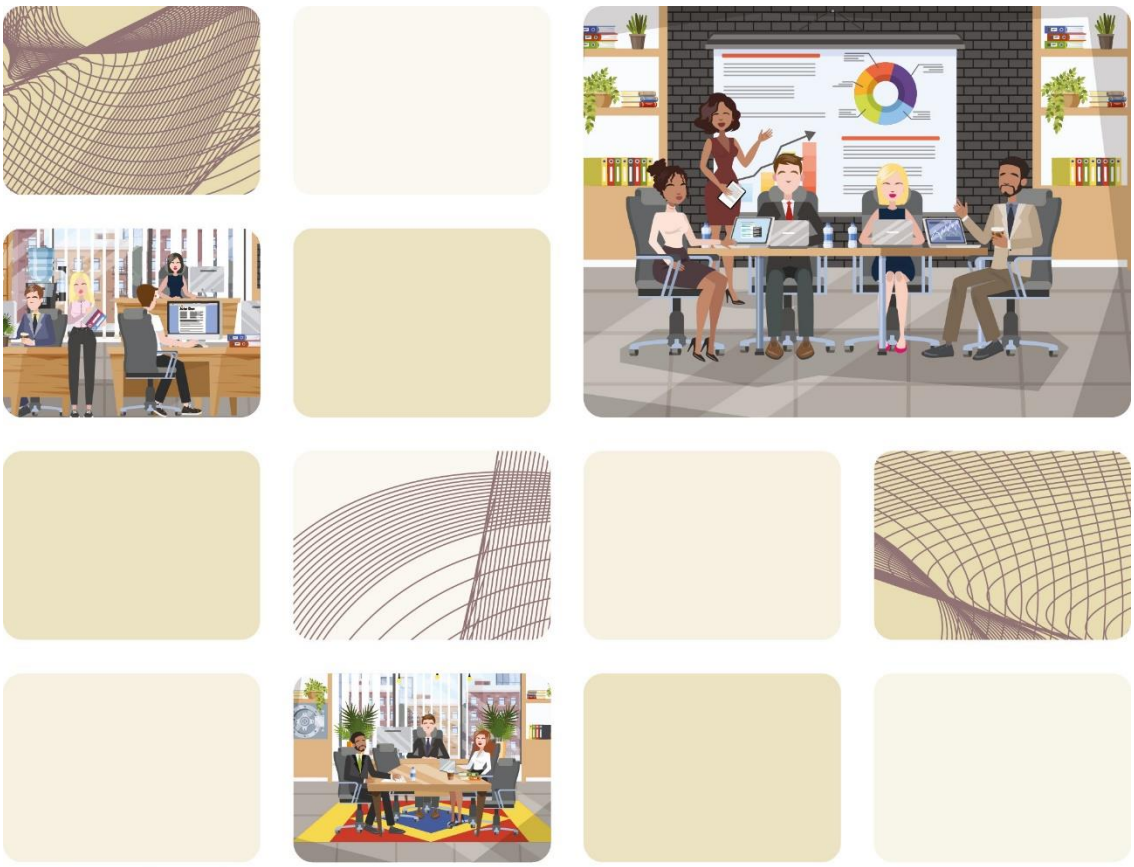
UK Health Security Agency

UK Standards for Microbiology Investigations

Review of users' comments received by Working group for microbiology standards in clinical bacteriology

Identification of *Neisseria* species



National Institute for Health and Care Excellence (NICE) has renewed accreditation of the process used by the **UK Health Security Agency** to produce **UK Standards for Microbiology Investigations (UK SMIs)**. The renewed accreditation is valid until **30 June 2026** and applies to guidance produced using the processes described in '**UK Standards for Microbiology Investigations Development Process' (2021)**. The original accreditation term began on 1 July 2011.

This publication was created by UK Health Security Agency (UKHSA) in partnership with the partner organisations.

Recommendations are listed as ACCEPT/ PARTIAL ACCEPT/DEFER/ NONE or PENDING

Issued by the Standards Unit, Specialised Microbiology and Laboratories, UKHSA

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Consultation: 07/09/2023 – 22/09/2023
Version of document consulted on: dg+

Section 6. Safety considerations

Comment number: 1

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

I am not sure 'vertical transmission' is correct here as that normally refers to transmission from mother to child. Do you mean direct inoculation?

Recommended action

1. Accept. Changed to direct inoculation.

Comment number: 2

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

Never heard the term 'vertical transmission' for lab workers, this usually refers to mother-to-child-transmission

Recommended action

1. Accept. Changed to direct inoculation.

Comment number: 3

Date received: 21/09/2023
Laboratory or organisation name: Institute of Biomedical Science

‘N. gonorrhoeae is also a Hazard group 2 organism which is responsible for the sexually transmitted infection, gonorrhoea and can also cause eye or throat infection - which is the most likely risk to laboratory workers through either vertical transmission, poor laboratory practice or inhalation of aerosols’.

This reads as though laboratory workers are at risk of acquiring N. gonorrhoeae by vertical transmission. As this is transmission from mother to child it doesn't fit as a route of transmission for laboratory workers.

Recommended action

1. Accept. Changed to direct inoculation.

Section 8. Identification

Comment number: 4

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

An immunological test for NG is still available - so suggest that when you mention biochemical and molecular tests, you also include immunological. Please also include the option of using 1% Vitox or IsoVitaleX in the primary agar plate for NG

Recommended action

1. Accept.

Comment number: 5

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

What molecular methods are implied here? If you mean NAATs these are routine in most labs and the last sentence is incorrect. Or do you mean WGS? Don't think anyone is using this, at least for NG. Need to be more specific.

Recommended action

1. Accept. This sentence has been removed.

Section 8.1 Cultural methods

Comment number: 6

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

Please state that all isolates must be submitted to ref lab.

Recommended action

1. Accept. Section 11. Referral to reference or specialist testing laboratories has been updated as appropriate.

Section 8.3.2.1 Polymerase Chain Reaction (PCR)

Comment number: 7

Date received: 22/09/2023
Laboratory or organisation name: Italian Association for Clinical Microbiology (AMCLI)

‘PCR is mainly used as complementary or confirmatory testing method for the identification of Neisseria species following MALDI-TOF MS results (47)’.

It is not clear if PCR is useful for all the Neisseria species or all the Neisseria species other than N. meningitidis.

Recommended action

1. None. Section 8.3.2.1 PCR has been removed.

Section 8.3.2.2 Next generation sequencing (NGS)

Comment number: 8

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

1. I am not sure this section is of value. I personally think we are some years from WGS replacing Maldi in its current form due to cost and time and the fact you still mainly need a culture for both methods anyway.

2. WGS has NOT replaced traditional phenotypic and polymerase chain reaction (PCR) methods for routine surveillance for NG.

Recommended action

1. Accept. This section has been updated.
2. Accept.

Sections 8.3.2.1 PCR and 8.3.2.2 NGS

Comment number: 9

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

1. PCR is not used to confirm NG cultures (I don't know about the other neisseria sp) so should say that clearly.

2. Similarly, WGS has not replaced traditional methods for NG at UKHSA.

Recommended action

1. None. This section has been removed.
2. Accept.

Section 8.4 Matrix-assisted laser desorption/ionisation - time of flight mass spectrometry (MALDI-TOF MS)

Comment number: 10

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

1. Are you missing reference to NG here: "the misidentification of commensal strains as N. meningitidis"

2. You mention a 'consistent' identification but it might be better to mention identification to species level and the other tests may be needed if this is not achieved.

3. Also, I wonder if some best practice should be mentioned, for example: ‘When MALDI-TOF MS is used for species identification, especially as the only identification method for N. gonorrhoeae, the method should be appropriately validated, manufacturer instructions carefully followed, available database updates installed and reviewed, and the use of an extraction step that can contribute to a more reliable species identification should be considered’.

Recommended action

1. None. The sentence is specifically referring to the misidentified of *N. meningitidis*.
2. Accept.
3. Accept.

Section 8.5.1 Biochemical tests and commercial identification systems

Comment number: 11

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

1. I think it is useful in the SMI to have a table of carbohydrate utilization and enzyme activity of different Neisseria species and other oxidase-positive species such as Moraxella catarrhalis and Kingella denitrificans.

2. As the Gonochek-II assay is still available in the UK then i think it is wise to continue to mention the following: N. gonorrhoeae that have a mutation in the proline iminopeptidase gene and therefore appear negative for this enzyme are prevalenthave been detected and kits that detect solely the production of aminopeptidases should not be used alone

Recommended action

1. None. Reference to the Manual of Clinical Microbiology provided instead.
2. Accept.

Comment number: 12

Date received: 22/09/2023
Laboratory or organisation name: Italian Association for Clinical Microbiology (AMCLI)

'The latex agglutination kits are designed for direct use on CSF or serum but will also work for cultures'. We think that the limited value of latex agglutination kits should be underlined. Also, the use from cultures should be allowed only if the test is validated for and the instruction for use (IFU) reports this indication.

We would propose: 'The latex agglutination kits are designed for direct use on CSF or serum, although the sensitivity and the NPV are low, but will also work for cultures according to the IFU of producers'.

The sensitivity of Pastorex for NmC was 80.0% (95% CI 65.4-90.4%) and the specificity was 94.4% (95% CI 72.7-99.9%). The positive likelihood ratio (LR) was 14.4 (95% CI 2.1-97.3) and negative LR was 0.2 (95% CI 0.1-0.4). The positive and negative predictive values (PPV and NPV) were 97.3% (95% CI 85.8-99.9) and 65.4% (95% CI 44.3-82.8).

References:

Trans R Soc Trop Med Hyg. 2016 Jul;110(7):381-5. doi: 10.1093/trstmh/trw046. Evaluation of Pastorex meningitis kit performance for the rapid identification of Neisseria meningitidis serogroup C in Nigeria Kennedy Uadiale 1, Agatha Bestman 1,

Charity Kamau 2, Dominique A Caugant 3, Jane Greig
4https://pubmed.ncbi.nlm.nih.gov/27496511/

J Clin Microbiol. 1995 Jun;33(6):1486-91. doi: 10.1128/jcm.33.6.1486-1491.1995.
Rapid bacterial antigen detection is not clinically useful M D Perkins 1, S Mirrett, L B Reller

Recommended action

1. None. The information on latex agglutination kits has been removed.

Section 8.5.2 Molecular methods

Comment number: 13

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

Please state that all isolates must be submitted to ref lab.

Recommended action

1. Accept. Section 11. Referral to reference or specialist testing laboratories has been updated appropriate.

Comment number: 14

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

1. I know you are trying to cover all Neisseria, but the most common one, NG is often detected by NAATS directly from clinical specimens and independent of any culture. I think this is lost in the text of the SMI.

2. I am not aware of labs using PCR as complementary or confirmatory testing method for the identification of Neisseria species following MALDI-TOF MS results other than the ref lab.

3. In this section (I think) you are suggesting to send an isolate to a ref lab when they don't have molecular tests for confirmation. In reality, other than UKHSA and labs that are keen to go off license with their NAATs and test a culture lysate, most labs will not use NAATs to confirm a maldi.

Recommended action

1. None. Detection is outside the scope of this document.
2. None. The section on PCR has been removed.
3. None. This sentence has been removed.

Section 8.4 Storage

Comment number: 15

Date received: 21/09/2023
Laboratory or organisation name: Institute of Biomedical Science

Note states N gonorrhoeae should be stored at -70°C but the document does not evidence this or cross reference where the figure was determined.

Recommended action

1. None. The suggested storage temperature is based on expert feedback. No supporting evidence was found.

Comment number: 16

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

Suggest to mention slopes to be stored in 5 - 10% CO_2 at 35 - 37°C.

Recommended action

1. Accept.

Section 9. Reporting

Comment number: 17

Date received: 13/09/2023
Laboratory or organisation name: NHS Lothian

Inform the infection specialist of all confirmed N. gonorrhoeae isolates, and of all Neisseria species from:

- minors
- cases of sexual assault, rape, or abuse
- cases of N. gonorrhoeae isolated from normally sterile sites or from invasive infection – also send to the appropriate reference laboratory
- multi-drug resistant isolates of GC from all site

Why does an infection specialist need to be informed about all Neisseria species in these conditions? If this is necessary it would be helpful to explain why

Recommended action

1. None. These are general guidelines that laboratories should adhere to and where appropriate follow local protocols. Further explanation in this section is not applicable.

Section 9.1 Infection specialist

Comment number: 18

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

Should say 'ceftriaxone resistant' not multi-drug resistant NG. Also, all ceftriaxone resistant NG should be sent to the UKHSA STI Ref lab

Recommended action

1. Accept.

Comment number: 19

Date received: 22/09/2023
Laboratory or organisation name: Italian Association for Clinical Microbiology (AMCLI)

Could an indication be given regarding the behaviour to be followed in case of isolation of meningococcus from non-sterile materials (respiratory samples, nasal swab, ...) other than CSF and blood? report and not notify? or notify and not report?

Recommended action

1. None. Outside the scope of this document.

Comment number: 20

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

Please add that N. meningitidis isolates should be sent to the appropriate reference laboratory.

Recommended action

1. Accept. Section 11. Referral to reference or specialist testing laboratories has been updated as appropriate.

Section 9.2 Presumptive identification

Comment number: 21

Date received: 13/09/2023
Laboratory or organisation name: NHS Lothian

Neisseria gonorrhoea is a typo and not the correct spelling

Recommended action

1. Accept.

Section 9.3 Confirmation of identification

Comment number: 22

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

Again, for NG, PCR is not used to confirm isolates. We use NAATs on clinical specimens (not cultures) - is that what you mean throughout? It's very unclear.

Recommended action

1. None. This information has been removed.

Algorithm 1. Identification of Neisseria gonorrhoeae

Comment number: 23

Date received: 13/09/2023
Laboratory or organisation name: NHS Lothian

Again, Neisseria gonorrhoea is incorrectly used throughout this algorithm

Recommended action

1. Accept.

Comment number: 24

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

Again, I think the use of NAATs for NG has been a bit mis-understood. Maldi is used for the ID of culture, NAATs are used for the ID in molecular clinical specimens. Clinics usually take one sample for culture and one sample for NAATs.

In the footnotes: If second pathway is followed, perform PCR on the clinical specimen. If further identification is required, refer to the appropriate reference laboratory. This suggests ref labs have molecular confirmation services for NG - we do not!

Recommended action

1. None. The second pathway and referral section have been removed from the algorithm.

Comment number: 25

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

Clinical specimen - molecular methods (why PCR specifically? Should say NAAT) - cannot refer these to Ref lab, we do not offer this confirmatory service.

Recommended action

1. None. The second pathway and referral section have been removed from the algorithm.

Algorithm 2. Identification of non-gonococcal Neisseria species

Comment number: 26

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

Please state in the final box of this algorithm that all isolates must be submitted to ref lab.

Recommended action

1. None. Referral section removed from the algorithm.

References

Comment number: 27

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

Referencing does not seem 100% correct

Recommended action

1. Accept. References updated.

General comments

Comment number: 28

Date received: 08/09/2023
Laboratory or organisation name: UK Health Security Agency

Apart from in the Taxonomy and Characteristics section, Neisseria gonorrhoeae is spelt incorrectly throughout the document as Neisseria gonorrhoea - missing the 'e' on the end.

Recommended action

1. Accept.

Comment number: 29

Date received: 08/09/2023
Laboratory or organisation name: UK Health Security Agency

Apart from the point above, the rest of the document looks OK.

Recommended action

1. None. No action required.

Comment number: 30

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

Throughout the document there is no instruction for all identified samples of disease-causing Neisseria meningitidis or for Neisseria meningitis samples isolated from a throat swab in a patient being treated with invasive disease to be sent to the appropriate reference laboratory.

It is vital that all samples/isolates are forwarded to the appropriate reference lab to:
• Inform appropriate case/contact/outbreak management
• Inform and evaluate national vaccine policies
• Allow for outbreak investigation both nationally and internationally
• Inform ongoing research (using isolate and specimen archives held by the MRU

Recommended action

1. Accept.

Comment number: 31

Date received: 07/09/2023
Laboratory or organisation name: RCGP

The document does not appear to include advice relating to testing in the community. It may be out of scope or require directing the reader to alternative documents. This may be increasingly relevant given the use of self-testing kits.

Recommended action

1. None. Outside the scope of this document.

Comment number: 32

Date received: 21/09/2023
Laboratory or organisation name: Institute of Biomedical Science

Whilst this document relates to the identification of Neisseria sp, it may be pertinent to add that any isolates of N gonnorrhoeae identified from specimens taken from children <16yrs may indicate safeguarding concerns and should be investigated accordingly. Add to introduction?

Evidence:

New HCPC standards of proficiency for Biomedical Scientist:

2.3 understand the importance of safeguarding by actively looking for signs of abuse, demonstrating understanding of relevant safeguarding processes and engaging in these processes where necessary

Recommended action

1. None. Outside the scope of this document.

Comment number: 33

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

Spelling of N. gonorrhoeae is not correct throughout

Recommended action

1. Accept.

Comment number: 34

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

gonorrhoea not gonorrhea
N gonorrhoeae not N gonorrhea

Recommended action

1. Accept.

Comment number: 35

Date received: 22/09/2023
Laboratory or organisation name: Italian Association for Clinical Microbiology (AMCLI)

As you probably saw already: the paragraph numbering is incorrect. 8.1.2.1 (page 8) 8.3.2.1, 8.3.2.2 and 8.4 (page 12-13)

Recommended action

1. Accept.

Comment number: 36

Date received: 22/09/2023
Laboratory or organisation name: Italian Association for Clinical Microbiology (AMCLI)

As you probably saw already: some names of species are incorrect page 10: N. Skkuensis; page 11: Neissria caviae, page 14 and algorithm 1: Neisseria gonorrhoea

Recommended action

1. Accept.

Financial barriers

Respondents were asked: 'Are there any potential organisational and financial barriers in applying the recommendations or conflict of interest?'.

Comment number: 37

Date received: 07/09/2023
Laboratory or organisation name: RCGP

Not applicable

Comment number: 38

Date received: 08/09/2023
Laboratory or organisation name: UK Health Security Agency

No

Comment number: 39

Date received: 11/09/2023
Laboratory or organisation name: Keith Shuttleworth and Associate

N/A

Comment number: 40

Date received: 13/09/2023
Laboratory or organisation name: NHS Lothian

None

Comment number: 41

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

No

Comment number: 42

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

No

Comment number: 43

Date received: 21/09/2023
Laboratory or organisation name: Institute of Biomedical Science

No

Comment number: 44

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

No

Health benefits

Respondents were asked: 'Are you aware of any health benefits, side effects and risks that might affect the development of this UK SMI?'.

Comment number: 45

Date received: 07/09/2023
Laboratory or organisation name: RCGP

Not applicable

Comment number: 46

Date received: 08/09/2023
Laboratory or organisation name: UK Health Security Agency

No

Comment number: 47

Date received: 11/09/2023
Laboratory or organisation name: Keith Shuttleworth and Associate

N/A

Comment number: 48

Date received: 13/09/2023
Laboratory or organisation name: NHS Lothian

No

Comment number: 49

Date received: 21/09/2023
Laboratory or organisation name: Meningitis Research Foundation

No

Comment number: 50

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

No

Comment number: 51

Date received: 21/09/2023
Laboratory or organisation name: Institute of Biomedical Science

No

Comment number: 52

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

No

Interested parties

Respondents were asked: 'Are you aware of any interested parties we should consider consulting with on the development of this document?'

Comment number: 53

Date received: 08/09/2023
Laboratory or organisation name: UK Health Security Agency

No

Comment number: 54

Date received: 11/09/2023
Laboratory or organisation name: Keith Shuttleworth and Associate

N/A

Comment number: 55

Date received: 13/09/2023
Laboratory or organisation name: NHS Lothian

No

Comment number: 56

Date received: 21/09/2023
Laboratory or organisation name: STI reference lab

No

Comment number: 57

Date received: 21/09/2023
Laboratory or organisation name: Institute of Biomedical Science

No

Comment number: 58

Date received: 21/09/2023
Laboratory or organisation name: STI Ref lab, UKHSA

No

Respondents indicating they were happy with the contents of the document

Overall number of comments: 1			
Date received	11/09/2023	**Lab name/Professional body (delete as applicable)**	Member of the public
Health benefits			