



Clinical Evaluation of a Mobile App-Based Respiratory Device in the Emergency Department Setting

Short Title: CLEAR-ED

Version 1A

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1.0 SIGNATURE PAGE

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

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 investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication 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.

Sponsor Representative Signature

Signature: SEE ELECTRONIC SIGNATURE AT THE END
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Date:

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Name (please print):

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Position:

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Chief Investigator Signature

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3.0 STUDY CONTACT INFORMATION

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4.0 SUMMARY OF PROTOCOL CHANGES

Summary of Changes to the Protocol			
Amendment Number	New Protocol Version and Date	Description of Change	Reason for Change
NA	NA	NA	NA

5.0 PROTOCOL SYNOPSIS

Study Summary

Protocol Title	Clinical Evaluation of a Mobile App-Based Respiratory Device in the Emergency Department Setting
Short Name	CLEAR-ED
Study Objectives	The primary objectives of this study are to evaluate the agreement and usability of the new device, namely the purpleDx smartphone video technology, for measuring patients' peak expiratory flow, forced expiratory volume in one second, respiratory rate and heart rate when compared to results measured using standard clinical reference methods during a single patient encounter in an Emergency Department setting. The secondary objectives are to demonstrate the safety of the purpleDx smartphone application and determine any subject subgroups or conditions of use of the new device that impair the quality or reliability of data.
Study Procedures	Subjects will undergo measurement of peak expiratory flow, forced expiratory volume in one second, respiratory rate and heart rate at one ED visit, using standard medical equipment/means and using the smartphone application purpleDx. Results will be recorded and analysed to determine the agreement and variation between traditional and new medical devices in this setting.
Study Sponsor	electronRx Ltd
Sponsor Representative	Dr Bipin Patel
Study Design	This is a prospective, comparative, single-visit medical device study to collect data to support a marketing application in the UK and EU. There is no Investigational Medicinal Product in this study. All subjects will undergo testing with traditional medical equipment/means and the Investigational Medical Device, purpleDx, thus each subject

	will act as their own control.
Investigational Medical Device	purpleDx is a non-interventional smartphone application which measures peak expiratory flow, forced expiratory volume in one second, respiratory rate and heart rate utilising the camera function and enhanced video quality of such mobile phones. It is categorised as Class IIA Software as a Medical Device (SaMD) and has been developed by electronRx Ltd in Cambridge.
Study Location	Cambridge University Hospitals NHS Foundation Trust (CUH) Emergency Department Addenbrooke's Hospital Hills Road Cambridge CB2 0QQ
Study Duration	Two months from date of site initiation visit to date of last subject recruited into the study.
Subject Population	Subjects will be male or female, aged 18 years and above, and must be able to sit up and read, understand and write in English. Subjects with and without a diagnosis of respiratory or cardiopulmonary disorder/s will be included.
Sample Size	Maximum of 160 subjects.
Primary Endpoint	1) Demonstration that measurements for physiological signals of peak expiratory flow obtained using purpleDx sufficiently agree with those obtained using standard clinical equipment/means to proceed to marketing application.
Secondary Endpoints	1) Demonstration that measurements for physiological signals of forced expiratory volume in one second, respiratory rate and heart rate obtained using purpleDx sufficiently agree with those obtained using standard clinical equipment/means to support

	proceeding to marketing application. 2) Establishment of thresholds for 'normal' ranges for peak expiratory flow, forced expiratory volume in one second, respiratory rate and heart rate. 3) Demonstration of usability and ease of use of purpleDx by subjects and clinical staff. 4) Demonstration of the safety of purpleDx. 5) Determination of any subsets of the patient population for which purpleDx may not be suitable. 6) Determination of any conditions or situations which impair the recording quality or reliability of data produced by purpleDx.
Reference Standards	● Medical UK Devices Regulation 2002 (SI 2002 No 618, as amended) [Part II is the relevant section for general medical devices including SaMD] ● Medical Device Regulation (EU) 2017/745 ● ISO 13485:2016 Medical devices – Quality management system – Requirements for regulatory purposes ● ISO 14155:2020 Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice ● ISO 14155-1:2009 Clinical Investigation of Medical Devices for Human Subjects – General Requirements ● ISO 14155-2:2009 Clinical Investigation of Medical Devices for Human Subjects – Clinical Investigation Plan ● IEC 62366-1 Part 1: Application of usability engineering to medical devices ● IEC 62304:2006 Medical device software – Software life cycle processes ● IEC 82304-1:2016 Health software Part 1: General requirements for product safety ● Declaration of Helsinki 2024 – Medical Research

	Involving Human Participants ● ICH GCP E6(R2): Guideline for Good Clinical Practice 2016
Health Economics	Utilisation of smartphones to enable patients to monitor and submit data to medical consultants for appraisal could revolutionise the identification and management of long-term health conditions such as asthma, Chronic Obstructive Pulmonary Disease and Interstitial Lung Disease. If a clinician could access the information held in the application, they may be able to amend a patient's treatment regime as clinically indicated following review of real-time data that could be compared to historical results, potentially without the need for the patient to attend a hospital clinic. This would alleviate demand for clinic slots, whilst simultaneously reducing waiting time and travel burden for patients, helping to revolutionise the patient management pathway.
Randomisation	Not applicable as there are no treatment arms in this study. Each subject will act their own control, by being tested with standard medical equipment and with purpleDx.
Eligibility Criteria	Inclusion Criteria 1) Sex at birth classified as male or female 2) 18 years of age and above, presenting to CUH Emergency Department 3) Able to read and understand the patient information sheet in English 4) Capacity and ability to sign an informed consent form 5) With or without respiratory or cardiorespiratory symptom/s Exclusion Criteria 1) Unable to sit up i.e. cannot lie completely flat (supine) 2) Known pregnancy in women of child-bearing potential 3) Unable to comply with the requirements of the investigation in any way

	4) Prisoners or young offenders
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6.0 ACRONYMS AND DEFINITIONS

Acronym	Definition
ADE	Adverse Device Effect
AE	Adverse Event
AF	Atrial Fibrillation
app	Smartphone Application
bpm	beats per minute
CA	Conformity Assessment
CI	Chief Investigator
COPD	Chronic Obstructive Pulmonary Disease
CTCAE	Common Terminology Criteria for Adverse Events v5.0
CUH	Cambridge University Hospitals NHS Foundation Trust
DD	Device Deficiency
DPO	Data Protection Officer
ECDS	Emergency Care Data Set
eCRF	Electronic Case Report Form
ED	Emergency Department
EU	European Union
FEV ₁	Forced Expiratory Volume in One Second
GB	Great Britain (England, Scotland and Wales)
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HR	Heart Rate
HRA	Health Research Authority

ICC	Intraclass Correlation Coefficient
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICO	Information Commissioner's Office
IEC	International Electrotechnical Commission
IFU	Instructions For Use
ILD	Interstitial Lung Disease
IMD	Investigational Medical Device
IRAS	Integrated Research Application System
ISF	Investigational Site File
ISO	International Organization for Standardization
LOA	Limits of Agreement
MDR 2002	Medical Devices Regulations 2002 (SI 2002 No 618, as amended)
MDR (EU)	Medical Device Regulation (EU) 2017/745
MHRA	Medicines and Healthcare products Regulatory Agency
NA	Not Applicable
NCRV	National Contract Value Review
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
PAH	Pulmonary Arterial Hypertension
PEF	Peak Expiratory Flow
PID	Participant Identifiable Data
PIS	Patient Information Sheet
POC	Proof of Concept
purpleDx	Medical Device under Investigation in this Clinical Study
QMS	Quality Management System

REC	Research Ethics Committee
RN	Research Nurse
ROC	Receiver Operating Characteristics
RR	Respiratory Rate
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SaMD	Software as a Medical Device
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDV	Source Data Verification
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
SSA	Site-Specific Approval
TMF	Trial Master File
UK	United Kingdom
UKCA	UK Conformity Assessment
USADE	Unanticipated Serious Adverse Device Effect
WHO	World Health Organisation
WOCBP	Women of Child-Bearing Potential

7.0 INTRODUCTION

7.1 Background

The ubiquitous distribution of smartphones amongst all population socioeconomic groups worldwide makes smartphone exploitation to access healthcare data a new axiom to stimulate change in the healthcare system. Indeed, in 2024, the Global System for Mobile Communications (GSM Association) stated that smartphones were owned by 57% of the global population, a staggering 4.6 billion people and the numbers are growing.¹ The prevalence of smartphones combined with consumer willingness to adopt novel technology provides an opportune platform to enable the healthcare sector to revolutionise and streamline the management of patients on a

platform that is already available to millions. Utilisation of smartphones can empower the public to use healthcare more efficiently and the technology has the potential to enable clinicians to make more rapid and accurate treatment decisions, reducing patient waiting times² and freeing up clinic appointments to increase the number of patients that can be dealt with over a given time. This is of particular importance given the increasing demand on health services due to the complex healthcare needs of an ageing population.³

The field of respiratory medicine lends itself to the introduction of smartphone technology to improve the care pathway for patients with long-term conditions such as Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Disease (ILD), Pulmonary Arterial Hypertension (PAH) and/or asthma. Currently, patients' physiological data, such as peak expiratory flow, forced expiratory volume in one second, respiratory rate and heart rate, is only collected by healthcare professionals when the patient attends hospital clinic visits, with no data collection during the intervening periods. In addition, there may be lengthy delays to accessing spirometry in the current NHS setting outwith the conventional follow up clinic structures. Indeed, there is considerable support in the extensive literature devoted to exploring the added value of home-based respiratory monitoring in at-risk groups to control disease, alter medication use and reduce hospital admissions as in COPD and Asthma.⁴ However, patients could assume a much more active role in their monitoring by downloading an application (app) such as purpleDx, onto their smartphones to generate data which could then be collated and securely stored in a cloud-based database in accordance with the General Data Protection Regulation (GDPR) requirements, building a repository of comprehensive data indicative of the individual patient's clinical profile over real time. Subsequently, if a patient became concerned that their clinical condition was deteriorating, the intention could be for their clinician to be alerted to consider any changes in purpleDx data amassed over time in conjunction with discussion of changing symptomology (such as increased breathlessness, cough or fatigue). The clinician may then be able to remotely affect changes to the subject's medication regimen to alleviate the issues being experienced quickly and without the need for them to attend the clinic. This early detection of exacerbations and consequent prompt treatment modification or introduction would provide a novel approach, for streamlined and personalised management of patients with long-term respiratory conditions, potentially saving time and resources^{5,6,7,8} and offering healthcare cost benefits.

The idea of using smartphone apps to aid clinical decision-making is not new and a variety of apps already exist on the market, such as the iPhone iSeismometer app which measures tremor frequency instead of the need costly for electromyogram analysis.⁹ Other examples of similar technology beginning to impact on healthcare would be FitBit and Apple watches now used widely for monitoring of atrial fibrillation (AF). The National Institute for Health and Care Excellence (NICE) in the UK has also

drawn attention to these devices singling out the Kardia device as a readily portable adjunct to the smartphone for AF monitoring.¹⁰ The simplicity of use versus the accuracy continues to be subject to controversy but the foothold these devices now have in the public domain confirm the enormous importance they represent for improving and extending healthcare initiatives. In the UK, before a new app can be approved for recognised clinical use, an MHRA approved clinical study must be carried out to 'verify that under normal conditions of use the performance characteristics of the device are those intended by the manufacturer and determine any undesirable side effects under normal conditions of use and assess whether these constitute risks when weighed against the intended performance of the device'.¹¹ Rigorous international standards must be complied with, including ISO13485:2016 and IEC 62366-1,^{12,13} and requirements are dependent on the level of risk posed by the medical device. This represents the major difference from 'Wellbeing' apps which are unproven and may over-diagnose or worse, under-diagnose critical issues of relevance to individual patients and their ongoing care.

This protocol aims to obtain clinical data to support the MHRA classification of this device and verify the broad equivalence of purpleDx and traditional medical equipment/means (Vitalograph spirometer, manual respiratory count and pulse oximeter), to measure four physiological parameters, namely peak expiratory flow (PEF), forced expiratory volume in one second (FEV₁), respiratory rate (RR) and heart rate (HR) in subjects with or without respiratory or cardiopulmonary conditions. The clinical data will be analysed and used to support a marketing application. Thus, establishing the data produced by smartphone and traditional devices/means is comparable for the measurement of physiological parameters is of paramount importance.

7.2 The Investigational Medical Device

The medical device under investigation in this study is a smartphone application (app), called purpleDx which has been developed by electronRx Ltd. It will be used to assess peak expiratory flow (PEF), forced expiratory volume in one second (FEV₁), respiratory rate (RR) and heart rate (HR) by a non-contact scan utilising the phone's camera function. According to the classification of Medical Devices by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK and the Medical Device Regulation in Europe (MDR EU), the app should be classified as Class IIA Software as a Medical Device (SaMD) and is currently pending approval for clinical use. Class IIA is medium risk as it has the potential to be used to inform changes to treatment regime if the app was further developed for such purposes.

The purpleDx app is designed to be easy to use, with two non-contact scans captured over the course of just one minute each. The subject should ideally sit on a chair in a

relaxed, upright position, preferably with their back against the chair. Alternatively, the subject may recline on a bed or trolley, with a note made of the corresponding angle of recline. The smartphone must be immobilised by using a phone stand or by being propped against a sturdy object. The phone should be perpendicular to the subject. The first one-minute scan is to determine Breath Scan namely Peak Expiratory Flow (PEF), Forced Expiratory Volume in One Second (FEV₁), and Respiratory Rate (RR), employing reference markers affixed to the subject's hands (one on each hand) to aid with visual tracking. The second one-minute scan is a Pulse Scan to measure Heart Rate (HR).

For PEF, FEV₁ and RR, the subject presses 'Breath Scan' on the smartphone and must then adjust their camera image profile on the screen according to the on-screen instructions. Once the image is correctly aligned, the recording starts automatically. A countdown of the sixty-second recording period will be displayed on the screen during the scan. The app will save the scan results to the cloud for analysis. The Breath Scan will be carried out 3 times. When the automatic analysis from the 3 Breath Scans is complete, the PEF, FEV₁ and RR results will be displayed on a results screen.

For HR, the subject presses 'Pulse Scan' and follows the on-screen instructions to position their face to fit the oval shown on the screen. Once the face is correctly positioned, the app will automatically start the recording. A countdown of the sixty-second recording period will be displayed on the screen during the scan. The HR results will appear after each Pulse Scan has been performed.

Screenshots of the various app screens are shown in Appendix 2.

Although not done as part of this clinical protocol, data could potentially be collated over time as the patient performed sequential testing.

7.3 Research Data to Date

The purpleDx app is the culmination of an extensive body of developmental work that has been carried out by electronRx over the past four years. Initial Proof of Concept (POC) testing, and subsequent in-house verification and validation testing, has been undertaken using previous iterations of several electronRx apps over the course of the developmental process, namely Blueprint and rCP. These earlier generations of the app were used in the primary care setting to capture video signal data from a number of subjects. The resultant data were analysed and used to adjust and inform the algorithms for the metrics to be captured in this clinical study, such that purpleDx has arisen from the learnings of the previous app investigations.

POC testing was undertaken on 98 subjects in a clinic setting in Japan to demonstrate the rCP app can perform a one-minute scan of the subject to produce results for heart

rate and respiratory rate. Approximately 400 additional subjects have undergone testing during the programme of verification and validation testing in the UK, mainly utilising the Blueprint and rCP apps but also a small number using purpleDx. The results of the user testing have been used to hone the algorithms for purpleDx to maximise the reliability of the parameter measurements for this clinical trial protocol.

Data accrued so far from approximately 500 subjects demonstrated improvement in agreement of measurements using the new device compared to the standard clinical devices (e.g. Vitalograph spirometer and pulse oximeter), as iterations in the algorithms used were improved. Following discussion with clinical experts in respiratory function, the thresholds for clinically useful agreement between the measurements from existing clinical devices and those achieved using the new smartphone device have been defined as targets for this clinical trial (see Table of Limits below).

In addition, we have also noted that as well as offering multiplication in accessibility to such clinical data the smartphone device offers considerable benefits to users in ease of capture of this data. We have also recognised for respiratory functions, that worsening clinical condition increases variation in an individual's sets of readings but on the other hand that often subjects find using the new device easier when they are clinically worse. Thus, as well as looking at parameter agreement we have included an analysis of 'usability' which we will link to clinical status.

7.4 Table 1: Table of Limits

This table shows the clinically acceptable variation in measurement between the new device and standard devices to remain clinically useful.

Parameter	Performance Range	Likely Performance of Device (% Within Limits of Reference Values)	Bias Target	Expected Acceptable Level Of Agreement
PEF	350 – 700 L/min	≥ 80% within ± 20%	± 10%	± 20%
FEV ₁	2 – 5 L	≥ 95% within ± 10%	± 0.1 L	± 0.2 – 0.25 L

RR	6 – 20 breaths per minute (Bpm)	≥ 95% within ± 10%	± 2 Bpm	± 4 Bpm
HR	50 – 120 beats per minute (bpm)	≥ 95% within ± 10%	± 5 bpm	± 1 bpm

This table details the current range for which data has been obtained. It states the expected capacity of the new device to determine the reference value based on the population data currently available (i.e. the agreement between devices). The table also proffers an estimate of the bias expected and the potential performance of the new device at determining reference values in practice across an unknown population as expected in this study.

8.0 RISK/BENEFIT ANALYSIS

8.1 Anticipated Risks

No clinically significant risks are expected to occur to the subjects from interacting with and using purpleDx. The scans are non-contact and the data being generated in this study will only be used to demonstrate comparability with existing methods of data capture to support a marketing application.

Hypoallergenic tape will be used to secure the reference marker fiducials to the skin on the back of subjects' hands to enable the purpleDx Breath Scan to function. There is a very low risk of reaction to the tape at the site of adherence to the skin. If a reaction does occur, the subject will be advised to apply a cold compress for 10 to 15 minutes at a time to help alleviate any swelling or itchiness. In the case of more serious reaction, the subject will be guided to use over-the-counter medication such as calamine lotion or 1% hydrocortisone cream.

The study has no bearing on any treatment the patient may receive through their conventional clinic structure consultation or as a result of their ED visit. However, if the subject encounters any problems in using purpleDx, they may experience transient frustration and anxiety whilst trying to resolve these difficulties.

If it becomes apparent through analysis of the data generated by purpleDx in this study that the app is not suitable for any subgroup of users, this information will be used to amend the intended user description in the device specification to ensure appropriate marketing application.

8.2 Potential Benefits

There are no particular clinical benefits for the subjects that take part in this clinical investigation, and there is no financial inducement to participate in the study. However, the subject may feel increased self-esteem or sense of altruism from participating in research that could potentially bring about improved management of respiratory or cardiopulmonary patients in the future.

9.0 STUDY OBJECTIVES

9.1 Primary Objectives

The primary objectives of this study are to determine whether the purpleDx non-interventional smartphone technology measures patients' peak expiratory flow (PEF), forced expiratory volume in one second (FEV₁), respiratory rate (RR) and heart rate (HR) within an acceptable agreement range and margin when compared to results measured using standard clinical testing equipment, and to demonstrate ease of use of purpleDx as opined by subjects and clinical staff.

9.2 Secondary Objectives

The secondary objectives of this study are to demonstrate the safety and usability of purpleDx in the Emergency Department setting, whether there are any subject subgroups or conditions of use for which purpleDx fails to generate sufficiently reliable data and establishment of thresholds for 'normal' ranges for PEF, FEV₁, RR and HR.

10.0 STUDY ENDPOINTS

10.1 Primary Endpoint

- Determination of the agreement in measurement of physiological signals of peak expiratory flow by traditional medical equipment and purpleDx to enable marketing application.

10.2 Secondary Endpoints

- Determination of the agreement in measurement of forced expiratory volume in one second, heart rate and respiratory rate by traditional medical equipment and purpleDx.
- Establishment of thresholds for 'normal' ranges for peak expiratory flow, forced expiratory volume in one second, respiratory rate and heart rate.

- Evaluation of the ease of using the User Interface and demonstration of usability by subjects and clinical staff.
- Demonstration of the safety of purpleDx.
- Determination of any subsets of the patient population for which purpleDx may not be suitable.
- Determination of any conditions or situations which impair the recording quality or reliability of data produced by purpleDx that have not already been determined during pre-clinical testing.

11.0 STUDY DESIGN

This study will take place at a single investigational site, namely Cambridge University Hospitals NHS Foundation Trust (CUH) in the Emergency Department, where the research team has extensive experience in performing clinical research studies in similar fields. The study will be conducted in compliance with the protocol, principles of Good Clinical Practice (GCP) and the applicable regulatory requirements.

Subjects will be male or female, aged 18 years and above. Subjects must be able to sit up and read, understand and write in English. Subjects with and without respiratory or cardiorespiratory symptom/s will be included. All participants will be required to sign an Informed Consent Form (ICF) and be allocated a unique study number by the Chief Investigator (CI)/Research Nurse (RN) or a suitably trained designee. Subjects will only be identified by the study number in all trial-related documentation i.e. there will be no patient identifiable information (PID) recorded for study purposes. At the hospital site, a subject identification log will be maintained to link the study subject number to individual PID, which will only be accessible to the subjects' clinical research team. This information will not be made available to the Sponsor. However, the study monitor will require access to ensure the correct subject's medical notes are reviewed during source data verification (SDV). The subjects will be made aware of this during the informed consenting process.

There are no treatment arms in the study. Each subject will be tested using standard clinical equipment to produce control data and by purpleDx to produce investigational data.

At the hospital visit, the following data points will be collected for each subject by the CI/RN or designee:

- Unique Subject Study Number
- Sex at birth
- Age in years

- Date of assessment
- Height in cm
- Weight in kg
- Chest circumference in cm (see Appendix 7)
- Skin tone (measured using device provided by Sponsor); see Fitzpatrick scale in Appendix 4
- Emergency Care Data Set (ECDS) presentation code
- Discharge diagnosis confirming chest illness
- 7, 14 and 30-day mortality status
- Smoking status (and number of pack years if smoker)
- Medical conditions (up to 5 relevant – respiratory or cardiorespiratory conditions, cardiac conditions, skeletal conditions e.g. scoliosis / mobility problems) to describe the population for intended use
- Confirmation of no known pregnancy in women of child-bearing potential (WOCBP); see Appendix 5
- Light Level (measured using device provided by Sponsor)
- Sitting or Reclining (and angle of recline if reclining)
- Peak expiratory flow (PEF) measured by purpleDx
- Peak expiratory flow (PEF) measured by conventional equipment (provided by Sponsor)
- Forced expiratory flow in one second (FEV₁) measured by purpleDx
- Forced expiratory flow in one second (FEV₁) measured by conventional equipment
- Respiratory rate (RR) measured by purpleDx
- Respiratory rate (RR) measured by manual count / visual inspection
- Heart rate (HR) measured by purpleDx
- Heart rate (HR) measured by conventional equipment
- Nurse/clinician assessment of subjects' ability to use purpleDx
- Subject evaluation of ease of using purpleDx
- Difficulties using purpleDx
- Adverse Event information
- Confirmation of new disposable mouthpiece for each subject's spirometry assessments.

During each purpleDx measurement, the following will also be recorded by the CI/RN or designee:

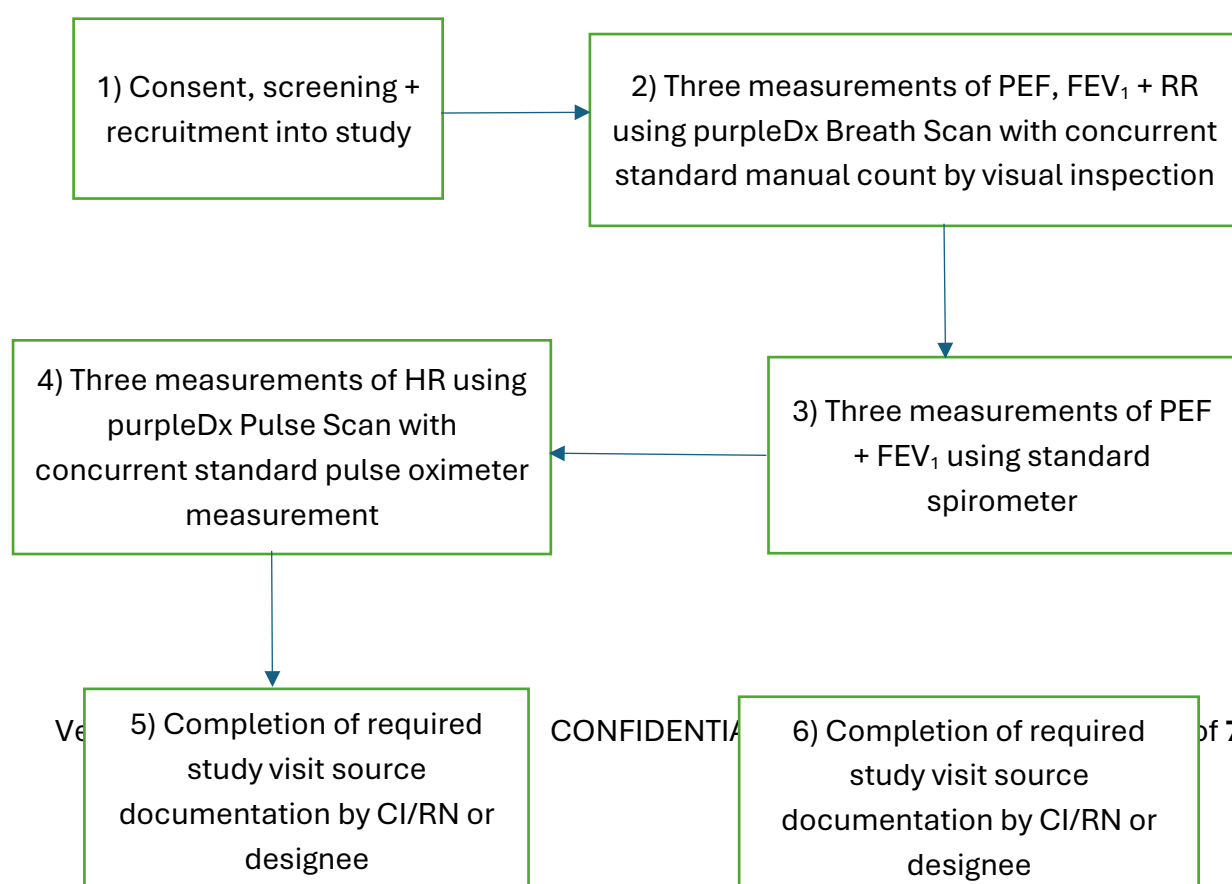
- Participant behaviour during recording, such as movement, talking, coughing, etc
- Facial obstructions, such as glasses, hats, beards, makeup, etc
- Chest obstructions, such as lanyards, loose clothing, top pattern (uniform versus patterned), etc
- Specific technical difficulties that may be encountered

- Details of any difficulties in following instructions.

The CI/RN or designee will use the light meter (see details in Appendix 6) provided by the Sponsor to ensure lighting levels are in the required range to allow purpleDx to function and will demonstrate how to use the purpleDx app to the subject. The Sponsor will provide the site with an iPhone containing the purpleDx app already downloaded and ready for use.

The subject will use the purpleDx device to perform the Breath Scan to measure PEF, FEV₁ and RR three times. Concurrently, the CI/RN or designee will observe the subject and count the number of breaths taken during each Breath Scan and will record the results on the source document. The CI/RN will use the standard Vitalograph spirometer equipment to obtain three sets of measurements for PEF and FEV₁. The subject will then use the Pulse Scan on the new device to obtain three HR readings. A standard pulse oximeter will be used concurrently to obtain three HR results. Thus, three sets of results will be produced for PEF, FEV₁, RR and HR by both the standard means and by the investigational equipment. Appendices 1 and 2 provide a detailed overview of the process and the app screenshots. For details of the equipment being used in the study, see Appendix 6. The purpleDx results will be displayed on the smartphone screen. The CI/RN or designee will copy the results from the new device and the standard equipment onto the subject's paper visit records to act as the source document for the parameter values. A PDF file will subsequently be emailed to the CI/RN or designated member of the clinical study team to verify the handwritten source document results from the purpleDx Breath Scan.

11.1 Figure 1: Overview of Study Visit Process





The CI/RN or designee will observe the subject using purpleDx and will use a simple tick-box Likert scale to answer a series of five questions about their ability to use the device. Each subject will also be asked to answer the same five questions using the simple tick-box scale to rate their ease of using the app (see Appendix 8 Section A – Device Setup and Use).

The CI/RN or designee will answer 3 additional questions (see Appendix 8 Section B – Time and Workflow).

Lastly, the CI/RN or designee and each subject will be asked to complete two open feedback questions to provide details of any difficulties or issues encountered during the process for setup, performing the scan, obtaining and recording results (see Appendix 8 Section C – Open Feedback).

All responses and required study information will be recorded in each subject's medical records or agreed form of source documentation. Data from purpleDx will be automatically uploaded to the Sponsor's database in the cloud. This information will only be identifiable by the subject study number i.e. no Patient Identifiable Data (PID) will be included.

Upon completion of the subject's visit, the CI/RN or designee will transcribe the information from any source documentation into the electronic Case Record Form (eCRF) within pre-agreed timelines (e.g. within 1 week of the date of the study timepoint).

The source documentation will be made available for external monitoring to ensure accuracy and validity of data transcribed into the eCRF.

All source documentation and the ISF must be kept for at least 10 years after the device is last placed on the market to comply with the medical device marketing requirements of regulators following completion of the study. Archival processes will be agreed between CUH and the Sponsor as part of the negotiation process to establish the Clinical Trial Agreement and ensure access can be arranged if required in future for auditing purposes.

The Sponsor will provide a secure database to act as the eCRF for the study raw data. Access to the eCRF will be password protected, and no patient identifiable data will be held within the eCRF. Each subject will only be identifiable by subject study number.



To access the eCRF, each user will require access rights to be granted by the Sponsor.

11.2 Definition of End of Study

The end of this study is defined as the 30 days after the date when the last recruited participant has completed the study testing procedures i.e. the last data point has been collected for the last study participant (30-day mortality status).

12.0 SUBJECT ELIGIBILITY CRITERIA

12.1 Inclusion Criteria

- 1) Sex at birth classified as male or female
- 2) 18 years of age and above, presenting to CUH Emergency Department
- 3) Able to read and understand the patient information sheet in English
- 4) Capacity and ability to sign an informed consent form
- 5) With or without respiratory or cardiorespiratory symptom/s

12.2 Exclusion Criteria

- 1) Unable to sit up i.e. cannot lie completely flat (supine)
- 2) Known pregnancy in women of child-bearing potential (WOCBP)
- 3) Unable to comply with the requirements of the investigation in any way
- 4) Prisoners or young offenders

13.0 STUDY PROCEDURES

13.1 Patient Screening and Recruitment

The RN or designee will approach potential subjects in the waiting area of the CUH Emergency Department to determine their interest in participating in the study. Subjects will be given a Patient Information Sheet (PIS) and Informed Consent Form (ICF), to read and consider and will be given sufficient time to ask any questions and receive satisfactory explanation to enable them to decide whether they want to take part.

Subjects will confirm their willingness to participate in the study by signing the study-specific ICF in the presence of the CI/designee. The original signed ICF will be scanned into the subject's electronic patient record then placed in the relevant section of the Investigator Site File (ISF). A photocopy of the signed ICF will be given to the subject. The subject will be assigned a unique anonymised study number. Signing the ICF and assignment of a study number constitutes recruitment into the study.

13.2 Informed Consent Process

Informed consent must be obtained prior to the participant undergoing any activities that are specifically for the purposes of the study.

Subjects will be approached in the CUH Emergency Department to determine interest in participating in the study. Subjects will be given sufficient time to read the PIS, receive answers to any questions they may have, and to consider whether they want to take part.

Subjects will confirm their willingness to participate in the study by signing the study-specific ICF. The original signed ICF will be placed in the ISF, and a photocopy will be filed in the subject's medical record and a photocopy will also be given to the subject.

This study requires participants to be capable of providing consent to take part and therefore a legal representative will not be able to sign consent on behalf of a subject. The assessment of capacity to consent involves consideration of whether the subject can understand the following points:

- the purpose and nature of the study
- what the study involves
- any risks and/or benefits of the study
- participation is voluntary
- decision whether to participate will not affect the subject's healthcare in any way.

The PIS and ICF will be printed on CUH headed paper and will have been approved by a Research Ethics Committee suitable for the assessment of medical device studies prior to the start of the study. Subjects will have the opportunity to ask any questions of the CI/RN to help them decide if they want to take part in the study.

13.3 Withdrawal of Consent

Subjects can withdraw their consent to participate in this study at any time and without affecting their subsequent clinical care in any way. This will be explained to the subject during the informed consent process.

If a subject withdraws consent to participate in the study after signing the ICF but prior to undergoing any study procedures, all study-related documentation will be destroyed. The subject will not be allocated a study number. No study information will be recorded. No study procedures will be undertaken.

If a subject signs the ICF, is allocated a study number and at least begins the measurement of any of the physiological parameters being investigated in the study but changes their mind and withdraws consent, the information will be kept as part of

the subject's medical record to maintain complete transparency but will not be included in the analysis in any way. The subject will still be asked to rate their ease of using the app but has the right to refuse. Their reason for withdrawal of consent will be ascertained as far as possible to determine if it was in any way due to using purpleDx.

13.4 Randomisation

This is not applicable to this clinical trial as all subjects undergo the same testing process and are not assigned to treatment arms. Each subject will act their own control, by being tested with standard clinical equipment and the SaMD.

13.5 Schedule of Events

13.5.1 Per-participant Activities

Activity	To be done at ED Visit
Review of PIS and signing ICF	x
Height	x
Weight	x
Chest circumference	x
Smoking status (number of pack years for smoker)	x
Relevant medical conditions (including confirmation of no known pregnancy in WOCBP)	x
Angle of recline (if subject is lying on bed/trolley)	x
Measurement of skin tone	x
Measurement of light level	x
Measurement of PEF, FEV ₁ , RR + HR using purpleDx [^]	x
Measurement of PEF, FEV ₁ , RR + HR using standard equipment/means ^{*^}	x
Completion of usability questions	x
Adverse event information	x

* standard equipment for PEF and FEV₁ is the Vitalograph spirometer and for HR is the Nonin pulse oximeter and standard means for RR is manual count by visual inspection

^ each parameter will be measured three times.

13.5.2 General Study Activities

Activity	Team Member	Estimated Time to complete activity per enrolled subject
Taking informed consent	CI/RN	15 minutes
Completion of visit assessments and source documentation	CI/RN/designee	45 minutes
Input of data into each subject's eCRF and CI sign off	CI/RN/designee	15 minutes
Maintenance of Investigator Site File and Essential Documentation	CI/RN/designee	30 minutes
Query resolution (arising from SDV)	CI/RN/designee	30 minutes

14.0 STATISTICAL ANALYSIS PLAN

The Statistical Analysis Plan (SAP) incorporates testing for peak expiratory flow (PEF) and forced expiratory volume in one second (FEV₁), heart rate (HR) and respiratory rate (RR) using the new device (PurpleDx), compared to these standard clinical measures using the Vitalograph spirometer, manual respiratory count and pulse oximeter in a single-visit A&E setting. The statistical approach evaluates agreement and usability for all four parameters.

14.1 Study Objectives

14.1.1 Primary Objective

- To evaluate **agreement** between the new device and standard clinical measures for assessment of Peak Expiratory Flow; **PEF** (Primary Endpoint).

14.1.2 Secondary Objectives

- To evaluate the agreement between the new device and reference methods for assessment of:
 - Forced Expiratory Volume in one second; **FEV₁**
 - Respiratory Rate; **RR**
 - Heart Rate; **HR**.
- To assess the **usability** of the new device for patients and clinicians.

14.2 Data Collection

- **Participants:** Adults (≥ 18 years) presenting to the ED with or without respiratory or cardiorespiratory symptoms.
- **Procedure:**
 - Three measurements of PEF, FEV₁ using the new device and reference method (best effort recorded).
 - Three measurements of HR and RR using the new device and standard clinical devices/means (average recorded).
 - Usability questionnaires (Likert scales) completed by patients and clinician post-use.
- **Reference Methods:**
 - PEF: Vitalograph spirometer
 - FEV₁: Vitalograph spirometer
 - RR: Manual count
 - HR: Pulse Oximeter

14.3 Outline Analysis Plan: Statistical Tests and Rationale

14.3.1 Bland-Altman Analysis (Agreement Testing):

Bland Altman is the required standard test to evaluate agreement between devices estimating the same clinical parameter¹⁴. To do this successfully we require a large enough sample (n large enough) to estimate the mean bias and limits of agreement (LOA) reliably and ensure stable estimates of variability of differences (standard deviation, SD). Bland Altman recommends at least 100 paired observations to estimate CI width around bias and LOA¹⁵.

- To assess the mean difference (bias) and Limits of Agreement (LOA) between the new device and the reference.

- Rationale: Identifies systematic bias and variability across measurement ranges.

14.3.2 Proportion Within Acceptable Limits:

- Calculation of % of measurements within a pre-defined acceptable range (e.g., $\pm 20\%$ for PEF).
- Rationale: Provides an intuitive clinical interpretation of device performance.

The level of agreement is calculated by showing the percentage of measurements taken by the two approaches that lie within specific limits as a performance measure. For example, using table 14.3.5 which is based on current available target performance data for purpleDx, performance can be used to describe how this agreement can be estimated.

For PEF it is hypothesised that $\geq 80\%$ of values taken by the two approaches in the same subject will lie within $\pm 20\%$ of each other. We will calculate for each set of paired data whether the two values are within 20% of each other, and then the proportion of subjects where there is success by this criterion will be calculated. A two-sided confidence level will be calculated around this proportion using the Wilson Score method. The study objective is to demonstrate that the proportion is $\geq 80\%$ so the study will be positive for this outcome if the lower bound confidence interval is $\geq 80\%$.

This figure will be used to determine the number of subjects that we will need to estimate this measure to this level (see section 14.4.2 below).

In a similar way we will use table 14.3.5 (our current estimate of performance) to say we expect to be able to demonstrate what percentage of readings for FEV₁, HR and RR from purpleDx (our secondary endpoints) will lie within $\pm$ an acceptable percentage of the conventional spirometry, or HR or RR standard device readings. We will calculate for each subject's paired readings, whether the two values lie within this percentage of each other and then the proportion of subjects where this is successful by this criterion for each measure will be calculated. A two-sided confidence interval will be calculated around this proportion using the Wilson Score method based on the subject numbers determined above. Subsequent sensitivity testing will allow upgraded description of device performance (see section 14.4.4).

Formula for deciding whether paired values are within a percentage range.

There are two approaches to this calculation, namely relative percent difference or the symmetric formula. The latter avoids bias, when either value could be the reference, but for this study we have our fixed 'gold' standard and hence we have chosen to use the relative percent difference.

Using: P_i = test device reading for subject i

G_i = gold standard reading for subject i

Success = $P_i - G_i \leq 0.2 \times G_i$

This approach measures deviation relative to the gold standard as in this study.

14.3.3 Intraclass Correlation Coefficient (ICC)^{16,17}:

- Used to assess reliability/agreement between two quantitative measurements.
- Rationale: ICC >0.75 indicates good agreement, ICC >0.90 indicates excellent agreement.
- Provides an important link with established literature for comparison.

14.3.4 Descriptive Statistics (Usability):

- Mean and SD for Likert-scale usability ratings.
- Error rates, setup time, and qualitative feedback summarised.

14.3.5 Parameter Hypothesis Table: Acceptable Agreement Thresholds

Parameter	Performance Range	Likely Performance of Device (% Within Limits of Reference Values)	Bias Target	Expected Acceptable Level Of Agreement
PEF	350 – 700 L/min	≥ 80% within ± 20%	± 10%	± 20%
FEV ₁	2 – 5 L	≥ 95% within ± 10%	± 0.1 L	± 0.2 – 0.25 L
RR	6 – 20 breaths per minute (Bpm)	≥ 95% within ± 10%	± 2 Bpm	± 4 Bpm
HR	50 – 120 beats per minute	≥ 95% within ± 10%	± 5 bpm	± 1 bpm

	(bpm)			
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14.4 Sample Size Calculation

14.4.1 PEF Sample Size Calculation (to show lower 95% CI bound $\geq 80\%$)

Study goal:

- True success proportion p_1
- Null threshold (target to exceed) $p_0=0.80$
- Type I error (2-sided): $\alpha=0.05$
- Power: $1-\beta=0.90$
- Use **Wilson score CI** to test whether lower bound ≥ 0.80 .

Approximate approach (one-sample proportion power analysis)

We can approximate using a **one-sample proportion test** (binomial test of $H_0: p = 0.80$ vs $H_1: p = p_1 > 0.80$):

$$n = \frac{\left[z_{1-\alpha/2} \sqrt{p_0(1-p_0)} + z_{1-\beta} \sqrt{p_1(1-p_1)} \right]^2}{(p_1 - p_0)^2}$$

This gives the approximate number of *paired comparisons* (subjects) needed.

Where:

- $z_{1-\alpha/2}=1.96$ for $\alpha=0.05$
- $z_{1-\beta}=1.2816$ for 90% power

Example calculation

Expected **true agreement proportion** $p_1=0.90$.

Then:

$$p_0 = 0.80, \quad p_1 = 0.90$$

$$n = \frac{(1.96\sqrt{0.8 \times 0.2} + 1.2816\sqrt{0.9 \times 0.1})^2}{(0.9 - 0.8)^2}$$

Computing:

$$\sqrt{0.8 \times 0.2} = 0.4, \quad \sqrt{0.9 \times 0.1} = 0.3$$

$$n = \frac{(1.96(0.4) + 1.2816(0.3))^2}{(0.1)^2} = \frac{(0.784 + 0.384)^2}{0.01} = \frac{1.168^2}{0.01} = \frac{1.364}{0.01} = 136.4$$

This means:

With 137 paired results (one per subject), if the *true* success rate is 90%, there is 90% power that the 95% lower Wilson bound will exceed 80%.

To ensure sample size of 137 can be achieved, the maximum number of patients recruited into the study will be 160. This allows for withdrawals or failures to capture measurements for any reason.

Once 150 patients have been recruited, the preliminary data will be reviewed to determine whether any further patients are required for the study or whether sufficient data has been collected to enable the statistics to be performed. Recruitment will cease once sufficient data has been shown to have been collected from at least 150 patients. A maximum of 160 patients will be recruited to achieve 150 analysable sets of data.

14.4.2 FEV₁ Sample Size Calculation

From Table 14.3.5 we might expect the performance of the purpleDx device to be closer to $\leq 10\%$ of the gold standard. However, across a broader range of clinical subjects as in this case, we are uncertain of the performance and to allow us to define the performance we will use the same threshold settings as for PEF.

However, we can calculate a table of performance of the device for p_0 and power for $n=150$, $p_1=0.95$ and $\alpha=0.05$ above using a rearrangement of the formula:

$$z_{1-\beta} = \frac{(p_1 - p_0)\sqrt{n} - z_{1-\alpha/2}\sqrt{p_0(1-p_0)}}{\sqrt{p_1(1-p_1)}}$$

Target p_0	Power
0.85	99%
0.88	84%
0.89	71%
0.90	54%

Thus with 150 subjects and a true agreement of 95% we can demonstrate that the lower CI exceeds 0.88 with about 80-85% power sufficient for this study.

14.4.3 HR and RR Sample Size Calculation

150 subjects (calculation as above for FEV₁)

Our aim as above is to define the percentage agreement as so that a positive result is achieved $\geq 80\%$ if the CI lower bound is $\geq 80\%$. Again, we would expect the agreement to be better than this but will need this number of subjects to ensure the precision of this proportion-of-agreement around the calculated CI margin. This ensures we can reliably quote the performance of the purpleDx device across these measures.

14.4.4 Sample Size for Intraclass Correlation

- FEV₁ (vs Vitalograph spirometry)
- HR (vs pulse oximeter)
- RR (vs manual count)

Our sample size needs to allow us to evaluate a Null Hypothesis: an ICC of less than or equal to 0.75 (moderate agreement) vs an Alternative Hypothesis: ICC equal to or better than 0.90 with a power of 0.80 and alpha of 0.05.

Using Bonnett's formula (2002)

$$n = \left[\frac{Z_{1-\alpha/2} + Z_{1-\beta}}{\ln\left(\frac{1+\rho_a}{1-\rho_a}\right) - \ln\left(\frac{1+\rho_0}{1-\rho_0}\right)} \right]^2 + 1$$

n ≈ 47–50 is needed to detect an ICC ≥ 0.90 versus null ICC of 0.75

n > 100 provides excellent power for secondary ICC analyses, especially if some readings are invalid.

14.4.5 Usability Sample Size

- Descriptive usability analyses benefit from larger samples.

- Able to detect differences in usability scores (effect size $d \sim 0.5$) with 80% power.
- **n = 100–125** provides a 90% usability rating with:
 - $\pm 6\%$ precision around usability proportions (95% CI).
 - Adequate numbers for subgroup comparisons.

14.5 Determination of Acceptable Usability

The Likert scale used to indicate usability is a 5-point scale where 3 represents a neutral or standard assessment. The scale allows subjects and clinicians to select a better or worse assessment.

The overall usability score will be computed as the mean of eight individual 5-point Likert items related to setup, ease of use, interpretation and satisfaction. This continuous usability index (range 1 – 5) will be summarized using mean and standard deviation. The null hypothesis is that the test usability index is no different from the population index of 3. Usability will be considered acceptable if the mean score is significantly greater than 3, assessed using a one-sample t-test. Internal consistency of the scale will be evaluated using Cronbach's alpha.

14.6 Sensitivity Testing

Within % criteria

It is intended with the data that we will refine the 'within x% criteria' by computing the proportion of paired readings within a range of limits e.g. $\pm 5\%$, $\pm 10\%$, $\pm 20\%$. By plotting these as a cumulative agreement graph, this will show how the devices converge as the tolerance band widens and enable users to decide how best to implement the device for their patients/subjects.

For each tolerance (e.g. 5%, 10%, 20%), we will also compute the **Wilson 95% CI** for the proportion within limit.

The Bland Altman plot

This is the industry standard for quantifying agreement. This allows systematic bias and spread to be visualised.

14.7 Handling of Missing Data

14.7.1 General Approach

- Every effort will be made to minimize missing data by thorough training of staff, checking of data at the point of entry, and rapid feedback to clinical teams.

- Missing data are anticipated to arise primarily from:
 - Patient inability to perform the measurement correctly,
 - Equipment malfunction or technical failure,
 - Clinician time pressure preventing data recording.

14.7.2 Specific Strategies

- **For PEF and FEV₁:**
 - If a patient is unable to provide three acceptable blows, the best available single reading will be used (if at least one acceptable effort exists).
 - If no valid readings can be obtained from either the new device or reference method, that data point will be recorded as **missing**.
- **For HR and RR:**
 - If standard or new device readings fail, a second attempt will be made immediately.
 - If still unsuccessful, the observation will be marked as **missing**.

14.7.3 Statistical Treatment of Missing Data

- **Primary Analyses:**
 - Analyses (Bland-Altman plots, ICC calculations, proportion within limits) will be conducted using **complete cases only** (i.e., patients with valid paired measurements for the parameter being assessed).
 - No imputation of missing PEF, FEV₁, HR, or RR values will be performed in the primary analysis.
- **Sensitivity Analyses:**
 - Sensitivity analyses will be considered if >10% of data for any parameter are missing.
 - For PEF, imputation methods such as **last observation carried forward (LOCF)** or **single imputation using median of available efforts** may be considered for exploratory purposes only.
 - For usability outcomes, missing questionnaire responses will not be imputed; proportions will be based on available data.

14.8 Reporting

- The amount and pattern of missing data will be summarized by parameter (PEF, FEV₁, HR and RR).
- The reasons for missing data (if known) will be categorized and reported descriptively.
- The potential impact of missing data on study conclusions will be discussed in the final study report.

14.9 Example Estimated Results Table

Parameter	Performance Range	Likely Performance of Device (% Within Limits of Reference Values)	Bias Target	Expected Acceptable Level Of Agreement
PEF	350 – 700 L/min	≥ 80% within ± 20%	± 10%	± 20%
FEV₁	2 – 5 L	≥ 95% within ± 10%	± 0.1L	± 0.2 – 0.25 L
RR	6 – 20 breaths per minute (Bpm)	≥ 95% within ± 10%	± 2 Bpm	± 4 Bpm
HR	50 – 120 beats per minute (bpm)	≥ 95% within ± 10%	± 5 bpm	± 2 bpm

14.10 Estimand Table¹⁹

Component	PEF	FEV ₁	RR	HR
Treatment	Measurement using new device	Measurement using new device	Measurement using new device	Measurement using new device
Comparator	Vitalograph spirometer	Vitalograph spirometer	Manual count	Pulse oximeter
Population	Adults ≥18 years presenting to ED with respiratory / cardiorespiratory symptoms	Same as PEF	Same as PEF	Same as PEF
Variable (Endpoint)	Peak Expiratory Flow; PEF (L/min)	Forced Expiratory Volume in One Second; FEV ₁ (L)	Respiratory Rate; RR (Breaths per minute)	Heart Rate; HR (beats per minute)
Summary Measure	Mean bias, 95% Limits of Agreement, % within ± 20% of reference	Mean bias, 95% Limits of Agreement, % within ±10%	Mean bias, 95% Limits of Agreement, % within ±10%	Mean bias, 95% Limits of Agreement, % within ±10%
Handling of Missing Data	Exclude invalid readings; perform sensitivity analysis if needed	Same as PEF	Same as PEF	Same as PEF
Intercurrent Events	Poor technique, device malfunction	Spirometry effort failure, device errors	Talking during measurement, movement artefact	Movement artefact, device connectivity issues
Interpretation	Agreement sufficient for clinical decision support at bedside	Agreement comparable to spirometry for diagnosis and monitoring	Agreement sufficient for respiratory distress assessment and monitoring	Agreement sufficient for accurate triage and monitoring

14.11 Access to the Final Study Dataset

The raw data contained in the eCRF will belong to the Sponsor. Only those members of the Sponsor team who are actively involved in performing the statistical analysis to produce the results for the study will be granted access to the final study dataset.

The investigational site team at CUH will be given the results of the study but will not have access to the raw data.

Study participants will have been asked as part of the informed consent process whether they agree to their anonymised data being used for future research purposes. If consent has been provided, the relevant raw data could be made available to the CI, providing separate approvals have been granted for such further research purposes.

15.0 ADVERSE EVENTS AND REPORTING

15.1 Definition of an Adverse Event

An Adverse Event (AE) is any untoward medical occurrence, unintended disease or injury or any untoward clinical sign in a clinical investigational subject, temporally associated with the subject's participation in research, whether or not it is considered related to the investigational medical device. This includes events related to the investigational medical device (IMD) or the comparator, and events related to the procedures involved in the clinical investigation plan. The Common Terminology Criteria for Adverse Events (CTCAE) v5.0 will be used to determine the most appropriate medical term for the AE (see Appendix 9).

15.2 Definition of a Serious Adverse Event (SAE)

A Serious Adverse Event (SAE) is any untoward medical occurrence that has results in any of the following:

- 1) Death
- 2) Life-threatening illness or injury
- 3) In-patient hospitalisation or prolongation of existing hospitalisation
- 4) Permanent impairment of a body structure or body function
- 5) Congenital abnormality or birth defect.

15.3 Definition of an Adverse Device Effect (ADE)

An Adverse Device Effect (ADE) is an Adverse Event (AE) related to use of an investigational medical device. This includes any AE resulting from insufficiencies or

inadequacies in the instructions for the use, deployment, operation or any malfunction of the investigational medical device. This includes any AE that is a result of a user error or intentional misuse of the device.

15.4 Definition of Device Deficiency (DD)

Device deficiency (DD) is the inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labelling. All occurrences of Device Deficiencies must be reported to the Sponsor using a DD Reporting Form (blank DD reporting forms will be provided to the site in the ISF).

15.5 Definition of a Serious Adverse Device Effect (SADE)

A Serious Adverse Device Effect (SADE) is an adverse device effect that has resulted in any of the following consequences:

- 1) Death
- 2) Life-threatening illness or injury
- 3) In-patient hospitalisation or prolongation of existing hospitalisation
- 4) Permanent impairment of a body structure or body function
- 5) Congenital abnormality or birth defect.

15.6 Definition of an Unanticipated Serious Adverse Device Effect (USADE)

An Unanticipated Serious Adverse Device Effect (USADE) is a Serious Adverse Device Effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report. All USADEs should be reported to the Sponsor using an SAE/SADE Reporting Form (see section 15.11).

15.7 Anticipated and Unanticipated Adverse Events

It is not anticipated that any AEs will occur during the testing of the medical device as the app utilises the smartphone's camera function to perform a non-invasive scan. Despite this, the reporting mechanism for site and Sponsor to handle any adverse events that do transpire is defined in this protocol to ensure all occurrences are captured and handled as necessary for patient safety and compliance with regulatory safety reporting requirements.

15.8 Classification of Adverse Event Causality

The CI is required to speculate as to the relationship between the SAE and the Investigational Medical Device (IMD), namely purpleDx. The classification of relationship is as follows:

- 1) Unrelated
- 2) Unlikely to be related
- 3) Possibly related
- 4) Probably related
- 5) Definitely related.

15.9 Classification of Adverse Event Seriousness

The CI is required to classify the seriousness of the SAE/SADE using the CTCAE v5.0 for the most appropriate grading from 1 to 5, where 1 is less serious and 5 is more serious. It should be noted that the term 'seriousness' is not the same as 'severity'. An AE may be considered severe but could be of minor medical significance. An AE is only considered to be serious if it results in any of the points as listed in 15.2, such that an AE can be considered severe but not serious, and vice versa.

15.10 Classification of Adverse Event Severity

The CI is required to classify the severity of the SAE/SADE. The severity is related to the intensity of the event, usually classified as mild, moderate or severe.

15.11 Reporting Requirements for SAEs/SADEs

Every SAE/SADE (including Unexpected Serious Adverse Device Effects; USADEs) must be reported to the Sponsor. The CI/RN must submit an initial SAE/SADE report to the Sponsor as soon as possible (within 24 hours of knowledge of the SAE/SADE taking place). A follow up form should be submitted to update the Sponsor as to further information within 7 days and as more information is available until the conclusion of the SAE/SADE. Blank SAE/SADE Reporting Forms will be provided to the site in the ISF. A new form should be used for each SAE/SADE and when providing follow up details.

The Sponsor must submit an initial report for each SAE/SADE to the MHRA and REC whether or not it is considered to be related to the IMD (purpleDx). A follow up report for each incident should be submitted to the MHRA and REC to provide full details of the investigation and outcome of the SAE/SADE.

16.0 ETHICS AND REGULATORY COMPLIANCE

Clinical studies taking place in the NHS setting require approval from a Research Ethics Committee (REC) and the Health Regulatory Authority (HRA), along with a Letter of No Objection from the MHRA and NHS Trust R+D approval, prior to the start of any study process or procedure.

16.1 Research Ethics Committee Approval

The Sponsor will seek approval (favourable opinion) for this clinical study from an appropriate Research Ethics Committee (REC) by completing and submitting Parts A and B of the online Integrated Research Application System (IRAS) forms.

The team at CUH will complete appropriate requirements to gain Health Research Authority (HRA) site-specific approval (SSA) to perform the clinical study at CUH. In parallel, approval will be sought from CUH Research and Development Department, which will include agreement of costings for undertaking and performing the study, and Clinical Trial Agreement.

16.2 MHRA Approval

The Sponsor will inform the MHRA of their intention to undertake the clinical study. Following confirmation of receipt of this information, the MHRA has 60 days to issue a Letter of Objection. If such an objection is not received by the Sponsor within that timeframe, it will be considered that the MHRA has no objections to the protocol, thus constituting regulatory authorisation to proceed with the clinical study.

16.3 Substantial Amendments to the Protocol

If the Sponsor amends the protocol in a way that it deems substantial, it will submit a Notice of Amendment to the REC to obtain approval for the amendment. The Sponsor will also inform the MHRA and site R+D department. The protocol changes cannot be implemented at site until all approvals have been received (unless required to ensure the safety of the study participant, in which case the change can be implemented immediately).

If the amendment is not deemed substantial, the Sponsor will inform the REC, MHRA and R+D department of the amendment for their records, but formal approval is not required. The amendment number and updated protocol version and date will be

recorded in section 4.0 of the protocol, along with description and reason for the change/s.

16.4 Study Documentation and Reporting Requirements

The site undertaking the clinical study will keep all correspondence with the REC and MHRA in their Investigation Site File (ISF). The CI will submit a Progress Report to the REC within 30 days of the start of the study, and an Annual Progress Report (APR) each year thereafter until the end of the study. The CI will submit an End of Study Report within one year of completion of the study, including any publications or study reports that have been produced. The CI will inform the REC if the study is terminated prematurely, explaining the reasons for this.

16.5 Data Protection and Patient Confidentiality

16.5.1 Data Protection

As this clinical study collects, stores and processes de-identified patient information, the risk of re-identification has been minimised. The Sponsor does not have access to the key required to decode the study numbers, making it impossible for the data to be traced back to individual participants. While fully anonymized data falls outside the scope of the General Data Protection Regulation (GDPR), the seven core principles of the Data Protection Act 2018 have been considered and enacted during the study's conception. The clinical site team must abide by these principles to ensure proper handling and safeguarding of participant data throughout the study.

1) Lawfulness, fairness and transparency: Subjects will be made aware of the information that will be captured for the purposes of this study, how it will be used and who will have access to the data during the informed consent process.

2) Purpose limitation: The data collected and generated by the study will only be used as outlined in this protocol. Data will not be manipulated or analysed in any other way. Data will be analysed to fulfil the aims of this clinical study and will not be used for any other purpose.

3) Data minimisation: Only the specific data points outlined in this protocol to achieve the aims of the study will be recorded. No additional or unnecessary details will be noted.

4) Accuracy: The data will be reviewed by a monitor to ensure information is accurate and reliable. Any errors or omissions will be rectified accordingly.

5) Storage limitation: The study records and information must be kept for at least 10 years following marketing to comply with the regulations for marketing new medical devices. This is detailed in the patient information sheet and expanded upon during the informed consent process as required.

6) Integrity and confidentiality: The Sponsor will provide a secure electronic repository for purpleDx data to be stored in the cloud. Access to this database will be password protected and restricted to those authorised Sponsor team members directly involved in the analysis process. Passwords will be allocated on an individual basis and will not be shared. Access to the database will be timestamped to provide an auditable record.

7) Accountability: The Sponsor is ultimately accountable for ensuring the principles of the Data Protection Act are adhered to and will achieve this via monitoring and auditing mechanisms.

16.5.2 Patient Confidentiality

To maintain patient confidentiality, the subjects who take part in this clinical study will each be identified by a study number that will consist of a sequence of seven numbers that are randomly generated (by the Vitalograph spirometer) and assigned completely independently of the patient details. The study number will replace all Patient Identifiable Data (PID) for the purposes of the study, and the Sponsor will have no access to PID.

The clinical site will maintain a subject log with details to link the study number to a specific patient. This log will not be kept in the Investigator Site File (ISF) and will not be accessible by the Sponsor but will be used by the monitor to ensure the correct subject medical notes are reviewed for the purposes of SDV. The log containing the linking code to individual patients will be securely stored in a password protected and encrypted digital file, in a separate location to any study data. During the informed consent process, subjects will be made aware of the need for the external review of PID in their hospital medical records for the monitoring process, to validate the depersonalised data for the study. It will be reiterated that no PID will be held in the study databases or accessible by the Sponsor. In this respect, the clinical site remains the data custodian in terms of any PID, whilst the Sponsor is responsible for the depersonalised data collected for study purposes as defined in this protocol.

Each subject will be required to provide consent for the Sponsor's monitor to access their PID solely for monitoring purposes. The ISF will be kept secure in a locked office only accessible by members of the site study team.

Although there is no patient identifiable data in this study, there is the potential for identifiable details to be sent to the Sponsor in error (e.g. on an email). Accordingly, methodology is in place to handle such a scenario.

If a breach of patient confidentiality occurs, the person discovering the breach must contact the Sponsor's designated Data Protection Officer (DPO) within 24 hours of discovery to inform them of the details. The Sponsor will then act in accordance with their internal Data Security and GDPR Compliance procedure.

The Sponsor will assess whether the breach is likely to result in a high risk to the rights and freedom of the individual/s concerned. If classed as high risk, the DPO will inform the Information Commissioner's Office (ICO) within 72 hours of discovery of the breach, along with the individual/s concerned without undue delay.

The Sponsor will maintain a log of all personal data breaches that occur during the clinical study, whether they constitute high risk or not.

16.6 Patient and Public Involvement

In line with the NIHR UK Standards for Public Involvement, previous versions of apps used during the development of purpleDx have been tested on 30 volunteers at CUH in December 2024 and a number of patients and members of the public at an outreach care home visit in May 2025. On these occasions, the participants found the new device to be acceptable to use and were happy to comply with the requirements of the preliminary testing procedures.

16.7 Peer Review

The protocol has been peer reviewed by a Clinician and a Statistician who are independent of and external to electronRx and CUH and are not involved in the study in any way. The Clinician has the necessary knowledge of the clinical services and issues involved with the management of patients with respiratory disease to comment on the protocol design and premise, and the Statistician has the expertise to comment on the protocol design and analysis techniques. As this is a small-scale study carrying little risk to participants, this level of peer review is deemed proportionate. Accordingly, no Data Monitoring Committee or Data Advisory Committee will be convened.

16.8 Audits and Inspections

16.8.1 Protocol compliance

The Essential Documents (all documentation in the ISF and subjects' source documentation) at the clinical site will be thoroughly reviewed by the study monitor to assess protocol compliance and validity of trial conduct. If the monitor detects any protocol deviations, these will be discussed with the Chief Investigator and relevant members of the site team to determine the reason for the deviation and to mitigate its future occurrence. Any deviations will be corrected where possible. If it is not possible to correct the deviation, the details will be highlighted to the Sponsor to determine whether data is still usable or should be eliminated from the analysis. The deviations will be classified as minor or major and will be recorded in the monitoring visit report. The study monitor will provide re-training to study team members following all protocol deviations. If a member of the study team continues to deviate from the requirements of the protocol despite attempts by the Sponsor to re-train the individual, the Sponsor may request a replacement person to carry out the role with any further participants.

The Sponsor understands that accidental protocol deviations can occur from time to time. If a member of the site team realises an accidental protocol deviation has occurred, they should immediately notify the Chief Investigator at site and the Sponsor representative, providing details of what has happened and how it differs from the approved protocol. The CI and Sponsor will discuss whether the deviation can be rectified in any way. If it is not possible to correct the error, the Sponsor will decide whether the data is still useful or whether it should be excluded from the analysis.

All protocol deviations (minor and major) must be documented for full transparency, using a Protocol Deviation Reporting Form (blank PD reporting forms will be provided in the ISF). A deviation will be considered major if the Sponsor deems it to have jeopardised the integrity of the data in any way. Details of major deviations will be reported to the Ethics Committee.

16.8.2 External Audit

All Essential Documentation (i.e. eTMF of the Sponsor and/or ISF at the investigational site) will be made available for external auditors for formal Inspection if/when requested.

16.9 Publication and Dissemination Policy

16.9.1 Dissemination Policy

The Sponsor will own the raw data collected for this clinical study. Upon completion of the study, the Sponsor will be responsible for analysing the data, producing a Final Study Report and ensuring the results are accessible to the public. The Sponsor will dedicate a section of their website to the clinical study results. Study participants will be provided with the website address, so they are able to access the results if they so wish in due course. For transparency, the website will clearly state if the results are pending and the date when the Final Study Report is expected to be published. If any study participant contacts the site research team to enquire about the study results, they will be referred to the Sponsor website for information.

The Sponsor will also aim to publish the study results in appropriate journal/s. The CI will be encouraged to publish aspects of the analysed version of the study data, recognising the contribution of the study design team.

The Final Study Report will be made available within 1 year from the completion of the study, with the expectation that submission to journals for publication would be made in parallel.

There are no additional funding streams for this clinical study and therefore no additional review or publication rights to consider.

Whilst the full complement of essential trial documents will be made available to the relevant Regulatory Authorities, these will not be publicly accessible.

16.9.2 Authorship Policy

The Sponsor does not intend to employ professional writers to produce the Final Study Report. Those involved in the design, development and implementation of the clinical study will be recognised in any publications.

17.0 INDEMNITY

The subjects that take part in this clinical trial will be covered by the Sponsor's insurance policy.

The insurance policy will cover:

1. Any potential legal liability of the Sponsor and/or Employers for harm to participants arising from the management of the clinical study.

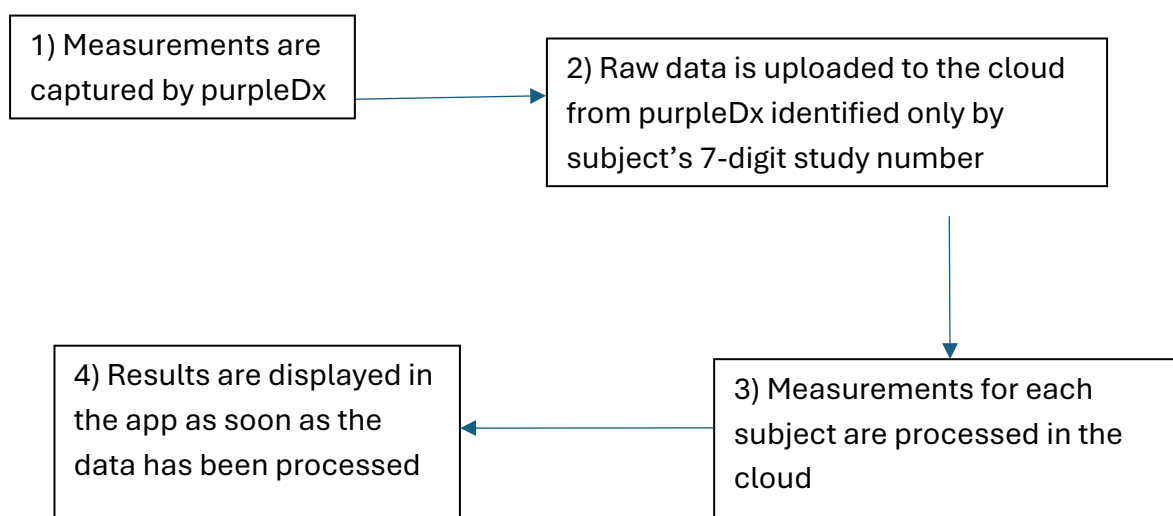
2. Any potential payment of compensation in the event of harm to participants where no legal liability arises.

3. Any potential legal liability arising in relation to any equipment provided by the Sponsor for use in the study, such as loss, damage, maintenance responsibilities for the equipment itself, harm to participants or site staff arising from the use of the equipment.

In addition, the clinical site will ensure their NHS indemnity scheme covers any potential legal liability of the investigators/collaborators arising from harm to participants in the conduct of the clinical study, prior to commencing recruitment of participants into the study.

18.0 DATA COLLECTION, HANDLING AND VERIFICATION

18.1 Figure 2: Overview of Data Flow



18.2 Source Documentation and Data Verification

The clinical site will confirm the location where all data will be recorded for the clinical study. This original documentation of data is referred to as source documentation. The clinical site will keep the source documentation secure and will provide it for review and verification by the study monitor as required. The data generated by purpleDx for the Breath Scan will be displayed on the phone screen then automatically submitted to the secure cloud storage. This will constitute the original source data for the purpleDx Breath Scan readings, which will be converted into a pdf document and returned to the

site for filing in the subject's medical record. The site team is required to transcribe the readings displayed on the screen at the time of measurement onto the visit paper record to serve as a backup in case an error occurs in the electronic process. If no pdf document is available, the handwritten visit record will constitute the source document. If any discrepancies are noted between the pdf document and the handwritten visit record, the Sponsor will be notified and asked to review the raw data to confirm correctness. If it is possible to provide the Pulse Scan measurements in a pdf document, this will also serve as the source document. However, if this is not possible, the handwritten visit record will constitute the source document.

18.3 Clinical Site Training and Initiation

The Sponsor will provide study-specific training to the site team at a Site Initiation Visit (SIV) to ensure the requirements of the protocol are fully understood and will be consistently complied with for all study subjects. The SIV may take place in person or via weblink and will include sufficient time to resolve all questions that may arise.

In addition, and before the clinical site can commence the recruitment of subjects into the clinical investigation, the site must provide all required documentation to the Sponsor as detailed in Appendix 13.

Upon receipt of the necessary documentation, the Sponsor will provide a formal letter of confirmation of site authorisation to begin the study to the local team. Recruitment of subjects into the clinical study can then begin at the site.

18.4 Retention of Source Documentation

To comply with the requirements of the regulators for marketing of new medical devices, the Essential Documentation for the clinical study must be retained by the site or Sponsor for at least 10 years following the end of the study or when the device was last placed on the market. If the paperwork is to be archived by CUH off site, the details of the location must be provided to the Sponsor in case access is required at any time.

19.0 REFERENCES

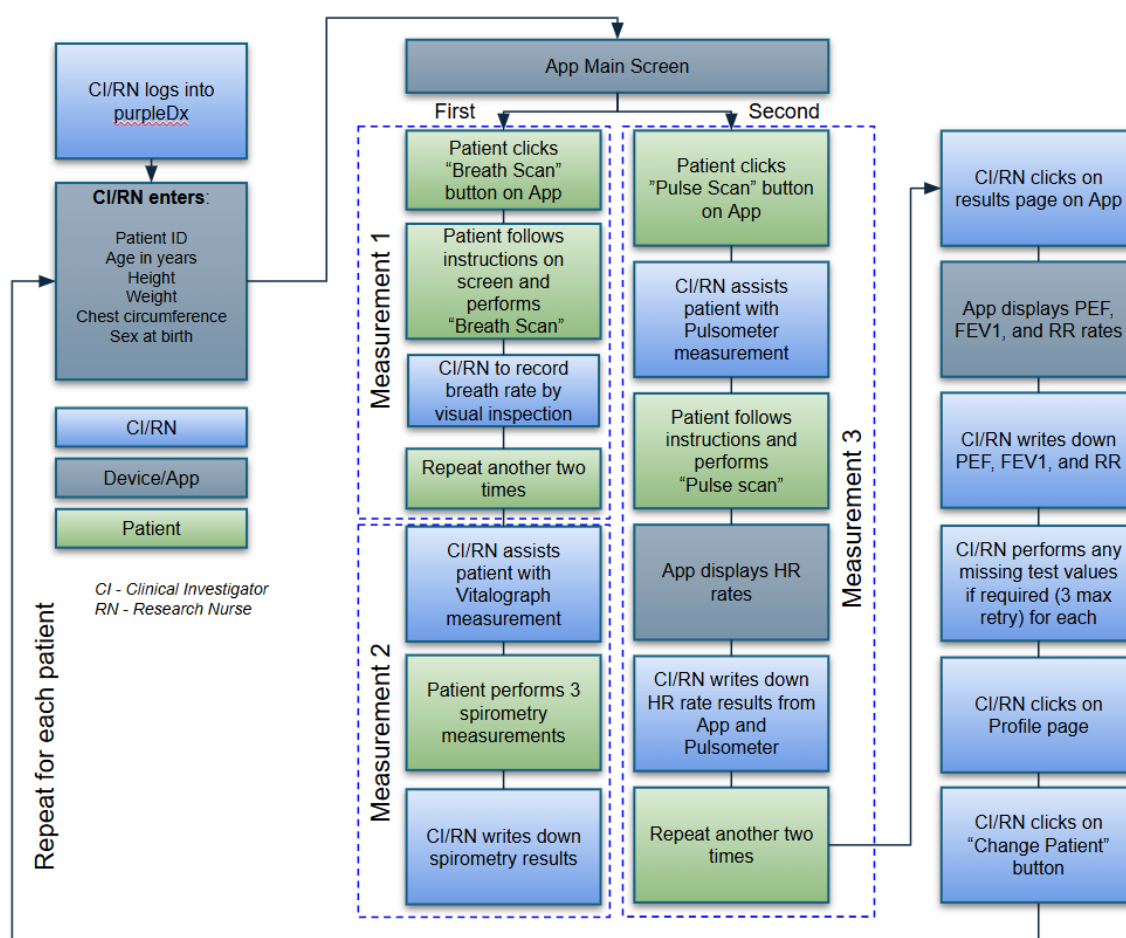
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20.0 APPENDICES

20.1 Appendix 1: purpleDx Interaction Workflow

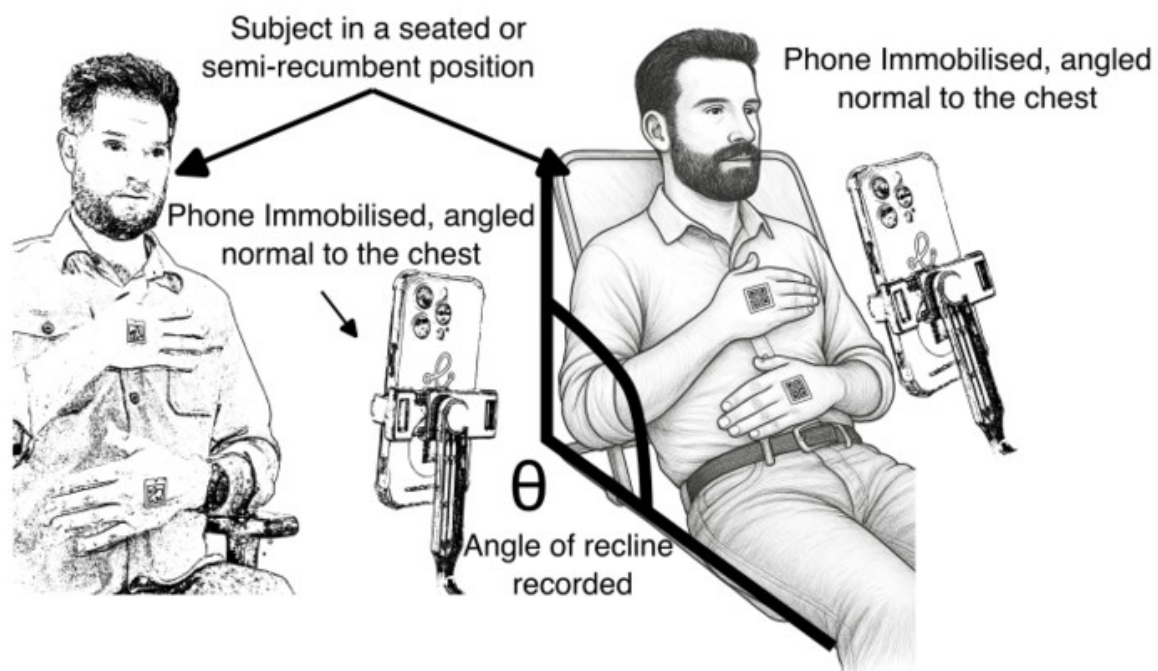
The diagram below illustrates the interaction and workflow between the CI/RN, subject and the investigational medical device (purpleDx app) to perform the measurement scans and collect results outlined for this protocol.



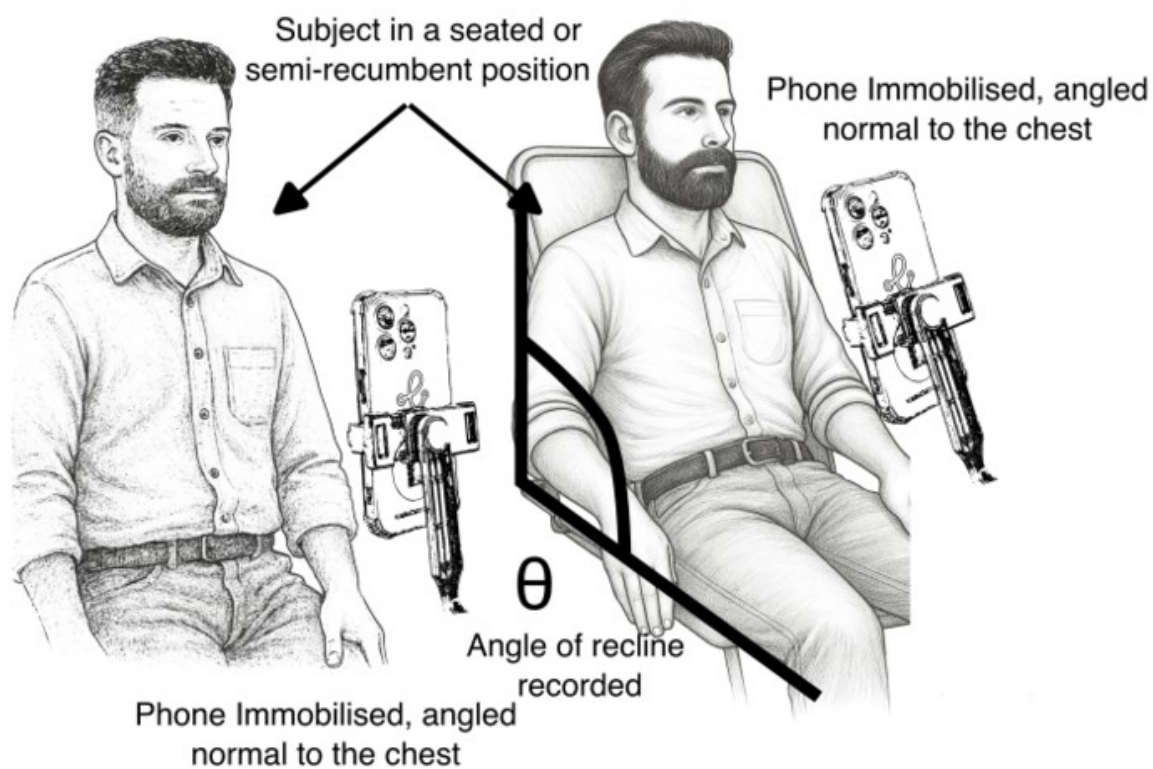
20.2 Appendix 2: Images of Subject Using purpleDx

The purpleDx app should be used with the subject sitting upright or reclining on a bed/trolley (with angle of incline recorded). For the trial purposes, the subject cannot lie completely flat (supine). The smartphone should be immobilised using a phone stand or by leaning it against a sturdy, static object.

20.2.1 Breath Scan (PEF, FEV₁ and RR) with Phone Stand



20.2.2 Pulse Scan (HR) with Phone Stand



20.2.3 Pulse Scan (HR) with Phone Against a Static Object

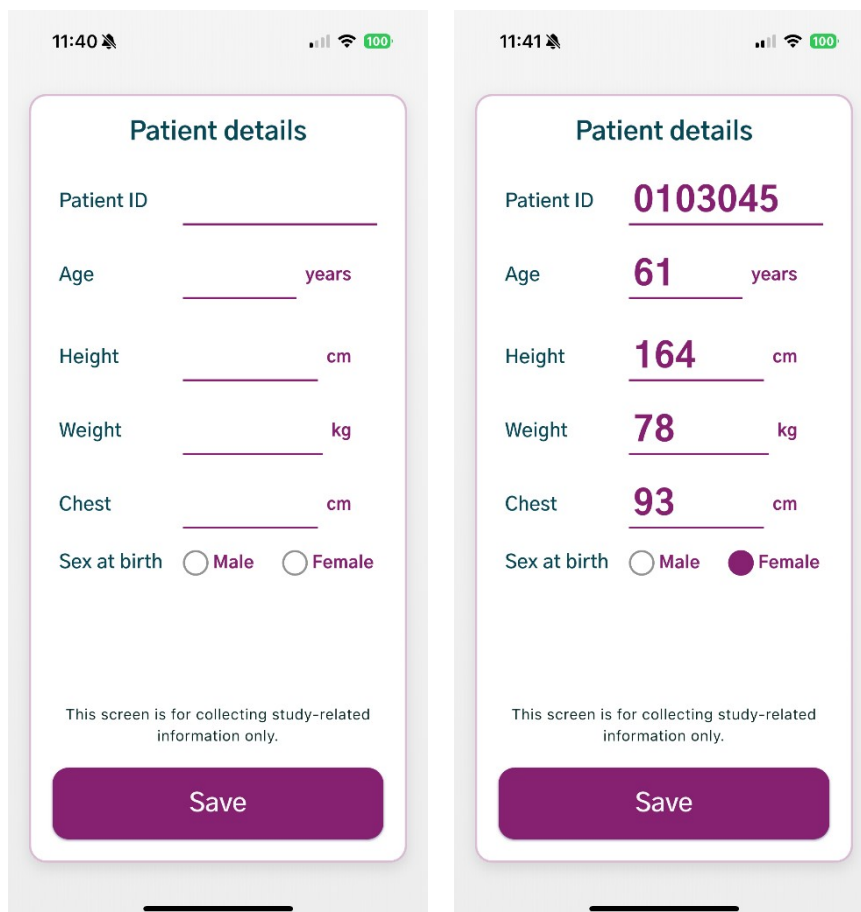


20.3 Appendix 3: purpleDx Screenshots

20.3.1 Subject Input Screen

Upon logging into purpleDx, the CI/RN or designee is taken to an initial screen where they must enter specific data required for the scans, as follows:

- Patient ID (Unique Subject Study Number)
- Age in years
- Height in cm
- Weight in kg
- Chest circumference in cm
- Sex at birth

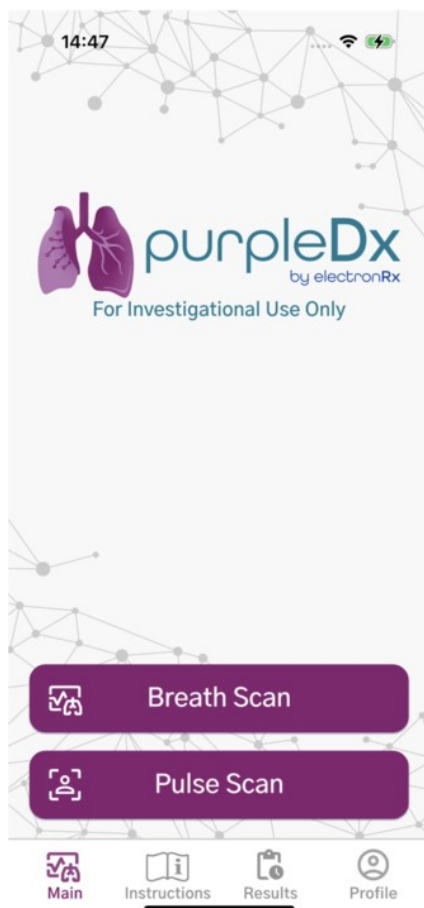


The image displays two side-by-side screenshots of the 'Patient details' screen in the purpleDx application. Both screenshots show a form with the following fields: Patient ID, Age (years), Height (cm), Weight (kg), Chest (cm), and Sex at birth (Male/Female). The left screenshot, taken at 11:40, shows the form with empty input fields. The right screenshot, taken at 11:41, shows the form with pre-filled data: Patient ID 0103045, Age 61 years, Height 164 cm, Weight 78 kg, Chest 93 cm, and Sex at birth Female. A 'Save' button is located at the bottom of the form in both screenshots. A disclaimer at the bottom of the form states: 'This screen is for collecting study-related information only.'

Field	Left Screenshot (11:40)	Right Screenshot (11:41)
Patient ID		0103045
Age (years)		61
Height (cm)		164
Weight (kg)		78
Chest (cm)		93
Sex at birth	☐ Male ☐ Female	☐ Male ☒ Female

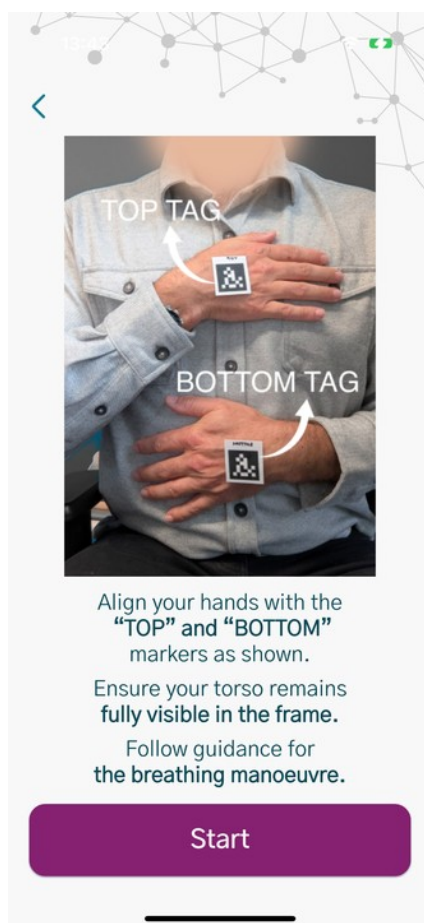
20.3.2 Scan Selection Screen

This screen allows the subject to select which type of scan to perform.

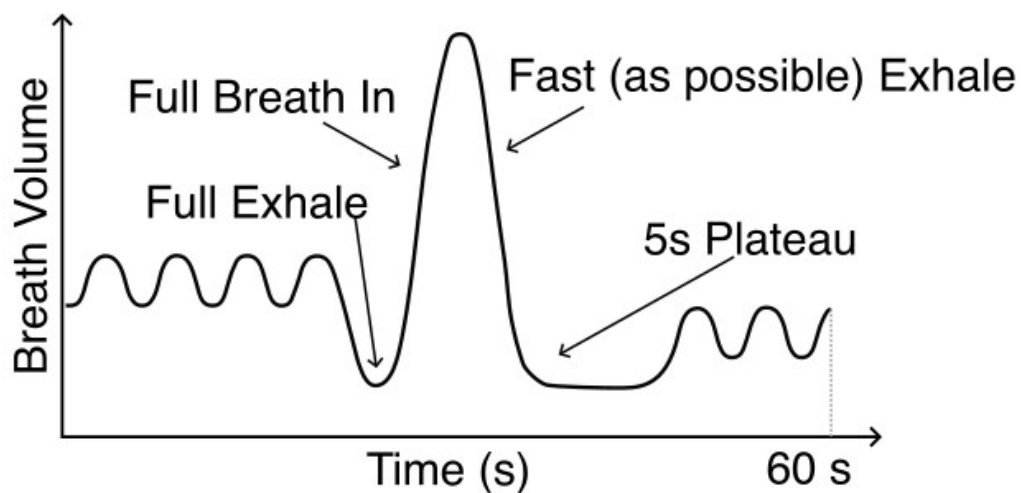


20.3.3 Instructions Screen for Breath Scan (PEF, FEV₁ and RR)

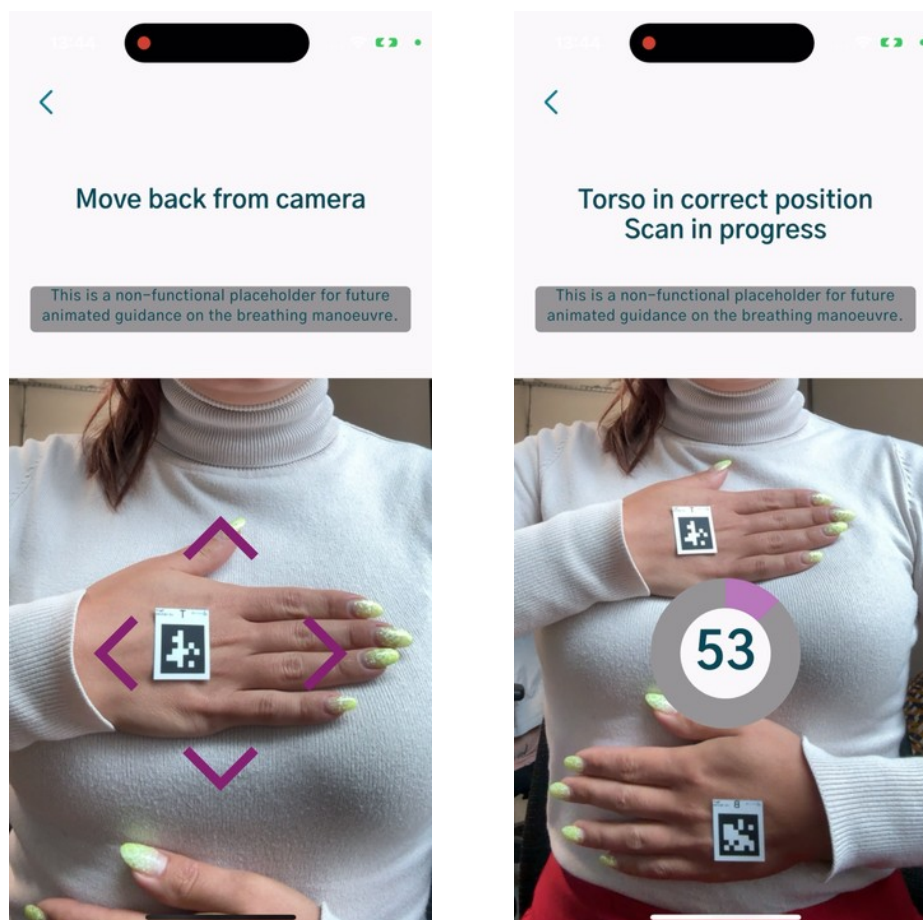
When the subject clicks on 'Breath Scan' on the Scan Selection Screen, they will be taken to the step-by-step instructions on how to properly position the smartphone and position themselves, as well as how to perform the breathing manoeuvre to complete the Breath Scan. Once the subject is correctly positioned, the app will automatically begin the scan.



The subject should breathe 'normally' for the first 4 breaths, followed by a full breath out, then a deep breath in. When they then next breathe out, it should be done as forcefully and quickly as possible. At the end of the exhale, the subject should hold their breath for 5 seconds before resuming breathing as 'normal'. This is shown in the graph below.



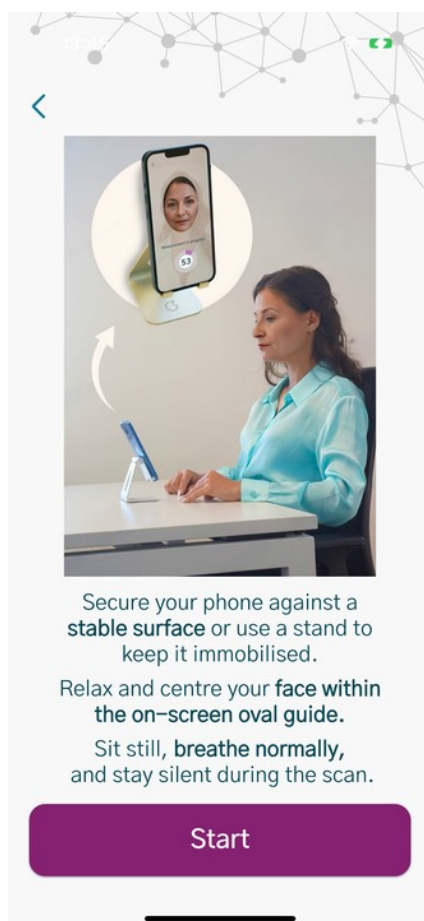
20.3.4 Recording Screens for Breath Scan (PEF, FEV₁ and RR)



The back arrow in the top lefthand corner of the screen can be used to prematurely stop the one-minute scan if something untoward happens and it is clear that an accurate and reliable scan will not be achieved e.g. if the subject sneezes or coughs.

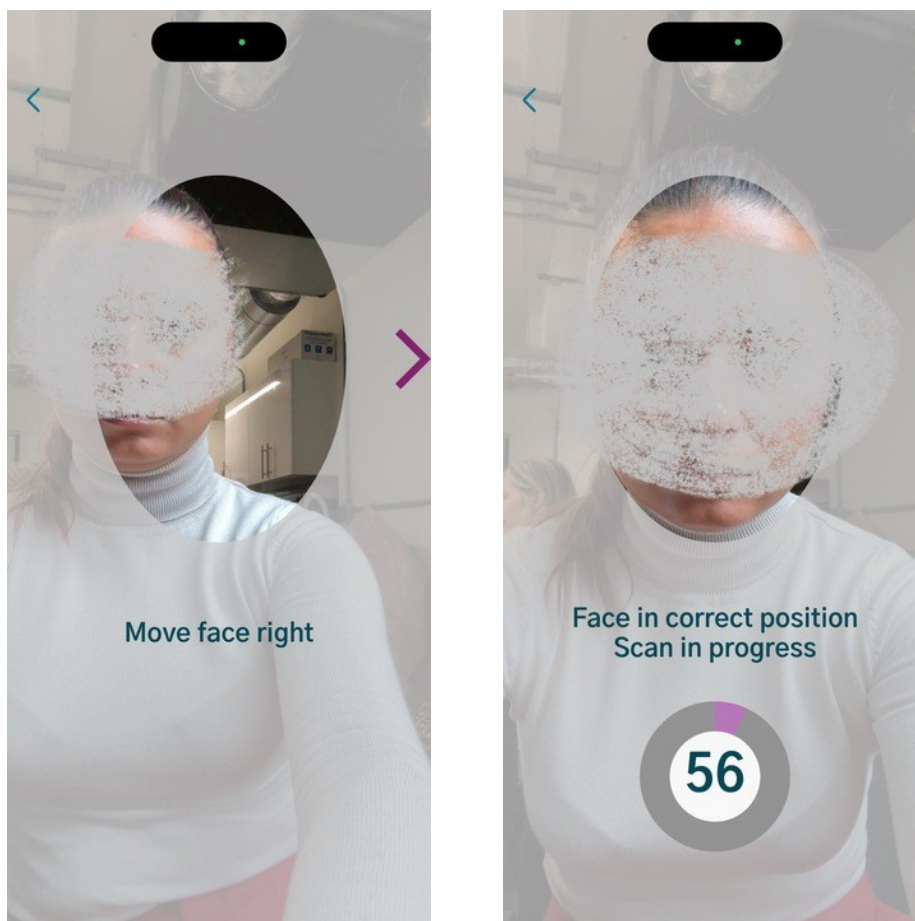
20.3.5 Instructions Screen for Pulse Scan (HR)

Similarly, clicking 'Pulse Scan' takes the subject to step-by-step instructions for how to position themselves so that their face is within the oval shown on the screen. Once the subject is in the correct position, the scan begins automatically.



20.3.6 Recording Screens for Pulse Scan (HR)

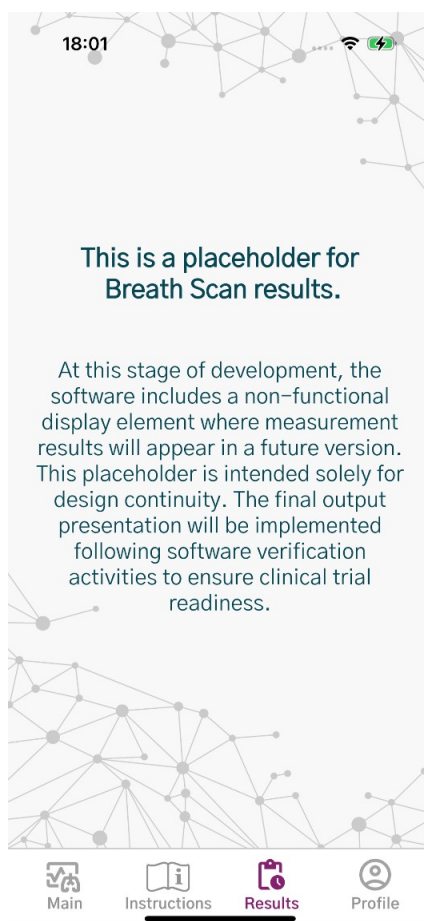
The screenshots below show the screens presented to the subject during the Pulse Scan.



The back arrow in the top lefthand corner of the screen can be used to prematurely stop the one-minute scan if something untoward happens and it is clear that an accurate and reliable scan will not be achieved e.g. if the subject sneezes or coughs.

20.3.7 Results Screen for Breath Scan (PEF, FEV₁ and RR)

The three sets of results for PEF, FEV₁ and RR will appear on the Results screen within 2 to 3 minutes of the measurements being taken, depending on the speed of the internet connection.



If any of the three sets of measurements have been unsuccessful and there are missing results, the CI/RN should ask the subject to repeat the Breath Scan. If there are any obvious reasons as to why the scan did not work, these will be noted by the CI/RN along with the need to perform a repeat scan. When the scan has been repeated, the results screen will be updated to include all successful measurements on the same screen.

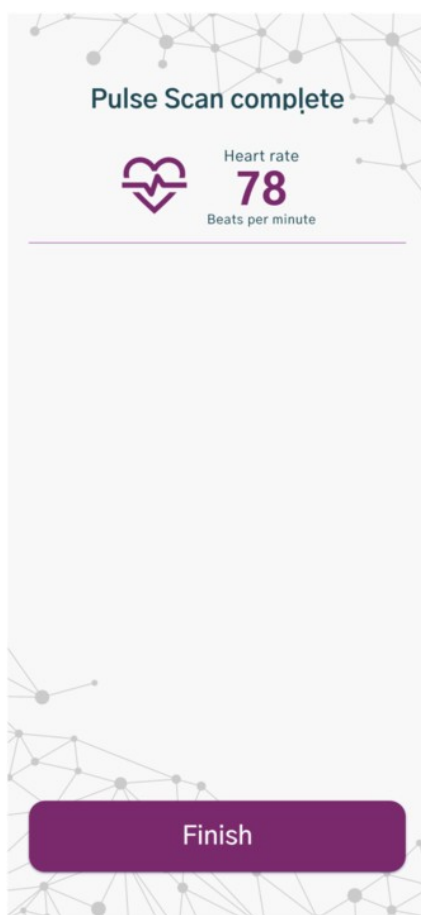
A maximum of 3 retry Breath Scans should be attempted as needed to produce 3 results for each of the 3 parameters PEF, FEV₁ and RR. If there are still missing data after 3 retry Breath Scans have been carried out, the missing results will be recorded as 'Not Available' (NA). The number of additional scans needed will be recorded.

Confirmation of the results for PEF, FEV₁ and RR will subsequently be sent to the CI/RN as a PDF document for filing in the subject's medical notes to enable verification.

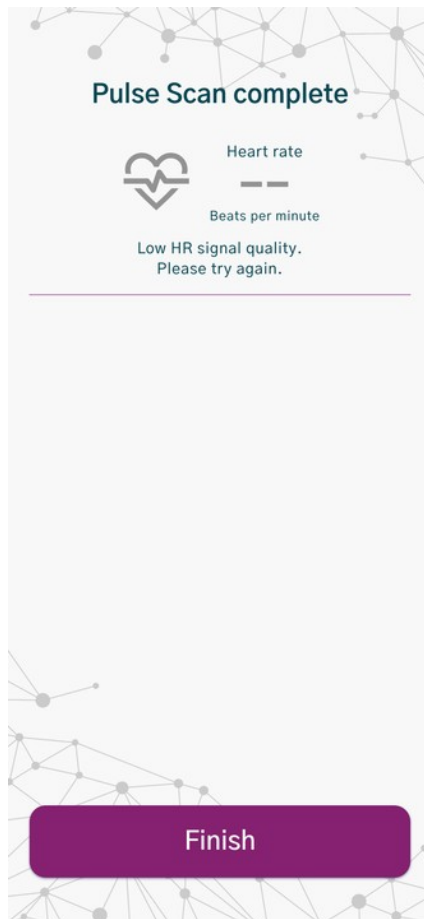
20.3.8 Results Screen for Pulse Scan (HR)

The screenshots below display the result for HR at the end of each Pulse Scan.

Following successful measurement of HR

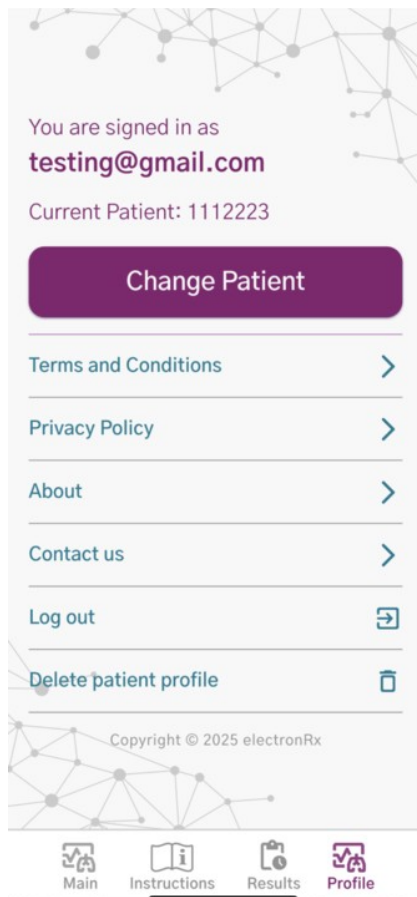


Following an unsuccessful measurement of HR



If the scan has been unsuccessful, the subject can perform the scan again. The protocol requires 3 readings for HR. A maximum of 3 additional retry pulse scans should be attempted if needed to produce the 3 readings. If 3 HR results are still not produced by the end of performing 3 pulse scans, the missing results will be recorded as 'Not Available' (NA).

20.3.9 Profile Screen and Change Patient Button



20.4 Appendix 4: The Fitzpatrick Scale

Type I	Type II	Type III	Type IV	Type V	Type VI
White skin. Always burns, never tans.	Fair skin. Always burns, tans with difficulty.	Average skin color. Sometimes mild burn, tan about average.	Light-brown skin. Rarely burns. Tans easily.	Brown skin. Never burns. Tans very easily.	Black skin. Heavily pigmented. Never burns, tans very easily.
					

The device Skin Colour Tester manufactured by PMUBEAUTY (Reference B0C772RJ33) will be used by the research nurse to assess each subject's skin tone according to the Fitzpatrick Scale. This device will be provided by the Sponsor to the clinical site and approved for use by their medical engineering team prior to study commencement.

20.5 Appendix 5: Determination of Pregnancy for Women Of Child-Bearing Potential

For the purposes of the inclusion/exclusion criteria for this clinical trial, it is not necessary to use a pregnancy test to exclude pregnancy in Women of Child-Bearing Potential (WOCBP). Since the app simply performs a non-invasive scan using the phone's camera functionality there is no risk to any subject or potential offspring. The CI/RN or designee will ask the subject if there is any possibility that they might be pregnant. If the subject thinks they may be pregnant they will be excluded from participation in the study. This is a precautionary measure as it may have a bearing on the ability of the app to produce reliable results (particularly in the second and third trimesters when lung capacity may be impinged by the developing offspring) and pregnant women have not been included in the verification and validation processes on the apps used during the developmental process of purpleDx.

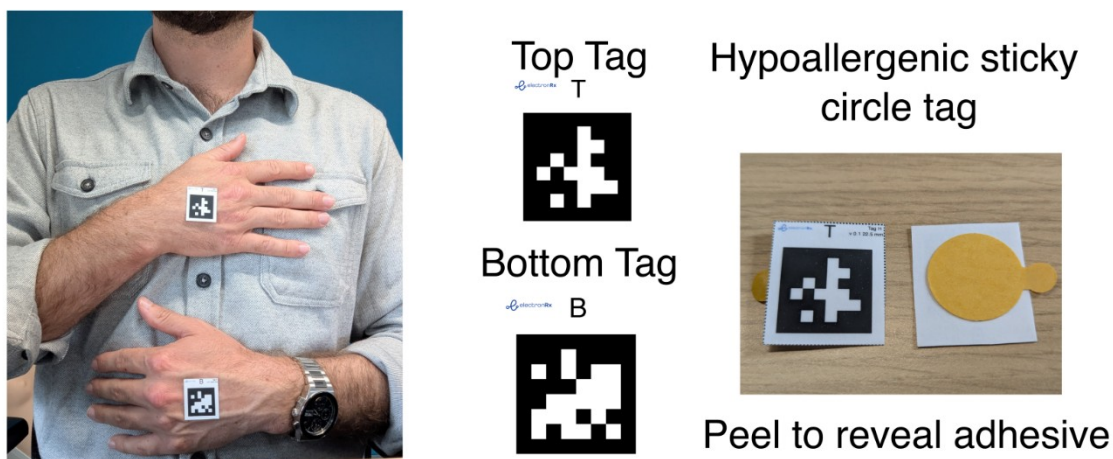
20.6 Appendix 6: Equipment Used in the Clinical Study

- iPhone version 15 with purpleDx app version 6.0.0 downloaded ready for use
- Vitalograph Pneumotrac Model 6800 with Spirotrac® 6 Software Model 7000 serial number PV11145 for standard measurement of PEF and FEV₁
- Nonin WristOx2 pulse oximeter for standard measurement of HR
- RSO PRO ILM 1337 Light Meter, +/- 3% +/-5 Digits
- Fitzpatrick skin tone meter: Skin Colour Tester manufactured by PMUBEAUTY (Reference B0C772RJ33)
- Reference fiducial markers to fix to subject's hands to aid visual tracking to enable purpleDx to measure PEF, FEV₁ and RR.

The Vitalograph spirometer, Nonin pulse oximeter, light meter and Fitzpatrick skin tone meter will be provided by the Sponsor and must be approved as safe for use by the site's medical engineering team prior to study commencement. The reference fiducial markers will also be provided by the Sponsor for use in the study.

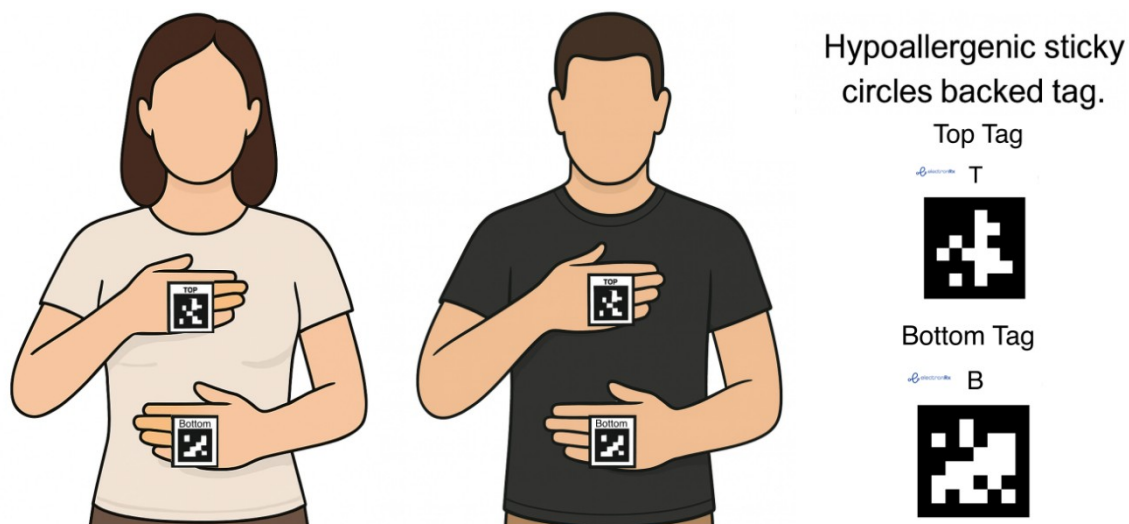
20.6.1 Reference Fiducial Markers

The Breath Scan to measure PEF and FEV₁ utilises reference markers (fiducials) to aid visual tracking.



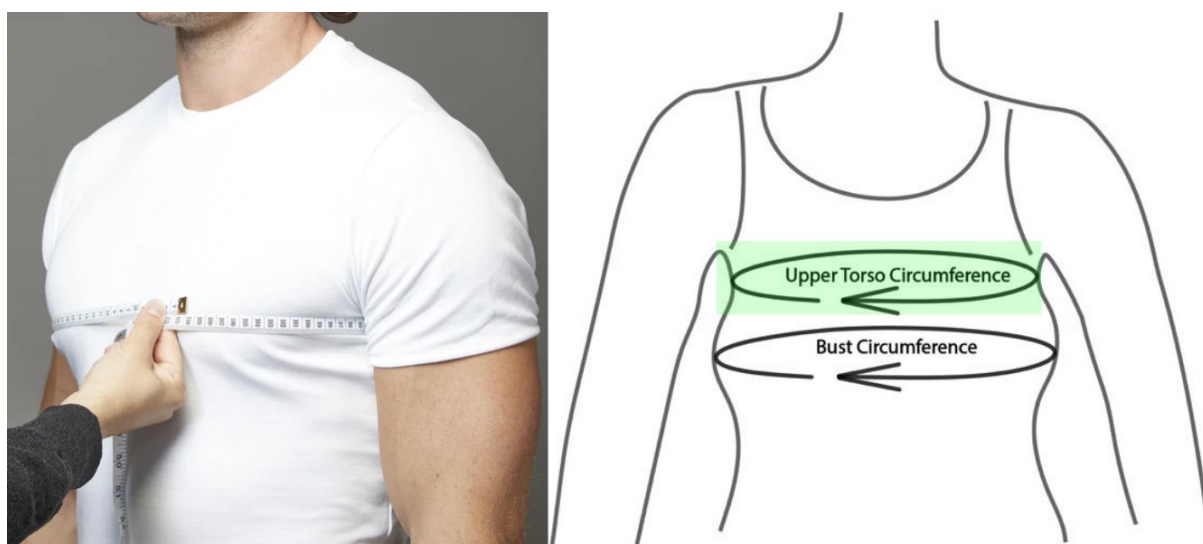
A new top and bottom fiducial are used for each subject. The fiducials are sticky on the reverse side so they can be affixed to the subjects' hands. The top and bottom fiducials are different so care must be taken to ensure they are affixed correctly. The top fiducial should be stuck on the back of the subject's right hand and the bottom fiducial on the

left hand. The subject then places their hands on their chest as shown in the image below:



20.7 Appendix 7: Measurement of Chest Circumference

The guidance below should be used to perform the measurement of chest (upper torso) circumference in centimetres:



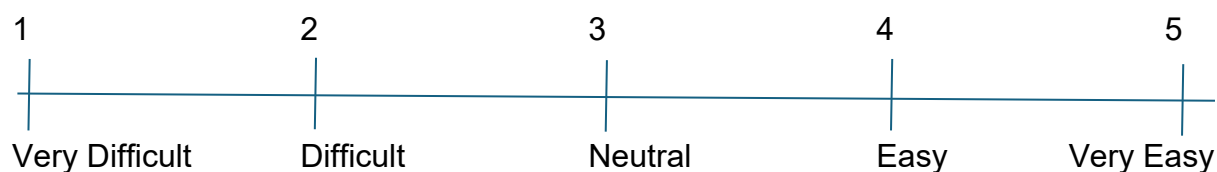
20.8 Appendix 8: Usability Questionnaire

This questionnaire is designed to be used by both patients and clinicians (CI, RN or designee) immediately after using the new device in the ED setting. It captures quantitative (Likert scale) and qualitative (free text) feedback for usability analysis.

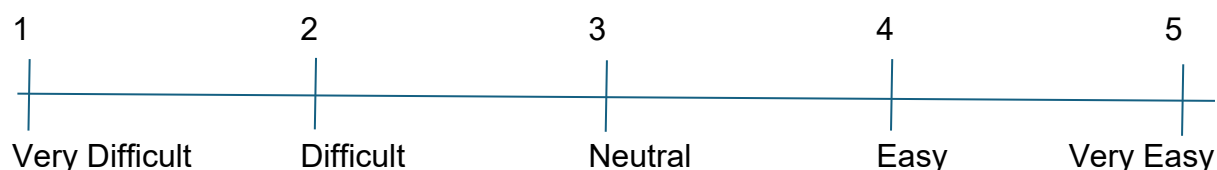
20.8.1 Section A – Device Setup and Use (for Patients and Clinician)

These questions should be answered by the subject and the clinician (CI/RN/designee) on separate sheets of paper, by ticking or circling the appropriate point on a scale of 1 to 5 as shown below:

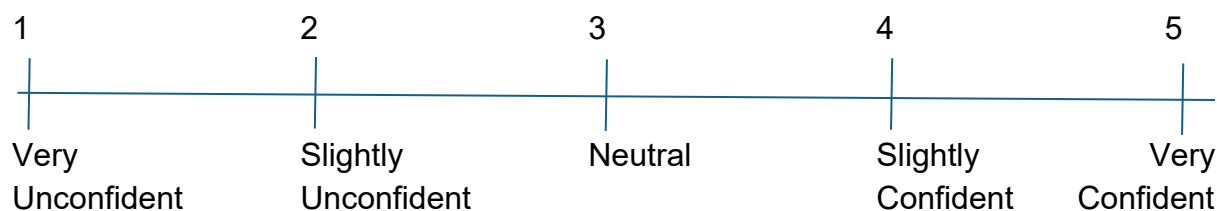
1) How easy was it to understand the instructions for using the purpleDx device?



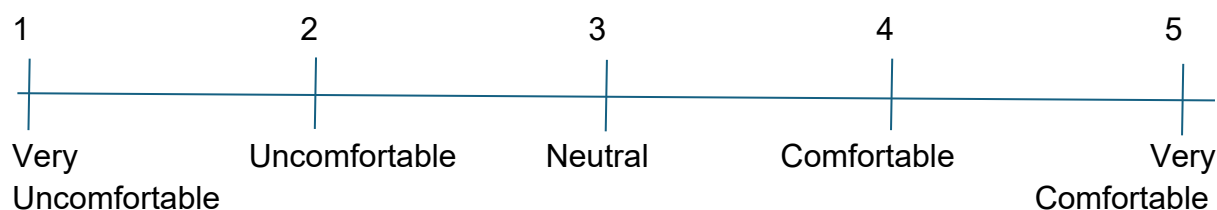
2) How easy was it to perform the test with purpleDx (such as sit still / follow prompts)?



3) How confident are you in the accuracy of the purpleDx device reading?



4) How comfortable was the device to use?





5) Would you be willing to use this purpleDx device again at a future visit?

1	2	3	4	5

Definitely Not	Probably Not	Neutral	Probably Yes	Definitely Yes

20.8.2 Section B – Time and Workflow (for Clinician only)

These questions should be answered by the clinician (CI/RN/designee) by ticking or circling the appropriate point on a scale of 1 to 5 as shown below:

6) How much time did it take to get a successful reading using purpleDx (approximate seconds)?

_____ seconds

7) How would you rate the purpleDx device's impact on workflow in a busy Emergency Department setting?

1	2	3	4	5

Very Disruptive	Slightly Disruptive	Neutral	Slightly Helpful	Very Helpful

8) Did the purpleDx device require technical assistance to use?

Yes ☐ No ☐

If Yes, please explain: _____

20.8.3 Section C – Open Feedback (for Patients and Clinician)

The questions below should be completed by the subject and the clinician (CI/RN/designee) on separate sheets of paper:

9) What did you like most about the purpleDx device?

10) What improvements would you suggest?

20.9 Appendix 9: Common Terminology Criteria for Reporting Adverse Events v5.0

See attached document.

20.10 Appendix 10: Documentation List for Site Authorisation

The following local documentation must be collected prior to Site Authorisation to commence the clinical study:

- Protocol Signature Page completed by CI
- CV and GCP certificate for each member of the research team
- Data Privacy Agreement
- Confidentiality Agreement
- Patient Information Sheet on local headed paper
- Informed Consent Form on local headed paper
- Delegation of Authority Log / Site Signature Sheet
- Site Training Log
- Clinical Trial Agreement including costings
- Local Equipment Validation Documentation for assessment of height, weight and heart rate
- Local Safety Testing Approval for use of Skin Tone meter, light meter, Nonin pulse oximeter and Vitalograph spirometer provided by the Sponsor for use in the study.

20.11 Appendix 11: Activity Durations for NHS Costings

The National Contract Value Review (NCVR) will be utilised to agree the costings for the clinical study to be undertaken in the NHS setting. The site will be reimbursed for each subject enrolled (as evidenced by signed ICF) into the study as follows:

- Consent procedure (discussing the protocol and PIS with the subject, answering any questions, completing the ICF)
- Clinic time for CI and RN to perform the registration of subjects to purpleDx and achieve assessments and documentation of data obtained via standard medical equipment and purpleDx
- Time for RN input of data into each subject's eCRF and CI sign off
- Time for RN maintenance of essential documentation to comply with protocol / GCP requirements (collation of CVs, GCP certificates, training logs etc)
- Time for RN to assist monitor with any queries arising from SDV.

The Sponsor will reimburse the costs for the study to the clinical site as agreed in the contract between Sponsor and Site. There are no additional funding routes.

Activity	Team Member	Estimated Time to complete activity per enrolled subject
Taking informed consent	CI/RN	15 minutes
Completion of visit assessments and source documentation	CI/RN/designee	45 minutes
Input of data into each subject's eCRF and CI sign off	CI/RN/designee	15 minutes
Maintenance of Investigator Site File and Essential Documentation	CI/RN/designee	30 minutes
Query resolution (arising from SDV)	CI/RN/designee	30 minutes

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Title: F006 - Clinical Investigation Plan - Addenbrookes Study Protocol

Approved By:

- Adrian Boyle	Fri Oct 17 09:55:48 GMT 2025
Approved	3ktLgEN+LBbp5C5pJldjtytmzfk
- Bipin Patel	Fri Oct 17 10:16:01 GMT 2025
Approved	QWN1MmwkTiatWKRxS0TKPTb+wak

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