

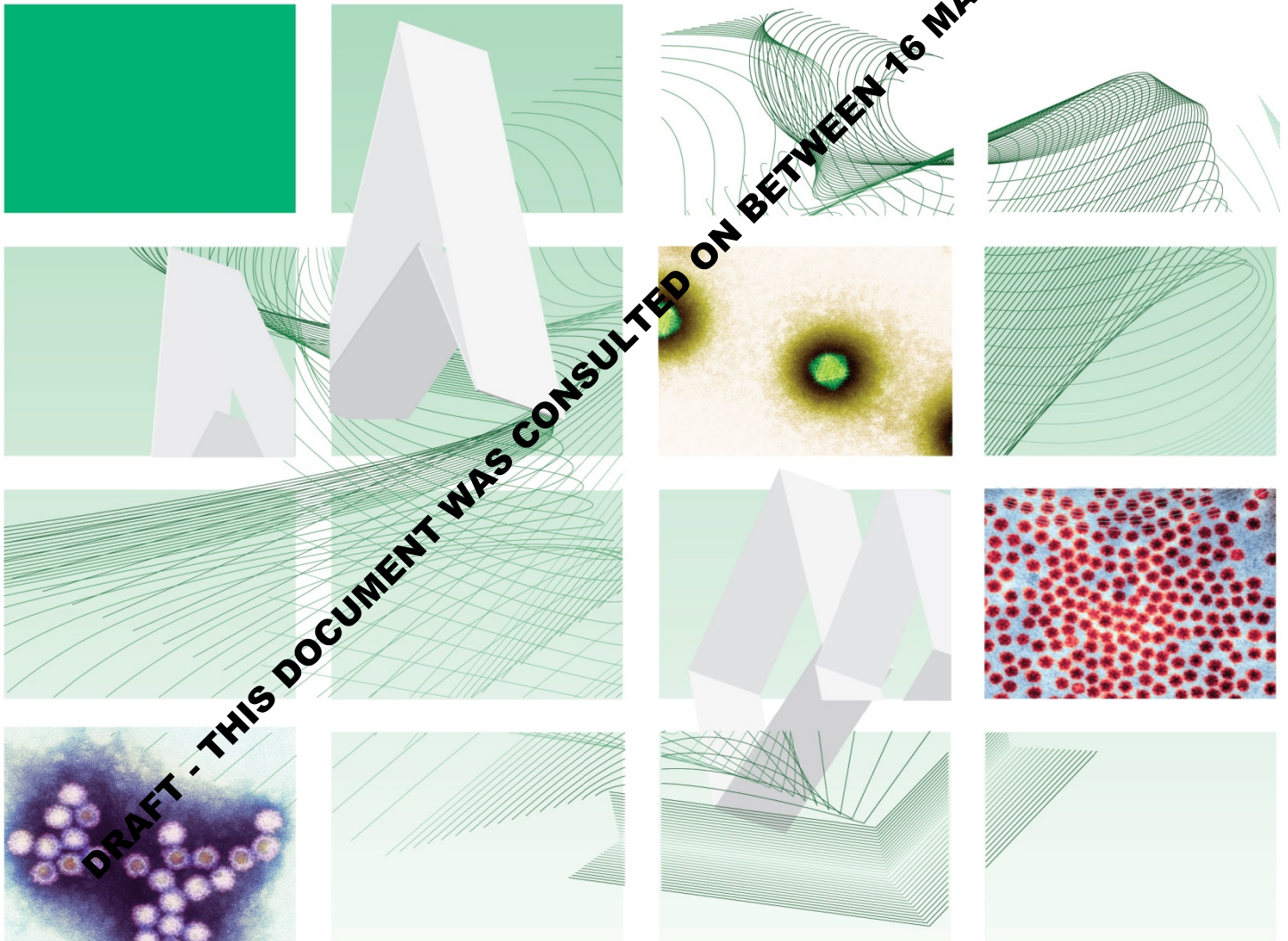


Protecting and improving the nation's health

UK Standards for Microbiology Investigations

Chlamydia trachomatis infection – testing by Nucleic Acid Amplification Tests (NAAT)

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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 <https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories>. SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see <https://www.gov.uk/government/groups/standards-for-microbiology-investigations-steering-committee>).

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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.	5/dd.mm.yy <tab+enter>
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Section(s) involved	Amendment

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UK Standards for Microbiology Investigations[#]: scope and purpose

Users of SMIs

- SMIs are primarily intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK.
- SMIs 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.
- SMIs 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 <https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories>.

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.

[#]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.

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 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 quality

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 <https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity>. 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

While every care has been taken in the preparation of SMIs, PHE and the partner organisations, 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 by an end user to an SMI for local use, it must be made clear where in the document the alterations have been made and by whom such alterations have been made and also acknowledged that PHE and the partner organisations shall bear no liability for such alterations. For the further avoidance of doubt, as SMIs have been developed for application within the UK, any application outside the UK shall be at the user's risk.

The evidence base and microbial taxonomy for the SMI is as complete as possible at the date 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.

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Scope of document

Type of specimen

Urine, vulvo-vaginal swabs, urethral swabs, endocervical swabs, rectal swabs, oropharyngeal swabs, pooled samples

Note: Avoid first-void urine in women.

Note: NAAT for extra-genital and pooled specimens should be validated locally¹.

Scope

This SMI covers the testing of clinical samples for the investigation of urogenital *Chlamydia trachomatis* infection (including rectal and oropharyngeal infection) by nucleic amplification tests (NAAT).

This SMI does not distinguish between lymphogranuloma venereum (LGV) serovars and non-LGV serovars of *C. trachomatis*. Send samples to the sexually transmitted bacteria reference unit (STBRU), or a local laboratory with a validated test for diagnosis^{2,3}.

This SMI does not include ocular trachoma or neonatal infections (including pneumonia and conjunctivitis). Refer to [S 2: Pneumonia](#) and [S 3: Conjunctivitis](#).

Refer to SMI [Q 4: Good laboratory practice when performing molecular amplification assays](#).

This SMI should be used in conjunction with other SMIs.

Definitions

For all antigen, antibody and NAAT testing the following definitions apply:

During testing process

Reactive – Initial internal stage positive result pending confirmation.

Not reactive – Initial internal-stage negative result.

Equivocal – Result is not clearly positive or negative. Further testing is required.

The term 'equivocal' may be different for various platforms eg 'indeterminate'.

Inhibitory – The term 'inhibitory' may be different for various platforms eg 'invalid'.

Reporting stage

These terms are used for final or preliminary reports.

Detected – Report-stage confirmed reactive result.

Not detected – Report-stage not reactive result.

Indeterminate – Reactive result that cannot be confirmed.

Inhibitory – The term 'inhibitory' may be different for various platforms eg 'invalid'.

Introduction

Chlamydia trachomatis infection is the most frequently reported bacterial, sexually transmitted infection in the UK, particularly in young adults. There are three biovars of *C. trachomatis* and fifteen serovars; trachoma biovars (serovars A-C), urogenital biovars (serovars D-K) and lymphogranuloma venereum (LGV) biovars (serovars L1-L3)⁴. This SMI covers the detection of urogenital *C. trachomatis* infection, but does not differentiate between LGV and non-LGV serovars. Several outbreaks of LGV have occurred in men who have sex with men (MSM) since the early 2000s and high rates of infection have been observed in MSM in the UK². However, increased rates may in part be due to increased use of NAAT for extra genital samples in this risk group⁵. Samples for LGV identification should be sent to the Sexually Transmitted Infection Reference Unit (STBRU) (or other laboratory with validated test) for diagnosis^{2,3}. Risk factors for *C. trachomatis* infection include <25 years of age, a new sexual partner or more than one sexual partner in the past year and inconsistent use of condoms.

Screening^{3,6,7}

Patients should be tested where there are symptoms or signs suggestive of chlamydial infection, in patients with reactive arthritis who are sexually active, in parents of children with chlamydial conjunctivitis/pneumonia and in egg and semen donors, or on request. Sexual partners of those with suspected or proven chlamydial infection should also be tested, as should all men or women with another sexually transmitted infection.

In England, routine screening is recommended in all sexually active men and women between the ages of 16 and 25 annually, or sooner if there has been a change of partner^{3,6}. Those over 25 may be screened if they have had a new sexual partner, or more than one sexual partner in the last 12 months. Repeat testing should be carried out 3-6 months following the completion of treatment in those diagnosed with chlamydial infection who are under 25 years old³.

Routine screening is not recommended in pregnant women unless from high prevalence populations; however, screening is recommended for those seeking termination of a pregnancy⁶.

Screening is also important in those undertaking IVF who may be asymptomatic⁸.

Laboratory diagnosis^{1,4,7}

Several diagnostic assays for the identification of *C. trachomatis* infection have been used. These include NAAT, cell culture, enzyme immunoassays and direct fluorescence assay. NAAT has been shown to be more sensitive and specific than other tests and therefore NAAT is recommended in this SMI for all cases, including medico-legal cases, and may be used for the investigation of extra-genital infections where validated locally. EIA and rapid tests are not recommended. The sampling sites should relate to the type of sexual activity reported and the patient category (see table 1 below)⁹.

Sample types⁹

The recommended sample type for women is a vulvo-vaginal swab which may be self-collected and submitted by post. Endocervical swabs have been shown to be less sensitive than vulvo-vaginal swabs and must be taken by a healthcare worker. The testing of first catch urine specimens from women may result in lower sensitivity and is not recommended by European guidelines^{3,10}.

In men, first void urine has been shown to be more sensitive than urethral sampling and is the sample type of choice. Urine should be held for a minimum of one hour and the first 20ml sampled.

Rectal samples may be taken by proctoscopy, or directly by the patient or healthcare worker. Where extra-genital specimens are being tested, local validation should be carried out (see [Q 1 – Commercial and in-house diagnostic tests: evaluations and validations](#) for further information).

Pooling of samples may be undertaken; however, pooled samples may not be appropriate if using a dual *Neisseria gonorrhoea/Chlamydia trachomatis* NAAT. Pooling of urine, rectal and oropharyngeal swabs may reduce testing costs; this method of pooling involves the pooling of samples from different sites from one patient (typically MSM)^{3,11}. If this type of pooling is carried out and is sent for LGV diagnosis to the reference laboratory, the method of pooling used should be stated on the referral paperwork. Validation of this method of pooling is required locally as it may lead to a reduction in sensitivity and if detected, the site of infection is unknown³. Samples from different patients can also be pooled for NAAT following DNA extraction¹². This method also needs to be validated locally for the platform used. If reactive, the DNA extracts are re-tested individually and the original sample or extract may be sent for LGV diagnosis at the reference laboratory.

In all cases laboratories should follow manufacturer's instructions regarding individual specimen types.

Table 1 – Appropriate sample sites dependent on sexual activity⁹

Type of sex	Oral	Vaginal	Anal
Patient			
MSM	Receptive: oropharyngeal swab Insertive: 1 st void urine		Insertive peno-anal: 1 st void urine Receptive peno-anal: rectal swab Receptive oro-anal: rectal swab
Heterosexual Male	Fellatio: 1 st void urine	1 st void urine	Peno-anal: 1 st void urine
Female	Fellatio: consider oropharyngeal swab	Self-taken V/V swab	Receptive: consider rectal swab

Note: Cunnilingus does not require a pharyngeal swab from the male.

Note: In MSM, where there is also sexual activity with women, refer to heterosexual male for appropriate sample type following vaginal sexual activity.

Laboratory tests

A Nucleic Acid Amplification Technique (NAAT) which can detect the Swedish new variant (nvCT) should be used. Dual NAAT for *C. trachomatis* and *Neisseria gonorrhoea* are available and are used in many laboratories in the UK¹³. Table 2 below compares estimated sensitivities and specificities for diagnostic tests in urogenital specimens from clinical trial data, package inserts and selected published papers¹⁴.

Table 2. Estimates of sensitivities and specificities for diagnostic tests for *C. trachomatis* in urogenital specimens¹⁴.

Diagnostic method	Sensitivity, %	Specificity, %
Tissue culture	70–85	100
Direct fluorescent antibody	80–85	>99
Enzyme immunoassay	53–76	95
Direct hybridization	65–83	99
Polymerase chain reaction		
Cervical swabs	89.7	99.4
Female urine	89.2	99.0
Male urine	90.3	98.4
Strand displacement amplification		
Cervical swabs	92.8	98.1
Female urine	92.8	98.4
Male urine	94.5	91.4
Male urethral swabs	94.6	94.2
Transcriptional mediated amplification		
Cervical swabs	94.2	97.6
Vaginal swabs	96.6–96.7	97.6–97.1
Female urine	94.7	98.9
Male urine	97.0	99.1
Male urethral	95.2	98.2
Real-time PCR		
Cervical swabs	80.9–87.7	99.4–99.7
Vaginal swabs	84.8–94.7	98.8–99.1
Female urine	92.6–95.7	99.2–99.5
Male urine	97.3–97.8	99.6–99.7
Male urethral	88.6–93.3	98.3–99.1

Note: It should be noted that this SMI recommends the use of vulvo-vaginal swabs in women.

Postal test-kits (PTK) have also been trialled as a form of sample collection for home-based screening¹⁵⁻¹⁷. Self-collected specimens (swabs or preserved urine) are posted to the laboratory for NAAT; results were found to be comparable to traditional

collection methods¹⁵⁻¹⁷. Assessment of these strategies in terms of test and cost effectiveness is ongoing. Validation should be carried out locally prior to use.

Point of care testing (POCT)

This SMI does not recommend the use of EIA based POCTs which have traditionally lacked sensitivity^{18,19}. Newly developed POCTs have been shown to have sensitivities of between 82% and 84%, however these tests are still inferior to NAAT^{3,20,21}. POCTs using NAAT are currently under development^{3,22}.

Confirmation¹³

C. trachomatis

As per national and international guidelines, for infections where the PPV of a test is less than 90%, and for specimens from extra-genital sites (eg rectal swabs), confirmatory testing, with a different target, for persons with a positive *C. trachomatis* screening test should be considered, taking into account local evaluation and validation data^{10,23}. In laboratories where confirmatory testing results are found to be consistently concordant following audit, confirmatory testing may be deemed unnecessary. However, if testing is associated with a medico-legal case then testing with a different target is required even in a high risk population³.

Samples for *C. trachomatis* confirmation can be sent to the sexually transmitted bacteria reference unit (STBRU). Samples may also be sent to STBRU or a local laboratory with validated test, to detect LGV serovars. Acceptable sample types include residual clinical specimens in which *C. trachomatis* has been detected by the local laboratory (by NAAT) or extracted DNA samples. The sample type must be made clear on all referral paperwork including whether it is a pooled sample.

Lymphogranuloma venereum

LGV testing is recommended in those with proctitis and in patients who are HIV positive MSM, with or without symptoms, who have *C. trachomatis* infection at any site^{2,3}. Consider sending *C. trachomatis* positive samples from rectal sites from both men and women for LGV diagnosis²⁴.

Window period and test of cure

Patients should undergo testing when they first present. If there is potential of sexual exposure within the previous two weeks, patients should return for a repeat NAAT test two weeks following exposure³.

Test of cure is not recommended for uncomplicated genital chlamydial infection³. Test of cure is recommended in pregnancy, where poor compliance is suspected and where symptoms persist. In addition, it is recommended in some cases of rectal infection depending on treatment type. Test of cure should occur at least three weeks after the completion of treatment³.

Persistent Infection

Persistent chlamydial infection has been demonstrated in patients who are at low risk of re-infection and who have tested positive for *C. trachomatis*, at least twice (using NAAT) despite having fully completed at least two rounds of therapy^{25,26}.

Asymptomatic patients with persistent infection may not be aware and may not be detected as test of cure is not recommended.

Medicolegal cases

Where results are likely to have medicolegal significance, specimens should be handled in accordance with Royal College of Pathologists' guidance^{27,28}. Legal precedent is limited, but for best practise, laboratories should confirm a reactive NAAT result by using a different target to ensure reproducibility³.

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.

Specimen containers

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".

NAAT inhibition

All sample types may contain inhibitors¹⁰. Many modern NAATs are able to remove inhibitors during the nucleic acid extraction process. Rectal specimens and urine from pregnant women and women in the third week after menstrual bleeding may contain high levels of inhibitors. It is likely that hormones have a role to play in this inhibition⁴. Manufacturer's instruction should be followed with regards to interpretation of inhibited test results. Use of an inhibition control in NAAT testing is recommended as false negative results may be caused by inhibitors.³

In duplex or multiplex assays, where several targets may be detected, competitive inhibition may be observed.

Safety considerations

Containment Level 2.

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.

Public health management

For information regarding notification to PHE (or equivalent in the devolved administrations) refer to page 15.

For further information on public health management refer to PHE web pages: <https://www.gov.uk/government/collections/chlamydia-surveillance-data-screening-and-management>.

For information regarding the national chlamydia screening programme refer to:

<http://www.chlamydia-screening.nhs.uk/ps/resources.asp>

Also refer to the British Association for Sexual Health and HIV guidelines and NICE guidelines for the management of *Chlamydia trachomatis* infection and lymphogranuloma venereum^{2,29}:

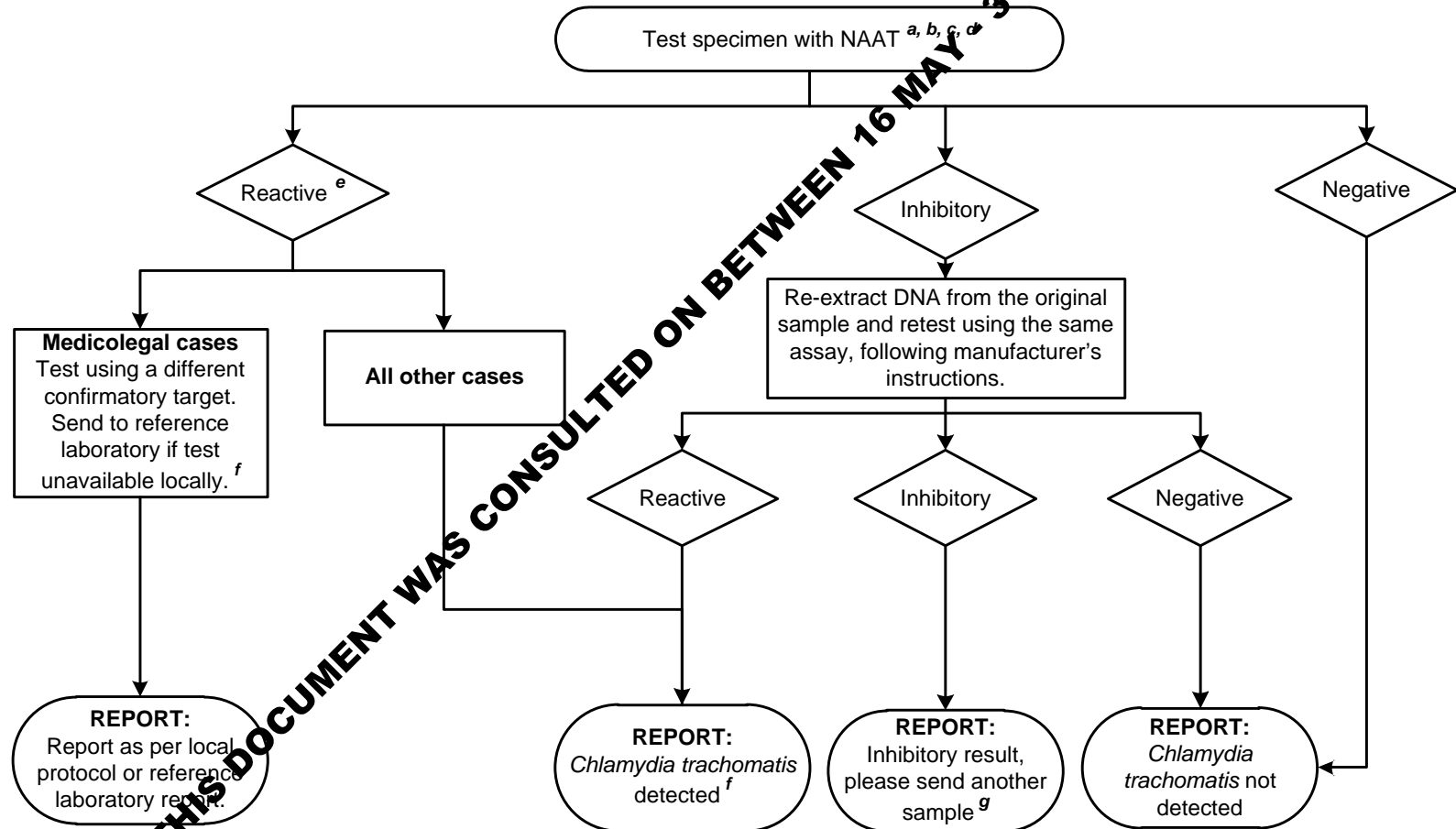
<http://www.bashh.org/BASHH/Guidelines/Guidelines/BASHH/Guidelines/Guidelines.asp>

<http://cks.nice.org.uk/chlamydia-uncomplicated-genital>

Partner notification should be discussed at the time of diagnosis. All sexual partners should be offered full STI screening³.

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Footnotes

- a) First catch urine (preferred) or urethral swab for men and vaginal swab (which may be self-collected) or endocervical swab for women are the recommended specimen types. Laboratories should ensure that their assay is capable of detecting the Swedish new variant *C. trachomatis* (nvCT).
- b) Laboratories using dual nucleic acid amplification tests (NAAT) capable of detecting both *C. trachomatis* and *N. gonorrhoeae* should follow nationally agreed algorithms and confirmatory strategy for the *N. gonorrhoeae* component of the test. In women, urine is not the optimal sample for *N. gonorrhoeae*/*C. trachomatis* combined NAAT.
- c) Laboratories should follow good practice when undertaking molecular testing. For *C. trachomatis* this should include environmental swabbing. See [Q 2 – Quality assurance in diagnostic virology and serology laboratory](#) and [Q 4 – Good laboratory practice when performing molecular amplification assays](#) for further information.
- d) It is recommended to use an inhibitory control for each specimen³. Failure to do so may lead to false negative results.
- e) Many authorities no longer recommend testing with a second platform unless testing is associated with a medico-legal case³. The decision to retest with a second platform depends on the sample type (for example samples from extragenital sites such as rectal swabs), which platform is used for screening and the prevalence of *C. trachomatis* in the population tested. In populations with low prevalence it is still necessary to confirm.
- f) Where appropriate send samples for *C. trachomatis* confirmation/LGV diagnosis to STBRU or local laboratory with validated tests.
- g) Consider sending to the reference laboratory (STBRU) for confirmation.

Notification to PHE^{30,31}, or equivalent in the devolved administrations³²⁻³⁵

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 Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCAs) and Creutzfeldt–Jakob disease (CJD) under 'Notification Duties of Registered Medical Practitioners': it is not noted under 'Notification Duties of Diagnostic Laboratories'.

<https://www.gov.uk/government/organisations/public-health-england/about/our-governance#health-protection-regulations-2010>

Other arrangements exist in [Scotland](#)^{32,33}, [Wales](#)³⁴ and [Northern Ireland](#)³⁵.

References

1. Geisler WM. Diagnosis and management of uncomplicated chlamydia trachomatis infections in adolescents and adults: Summary of evidence reviewed for the 2010 centers for disease control and prevention sexually transmitted diseases treatment guidelines. *Clinical Infectious Diseases* 2011;53:S92-S8.
2. White J, O'Farrell N, Daniels D. 2013 UK National Guideline for the management of lymphogranuloma venereum: Clinical Effectiveness Group of the British Association for Sexual Health and HIV (CEG/BASHH) Guideline development group. *International journal of STD & AIDS* 2013;24:593-601.
3. BASHH. 2015 UK national guideline for the management of infection with *Chlamydia trachomatis* 2015.
4. Lanjouw E, Ossewaarde JM, Stary A, Boag F, Van Der Meijden WI. 2010 European guideline for the management of *Chlamydia trachomatis* infections. *International Journal of STD and AIDS* 2010;21:729-37.
5. Haidari G, Perry MEO, White JA. Are we seeing a true rise in *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in men who have sex with men in the UK? *Sexually Transmitted Infections* 2014;90:308.
6. National Institute for Health and Care Excellence. *Chlamydia* uncomplicated genital 2011.
7. Public Health England BIA. *Diagnosis of Chlamydia trachomatis: Quick reference guide for general practices* 2011.
8. Akande V, Turner C, Horner P, Horne A, Pacey A. Impact of *Chlamydia trachomatis* in the reproductive setting: British fertility society guidelines for practice. *Human Fertility* 2010;13:115-25.
9. BASHH. 2015 BASHH CEG guidance on tests for sexually transmitted infections 2015.
10. IUSTI. European guideline for the management of *Chlamydia trachomatis* infections. 2010.
11. Sultan B, White JA, Fish R, Carrick S, Brima N, Copas A et al. The "3 in 1" Study: Pooling Self-Taken Pharyngeal, Urethral, and Rectal Samples into a Single Sample for Analysis for Detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in Men Who Have Sex with Men. *Journal of clinical microbiology* 2016;54:650-6.
12. Rours GI, Verkooyen RP, Willemse HF, van der Zwaan EA, van Belkum A, de Groot R et al. Use of pooled urine samples and automated DNA isolation to achieve improved sensitivity and cost-effectiveness in large-scale testing for *Chlamydia trachomatis* in pregnant women. *Journal of clinical microbiology* 2005;43:4684-90.
13. Toby M, Saunders P, Ison CA. Survey of the laboratory diagnosis of gonorrhoea and chlamydia infection in the UK. *Sexually Transmitted Infections* 2015;91:299.
14. Gaydos C *Chlamydia trachomatis: Molecular testing methods* Vol 7. Basel: Karger; 2013. 78-88.
15. Jamil MS, Hocking JS, Bauer HM, Ali H, Wand H, Smith K et al. Home-based chlamydia and gonorrhoea screening: a systematic review of strategies and outcomes. *BMC public health* 2013;13:189.
16. McNicol J, Debattista J. Use of the UriSwab collection device for testing of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: Implications for a postal testing service. *International Journal of STD and AIDS* 2013;24:477-80.
17. Gaydos CA, Farshy C, Barnes M, Quinn N, Agreda P, Rivers CA et al. Can mailed swab samples be dry-shipped for the detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* by nucleic acid amplification tests? *Diagnostic Microbiology and Infectious Disease* 2012;73:16-20.

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18. Hislop J, Quayyum Z, Flett G, Boachie C, Fraser C, Mowatt G. Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital chlamydia infection in women and men. *Health Technology Assessment* 2010;14:i-125.
19. Jain A, Ison CA. Chlamydia point-of-care testing: Where are we now? *Sexually Transmitted Infections* 2013;89:88-9.
20. Hesse EA, Patton SA, Huppert JS, Gaydos CA. Using a rapid communication approach to improve a POC Chlamydia test. *IEEE Transactions on Biomedical Engineering* 2011;58:837-40.
21. Huang W, Gaydos CA, Barnes MR, Jett-Goheen M, Blake DR. Comparative effectiveness of a rapid point-of-care test for detection of *Chlamydia trachomatis* among women in a clinical setting. *Sexually Transmitted Infections* 2013;89:108-14.
22. Dean D, Turingan RS, Thomann HU, Zolotova A, Rothschild J, Joseph SJ et al. A Multiplexed Microfluidic PCR Assay for Sensitive and Specific Point-of-Care Detection of *Chlamydia trachomatis*. *PloS one* 2012;7.
23. British Association for Sexual Health and HIV. *Chlamydia trachomatis* UK testing guidelines. 2010.
24. Van Liere GAFS, Hoebe CJPA, Wolffs PFG, Dukers-Muijers NHTM. High co-occurrence of anorectal chlamydia with urogenital chlamydia in women visiting an STI clinic revealed by routine universal testing in an observational study; a recommendation towards a better anorectal chlamydia control in women. *BMC Infectious Diseases* 2014;14.
25. Pitt RA, Alexander S, Horner PJ, Ison CA. Presentation of clinically suspected persistent chlamydial infection: A case series. *International Journal of STD and AIDS* 2013;24:469-75.
26. Puolakkainen M. Laboratory diagnosis of persistent human chlamydial infection. *Frontiers in Cellular and Infection Microbiology* 2013;3.
27. Royal College of Pathologists. Guidelines for handling medicolegal specimens and preserving the chain of evidence. 2008.
28. British Association for Sexual Health and HIV. UK National Guidelines on the Management of Adult and Adolescent Complainants of Sexual Assault. 2011.
29. NICE. Chlamydia - uncomplicated genital 2011.
30. Public Health England. Laboratory Reporting to Public Health England: A Guide for Diagnostic Laboratories 2013. 1-37.
31. Department of Health. Health Protection Legislation (England) Guidance. 1-112. 2010.
32. Scottish Government. Public Health (Scotland) Act. 2008.
33. Scottish Government. Public Health etc. (Scotland) Act 2008. Implementation of Part 2: Notifiable Diseases, Organisms and Health Risk States. 2009.
34. The Welsh Assembly Government. Health Protection Legislation (Wales) Guidance. 2010.
35. Home Office. Public Health Act (Northern Ireland) 1967 Chapter 36. 1967.