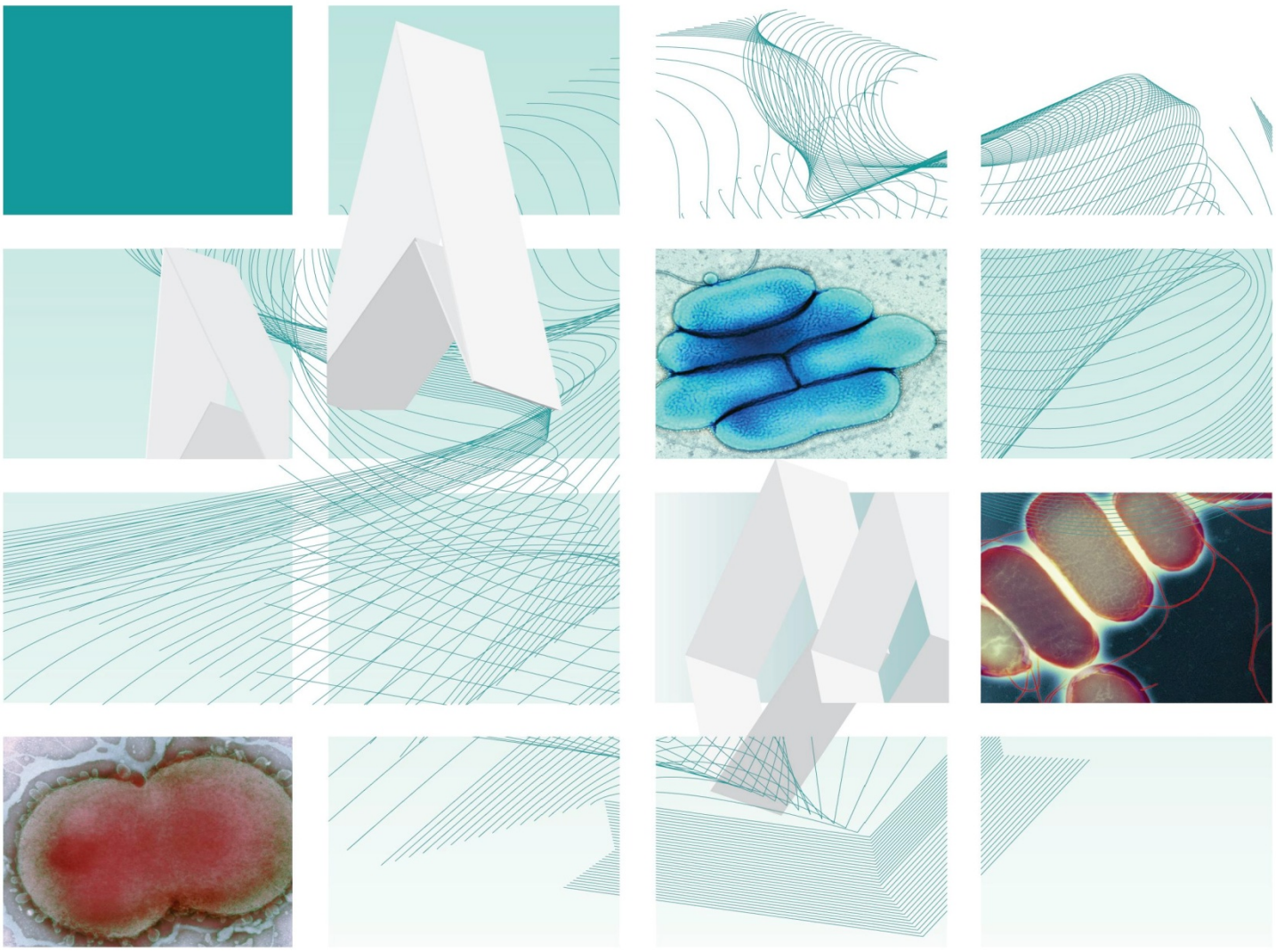
Public Health England

NHS

UK Standards for Microbiology Investigations

Screening for *Neisseria meningitidis*



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Acknowledgments

UK Standards for Microbiology Investigations (SMIs) are developed under the auspices of Public Health England (PHE) working in partnership with the National Health Service (NHS), Public Health Wales and with the professional organisations whose logos are displayed below and listed on the website http://www.hpa.org.uk/SMI/Partnerships. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see http://www.hpa.org.uk/SMI/WorkingGroups).

The contributions of many individuals in clinical, specialist and reference laboratories who have provided information and comments during the development of this document are acknowledged. We are grateful to the Medical Editors for editing the medical content.

For further information please contact us at:

Standards Unit
Microbiology Services
Public Health England
61 Colindale Avenue
London NW9 5EQ
E-mail: standards@phe.gov.uk

Website: http://www.hpa.org.uk/SMI

UK Standards for Microbiology Investigations are produced in association with:

Contents

Amendment Table

Each SMI method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from standards@phe.gov.uk.

New or revised documents should be controlled within the laboratory in accordance with the local quality management system.

Amendment No/Date.	3/12.03.14
Issue no. discarded.	1.2
Insert Issue no.	2
Section(s) involved	**Amendment**
Whole document.	Document has been transferred to a new template to reflect the Health Protection Agency's transition to Public Health England. Front page has been redesigned. Status page has been renamed as Scope and Purpose and updated as appropriate. Professional body logos have been reviewed and updated. Standard safety and notification references have been reviewed and updated. Name changed to 'Screening for *Neisseria meningitidis'* from 'Screening for meningococci'. Minor textual and formatting changes.
Scope.	Type of specimen - Naso and Pernasal swabs removed, Nasopharyngeal swabs added. Scope - expanded to include when to screen for *Neisseria meningitidis*. Hyperlinks to other relevant SMI added.
Introduction.	Updated to include routes of transmission and risk factors, PHE and NICE guidelines, and information regarding serogroups. Updated carriage, spectrum of disease and epidemiology sections.
Safety considerations.	Restructured and reworded in line with new template. Safety consideration statements regarding *N. meningitidis* updated; processing of samples can be carried out at containment level 2. Standard safety references have been reviewed

	and updated.
Referral to Reference Laboratories.	Text updated, links for Scotland and Ireland added.
Notification to PHE or equivalent in the devolved administrations.	Reference updated, reference to Northern Ireland added.
Appendix 1.	Addition of Appendix 1 – Flowchart.
References.	References reviewed and updated.

Amendment No/Date.	2/01.08.12
Issue no. discarded.	1.1
Insert Issue no.	1.2
Section(s) involved	**Amendment**
Whole document.	Document presented in a new format. The term “CE marked leak proof container” is referenced to specific text in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) and to the Directive itself EC[1,2]. Edited for clarity. Reorganisation of [some] text. Minor textual changes.
Sections on specimen collection, transport, storage and processing.	Reorganised. Previous numbering changed.
References.	Some references updated.

UK SMI[#]: Scope and Purpose

Users of SMIs

Primarily, SMIs are intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK. SMIs also provide clinicians with information about the available test repertoire and the standard of laboratory services they should expect for the investigation of infection in their patients, as well as providing information that aids the electronic ordering of appropriate tests. The documents also provide commissioners of healthcare services with the appropriateness and standard of microbiology investigations they should be seeking as part of the clinical and public health care package for their population.

Background to SMIs

SMIs comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages. Syndromic algorithms are supported by more detailed documents containing advice on the investigation of specific diseases and infections. Guidance notes cover the clinical background, differential diagnosis, and appropriate investigation of particular clinical conditions. Quality guidance notes describe laboratory processes which underpin quality, for example assay validation.

Standardisation of the diagnostic process through the application of SMIs helps to assure the equivalence of investigation strategies in different laboratories across the UK and is essential for public health surveillance, research and development activities.

Equal Partnership Working

SMIs are developed in equal partnership with PHE, NHS, Royal College of Pathologists and professional societies. The list of participating societies may be found at http://www.hpa.org.uk/SMI/Partnerships. Inclusion of a logo in an SMI indicates participation of the society in equal partnership and support for the objectives and process of preparing SMIs. Nominees of professional societies are members of the Steering Committee and Working Groups which develop SMIs. The views of nominees cannot be rigorously representative of the members of their nominating organisations nor the corporate views of their organisations. Nominees act as a conduit for two way reporting and dialogue. Representative views are sought through the consultation process. SMIs are developed, reviewed and updated through a wide consultation process.

Quality Assurance

NICE has accredited the process used by the SMI Working Groups to produce SMIs. The accreditation is applicable to all guidance produced since October 2009. The process for the development of SMIs is certified to ISO 9001:2008. SMIs represent a good standard of practice to which all clinical and public health microbiology laboratories in the UK are expected to work. SMIs are NICE accredited and represent

[#] Microbiology is used as a generic term to include the two GMC-recognised specialties of Medical Microbiology (which includes Bacteriology, Mycology and Parasitology) and Medical Virology.

neither minimum standards of practice nor the highest level of complex laboratory investigation possible. In using SMIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. SMIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. SMIs also provide a reference point for method development. The performance of SMIs depends on competent staff and appropriate quality reagents and equipment. Laboratories should ensure that all commercial and in-house tests have been validated and shown to be fit for purpose. Laboratories should participate in external quality assessment schemes and undertake relevant internal quality control procedures.

Patient and Public Involvement

The SMI Working Groups are committed to patient and public involvement in the development of SMIs. By involving the public, health professionals, scientists and voluntary organisations the resulting SMI will be robust and meet the needs of the user. An opportunity is given to members of the public to contribute to consultations through our open access website.

Information Governance and Equality

PHE is a Caldicott compliant organisation. It seeks to take every possible precaution to prevent unauthorised disclosure of patient details and to ensure that patient-related records are kept under secure conditions. The development of SMIs are subject to PHE Equality objectives http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317133470313.

The SMI Working Groups are committed to achieving the equality objectives by effective consultation with members of the public, partners, stakeholders and specialist interest groups.

Legal Statement

Whilst every care has been taken in the preparation of SMIs, PHE and any supporting organisation, shall, to the greatest extent possible under any applicable law, exclude liability for all losses, costs, claims, damages or expenses arising out of or connected with the use of an SMI or any information contained therein. If alterations are made to an SMI, it must be made clear where and by whom such changes have been made.

The evidence base and microbial taxonomy for the SMI is as complete as possible at the time of issue. Any omissions and new material will be considered at the next review. These standards can only be superseded by revisions of the standard, legislative action, or by NICE accredited guidance.

SMIs are Crown copyright which should be acknowledged where appropriate.

Suggested Citation for this Document

Public Health England. (2014). Screening for *Neisseria meningitidis*. UK Standards for Microbiology Investigations. B 51 Issue 2. http://www.hpa.org.uk/SMI/pdf.

Scope of Document

Type of Specimen

Oropharyngeal swabs, nasopharyngeal swabs

Scope

This SMI describes the investigation of swabs for the presence of *Neisseria meningitidis.*

Screening for *Neisseria meningitidis* (the meningococcus) should be performed when investigating a suspected case of meningococcal disease, for screening contacts of a case, and in outbreak situations to determine the extent of carriage and/or the need for prophylaxis.

B 5 - Investigation of Nose Swabs, B 9 - Investigation of Throat Swabs and ID 6 - Identification of *Neisseria* species are recommended for additional background information.

This SMI should be used in conjunction with other SMIs.

Introduction

Neisseria meningitidis forms part of the normal nasopharyngeal flora. Person to person transmission is the only known route of acquisition and usually occurs via aerosol droplets or secretions from the upper respiratory tract of an asymptomatic carrier or a close contact with invasive meningococcal disease[3]. The majority of cases (97%) of meningococcal disease which occur in the UK are sporadic, close contacts of a case are however recognised to be at an increased risk of infection[4]. To prevent onward transmission of virulent meningococci, prophylaxis (antibiotic chemoprophylaxis and vaccination if appropriate) is recommended for such contacts. The aim is to eliminate carriage of the virulent organism from the case's immediate social network. PHE recommends that nasopharyngeal swabs should be collected from all suspected cases, and the request form should specify that *N. meningitidis* is being sought[4-7]. NICE guidelines for the management of bacterial meningitis do not however recommend the use of throat swabs for the investigation of meningococcal disease in children under 16[8]. Management of outbreaks of meningococcal disease and prophylaxis is usually led by the consultant in communicable disease control (CCDC) or consultant in public health medicine (CPHM)[4].

Characterisation of the causative organism is an important consideration in outbreak management, as it determines whether cases may be related and whether vaccination of contacts may be necessary. The use of intravenous antibiotics in the community prior to hospital admission may decrease the yield of *N. meningitidis* from blood and CSF samples, nasopharyngeal swabs are less affected by prior antibiotic therapy and have been shown to yield *N. meningitidis* in 40-50% of clinical cases[4]. Confirmation of cases by non-culture (molecular) methods does not provide isolates for typing and determination of antimicrobial susceptibilities. Isolation of the organism from diagnostic or screening swabs from cases and close contacts may therefore be necessary for strain identification. Typing is important for outbreak investigations and surveillance, for the national serogroup C meningococcal vaccination programme and for detection of vaccine failures[9].

Carriage

N. meningitidis is carried on the posterior pharyngeal wall and can be detected from oropharyngeal or nasopharyngeal swabs[10]. Specimens for meningococcal screening are from two types of individuals: those infected and who may have been treated with antibiotics; and untreated asymptomatic contacts of the index case. Oropharyngeal swabs (sampling the posterior pharyngeal wall through the mouth) are ideal, but nasopharyngeal swabs (although they may be difficult to obtain) are also acceptable.

The carriage rate in the general population has been estimated to be around 10%[11]. This may be substantially higher in teenagers (25%) and young adults (32%), probably as a result of increased social activities leading to inhalation of infected respiratory secretions and by direct contact (kissing)[3,11]. Carriage rates may also be higher in close contacts of a case, in closed or semi-closed communities such as military establishments and university students, during mass public gatherings (eg the Hajj pilgrimage) and particularly during outbreaks[12]. The risk of carriage also increases with damage to the nasopharyngeal mucosa from smoking (and passive smoking) and from co-infection with influenza and *Mycoplasma* species[11]. Chemoprophylaxis should be offered to close contacts of a case who have had prolonged close contact (eg those in a household setting), and to those who have had transient close contact but who have been exposed to large droplets or secretions from the respiratory tract at the time of case admission to hospital[4]. Where there is more than one case the decision on when to extend prophylaxis will be taken by the CCDC.

Spectrum of Disease

Infection with *N. meningitidis* produces a wide spectrum of disease manifestations ranging from a mild illness with transient fever and bacteraemia to fulminant meningococcal sepsis characterised by a rapidly progressive, widespread purpuric skin rash, coagulation defects, septic shock and death within a few hours of onset of symptoms[11]. Other presentations include a predominantly meningitic illness which may or may not be accompanied by a purpuric rash, primary meningococcal arthritis, pneumonia, conjunctivitis and, more rarely sinusitis, endocarditis and necrotising fasciitis[13-15]. Occasionally a more chronic picture may be encountered in association with positive blood cultures often with cutaneous lesions and arthritis.

N. meningitidis may also be isolated from the lower genital tract or rectum in men and women during screening for gonorrhoea and may be implicated in genital tract infections[16,17]. Rare deficiencies of the later stages of the complement and properdin pathway (or treatments that inhibit the complement pathway) can predispose to recurrent infections with uncommon *N. meningitidis* serogroups, non-groupable meningococci and *Neisseria*-related bacteria presenting as meningococcal disease[18]. Disseminated meningococcal infection, although rare, may also be found in patients who are infected with HIV[19].

Epidemiology

Meningococcal disease occurs worldwide. Thirteen serogroups have been identified (based on unique capsular polysaccharides), six of which cause the majority of infections (A, B, C, W135, X and Y)[20]. Serogroup B is the most prevalent serogroup in the UK followed by serogroup C[21,22]. Incidence of invasive serogroup Y in the UK has increased over recent years. Natural immunity in the population to group W135 and Y meningococci has been shown to be low across all age groups[23].

The incidence and case fatality are highest in infants less than one year of age in whom the signs of early infection may be more difficult to detect[8,21,22]. There is a second but lower peak of infection in the 15-24 year age group and a seasonal peak in the winter months[24].

Technical Information/Limitations

Limitations of UK SMIs

The recommendations made in UK SMIs are based on evidence (eg sensitivity and specificity) where available, expert opinion and pragmatism, with consideration also being given to available resources. Laboratories should take account of local requirements and undertake additional investigations where appropriate. Prior to use, laboratories should ensure that all commercial and in-house tests have been validated and are fit for purpose.

Selective Media in Screening Procedures

Selective media which does not support the growth of all circulating strains of organisms may be recommended based on the evidence available. A balance therefore must be sought between available evidence, and available resources required if more than one media plate is used.

Specimen Containers[1,2]

SMIs use the term “CE marked leak proof container” to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: “The design must allow easy handling and, where necessary, reduce as far as possible contamination of, and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes”.

1 Safety Considerations[1,2,25-39]

1.1 Specimen Collection, Transport and Storage[1,2,25-28]

Use aseptic technique.

Collect swabs into appropriate transport medium.

Transport swabs in transport medium in sealed plastic bags.

Compliance with postal, transport and storage regulations is essential.

1.2 Specimen Processing[1,2,25-39]

N. meningitidis is a Hazard Group 2 organism and the processing of diagnostic samples can be carried out at Containment Level 2.

Due to the severity of the disease and the risks associated with generating aerosols of the organism, any manipulation of suspected isolates of *N. meningitidis* should always be undertaken in a microbiological safety cabinet until *N. meningitidis* has been ruled out (as must any laboratory procedure giving rise to infectious aerosols)[31].

N. meningitidis can cause severe and sometimes fatal disease. Laboratory acquired infections have been reported[40,41]. The organism infects primarily by the respiratory route. An effective vaccine is available for some meningococcal groups.

Refer to current guidance on the safe handling of all organisms documented in this SMI.

The above guidance should be supplemented with local COSHH and risk assessments.

2 Specimen Collection

2.1 Type of Specimens

Oropharyngeal swabs, nasopharyngeal swabs

2.2 Optimal Time and Method of Collection[42]

For safety considerations refer to Section 1.1.

Unless otherwise stated, swabs for bacterial and fungal culture should then be placed in appropriate transport medium[43-47].

2.3 Adequate Quantity and Appropriate Number of Specimens[42]

N/A

3 Specimen Transport and Storage[1,2]

3.1 Optimal Transport and Storage Conditions

For safety considerations refer to Section 1.1.

Collect specimens before antimicrobial therapy where possible[42].

Specimens should be transported and processed as soon as possible[42].

Recovery of meningococci is compromised if culture is delayed[10].

If processing is delayed, refrigeration is preferable to storage at ambient temperature[42].

Direct plating when the swab is taken should be considered.

4 Specimen Processing/Procedure[1,2]

4.1 Test Selection

N/A

4.2 Appearance

N/A

4.3 Sample Preparation

N/A

4.4 Microscopy

N/A

4.5 Culture and Investigation

Inoculate each plate with swab. (Q 5 - Inoculation of Culture Media for Bacteriology).

For the isolation of individual colonies, spread inoculum with a sterile loop.

4.5.1 Culture media, conditions and organisms

Clinical details/ conditions	Specimen	Standard media	Incubation			Cultures read	Target organism(s)
			Temp °C	Atmos	Time		
Screening for *N. meningitidis* case or contact	Swab	GC selective agar	35-37	5-10% CO2	40-48hr	daily	*N. meningitidis*

4.6 Identification

Refer to individual SMIs for organism identification.

4.6.1 Minimum level of identification in the laboratory

Neisseria species	species level ID 6 - Identification of *Neisseria* species

Organisms may be further identified if this is clinically or epidemiologically indicated.

4.7 Antimicrobial Susceptibility Testing

Refer to British Society for Antimicrobial Chemotherapy (BSAC) and/or EUCAST guidelines.

4.8 Referral for Outbreak Investigations

N/A

4.9 Referral to Reference Laboratories

For information on the tests offered, turn around times, transport procedure and the other requirements of the reference laboratory click here for user manuals and request forms.

Organisms with unusual or unexpected resistance and whenever there is a laboratory or clinical problem, or anomaly that requires elucidation should be sent to the appropriate reference laboratory.

Contact appropriate devolved nation reference laboratory for information on the tests available, turn around times, transport procedure and any other requirements for sample submission:

England and Wales
http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1158313434370?p=1158313434370

Scotland

http://www.hps.scot.nhs.uk/reflab/index.aspx

Northern Ireland

http://www.publichealth.hscni.net/directorate-public-health/health-protection

Refer *N. meningitidis* for confirmation of identification, typing and susceptibility testing.

5 Reporting Procedure

5.1 Microscopy

N/A

5.2 Culture

Negative

N. meningitidis not isolated.

Positive

N. meningitidis isolated and report serogroup if known or state “Further identification to follow”.

5.2.1 Culture reporting time

Clinically urgent culture results to be telephoned or sent electronically when available.

Interim/final written report, 16 – 72hr stating, if appropriate, that a further report will be issued.

5.3 Antimicrobial Susceptibility Testing

Report susceptibilities as clinically indicated. Prudent use of antimicrobials according to local and national protocols is recommended.

6 Notification to PHE[48,49] or Equivalent in the Devolved Administrations[50-53]

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify Public Health England (PHE) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days.

For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local PHE Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

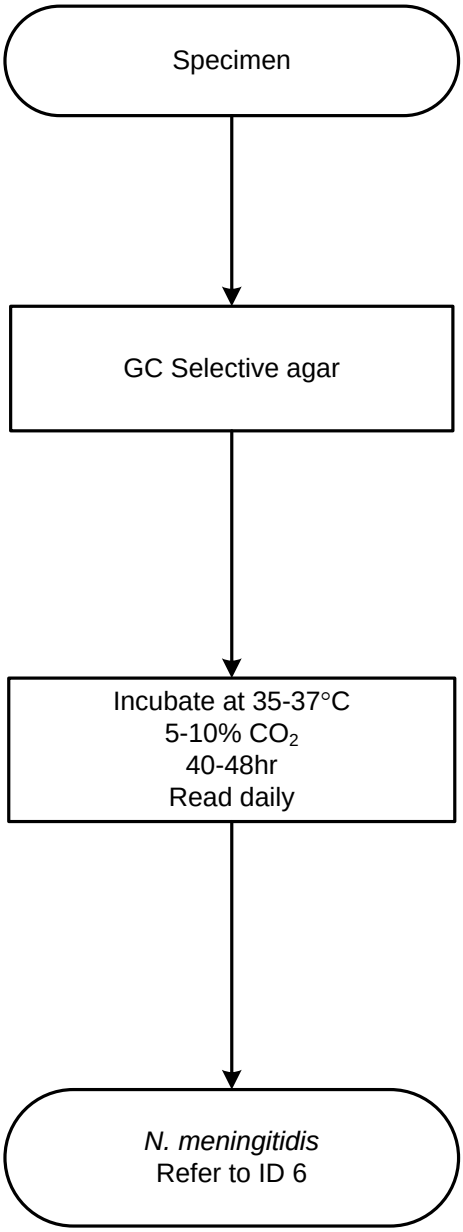
Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to PHE. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to PHE and many PHE Health protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

Note: The Health Protection Legislation Guidance (2010) includes reporting of HIV & STIs, HCAIs and CJD under 'Notification Duties of Registered Medical Practitioners': it is not noted under 'Notification Duties of Diagnostic Laboratories'.

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/HealthProtectionRegulations/

Other arrangements exist in Scotland[50,51], Wales[52] and Northern Ireland[53].

Appendix: Screening for *Neisseria meningitidis*



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