



National Public Health Monitoring of Incident HIV-1 Infections and Primary Drug Resistance

Laboratory Protocol

Health Protection Agency

Centre for Infections

Version 4.3 01/11/08

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1. Background

HIV poses a unique challenge to the public health monitoring of communicable diseases as a result of the extended period between infection and the onset of symptoms, which is typically between eight and eleven years. Current tests for HIV are unable to distinguish recently acquired infections (incident infections) from long standing infections. As a result, we have no way of directly assessing whether the increases seen in the number of newly diagnosed infections in the UK is a result of the success in promoting HIV testing, or a failure to reduce HIV transmission.

Recent laboratory advances, however, have made it possible to identify infections that are likely to have been acquired within a well defined recent time frame, which can be used as a basis for determining the incidence of infection as a key indicator of HIV transmission. The generic term 'Recent Infection Testing Algorithm' (RITA) has been coined to cover the several serological methods that have been described to distinguish a recent infection.

The HPA is establishing an enhanced HIV virological surveillance program to incorporate these new methodologies into existing national HIV surveillance systems to provide accurate estimates of HIV incidence. Our intention is to better characterise the HIV epidemic by identifying populations and/or subpopulations where a greater risk of transmission, and therefore a greater need for intervention exists. Estimates of HIV incidence can also supply additional information for advocating, designing and planning public health action as well as providing the most direct means for evaluating the impact of intervention initiatives.

2. Aims

Working in close collaboration with national and local laboratory and GUM services, the aims of the National Public Health Monitoring of Incident HIV-1 Infections and Primary Drug Resistance are to:

Locally:

- Provide the proportion of local infections that are likely to be recent.
- Provide links between resistance and incidence results for the local monitoring of primary drug resistance.
- Provide data to inform and evaluate local health promotion and HIV prevention initiatives.

Nationally:

- Provide appropriately stratified national estimates of HIV incidence.
- Integrate the national database of newly diagnosed HIV infections with the MRC HIV resistance database for the national monitoring of primary drug resistance.
- Provide data to inform and evaluate national health promotion and HIV prevention initiatives

3. Sample Requirements

i. Eligibility Criteria

To be included into the HIV-1 incidence and resistance public health monitoring program, an aliquot of all confirmed HIV positive samples should be sent to the Virus Reference Division, at the Health Protection Agency (HPA), Colindale, for RITA testing. The HPA have the resources in place to offer RITA testing at no additional charge, providing that the cost of transporting samples to the HPA, Colindale, can be met by the collaborating centre. Serum or plasma specimens should be submitted only for newly diagnosed infections, and where an individual is:

- Confirmed to be anti-HIV-1 antibody positive;
- First HIV diagnosis
- Over 16 years old;
- Total sample volume available for submission is >0.5mls, although samples in excess of 0.2mls can still be submitted, but will allow only minimal testing.

ii. Sample Information

All necessary epidemiological information for each of the HIV positive samples will be collected through a combination of the laboratory and clinician report forms that we routinely receive for all new HIV diagnoses. However, with the added complexities of estimating HIV incidence and the potential for misclassification, we will be seeking feedback from the clinic on any medical condition that may affect the serological testing methodologies (e.g. hyper- or hypo- gammaglobulinemia) and on instances where the clinical data suggests a non-recent infection.

iii. Sample Test Request Form

Specimens should be submitted using the test request form, an example of which can be found in section 9. All centres will receive a personalised copy of the specimen submission form, with the senders name and address pre-filled. Although it is important that as much of the form is completed as possible, it is particularly important that the 'patient/source information' section is complete, as these data will be used to link the results of the RITA test to the epidemiological data collected from the clinic. The 'hospital number' field can be completed using the clinic number for GUM patients. Please also ensure that the RITA box is ticked. If you would prefer to submit samples with an alternative test request form, we would be happy to discuss this with you, providing it contains sufficient information to enable each sample to be linked with the national surveillance data.

iv. Frequency of Specimen Submission

Samples can be submitted for RITA testing at intervals convenient for the individual laboratory, providing samples are stored inline with the sample storage and transportation guidelines. RITA testing will be carried out at the HPA on a weekly basis for all available samples.

v. Sample Storage and Transportation

Variations in sample storage conditions can have significant repercussions on the results of the serological testing algorithms which form an integral component of this project. For short periods of time (less than one week), samples can be stored at standard refrigeration temperatures (2-8oC). For long term storage, the sample must be frozen at -20oC or lower, with care taken to avoid freeze-thawing specimens more than 4 times.

Samples should be sent in accordance with the laboratory's standard guidelines and procedures, ensuring that the integrity of the samples is not compromised. Accompanying each set of samples should be a copy of the 'RITA Testing Submission Form', which details the contact information for the originating laboratory and a list of the unique local sample identifiers for the samples contained in each shipment.

vi. Linking Recent Infections to New Diagnoses and the UK Resistance Database

All newly diagnosed HIV infections within the UK are routinely reported to the Health Protection Agency (HPA), and in line with the British HIV Association (BHIVA) guidelines, all new diagnoses are recommended to be accompanied by a resistance test. The collection of patient identifiers will enable the results of the RITA test to be accurately linked with the national databases containing the epidemiological information supplied by the clinic for each

new diagnosis, and the associated resistance tests. This level of linkage will form the foundation for incidence and primary drug resistance monitoring at the local and national level.

vii. RITA Testing Retrospective Samples

Our intention is to extend RITA testing to stored diagnostic material from HIV diagnoses made between 1st January 2005 and the date at which each centre enrolls in the collaboration. This will enable data from the prospective service to be compared to data for previous years, and provide immediate information on the trends in HIV incidence. We will also be able to more rigorously address additional issues such as the representativeness and biases in the retrospective study outcomes. Retrospective RITA test results will be returned to their originating clinic using the same mechanism as the proposed prospective programme.

4. Conformity with the Human Tissue Act

All diagnostic samples received by the HPA will be accompanied by only minimal data equivalent to a subset of that already collected for each newly diagnosed individual in the UK. Data is collected to allow linkage to existing databases for the purpose of local and national public health monitoring, and informing public health action.

5. Conformity with Confidentiality and Caldicott

Appropriate registration is in place for the handling of all data associated with this project, full details of which are available upon request ^{1 2 3}.

¹The HPA is registered under the [Data Protection Act 1998](#) (registration number Z7749250) to handle data for diagnostic, public health and other purposes. The Agency is very careful to maintain its procedures strictly within the requirements of the DPA.

² The HPA is also registered under Section 60 of the [Health and Social Care Act 2001](#) and has approval from the Patient Information Advisory Group (PIAG) to handle data for purposes that include surveillance and the control of disease, even where specific patient consent has not been given.

³ Statutory Instrument 2002 No. 1438 in [The Health Service \(Control of Patient Information\) Regulations 2002](#) provides the legal basis for this data handling. It is included on the HPA website and may also be found at

6. Ethical Considerations

The Public Health Monitoring of Incident HIV-1 Infections and Primary Drug Resistance is an extension of the HIV and AIDS surveillance system established in the mid-1980s for all new diagnoses of HIV and AIDS. However, to address any possible ethical concerns that may arise during the implementation of HIV incidence monitoring, we have applied for, and received SSA exempt NHS Research Ethics Committee (MREC) approval.

7. Outputs

i. Reporting HIV Incidence results

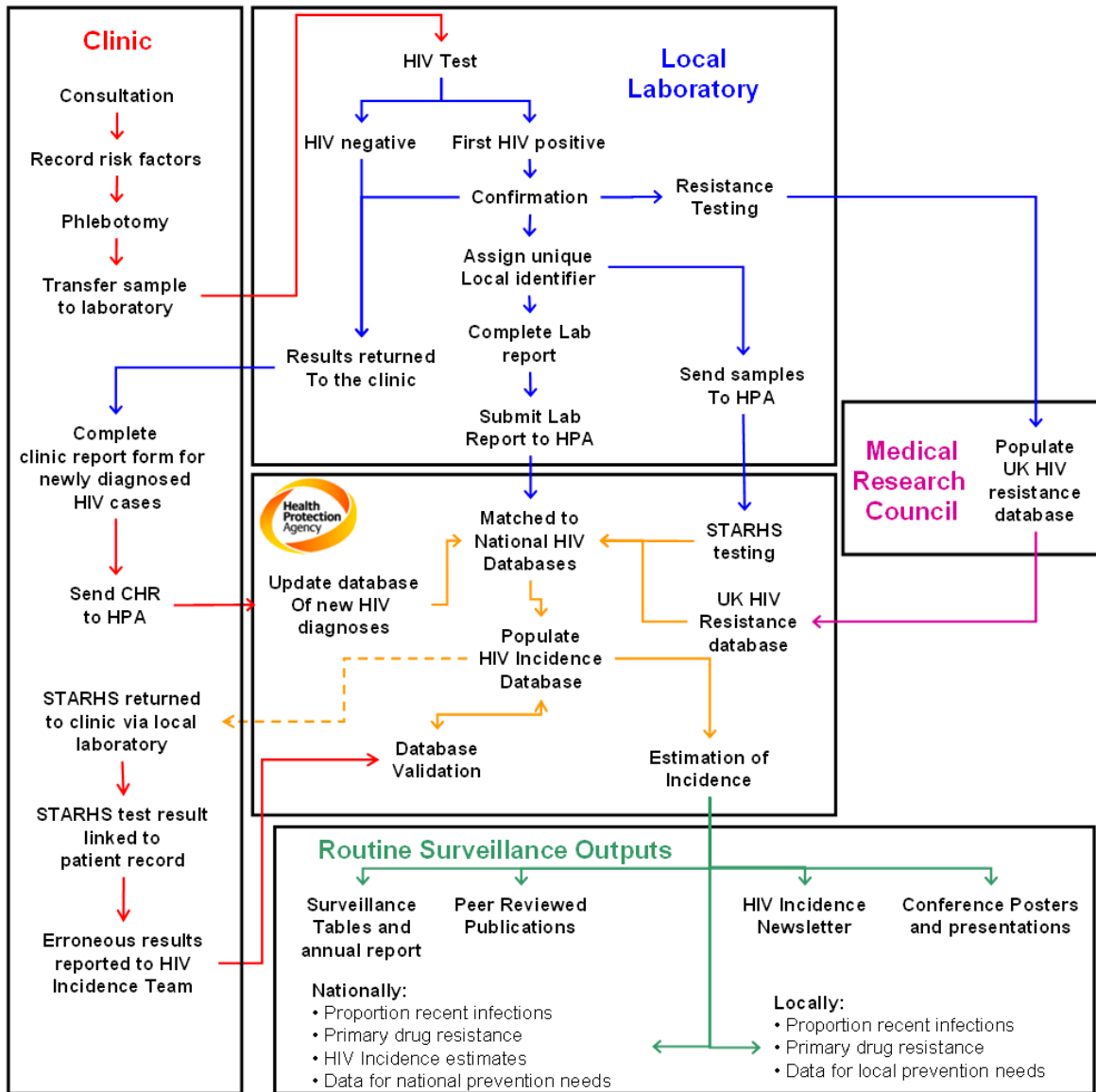
Results of the RITA test are intended to be returned directly to the associated laboratory and clinic within two weeks of receiving the batched samples. Reports will be made at the individual patient level, identified by the same laboratory ID that those samples were initially submitted to the HPA with.

ii. Additional Reports

Regular outputs from the UK incidence project are intended to be circulated to all collaborating laboratories and clinics and will include:


- HIV incidence newsletters
- National and regional quarterly HIV incidence surveillance tables
- HIV/STI Annual Reports
- Conference presentations and abstracts
- Peer reviewed publications

8. Overview



9. Example Test Request Form

Centre for Infections request form



HIV Reference Test

Virus Reference Department
61 Colindale Avenue
London NW9 5HT

Phone +44 (0)20 8327 6017/6266
VRDqueries@hpa.org.uk
www.hpa.org.uk/SRMTTests

HPA Colindale
CFI (VRD)
DX 6530006
Colindale NW

Please write clearly in black ink

S3

SENDER'S INFORMATION

Sender's name and address

Postcode

Phone Ext

Purchase order number

Project code

PATIENT/SOURCE INFORMATION

Human Animal* Other*

*please specify

NHS number

Surname (or surnames)

Forename

Sex male female

Date of birth D D M M Y Y Y Y | Age

Patient's postcode

Ethnic group

w White m Black Caribbean n Black African

p Black other y Indian/Pakistani/Bangladeshi x Other/Mixed

Hospital name (if different from sender's name)

Ward/clinic name

Hospital number

Patient's CCDC

Medico-legal case

Have previous samples from this patient been sent for reference test?

Yes No

Last known HPA reference number

Important: For MTCT investigations, please provide the following information for the corresponding mother/child

Name

Date of birth D D M M Y Y Y Y

HPA reference no.

SAMPLE INFORMATION

Your reference

Sample type Serum/plasma EDTA whole blood

Date of collection D D M M Y Y | Time

Date sent to HPA D D M M Y Y

Priority status

Facility where the sample was collected (tick one)

1 <input type="checkbox"/> Accident and Emergency	7 <input type="checkbox"/> In patient
2 <input type="checkbox"/> Transfusion/transplant recipient	8 <input type="checkbox"/> Infectious disease unit
3 <input type="checkbox"/> Blood transfusion service	9 <input type="checkbox"/> Paediatric
4 <input type="checkbox"/> Drug dependency unit	10 <input type="checkbox"/> Postmortem specimen
5 <input type="checkbox"/> GP	11 <input type="checkbox"/> Prison
6 <input type="checkbox"/> GUM clinic	12 <input type="checkbox"/> Other (please specify)

TESTS REQUESTED

Anti HIV confirmation

Seroconversion

Maternal transmission

HIV proviral DNA PCR

HIV RNA PCR (qualitative)

HIV RNA viral load

STARHS (HIV-1 incidence test)

Other tests

SENDER'S LABORATORY RESULTS

	ASSAY/KIT	Product no.	OD 1	OD 2	Cut off	Result/Interpretation
1						
2						
3						
4						

Current HIV test results (where available)

1 HIV-1 positive 3 HIV-2 positive

2 Untyped 4 Indeterminate

Has the patient ever received an HIV test prior to this diagnosis?

No Yes (please specify date(s) below)

Date last negative (if any) D D M M Y Y

Date earliest positive in the UK D D M M Y Y

CLINICAL/EPIDEMIOLOGICAL INFORMATION

Probable route of infection/reason for test

a Heterosexual f Blood/tissue recipient

b Sex between men g Needlestick injury recipient

c IV drug user h Needlestick injury donor

d Vertical transmission e Other (please specify)

Clinical information (tick one)

o No symptoms h HIV related symptoms

s HIV seroconversion symptoms a AIDS related symptoms

Has the patient received ARV in the last 6 months?

Yes No Unknown

CPA

All requests are subject to HPA standard terms and conditions, available at www.hpa.org.uk/hoj/standardterms.htm

VV0145.02

Please complete and submit an original copy of this request form for each specimen, a copy of which is available in PDF format from ruth.smith@hpa.org.uk if you do not already have one.