ISRCTN60488657 https://doi.org/10.1186/ISRCTN60488657

New 6-in-1 vaccine study to guide UK vaccine policy

Submission date 02/06/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 04/09/2023	**Overall study status** Ongoing	
Last Edited 20/05/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims

A vaccine protecting against Haemophilus influenzae type b (Hib) and group C meningococcus (MenC), currently given in the UK routine immunisation programme at age 12 months, branded Menitorix, will be unavailable from 2025. The Joint Committee on Vaccination and Immunisation (JCVI) has considered options for adapting the current schedule. This study will evaluate a proposed schedule before its implementation.

The JCVI suggests that MenC vaccination is no longer required in the UK infant schedule, as a successful vaccination programme in adolescents has led to effective “herd immunity” against MenC. The JCVI also suggests a new vaccination timepoint in the routine schedule at age 18 months, to give a second dose of measles, mumps, rubella (MMR) vaccine and a booster dose of the “6-in-1” vaccine (which protects against diphtheria, tetanus, poliovirus, pertussis, hepatitis B and Hib). Moving forward the second dose of MMR vaccine (currently given at pre-school age) may improve vaccination uptake. An initial course of the 6-in-1 vaccine is currently routinely given at 2, 3 and 4 months of age. The boost to Hib immunity currently achieved with Menitorix may instead be achievable by giving the 6-in-1 vaccine at 18 months.

There are two licensed 6-in-1 vaccines, Infanrix hexa and Vaxelis, whose components differ. Currently, the same vaccine is recommended for each of the initial three doses. This study will investigate whether the vaccines may be used interchangeably for the booster, which would facilitate the delivery of the vaccine programme. In addition, the researchers will study the difference in immune response to routine vaccinations between infants born at less than 37 weeks gestational age versus those born at greater than or equal to 37 weeks gestational age receiving this vaccine schedule.

Who can participate?

Children aged 12 months who have completed the infant UK immunisation schedule before 6 months of age

What does the study involve?

Participants will be given the vaccinations routinely scheduled at 12 months (except Menitorix). At age 18 months, they will be given either Infanrix hexa or Vaxelis (determined by

randomisation) and MMR vaccine. Participants will also be offered two doses of chickenpox vaccine (which is not routinely given in UK) as an optional benefit. Blood samples will be taken at ages 18 and 19 months to assess immune responses to the vaccines.

What are the possible benefits and risks of participating?
The following benefits are possible when participating in this study:
Participants will be given routine vaccines in their own homes or in a suitable and convenient location.
Participants will be offered two doses of a vaccine which helps to prevent chicken pox. This vaccine is not routinely offered in the UK.
Participants will have 24-hour telephone access to an on-call study team member for urgent clinical queries related to the study.
Participants in the study will receive their booster dose of an MMR vaccine at the age of 18 months old instead of at 40 months; this may result in increased protection against measles, mumps and rubella from an earlier age. Similarly, by receiving the 6-in-1 vaccine at the age of 18 months old, participants may gain increased immunity against tetanus, diphtheria, pertussis, polio and hepatitis B.

Participants in this trial will be receiving licensed vaccines which are already included in the childhood routine UK immunisation schedule or licensed for use in the UK. The risks to participants include the common side effects of each vaccination, listed within the summary of product characteristics. These include local injection site reactions such as pain, erythema, swelling, pruritis and induration and systemic side effects including fever, irritability, rash, malaise, drowsiness, vomiting and loss of appetite. Both MMR and varicella vaccines are associated with an increased risk of febrile seizures, typically 7 to 10 days following vaccination.
A delay in administration of the Hib booster from 12 to 18 months may result in reduced immunity against Hib, however, this risk is minimal due to low numbers of Haemophilus influenzae Type B cases reported in the UK.
Removal of the MenC booster from the vaccinations given at 12 months may result in reduced immunity against MenC. The risk of disease resulting from this is extremely low, given the low rates of carriage in the UK since the introduction of routine adolescent MenACWY vaccination in 2015.
As with all vaccines, there is a small chance of an allergic reaction including severe reactions such as anaphylaxis (the risk is less than one in a million doses for existing vaccines).
The risks associated with blood sampling include bleeding, pain at the injection site, bruising and infection. Anaesthetic cream is offered to minimise any pain during blood sampling. The volume of blood taken at each visit does not exceed the recommended European limits for infants.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
May 2023 to June 2026

Who is funding the study?
MCM Vaccine (Netherlands)

Who is the main contact?
Prof. Dominic Kelly, info@ovg.ox.ac.uk (UK)

Study website
https://trials.ovg.ox.ac.uk/trials/6-1-part-2-vaccine-study

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2022-003425-22

IRAS number
1006942

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
OVG2022/04, IRAS 1006942, CPMS 57091

Study information

Scientific Title
Heterologous boosting for hexavalent paediatric vaccines in the UK schedule

Acronym
The 6-in-1 Part 2 Vaccine Study

Study objectives
Primary objective:
To determine if the anti-PRP seroprotection rate in the heterologous hexavalent schedule is non-inferior to the homologous schedule at 1 month following boost with either Hex-I or Hex-V

Secondary objectives:
1. To determine if the anti-PRP seroprotection rate in the heterologous schedule is superior to the homologous schedule at 1 month following boost
2. To characterize the immunogenicity of selected antigens in Infanrix-hexa and Vaxelis at 18 months in study participants after receiving homologous Infanrix-hexa or Vaxelis as prime

vaccination at 2, 3 and 4 months
3. To characterize the immunogenicity of selected antigens in Infanrix-hexa and Vaxelis at 18 and 19 months in study participants receiving either homologous or heterologous Infanrix-Hexa or Vaxelis as boost vaccination at 18 months
4. To characterize the immunogenicity of a schedule of MMR prime at 12 months and MMR boost at 18 months
5. To characterize rates of solicited and unsolicited adverse events for both heterologous and homologous schedules

Added 22/03/2024:
6. To determine if there is a difference in anti-PRP seroprotection rates after the primary vaccination series of 6-in-1 at 18 months of age in infants born at ≥32 weeks gestational age compared to infants born at <32 weeks gestational age
7. To determine if there is a difference in anti-PRP seroprotection rates at one month following the 6-in-1 booster vaccination in infants born at ≥32 weeks gestational age compared to infants born at <32 weeks gestational age
8. To characterize the immunogenicity of selected antigens at 18 months in infants born at ≥32 weeks gestational age and in infants born at <32 weeks gestational age, after receiving 6-in-1 prime vaccination at 2, 3 and 4 months
9. To characterize the immunogenicity of selected antigens at 19 months in infants born at ≥32 weeks gestational age and in infants born at <32 weeks gestational age, after receiving 6-in-1 boost vaccination at 18 months

Updated 29/01/2025:
6. To determine if there is a difference in anti-PRP seroprotection rates after the primary vaccination series of 6-in-1 at 18 months of age in infants born at ≥37 weeks gestational age compared to infants born at <37 weeks gestational age
7. To determine if there is a difference in anti-PRP seroprotection rates at one month following the 6-in-1 booster vaccination in infants born at ≥37 weeks gestational age compared to infants born at <37 weeks gestational age
8. To characterize the immunogenicity of selected antigens at 18 months in infants born at ≥37 weeks gestational age and in infants born at <37 weeks gestational age, after receiving 6-in-1 prime vaccination at 2, 3 and 4 months
9. To characterize the immunogenicity of selected antigens at 19 months in infants born at ≥37 weeks gestational age and in infants born at <37 weeks gestational age, after receiving 6-in-1 boost vaccination at 18 months

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/08/2023, East of England - Cambridge South Research Ethics Committee (Equinox House, City Link, Nottingham , NG2 4LA, United Kingdom; None available; cambridgesouth.rec@hra.nhs.uk), ref: 23/EE/0121

Study design
Single-blind randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
University/medical school/dental school

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
This study is to evaluate a proposed new vaccine schedule before its potential implementation

Interventions
All participants receive the following vaccines at 12 months of age:
• Meningococcal Group B vaccine (Bexsero), 0.5 ml by intramuscular injection
• Pneumococcal polysaccharide conjugate vaccine (Prevenar 13), 0.5 ml by intramuscular injection
• Measles, mumps and rubella vaccine (Priorix or M-M-RvaxPro), 0.5 ml by intramuscular injection

Participants do not receive the Hib/MenC vaccine (Menitorix), which is currently routinely given in the UK immunisation schedule at 12 months.

All participants receive the following vaccine at 18 months of age:
• Measles, mumps and rubella vaccine (Priorix or M-M-RvaxPro), 0.5 ml by intramuscular injection

All participants are randomised to receive at 18 months of age:
EITHER hexavalent DTaP/IPV/Hib/HepB vaccine (Infanrix hexa), 0.5 ml by intramuscular injection
OR hexavalent DTaP/IPV/Hib/HepB vaccine (Infanrix hexa), 0.5 ml by intramuscular injection

Randomisation (1:1) will be achieved by computer-generated randomisation lists, prepared by the study statistician using stratified block randomization

There will be four study groups, determined by the hexavalent vaccine received for priming in infancy (Infanrix hexa or Vaxelis) and by the hexavalent vaccine received at 18 months of age (Infanrix hexa or Vaxelis). In addition, all study participants will be offered varicella vaccine (either Varivax or Varilrix) at 12 and 18 months of age (each dose 0.5 ml, by intramuscular injection). This is optional and decided by the participant's parent/legal guardian, who may opt for 0, 1 or 2 doses of the varicella vaccine to be given.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Others (immunogenicity, reactogenicity)

Phase
Phase IV

Drug/device/biological/vaccine name(s)

Infanrix hexa, Powder and suspension for suspension for injection [Diphtheria toxoid, Tetanus toxoid, Bordetella pertussis toxoid, Bordetella pertussis Filamentous Haemagglutinin, Bordetella pertussis pertactin, Hepatitis B surface antigen, Poliovirus (inactivated) type 1 (Mahoney strain), Poliovirus (inactivated) type 2 (MEF-1 strain), Poliovirus (inactivated) type 3 (Saukett strain), Haemophilus influenzae type b polysaccharide, Tetanus toxoid (as carrier protein for Haemophilus influenzae type b polysaccharide), Aluminium hydroxide (hydrated), Aluminium phosphate] , Vaxelis [Diphtheria Toxoid, Tetanus Toxoid, Bordetella pertussis toxoid, Bordetella pertussis Filamentous Haemagglutinin, Bordetella pertussis Pertactin, Bordetella pertussis Fimbriae Types 2 and 3, Hepatitis B surface antigen, Poliovirus (Inactivated) Type 1 (Mahoney), Poliovirus (Inactivated) Type 2 (MEF-1), Poliovirus (Inactivated) Type 3 (Saukett), Haemophilus influenzae type b polysaccharide (Polyribosylribitol Phosphate), Meningococcal protein (as carrier for Haemophilus influenzae type b polysaccharide), Aluminium phosphate, Amorphous aluminium hydroxyphosphate sulfate] , Priorix [Measles virus Schwarz strain (live, attenuated), Mumps virus RIT 4385 strain, derived from Jeryl Lynn strain (live, attenuated), Rubella virus Wistar RA 27/3 strain (live, attenuated)] , M-M-RvaxPro [Measles virus Enders' Edmonston strain (live, attenuated), Mumps virus Jeryl Lynn™ (Level B) strain (live, attenuated), Rubella virus Wistar RA 27/3 strain (live, attenuated)]

Primary outcome measure

Anti-PRP (Hib) IgG concentrations ≥1.0 mcg/ml, measured by ELISA at 19 months of age

Secondary outcome measures

1. IgG concentrations against PRP (Hib), diphtheria toxoid, tetanus toxoid, hepatitis B surface antigen and pertussis toxoid (PT, FHA, fimbriae, pertactin), measured by ELISA at 18 and 19 months of age
2. Antibody against polio types 1, 2 and 3, measured by poliovirus binding inhibition multiplex immunoassay at 18 and 19 months of age
3. IgG concentrations against measles, mumps and rubella, measured by ELISA at 18 and 19 months of age
4. Solicited events recorded in participant diaries, from the vaccination at age 18 months until 7 days post-vaccination
5. Daily temperature recorded in participant diaries, from the vaccination at age 18 months until 21 days post-vaccination
6. Unsolicited medically attended adverse events reported by participants from the vaccination at age 18 months until 28 days post-vaccination
7. Serious adverse events (SAEs) reported by participants from the vaccination at age 12 months until the final study visit

Added 22/03/2024:
8. Anti-PRP (Hib) IgG concentrations ≥1.0 µg/ml and anti-PRP (Hib) IgG concentrations ≥0.15 µg /ml at 18 months of age, as measured by ELISA
9. Anti-PRP (Hib) IgG concentrations ≥1.0 µg/ml and anti-PRP (Hib) IgG concentrations ≥0.15 µg /ml at 19 months of age, as measured by ELISA
10. IgG concentrations at 18 months against PRP (Hib), diphtheria toxoid, tetanus toxoid, hepatitis B surface antigen, pertussis toxoid (PT, FHA, fimbriae, pertactin), measles, mumps, rubella, measured by ELISA
11. Antibody against polio types 1, 2, 3 determined by MIA* at 18 months
12. IgG concentrations at 19 months against PRP (Hib), diphtheria toxoid, tetanus toxoid, hepatitis B surface antigen, pertussis toxoid (PT, FHA, fimbriae, pertactin), measured by ELISA
13. Antibody against polio types 1, 2, 3 determined by MIA* at 19 months

Overall study start date
05/05/2023

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. Children aged 12 months (up to 12 months +42 days), who have completed the infant UK immunisation schedule before 6 months of age [including 3 (homologous) doses of Hex-I or Hex-V]
2. Parents/legal guardians are willing and able to comply with study procedures
3. Parents/legal guardians who are over 18 years of age and willing to provide written informed consent for their child's participation in the study

Added 22/03/2024:
4. For cohort B only: children born at <32 weeks gestational age

Updated 29/01/2025:
4. For cohort B only: children born at <37 weeks gestational age

Participant type(s)
Healthy volunteer

Age group
Child

Lower age limit
12 Months

Sex
Both

Target number of participants
572

Key exclusion criteria
Children may not participate in the study if they have:
1. Received any of the vaccines/vaccine doses scheduled for the UK '12-month' immunisation episode
2. Received any additional doses (outside the routine schedule) of any vaccines containing antigens for diphtheria, tetanus, pertussis, polio, hepatitis B, Hib, measles, mumps, rubella or varicella
3. Received influenza vaccine
4. Confirmed or suspected immunodeficiency
5. Household contacts with severe immunodeficiency
6. Any of the contraindications to the study vaccinations as specified in The Green Book
7. Confirmed anaphylactic reaction to any constituent or excipient of the study vaccines
8. Confirmed anaphylactic reaction to neomycin, streptomycin or polymyxin B (which may be

present in trace amounts in the tetanus vaccine), kanamycin, histidine, sodium chloride or sucrose (which may be present in trace amounts in the Meningococcal B vaccine) or to gelatin (which may be present in trace amounts in the MMR vaccine)
9. Latex hypersensitivity (the syringe cap of the Meningococcal B vaccine Bexsero may contain natural rubber latex)
10. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk through participation in the study, or may influence the result of the study or the participant's ability to participate in the study
11. Parents/legal guardians who are on the delegation log of this study

Added 22/03/2024:
Temporary exclusion criteria
Children are temporarily excluded from participating if they:
1. Within the 28 days prior to study vaccines have received live yellow fever, varicella or any other live vaccine that requires a 28-day interval before receiving MMR or varicella vaccine
2. Have received any other vaccine within 14 days prior to study vaccines
3. Have scheduled elective surgery, planned admission or other procedures requiring general anaesthesia within 7 days of receiving a vaccine
4. Have a febrile illness (axillary temperature ≥38.0°C) within the previous 24 hours of a scheduled vaccination
5. Are currently participating in another interventional clinical trial
6. Have had a tuberculin skin test (Mantoux) which has not been read (MMR vaccine should be delayed until after the test has been read unless protection against measles, mumps and rubella is required urgently)

Date of first enrolment
12/09/2023

Date of final enrolment
31/07/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford Vaccine Group
Centre for Clinical Vaccinology & Tropical Medicine (CCVTM)
Churchill Hospital
Oxford
United Kingdom
OX3 7LE

Study participating centre

Bristol Royal Hospital for Children
Bristol Vaccine Centre
Upper Maudlin St,
Bristol
United Kingdom
BS2 8BJ

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

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

Study participating centre
The Adam Practice
Upton Surgery
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Poole
Dorset
United Kingdom
BH16 5PW

Sponsor information

Organisation
University of Oxford

Sponsor details
Research Governance, Ethics & Assurance Team (RGEA)
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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
MCM Vaccine

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

Participants will not be identifiable from shared or published data. De-identified participant data will be made available upon requests directed to the chief investigator. Proposals will be reviewed and approved by the sponsor, chief investigator, and collaborators on the basis of scientific merit. After approval of a proposal, data can be shared through a secure online platform after signing a data access agreement.

Intention to publish date
30/06/2026

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date