UK Health Security Agency

Meningococcal reference unit
User manual

November 2021

Contents

Executive summary

This document contains information on reference services for:

- *Neisseria meningitidis* (meningococcal) isolate characterisation
    - Capsular polysaccharide antigen detection (serogrouping)
    - Porin B (PorB) serotyping
    - Porin A (PorA) serosubtyping
    - Antimicrobial susceptibility testing
- meningococcal (and *Streptococcus pneumoniae*) DNA detection and meningococcal capsular grouping by real-time polymerase chain reaction (PCR)
- meningococcal serology including vaccine response (performed by the Vaccine Evaluation Unit (VEU))

Authorised By: Prof Ray Borrow (Deputy Head of Meningococcal reference unit)

Effective Date: November 2021

Introduction

Meningococcal reference unit overview

The Meningococcal reference unit (MRU) for England and Wales and Northern Ireland (NI) has been situated in Manchester since 1978. Originally established to provide phenotypic characterisation of meningococci isolated from cases of invasive meningococcal disease throughout the country, the nature and scope of the confirmation and surveillance activity has widened as has the range of tests available.

The MRU is located at the Manchester Royal Infirmary (MRI) and is an integral component of the Manchester Medical Microbiology Partnership (MMMP). The MMMP is part of the recently established Manchester University NHS Foundation Trust (MFT), formerly Central Manchester Foundation Trust (CMFT).

The MRU works closely with other parts of the UKHSA, particularly the Immunisation and Countermeasures Department based at Colindale, to optimise meningococcal disease ascertainment through enhanced surveillance, often with direct communication with UKHSA Health Protection teams.

Accredited to ISO 15189, the MRU has been a world leader in developing and making nationally available tests for non-culture case confirmation of meningococcal infection by PCR. Initially designed to identify the major disease-causing serogroups (A, B, C, Y and W), the test repertoire has been extended to provide more detailed additional characterisation utilising molecular techniques including DNA sequencing from cultured isolates and directly from clinical specimens, where possible. Since July 2010 all invasive disease isolates undergo whole genome sequence analysis.

The optimised surveillance, along with serological studies performed in the co-located Vaccine Evaluation Unit (VEU), were key elements in supporting and monitoring the successful introduction of the meningococcal serogroup C conjugate vaccine in the UK in 1999, the introduction of serogroup A conjugate vaccine in sub-Saharan Africa from 2010, and serogroup B (MenB) and ACWY vaccination in the UK in 2015, and have contributed significantly to establishing the international reputation of the MRU. In addition to providing confirmatory laboratory services and strain characterisation, staff from the MRU advise on the investigation and management of individual cases and outbreaks.

The MRU has been active in establishing and maintaining collaboratortive networks between national reference laboratories, collaborating to harmonise and optimise surveillance throughout Europe and sharing this experience with other interested groups worldwide. This has resulted in the establishment of the European Meningococcal and Haemophilus Disease Society (EMGM). The MRU supports work-packages in the European Centre for Disease Control (ECDC) Invasive Bacterial Diseases Laboratory Network (IBDlabnet), with particular regard to the provision of External Quality Assessment (EQA) in collaboration with UKHSA Colindale and UK NEQAS. The MRU was until recently a global reference laboratory for the World Health

Organization (WHO) Invasive Bacterial Diseases EQA but since 2013 has managed WHO EQA panels (with UKHSA and UK NEQAS) for WHO Regional, National and Sentinel Laboratories.

National meningococcal immunisation programmes

On the 1st September 2015, a MenB vaccine (Bexsero®) was added to the National Infant Immunisation Programme in England to help protect children against meningitis and septicaemia, which are serious and potentially fatal illnesses. Infants are offered the MenB vaccine with the other routine vaccinations at 2 months, 4 months and 12 months of age. Vaccinating infants at these times helps protect them when they are most at risk of developing MenB disease. Infants under 1 year of age are most at risk of MenB and the number of cases peaks at around 5 to 6 months of age.

The national surveillance protocol for invasive meningococcal disease in England has been extended in recognition of changes to the meningococcal group C conjugate (MCC) vaccination programme, including the removal of the infant MCC dose at 3 months and the introduction of an adolescent ACWY vaccine in August 2015.

There was a slow and steady increase in invasive meningococcal disease due to capsular group W (MenW) since 2009.

This increase was due to expansion of a single hyper-virulent strain belonging to the ST-11 clonal complex (cc11) and has been observed across all regions. MenW cases were not associated with travel, indicating that this strain was now endemic in England (Lucidarme J and others, 2015 (1)). Since 2011, MenW cases have been diagnosed across all age groups and are associated with a higher case fatality rate than the more common MenB cases.

Further information, with links to related resources, can be found at the meningococcal disease: guidance, data and analysis web page.

MRU services and resources

- clinical advice for case and outbreak investigation and management
- technical laboratory advice and support for large scale investigations and carriage studies
- meningococcal cultured isolate confirmation and characterisation
- meningococcal DNA detection by real-time PCR
- molecular characterisation from meningococcal isolates and non-culture material
- collection of >50,000 phenotypically characterised meningococcal isolates
- collection of >4,500 fully sequenced meningococcal case isolates (by whole genome sequencing)
- archive of thousands of meningococcal PCR-positive clinical samples (stored under HTA licence).
- electronic datasets of all laboratory-confirmed IMD cases since 1984
- support for collaborative scientific projects and audits
- takes part in a range of EQA activities.
- response to meningococcal vaccination (Vaccine Evaluation Unit)

Personnel and contact information

MRU postal addresses

DX address:

DX 6962410
Manchester 90 M

Courier address:

Meningococcal reference unit
UK Health Security Agency
Manchester Medical Microbiology Partnership
Clinical Sciences Building 2
Manchester Royal Infirmary,
Oxford Road
Manchester, UK
M13 9WL

Postal address (paper mail):

Meningococcal reference unit
UK Health Security Agency
Manchester Medical Microbiology Partnership
PO Box 209
Clinical Sciences Building 2
Manchester Royal Infirmary,
Oxford Road
Manchester, UK
M13 9WL

Telephone contacts

General laboratory results enquiries (Mon to Fri, 9am to 5pm):

+44 (0)161 276 8788

Select option 1 for authorised results for:

- meningococcal isolate characterisation (serotyping and sensitivities)
- meningococcal PCR
- pneumococcal PCR
- meningococcal serology (A, B, C, W,Y)

Technical or clinical enquiries (Mon to Fri, 10am to 3pm):

For MRU or VEU clinical advice use +44 (0)161 276 8788

Select option 4.

Alternatively, for technical or clinical enquires, use the telephone contact numbers for relevant MRU or VEU personnel (refer to Personnel page).

Out-of-hours enquiries:

For urgent enquiries out of hours, contact the Manchester University NHS Foundation Trust switch board on +44 (0)161 276 1234 and ask for the Medical Microbiologist on-call.

Personnel

Meningococcal reference unit: Technical laboratory enquiries	
• meningococcal isolate identification and phenotyping: speciation, serotyping and antibiotic susceptibility testing • meningococcal molecular detection or capsular grouping by real-time PCR • meningococcal molecular characterisation: gene sequencing, whole genome sequencing • meningococcal vaccine antigen detection • outbreak and cluster investigation	**For general results enquiries please see previous page** **Xilian Bai PhD** Pre-registration Clinical Scientist Tel: +44(0)161 276 6764 xilian.bai@phe.gov.uk **Jay Lucidarme PhD** Senior Scientist Tel: +44(0)161 276 6764 jay.lucidarme@phe.gov.uk **Stephen Clark PhD** Senior Scientist Tel: +44(0)161 276 5689 stephen.clark@phe.gov.uk
Meningococcal reference unit: Medical enquiries	
• patient investigation and clinical advice • clinical interpretation of laboratory results • outbreak management advice	**Prof Ray Borrow PhD., FRC/Path,** Consultant Clinical Scientist (HCPC: CS00231) Deputy Head of MRU Head of Vaccine Evaluation Unit (VEU) Tel: +44(0)161 276 8850 ray.borrow@phe.gov.uk

Vaccine Evaluation Unit (VEU)	
• vaccine evaluation, research and development • vaccine response assessment • vaccine research projects • service and molecular research projects	**Vaccine Evaluation Unit (VEU)** General enquiries- Serum bactericidal assays Tel: +44(0)161 276 6793 **Prof Ray Borrow PhD., FRC/Path,** Deputy Head of MRU Head of Vaccine Evaluation Unit (VEU) Tel: +44(0)161 276 8850 ray.borrow@phe.gov.uk
UKHSA Immunisation Division (Colindale)	
• immunisation and public health response queries	Clinical advice is available through the UKHSA Colindale Duty Doctor service. Dial 020 8200 4400 and ask for the duty doctor. Out of hours service is available on this number. Email Immunisation.Lead@phe.gov.uk

Meningococcal isolate characterisation

Species confirmation

Phenotypic confirmation of *Neisseria meningitidis* isolates based on morphology, conventional biochemical and serological reactions.

Meningococcal phenotyping

- serogroup: identification of capsular polysaccharide antigens by serological reactions: dot-blot ELISA using monoclonal antibodies (supplied by NIBSC). Co-agglutination using in-house polyclonal antibodies or commercial latex antigen kits may also be used to aid characterisation.
- serotype: identification of PorB (class 2 or 3) outer membrane proteins by in-house dot-blot ELISA using monoclonal antibodies (supplied by NIBSC)
- serosubtype: identification of PorA (class 1) outer membrane proteins by in-house dot-blot ELISA using monoclonal antibodies (supplied by NIBSC)

Meningococcal genotyping

Whole genome sequence (WGS) analysis: Since July 2010, all meningococcal case isolates undergo WGS as part of invasive meningococcal disease surveillance. The indexed genomic data is stored in Meningitis Research Foundation Meningococcus Genome Library.

WGS allows the characterisation of the majority of (if not all) meningococcal genes including typing and vaccine antigens. From this data, high resolution genomic analyses can be performed to determine the relatedness of isolates. This can be utilised in outbreak or cluster scenarios to support public health decisions. Sequencing on the Illumina platform is currently outsourced and is routinely performed on isolates in batches. Turn-around times for WGS can vary widely. However, WGS on isolates of particular interest can be expedited, if required.

Vaccine antigen sequencing: Whilst WGS provides characterisation of vaccine antigen genes, the lead time for WGS can vary. In urgent cases, individual characterisation of vaccine antigens (for example, Factor H-Binding Protein (fHbp) and PorA) can be performed by PCR-sequencing when requested.

Antibiotic susceptibility testing

Minimum Inhibitory concentrations (MICs) for benzylpenicillin, cefotaxime, rifampicin and ciprofloxacin are routinely determined using commercial gradient diffusion strip methodology and reported for all submitted isolates. Other antibiotic susceptibility tests may be available upon request.

Antimicrobial breakpoints are defined by The European Committee on Antimicrobial Susceptibility Testing (EUCAST). These breakpoints can be found on the EUCAST website.

Please note that it is not unusual to observe reduced susceptibility to penicillin for meningococcal case isolates. Approximately 30% of isolates show reduced susceptibility. However, if penicillin is used, effective therapeutic levels may be achieved. Please discuss with the MRU if there are concerns. Isolates with penicillin MICs > 0.5 mg/L should warrant further investigation.

PCR and molecular testing

Meningococcal screening and genogrouping assays

Meningococcal-specific real-time PCR (ABI Taqman™ or Roche LightCycler™ (Flow flex system)) assays are used to detect *N. meningitidis* DNA and determine the capsular group (genogroup) where possible.

The MRU screening assay is performed on all submitted PCR specimens. This 4-component multiplex assay comprises the following 4 gene targets:

- meningococcal *ctrA*: detects *N. meningitidis* DNA (encapsulated meningococci only) (Guiver and others, 2011; Gray and others, 2014; McHugh and others, 2015) (3,4,5)
- meningococcal *siaDB* (or *csb*): capsular group B-specific meningococcal DNA
- pneumococcal *ply*: *Streptococcus pneumoniae* DNA
- in-house internal control (IC): Added during extraction. Screening assay results valid only if IC is positive. A negative IC could indicate presence of PCR inhibitors

Upon confirmation of *ctrA* positivity **and** in the absence of *siaDB* positivity (probable non-group B meningococcus), secondary group-specific PCR assays based on capsular polysaccharide synthesis genes are used. Firstly, samples are tested for groups C (*siaDc/csc*), W (*siaDw/csw*) and Y (*siaDy/csy*). Finally, if still negative, a group A-specific (*mynA*) may be used, although group A disease or carriage is rare in the UK.

It is possible for low level positives (low DNA concentration) to be weakly positive with the sensitive ctrA screening assay but not detected with the specific siaD capsular grouping assays. Hence meningococcal DNA may be detected but genogroup not determined.

Pneumococcal detection

The samples found positive with the pneumolysin (*ply*) PCR screen in the 4-component multiplex PCR assay are tested for confirmation using a pneumococcal specific autolysin (*lytA*) PCR. Samples found to be positive with both ply and *lytA* are reported as pneumococcal PCR positive.

Samples that are positive for *ply* alone may indicate detection of a non-pneumococcal streptococcal species and are reported as pneumococcal PCR negative.

DNA from pneumococcal carriage can be detected in the blood samples of children under the age of 2 years. Consequently, clinical interpretation of the molecular results is recommended for all positive pneumococcal reports among children less than 2 years of age (Dagan and others, 1998 (6)). A comment is made therefore on all MRU pneumococcal PCR positive reports for children <2 years to that effect.

Meningococcal serology (VEU)

The following serum bactericidal antibody (SBA) assays are performed by the Vaccine Evaluation Unit (VEU), co-located with the MRU at Manchester Royal infirmary.

MenACWY rSBA

This assay measures functional (bactericidal) antibody titres against capsular polysaccharide among group A, C, Y or W meningococcal control strains. The assay utilises baby rabbit serum as an exogenous complement source. An rSBA titre of ≥1:8 is the internationally recognised surrogate for protection against group C strains.

MenB hSBA

This assay measures functional (bactericidal) antibody titres against sub-capsular protein antigens expressed by a panel of serogroup B meningococcal strains. This assay utilises exogenous human complement. An hSBA titre of ≥4 is the internationally recognised surrogate for protection against group B strains.

Serodiagnosis of meningococcal disease is not available.

MRU clinical specimen archive

In 2006, the MRU began storing a sub-set of meningococcal PCR-positive clinical specimens under an MMMP HTA licence for the purposes of quality control, assay development, epidemiological investigations or experimental research. In more recent years, all residual PCR-positive clinical material from living persons (at time of collection) is retained under the licence.

The specimens in this archive are available for use in relevant external projects with appropriate ethical approvals. Please contact Personnel page for further information. Details on MRU specimen retention and HTA compliance can be found in the Data and Tissue Handling Section (Page 24).

Submitting samples to the MRU

Submitting meningococcal cultures/isolates

Suspected meningococcal isolates must be submitted along with a completed UKHSA MRU Request Form in accordance with the MMMP Specimen Acceptance Policy. Please refer to page 8 for MRU postal addresses.

Please send pure, viable cultures from all positive sites of invasive meningococcal disease cases: sterile (such as CSF, blood, joint fluids) and any non-sterile sites (for example, nose, throat, bronchial lavage, sputum), if available. Meningococcal isolates from genitourinary tracts should not be routinely submitted unless they appear resistant (penicillin MICs of > 0.25 mg/L and/or ciprofloxacin MICs >0.03 mg/L) or are clinically significant (in particular urethritis/proctitis, Brooks and others, 2020 (2)) or believed to be epidemiologically-linked to cases of invasive disease.

Neisseria gonorrhoeae reference services are provided by the AMRHAI (antimicrobial resistance and healthcare associated infections) reference unit, UKHSA Colindale. Refer to AMRHAI Reference Unit's reference and diagnostic services for submission requirements.

Slopes (preferred)

The preferred media for transport of cultures are agar slopes (chocolate (heated) blood agar slopes, blood agar slopes or Dorset egg slopes) after establishing growth by overnight incubation at 37 ºC. Short-term storage of sloped cultures at 30 ºC is optimal if there are delays before submission. Should it be necessary to submit an un-incubated culture, apply a heavy inoculum to ensure survival of the organism during transport. Please indicate on the request form if the material (slope) has not been incubated.

Swabs

Specific transport swabs in Amies medium are accepted, although the presence of charcoal may interfere with direct, rapid agglutination reactions if urgent results are required. The use of liquid transport swabs is not recommended as there is a risk of leakage during transport and receipt. Liquid transport systems for (automated) clinical investigation may not be appropriately designed for pure culture shipment: If in doubt please discuss with MRU staff before submission.

Frozen suspensions

If you wish to submit meningococcal isolates as frozen liquid suspensions, please contact senior MRU staff (see Personnel) beforehand to ensure material is received or stored appropriately. Frozen liquid suspensions (for example microbead storage systems) is the preferred method for transport of large batches of isolates (for example for research studies). When sending frozen liquid suspensions, special attention must be made to the appropriate packaging and transportation requirements (refer to MMMP Specimen Acceptance Policy).

Other media

If you wish to submit meningococcal cultures on any other type of media, please contact senior MRU staff (see Personnel) beforehand to discuss.

Submitting specimens for PCR testing

Samples for PCR testing must be sent alongside a completed MRU Request Form in accordance with the MMMP Specimen Acceptance Policy. Please refer to page 8 for MRU postal addresses.

PCR sample collection

A minimum of 400 µL (0.4 mL) of fluid (for example EDTA, CSF) is required for extraction without dilution. Smaller volumes will be diluted as required and resulting in reduced detection sensitivity. Greater volumes (up to 2 mL) are preferred to allow repeat testing.

It is recommended that samples for meningococcal PCR are collected less than 48 hours following disease onset, admission to hospital or administration of antibiotics. The likelihood of a positive PCR result decreases with time following antimicrobial administration. Blood samples for PCR taken more than 48 hours after commencement of antibiotic therapy are unlikely to remain positive, however, CSF may remain positive for longer periods.

PCR sample storage

Samples should be stored at 4ºC (not frozen) prior to transport. Freeze-thawing may reduce the likelihood of positivity with low genome copy samples and can result in cracked or broken containers.

Preferred PCR sample types

The MRU DNA extraction platforms and PCR assays have been validated for:

- whole blood (EDTA)
- coagulated whole blood
- CSF
- serum
- plasma
- joint fluids

Whole blood EDTA is preferred, although heparinised or citrated bloods can be tested. Plasma or serum can be tested, although sensitivity may be compromised. Only the serum fraction of coagulated bloods can be tested.

Original CSF (uncentrifuged) or re-suspended CSF deposits are preferred to CSF supernatants in order to increase the sensitivity of detection. Definitive laboratory confirmation of meningococcal meningitis can only be made by analysis of a CSF sample.

Other PCR sample types

DNA extracts from primary molecular laboratories are accepted, however, the submitted extract would be put through the in-house DNA extraction process so that the internal PCR control is added to the sample. Some sensitivity may be lost due to this additional extraction process.

Other specimens from normally sterile sites (for example tissue samples or blocks) may be examined after prior consultation with the MRU. They are not currently considered a routine investigation as they require bespoke manual processing with concomitant increases in turnaround time. The results from such samples should be considered 'unvalidated' and interpreted as such.

Blood culture bottle fluid (from automated culture detection systems) can be tested but will require an additional purification step to remove PCR inhibitors. As such, the detection sensitivity may be reduced. As with all samples, please ensure that culture bottle fluid is clearly identified as such. This is especially important owing to the additional safety risks associated with this sample.

Repeat or additional testing

Additional testing can be requested by telephone or letter. Please note, additional testing is subject to sufficient sample volume being available.

Urgent MRU specimens (submitted via courier)

Arrangements to accept urgent couriered samples must be agreed with the MRU before the samples are despatched. Failure to do so may result in the specimen(s) being lost or not being tested in a timely fashion.

Submitting samples via an OVERNIGHT courier to arrive from 8:30am the following day has proven to be the most reliable transport.

Sending urgent specimens out of hours

We strongly discourage sending urgent couriered samples for delivery out of hours (after 5:30pm, Monday to Friday, at weekends, or on Bank Holidays). If unavoidable, specimens should be labelled as urgent and addressed to the 'Virologist On-Call' or 'Microbiologist' 'On-Call'. The specimen should be left at the Manchester Royal Infirmary Autolab reception (the ground floor of Clinical Sciences Building 2, or the drop-off point or 'hatch' of Autolab, accessible via the Main Boulevard under the link-bridge).

Submitting samples to the VEU for meningococcal serology

For serum bactericidal antibody (SBA) assays, all samples should be submitted along with the completed Vaccine Preventable Serology request form in accordance with the MMMP Specimen Acceptance Policy.

A minimum sample volume of clotted blood or serum of 500 µL is required. Post-vaccination samples of clotted blood or serum should be collected 3 to 8 weeks following vaccination.

It is important that the patient's relevant immunisation details, eculizumab therapy or any current antibiotics are recorded on the request form.

Turnaround times and result reporting

The estimated turnaround times for MRU services are outlined in the table below. These are given as a general guide and may vary widely depending on the time of receipt, sample type and the analyses performed.

All times include working days only (Monday to Friday)

Service	Time to provisional telephone result	Time to final printed report
Meningococcal isolate characterisation	24 to 72 hours (serogroup only)	7 to 10 working days (serogroup and susceptibilities)
Meningococcal PCR testing	24 hours	48 hours
Meningococcal serology - serum bactericidal antibody (SBA) assay (performed by Vaccine Evaluation Unit)	N/A	28 working days

PCR samples must be received at the MRU by 10am weekdays to be tested the same working day. PCR negative and meningococcal group B positive results are typically available within 24 hours of receipt. Results on samples requiring additional meningococcal genogrouping or pneumococcal PCR (*lytA*) confirmation are typically available within 48 hours of sample receipt.

Results are telephoned up to 5:30pm or the following morning of the next working day. Urgent samples may be processed more rapidly provided the laboratory is notified in advance of receipt.

From late 2018 there has been a phased roll-out of MRU eLab (electronic) reporting for submitting laboratories in order to reduce reporting and therefore overall turnaround times. Contact Mr Mark Hasselholdt for MRU eLab enquiries. mark.hasselholdt@phe.gov.uk

Although hardcopies of the PCR results are sent to the local Health Protection Team (HPT) based on the patient's postcode, it is currently the responsibility of the requesting laboratory to inform their local Consultant in Communicable Disease (CCDC) or HPT of positive meningococcal PCR results in an appropriate, timely fashion.

Charges

MRU charges

Isolate characterisation and meningococcal PCR testing are provided free of charge for users in England and Wales.

Users from Northern Ireland and other countries will be charged for PCR testing.

VEU charges

Users will be charged for meningococcal serology requests (vaccine response testing) if not initiated as part of an MRU or UKHSA epidemiological or case investigation. Current prices can be obtained from Mr Mark Hasselholdt (mark.hasselholdt@phe.gov.uk).

Sample packaging and transportation

MMMP Specimen Acceptance Policy

All samples submitted to the MRU or VEU must meet the requirements of the MMMP Specimen Acceptance Policy. Failure to meet these criteria may result in delays in testing.

Sample transportation

It is the responsibility of senders to comply with the current transport legislation and safety recommendations. All samples must be submitted in packaging appropriate for the transport of biological substance category B (UN3373). Refer to IATA category B Packing Instruction 650. Please contact MRU staff for guidance regarding sample packaging or transportation of meningococcal cultures and PCR samples.

MRU request form (cultures and PCR samples)

All culture and PCR samples should be submitted along with the completed the MRU request form.

Please ensure **all** essential information (as indicated on the form) is provided and that any information matches the information on the corresponding sample or culture label. If important

information is missing, or there are discrepancies, sending laboratories may be need to be contacted which could result in a delay in testing.

VEU request form (meningococcal serology)

All serology samples should be submitted along with the completed the VEU request form.

Please ensure all information matches the information on the corresponding sample label. If important information is missing, or there are discrepancies, sending laboratories may be need to be contacted which could result in a delay in testing.

Data and tissue handling

MRU policies strictly adhere to the guidelines set out in the relevant data and tissue handling legislation, including the Caldicott Report (1997) and the Human Tissue Act (2004).

Data handling

The recommendations of the Caldicott Report (1997) and The General Data Protection Regulation GDPR (2016) have been adopted by UKHSA and by the National Health Service as a whole. These recommendations relate to the security of patient identifying data (PID) and the uses to which they are put. MRU, as an integral part of Manchester Medical Microbiology Partnership, observes Caldicott guidance in handling PID. The MMMP has appointed its own Caldicott Guardian who advises on confidentiality issues and is responsible for monitoring the physical security of PID. This also applies to the transfer of results of investigations to and from MMMP, whether by mail services, telephone or fax. The value of 'safe haven' arrangements or other means of the sender and receiver of information identifying themselves to each other before data are transferred is emphasized.

MMMP audits the security of its PID in collaboration with its customers. Customers are invited to review our arrangements in conjunction with the Caldicott Guardian. Customers are also asked to draw to the Caldicott Guardian's attention any instances where PID security has been threatened or has broken down. Uses that PID are put to outside clinical diagnostic services generally allow patient identifiers to have been removed before hand, and when PID is used for research purposes the proposals are considered first by the National Research Ethics Committee. All enquiries about the security and use of PID should be addressed to the Caldicott Guardian, William Welfare (Tel: 0161 234 9473), e-mail william.welfare@phe.gov.uk

Data containing patient information will not be sent using fax. Sending patient information via email is discouraged. Only email accounts that can guarantee data encryption (secure or closed email systems) are used for this purpose.

Human Tissue Act (HTA) compliance

The MRU adheres to the HTA and its application within the Manchester University NHS Foundation Trust site.

Tissue samples (such as CSF, whole blood, joint fluid) from patients are submitted to the MRU with their consent (obtained at time of sampling) for disease confirmation, epidemiological or public health investigations. Samples are tested and retained in accordance with the MRU specimen retention policy. Any residual original sample is retained for 1 year following initial processing.

Since 2006 in accordance with the HTA, post mortem samples or samples from the deceased (patients known by the MRU to have died at the time of submission) have been returned if requested or destroyed sensitively.

Where possible, all meningococcal PCR positive residual clinical samples (from persons living at time of collection) are retained for quality control, assay development or epidemiological investigation under the local Research and Development HTA license.

Should it be necessary to contact the MRU regarding a HTA issue, the nominated persons within MMMP are: Research and Development Person Designated (PD) is Professor Ray Borrow and Post Mortem PD (MFT Bacteriology), Mr Ben Kirkman (Tel. 0161 276 8851).

References

1 Lucidarme J and others. 2015. Genomic resolution of an aggressive, widespread, diverse and expanding meningococcal serogroup B, C and W lineage. Journal of Infection 2015 volume 71 issue 5 pages 544-52.

2 Brooks A and others. Detection of the United States Neisseria meningitidis urethritis clade in the UK and the emergence of multiple antibiotic resistance – a call for vigilance. Eurosurveillance 2020 volume 25 issue 15.

3 Guiver M and others. Modifications to a Published ctrA PCR Assay for the Improved Non-Culture Confirmation of Meningococcal Disease in England and Wales. Meningitis Research Foundation meningitis and septicaemia in children and adults conference 4-5 November 2011, London, UK. Poster abstract.

4 Gray SJ and others. Quality improvements for the non-culture (PCR) confirmation of meningococcal disease in England. XVIIIth International Pathogenic Neisseria Conference (IPNC), Wuerzburg, Gemany, 9-14 September 2014. Poster abstract 121, page 261.

5 McHugh MP and others. Reduced turnaround time and improved diagnosis of invasive serogroup B Neisseria meningitidis and Streptococcus pneumoniae infections using a lyophilized quadruplex quantitative PCR. Journal of Medical Microbiology 2015 volume 64 issue 11 pages 1321-1328.

6 Dagan R and others. Prospective study to determine clinical relevance of detection of pneumococcal DNA in sera of children by PCR. Journal of Clinical Microbiology 1998 volume 36 issue 3 pages 669-673.

7 World Health Organization. Laboratory Methods for the Diagnosis of Meningitis caused by Neisseria meningitidis, Streptococcus pneumoniae , and Haemophilus influenzae. WHO Manual, 2nd Edition. World Health Organization, 2011.

About the UK Health Security Agency

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