PROTOCOL FOR THE MANAGEMENT OF THE BABY BIO BANK (BBB)

VERSION 7.0

25th May 2016

CONTENTS **1**

1. What is a biobank **3**

2. The aim of the Baby Bio Bank (BBB) **3**

3. Primary Sites of the BBB **4**

4. Participating Sites of the BBB **4**

5. Personnel Structure of BBB **4**

6. The Resource Management Board (RMB) **5**
6a. Structure of the RMB **5**

6b. Function of the RMB **6**

7. Ethical Issues **7**
7a. Informed Consent 7
7b. Obtaining Consent 7
7c. Public Access to Information 9

9g. Processing of Buccal Swab for DNA 16

10. Quantification of Biological Specimens 16
10a. Quantification of DNA 16
10b. Quantification of RNA 17
10c. Quantification of Proteins 17

11. Quality Control 17
11a. Equipment maintenance and repair 17
11b. Staff training 17
11c. Data management 18
11d. Record keeping 18

12. Database Requirements 21

13. Storage of Specimens 20
13a. Long Term Storage of Blood 21
13b. Long Term Storage of Tissues 21
13c. Long Term Storage of Plasma and Serum 21
13d. Long Term Storage of Urine 21
13e. Long Term Storage of DNA 21
13f. Long Term Storage of RNA 21

14. Transfer of Biological Specimens from Different Sites 21

15. Transfer of Data 22

16. Conditions for Use and Access to BBB Biological Specimens 22

17. Equipment and Reagents 23
17a. Reagents 23
17b. Equipment 24

APPENDIX 1 25
APPENDIX 2 26
APPENDIX 3 29

3. Primary Sites of the BBB

3a. Institute if Child Health (ICH)

E 6W 0DU\¶V +RVSLWDO 60+

4. Participating Sites of the BBB

4a 6W 0DU\¶V +RVSLWDO 60+

E .LQJ¶V &ROOHJH +RVSLWDO .&+

F 4XHHQ &KDUORWWH¶V DQG &KHOVHD +RVSLWDO 4&&+

4d. University College Hospital London (UCLH)

4e. Chelsea and Westminster Hospital (CWH)

5. Personnel Structure of BBB

5a. BBB Principal Applicants: Professor Gudrun Moore and Professor Lesley Regan

5b. BBB Research Manager: Dr Nita Solanky/ Dr Sayeda Abu-Amero

5c. BBB Principal Collaborators: Professor Mark Johnson (CWH), Professor Kypros Nicolaides (KCH), Professor Catherine Williamson (QCCH), Professor Donald Peebles (UCLH), Professor John Whittaker (London School of Hygiene and Tropical Medicine (LSHTM)

5d. Head Research Nurse Ms Katherine Rogers

5e. Research Associates Dr Nita Solanky (CWH), Dr Ana Maria Miranda Perez (QCCH), Dr Anna Thomas (ICH) and Dr Shawnelle White (SMH)

7. Ethical Issues

7a. Informed Consent

One of the funda

recognised centre for mothers' suffering from recurrent miscarriage and this will be the centre targeted for this cohort.

There is overlap among the four cohorts above and patients will only be recruited once per pregnancy even if they fall into multiple cohorts.

5. Normal: in order to understand the genetic causes of the complications of pregnancies detailed above, comparisons need to be made to a reference normal cohort without any of the above or other complications.

The potential donors will then be recruited by highly motivated research nurses/midwives/associates. These nurses/midwives/associates will approach the potential donors and provide written information on the study which will be verbally explained in a language suitable for the donor. The research nurses/midwives/associates will answer all queries regarding the purpose, methods, demands, risks, inconveniences, discomforts and putative outcome of the study. The research nurses/midwives/associates will also point out contact details if the donor has any further queries. They will allow the donor to make an independent decision regarding their participation in the study or not, and assure the potential donor that their medical care is not governed by their decision to participate or not.

If the donor decides to participate, then they will be asked to sign a consent form stating that they have read the information sheet which they have understood and that they have voluntarily agreed to participate. The consent form also states that their clinical data will be used and that they are free to withdraw at any time during the study. The donor will receive a copy of the signed consent, and a copy will be held by the BBB and in the participants' hospital notes.

the sample to be scanned and associated with clinical data, without the need for personal identifiers such as donor name, the traditionally used date of birth (DOB) or donor hospital number written on the sample container. The label will be resistant to extremes of cold storage temperatures (-80ºC) and will survive repeated freeze-thawing of the sample.

The barcode label will associate multiple samples of the same source from the same donor; multiple samples from different sources from the same donor and it will also associate the unique trio identifier code i.e. maternal, paternal and fetal samples from one family. Clinical data for each individual in the trio will be encoded into the unique trio identifier code.

8d. Collection of Urine

Urine will be collected in standard specimen containers by the donor and will be aliquoted within 1 hour for long-term storage at -80ºC. Urine can be used for proteome mapping and biomarker discovery.

8e. Collection of Placental Tissue for DNA and RNA

It is best to collect and process tissues within an hour of excision to minimize degradation of RNA and minimize the effect of hypoxia on gene expression. As excised tissues stored for extraction of DNA will be the same source for RNA extraction, the same care will be taken for both end point.024 584.i0 0 1fowill ber DNA

placed in 5 x volume

The SK-2 Isohelix Swab (SK-2S; Isohelix, Cell Projects) will be used for collection of a buccal sample (see 8j above).

9g. Processing of Buccal Swab for DNA

DNA from buccal swabs will be extracted using the Invitrogen iPrep™ ChargeSwitch® Buccal Cell Kit in conjunction with the iPrep™ Forensic Card. 1 ml ChargeSwitch® Lysis Buffer and 10 ul Proteinase K are added together to make the Lysis Mix and this added to the buccal swab in a sterile 1.5 ml microcentrifuge tube. The buccal swab is completely immersed in the Lysis Mix and vortexed for 10-15 seconds to facilitate mixing and then incubated for 20 minutes at 37^{o}C. The sample is then transferred to the iPrep Sample and Elution Tube and DNA extracted using the Invitrogen iPrep™ ChargeSwitch® Buccal Cell Kit according to the manufacturer's instructions. DNA is eluted in a volume of 75 -150 µl Elution Buffer (supplied) with an expected yield around 1 - 3 ug.

10. Quantification of Biological Specimens

All nucleic acid extraction will be quantified using the Nanodrop® ND 1000 (Nanodrop Technologies Inc.). Although the sample size is not critical, it is essential that a liquid column be formed so that the gap between the upper and lower measurement pedestal is bridged by the sample.

On start up, the pedestal surfaces will be thoroughly wiped with water and a clean water sample loaded to initialize the instrument. The Nanodrop® ND 1000 will then prompt to blank the instrument which should be the buffer used to resuspend or elute the samples. The Nanodrop® ND 1000 is ready for use.

10a. Quantification of DNA

The minimum amount of DNA for accurate quantification using the Nanodrop® ND 1000 is 1 µl. Select the Nucleic Acid option and from the drop down menu select dsDNA (double stranded DNA). Enter the identification of the sample and quantify according to the on-screen instructions (see manufacturer's instructions for details).

10b. Quantification of RNA

The minimum amount of RNA for accurate quantification using the Nanodrop® ND 1000 is 1 µl. Select the Nucelic Acid option and from the drop down menu select RNA. Enter the identification of the sample and quantify according to the on-screen instructions (see manufacturer's instructions for details).

10c. Quantification of Proteins

The minimum amount of protein for accurate quantification using the Nanodrop® ND 1000 is 2 µl. Select the Protein option and from the drop down menu select the type of protein. Enter the identification of the sample and quantify according to the on-screen instructions (see manufacturer's instructions for details).

Before dispatch a subset of both DNA and RNA samples will additionally be verified by UCL Genomics using an Agilent 2100 Bioanalyser. (https://www.ucl.ac.uk/ich/research/genetics-genomic-medicine/ucl-genomics).

Researchers are able to request bioanalyser verification and results of samples prior to dispatch at a cost.

11. Quality Control

11a. Equipment maintenance and repair

All equipment is maintained under contract with their supplier's and serviced annually.

11b. Staff training

All BBB staff employed by the two universities requires 10 days of new skills training annually. Training includes course such as: Good Clinical Practice; research and human tissue legislation and statistical analysis.

All recruiting staff are certified phlebotomists.

Standard Operating Protocols (SOPs)

SOPs are documented in the PROTOCOL FOR THE MANAGEMENT OF THE BABY BIO BANK which are approved by the ethics committee and are in

will have multiple aliquots which need to be identifiable. Each biological sample will be processed into DNA, RNA and protein which needs to be identifiable.

3. The clinical data (and research data) associated with each donor will be linked through the unique identifier.

4. All biological and processed specimens, and clinical data comprising the trio (mother, father, baby) will be linked.

5. Consent (and withdrawal of consent) will be tracked through the database.

6. The location, availability and usage of the donor sample will be tracked through the database.

7d

We will have duplicated samples stored on the two primary sites, ICH and SMH, to ensure that no sample is lost due to breakdown of storage facilities.
For storage of biological specimens it is generally preferable for them to be cooled gradually to minimize formation of ice crystals but thawing should be as quick as possible. Repeat freeze thawing should be avoided by generating aliquots. Generally, the lower the temperature the longer the viable storage period.

An important consideration is the type of storage vehicle e.g. cryovials, sample containers etc which have to withstand extremes of cold (-80ºC) and sudden rises in temperature (thawing) and therefore need to be resistant. Additionally, the use of appropriate barcode labels which can remain adherent and readable is critical.

13a. Long Term Storage of Blood

Whole blood and white cell pellets will be storc9uots.

BT1 0 0 1 39J.18 418oraa170.54TJs.

13f. Long Term Storage of RNA

Extracted RNA will be stored at -80ºC.

14. Transfer of Biological Specimens from Different Sites

For the transfer of biological and processed samples from QCCH and CWH to SMH, the research midwives/nurses/associates will use dry ice in polystyrene boxes or cool bags/boxes for the safe and efficient transfer from the collection site to the deposit site. It is anticipated that movement among these sites will be an hour or less and that this method is appropriate. Individual samples will be in appropriately sealed containers and bagged to ensure spillages are minimized.

For samples to be transferred to research users, the above methodology will be used with consideration for shipping time, distance, climate, method of transport, type and number of samples and regulations of the carrier. Packages will be labeled with standardized BIOSPECIMEN HAZARD labels. Samples will not be shipped without an authorized MTA (Template academic MTA Appendix 3).

15. Transfer of Data

Research midwives/nurses/associates

APPENDIX 1
Informat

APPENDIX 2

APPLICATION FORM FOR USE OF BBB BIORESOURCES version 2.0

BBB APPLICATION REFERENCE 1 8 0 % (5 « « « « « « «

PLEASE READ AND SIGN OUR TERMS AND CONDITIONS FOR BBB USE AND UPLOAD WITH YOUR APPLICATION AND ACCOMPANYING DOCUMENT

BY SIGNING THIS AGREEMENT YOU ARE ALSO AGREEING TO DEPOSIT YOUR DATA IN THE BBB AFTER PUBLICATIONS AND IP ACKNOWLEDGED

APPLICATIONS ARE CONSIDERED APPROXIMATELY EVERY FOUR MONTHS APRIL, JULY AND NOVEMBER. YOU WILL HEAR BACK REGARDING YOUR APPLICATION WITHIN TWO WEEKS OF THE OF THE COMMITTEE MEETING.

COMPLETE ALL FIELDS AND SUBMIT VIA THE BBB WEBSITE

IF YOU HAVE ANY QUERIES REGARDING THIS FORM PLEASE EMAIL THE BBB MANAGER s.abu-amero@ucl.ac.uk

NAME OF APPLICANT, TITLE	
ADDRESS	
EMAIL ADDRESS	

APPROVAL NUMBER	
APPROVING BODY	
TITLE OF PROJECT	
COLLABORATORS AND THEIR AFFILIATIONS-ADD AS NECESSARY	
500 WORD SUMMARY OF PROJECT	
TYPE OF SPECIMENS REQUESTED-PLEASE TICK BOX *OR* SEE BBB WEBSITE FOR LIST OF TYPE OF SPECIMENS AVAILABLE	FETAL PLACENTAL TISSUE FETAL UMBILICAL CORD FETAL CORD BLOOD EDTA FETAL CORD BLOOD SERUM FETAL CORD BLOOD PLASMA PLACENTAL MEMBRANES MATERNAL BLOOD EDTA MATERNAL SERUM MATERNAL PLASMA MATERNAL WHITE BLOOD CELLS MATERNAL URINE PATERNAL BLOOD EDTA PATERNAL SERUM PATERNAL PLASMA PATERNAL WHITE BLOOD CELLS FETAL DNA FROM PLACENTAL TISSUE FETAL RNA FROM PLACENTAL TISSUE FETAL DNA FROM UMBILICAL CORD FETAL RNA FROM UMBILICAL CORD

CATEGORY OF SPECIMENS	PRE-ECLAMPSIA PREMATURE RECURRENT MISCARRIAGE IUGR NORMAL
VOLUME/AMOUNT OF SPECIMEN REQUESTED	
NUMBER OF SPECIMENS REQUIRED PER CATEGORY	
FUNDING BODY DETAILS	

PLEASE PROVIDE ONE COPY OF THE APPLICANTS CV.

PLEASE ATTACH ONE COPY OF THE APPROVED PROJECT.

PLEASE ATTACH ONE COPY PROOF OF FUNDING.

THANK YOU.

SIGNATURE OF APPLICANT-DATE	SIGNATURE OF R&D OFFICE/HOST INSTITUTION-DATE

account number 4017 8691, sort code 20 10 53, account name University College London, held with Barclays Bank plc,6 – 17 Tottenham Court Road, London, W1T 1AZ. In addition, the Recipient shall use a courier with suitable skill and experience to safely transport the Material in accordance with all applicable laws and will bear the cost of shipping and any necessary insurance. If so requested by the Provider, the Recipient shall provide it with written confirmation of the safe receipt of the Material promptly after their delivery to the Recipient's premises.

Schedule 1

[Attach A

Schedule 2

[Insert cost]

Agreed by the Parties though their authorised signatories:

University College London

Signed:

Name:

Title:

Date:

[Insert name of the recipient institution]

Signed:

Name:

Title:

Date: