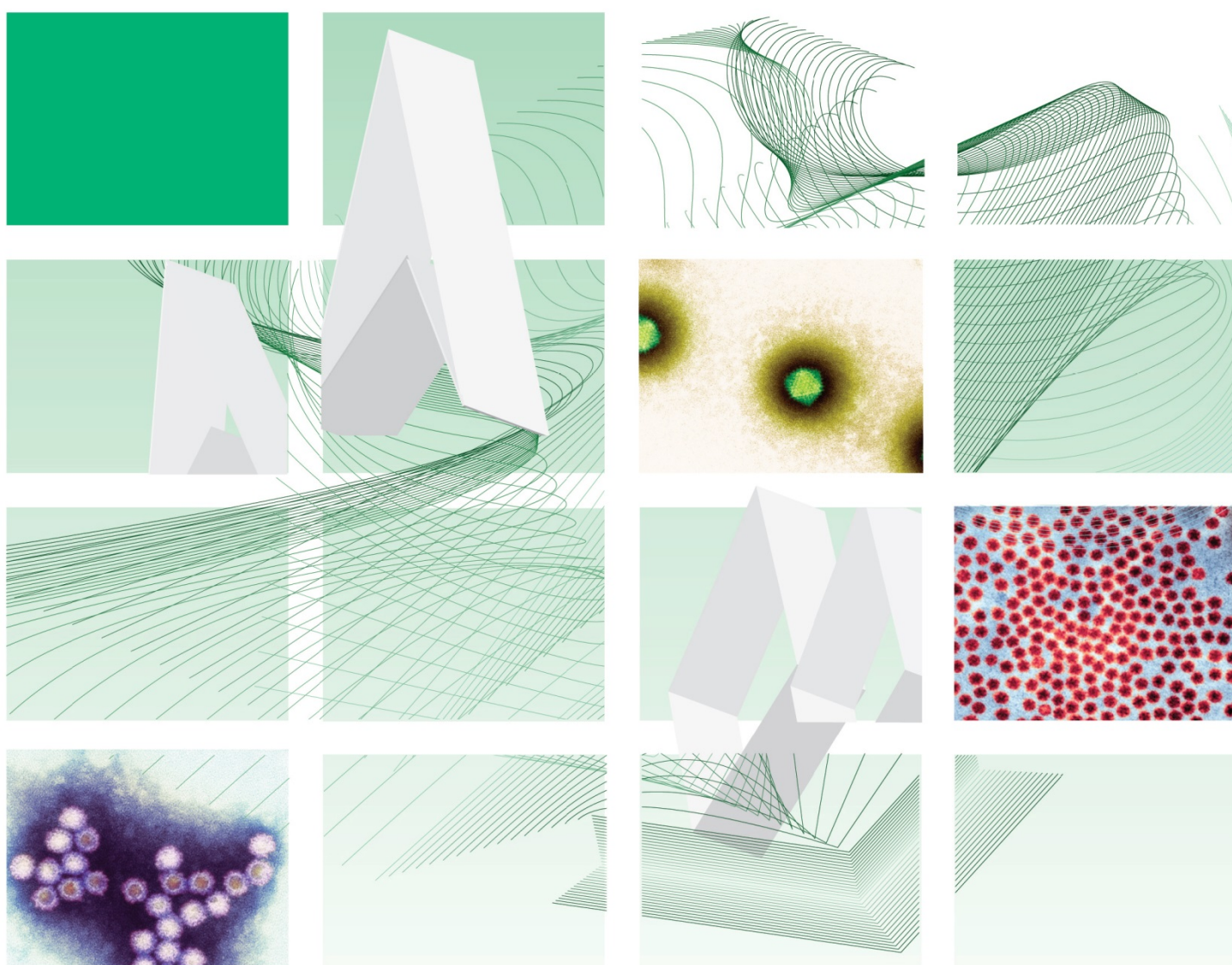




UK Standards for Microbiology Investigations

HIV screening and confirmation



"NICE has renewed accreditation of the process used by **Public Health England (PHE)** to produce **UK Standards for Microbiology Investigations**. The renewed accreditation is valid until **30 June 2021** and applies to guidance produced using the processes described in **UK standards for microbiology investigations (UKSMIs) Development process, S9365', 2016**. The original accreditation term began in **July 2011**."

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Acknowledgments

UK Standards for Microbiology Investigations (UK 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>. UK 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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For further information please contact us at:

Standards Unit
National Infection Service
Public Health England
61 Colindale Avenue
London NW9 5EQ

E-mail: standards@phe.gov.uk

Website: <https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories>

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Amendment table

Each UK 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.	6/03.01.17
Issue no. discarded.	4
Insert issue no.	4.1
Section(s) involved	Amendment
Whole document.	New NICE/PHE guideline added in the Introduction and Public Health Management sections of the document.

Amendment no/date.	5/22.11.16
Issue no. discarded.	3.2
Insert issue no.	4
Section(s) involved	Amendment
Whole document.	<p>Title of document updated to HIV Screening and Confirmation.</p> <p>Scientific content updated.</p> <p>The Virology template format updated with new sections.</p> <p>Definitions of different terms used during testing and reporting stages have been explained.</p> <p>Technical limitations/information added.</p> <p>Reporting section included.</p> <p>Links to documents and websites updated.</p> <p>Evidence grading added in the References section. A summary table which defines the grades has been added and this should be used in conjunction with the reference list.</p> <p>References updated.</p>
Appendix.	The algorithm from the previous UK SMI document has been split one for HIV screening and the other for HIV confirmation. These new recommended

	<p>algorithms brings clarity to the laboratory diagnosis of acute and established HIV infection, fewer situations for inconclusive results and quicker turnaround times of final reports for tests.</p> <p>A HIV reporting table for patients has been included to summarise the combination of results that do occur and the individual comments that could be added.</p>
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UK SMI[#]: scope and purpose

Users of UK SMIs

Primarily, UK SMIs are intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK. 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 UK SMIs

UK 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 UK 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

UK 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 UK SMI indicates participation of the society in equal partnership and support for the objectives and process of preparing UK SMIs. Nominees of professional societies are members of the Steering Committee and working groups which develop UK 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. UK SMIs are developed, reviewed and updated through a wide consultation process.

Quality assurance

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

[#] 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.

accredited and represent neither minimum standards of practice nor the highest level of complex laboratory investigation possible. In using UK SMIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. UK SMIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. UK SMIs also provide a reference point for method development. The performance of UK 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 UK SMI working groups are committed to patient and public involvement in the development of UK SMIs. By involving the public, health professionals, scientists and voluntary organisations the resulting UK 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 UK SMIs is subject to PHE Equality objectives <https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity>.

The UK 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 UK 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 UK SMI or any information contained therein. If alterations are made by an end user to an UK 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 UK 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 UK 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.

UK SMIs are Crown copyright which should be acknowledged where appropriate.

Suggested citation for this document

Public Health England. (2017). HIV screening and confirmation. UK Standards for Microbiology Investigations. V 11 Issue 4.1. <https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories/>

Scope of document

Type of specimen

Whole blood, serum or plasma

Note: Venous blood is the preferred specimen for HIV testing. Dried blood and dried plasma spots have been validated and are commonly used for HIV testing and monitoring of hard to reach groups^{1,2}.

This algorithm outlines the laboratory-based detection and exclusion of HIV infection using serology and nucleic acid amplification tests.

Testing of oral fluid/saliva is not covered by this UK SMI. Such samples should be referred to reference laboratories, as they may be subject to more sampling variation which must be taken into consideration when assessing the sensitivity and utility of the test in various settings.

The scope of this algorithm does not include investigation of potential mother to child transmission of HIV in children under 18 months of age, or the testing of blood prior to organ donation. Refer to the SaBTO Guidance on the microbiological safety of human organs, tissues and cells used in transplantation³.

Laboratory-based HIV diagnostic algorithms should provide appropriate certainty for exclusion and detection of HIV-1 and 2 infections in all patient groups and clinical settings, and should also distinguish HIV-1 from HIV-2 infection. Early detection enables initiation of antiretroviral therapy and thereby better preservation of immunological function, quicker viral load suppression and reduction of HIV transmission to sexual partners by more than 96%. Suppression of viral replication also has potential to reduce both the emergence of viral mutations and the severity and duration of symptoms due to acute HIV infection⁴⁻⁷.

Refer to UK SMI [Q 7 - Good practice when undertaking serology assays for infectious diseases](#) for information regarding good laboratory practice in serological testing.

This UK SMI should be used in conjunction with other UK SMIs.

Definitions

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

During testing process

Reactive – Initial internal stage positive result pending confirmation.

Not-reactive – Initial internal stage negative result.

Indeterminate/ equivocal – Result is not clearly positive or negative. Further testing is required. This is used for preliminary reports.

Reporting stage

Indeterminate – Reactive result that cannot be confirmed. This is used for final or preliminary reports.

Detected – Report stage confirmed reactive result.

Not detected – Report stage not reactive result.

Introduction

Human immunodeficiency virus (HIV) is a retrovirus that causes a chronic infection in the cells of the immune system. It is transmitted via exposure to body fluids containing free virus particles. Without treatment, most persons with HIV develop acquired immunodeficiency syndrome (AIDS) within 10 years of infection, which is associated with substantial morbidity and premature death.

Over 100,000 people were living with HIV infection (diagnosed and undiagnosed) in the UK in 2013 and, globally, 2 million people acquired the infection in the following year, resulting in almost 37 million people living with HIV in total. Almost 70% of all new HIV infections currently occur in sub-Saharan Africa⁸.

There are two recognised HIV types – HIV-1 and HIV-2. HIV-1 is found largely throughout the world including UK, USA and the rest of Europe. It is divided into three groups on the basis of differences in the envelope region, HIV-1 major group (HIV1-M), outlier (HIV1-O) and HIV1-N group. The HIV1-M major group can be classified further into 9 subgroups designated A through to K excluding E and I. These subgroups have envelope gene sequences that vary based on genetic similarities. They differ in geographical distribution, biological characteristics and major mode of transmission etc. HIV-1 groups O and N are more distant to all other HIV-1 subgroups (but less so compared to HIV-2) and therefore are classified under HIV-1 only, with a limited distribution in West Africa.

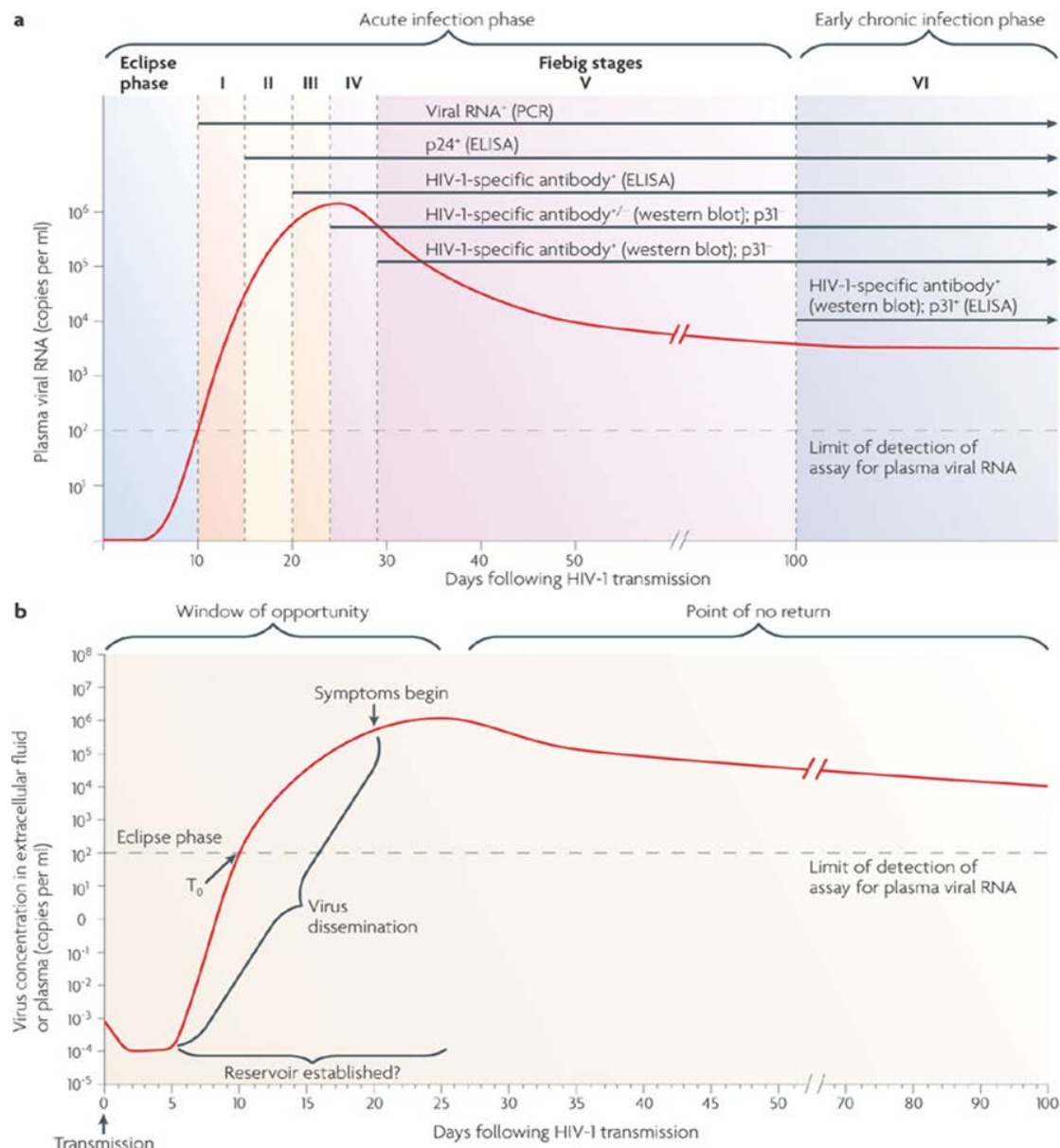
HIV-2 is found largely in West Africa and also comprises of a heterogeneous group of viruses that has been divided into 5 subgroups designated A through to E⁹.

Accurate laboratory diagnosis of HIV is essential to identify those who could benefit from treatment, to reduce HIV transmission and to reassure persons who are uninfected. Expansion of HIV testing in health care settings has been strongly recommended in guidelines from the European Centre for Disease Prevention and Control (ECDC), World Health Organisation (WHO), British HIV Association (BHIVA), British Association of Sexual Health and HIV (BASHH) and the British Infection Society (BIS), in order to facilitate earlier diagnosis^{7,10,11}. Public Health England (PHE) and National Institute for Health and Care Excellence (NICE) guidelines also support these recommendations in health care settings in the UK¹²⁻¹⁶. There are 3 categories of HIV indicator conditions that should prompt consideration of HIV testing¹⁰:

- patients presenting with potentially AIDS defining conditions, or symptoms suggestive of primary HIV⁷;
- patients presenting with conditions or risk factors associated with a likely undiagnosed HIV prevalence of >0.1%;
- conditions where not identifying the presence of HIV infection may have significant adverse implications for the patient's correct diagnosis or clinical management. This includes dialysis, conditions requiring aggressive immunosuppressive therapy (such as cancer, transplantation, or auto-immune disease), primary space occupying lesion of the brain and idiopathic/thrombotic thrombocytopenic purpura.

Window period of infection^{9,17-19}

This is the period between exposure and the ability to detect markers of HIV infection (such as antibodies, antigens and RNA) in the peripheral blood. The graphs and the table below show the window period for RNA detection and its duration.



Nature Reviews | Immunology

Figure 1: The different window periods/stages in HIV infection. *Courtesy of AJ McMichael Nature, 2010²⁰.*

The Fiebig stages (figure 1) characterises early HIV infection and HIV seroconversion in relation to the time at which different HIV tests will give a positive reaction. They reflect the immunological and pathological events that occur, sequentially, in patients on and after exposure to HIV infection and post infection. These stages and their durations are described in Table 1:

Table 1: Fiebig Stage Classifications for Substages of Human Immunodeficiency Virus Type 1 Primary Infection, with Durations. *Courtesy of MS Cohen et al. J Infect Dis. 2010²¹.*

Stage	Defining finding and/or marker	Duration, mean (range), days	
		Individual phase	Cumulative duration
Eclipse		10 (7-21)	10 (7-21)
I	vRNA positive	7 (5-10)	17 (13-28)
II	P24 antigen positive	5 (4-8)	22 (18-34)
III	ELISA positive	3 (2-5)	25 (22-37)
IV	Western blot positive or negative	6 (4-8)	31 (27-43)
V	Western blot positive, p31 antigen negative	70 (40-122)	101 (71-154)
VI	Western blot positive, p31 antigen positive	Open-ended	...
Note: ELISA, enzyme-linked immunoassay; vRNA, viral RNA.			

Thus, depending on the type of screening test and the sample being tested, the window period for detecting HIV infection could range from 4 weeks for 4th generation HIV blood tests up to three months for 3rd generation HIV blood tests. This reflects the ability of 4th generation HIV assays to detect HIV p24 antigen, whereas third generation HIV assays detect only antibodies (IgM and IgG) against HIV-1 and HIV-2. This antibody response occurs after p24 antigen but, at 12 weeks post-exposure, 99% of all true infections should be picked up by 3rd generation assays. The type of sample is another variable affecting the window period for different assays. Venous and capillary blood samples will give reactive results within the 4 week window period in 4th generation assays. The joint [BASHH/EAGA \(Expert Advisory Group on AIDS\) statement](#) on the HIV seroconversion window period, November 2014, acknowledges the improvements in assay sensitivity and the information shown above²²:

“HIV testing using the latest (fourth generation) tests is recommended in the BHIVA / BASHH / BIS UK guidelines for HIV testing (2008). These assays test for HIV antibodies and p24 antigen simultaneously. A fourth generation HIV test on a venous blood sample performed in a laboratory will detect the great majority of individuals who have been infected with HIV at 4 weeks after specific exposure.

Patients attending for HIV testing who identify a specific risk occurring less than 4 weeks previously should not be made to wait before HIV testing as doing so may miss an opportunity to diagnose HIV infection (and in particular acute HIV infection during which a person is highly infectious). They should be offered a fourth generation laboratory HIV test and be advised to repeat it when 4 weeks have elapsed from the time of the last exposure.

A negative result on a fourth generation test performed at 4 weeks post-exposure is highly likely to exclude HIV infection. A further test at 8 weeks post-exposure need only be considered following an event assessed as carrying a high risk of infection.

Patients at ongoing risk of HIV infection should be advised to retest at regular intervals.

Patients should be advised to have tests for other sexually transmitted infections in line with advice on window periods for those infections (see BASHH guidelines at: www.bashh.org).

Testing after occupational exposure

While the BASHH / EAGA statement may also apply to healthcare workers who are exposed to HIV infection in the occupational setting, reference should be made to the Department of Health, UK Expert Advisory Group on AIDS (EAGA) guidance on [HIV post-exposure prophylaxis](#)^{9,17,18,22}. This states that 'A negative HIV test result at 12 weeks post-exposure or post cessation of PEP provides a very high level of confidence of freedom from HIV infection related to the occupational exposure'.

Elite controllers

A few HIV-1 infected patients are able to maintain better immunological control of HIV infection, with consequent lower or undetectable HIV-1 viral loads and higher mean CD4 cell counts. This phenomenon is encountered rarely, being identified in approximately 1% of patients in some cohorts, however varying case definitions have been employed^{23,24}. Recent consensus defines elite controllers as patients who are treatment naïve with CD4 count >500 cells/mm and either all plasma HIV viral load measurements below limit of assay detection for over a 6 month period, or >90% plasma HIV viral load measurements of <400 copies/mL over a 10 year period²⁵. These parameters are associated with a lower hazard ratio for disease progression, but can also modulate some of the expected laboratory findings during early infection. It is important to recognise this rare clinical possibility when diagnosing a new HIV infection: HIV proviral DNA testing might be helpful in the initial diagnostic stages, although in some viral suppressors, even this test could still be negative.

Types of HIV diagnostic tests

There are several test types that could be used for HIV diagnosis. They are as follows:

Serological assays detect HIV antigens and/or antibodies and are grouped into "generations", as follows:

Third generation tests

These tests detect all types of HIV antibodies, but not antigens. The third generation tests are reactive by 20 to 30 days, at the earliest, following exposure¹¹. Although it has been recommended that laboratories use fourth generation assays as screening tests, a third generation assay may be used as a supplementary test to differentiate antigen from antibody signals in samples reactive in fourth generation assays¹²⁷.

Fourth generation tests

They are the first line choice tests depending on clinical scenarios and are recommended by BHIVA /BASHH /BIS guidelines in the UK for use for initial testing and are better at detecting acute, established or very late HIV infection than other forms of testing²². These are synthetic peptide or recombinant protein antigens used in the same antigen sandwich format as third generation assays to detect IgM and IgG antibodies, and monoclonal antibodies are also included to detect p24 antigen. Inclusion of p24 antigen capture allows detection of HIV-1 infection before antibody production. These do not usually distinguish antibody reactivity from antigen reactivity.

The window period for these tests can be 15 to 20 days in most patients; and clinical guidelines classify the window period as 4 weeks²⁶. They are the current standard of care for HIV screening in UK.

Fourth generation point - of - care tests (POCTs)

These rapid tests can be performed on blood or other sample types and also detect HIV antibodies and p24 antigens. However, it should be noted that the ability to detect p24 antigen, as in the setting of acute infection, has been reported to be very low²⁷. Fourth generation POCTs may also vary in their ability to discriminate between HIV-1 and HIV-2.

According to BASHH, these rapid HIV blood tests are generally satisfactory for detection of uncomplicated, established HIV infection⁷. The window period for these tests can be highly variable but they should detect most infections within 6 weeks of exposure to HIV and results are available within 30 minutes of testing²⁸. They are recommended only in certain settings, such as community outreach projects and drop in clinics, as well as for screening hard-to-bleed high risk patients.

Point-of-care testing should be either overseen by local laboratories that can help to deliver a robust quality assurance system or used under professional supervision with clear pre- and post-test counselling. Further tests must be performed for all patients with positive rapid test results and for those with negative results where there is suspicion of infection or continued high risk of exposure⁷.

p24 only tests²⁹

These tests detect the viral capsid p24 protein in a blood/serum specimen. As noted above, p24 antigen is detectable before HIV antibody during acute infection. A limitation of the p24 antigen test during seroconversion is that antigenemia is transient: it can appear as early as 2 weeks after infection and disappear quite quickly; or last 3 to 5 months depending on the host's immune response and other viral regulatory factors. Thus the window period for these tests is around 2 to 4 weeks. However, p24 antigen can become detectable again in advanced HIV infection due to the prolonged immunosuppression of HIV antibodies by the virus²⁹.

The specificity of a reactive p24 antigen result should be confirmed by a p24 antigen neutralisation test, or by detection of HIV-1 RNA in plasma.

Nucleic Acid Amplification Tests (NAATs)

NAAT can detect viral genetic material (RNA or DNA). Most assays measure HIV-1 RNA, though HIV-2 RNA testing is available at a few laboratories in the UK. HIV-2 RNA tests are not currently approved by MHRA, and are used only on an individual patient basis where clinically indicated.

Quantitative HIV-1 NAAT can be used as a supplementary test when a patient gives persistently indeterminate immunoblot/immunoassay results, or in suspected primary HIV infection but should only be performed with specialist input^{7,9,30}. NAATs are not recommended or licensed for initial HIV screening because they may give false positive results^{3,28,31}. In addition, NAAT tests offer very little advantage over fourth generation assays in terms of earlier detection of acute infection.

Blood donations are screened for viral RNA to reduce the risk of transmitting HIV from blood donated during the serological window period of antigen and antibody assays^{3,24}.

Proviral DNA testing may be useful for confirming the status of patients with indeterminate serology and undetectable HIV RNA or for testing infants born to HIV-infected women³².

Note: A few qualitative HIV-1 NAATs are commercially available; however such tests are not currently part of standard testing algorithms in the UK³³.

Other commercial alternatives

Home testing kits^{13,28}

There are two different types of HIV home testing kits: instant result self-testing kits and home sampling kits. However, these will not be covered in detail here as it is not within the scope of the document.

Technical limitations/information

Limitations of UK SMIs

The recommendations made in UK SMIs are based on evidence (for example, 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 tests have been verified and in-house tests have been validated and are fit for purpose.

Specimen containers^{1,2}

UK 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”.

Safety considerations

Collect specimens in appropriate CE marked leak proof containers and transport in sealed plastic bags. In resource limited countries, dried blood spots (on filter paper) for sample collection are used rather than blood samples because the storage conditions in these settings are impractical. DBS has been shown to keep the viral nucleic acid in good condition during transportation³⁴.

Compliance with postal, transport and storage regulations is essential.

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

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

Public health management

Early HIV screening and testing of patients helps in controlling the HIV epidemic and reducing late HIV diagnosis. Programmes that have been introduced to increase HIV testing have been shown to be cost-effective and provide a positive return on investment.

For information regarding notification to PHE (or equivalent in the devolved administrations), refer to the section for Notification to PHE or equivalent in the devolved administrations.

For more information on promotion of HIV testing, refer to the joint PHE and NICE guideline: <http://nice.org.uk/guidance/ng60>.

For further information on public health management of HIV, refer to PHE guidance: <https://www.gov.uk/government/collections/hiv-surveillance-data-and-management>.

For information on healthcare workers who are exposed to blood borne viral infections in the occupational setting, refer to <https://www.gov.uk/government/groups/uk-advisory-panel-for-healthcare-workers-infected-with-bloodborne-viruses> and for information on post exposure prophylaxis, refer to http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_088185?ss=SourceSiteId=ab.

Other sources of information

For other international guidelines that may be useful see below, bearing in mind that practice in some countries differs significantly from UK practice due to regulatory requirements:

Public Health Agency of Canada (PHAC)

<http://www.phac-aspc.gc.ca/aids-sida/guide/hivstg-vihgdd-eng.php>

CDC

This link <http://www.cdc.gov/hiv/guidelines/testing.html> leads to all the links below:

[Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations](#)

[Quick Reference Guide—Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations,](#)

[Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm](#)

WHO has important details on rapid tests

http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/unaidspublication/2014/JC2603_self-testing_en.pdf

http://www.who.int/diagnostics_laboratory/evaluations/hiv/en/

http://www.who.int/diagnostics_laboratory/publications/15032_hiv_assay_report18.pdf?ua=1

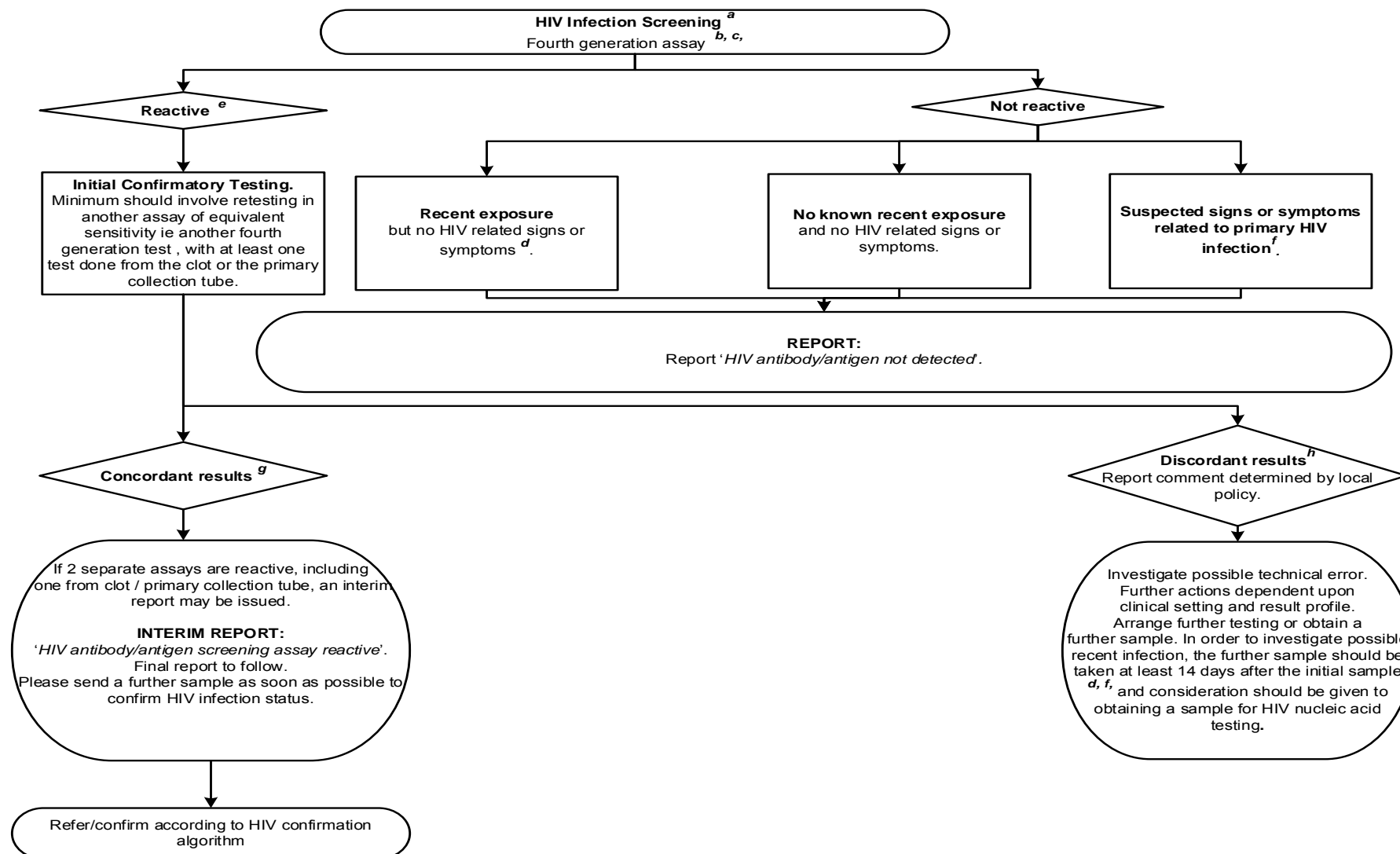
ECDC

http://ecdc.europa.eu/en/publications/Publications/101129_TER_HIV_testing_evidence.pdf

<http://hiveurope.eu/Portals/0/Guidance.pdf.pdf>

<http://www.iusti.org/regions/europe/pdf/2014/2014IUSTIguidelineonHIVtesting.pdf>

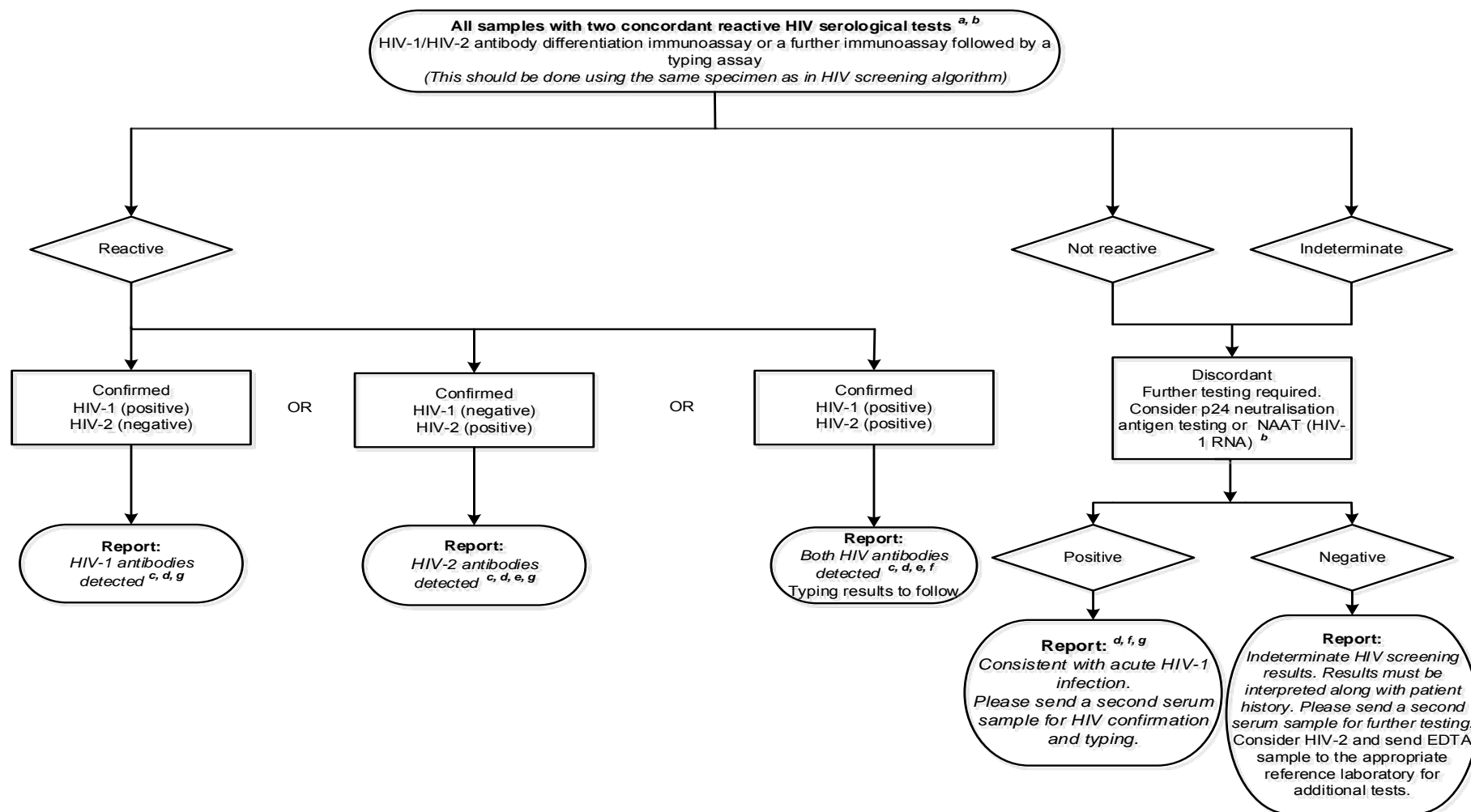
HIV screening^{7,9,11,26,34-40}



Footnotes relating to HIV screening

- a) This algorithm is not applicable to investigation of potential mother to child transmission of HIV in children under 18 months of age or screening for organ donation.
- b) BASHH UK national guidelines on HIV testing recommend point-of-care tests to be considered for use where very rapid availability of test results is desirable, such as in outreach care settings, GUM clinics, community testing sites, urgent source testing and circumstances in which venepuncture is refused⁷. Such rapid tests (antibody only, or combined antibody/antigen) may be indicated in certain settings where the overall benefit of increased testing outweighs any potential disadvantage of poorer test performance.
- c) HIV RNA NAATs (viral load tests) are not recommended for initial diagnostic HIV screening. Although they may offer the marginal benefit in detecting early HIV infection, they are not licensed for diagnostic use and have the potential to give both false positive and false negative results^{1,39,41}. Furthermore, most RNA NAATs detect only the more common HIV-1 and not HIV-2 virus.
- d) See [BASHH statement](#) on HIV seroconversion window period, November 2014²².
- e) HIV vaccine recipients (having a HIV test) with reactive immunoassay results are encouraged to contact a vaccine trial site for specialised testing to determine their HIV infection status.
- f) If sample is negative on testing in a case of suspected primary HIV infection, send further sample for retesting within 14 days²².
- g) Results are considered concordant when both the initial fourth generation screening test and a second fourth generation assay of differing specificity (but equivalent sensitivity) are reactive.
- h) Results are considered discordant either when results differ between the clot sample/ primary collection tube and the aliquot sample, or when reactivity in the initial fourth generation assay is not reproduced in the second fourth generation assay. When discordant results occur, further investigations should be performed using samples from the primary collection tube.

HIV confirmation^{26,34,39}



Footnotes relating to HIV confirmation

- a) An HIV-1/HIV-2 antibody differentiation immunoassay should be used to confirm reactive serology results because it distinguishes between HIV-1 and HIV-2 and therefore has important implications for treatment.
- b) HIV NAATs may help to confirm suspected infection and may be used as an optional alternative to confirmatory immunoassays, or to resolve discordant results, but local policies should define their use and interpretation. It should be noted that some HIV NAAT assays are only validated for treatment monitoring and not for use as diagnostic assays.
- c) Repeat serology testing of a second sample is recommended to rule out mislabelling and confirm patient identity. A separate sample giving a positive NAAT result could fulfil this requirement. Where viral load is undetectable or below the detection limit of the assay, a further sample should be collected for serological testing. Attention should be paid to the final diagnosis, whether HIV-1, HIV-2 or both as it has important treatment implications.

Note: When testing patients who are known to be HIV positive but are new to laboratory records, a second sample should still be requested for completeness.

- d) Laboratory reports of newly identified HIV positive individuals from clinics and laboratories in England and Wales should be forwarded to the HIV Reporting Section of Public Health England, Colindale (<https://www.gov.uk/government/collections/hiv-surveillance-data-and-management>), while new cases in Scotland should be reported to Health Protection Scotland (<http://www.hps.scot.nhs.uk/bbvsti/surveillancesystems.aspx>). In Northern Ireland, new HIV diagnoses are reported via CoSurv to the Public Health Agency Northern Ireland.

A definitive diagnosis of HIV infection should not be reported to the relevant agency unless the full confirmatory testing algorithm has been completed with a positive result AND the results are confirmed by testing a second specimen.

- e) There are currently no MHRA approved tests for HIV-2 RNA or DNA; they are available at a few centres in the UK on an individual patient basis.
- f) A confirmed reactive HIV test result which cannot be typed should be referred to the appropriate reference laboratory for further HIV testing.
- g) HIV avidity testing distinguishes recent infections from established infections and is primarily used for monitoring at a population level. HIV avidity testing is available as a public health surveillance tool at PHE Colindale, London Edinburgh and in Glasgow, West of Scotland. In England, Wales and Northern Ireland, clinics and laboratories can have specimens tested for evidence of recent HIV infection by antibody avidity testing through agreeing a memorandum of understanding with PHE, Colindale. Specimens for HIV avidity testing should be the first confirmed anti-HIV positive specimen from the patient if available, however where not available, the laboratory should ask for another specimen. Clinicians should be aware that the avidity test is not diagnostic and the result should be considered with clinical and other laboratory data. The avidity test can be affected by infecting HIV subtype, current or previous

treatment with ARV's and declining immune status such as found in patients with AIDS.

Report comments

The table below is a summary of the combinations of confirmation results that may occur and require individual comments based upon profile and clinical setting, along with a further sample. Refer to footnotes for further information and actions.

Note: Two fourth generation tests have already been performed in the screening stage.

Further testing of HIV screening test reactive samples by using HIV-1/HIV-2 antibody differentiation immunoassay or a further immunoassay followed by a typing assay.

	HIV-1	HIV-2	Interpretative comment	Notes
1	Reactive	Not reactive	HIV- 1 antibodies detected. Evidence that HIV-1 infection is present.	Please send a repeat sample to confirm.
2	Not reactive	Reactive	HIV- 2 antibodies detected. Evidence that HIV-2 infection is present.	Please send a repeat sample to confirm.
3	Reactive	Reactive	HIV- 1/HIV-2 antibodies detected. Evidence that HIV infection is present. HIV antibodies could not be differentiated as HIV-1 or HIV-2.	Suggest sending sample to reference laboratory for further testing. Additional testing for HIV-1 RNA or HIV-2 RNA should be performed. Please send a repeat sample to confirm.
4	Not reactive/ Indeterminate	Not reactive/ Indeterminate	HIV antibodies are not confirmed. Further testing required.	Follow up testing HIV p24 antigen or by HIV-1 RNA. <ul style="list-style-type: none"> HIV-1 RNA positive / p24 antigen neutralised Consistent with acute HIV-1 infection Please send a repeat serum sample for confirmation and typing if confirmed by p24 antigen. HIV-1 RNA negative / p24 antigen not

				<p>neutralised</p> <p>Indeterminate HIV screening results. Results must be interpreted along with patient history. Please send a second serum sample for further testing. Consider HIV-2 and send EDTA sample to the appropriate reference laboratory for additional tests.</p> <p>Note: HIV-2 RNA testing should be performed if clinically indicated.</p>
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Notification to PHE^{42,43}, or equivalent in the devolved administrations⁴⁴⁻⁴⁷

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](#)^{44,45}, [Wales](#)⁴⁶ and [Northern Ireland](#)⁴⁷.

References

Modified GRADE table used by UK SMLs when assessing references

Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) is a systematic approach to assessing references. A modified GRADE method is used in UK SMLs for appraising references for inclusion. Each reference is assessed and allocated a grade for strength of recommendation (A-D) and quality of the underlying evidence (I-VI). A summary table which defines the grade is listed below and should be used in conjunction with the reference list.

Strength of recommendation		Quality of evidence	
A	Strongly recommended	I	Evidence from randomised controlled trials, meta-analysis and systematic reviews
B	Recommended but other alternatives may be acceptable	II	Evidence from non-randomised studies
C	Weakly recommended: seek alternatives	III	Non-analytical studies, for example, case reports, reviews, case series
D	Never recommended	IV	Expert opinion and wide acceptance as good practice but with no study evidence
		V	Required by legislation, code of practice or national standard
		VI	Letter or other

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