# Feasibility study for the development of a serocorrelate of protection against invasive Group B Streptococcus disease (the iGBS study)

Submission date 02/07/2018	<b>Recruitment status</b> No longer recruiting	[ [2
Registration date 09/07/2018	<b>Overall study status</b> Completed	[ []
Last Edited 19/08/2022	<b>Condition category</b> Infections and Infestations	Ľ

Prospectively registered

[X] Protocol

[] Statistical analysis plan

[X] Results

Individual participant data

#### Plain English summary of protocol

Background and study aims

Group B Streptococcus (GBS) is a bacterium (bug) that causes infection in young infants in all regions of the world. Worldwide in 2015 it was estimated that there were at least 319,000 infants under 3 months of age with GBS disease, resulting in 90,000 deaths and at least 10,000 children with long-term disabilities. Babies mostly acquire the GBS bacteria from their mothers around the time of birth and around 20% of all pregnant women carry GBS in their bowel and vagina. The global burden of GBS is therefore high and the options for prevention are currently limited. An effective vaccine that could be given to pregnant women has the greatest potential to benefit mothers and babies worldwide and such vaccines are now being tested in clinical trials, including in pregnant women. To license a new vaccine so that it can be recommended for routine use usually requires evidence that the vaccine is safe and effective in preventing the disease. This usually means undertaking a large trial in which the new vaccine is given to half of the subjects, who are then compared to the other half who did not receive the new vaccine. Such trials are expensive and time-consuming to perform. Another way of licensing a new vaccine is to show that when it is given to relevant groups of people it is able to produce levels of immunity (usually measured as antibodies) in their blood that are known to result in protection. Such levels are called serocorrelates (because they "correlate" with protection). Although there is considerable evidence that high levels of antibody against GBS in pregnant women do correlate with protection against GBS disease in their babies, the precise level (the serocorrelate) is not currently known. Although GBS is the most common cause of serious early infections in UK babies it is still relatively rare overall, so around 150,000 babies will need to be followed in order to find at least 150 babies with GBS disease, which is around the number needed to establish the serocorrelates of protection. The aim of this smaller (feasibility) study of around 4000 women is to assess the recruitment and test the methods. If this feasibility study works well this will lead to a larger study to address the question of how much antibody is needed to protect against invasive infant GBS disease.

#### Who can participate?

Pregnant women aged 18 and over who are delivering at one of the selected hospitals

What does the study involve?

A small sample of blood is collected from pregnant women and/or from the cord of their newborn babies at delivery and stored in the laboratory. With the cooperation of paediatricians and microbiologists the researchers are alerted if any of the babies develop GBS disease over the next 3 months. For those who do, the level in their blood samples at birth is then compared with that of other babies who did not develop GBS disease. Because many babies acquire GBS from their mothers at birth a smaller number of the mothers have a swab taken to see if they are carrying GBS around the time of birth.

What are the possible benefits and risks of participating?

The antibody tests will help in the development and licensure of GBS vaccines for pregnant women. It is hoped that the results of this study will help to stop babies from becoming sick with GBS disease in the future. A blood sample can cause anxiety for some people and is associated with mild, temporary discomfort. There is a small risk of fainting, bruising and infection. All blood sampling is performed by trained members of the study team. If required, a blood sample may be needed from the baby at 1-3 months (less than a teaspoon full). This can cause discomfort but common distraction techniques, such as breastfeeding, can be used to minimize this. In the unlikely case of a stillbirth, participants are still asked if they are happy to consent for a blood test. This can provide useful information as GBS is a cause of stillbirths.

Where is the study run from?

- 1. St George's University Hospitals NHS Foundation Trust (UK)
- 2. Kingston Hospitals NHS Trust (UK)
- 3. Croydon University Hospitals NHS Trust (UK)
- 4. East Surrey Hospitals NHS Trust (UK)
- 5. Poole Hospital NHS Trust (UK)

When is the study starting and how long is it expected to run for? June 2018 to August 2020

Who is funding the study? NIHR Health Technology Assessment Programme (UK)

Who is the main contact? Prof. Paul Heath

Study website https://www.sgul.ac.uk/igbs

## **Contact information**

**Type(s)** Scientific

**Contact name** Prof Paul Heath

ORCID ID http://orcid.org/0000-0002-7540-7433

**Contact details** 

St George's University of London Cranmer Terrace Paediatric Infectious Diseases Research Group Jenner Wing, Level 2 London United Kingdom SW17 0RE

## Additional identifiers

EudraCT/CTIS number

**IRAS number** 

ClinicalTrials.gov number

Secondary identifying numbers 1.0; HTA 17/153/01

## Study information

#### Scientific Title

Feasibility study for the development of a sero-correlate of protection against invasive Group B Streptococcus disease

Acronym

iGBS

#### **Study objectives**

What are the Group B Streptococcus (GBS) capsular polysaccharide serotype-specific IgG immunecorrelates of protection against the most prevalent serotypes of GBS causing invasive infant disease (iGBS)?

Aims and objectives:

Given the anticipated study size of this study and its logistic complexities, the aim of this initial feasibility study is to test key operational aspects of the study design of such a study. The feasibility study aims to collect data on maternal GBS colonizing serotype prevalence, anticapsular IgG concentrations, kinetics of antibody transfer and IgG decay in the first three months of life and enable sample size and power assumptions for the main study to be assessed.

#### Ethics approval required

Old ethics approval format

**Ethics approval(s)** West Midlands - Solihull, 15/06/2018, REC ref: 18/WM/0147

**Study design** Multicentre prospective cohort study

Primary study design

#### Observational

**Secondary study design** Cohort study

**Study setting(s)** Hospital

**Study type(s)** Other

#### Participant information sheet

https://www.sgul.ac.uk/images/iGBS/PIS%20for%20website%20KH,%20SGH.pdf

#### Health condition(s) or problem(s) studied

Invasive infant disease caused by Group B Streptococcus

#### Interventions

The trialists will establish maternal delivery/infant cord serum collection from 5 maternity units (around 4000 women) and test the feasibility of their strategies. They will collect a small sample of blood from pregnant women and/or from the cord of their newborn babies at delivery and store these samples in the laboratory. With the cooperation of paediatricians and microbiologists they will be alerted if any of the babies develop GBS disease over the next 3 months (cases). For those who do, the trialists can then compare the level in their blood samples at birth with that of other babies (controls) who did not develop GBS disease.

Because many babies acquire the GBS from their mothers at birth the trialist will also carry out a sub-study in which 1000 mothers will have a vaginal-rectal swab taken to see if they are carrying GBS around the time of birth. The babies of mothers identified as carrying GBS will be the control babies as they were known to be exposed to GBS at birth but didn't develop GBS disease.

The trialists will assess the following parameters:

1. Enrollment rate (the rate (proportion) of eligible women who are willing to participate in the blood collection study)

- 2. Maternal and/or cord blood collection rate
- 3. The impact of different timings related to blood sample processing and storage
- 4. Key clinical data collection rate
- 5. Rectovaginal swab/delivery blood sample study enrollment rate
- 6. Rectovaginal swab and delivery blood sample collection rate
- 7. Infant blood sample study consent rate
- 8. Infant surveillance consent rate

The collection of blood samples in colonised women will be used to derive estimates of GBS anticapsular IgG concentrations using a standardised assay.

#### Intervention Type

Other

#### Primary outcome measure

The feasibility of collecting serum at delivery (either maternal or cord or both) from a large cohort of pregnant women, assessed using:

1. Enrolment rate (the rate (proportion) of eligible women who are willing to participate in the

delivery blood collection study)

2. Maternal and/or cord blood collection rate

3. Key clinical exclusion data (gestation at birth, receipt of IAP in labour (yes/no), type of IAP

(list), time between administration of IAP and delivery (in hours) collection rate)

4. Infant iGBS surveillance consent rate

#### Secondary outcome measures

In the sub-study the following are assessed at delivery:

- 1. Rectovaginal swab study consent rate
- 2. Rectovaginal swab collection rate
- 3. Rectovaginal GBS colonisation rate
- 4. Rectovaginal GBS CPS serotype-specific colonisation rates

In the sub-study where samples of maternal/cord blood and rectovaginal swabs are available, the following are assessed at delivery:

- 1. Infant blood sample study consent rate
- 2. Infant Guthrie card consent rate
- 3. Infant Guthrie card collection rate

#### Overall study start date

01/06/2018

#### **Completion date**

31/08/2020

## Eligibility

#### Key inclusion criteria

1. Pregnant

- 2. ≥ 18 years of age
- 3. Delivering at one of the selected hospitals
- 4. Consented to participate during the study period

#### Participant type(s)

Patient

**Age group** Adult

Lower age limit

18 Years

**Sex** Female

**Target number of participants** Approximately 4000

**Total final enrolment** 1823 **Key exclusion criteria** Does not meet the inclusion criteria

Date of first enrolment 02/07/2018

**Date of final enrolment** 31/12/2018

## Locations

**Countries of recruitment** England

United Kingdom

#### Study participating centre

**St George's University Hospitals NHS Foundation Trust** Blackshaw Road London United Kingdom SW17 0QT

**Study participating centre Kingston Hospitals NHS Trust** Galsworthy Rd Kingston upon Thames Kingston United Kingdom

KT2 7QB

**Study participating centre Croydon University Hospitals NHS Trust** 530 London Rd Croydon United Kingdom CR7 7YE

**Study participating centre East Surrey Hospitals NHS Trust** Canada Ave Redhill United Kingdom RH1 5RH

**Study participating centre Poole Hospital NHS Trust** Longfleet Rd Poole United Kingdom BH15 2JB

### Sponsor information

Organisation

St George's University Hospitals NHS Foundation Trust

#### **Sponsor details**

St George's Joint Research Enterprise Services Hunter Wing, Ground Floor Cranmer Terrace London England United Kingdom SW17 0QT +44 (0)208 725 0794 researchgovernance@sgul.ac.uk

**Sponsor type** Hospital/treatment centre

Website https://www.stgeorges.nhs.uk/

ROR https://ror.org/039zedc16

### Funder(s)

Funder type Government

**Funder Name** 

Health Technology Assessment Programme

Alternative Name(s) NIHR Health Technology Assessment Programme, HTA

**Funding Body Type** Government organisation

Funding Body Subtype National government

**Location** United Kingdom

## **Results and Publications**

#### Publication and dissemination plan

The protocol has not been published but is available on request. The trialists are planning to publish the outcomes of the feasibility study and sub-studies in early 2019.

#### Intention to publish date

01/06/2019

#### Individual participant data (IPD) sharing plan

All data will be stored in an online format on the RedCap database. Data in this database will be anonymised, with each participant being identified by a unique participant ID. No patient identifiable information will be stored on RedCap. Research midwives and members of the research team all have secure password protected accounts that allow them to input data onto this form.

#### IPD sharing plan summary

Stored in repository

#### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2019	20/12/2019	Yes	No
Protocol file	version 9.0	06/10/2020	19/08/2022	No	No