Project proposal

Application of Point of Care Testing (POCT) Full Blood Count (FBC) analyser in neonatal (<2 months) clinical care

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Confidentiality Statement
This document contains confidential information that must not be disclosed to anyone other than the Investigator Team, host NHS Trust(s), regulatory authorities, and members of the Research Ethics Committee.

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1. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
0	1	15/11/2023		Initial draft
1	2	24/04/2024	N. Hollowood	REC recommendations
2	3	08/06/2024	N. Hollowood	REC recommendations
3	4	04/07/2024	N. Hollowood	Change to neonatal age (<3months to < 2 months)

2. SYNOPSIS

Study Title	Application of Point of Care Testing (POCT) Full Blood Count (FBC) analyser in neonatal (<2 months) clinical care
Study Design	Laboratory and POCT analysis
Participants	Neonatal patients < 2 months of age
Planned Sample Size	30
Study Period	01/06/2024 – 31/09/2024
Primary Objective	To ascertain whether the device is suitable for a larger scale CE marking research project to enable clinical use of the device in neonates< 2 months of age.
Secondary Objective	To determine whether the device could offer a solution for the clinical issue of clotted samples from this population group.

3. ABBREVIATIONS

AE	Adverse event
AR	Adverse reaction
GP	General Practitioner
HDFT	Harrogate and District NHS Foundation Trust
ICF	Informed Consent Form
IPS	Integrated Pathology Solutions
NHS	National Health Service
PICU	Paediatrics Intensive Care Unit
PI	Principal Investigator
PIL	Participant/ Patient Information Leaflet
POCT	Point of Care Testing
R&D	NHS Trust R&D Department
REC	Research Ethics Committee

UKAS UK Accreditation Services

4. BACKGROUND AND RATIONALE

Performing a full blood count (FBC) is a common clinical practice in neonatal care. Samples reported as “clotted” are not able to be analysed and require redraw. A perceived “high” clotting rate elicits frustration among clinical team members and has negative effects on patient flow and patient satisfaction. The overall % rejection rate of neonatal FBC samples due to the presence of clots is high and has been estimated at 20-30% by the neighbouring neonatal units in large teaching hospitals in the region. The literature confirms clotting rejection rate of 30%.[1] Capillary blood is the main technique used to collet blood from neonates. Typically, platelet activation is triggered when there is a break in the vascular endothelium (heel prick). There are studies indicate that capillary blood sampling collection increases the risk of clotting.[2] There were preliminary evidence show that venous samples have a lower clotting rate but the latter is not an option except in few PICU cases. There are few postulated mechanisms for the cause of clotting in neonates such as the sample transfer time to the laboratory, the blood collection technique, prematurity, neonate weight or coexisting maternal or neonate’s clinical conditions. A recent study demonstrated that a child's increasing body weight reduced the risk of pre-analytical errors, including risk of clotting.[2] Therefore, the clotting rate is not a large pre-analytical problem is neonates older than 3 months old. However, to date, there are no studies to elucidate the main reason for the high clotting rate in neonates.

There has been ongoing audit work undertaken to establish the exact cause of why these samples seem to be clotting. Sampling technique and a change in blood collection bottles have been considered and implemented but with no clear consistent root cause being identified.[3]

Recently, POCT devices that measure FBC at the patient bedside have become available for clinical use and as such provide the potential to reduce the risk of clot formation. Currently, there are only two commercial POCT devices available for FBC measurement, both of which are not clinically validated for the age group from 0-3 months old. The HemoScreen is one of the two devices, which has a small footprint, requires a small sample of capillary or venous blood (40µL in each capillary) and gives 20 FBC results in 5 minutes across the 5-part differential. This device however, has only been clinically validated for patients 2 month old and onward. To realise the full potential of HemoScreen POCT device, it needs to be clinically validated in neonates < 2months old.
Although, HemoScreen POCT device is CE marked and clinically validated in the age group of > 2 months old onward. It is important to mention that HemoScreen is reasonably new to the healthcare market; hence, clotting studies for the <2 months old are not available yet.

5. OBJECTIVES

5.1 Primary Objectives

To ascertain whether the device is suitable for a larger scale CE marking research project to enable clinical use of the device in neonates< 2months of age.

5.2 Secondary Objectives

To determine whether the device could offer a solution for the clinical issue of clotted samples from this population group.

6. ELIGIBILITY

Participants will be neonatal patients resident at Special Care Babies Unit (SCBU) at Harrogate Hospital. The GCP trained neonatal unit nurses will do recruitment verbally. Potential participant's guardian will be approached and their child will be invited to participate, they will be provided with an information sheet about the study (**Attachment 1**) and they will be allowed at least 24h to think about participation. Enrolment is voluntary will only be accepted the guardian of the child signs an informed consent form (**Attachment 2**)

Inclusion Criteria:

1. Patients 2 months old or younger.

Exclusion Criteria:

1. Patient over 2 months old.
2. Participants in another research study involving an investigational product in the past 12 weeks.

7. ENROLEMENT

7.1 Description of Enrolment Process

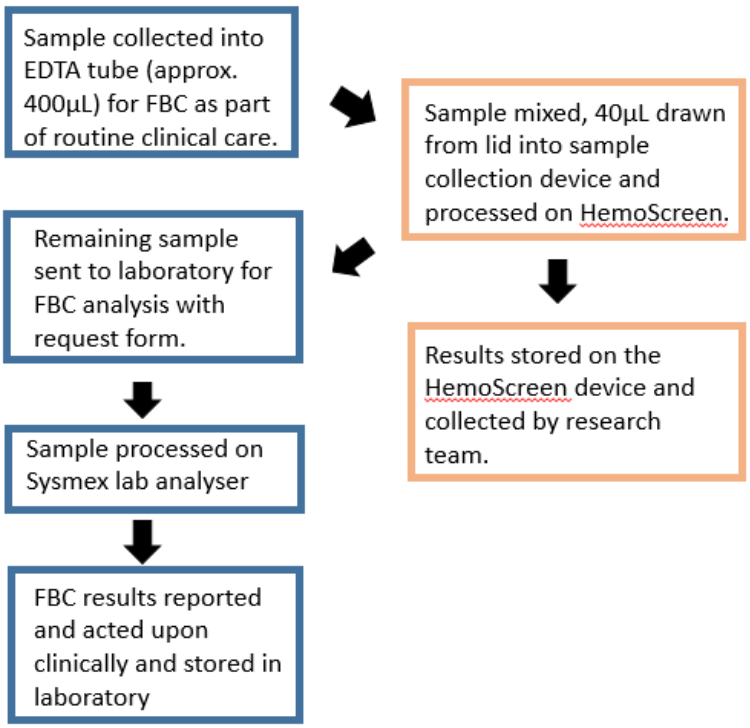
Subjects will be recruited by the staff nurses involved in the trial approaching the parents on the ward. Participant's guardians will be issued with an information sheet outlining the trial requirements and aims. The study will be discussed and participants parents will be made aware they do not have to take part in this trial.

7.2 Informed consent

The participant's guardian will personally sign and date the approved version of the informed consent form before any study specific procedures are performed. Written and verbal information will be presented to the participants guardian detailing the exact nature of the study and any risks involved in taking part. (Appendix) It will be clearly stated that the participant is free to withdraw from the study at any time for any reason with no obligation to give the reason for withdrawal. The participant guardian will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant guardian dated signature and dated signature of the person who presented and obtained the informed consent. A copy of the signed Informed Consent will be given to the participants guardian. The original signed form will be retained at the study site.

7.3 Sample Collection

The sample collection, analysis and storage is outlined below:



1. When the patient's clinical care requires a FBC result, the sample will be collected with from the baby's heel (capillary) or as a venous sample into a purple topped paediatric EDTA tube. The standard quantity that is collected for this analysis is 400µL.
2. The sample will then be mixed to ensure dispersion of the EDTA anticoagulant through the blood and to ensure an even distribution of blood products. From this sample, 40µL will be drawn from the blood that has collected from the lid of the sample into the HemoScreen capillary sample collection device. The sample collection device will be placed into the HemoScreen cartridge and processed on the analyser by a trained user.
3. The FBC and 5 part differential results will be stored on the analyser and collected by the principal investigator. The clinical team will not report or act on these results.
4. The remaining sample will be labelled up and sent to the laboratory with a request card for FBC analysis.
5. The Laboratory sample will be processed as usual on the Sysmex XN1000 for FBC including 5 part differential.
6. The results will be reported to the clinical team for clinical management. The EDTA sample will be stored in the laboratory for a few days and then disposed as per normal laboratory procedure.

7. The laboratory results will be statistically compared to the retrieved results from HemoScreen (using Altman Bland and Passing Bablock Regression).

7.4 Target recruitment

A minimum of 15 patients are to be recruited to make a library of a minimum of 30 samples (max. 2 samples per single patient) is recommended by Altman and Bland graphical method as described in the Lancet 1986[37]. This sample size would give a 95% Confidence Interval (CI) of about +/- 0.34S, where S is the standard deviation of the difference of the two methods used in this study (HemoScreen and Sysmex).

8. DATA ANALYSIS

8.1 Demographic Data

Analytical results will not take demographic data into account.

8.2 Laboratory Methods

The EDTA sample will be processed on the HemoScreen POCT analyser for FBC including 5 part differential.

The EDTA sample will be then be sent to the laboratory and processed on the Sysmex XN1000 for FBC including 5 part differential.

8.3 Analytical Results

The analytical results will be returned to the Investigator in electronic format.
Statistical analysis will be performed using Analyse-it add-in package for Microsoft Excel.

8.4 Spurious Data

Extreme values “outliers” will be ruled out using Box-Cox statistical test.

8.5 Successful Criteria

The comparison will be considered successful if a minimum of 95% of HemoScreen results for all parameters are within 2SD (Standard Deviations) from the Laboratory (Sysmex XN1000).

8.6 Termination Criteria

A clotting rate of 10% on the Hemoscreen will result in the early termination of the study. The study will run until we have collected 30 suitable samples. Once we have the data from 30 samples the trial will close

9. QUALITY ASSURANCE PROCEDURES AND SAFETY

The study will be conducted in accordance with the current approved protocol, relevant regulations and procedures. All sample analysis will be undertaken in a UKAS

accredited laboratory. Dedicated storage arrangement will aim to maintain sample quality prior to analysis.

The HemoScreen results cannot be used as an alternate to the laboratory results as they are not available to the medical team; the risk associated with this study have been assessed and minimised. They are as follows:

The clinical staff may be tempted to act upon the results generated instead of following the approved care procedure which is to ignore the results as they are for data collection only. To reduce the risk of this, only trained users have access to the device, only research trained nursing staff (not medics) have access to the device, the option to look results up on the analyser has been removed, the printer has been removed. The results will be stored in the device and can only be accessed and retrieved periodically by the principal investigator. A full risk assessment has been written to ensure these risks are minimised. The HemoScreen device will be labelled as under investigation as long as it is in use for this pilot. All the research nurses involved in this study are GCP trained.

10. ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be restricted to the investigating team at the host institution.

11. ETHICS

11.1 Declaration of Helsinki

The Investigator will ensure that this study is conducted in full conformity with the current revision of the Declaration of Helsinki (October 2008).

11.2 Ethical Approval

The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to the Yorkshire Research Ethics Committee (REC) favourable opinion. The Investigator will submit and obtain favourable opinion for all substantial amendments to the original approved documents.

11.3 Participant Confidentiality

The investigating team will ensure that the participants' anonymity is maintained. The participants will be identified only by initials and a participants ID number on any electronic database. All documents will be stored securely and only accessible by the investigating team. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

12. DATA HANDLING AND RECORD KEEPING

All study data will be entered into a secure HDFT pathology results server. The participants will be identified by a study specific participants number and/or code in any database. The name and any other identifying detail will NOT be included in any study data electronic file after the participants have received a copy of their test

results.

13. FUNDING

This project will be funded by the commercial company Pixcell medical who own the HemoScreen POCT analyzer. They will cover the analyzer costs, reagents and consumables, and any research application costs.

The cost of the research staff time and contingencies will be funded by a bursary provided as part of the healthcare research fellowship from the NIHR and devices for dignity.

14. POTENTIAL IMPACT OF THE STUDY

This pilot is well-timed to add further to the ongoing efforts for improvement of neonates' clinical care. The project will be running between May 2024 and will be completed by May 2025.

If successful, a larger scale multi-centre study would be required to fully validate and CE mark the device for clinical use in neonates (<2 months). The investigating team will seek to publish their findings in relevant peer reviewed journals.

15. RESEARCH TEAM

Research nurses will be involved in the recruitment of participants to ensure suitability and signing of informed consent forms, they will help in the collection of blood samples The chief and principal investigators will ensure proper documentation of the generated data and will participate in the statistical analysis, drawing conclusions and writing the report for publication.

16. REFERENCES

[1] Jennifer McCoy, Tanya Tichon, and Michael Narvey . Reducing CBC clotting rates in the neonatal patient Care Areas. BMJ Qual Improv Rep. 2016; 5(1): u215456.w4946. doi:10.1136/bmjquality.u215456.w4946

[2] Henrik Hjelmgren. Anna Nilsson, Ida H. Myrberg et al. Capillary blood sampling increases the risk of preanalytical errors in pediatric hospital care: Observational clinical study. J Spec Pediatr Nurs. 2021;26:e12337. https://doi.org/10.1111/jspn.12337.

[3] Moiseiwitsch N, Brown AC. Neonatal coagulopathies: A review of established and emerging treatments. Exp Biol Med (Maywood). 2021 Jun; 246(12):1447-1457. doi: 10.1177/15353702211006046. Epub 2021 Apr 15.