# PALOH-UK

## Pharmacogenetics to Avoid Loss of Hearing – UK (PALOH-UK)

### Participant Information Sheet (PIS)

In many hospitals around the country babies now have a cheek swab test to help identify if they are at risk of hearing loss as a side effect of their antibiotics. If they are, an alternative but equally effective antibiotic will be used. The test (known as the genedrive test) itself is now part of routine clinical practice and is not performed under research. However, sites using the system are collecting data on the performance of this test to assess whether it should be rolled out across the country. This data is being collected as part of the Pharmacogenetics to Avoid Loss of Hearing Trial – UK (PALOH-UK).

Your child's anonymised sample and data will be collected as part of this assessment. You have the right to withdraw your child's sample and data from this assessment if you wish. Please take time to read the following information carefully and discuss it with members of your child's medical team if you wish. Please ask if there is anything that is not clear or if you would like more information. Thank you for taking the time to read this.

## About the research

- **Who will conduct the research?**

This project is sponsored by the University of Manchester (UoM) and the research team is made up of a collaboration between 1) clinical sites across the United Kingdom, 2) clinical academics based at the Manchester Centre for Genomic Medicine, and 3) a technology partner, genedrive plc. The research is led by Professor William Newman and Dr John McDermott, both of whom are based at The University of Manchester, School of Biological Sciences, Division of Evolution and Genomic Sciences.

**What is the purpose of the research?**

**Background**

- Over 90,000 babies are admitted to Newborn Intensive Care Unit's (NICU's) every year in the UK, with many more admitted to local neonatal units (LNUs) and special care baby units (SCBUs). A large proportion of these babies will be prescribed and given antibiotics for protection against or treatment of bacterial infection.

- In what is often referred to as the “golden hour”, the medical team will aim to screen babies who may be at risk of bacterial infection, prescribe and administer antibiotics within one hour of admission.
- The antibiotic, Gentamicin is an aminoglycoside and is the first-choice antibiotic recommended nationally to treat or protect against suspected bacterial infection or to treat babies with a known bacterial infection. It is given alongside a second antibiotic (Benzylpenicillin) and this combination has the major advantage of being effective and a lower risk of antibiotic resistance compared to alternative antibiotics.
- However, some children have the inherited 1555A>G change in the MT-RNR1 gene that may cause severe hearing loss or deafness if they are treated with even a single dose of Gentamicin.
- It is estimated that 1 in 500 people have this genetic change. People with this change may suffer complete deafness or severe hearing loss if they have even just a single dose of the antibiotic, Gentamicin. By testing babies on admission to NICU’s in the UK, before they receive their first dose of Gentamicin, we have the potential to avoid approximately 180 cases of permanent severe hearing loss or complete deafness caused by this antibiotic every year.

**The Study**

- Testing for the m.1555A>G change usually takes 3-4 days through a genetics laboratory, which is not quick enough for babies admitted to a NICU with suspected infection. Genedrive PLC have developed a rapid test which takes 26 minutes and was tested in a large study (PALOH) in 2022.
- The test was provisionally recommended for use in clinical practice by the National Institute for Health and Care Excellence (NICE), but more evidence is required before it can be deployed nationally.
- This study (PALOH-UK) aims to collect that evidence.
- Hospitals around the UK will have access to the genedrive test, and testing will take place as part of routine clinical practice.
- The study looks to collect anonymised cheek swab samples and data on how the test was used in clinical practice, and how well it performs against.
- The study will use the anonymised cheek swabs samples to compare the results of point-of-care test to an alternative laboratory test, to confirm the performance of the point-of-care test. Testing will also be performed to check the reasons for any test failures.

Your child was chosen to be tested with the genedrive test as part of their routine practice and we are hoping to test approximately 5,550 babies across the United Kingdom.

➢ **Why was my child selected to participate?**

All babies admitted to the recruiting hospital sites will be tested with the genedrive test as part of routine practice and will be included in this study during the research study period commencing from the trial start date at the corresponding site.

The attending clinician may decide not to perform the genetic test straight away on a baby if immediate antibiotic treatment is required upon admission and IV access has already been established, as the risk of waiting for the genetic results would be too great. In this case, the genetic

test will not be performed, and the baby will not be included in the research study. If the genetic test is performed at a later time during your baby's admission, then they will be included in the research study.

- **What are the risks and benefits of my child taking part in the study.**

If completed, the opt out form would include a baby's NHS or district number as well as a parent's name and so the form will be held on the NHS site in a secure location with your baby's medical notes. It will not be accessed by the study research team.

The purpose of this study is to assess whether this test could cause a delay to a baby being given an antibiotic. We have shown in our previous study of 750 babies, there was no delay in the time to give babies antibiotics and we believe there is a very low risk of a delay in antibiotics being given. To further reduce this risk, as described at the bottom of page 2 of this document, babies that require immediate antibiotics may not have the genetic test performed, as the risk of delay would be too great in this instance.

If a baby is found to carry the gene change, they will be prescribed an alternative antibiotic which is as effective as gentamicin but reduces the risk of permanent hearing loss. The expected benefit is for participants to be part of a study that will aim to allow wider adoption of the genetic test.

- **Will the outcomes of the research be published?**

Yes, we plan to publish the outcomes of this work to help support other hospitals in deciding whether they should use the test and how it might be implemented. No personal or identifiable details about your child will be included in any publication.

- **Who has reviewed the research project?**

This project has been reviewed by London - West London & GTAC Research Ethics Committee, REC Reference: 24/LO/0854**.**

- **Who is funding the research project?**

This work has been funded by the National Institute for Health and Care Research (NIHR) as part of the NIHR and Office for Life Sciences Real World Evidence Call.

## What would my involvement be?

- **What would happen to my child and their data if they took part?**

**The Test**

- On admission, a single swab will have been taken from the inside of your baby's cheek. This is a harmless test, will not cause any discomfort to your baby and it will be taken at the same time as other routine swabs are taken from your baby. The swab will be used in the test their DNA to detect the m.1555A>G gene change.
- The team caring for your baby will process the test on the neonatal unit to give a result back in less than 30 minutes. Whilst the test is running, the other routine admission procedures can continue so it will not delay your baby's treatment. The buccal (cheek) swab is mixed in a buffer solution and reagents in a cartridge. The cartridge is then inserted into the Genedrive device for

analysis giving a “detected” or “not detected” result in 26 minutes. Once a result is available, the team caring for your baby will be able to decide on which antibiotic is most suitable and is safe for your baby.

- The test only looks for the m.1555A>G gene change, there is no other genetic testing or information produced about your baby’s genes or inheritance because of performing this test.
- This testing is undertaken as part of routine care and is not a formal part of the research study itself.

**Possible Results**

- Most babies tested will not have this genetic change. If your baby needs antibiotics and we do not detect the m.1555A>G gene change, your baby will be prescribed and administered the antibiotic, Gentamicin for the protection against and treatment of newborn infection.
- If we do detect the m.1555A>G gene change that causes the sensitivity to Gentamicin (a positive result), your baby can still be protected against and treated for infection because we will give a different effective antibiotic (for example one called Cefotaxime).
- The purpose of this study is to assess whether this test could cause a delay to a baby being given an antibiotic. We have shown in our previous study of 750 babies, there was no delay in the time to give babies antibiotics and we believe there is a very low risk of a delay in antibiotics being given. To further reduce this risk, as described at the bottom of page 2 of this document, babies that require immediate antibiotic may not have the genetic test performed, as the risk of delay would be too great in this instance.
- If your baby tests positive, you will be offered a genetics appointment at a time that suits you to discuss with you what this genetic test result means in more detail for your baby and for other relatives. This will be an opportunity to answer any questions that you may have. They would ensure that this result is included on your baby’s medical records so that they are not treated with aminoglycoside antibiotics in the future.
- If there is a “test fail” (meaning the test does not produce a result) your baby will receive antibiotic therapy as normal, which may be gentamicin or an alternative antibiotic which is just as effective. This will be decided by your child’s care team.

**The Research Study**

- Once your baby’s cheek swab sample has been taken, it will be stored securely at the hospital and then after 28 days it will be fully anonymised. It will then be sent to the main study laboratory in Manchester where the m.1555A>G change will be tested for using a different approach. This will allow us to confirm the accuracy of the genedrive system.
- If we are unable to get a result from the cheek swab (i.e. a test fail), we will try to establish why this happened. These investigations, of the reason of the test fail, will take place in the laboratories at the Manchester Centre for Genomic Medicine, or in the laboratories of our colleagues who developed the test (genedrive).
- Your baby’s cheek swab sample will only be used within the PALOH-UK study and assessed by members of the research team.
- Once the study ends, the anonymised samples will be destroyed and will not be used in any future research.
- We will also collect data on how long it takes for babies to receive antibiotics, the types of antibiotic given, and the proportion of admissions who underwent the test. None of this will include any personal identifiable information from your baby being sent to the research team, but your baby’s data may contribute to those assessments.

- **Will I or my child be compensated for taking part?**

No compensation will be offered for participation in this study.

- **What happens if I do not want my child to take part or if I change my mind?**

It is up to you to decide whether or not your child takes part. If you do not want us to include your baby's sample and data in this study, you can opt out. We have provided an "opt out form" for you to do this. Please let your care team know if you wish to opt out so that we can remove your baby's data and destroy any samples, but this can be only done prior to the cheek swab sample being anonymised – which will take place after 28 days from when your baby was admitted.

Completed opt out forms will be retained in secure manual files by your local neonatal unit, as this will contain identifiable information on your baby and the name of the parent or guardian. This form will not be accessed by the study research team and will remain at your local NHS site.

If you do decide you are happy for your baby to take part, you are still free to withdraw at any time without giving a reason and without detriment to your child. However, as detailed above, it will not be possible to remove your sample and data from the project once it has been anonymised as we will not be able to identify your specific data. This does not affect your data protection rights.

## Data Protection and Confidentiality

- **What information will you collect about my child?**

All the data collected about your child will be undertaken as part of routine practice and would have been collected even if a study were not ongoing. The research team does not need to know specific information about your child, but we ask that each hospital site reports average data about all admissions to us.

In addition, we will ask to look at the cheek swab sample from your child to check the accuracy of the system. This sample will be completely anonymised, so the research team will not be able to tell that this was from your child

These data include:

- Average time to antibiotic (i.e. how long it took your baby to get their antibiotics)
- Whether the test was performed
- Ethnicity data
- Additional data linked to the cheek sample to confirm the point-of-care test performance and to determine the root-cause of any test failures.

- **Under what legal basis are you collecting this information?**

We are collecting and storing this personal identifiable information in accordance with UK data protection law which protect your child's rights. These state that we must have a legal basis (specific reason) for collecting your child's data. For this study, the specific reason is that it is "a public interest task" and "a process necessary for research purposes".

- **What are my child's rights in relation to the information you will collect about them?**

You have a number of rights under data protection law regarding your child's personal information. For example, you can request a copy of the information we hold about you. However, as detailed above, the study team will hold no personal information about your child.

If you would like to know more about different rights or the way we use personal information to ensure we follow the law, please consult our Privacy Notice for Research:

Full URL **https://documents.manchester.ac.uk/display.aspx?DocID=37095**

- **Will my child's participation in the study be confidential and their personal identifiable information be protected?**

In accordance with data protection law, The University of Manchester is the Data Controller for this project. This means that we are responsible for making sure your personal information is kept secure, confidential and used only in the way you have been told it will be used. All researchers are trained with this in mind, and your data will be looked after in the following way:

- We have designed the study so that no personal identifiable information needs to be sent to the central research team.
- As such, any data will be fully anonymised at the hospital sites, and the research team will not be able to identify participants.
- Any study data will be stored securely on University of Manchester managed systems.
- You will not be contacted to participate in future research
- Anonymised data will be uploaded into study repositories, as this is good research practice.

- **What are the insurance and indemnity arrangements in place for this study?**

The University of Manchester will arrange insurance for research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students, subject to policy terms and conditions.

## What if I have a complaint?

In the unlikely event that something does go wrong, and you are harmed during the research you may have grounds for a legal action for compensation against the University of Manchester (or the NHS Trust) but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

If you have a complaint that you wish to direct to members of the research team, please contact:

**PI - Dr Helen McDevitt**

**Email address - ggc.obstetric.gcrf@nhs.scot**

**Telephone number - 0141 232 7600**

For complaints about all acute hospital services across Glasgow and Clyde, you can: Call: 0141 201 4500 Email: complaints@ggc.scot.nhs.uk Write to us at: Complaints Department North East Sector Offices, Stobhill Hospital 300 Balgrayhill Road Glasgow G21 3UR

The NHS in Scotland has in place arrangements to provide a Patient Advice and Support Service (PASS) for all NHS users. The service is free, confidential, independent of NHSGGC, and fully impartial. Helpline telephone number: 0800 917 2127 For more information about this service and to find your local bureau, including contact details: https://www.cas.org.uk Patient Advice & Support Service.

**If you wish to make a formal complaint to someone independent of the research team or if you are not satisfied with the response you have gained from the researchers in the first instance then please contact**

The Research Ethics Manager, Research Office, Christie Building, The University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 306 8089.

If you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, The University of Manchester, Oxford Road, M13 9PL at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office about complaints relating to your personal identifiable information Tel 0303 123 1113

Full URL **https://ico.org.uk/make-a-complaint/**

## Contact Details

If you have any queries about the study, then please contact the research team:

**PI - Dr Helen McDevitt**
Email address - ggc.obstetric.gcrf@nhs.scot
Telephone number - 0141 232 7600