Clinical Investigation Plan

Evaluation of the GRI gentleheel® incision device for adult fingertip blood sampling – intended use extension

1 Title Page

FULL/LONG TITLE OF THE STUDY

Evaluation of the GRI gentleheel® incision device for adult blood sampling. - Intended Use Extension

SHORT STUDY TITLE / ACRONYM

Evaluation of GRI gentleheel® incision device for adult blood sampling

PROTOCOL VERSION NUMBER AND DATE

Version 1.0 15/02/2022

2 Research Reference Numbers

IRAS Number: **311621**

SPONSOR Number: **00023**

SPONSOR

Mowgli Innovation

Representative of the Sponsor:

Georges-Alexandre Haines

69 Portnall Road

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3 Signature Page

Principle Investigator Declaration

I confirm that the following protocol (Version 1.0, dated 15/01/2022), has been written by me and I, as the Principle Investigator, agree to conduct the trial in compliance with this version of the protocol.

The undersigned confirm that the following protocol has been agreed and accepted and that the Principle Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki (1996), the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the sponsor.

I also confirm that I will make the findings of the study publically available through publication and/or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Date: 15/02/2022

Signature:

.....

Name (please print):

.....Georges-Alexandre Haines.....

Position: ..Director Mowgli Innovation.....

Principle Investigator Site: Date: 15/02/2022

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Principle Investigator: Yazan Ajam

Signature:
.....

Name: (please print):

.....Yazan Ajam.....

4 Key Study Contacts

Principle Investigator	**Mr Yazan Ajam, MBChB, FRCS (Plast)** Email: yazan.al-ajam@nhs.net Telephone: 020 7794 0500 ext 38589
Study Co-ordinator/Manager	Georges-Alexandre Haines
Sponsor	**Mowgli Innovation**
Funder(s)	**Mowgli Innovation**
Key Protocol Contributors	**Mr Yazan Al-Ajam, MBChB, MRCS** Email: yazan.al-ajam@nhs.net Telephone: 020 7794 0500 ext 36988

5 Study Summary

Full Study Title	Evaluation of the GRI gentleheel® incision device for adult fingertip blood sampling - intended use extension
Internal ref. no. (or short title)	Evaluation of the GRI gentleheel® incision device for adult blood sampling.
Study Design	Prospective, interventional, non-randomised, single-centre study.
Study setting	Single site
Planned Size of Sample	50
duration	5 days
Planned Study Period	4 weeks for the purpose of recruitment
Research Question/Aim(s)	Can GRI gentleheel® incision device be safely used by lay members of the adult population for the purpose of capillary blood sampling from the fingertip.

6 Funding and Support

FUNDER	FINANCIAL AND NON FINANCIAL SUPPORT GIVEN
Mowgli Innovation	Financial support
Mowgli Innovation	Non-financial support (Sponsor)

ROLE OF STUDY SPONSOR AND FUNDER

The role of the study funder is to provide financial support to the study. The sponsor takes on ultimate responsibility for the initiation and management the research, providing the facilities in which the study patients will take part in the trial. The sponsor will ensure primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

The Principle Investigator and the study co-ordinator will be responsible for patient recruitment, and randomisation, data collection and analysis, annual progress report as well as final report preparation. Patient & Public Involvement Groups will not be involved in the design and implementation of the study.

7 Protocol Contributors

The study sponsor (Mowgli Innovation) will be involved in the review of the study protocol, data analysis and interpretation as well as manuscript writing and dissemination of the results. The key protocol contributors, the principal investigator and the study co-ordinator will assist the study sponsor in these tasks, however, the final decision regarding the study design, conduct of the study, data collection and analysis, annual progress report and final report preparation lies with the principle investigator.

Key Protocol Contributor	**Mr Yazan Al-Ajam, MBChB, MRCS** Email: yazan.al-ajam@nhs.net Telephone: 020 7794 0500 ext 36988

8 Contents

STUDY FLOW CHART

Parameter/Examination	Day of Procedure	Within 5 days of procedure (Follow-up telephone call)
Obtain Signed informed consent	X	
Patient Demographics/Medical History	X	
Concomitant medication	X	
Blood collection with gentleheel® device	X	
Assessment of pain rating	X	
Assessment of Adverse Events	X	X
Follow-up Telephone call		X

9 List of Abbreviations/Glossary of Terms

ADE	Adverse Device Event
AE	Adverse Event
CI	Confidence Interval
CIP	Clinical Investigation Plan
CRF	Case Report Form
EC	Ethics Committee
IFU	Instructions For Use
ITT	Intention to Treat
POCT	Point of Care Testing
SADE	Serious Adverse Device Effects
SAE	Serious Adverse Event
SD	Standard Deviation
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analogue Scale
WHO	World Health Organization

10 Involved parties

Sponsor

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Contact:	07806602491

CRO/Study coordinator (If applicable)

Name:	Georges-Alexandre Haines
Address:	69 Portnall Road, London, W9 3BB
Contact:	07806602491

Principal Investigator

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Legal Manufacturer of the investigational device (gentleheel®)

Name:	**GRI Medical & Electronic Technology Co., Ltd.**
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Contact	+86057383617397

11 Approvals

	Signature	Date
Sponsor	Georges-Alexandre Haines	15/02/2022
Principal Investigator	Yazan Ajam	15/02/2022
Legal Manufacturer	Sidonia Dong	15/02/2022

12 Introduction

12.1 Background – Current Solutions (Principles and Disadvantages)

One of the most commonly performed procedures in the health sector is venepuncture, with millions carried out every year in the United Kingdom. Until recently, venepucture has been the mainstay of obtaining intravenous access for the purpose of blood sampling. This involves using a needle to puncture a peripheral vein in order to access the venous circulation in order to draw blood, which is then sent to the lab for analysis. However, venepuncture is not without potential complications, which include patient discomfort, echhymosis, risk of sharp injury to the phlebotomists, and anemia associated with repeat venepuncture (1–3). Furthermore, in patients with inadequate or damaged veins (such as burns patients), those with arms in casts, and in cases of obesity, venepuncture can be challenging, often requiring multiple attempts to obtain an adequate blood sample. Repeated large-volume sampling is undesirable for patients, especially for patients with chronic disease who require regular sampling or when maintaining blood volume is critical (4,5). In such instances, capillary blood testing can be performed (6). This involves using a micro lancet to make a small, 1-2mm incision in the fingertip resulting in pin-point bleeding. This blood is collected into blood collection tubes and sent for analysis. The use of micro lancets to extract blood for analysis is not new. Diabetics have been using this for decades to obtain real-time blood sugar measurements (7), and their use is commonplace in neonates, using the heal to extract blood samples.

With the advent of point-of-care testing (POCT) in a variety of locations such as GP surgeries, the community and in the Emergency Department, the concept of capillary blood testing is becoming increasingly more relevant (4,8). POCT is any diagnostic testing performed onsite, with the results leading to potential change in patient care. Capillary blood samples are now routinely used for checking a variety of blood parameters such as glucose, glycosylated haemoglobin, cholesterol, haemoglobin, bilirubin and electrolytes (4,8,9). Capillary blood sampling has also been used for rapid screening for HIV, hepatitis B & C and for drug monitoring (10,11).

Capillary blood sampling has clear advantages over traditional venepucture: it is less invasive, less painful, requires fewer consumables, is less resource intensive with regards to the need for a phlebotomist, clinical space, storage and logistical requirements (4,12). Furthermore, venipuncture requires substantial training to perform the collection, and success in obtaining a sample is dependent on the skill of the phlebotomist performing the blood draw in addition to the accessibility of the patient's veins. The use of a hypodermic needle for venipuncture not only poses the risk of needle-stick injury to the phlebotomist but can also cause pain and anxiety for the patient, which can be a barrier to receiving proper healthcare. Therefore, there is a real need for a reliable and easy way to obtain blood for use in capillary blood sampling to meet the growing need in this area of healthcare provision.

12.2 Challenges with Capillary Blood Collection

Traditional methods of capillary blood sampling work by using a micro lancet to puncture the skin. A small plastic device comes pre-loaded with a sterile lancet. The device is held against the side of the fingertip and is either pushed into the finger to activate (for contact-activated lancets) or a button is pressed on the device, deploying the spring-loaded lancet at high speed, piercing the capillaries located in the dermis and resulting in bleeding. The finger is squeezed to expedite the flow of blood, which is collected and used for analysis.

One potential disadvantage of capillary blood sampling is difficulty in reliably obtaining a blood sample of sufficient volume and quality for testing. The practice of lancing 'alternate sites' such as the arm, thigh, or palm has been used to alleviate the pain associated with fingertip sampling, but the lower capillary densities of these regions make it even more

difficult to obtain an adequate sample volume for testing (13).

A recent review article tested several lancet-based finger capillary blood sampling devices available on the market on adult volunteers. It found the mean volume of blood extracted varied from 37.3 µL to 265.0 µL, depending on the design of the lancet (needle versus blade), with all needle-based devices yielding a volume below 100 µL (8).

Typical routine blood tests require two separate blood bottles (one for conducting haematological tests such as haemoglobin levels, and another for biochemical profile, renal and liver function tests). The volume of blood required to analyse these samples varies according to the lab, and typically this ranges from 100 µL to 500 µL. With the current lancet-based systems, it is not uncommon to require the puncture of several fingers to obtain sufficient volume, resulting in increased pain to the patient.

Hemolysis (breakdown of red blood cells), lipaemia (contamination of the sample with micro-fat particles) and sample dilution with extracellular fluid are recognized complications of capillary blood sampling (6,14), which are often due to repetitive squeezing of the finger at the puncture site in order to extract sufficient blood from the finger.

Therefore, there is a real need for a lancet-based device that is not only safe and easy to use but more importantly one that can provide sufficient blood volume.

12.3 Proposed Solution

Our solution to the problem is to modify the use of a pre-existing device on the market (gentleheel®) to address the shortcomings of blood capillary sampling devices with regards to obtaining an adequate volume of blood. The gentleheel® device, is a heel incision device designed for use in new-born blood sampling. This device is CE-marked and FDA approved. It offers a safe and efficient way of acquiring blood samples from the heels of new-borns and toddlers. The device is engineered with the following features to ensure ease of use and minimal discomfort for the patient:

- Ergonomic design for improved handling.
- Multiple visual indicators reinforce incision site.
- Incision devices are less traumatic than punctures.
- Tri-bevel blade generates a smoother, less traumatic incision.
- Hardened stainless steel blade improves incision accuracy.
- Permanent blade retraction minimizes possible reuse or injury.
- Welded plastic casing prevents accidental exposure to the blade.

The fundamental difference between gentleheel® and other devices is the greater volume of blood that can be extracted from a single finger prick. This is due to the type of lancet and the way it is deployed. In contrast to traditional devices that use a needle as a lancet that punctures the skin, gentleheel ® utilises a blade, creating a 3.0 mm area of dermal bleeding, resulting in improved blood flow, allowing for increased volume of blood to be collected with the potential to reduce the aforementioned limitations with needle-based lancets. The incision depth is 2.0 mm, in accordance with safety limits recommended by the World Health Organization (WHO) guidelines on the use of capillary blood sampling devices (6).

This device, however, is only licensed for use by healthcare professionals on the heels of new-borns and toddlers. The intention of this study is to extend the utility of this device by investigating its use in capillary blood sampling from adult fingertips.

12.4 Investigational Device

This section shows gentleheel® device and contains a schematic of the mechanism of action.

Figure 1: Picture of the gentleheel® device model Toddler.

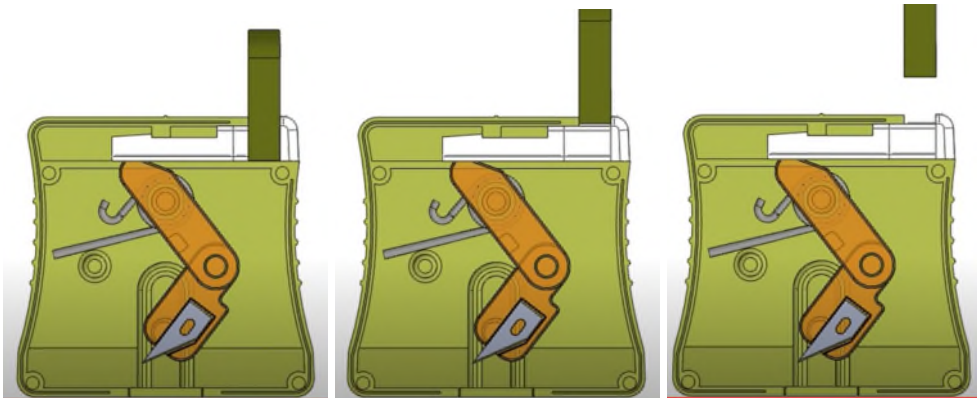

Figure 2: Schematic drawings showing from left to right the removal of the trigger lock.

Figure 3: Schematic drawings showing from left to right the sweeping motion of the tri-bevel stainless steel blade after the blade is deployed.

13 Research Question/Aims

Can gentleheel® incision device be used by lay members of the public without intervention from medically qualified practitioners for the purpose of capillary blood sampling in the fingertip?

14 Study Objectives

This clinical investigation is designed to collect information related to the performance and safety of this device during blood sampling in adult fingertips.

14.1 Primary Objectives

1. To determine if a volume of 500 microlitres to 1.1 millilitre of blood can be collected after a single lancing of the fingertip with gentleheel®.
2. To assess pain from fingertip lancing with gentleheel®.

14.2 Secondary Objectives

Reporting of adverse events.

15 Study Design, Data Collection and Data Analysis

15.1 Recruitment and baseline assessments

When the Investigator has determined the eligibility of a specific subject as per the defined inclusion and exclusion criteria, the Investigator or a person designated by the Principal Investigator who has been trained on the Clinical Investigation Plan, will explain the nature and scope of the clinical investigation, potential risks and benefits of participation, and answer any question of the patient. The patient will be provided ample time to read and understand the Informed Consent Form and to consider his/her participation in the study. If the patient agrees to participate, the informed consent form must be signed and personally dated by the patient. The Investigator must also sign and date the Informed Consent Form, prior to enrolment of the patient. The Investigator will maintain a copy of the relevant study approval along with a copy of each patients signed Informed Consent Form in a designated study file. The investigator will provide patients with a copy of their signed Informed Consent Form. If new information about the clinical study becomes available, the patients will be notified by the Principal Investigator or study personnel. If the approving committee of the study requires an updated Informed Consent Form to be administered, all actively participating subjects will sign the new form.

After the subject signs the Patient Consent Form, he/she is considered enrolled into the study.

15.2 Randomisation and blinding

Since this is a prospective, interventional, non-randomised study, no randomisation will be necessary. As only one device will be used there will be no need for blinding.

15.3 Investigation Design

A sample size of 50 patients will be used. Each patient will perform two separate incisions on the middle and ring fingers, resulting in 100 blood draws. During the procedure, the following data will be documented:

- the location of the incisions (which finger – middle/ring and which side of the fingertip – ulnar/radial).
- the volume of blood obtained from each incision;
- the pain level experienced for each incision;

After appropriate explanation of the procedure to the patient, he/she will sign the Informed Consent Form to confirm that their participation in the study is voluntary. All required data as per the CRF will be obtained and the patient will then collect blood from 2 incisions on his/her fingertips.

All collected blood samples will be used for volume measurement and discharged afterwards. Following the blood collection from all 2 incisions, the patient will be appropriately monitored, until he/she leaves the investigational site. Any adverse event if presented will be documented before the patient leaves the investigational site.

Please see Table 1 for an overview of the data being collected for each subject on the day of the blood collection procedure.

Table 1: Overview of the data to be collected for each subject in the day of the blood collection procedure.

Incision #	**Finger identification (middle/ring)**	**Incision position (radial/ulnar)**	**Volume of blood collected (µl)**	**Pain level (0 to 10)**
1				
2				

Within 5 days of procedure, a follow-up telephone call will take place in order to assess if any adverse events occurred.

15.4 Table Summary of Key Timelines

Data Collected	Recruitment	Procedure	Telephone Follow up
	Up to 4 weeks pre-procedure	Day 0	Day 5
Informed consent	X	X	
Blood volume collection		X	
Pain score		X	
Adverse events (CRF's)		X	X

15.5 Procedure for Capillary Sampling

This protocol is based on the recommendations set out by the WHO guidelines on drawing blood: Capillary blood sampling (6)**.** A patient information sheet will be provided to the patient with written instruction on how to use the device.

Material Required

The following materials will be provided with gentleheel®:

- Alcohol wipe
- Sterile gauze pads
- Blood collection container, with marker lines to indicate the volume of blood collected

Preparation

- Wash your hands under warm water for 2 minutes.
- While standing up swing your arms several times to stimulate the blood flow.
- Use the alcohol wipe to clean the finger you intend to use – we recommend using the middle or ring finger of your non-dominant hand.

Procedure for sample collection

- When making an incision on the adult's finger, the incision site must be on the fingertip (see illustration below), and indicated as radial/ulnar.

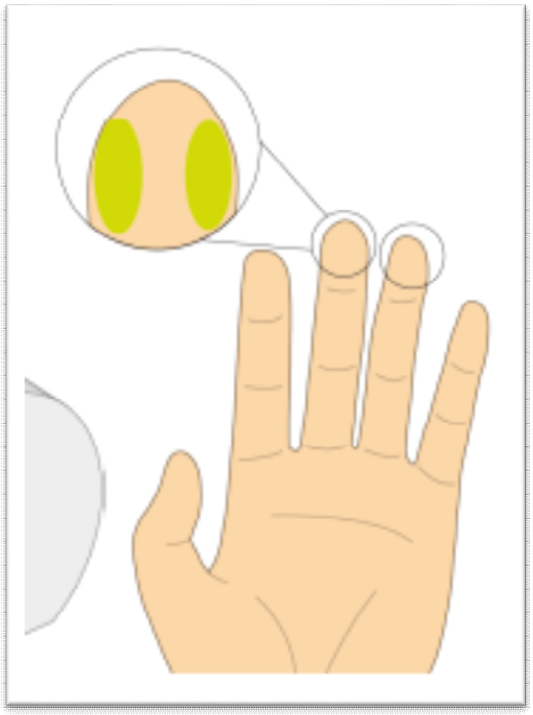

Figure 2: Illustration of the incision site in an adult fingertip.

- **Remove gentleheel® from its packaging.**
- **Remove the trigger lock.** Once the trigger is removed, do not depress the trigger or place anything in front of the opening at the base of the device.
- **Incision.** Place the opening (at the base of the device) against the cleansed incision site ensuring that the base of the device is flush with the fingertip's skin. After depressing the trigger, immediately remove the device.
- **Remove first drop of blood.** The first drop of blood should be wiped away from the incision with a dry sterile gauze pad.
- **Collect sample.** A second drop of blood should form over the incision site. Collect the blood sample and fill it in the collection container provided. Avoid squeezing the finger too tightly. Fill both blood tubes to the fill line.
- **Compression.** When the blood collection procedure is complete, apply firm pressure to the site to stop the bleeding using the dry sterile gauze pad provided.
- Note down your perception of pain on a scale of 0-10, with 0 being no apin and 10 the worse imaginable pain.

15.6 Procedure

After appropriate explanation of the procedure to the patient, he/she will sign the Informed Consent Form to confirm that their participation in the study is voluntary. All required data as per the CRF will be obtained and the patient will then collect blood from 2 incisions on his/her fingertips. No more that a maximum of 4 ml of blood will be collected per patient. The patient will then be asked to rate their pain using the Numerical Pain Rating Scale of 0-10, with 0 being no pain and 10 the worse imaginable pain.

All collected blood samples will be used for volume measurement and discharged afterwards. Following the blood collection from all 2 incisions, the patient will be appropriately monitored, until he/she leaves the investigational site. Any adverse event if presented will be documented before the patient leaves the investigational site.

15.7 Follow-up

The following assessments will be completed via a telephone call within five days after the procedure:

- Adverse Events – any adverse events that occurred since the day of the procedure.

If no adverse events have occurred, it will be documented in the CRF accordingly.

15.8 Study Population

A total of 50 subjects will be enrolled in the study.

15.8.1 Inclusion Criteria

- Subjects older than 18 years (adults).
- Subjects able to provide informed consent.

15.8.2 Exclusion Criteria

- Subjects younger than 18 years.
- Subjects unable to provide informed consent.
- Subjects who may be dehydrated.
- Subjects diagnosed with poor peripheral circulation from other causes.
- Subjects who present with a callus, skin ulceration, or blister at the intended puncture site.
- Subjects with thrombocytopenia and/or Platelet abnormalities.
- Subjects diagnosed with peripheral edema. Pregnancy or breastfeeding (self-reported).
- Confirmed or suspected malignant cancer.
- Anxiety with needles or finger pricks.
- History of blood borne infection (e.g., HIV, hepatitis B or C, syphilis, malaria, babesiosis, brucellosis, leptospirosis, arboviral infections, relapsing fever, T lymphotropic virus Type 1, Creutzfeldt-Jakob disease).
- Currently participating in another study.
- Donation or loss of 400 mL or more of blood within 4 weeks prior to the start of the study.
- Any other condition that in the Investigator opinion may negatively influence Subject's participation in the study.
- Intake of medicines that affect blood coagulability (including anticoagulants such as vitamin K, antivirals and anticoagulants such as heparin, aspirin, thrombin inhibitors, vitamin K antagonists).

15.9 Withdrawal Criteria

Patients have the right to withdraw from the study at any time and for any reason without prejudice to their future medical care by the investigation team or investigation site. The Investigator will record all information regarding the subject discontinuation. A patient may be

withdrawn from the study for the following reasons, and data until the date of withdrawal will be recorded in the Case Report Form (CRF):

- Subjects may choose to withdraw from the study under the terms of the Declaration of Helsinki and their consent documentation without having to give a reason;
- Any unanticipated adverse event which is, in the opinion of the Investigator, related to the treatment and will endanger the well-being of the patient if treatment is continued;
- Development of any intercurrent illness(es), infection or condition(s) that might interfere with the protocol;
- Non-compliance with the clinical investigation procedures deemed by the Investigator to be sufficient to cause discontinuation;
- Any problem deemed by the Investigator to be sufficient to cause discontinuation.

16 Statistical Considerations

16.1 Sample Size

Considering the design and objective of this investigation, the nature of the results needed to conclude on the safety and performance of gentleheel® as incision device for adult fingertips, and the fact that the device is already CE-marked as heel incision device for new-born sampling, the inclusion of 50 subjects in the investigation, a 2 incisions per subject, which will result in 100 blood draws to be assessed, appears therefore sufficient to obtain conclusive findings. This was based on the precision of the 90% CI for the primary objectives as this is a single-arm study. Under this approach, no statement of power is required and alpha = 0.10 will be used as the CI specified as a two-sided 90%.

16.2 Study Populations Definitions

In this study one study population is defined.

The Intent-to-Treat (ITT) population will comprise of all subjects who match the inclusion criteria, have signed their Informed Consent Form and are willing to take-part in the study.

16.3 Analysis Method

All data will be anonymised prior to analysis.

The statistical analysis will be done on the ITT population. In case more than 10% of patients present major violations to the protocol (defined as any deviation which may significantly impact the evaluation of the endpoints), primary endpoints analysis will be re-assessed and documented appropriately.

Descriptive statistical data will be used to summarize the characteristics of subjects at the time of inclusion (demographics, baseline and procedure data).

The primary and secondary objectives will be presented as a proportion with 90% confidence intervals (CIs). For other objectives, quantitative variables will be summarized by the number of patients (n), mean, standard deviation (SD) and range; qualitative variables will be summarized by frequency and percentage of patients; rates will be summarized by the numerator, denominator, rate, and its 90% CI. Descriptive statistics only will be provided for AE data.

A complete adverse event description will be done: total number of events and number of patients with at least one of the respective categories AEs, ADEs, SAEs, SADEs, USADEs.
Investigation Assessments

17 Participating Investigator and Site

One investigational site in the United Kingdom will be chosen for this study. This will take place at King's College London, in a dedicated research facility which routinely carries out blood sampling related studies.

The Principal Investigator is experienced in the field of phlebotomy and capillary blood sampling and collection. All training on how to use the gentleheel® device will be provided to the Investigator by the Sponsor of the study. A Study Coordinator will be available to ensure the data is collected, and any immediate adverse events noted.

18 Investigation Handling Procedures

The investigational device will be provided to the site by the sponsor. Each device will be entered and tracked on the Device Accountability Log. Once an investigational device is used, it should be discarded per the investigational site's disposal procedure. All devices are one-time use only. The devices should be kept in a secure location, in a cool, dry place.

19 Anticipated Adverse Events

Adverse events that may possibly be caused by, or associated with, the use of the gentleheel® for capillary blood sampling in adult fingertips include:

- Fainting during the incision procedure.
- Pain during and after the incision procedure.
- Bruising.
- Hematoma.
- Excessive bleeding requiring more than 5 minutes of compression to stop.
- Infection at the incision site.

20 Anticipated Benefits to the Patients

The anticipated benefits of the gentleheel® for capillary blood sampling in adult fingertips is to improve the user / patient experience of capillary blood collection:

- Ensure collection of an adequate volume of blood from a single finger puncture.
- Minimal discomfort from the procedure - blade-based incision devices are less traumatic than needle-based puncture devices (15). The sweeping motion of the tri-bevel stainless steel blade of the gentleheel® device allows for a smoother and less traumatic incision.
- The gentleheel®'s ergonomic design is easy to use and user friendly.

21 Minimization of Risks

This investigation will be monitored to ensure the identification, documentation and analysis of all adverse events, compliance with the Clinical Investigation Plan, the terms of the participating study approval committee to protect the safety and rights of all patients, and applicable local regulations. In addition, risks have been minimized through selection of the Investigator who is experienced in capillary blood sampling.

Although all risks associated with the intended procedure and device may not be fully known at this time, the risks have been identified through an exhaustive literature search and represent the most up-to-date understanding of risks associated with the proposed procedure. The sponsor will employ the following measures throughout the course of this investigation to minimize these risks.

- The Sponsor has clearly defined inclusion and exclusion criteria and will monitor adherence to them, to ensure that only appropriate patients are enrolled.
- The Investigator will obtain informed consent.
- The Sponsor will select the investigational site that has a sufficient level of expertise needed to support and to manage adverse events that could arise and to provide appropriate alternative measures if needed.
- The Investigator will ensure that the follow-up of the patients are consistent with current medical practices and provide the institutional standard of care in line with expert medical judgment.
- The Investigator will report all Safety Adverse Events (SAE).

22 Follow-up of Adverse Events and Adverse Device Effects

Any Adverse Event (AE) or Adverse Device Event (ADE) will be followed until it has resolved, has a stable level of sequelae or in the Investigator's opinion is no longer clinically significant.

22.1 Adverse Events and Device Deficiency Recording on the CRF

All AE must be reported for each patient with a full description, including the nature, the date of onset and resolution, the determination of seriousness, the severity, the action taken, the corrective treatment and the relationship to the device and/or procedure assessed by the Investigator. All investigational device deficiencies will be documented on the CRF and reported to Sponsor.

23 Protocol Synopsis

Title of the investigation: Evaluation of the GRI gentleheel® incision device for adult blood sampling. - Intended Use Extension	
Objective:	The objective of the proposed clinical investigation is to evaluate the safety and performance of the gentleheel® incision device for capillary blood sampling in adults' fingertips.
Intended Use:	The gentleheel® device as a fingertip incision device intended for blood sampling in adults.
Investigational Device:	gentleheel® model Toddler, Blue Incision depth 2.00 mm Incision length 3.00 mm
Investigation Design:	Prospective, interventional, non-randomized, single-centre
Participating Sites:	1 site in the UK
Planned Number of Patients:	50 patients
Sample size	100 blood draws, 2 finger incisions per patient
Participation Duration:	Procedure: 20 minutes Follow-up: 5 days (Telephone Call)
Total estimated duration of the investigation:	1 Month
Outcomes:	**Primary Objectives:** • Determine the capillary blood volume collected after a single lancing of the fingertip. • Assessment of pain during finger incision using the 0-10 Numerical Pain Rating Scale **Secondary Objectives:** Adverse events.
Inclusion Criteria:	• Subjects older than 18 years (adults) • Subjects able to provide informed consent

Exclusion Criteria:	• Subjects younger than 18 years • Subjects unable to provide informed consent • Subjects with cognitive impairment which is sufficient to adversely affect the participants understanding of the study, their ability to respond to patient questionnaires or their ability to cooperate with post-procedure assessment. • Subjects who may be dehydrated • Subjects diagnosed with poor peripheral circulation from other causes • Subjects who present with a callus, skin ulceration, or blister at the intended puncture site • Subjects with thrombocytopenia and/or Platelet abnormalities • Subjects diagnosed with peripheral edema. Pregnancy or breastfeeding (self-reported) • Confirmed or suspected malignant cancer • Anxiety with needles or finger pricks • History of blood borne infection (e.g., HIV, hepatitis B or C, syphilis, malaria, babesiosis, brucellosis, leptospirosis, arboviral infections, relapsing fever, T lymphotropic virus Type 1, Creutzfeldt-Jakob disease) • Currently participating in another study • Donation or loss of 400 mL or more of blood within 4 weeks prior to the start of the study • Any other condition that in the Investigator opinion may negatively influence Subject's participation in the study • Intake of medicines that affect blood coagulability (including anticoagulants such as vitamin K, antivirals and anticoagulants such as heparin, aspirin, thrombin inhibitors, vitamin K antagonists)

24 General Study Conduct

24.1 Ethical and Regulatory Considerations

The study will be performed in accordance with the standard ISO 14155 on clinical investigations with medical devices on human subjects and recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland,1964 and later revisions.

The Clinical Investigational Plan, Informed Consent Form, any other specific study documents and all amendments to these study documents will be reviewed and approved by the appropriate Ethics Committees (ECs) and Competent Authority (MHRA) before enrolment of any patients. In addition, the Sponsor will keep the regulatory authorities informed of any SAEs throughout the study course.

24.2 Data collection, Data handling, Monitoring

The Investigator and the investigational site will permit authorized personnel to review (monitor) completed CRFs, approval committee decisions, and investigator and clinical site records throughout the course of the study. Additionally, patient charts and clinical records will be reviewed by the Sponsor and/or designee(s) so that protocol adherence and source documentation can be verified. All data will be appropriately anonymised.

The subjects will be identified in the CRFs only with a patient number. The subject will be informed that his/her data will be stored and analyzed by computer, that national regulations for handling of computerized data will be followed and that only the Investigator and representatives of the Sponsor will have access to individual subject data. Furthermore, the patients should be informed about the possibility of inspection of relevant parts of the records by the Investigator and/or Health Authorities.

Data collected on the CRFs shall be entered into a database. Accuracy of data entry shall be verified by Data Management staff and monitors. Any inconsistencies observed on data (missing values, failed logic controls) or any discrepancies between data filled and source data on site will generate queries to be answered by the Investigator. Once all queries are answered and data fully corrected, the database will be frozen and access to database will be retired to the Investigator and it will be impossible to perform any additional changes on stored data. Export of the database will then be programmed and accomplished to allow the statistical reporting on a cleaned and validated database. Access to the database shall be limited to appropriate personnel in order to preserve data integrity.

24.3 Record Retention

The Investigator must retain records for this investigation for a minimum of 10 years.

24.4 Device Accountability

The Investigator is responsible for ensuring that investigational devices are kept in a secure location and are available only to authorized personnel who are part of the research team for this investigation. The accountability of each investigational device will be documented.

24.5 Financing and Insurance

For any injuries, which can be traced to the study, subjects participating in the study are covered by insurance policies, as required by regulation for clinical studies. A product liability insurance policy taken out by the Sponsor and will cover liability for possible injury to the patient, provided the investigator and his/her staff have followed the instruction of Sponsor in accordance with this protocol and any amendments, that the product administered to the subject in this study have been supplied by Sponsor and that the Investigator and his/her staff have in general performed this study in accordance with scientific practice and currently acceptable techniques and know how.

24.6 Publication Policy

Any written or oral communication of the results of the clinical investigation must receive the preliminary agreement of the Investigator and of the Sponsor. This policy does not affect any applicable legal publication obligations of the Sponsor.

24.7 Sponsor Responsibilities

Sponsor has the overall responsibility for its conduct, including assurance that the study meets the regulatory requirements of the standard ISO 14155 on clinical investigations with medical devices on human subjects. Sponsor or its representative will ensure adherence to the ISO 14155 standard and Sponsor's general duties, selection of Investigators, monitoring, supplemental applications, maintaining records, and submitting periodic and final reports. Sponsor will select a qualified Investigator experienced in the field of application and trained in the use of the device with consideration of familiarity with the background and requirements of the clinical investigation methodology. Sponsor will provide devices only to the participating Investigator, obtain a signed Investigator's Agreement and provide the Investigator with the information necessary to conduct the investigation. The training of appropriate clinical site personnel will be the responsibility of the Sponsor. To ensure uniform data collection and clinical protocol compliance, the Sponsor will present a formal educational session to study site personnel which will review the clinical protocol, techniques for the identification of eligible subjects, instructions on data collection, methods for soliciting data from alternative sources, schedules for follow-up with the study site coordinators, and regulatory requirements, as mentioned. Sponsor will maintain copies of correspondence, data, (S)ADEs and other records related to the investigation.

24.8 Investigator Responsibilities

Investigators will ensure that all work and services they provide will be conducted in compliance with the standards of good clinical and research practice, i.e. ISO 14155. The Investigator will ensure that the study is conducted in compliance with the Clinical Investigation Plan and the Investigator's Agreement, as applicable. The Investigator will be responsible for the day to day conduct of the clinical investigation as well as for the safety and well-being of the human subjects involved in the clinical investigation.

The Investigator will have the resources to conduct the clinical investigation properly and obtain from the Sponsor information which he judges essential about the device and be familiar with this information.

The Investigator shall ensure that adequate information is given to the subject both in oral and written form, on the nature of the study. This information shall be easily understandable by the subject. This information shall include the aims, expected benefits for him/her and/or others, risks and inconveniences and an explanation of any alternative methods, and of possible consequences of any withdrawal from the study. Subjects shall be allowed sufficient time to understand the Informed Consent Form, and to decide whether or not they wish to participate. The subjects shall be informed that his/her participation in the clinical investigation is confidential. Patients shall be made aware that the data relating to the study may be made available to third parties while maintaining anonymity. The Investigator will maintain study records for an appropriate time and the subject's identity shall not be released to third parties without the subject's prior consent. Record retention periods will be provided to all concerned by Sponsor. All information and data concerning subjects or their participation in this study will be considered confidential. Only authorized personnel will have access to this confidential information. All data used in the analysis and reporting of this evaluation will be without identifiable reference to individual subjects.

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