National enhanced surveillance of vaccination programmes targeting invasive meningococcal disease in England

Public Health England Immunisation Department and Meningococcal Reference Unit
About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. It does this through advocacy, partnerships, world-class science, knowledge and intelligence, and the delivery of specialist public health services. PHE is an operationally autonomous executive agency of the Department of Health.

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Version 1.2 summary of revisions

- Section 6: tables 6.1 and 6.2 have been replaced with a flowchart in order to clarify the role of the PHE HPT and the text has been updated accordingly.
- Simplified surveillance sample submission for all age groups.
- The document has been updated to include specific mention of meningococcal infection of the conjunctiva.
- The MENSVO1 surveillance form has date of onset and a new Part H included.
- All notable changes are identified in blue text.

Version 1.1 summary of revisions

- Changes consisted of minor edits. No substantive changes were made.
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Executive Summary

This document updates and replaces the Joint protocol from the Public Health Laboratory Service (now Public Health England, PHE) and the Institute of Child Health for Surveillance of the impact of the meningococcal group C (MCC) conjugate vaccination programme and protocol for investigation of vaccine failures in England and Wales, published in November 1999. The national surveillance protocol for invasive meningococcal disease (IMD) in England has been extended in recognition of:

- Changes to the MCC programme, including the removal of the infant MCC dose at 4 months and the introduction of an adolescent MCC dose in June 2013.
  

- The emergency introduction of a quadrivalent conjugate vaccine against meningococcal groups A, C, W, and Y (MenACWY) for 14-18 year-olds in August 2015 in response to a national outbreak of a hypervirulent MenW strain belonging to ST-11 clonal complex (Ladhani et al., 2015; Campbell et al., 2015)
  

- The introduction of a MenB vaccine, Bexsero®, into the national infant immunisation schedule in September 2015 at 2, 4, 12 months of age (2+1), with a small catch-up for 3 month olds (3-4-12 months) and 4 month olds (4-12 months) when they attend their routine immunisation visits
  

This protocol covers the enhanced surveillance plan for invasive meningococcal disease in England with the aim of collecting data for the JCVI to inform national vaccination policy.
1. Background

1.1 Meningococcal C conjugate (MCC) vaccines were introduced into the routine infant schedule in England from November 1st 1999 (Campbell 2010). A phased catch-up programme for all other children up to 18 years began concurrently and was later extended to all students aged up to 25 years. In clinical trials MCC vaccines were found to be safe, immunogenic and to prime for memory and licensure was based on immunogenicity rather than efficacy data. At that time the fundamental requirement for enhanced case confirmation, strain characterisation and surveillance was recognised in order to monitor the impact of these MCC immunisation programmes. An appropriate surveillance strategy was, therefore published in November 1999 and has been in place ever since. Information generated from this surveillance has been key in furthering understanding of the impact of MCC vaccines and has influenced the way that meningococcal conjugate vaccines vaccine programmes were subsequently introduced in other countries, including the MenA vaccination programme in African countries across the meningitis belt. It has also led to changes in the MCC programme in England with a reduction from a 3-dose to 2-dose infant programme based on comparable immunogenicity and the introduction of a Hib-MCC booster at 12 months of age to address waning immunity (Campbell et al., 2010).

1.2. The MCC immunisation programmes had a very rapid and marked impact on invasive MenC disease in the cohorts targeted by vaccine. An indirect effect on age groups outside the immunised group was also apparent with a large reduction in cases in older ages. There have been around 30 MenC cases confirmed annually in England and Wales since 2006/07. MenB now accounts for the vast majority of invasive meningococcal disease (IMD) (Ladhani et al., 2012). In 2014, there were 400 laboratory-confirmed MenB cases in England, with a quarter of cases occurring in infants (<1 year) and a further quarter in 1-4 year-olds (PHE data available here).

1.3. Two quadrivalent conjugate vaccines (offering protection against capsular groups A, C, W and Y; Nimenrix® and Menveo®) are currently licensed for use in the UK (Tan et al., 2010). MenACWY vaccine is currently recommended for travel to endemic areas and for children and adults with asplenia or splenic dysfunction or complement deficiency who may be at increased risk of invasive meningococcal infection. It is also offered to those at close prolonged contact with individuals with confirmed capsular group A, W or Y disease or probable cases with capsular group A, W or Y from a nasopharyngeal swab to reduce the risk of late disease.

1.4. Efforts to develop an effective MenB vaccine initially focussed on MenB outer membrane vesicles (OMVs), which have exhibited varying efficacy and are usually restricted to specific epidemic strains because the immune-dominant antigen (PorA) is highly variable (Tan et al., 2010). In order to provide broader, cross-protective immune responses, more recent vaccines have incorporated outer membrane vesicles from multiple strains with or without recombinant surface proteins such as factor H binding protein (fHbp), Neisserial Heparin binding Antigen (NHBA) and Neisserial adhesin A (NadA). The first of these vaccines, Bexsero® (GSK Biologicals), was licensed in Europe in January 2013 and introduced into the UK infant immunisation programme on 01 September 2015 (https://www.gov.uk/government/collections/meningococcal-b-menb-vaccination-programme).
1.5. This national surveillance plan has been adapted from previous surveillance strategies implemented when the Hib, MenC and pneumococcal vaccines were introduced into the national immunisation programme. It describes the public health actions for collecting epidemiological and clinical information as well as additional blood samples from patients with meningococcal disease in order to inform and evaluate future vaccine policy. The PHE HPT role is vital to meningococcal surveillance because their early involvement with cases can help ensure the correct surveillance information can be collected quickly and the acute surveillance blood samples can be obtained in a timely manner. This plan aims to encompass all meningococcal vaccines in the national immunisation programme and their impact on all meningococcal capsular groups across all ages in England. The surveillance plan will be reviewed at regular intervals in the light of: the surveillance data generated, the programmes adopted and actual vaccine usage, which at present is uncertain.

2. Objectives

a) To continue to monitor the impact and age-specific vaccine-effectiveness of the MCC immunisation programme
b) To monitor the impact and age-specific vaccine-effectiveness of the MenB immunisation programme in children
c) To monitor the impact and age-specific vaccine-effectiveness of the MenACWY immunisation programme in adolescents and evidence of any indirect impact across the population
d) To continue to monitor the phenotypic and genetic characteristics of invasive meningococcal isolates
e) To describe the clinical characteristics, risk factors and outcomes of IMD as well as acute and convalescent serology in children aged <5 years with laboratory-confirmed IMD following the introduction of the MenB immunisation programme.

The monitoring of vaccine safety is also a key aspect of immunisation programme surveillance and will be undertaken by the Medicines and Healthcare Regulatory Agency (MHRA) in collaboration with PHE.

3. Definition of a confirmed case of IMD

(a) A case of IMD is defined as an individual with a culture of N meningitidis or identification of meningococcal DNA from a normally sterile site.

As set out in the Guidance for the Public Health management of meningococcal disease in the UK, meningococcal infection of the conjunctiva is considered an indication for public health action because of the high immediate risk of invasive disease but this does not meet the definition for a confirmed case of invasive meningococcal disease (https://www.gov.uk/government/publications/ meningococcal-disease-guidance-on-public-health-management).

For the purposes of surveillance, cases will be further classified below.
3.1 Men A/C/W/Y IMD

A case of Men A/C/W/Y IMD is defined as an individual meeting the case definition for IMD and one or more of the following:

- Phenotypically Men A/C/W/Y culture positive from samples taken from a normally sterile site or from rash aspirate
- PCR capsular group (siaD) A/C/W/Y positive from sample taken from a normally sterile site or rash aspirate
- Meningococcal A/C/W/Y antigen detected by latex in blood, CSF or urine. Note: Positivity by a latex method which does not distinguish between A, C, Y and W will not be considered confirmation of any individual group.

3.2 MenB IMD

A confirmed case of MenB IMD is defined as an individual meeting the case definition for IMD with isolation of MenB or positive capsular group B specific PCR from a normally sterile site.

The licensed MenB vaccine, Bexsero®, does not target the polysaccharide capsule (which determines the capsular group) but is based on recombinant surface proteins including an outer membrane vesicle from a specific New Zealand outbreak strain. Although the vaccine was developed to maximise protection against MenB, it also has the potential to protect against invasive disease caused by other capsular groups. Similarly, the vaccine will not protect against all MenB strains – in England, it is estimated that Bexsero® will protect against 73-88% of currently circulating MenB strains (Vogel et al., 2013; Frosi et al., 2013). Thus, additional definitions are required to capture antigen-specific vaccine effectiveness against MenB cases and against all IMD cases.

The impact of Bexsero® (4CMenB) will be monitored using the Meningococcal Antigen Typing System (MATS) assay undertaken for all invasive MenB isolates by the MRU.

The definition of an isolate with a positive MATS assay result (“MATS positive”) is a N. meningitidis strain with at least one vaccine antigen (fHbp, NadA, NHBA) above the positive bactericidal threshold (PBT) or a positive result for PorA P1.4 by sequencing of VR2 and/or by serosubtyping.

3.2.1 A confirmed case of MATS positive MenB IMD case is defined as:

- A confirmed case meeting case definition plus MATS positive; OR
- A confirmed case meeting case definition with no sterile isolate, but positive MenB-specific PCR from a sterile site plus isolation of MenB from a throat swab, which is MATS positive.

4. Enhanced Surveillance for meningococcal disease

4.1 Existing national surveillance activities

Surveillance of meningococcal disease in England currently relies on collation of information on cases of laboratory-confirmed infection identified by the PHE Meningococcal Reference Unit (MRU) in Manchester. Confirmation of IMD cases by MRU relies on serogrouping
isolates from culture proven cases and identification of the responsible capsular group by PCR. Regular electronic downloads are made from MRU to the Immunisation Department, PHE Colindale, reporting all meningococcal infections confirmed by MRU and those known by MRU to have a fatal outcome. Ascertainment of fatal laboratory-confirmed cases is supplemented at the PHE Immunisation Department by linkage of laboratory reports with meningococcal deaths reported to the Office of National Statistics (ONS). MenC cases have been routinely followed-up since the introduction of the MCC vaccine in November 1999 in order to ascertain vaccination history and other epidemiological data.

4.2 Routine laboratory investigation of IMD at MRU

This section summarises the current routine investigations offered by the PHE MRU for suspected cases of IMD. The MRU user manual can be accessed directly for more detailed information on the use of these services (https://www.gov.uk/government/collections/meningococcal-reference-unit-mru). The MRU offers a national reference service for confirmation and characterisation of invasive meningococcal isolates. The MRU also offers a free national reference service for meningococcal PCR of clinical samples from suspected IMD cases. If IMD is confirmed by a local diagnostic laboratory (including private laboratories), then the original sample, including extracts from PCRs, should be referred to MRU to allow the capsular group to be identified. In addition to the routine testing, additional typing may be undertaken in certain situations such as outbreaks. All invasive meningococcal isolates should be submitted to the MRU for additional characterisation, even if the diagnosis has already been confirmed locally (including confirmations by private laboratories) or nationally by PCR.

4.3 Neisseria meningitidis isolate characterisation

4.3.1 Phenotypic characterisation

Phenotypic confirmation of *N. meningitidis* isolates is based on morphology and biochemical reactions. Phenotype identification is routinely undertaken by:

- Serogroup
- Identification of capsular polysaccharide antigens by serological reactions is available on request but PCR is preferred for acute samples.
- Serotype
- Identification of PorB outer membrane protein (OMP) by a dot-blot ELISA using monoclonal antibodies (mabs).
- Serosubtype
- Identification of PorA OMP by a dot-blot ELISA using monoclonal antibodies.

4.3.2 Genotypic characterisation

Genotype confirmation is routinely based on identification by:

- Capsular group: Use of PCR based capsular group confirmation enables identification of non-viable organisms. All suitable submitted samples are tested with an internal control in a *N. meningitidis* specific (capsular transport gene, ctrA) screening PCR test which also incorporates the PCR MenB-specific assay (based on the sialyltransferase gene, siaD B) and the pneumolysin assay. All non-MenB *N. meningitidis* reactive specimens are then tested by the capsular group-specific PCR
assays (based on siaD) to detect and distinguish MenC, MenY and MenW. Testing for MenA can be performed where indicated using the mynA assay.

- **Subtype:** Genetic characterisation of subtype (PorA) by DNA sequencing has been routinely undertaken and reported on all clinical isolates since October 2007. From Jan 2012, MRU has introduced porA subtyping for non-culture samples that are ctrA +ve under cycle number 34.

- **Additional characterisation:** following the introduction of the infant MenB immunisation programme, an additional 2 ml EDTA sample will be requested from all suspected IMD cases to undertake additional phenotypic/genotypic characterisation to assess whether the strain was potentially vaccine-preventable. This additional EDTA sample must be accompanied by the Sample Submission Form (MenSAM01) in Appendix 3 when it is sent to the MRU, or else it will be processed along with routine clinical samples for diagnostic testing.

### 4.4 Antibiotic susceptibility testing

The Minimum Inhibitory Concentrations (MICs) routinely determined on submitted isolates are: penicillin, ceftaxime, rifampicin and ciprofloxacin using Etest (Biomerieux) gradient diffusion methodology. Other antibiotic susceptibility tests may be performed on request.

### 4.5 Acute and Convalescent serum samples

Acute and convalescent serum samples are already routinely being requested from all vaccine-eligible confirmed/probable MenC cases to help decide on future vaccination of these cases and to investigate the mechanism of disease post-vaccination.

Following the introduction of the MenB programme, acute and convalescent serum samples are also being requested from all children younger than 5 years with laboratory-confirmed IMD, irrespective of the meningococcal capsular group responsible or the child’s prior meningococcal immunisation status.

### 4.6 Optimum clinical specimens for suspected meningococcal disease

Clinicians should be advised to follow their local or national guidelines for the clinical management of children and adults with meningitis and/or septicaemia. For public health management of meningococcal disease in the UK, the following samples should be taken as soon as possible after hospital admission (https://www.gov.uk/government/publications/meningococcal-disease-guidance-on-public-health-management):

- Blood culture
- EDTA blood for PCR (2 ml) to be sent to the MRU
- CSF culture (if meningitis suspected and LP not contra-indicated)
- CSF for PCR (if meningitis suspected and LP not contra-indicated)
- Throat swab for culture (even if antibiotics have been administered).
- Culture/PCR of other sterile sites if clinically indicated (e.g. joint fluid, etc)
- Rash aspirate (if this investigation identified as useful locally).
5. National surveillance database

The existing system of electronic downloads from MRU to the PHE Immunisation Department of all laboratory-confirmed IMD cases will continue but at shorter intervals of 1-3 times a week. In the near future, this process will be succeeded by a joint PHE Immunisation Department and MRU meningococcal database currently in development. National data on laboratory-confirmed IMD cases will continue to be published quarterly in the Health Protection Report (HPR). A reconciled database holding demographic, clinical, serological and immunological information from the follow up of all cases will be maintained and used to monitor the impact of the meningococcal vaccination programmes.

6. Public Health Surveillance Actions

The public health actions for patients with probable/confirmed IMD will depend on the age of the patient (< 5 years or ≥5 years). These procedures have been summarised in the Flowchart below.

6.1 SUSPECTED IMD CASES reported to PHE HPTs

- PHE Health Protection Teams (HPTs) informed of a suspected case of IMD are requested to collect information needed to undertake Public Health action using the short epidemiological surveillance questionnaire (Form MENSV01, see Appendix 1) or a local equivalent. It may be necessary to contact the GP to obtain an accurate vaccination history for confirmed IMD cases in the vaccine-eligible age-group. The completed MENSV01 surveillance form or local equivalent should be uploaded to the appropriate HPZone record for the case. The MENSV01 form is available on HPZone.

- PHE HPTs can discuss with clinicians the samples that need to be taken to confirm the diagnosis (see Section 4.6 above). For cases that require public health action, it is important to request the following additional enhanced surveillance samples as soon as possible after hospital admission. These can be taken when the patients have their next blood test:
  - **Children under 5 years:** require an acute serum sample and an additional EDTA sample which should both be sent to the MRU using the SAMPLE SUBMISSION FORM (MenSAM01, Appendix 3). For confirmed cases, the PHE Immunisation Team will contact the laboratory to confirm that the samples have been forwarded.
  - **Adults and children ≥5 year-olds:** an additional EDTA sample to be sent to the MRU using the SAMPLE SUBMISSION FORM (MenSAM01, Appendix 3). This sample is in addition to the EDTA sample for PCR-testing to confirm the diagnosis, which should be sent to the MRU according to local hospital procedures.

- Because of the importance of ensuring maximal confirmation of cases of IMD by capsular group, PHE HPTs, clinicians and microbiologists are reminded of the importance of taking a throat swab on admission. With immediate plating, positive cultures can be obtained in up to 45% of cases of meningococcal disease. Throat swabs are now routinely recommended for investigation of suspected meningococcal disease, even if the patients have already received IV antibiotics, because they allow detailed
characterisation of the meningococcal isolate in cases that not confirmed by culture (e.g. PCR-confirmed cases).

- In order to monitor the different national meningococcal immunisation programmes currently in place, it is also critical that all IMD positive samples are sent to the MRU for confirmation and characterisation, even for cases where the diagnosis has already been confirmed by PCR.

Cases with meningococcal infection restricted to the conjunctiva but without evidence of invasive disease should be assessed for public health action but should not be included in the enhanced surveillance unless the patient goes on to develop invasive disease.

In summary, the help of PHE HPTs is requested for completion of the epidemiological surveillance form and to request clinicians take the additional acute surveillance blood samples. PHE immunisation team will liaise with the local hospital to identify whether the additional samples were taken and to ensure these are forwarded to the MRU.

6.2 CONFIRMED CASES reported to the PHE Immunisation Team

- The PHE Immunisation Team will liaise with the PHE HPTs for any incomplete or missing surveillance forms (Form MENSV01) for confirmed IMD cases.
  
  - The PHE Immunisation Team will also liaise with the hospital to ensure that the appropriate clinical samples for confirmed cases have been forward to the MRU using the SAMPLE SUBMISSION FORM (MenSAM01, Appendix 3) if this has not already been done. For <5 year-olds, this will include serum (2 ml within 72 hours of treatment) for acute serology and the additional EDTA (2 ml) sample for further bacterial characterisation

- For children younger than 5 years, PHE Immunisation Team will request paediatricians (letters at Appendix 2):
  - Complete the clinical questionnaire (Form MENSV02) and return the form to the PHE Immunisation Team by fax, post or email (see Appendix 4)
  - Arrange for the child with confirmed IMD to have an additional blood test at 3-6 weeks after diagnosis for convalescent serology (2 ml serum sample).

- The PHE Immunisation Team may contact the GP if further epidemiological, clinical and/or immunisation information is required.
Surveillance Plan Flowchart

Local hospital: action according to local procedures
- Throat Swab for local culture
- EDTA sample (2ml) sent to MRU for PCR-testing
- Take other samples as clinically indicated (CSF, joint, etc.)

Flowchart: surveillance actions for suspected and confirmed IMD cases
(Version 1.1, Dated 10 Dec 2015)

Local PHE HPT informed

PHE HPT routine surveillance
- Check throat swab has been taken for local culture
- Check EDTA +/- other clinically-indicated samples are sent to MRU for PCR-testing
- Remind that all meningococcal positive isolates should be sent to the MRU
- Collect detail needed for PH action (epi surveillance form MENV01 or local equivalent)

PHE HPT enhanced surveillance

Suspected case under 5 years of age
- Request ACUTE serum (2ml) and additional EDTA sample (2ml) for non-culture typing of vaccine antigens be taken (ideally within 72 hours of treatment) & sent to MRU using the PHE sample submission form (Appendix 3)

Suspected case 5 years of age or older
- Request additional EDTA sample (2ml) to be sent to MRU for non-culture typing of vaccine antigens using the PHE sample submission form (Appendix 3)

All cases confirmed as IMD
- Ensure epi surveillance form MENV01 is completed and uploaded to HPZone or is returned to PHE for all confirmed cases

PHE Immunisation team enhanced surveillance
- Confirm age appropriate samples for confirmed cases have been sent to MRU including second EDTA samples and acute serum for <5 years
- Request CLINICIANS to complete the clinical questionnaire MENV02 for confirmed cases <5 years
- Request PHE HPTs to complete epi surveillance form MENV01 (if not complete)

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7. Possible future considerations for further investigations

Under HTA license acute EDTA samples or CSF samples sent to MRU will be stored where possible to allow further studies on cases of IMD. Ethics committee approval will be sought before any such use of stored samples is made.

8. Measurement of vaccine coverage

- Routine coverage data for the proportion of children receiving 2 doses of MCC vaccine by 1st, 2nd and 5th birthday is collected and the proportion of children receiving a dose of MCC-Hib vaccine by 2nd and 5th birthday is currently collected on a quarterly basis through the PHE COVER scheme. National data are also published annually for England by the Department of Health.

- Vaccine coverage data collection for the teenage age group targeted by MCC and MenACWY conjugate vaccine is under review. Routine collection of vaccine coverage data in teenagers is likely to operate in a similar way to detail currently collected by PHE for the HPV vaccine delivered to teenage girls. These data are collected using the ImmForm website managed by PHE which coordinates and manages the collection and reporting of national data.

- Coverage data collection will be extended to provide rapid measurement of the proportion of children who are appropriately vaccinated with the MenB vaccine by relevant ages.

9. Calculation of vaccine effectiveness

- Vaccine effectiveness (VE) is generally defined as the % reduction in the attack rate in vaccinated compared with unvaccinated children in the same birth cohorts. VE will be assessed by the screening method. For this method, the VE can be estimated using the formula below, where PCV is the proportion of cases that are vaccinated and PPV is the proportion population vaccinated (coverage):

\[
VE = \frac{1 - (PCV \times (1-PPV))}{(1-PCV) \times PPV}
\]

- This requires knowledge of the numbers vaccinated and unvaccinated in the population (by birth cohort or age group) at any given time and the numbers of cases by vaccination status arising in the same period (by birth cohort or age group).

- Information on the proportions vaccinated by age group and birth cohort will be generated through the COVER scheme described above. The vaccination status of confirmed cases by meningococcal capsular group will be ascertained by routine follow-up.
- Age specific vaccine effectiveness estimates will be carried out using cases occurring after implementation of the relevant vaccination campaign in that age group. VE estimates will be generated for the various meningococcal vaccines in eligible cohorts targeted for immunisation. Where possible, VE will also be estimated for vaccine-specific antigens.

- MenACWY conjugate vaccine effectiveness in teenagers will be undertaken using the indirect cohort method and case control follow up.

10. Dissemination of information and outputs

Successful implementation of the national surveillance programme will continue to depend on collaboration of health protection units, immunisation co-ordinators, microbiologists and clinicians looking after patients with IMD. Information on the surveillance scheme will be disseminated widely through PHE Web Pages. This information will include names, contact numbers and addresses of lead individuals for different parts of the programme.

Regular reporting already undertaken through publication in the HPR will continue. It is recognised that the MenB vaccine programme will require rapid monitoring and early feedback to assess the impact of the programme.

Reports to Joint Committee on Vaccination and Immunisation (JCVI) to include disease incidence and coverage and VE when this becomes available.
11. References


Appendix 1: Surveillance questionnaire
(Form MENSV01, December 2015)
# National Epidemiological Surveillance - Confirmed Invasive Meningococcal Disease

**Form MENSVO1**  
December 2015

**Public Health England Immunisation, Hospitals and Blood Safety Department**  
61 Colindale Avenue, London NW9 5EQ  
Tel. 020 8327 7828 or 6058  
Secure Fax: 020 8327 7404  
Email: meningoc@phe.gov.uk

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**PLEASE COMPLETE IN BLOCK CAPITAL LETTERS**

---

### IN CONFIDENCE

**Patient Details**

Surname:  
Forename:  
D.O.B. (DD/MM/YYYY):  
Gender: Male  Female

NHS number:  
HPZone reference number:  
PHE reference:  
Onset date:  

---

### PART A: Ethnicity – please tick below

- White British
- White other
- Black Caribbean
- Black African
- Indian
- Pakistani
- Bangladeshi
- Chinese
- Mixed*
- Other*  
*Please specify

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### PART B: Vaccination History. This covers Men B, Men C and MenACWY vaccination.

Please complete details for all vaccines below as fully as possible.

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<th>Did this case receive any doses of each vaccine before disease onset?</th>
<th>1st dose date</th>
<th>1st dose batch number</th>
<th>1st dose manufacturer/brand</th>
<th>2nd dose date</th>
<th>2nd dose batch number</th>
<th>2nd dose manufacturer/brand</th>
<th>3rd dose date</th>
<th>3rd dose batch number</th>
<th>3rd dose manufacturer/brand</th>
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<td>Boxero®</td>
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<td></td>
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1. Men B vaccine (Boxero®) included in the routine infant programme since 2/9/2013 and any baby born from 2/9/2013 should have been offered the vaccine at 2-4 months.

2. Men C vaccine (Menitor® or Menitor® or Menitor®) included in the routine infant programme since 2/9/1999. Catch-up vaccination means all those born from 1/9/1991 should have been offered at least one dose of MenC vaccine. MenC vaccine was offered to teenagers aged 13-14 years and Ershina June 2013- May 2015

3. A single dose of MenCHb vaccine (combined 14-valent polysaccharide type B [Hib]) has been offered at 12-13 months of age from 1/9/2006 (DOE-V/9/2006).

4. MenACWY vaccine (MenzB, Menitor®) replaced MenC vaccine for teenagers and the booster doses given from 2/9/2015; catch-up vaccination is also being offered for those aged 14-18 years (DOE-V/9/1996 and aged 14+ years).
### PART C: Clinical presentation

1. What was the clinical presentation?
   - [ ] Meningitis
   - [ ] Septicaemia
   - [ ] Both meningitis & septicaemia
   - [ ] Septic arthritis
   - [ ] Epiglottitis
   - [ ] Pneumonia
   - [ ] Other
   - [ ] Unknown

   Comments: ........................................

### PART D: Risk factors

2. At the time of onset did the patient have any known risk factors for meningococcal disease?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

   2.1 If yes, what were their risk factors?
   - [ ] Asplenia/ splenic dysfunction
   - [ ] Complement deficiency
   - [ ] Malignancy/ Immune Deficiency
   - [ ] Immunosuppressive drug
     - (Including complement inhibitors, e.g. eculizumab)

   Comments: ........................................

### PART E: Co-morbidities and pregnancy

3. At the time of meningococcal disease, did the patient have any co-morbidities?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

   3.1 If yes, what were their co-morbidities?
   - [ ] Chronic heart disease
   - [ ] Congenital or chromosomal abnormality
   - [ ] Chronic lung disease
   - [ ] CNS disease (CSF leak, VP shunt etc)
   - [ ] Chronic renal disease
   - [ ] Chronic gastrointestinal disease
   - [ ] Metabolic disease
   - [ ] Other

   Comments: ........................................

4. Was the patient pregnant at the time?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

### PART F: Outcome

5. Was the patient admitted to ITU?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

6. Is the patient currently alive?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

6.1 If patient died, Date of death
   ........................................ (dd/mm/yyyy)

### PART G: Travel History

7. Was the patient born in the UK?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

   7.1 If no, when did they arrive in the UK
   ........................................ (mm/yyyy)

7.2 Country of birth:

8. Has the patient recently travelled abroad (returning in the last 28 days)?
   - [ ] Yes
   - [ ] No
   - [ ] Unknown

8.1 If yes, where did they travel?

8.2 When did they return?
   ........................................ (dd/mm/yyyy)

### PART H: Is the case at working or attending any of these situations?

- [ ] child minder
- [ ] nursery
- [ ] school
- [ ] university
- [ ] care/nursing home
- [ ] barracks
- [ ] other

### PART I: Please provide any further comment

........................................

Thank you for your time and assistance. Please return by post, secure fax, email (both as detailed overleaf) or upload to HPZone.
Appendix 2: PHE Letters

a) Requesting Acute Serum Sample
b) Requesting Convalescent Serum Sample
c) Requesting additional EDTA sample for non-culture characterisation of meningococcal antigens
Public Health England

Meningococcal disease enhanced surveillance plan

Immunisation Department
61 Colindale Avenue
London NW9 5EQ, UK

T 020 8327 7828 or 6058
F +44 (0)20 8 327 7404
E PHE.meningo@nhs.net
www.gov.uk/phe

Surveillance of Invasive Meningococcal Disease

Request for Acute Serology

Doctor ___________________________ PHE ref. ________________
………………………………
………………………………
………………………………

Dear Dr. ________________________,

Patient Name: ____________________________ NHS No. _____________

HOSPITAL:________________________________ DOB _____/_____/_____

Public Health England (PHE) is conducting enhanced national surveillance of invasive meningococcal disease (IMD) to monitor the impact of meningococcal vaccines in the national immunisation schedule. As part of the surveillance, we are requesting acute serum samples from children with laboratory-confirmed IMD. Since more than half the cases are now diagnosed by PCR only, we are also developing non-culture characterisation of meningococci to monitor vaccine effectiveness. We would, therefore, be grateful if you could also send an extra EDTA sample (2 ml) with the acute serum using the enclosed Sample Submission Form (MenSAM01).

- It is critically important that all positive meningococcal samples are sent to the Meningococcal Reference Unit for confirmation, capsular grouping and genetic/molecular characterisation

- Could you please also arrange for a blood test for convalescent serology (2ml serum), ideally at 3-6 weeks after diagnosis, and send the sample to the Meningococcal Reference Unit (MRU) using the enclosed Sample Submission Form (MenSAM01)

Our contact details are on the top right-hand corner of this letter. Thank you for your time and help.

Yours sincerely

Dr Shamez Ladhani
Paediatric Infectious Diseases Consultant

Professor Ray Borrow
Deputy Head of MRU

Dr Mary Ramsay
Head, Immunisation Department

Public Health England has approval under PIAG Section 60 of the Health and Social Care Act 2001 (now subsumed into the National Information Governance Board for Health and Social Care with Section 60, now Section 251 of the NHS Act 2006) to process confidential patient information for public health purposes (see http://www.legislation.hmso.gov.uk/si/si2002/20021438.htm).

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Surveillance of Invasive Meningococcal Disease

Request for Convalescent Serology & Clinical Questionnaire completion

Doctor ..................................................  PHE ref. _______________
..................................................
..................................................
..................................................

Dear Dr. ..............................,

Patient Name: ____________________________  NHS No. _____________
HOSPITAL:________________________  DOB _____/_____/_____

Public Health England (PHE) is conducting enhanced national surveillance of invasive meningococcal disease (IMD) in England to monitor the impact of meningococcal vaccines in the national immunisation schedule. We would be grateful if you could complete the enclosed CLINICAL QUESTIONNAIRE for the above-named patient and return it to us by fax, email or in the pre-paid envelope provided, along with a copy of the patient’s HOSPITAL and INTENSIVE CARE (if admitted) discharge summaries.

Please complete the questionnaire and send us the requested information even if the patient has since been discharged, transferred to another hospital or died following the infection.

Could you please also arrange for a blood test for convalescent serology (2ml serum), ideally at 3-6 weeks after diagnosis, and send the sample to the Meningococcal Reference Unit (MRU) using the enclosed Sample Submission Form (MenSAM01)

Our contact details are on the top right-hand corner of this letter.
Thank you for your time and help.

Yours sincerely

Dr Shamez Ladhani  Professor Ray Borrow  Dr Mary Ramsay
Paediatric Infectious Diseases  Consultant Deputy Head, MRU  Head, Immunisation Department

Public Health England has approval under PIAG Section 60 of the Health and Social Care Act 2001 (now subsumed into the National Information Governance Board for Health and Social Care with Section 60, now Section 251 of the NHS Act 2006) to process confidential patient information for public health purposes (see http://www.legislation.hmso.gov.uk/si/si2002/20021438.htm).
Surveillance of Invasive Meningococcal Disease

Request for EDTA sample (≥ 5 year-olds)

Doctor ……………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………………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Appendix 3: Sample submission form (MenSAM01 December 2015)
# Surveillance of Invasive Meningococcal Disease

**Sample Submission Form**

**MenSAM01 version December 2015**

## Patient Information

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Name</td>
<td>____________________________</td>
</tr>
<tr>
<td>NHS No.</td>
<td>_____________</td>
</tr>
<tr>
<td>HOSPITAL</td>
<td>_______________________________</td>
</tr>
<tr>
<td>DOB</td>
<td>____ / ____ / ____</td>
</tr>
<tr>
<td>Name of Paediatrician</td>
<td>__________________________</td>
</tr>
</tbody>
</table>

## Blood Sample(s) for Meningococcal Surveillance

This form should be completed and sent with any blood sample taken for meningococcal surveillance. Please write the date when the sample was taken and tick the appropriate box.

**DATE Sample Taken:** ____ / ____ / ____

1. **ACUTE SAMPLES (ideally within 72 hours of starting treatment)**
   - [ ] Serum sample (2 mL) for acute antibody measurement
   - [ ] EDTA sample (2 mL) for non-culture meningococcal characterisation

2. **CONVALESCENT SAMPLE (ideally 3-6 weeks after diagnosis)**
   - [ ] Serum sample (2 mL) for convalescent antibody measurement

**Completed By:** __________________________ **Tel:**____________________ **Date:**...../...... /……

Thank you very much for your co-operation.

---

All samples should be sent through your local laboratory where they will be packaged in accordance with current transport and postal regulations, and **MUST BE ACCOMPANIED BY THIS FORM**

Please send **Sample(s) with Form** to:

Professor Ray Borrow, PHE Meningococcal Reference Unit, Manchester Medical Microbiology partnership, Clinical sciences Building, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WZ.
Tel: 0161 276 6793. E-mail: ray.borrow@phe.gov.uk.
(HAYS DX Meningococcal Reference Unit, DX 6962410, Manchester 90M)

**LAB use only (comments):**
Appendix 4: Clinical questionnaire (Form MENSV02, December 2015)
Enhanced National Surveillance of Meningococcal Disease
Clinical Questionnaire Form MENS02, December 2015

Patient Details
- Patient name: ____________________________ Date of Birth: ____________
- NHS Number: ____________________________
- PHE reference: __________________________

Section A: Reporter Details
- Date of completion of questionnaire: ____________
- Consultant responsible: ________________________
- Telephone number: __________________________ Email: _______________________

Section B: Demographics

B1 Ethnicity
- White / Black African / Black Caribbean / Indian / Pakistani / Bangladeshi / Chinese / Mixed/Other (specify):

B2 If born prematurely, gestation at birth: ____________ weeks

B3 Underlying Risk Factors
- None
- Asplenia / Splenic Dysfunction (including sickle cell disease)
- Known complement deficiency (including complement inhibitor therapy)
- Immunosuppression (including HIV)
- Comments: ________________________________

B4 Any other underlying medical condition: Yes □ No □
- Comments: ________________________________

B5 Travel abroad in the previous 28 days: Yes □ No □ NK □
- If yes, where & date of return:

B6 Recently entered UK? Yes □ No □ NK □
- If yes, country of origin & date of entry:
## Section C: Presentation/Clinical features

### C1 Date of onset of illness:

### C2 Date of hospital admission:

Time at Presentation: ____ : ____ am/pm

### C3 Date of hospital discharge:

### C4 Symptoms and signs at presentation: (tick all that apply)

**History**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Symptom</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (≥38°C)</td>
<td>Lethargy</td>
<td>Irritability</td>
</tr>
<tr>
<td>Sore throat/ coryza</td>
<td>Breathing difficulty</td>
<td>Bulging fontanelle</td>
</tr>
<tr>
<td>Reduced feeding/appetite</td>
<td>Apnoea</td>
<td>Headache</td>
</tr>
<tr>
<td>Thirst</td>
<td>Floppy muscle tone</td>
<td>Neck Stiffness</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>Leg pain</td>
<td>Photophobia</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>General aches</td>
<td>Confusion/delirium</td>
</tr>
<tr>
<td>Abnormal skin colour</td>
<td>Cold hands and feet</td>
<td>Drowsy</td>
</tr>
<tr>
<td>Rash</td>
<td>Bone joint pain/swelling</td>
<td>Seizures/Convulsions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unconscious</td>
</tr>
</tbody>
</table>

### C5 Examination on admission

**Tick all that apply**

- Fever: temp on admission [ ] [ ] [ ] °C
- Rash: [ ] If yes, please tick all that apply:
  - macular [ ] papular [ ] maculo-papular [ ] petechial [ ] purpuric [ ] fulminant [ ]
- Reduced GCS (state score if reduced):
- Seizure: [ ] Total seizure duration _____ mins [ ] focal or [ ] generalised [ ] Required anticonvulsants in A&E
- Signs of shock [ ] [ ] Required fluid boluses: total volume: _____________ ml/kg [ ] Required inotropes

*Signs of shock: Cap. Refill time >2 secs, tachycardia >160 beats/min, hypotension, pale/mottled skin, cold hands/feet, urinary output <2ml/kg/hr
Section D: Complete if admitted to PICU (attach discharge summary if available)

D1. Date of PICU admission: __/__/____ discharge: __/__/____

D2. Reason for admission: ________________________________

D3. Type of Support
   a) Ventilation  Yes  No  NK  If Yes No. days __________
   b) Inotropes  Yes  No  NK  If Yes No of days __________
   c) Haemofiltration  Yes  No  NK  If Yes No of days __________
   d) Surgical procedures  Yes  No  NK  If Yes, explain: __________

Section E: Lumbar Puncture (cross out this section if not applicable)

E1. If LP done, date: __/__/____ Time taken: _____ : _____ am/pm

E2. LP performed before ☐ or AFTER ☐ antibiotics?  If after, how many hours after? __________

E3. If No, state why: cardiovascular instability ☐ respiratory instability ☐ unable to ☐ other_______

E4. CSF WBC count ______ per mm$^3$  Neutrophils %  Lymphocytes %
   CSF RBC count ______ per mm$^3$  CSF protein ______ mg/dl
   CSF glucose _______ mmol/l  Plasma glucose ______ mmol/l

Section F: Blood Investigations (on admission)

F1. Full Blood count: Hb: _____ g/dL  WBC count _____ x10$^9$/L  Neutrophil count _____ x10$^9$/L
   Platelets _____ x10$^9$/L  C-reactive protein: _____ mg/L  Not done: ☐

F2. Liver Function Test: Bilirubin _____ mg/dL  Alanine Transaminase (ALT) _____ IU/L  Not done: ☐

F3. Urea and Electrolytes: Urea: _____ mmol/L  Creatinine: _____ mg/dL  Not done: ☐

F4. Clotting: APTT: _____ seconds  INR: _____  Not done: ☐

Section G: Treatment

G1. Antibiotics on admission: ________________________________
   Time of FIRST antibiotic dose: _____ : _____ am / pm
   Total duration of antibiotics: IV _________ (days) then oral: ___________ (days)

G2. Steroid given for meningitis diagnosis: Yes ☐  No ☐  NK ☐
   If yes, how many hours after the first antibiotic dose? _____________
### Section H: Please complete if any imaging performed

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Performed</th>
<th>Scan Normal?</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes  No  NK</td>
<td>Yes  No  NK</td>
<td></td>
</tr>
<tr>
<td>H1 Cranial Ultrasound</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H2 CT Head</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H3 MRI Head</td>
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<td></td>
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</tbody>
</table>

**H4 Major findings (you can please attach copy of report instead):**  

---

### Section I: Outcomes

11. Did the patient survive the infection? **Yes** ☐  **No** ☐  
   
   If died, date: ☐/☐/☐ ☜Cause of death: ☐/☐/☐

If survived:

12. Date of last follow-up: ☐/☐/☐

13. At follow-up, did the patient have any of the following?:
   
   a) Epilepsy        ☐ ☐ ☐
   b) Other Neurological complications ☐ ☐ ☐
   c) Amputations     ☐ ☐ ☐

If yes to (a)-(c) above, give details:

---

14. Date of hearing test: ☐/☐/☐  Any Hearing loss? **Yes** ☐  **No** ☐  **NK** ☐

   If yes, please indicate:
   - RIGHT EAR: Mild ☐  Moderate ☐  Severe ☐
   - LEFT EAR: Mild ☐  Moderate ☐  Severe ☐

### Section J: Additional Comments

---

**Thank you for taking the time to complete the Questionnaire**

*Please return the completed form to: Immunisation Department, Public Health England, 61 Colindale Avenue, London NW9 5EQ, UK.*

*Any questions? Please call or email us using meningoc@phe.gov.uk or the details provided on page 1.*