Protocol: Collection of Blood Products for Use in the Development and Validation of Point-of-Care *In Vitro* Diagnostic Liver Function Test Devices

Study GKD001

NCT # Not Yet Assigned

IRB Approved Date 6/23/2022

Clinical Study Protocol

Title of Clinical Study:	Collection of Blood Products for Use in the Development and Validation of Point-of-Care *In Vitro* Diagnostic Liver Function Test Devices
Protocol Short Title:	Blood Collection for Development of Diagnostic Tests
Protocol Number:	GKD001
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Study Sponsor:	Group K Diagnostics 1015 Chestnut St Suite 1010 Philadelphia, PA 19107
Study Site	Group K Diagnostics 1015 Chestnut St Suite 1200 Philadelphia, PA 19107
Number of Subjects	150 Adults over 6 months
Study Start Date:	June 27, 2022

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ATTACHMENTS

1. Study Overview

The present clinical study is designed to collect blood samples to support the development and validation a new diagnostic device platform for quantitative point-of-care and at-home testing of blood for various analytes instructive of patient health. The blood analytes of initial interest are instructive of liver health. The target population for this study includes adults who are healthy or who may have liver disease or be on medications that may impact liver function. Initial reach activities will rely on standard venous blood draws and later activities will include finger stick capture of capillary blood, as well.

2. Study Objectives

2.1 To collect blood samples for use as both fresh and frozen specimens in the development and validation of quantitative tests for bilirubin, ALT (alanine transaminase), and AST (aspartate aminotransferase) using a novel investigational *in vitro* diagnostic (IVD) device.

2.2 To perform structured testing protocols using investigational test devices to support statistical analysis of the device analyte test results to confirm reproducibility, linearity, repeatability, and other assessments to demonstrate the devices will be safe and effective when used as intended.

2.3 To prepare investigational study reports for evaluation of the IVD tests for 510(k) clearance by the FDA.

3. Study Background

Outpatient diagnostics are time-consuming and expensive due to the long test turnaround times, difficult result release workflows, and the need for specially trained staff involvement. Turnaround time for diagnostics tests can be up to 5 days or more, as patients may have to travel to a separate facility to have labs drawn, and those lab draws follow a complex workflow. Since testing is offsite, a significant number of patients never make it to their appointments and are therefore not retained in the system. Time delay or non-compliance can make acute problems even more serious. Additionally, lab samples may have to be sent to a third location to have actual clinical testing performed on them. This causes patients to be lost to follow up when doctors attempt to provide patients with results but are unable to get in touch. Beyond time and workflow difficulties, tests can cost anywhere from $15-$100 per test depending on a myriad of factors such as insurance, plan coverage, and provider. Given that over two-thirds of all clinical decisions are based on laboratory testing (COLA, 2015) and in a 2002 survey of the US, 77% of providers were unable to contact their patients with abnormal diagnostic results (White, 2002), diagnostics are not working efficiently for outpatient providers. These studies show that lack of access to fast point of care results leads to significant problems in continuum of care and effective care. Very few rapid diagnostics are used by doctors, as modular machines are often cost or workflow prohibitive. Many rapid diagnostics require a trained technician and have high-cost hardware and certifications. The rapid diagnostics that are often used are tests such as pregnancy tests or rapid strep tests that are in multiple different platforms and are rate-limited in how many tests a practice can adopt.

Group K Diagnostics (GKD) intends to transform healthcare through innovative, rapid diagnostics. Inefficiencies of current lab solutions will be solved by bringing the "lab" to the provider and allowing practitioners to run diagnostic tests onsite in doctors' offices and clinics. With a low-cost reliable system, providers have actionable information before the patient leaves the office. GKD is developing a paper microfluidic platform (KromaHealth Kit) with an accompanying mobile application (KromaViewer). The KromaHealth Kit is a simple, cost-effective device with one or more test windows. These windows have a mix of dried proprietary reagents that when combined with a patient's drop of blood or serum will produce a colorimetric change. The KromaHealth Viewer on a mobile phone in concert with a low-tech viewing light box is then used to interpret the color change and transmit results to a doctor or to the patient.

Group K currently has a 510(k) submission under review with the FDA for a bilirubin only test device that will be used in clinical laboratories. The present study will support obtaining newly requested performance data on the IVD device under review and the development and validation of a 3-analyte test IVD device on the same platform.

4. Study Design

4.1 Enrolled subjects will provide one standard venous blood draw performed by a certified phlebotomist. The blood will be captured in a barcoded venipuncture tube with a copy of the barcode affixed to the enrollment form. Some enrolled subjects will also have a finger stick of blood captured in a measured capillary tube. Subjects will be allowed to participate in the study up to 1 time per week or may choose to only participate once.

4.2 Development and validation protocols will be performed using aliquots of the fresh blood samples and remaining serum will be aliquoted and stored for further validation work. Some studies will require fresh samples while others can be performed using frozen.

4.3 Statistical analysis of the development protocols will dictate the number of samples required for validation studies. At this time, it is projected that less than 300 individual fresh blood samples will be required to complete the entirety of the work for submission of the validation reports to the FDA.

4.4 The study duration is approximately six months with completion expected by December 31, 2022.

4.5 All study staff will be well trained on the study protocol and have current certifications for the roles they will perform in this study.

4.6 Study subjects will be consented, enrolled, and have blood drawn in a private area of the office with only the phlebotomist, staff member obtaining informed consent, and possibly the study PI present. Patients will be given ample time to have all their questions answered.

5. Characteristics of the Study Population

5.1 Target population: adults, 18 years of age and older, with varying liver health.

5.2 Key inclusion criteria:

5.2.1 18 years of age and older
5.2.2 Able to read and understand an informed consent form written in English

5.3 Key exclusion criteria:

5.3.1 Pregnancy
5.3.2 Participated in the present study within the last 6 days
5.3.3 Subject is subjectively unwell at the time of enrollment visit
5.3.4 Subject previously participated and has asked to be withdrawn from the study

6. Subject recruitment

The study recruitment will involve posting of the study's call for volunteers on physical displays in public areas near the study site, on social media platforms, via email list serves, and on the sponsor's website. Sponsor employees will also send links to the study recruitment pages on social media and the sponsor's website to their friends and family. The physical and electronic recruitment posts will include a phone number to contact to gain more information. Potential subjects will be informed of the criteria for study inclusion, data to be collected during study enrollment, as well as the risks and benefits study enrollment. This information is provided in the consent form and presented verbally during the consent process.

7. Study Procedures

7.1 Subject Enrollment

7.1.1 Subjects contact study phone number supplied on recruiting postings and are asked the following screening questions:

a. Are you 18 years of age or older?
b. Can you read and understand an informed consent form written in English?

c. Are you currently pregnant?

7.1.2 Based on the answers to the screening questions, a subject will be invited to enroll in this study and a study visit will be scheduled.

7.1.3 When the subject arrives for the scheduled visit, they will be asked the screening questions again for confirmation. Based on the answers, they will be given the informed consent form to read and discuss with study staff. They will be encouraged to ask any questions about the conduct of this study that they wish.

7.1.4 Informed consent will be obtained by signature, and a copy made for the subject to take.

7.1.5 Once enrolled, the following information will be gathered and recorded in the Study Enrollment Form:

a. Full name
b. Date of birth
c. Phone number
d. If they are feeling healthy today
e. If they have any diagnosed liver conditions or are on any medications that may affect liver function, and if so, what these are

7.1.6 A phlebotomist will perform a standard venous blood draw to collect roughly 3 mL (milliliters) of blood using a 3.5 mL barcode-labeled venipuncture tube. (At a later phase in study research, volunteers will also have 30 μL of blood taken by finger stick).

7.1.7 Subjects will be monitored for any immediate adverse effects of the blood collection procedure.

7.1.8 Subjects will be given the copy of the informed consent form and a $25.00 pre-loaded gift card as reimbursement for their time and transportation to the study site.

7.1.9 Subjects will be invited to contact the study Principal Investigator should any questions or concerns arise after leaving the study site and reminded that they may request to participate again in the study if they so choose.

7.2 Biobanking of Blood Samples

Venous blood samples will be allowed to clot, and serum will be drawn off. Serum will be aliquoted for use in barcode-labeled tubes. Some aliquots will be used fresh, and others stored frozen. The retained samples will used to continue development and validation of the *in vitro* diagnostic tests.

Finger stick blood samples will be used immediately for testing.

7.3 Laboratory Testing

Various structured testing protocols will be performed using investigational test devices to support statistical analysis of the device analyte test results to confirm reproducibility, linearity, repeatability, and other assessments to demonstrate the devices will be safe and effective when used as intended. Investigational device test results will not be provided to study subjects.

7.4 Data Analysis Plan

Structured testing protocols and statistical analysis plans have been created based on CSLI standards for assessment of critical performance parameters. These parameters include single and multi-site precision and repeatability, linearity, Limit of Blank/Limit of Determination, device stability, and interference of anticipated compounds. Other parameters may be assessed based on the outcome of the pre-planned analytics. Investigational device study reports will be submitted to the FDA in support of making the new test devices available to the healthcare community.

8. Subject Confidentiality

Subject enrollment logs will be kept on a secure server with access only by PI and one study staff member designate. Enrollment logs will be the only documentation linking the blood sample barcode to the individual subject. Blood and corresponding test results will be linked via unique barcode identifiers. The linking set will be maintained in a 21 CFR Part 11 compliant electronic laboratory management system. The investigator assures that subject's anonymity will be maintained and that their identities are protected from unauthorized parties. The subjects will be informed that representatives of the Sponsor of the study, the overseeing IRB, FDA, or EC, or regulatory authorities may inspect their study enrollment records to verify the information collected, and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws. Only necessary study staff will have access to data. Though we do not expect any breaches of confidentiality, if they do occur, they will be reported directly to the IRB within 24 hours of after discovery.

All potential participants will have their questions answered and will be consented in a private area of the study site.

9. Data Disclosure

Investigational device study reports supplied to the FDA will contain no identity information about the subjects who participated in this clinical trial

10. Risk / Benefit

10.1 Potential Study Risks

Study inclusion involves the minimal risk inherent to standard venipuncture and finger stick procedures. Some slight risks of standard venous blood draws are pain from the needle going through skin into the vein, mild bruising, clots under the skin, lightheadedness, possible fainting, and rarely, infection. Subjects will have clear instructions as to how to reach the team if questions, concerns or adverse events occur after leaving the study site. There is a potential risk of loss of privacy and breach of confidentiality which will be minimized only using barcode and de-identified demographic information outside of the enrollment process. No aspect of the study data analysis plan requires accessing the original enrollment documentation, by either hard copy or electronic form.

10.2 Potential Study Benefits

There will be no direct benefit to the subjects from participation in this study; the data and conclusions derived from this study, however, will support evaluation of technology designed to increase access to clinical diagnostic tests.

10.3 Alternatives to Participation

Participation is voluntary and optional. Potential subjects may chose not to participate.

11. Data and Safety Monitoring

Enrollment data and subject safety will be monitored by the PI and/or study staff during subject visits. Any adverse events that occur during subject visits or any study-related adverse events that arise after the subject visit, will be reported to the IRB. Investigation device test data will not be shared with subjects.