



WHO WORKING GROUP ON HIV INCIDENCE ASSAYS
Brief Meeting Report

Geneva, 28-30 January 2008

1. Background

A central objective of HIV programs is to reduce HIV transmission. Most HIV surveillance systems rely on population HIV prevalence estimates in combination with behavioral data to monitor trends in HIV transmission. However given the delay between HIV and AIDS and the increasing survival time due to increasing availability of ART, prevalence data are of limited use in this regard. Incident HIV infection rates are more valuable indicators of the rate of HIV transmission and help determine both the need for programs and their effectiveness.

Several groups have developed specialized serological assays that can distinguish recent from established HIV infections. These tests have been referred to as STARHS (serological testing algorithms for recent HIV seroconversion). As the assays have been developed, their accuracy has been investigated by comparing estimates of incidence that are derived from their use, with HIV incidence estimates obtained by other means and believed to measure close to the real incidence. These investigations have been conducted in a variety of settings, using a range of different 'gold standard' estimates. There has not been an agreed approach to validation, and comparison of findings across assays has been problematic.

During the XVI International AIDS Conference held in Toronto in 2006, the Ontario HIV Treatment Network (OHTN) organized a symposium on the Serologic Testing Algorithm for Recent HIV Seroconversion (STARHS). During the meeting, participants agreed that there was a need for standardization of approaches used for assay validation. The Centers for Disease Control and Prevention (CDC) began drafting a validation protocol to provide guidance on calibration and validation of HIV incidence assays. There was a consensus that in order to move forward this agenda, WHO should lead the work and a more formal Working Group on HIV Incidence Assays should be established. Additional meetings took place during the international conferences of CROI 2006 and IAS 2007, to further develop the protocol that would be internationally endorsed. To support the development of this protocol, the group agreed that a comprehensive literature review on the calibration and validation of HIV incidence assay should be also undertaken, and the World Health Organization undertook to support this review.

2. Objectives of the Meeting

1. To formally establish a WHO Working Group on HIV incidence assays
2. To review approaches that have been used to validate HIV incidence assays
3. To seek agreement on the protocol for validation of existing and future HIV incidence assays (currently in draft format)
4. To determine the next steps, particularly in relation to identification and collection of specimens for assay validation

3. Meeting Proceedings

Throughout the meeting a number of key terms were referred to. Definitions are provided below:

Calibration: To determine the “mean incident window period” and corresponding “cut-off” for recent infection classification by assessing performance in longitudinal specimens from seroconverting individuals. .

Measuring performance characteristics: determining sensitivity & specificity, from use of the assay in samples from populations with known durations of HIV infection. Sensitivity being the ability to correctly determine recent HIV infections, whereas specificity is the ability to correctly detect longstanding HIV infections. Additional performance characteristics include reproducibility of the assay and coefficient of variation (% CV) in the dynamic range of measurement.

Validation: comparing assay incidence in a population, to concurrent estimates of incidence in the same population obtained by an alternative means that is believed to provide a reliable measure of incidence (‘observed incidence’ based on ‘gold standard’).

Seroconversion panels: series of specimens obtained from individuals before and after the time of their infection with HIV. For precise estimation of the timing of HIV-seroconversion and the window period, the series should be closely-spaced around, and after, the time of seroconversion.

Mean Window period (for a STARHS method) for an HIV incidence assay: mean period between HIV-seroconversion and the time at which the STARHS optical density reaches a pre-set cut-off.

3.1 *Session One: Presentation of the literature review on HIV incidence assays*

Rebecca Guy presented the review of literature on HIV incidence assays.

The review objectives were to describe and assess the approaches used to calibrate HIV incidence assays, assess performance characteristics and validate them in comparison to ‘gold standard’ incidence estimates. The published results obtained by these approaches were assessed.

The review concluded that calibration is a crucial step in the development of an incidence assay. The review found that in many papers, key calibration information (such as sample size, methods of determining date of HIV seroconversion, risk group and the presence of other infections) was not presented. Of information available; half of the published calibrations related to subtype B infection, there were often wide confidence intervals around the estimated window period and there was no evidence of the use of multiple sites or laboratories to confirm estimated window periods using comparable specimens.

Assessment of assay performance characteristics was described as being required to provide confidence that an assay is able to effectively separate recent and established infections in a field setting. The review found that most samples used for these assessments were from US-based cohorts, there was considerable variation in the detail provided on the source and characteristics of the specimens, there were very few assessments of duration of longstanding infections within categories, particularly 2 or 3 years post-seroconversion and the effect of antiretroviral therapy on assay specificity had not been not comprehensively explored.

Validation of assay-derived incidence estimates against estimates determined from another gold standard source was reported to be the ultimate means by which incidence assays must be tested. The review found a range of items that were not reported in published papers - subtype and sample numbers and there were limited findings on non-subtype B infections. There was also great variation in the way comparisons had been undertaken - choice of specimens and source of the alternative incidence estimate. Alternative incidence methods described in papers included

cohorts, databases of repeat HIV testers; self reported repeat testing, other assays and mathematical techniques. Finally the greatest discordance between assay and alternative incidence were in studies conducted with non-identical samples where the assay incidence was derived from cross sectional surveys of heterosexual populations from Africa However other recent studies in South Africa have found a close matched results..

General discussion

Meeting participants made a number of suggestions related to the review including:

- The summary of mean window period estimates by assay should be subtype specific
- The performance characteristics section of the report would benefit from indicating which estimates were derived from the same study
- The appropriateness of using the terms sensitivity and specificity estimates when assessing assay performance before and after the mean window period was raised. There were no suggestions about alternative terminology and the participants recognized that these terms were commonly used in published papers.
- To be able to compare assay specificity among longstanding and AIDS cases, it was suggested that only findings within the same population should be compared as overall there were more studies with estimated for AIDS cases than longstanding infections (> 1 year since seroconversion).
- The differences between the assay and observed incidence validation estimates should be presented by subtracting the observed incidence from the assay incidence, rather than the opposite.
- The final groupings used to show how the comparability of specimen source impacts on the discrepancy between observed and assay incidence, should be broken down into further detail i.e. proportion prevalent infections in the assay incidence estimate.

3.2 *Session Two: Update on existing HIV incidence assays (it can be put in annexes)*

S Le Vu presented data resulting from evaluation of the EIA-RI assay performance for detecting recent infection among new HIV diagnoses in France, during the period 2003-2006. This evaluation takes into account the new HIV infections reported by the French

national HIV surveillance reporting system and compares the EIA-RI (V3-IDE) assay with the epidemiological surveillance data. Among the main activities planned by INVS for the future are considering modeling the main marker (ratio IDE), determination of empirical cutoff to target a convenient window period plus addition of subtype/ethnicity covariates.

B Suligoi presented the avidity index assay that is based on the principle of an increasing functional affinity (“avidity”) of antibody response to pathogens over time after a primary infection. The future plans for this assay include broadening the use of the assay in Italy, to establish an external quality assurance scheme and to implement further studies on individuals infected with non-B subtypes and to explore the relation with long-standing infections, long term non-progressors and individuals on ART.

N Constantine presented a simple and inexpensive particle agglutination Test to distinguish recent from established HIV-1 infection with an existing commercial test adapted using the sensitive/less sensitive methodology. It has been validated with clade B and currently in process to validate with non-B clades from India and Nigeria.

M Busch presented sensitive/less sensitive HIV immunoassays for detection of recent seroconverters and incidence projection applied in blood donors. Several limitations were highlighted with these methodology including availability of commercial assays i.e. manufacturers discontinue manufacturing when they develop enhanced assays (HIV-2, group O, 3rd and 4th generation EIAs, ChIAs), the S/LS application has not been approved by FDA, requires IND or IDE and need for additional quality control (QC) measures. The HIV clades have different S/LS-EIA window periods. In individuals with AIDS or those on ART, there may be a loss of antibodies that can falsely assign these individuals as recently infected.

J Parry presented the Euro HIV Work Package 7, a collaboration of European research groups working on HIV incidence assays. They aim to investigate whether an HIV incidence assay currently employed in one laboratory is transferable to another laboratory and to compare the performance of up to five incidence assay approaches on panels of well-characterized specimens.

E Dax presented the work on the IgG3 Immunoassay and its developments. There is a specific IgG3 antibody response to the p24 antigen that may be useful as a marker of established infection. To date a number of commercially acquired seroconversion panels have been tested using this methodology with promising results.

B Parekh presented an update on the status of the BED Assay based on the competitive capture format of the assay (proportion of specific HIV-IgG to total non-HIV-IgG). The calibration and validation studies done in different countries and with different clades were discussed. The BED assay is commercial available and used in several countries. Several studies have reported plausible incidence estimates or overestimation of incidence using the BED assay suggesting that further work is required to better understand performance of the assay in different population.

J Hargrove presented the work done comparing the BED assay with the ZVITAMBO cohort seroconversion data. He concluded saying that the best scenario would be to have a test which accurately identifies long-term HIV positive cases either using a stand-alone assay or combined with the BED assay. In the mean time, we need urgently to measure the proportion of recent-by-BED cases (ϵ or false recent infections) in people HIV positive > 1yr. Present results suggest that there is significant change in above a value of 50 and. Only Current results suggest that only CD4 < 50 and ART are associated with elevated levels of ϵ , but further significant variation might become apparent through studies using larger sample sizes. The need to think more carefully about how we estimate the window period was highlighted.

3.3 Session Three: Update on new HIV incidence assay development

B Parekh presented a new assay utilizing a novel recombinant antigen (rIDR-M) based on the gp41 immunodominant region = IDR. The assay principle operates on the basis that all HIV-infected people will develop antibodies to this region and there is minor but immunologically important variation among subtypes. IDR-M has been designed to cover all subtypes and recombinants forms of the virus (group M).

Two new approaches were presented utilizing the rIDR-M recombinant antigen. The first is based on coating the plate with limiting antigen and then performing a dissociation step to measure relative avidity (LAg-Avidity EIA). In this single well avidity assay, specimens with low avidity antibodies (assumed to be early in infection) are easily dissociated and give comparable results to two-well avidity index approach. The second test in development is a Rapid Incidence Test using rIDR-M to detect recent HIV infection. This test has been recently licensed to a commercial partner by CDC for kit development. It was suggested that combining two different methods, based on two different principles, should significantly improve predictive value and accuracy of incidence estimates.

Further work will determine the cutoff and window period determination using seroconversion panels and direct comparison with the Avidity Index Assay. Other planned research includes estimation of the rate of false-recent classification in known long-term infections such as with AIDS, tuberculosis/malaria and other co-infections, pregnant women, those on ART and those with elevated IgG due to factors other than HIV infection. Validation will take place in different populations (comparing modeled to measured incidence estimates) and evaluation will proceed of LAg-Avidity EIA as an independent assay or as part of an incidence algorithm to increase predictive value of detecting recent infection.

3.4 Session Four: Review of draft protocol for validation of existing and future HIV incidence assays

Andrea Kim presented the last version of the draft protocol (here after referred to as the 'Protocol').

The aim of the Protocol is to provide guidance on standard procedures for validating existing and future HIV incidence assays and algorithms for estimating incidence from cross-sectional surveys.

There are several limitations of current HIV incidence assays including the possibility of commercial assays being discontinued; some in-house assays may not be reproducible. Some approaches are known to overestimate HIV incidence due to misclassification of long-term infections as recent infections, while other assays remain to be evaluated in larger samples with diverse HIV-1 subtypes and some must have an HIV incidence formula established.

The objectives of the Protocol are to provide recommendations for the preferred method to integrate validation of HIV incidence assays into existing or planned longitudinal cohort studies of HIV infection and to suggest methods to quantify, adjust for and report on potential assay misclassification of recent vs. longstanding HIV infection, so that the limits of assays and potential effects on incidence estimates are clearly described.

The need for standardization and the Protocol was highlighted by a description of assay limitations including:

- Commercial assays may be discontinued
- Some of the in-house assays may not be reproducible
- Some assays misclassify longstanding infections as recent infections
- Some assays have not been assessed using larger sample populations with diverse HIV-1 subtypes

In the Protocol the longitudinal cohort study of persons at risk for HIV infection was described as the preferred validation design, with continued follow-up for incident seroconverters, and also follow-up (for at least a year) of persons determined to already be HIV-infected at inception of the cohort. The prospective cohort study enables comparison of HIV incidence estimated by the incidence assay at various cross-sectional time points after enrollment into the cohort vs. the estimated incidence calculated in a standard epidemiologic approach (incident cases per person-years of observation). The study should include frequent serial blood collection (ideally every 3 months; otherwise every 6 months) and HIV-antibody testing to identify incident HIV infections. The cohort must have sufficient sample size and duration (see statistical considerations section) to permit identifying enough incident HIV infections. Suitable longitudinal studies include HIV vaccine preparedness cohorts and HIV prevention intervention trials (e.g., Thai BMA; VaxGen trials; ZVITAMBO, IAVI). Additional validation designs were presented and are available in the Annex 4 of the protocol.

The Protocol also recommends that a number of variables be collected for HIV-seroconverters and prevalent HIV-seropositive persons in epidemiological validation studies, to better define the factors associated with assay misclassification: mode of transmission, HIV-1 subtype, sex, age, race, IgG levels, co-infections, CD4 cell count and HIV-viral load information, presence of opportunistic infections, AIDS status and ART use.

General discussion

After the protocol was presented meeting participants raised the following points;

- Appendix 4A of the protocol (Calibration): Should this be restored to become part of the main document or remain as an appendix? If part of the main document there could be two separate sections of the protocol; calibration and validation.
- There was a suggestion to change the terminology from ‘Calibration’ to ‘Window Period Estimation’
- The characteristics of the samples used will depend on the assessment purpose i.e. assessing false recently among long standing infections compared to assay validation
- Serial bleeds from one person should be treated as independent samples
- Should we investigate the window period of blood donors versus other groups
- Panels of two types: Seroconverter panels (RNA+) and Interval Seroconverters

Several specific issues were deemed to require discussion by two groups, made of participants from the meeting. The issues and corresponding suggestions from the groups are listed below.

.

Issue 1: Spacing of specimens for calibration

What is the optimal and minimum spacing requirement of specimens for calibration of the assays ? For example, is 6 months OK or too wide? Note, for the ZVITAMBO study, analysis was restricted to data where the spacing was <100 days. The current Protocol states ‘Requisite number of HIV-positive specimens per seroconverter: first confirmed HIV-seropositive specimen plus at least 2-3 more spaced a few months apart, over at least 12 month span”.

Group suggestions:

The specimens should include seroconversion panels. Prior to testing positive, the specimens should be spaced a maximum of 3-4 months apart (similar to the Thai BAM trial) over a 12

month period but ideally one month apart (consistent with microbicide trials). After testing positive, at least two additional specimens should be collected, spaced four months apart over nine months.

Issue 2: Spacing of specimens for validation

What is the optimal and minimum spacing requirement for validation of the assays ?

Similar criteria should apply for seroconversion panels used for validations of the assays. In addition, however, it was highlighted that there needs to be better characterization of longstanding infections for use in validation (greater than 1 year after seroconversion). These longstanding infections could be obtained by continued follow-up and testing of person after seroconversion at subsequent visits, or until initiation of treatment.

The long-term specificity is important for mathematical adjustment methods which have been used previously to overcome the issue of assay misclassification of recent infections (see below). This specificity will vary according to different populations; therefore it is important to assess assay performance against longstanding infections as part of the key performance characteristics of a test. The samples should include low CD4 count levels (<50). When assessing assay incidence in field study i.e. cross sectional, you would need to know the percent of persons in the population with a low CD4 count and the adjustment factor could be applied to overcome any misclassification bias. Some discussion took place about the practicality of testing for CD4 count in some surveys and options of a subset of the population being tested.

Issue 3: Window period estimation:

What are the different approaches for determination of the window period using data from seroconverters? What are the pro and cons of each method? How should the window period estimation take into account apparent bends in the curve, as observed with the BED? (E.g. BED ODn value stable at baseline for first 25 days).

In addition, difference between mean window period (important for population incidence estimates) and inclusive window period (important for individual diagnosis of recent infection)

was emphasized. Mean window period describes time period when approximately 50% of people will move from recent to long-term classification while include window period describes time period since seroconversion when 95% of incident infections will move from recent to long-term classification.

Group suggestions:

There were (at least) two different approaches that could be used to calculate the window period (i) mixed model approach - regression and random coefficient - linear relationship and (ii) random intercept - population of slopes technique. However there was no agreement by the group on the ideal method and there was a suggestion that more work needs to be done on this topic.

It is important for the methods to be transparent and consistent between studies. Key factors that should be described in each study include; the number and characteristics of specimens assessed, the timing of seroconversion specimens, the structure of the data is it independent data or not? It was also highlighted that a standard graphical format is preferred for presentation of calibration curved i.e. cumulative percent over time.

There are manuscripts and publications evaluating incidence assays using described mean window but applying it to individual diagnosis. This is totally inappropriate and does not contribute in any way in assessing performance of the assay. Those reviewing the manuscripts should be aware of these differences and should provide comments appropriately.

Issue 4: Number of calibration cutoffs - See above – the same applies to cut-off

Do we need 2 cut-offs? a) One for distinguishing people as recent and b) one for estimation incidence in the population? (“a” will need to be conservative in cut-off and will have a different window period from “b”).

Group suggestions:

Identifying recent infections is important for clinical, research purposes, contact tracing and may need a higher specificity compared to estimating population trends. However having different cutoffs would entail considerable education of users to prevent confusion. It was thought that this discussion fell more into the area of application, not validation. It was suggested that additional testing (e.g. CD4 determinations) could be used to identify misclassified long standing infections.

Issue 5: Optimal validation designs

Other than the design specified in section x of the protocol are there other optimal designs for validation that should be highlighted i.e. military cohorts and repeat blood donors.

Group suggestions:

The optimal design specified in the protocol was best. The others designs described in the Protocol are not as useful but probably should not be ruled out. A hierarchy of designs was suggested:

1. Cohort
2. Database of repeat testers i.e. blood bank, clinic
3. Comparison against another assay?
4. Preferably not mathematical outputs

It was pointed out that in design 2 there may not be a sufficient supply of 'long standing infections' or 'prevalent infections' to assess the issue of false recency. Therefore these samples may need to be obtained from another source, but a similar population. The 'long standing infections' or 'prevalent infections' should be well characterized.

Issue 6: Other characteristics for validation and calibration specimens

What are the desired and required characteristics e.g. mode of transmission, gender

Group suggestions:

Other than those timing criteria mentioned in response to issue 1, specimens used for validation and calibration should have a subtype and geographical coverage, the specimen suppliers should have processed the specimens within eight hours, the specimens should not have been refrigerated for longer than 1 week (preferably not longer than two days), the volume should be at least 3-5 ml (preferably 10 ml), the specimen could be plasma or serum, the specimens should be frozen when transported (or at least kept at a minimum of 4°C) and once received at the proposed central specimens repository (serum/plasma bank)* should be aliquotted and stored at -70°C for max ten years. The issue of freeze thaw and was discussed and based on previous experience with HIV antibody assay quality assurance assessments, repeat specimen

freeze-thaw should not impact on assay performance. In general freeze thaw cycles should be limited as much as possible.

* For long term assessment of HIV incidence assays it was agreed that a central bank of specimens was needed, similar to HIV antibody assay

Issue 7: HIV incidence risk factor analysis

How far can stratification be conducted for identifying risk factors for population incidence estimates? One level at a time? Is multivariate analysis possible?

Group suggestions:

Multivariate analysis for risk factors of HIV incidence (using incidence assays) was an appropriate epidemiological analysis, however a few possible issues should be considered - sample size of incident infections may be small in some situations, large confidence intervals may result and there may be biases introduced by the inherent nature of assigning recent infections based on a mean window period i.e. sensitivity approximately 80-90%. The latter may be overcome by applying a lower OD cut-off to increase the sensitivity of the assay. However perhaps the first step would be to simply conduct the analysis using the usual cutoff and review the findings to see if they appear valid and consistent with other studies.

Issue 8: Calculation of incidence from NAAT testing

How do we estimate HIV incidence from NAAT testing? Previous attempts have produced highly inflated estimates that are not plausible. Can BED and NAAT be combined to distinguish between recent and acute infections?

Group suggestions:

NAAT incidence testing is useful in a blood bank setting. There is evidence (Busch), that NAAT and SLS findings are comparable when the assays were used to test samples from a database of repeat testers. On the other hand, anecdotal evidence from an unpublished study (Pilcher) suggests that NAAT incidence was higher compared to assay incidence. The group suggested more information is required to conclude on this issue.

Issue 9: Assay sensitivity and specificity

What is acceptable assay specificity for recent classification?

Group suggestions:

Since we are measuring a continuous parameter, such as increasing levels of antibodies or increasing antibody avidity, it is not likely that we can achieve sensitivity or specificity anywhere close to 100%. The window periods are determined by using an arbitrary cut-off which is not reached by all people at the same time due to individual /biologic variation. Therefore some compromise is inevitable as long as loss in sensitivity is balanced by gain specificity or vice versa, especially for incidence estimates. Like all assays there is a trade off of sensitivity versus specificity and the importance of the parameters may depend on the application of assay i.e. clinical or surveillance perspective. Overall, for long term trends the specificity is most important.

What are implications of assays with poor sensitivity?

Group suggestions:

Overall the sensitivity of all available assays appears generally good i.e. >80%. If the incidence is very low in a population a poor sensitivity will impact on the interpretation of the findings. It is also important to have some consistency in the sensitivity estimates to interpret trends over time and interpret inter-regional estimates. It would be ideal for a sensitivity standard to be set, as part of a quality assurance profile, and only assays used which meet this standard.

Issue 10: Future validation studies:

Are there suggestions for existing or imminent large cohorts that may already be collecting the types of specimens we need for ideal validation studies (including follow-up of prevalence HIV positives) and are potentially willing to collaborate?

A specimen bank should be developed and critical assessment steps are defined including validation:

1. Calibration – can it produce a curve, window period estimation?
2. Assess ability to distinguish recent from long-term infections.

3. Assess performance against false recent infections.
4. Assess ability to measure cohort incidence.
5. Apply in a cross sectional study, could occur within the same cohort, assess application of correction factor.

The findings from steps 1-5 above should be presented as part of an overall assay description including assay frame work, cost, transferability, availability, type of antibody measured, the primary assay reference, equipment required, assay dilution needed, automations, QA programs.

To access cohort specimen for validation, institutes with existing cohorts from a variety of regions could be approached and offered funding to supply the specimens. An 'expression of interest' may be the best process. The specimens required and the validation methods should be in accordance with the Protocol Recommendations.

Session five: Roles and responsibilities of the HIV incidence working group

The following objectives were suggested, but would be further developed by the Working Group following the meeting

Objectives

1. To provide a framework and guidance in which to measure HIV incidence (review agenda)

Other possible objectives

1. To support the establishment of appropriate specimen panels.
2. Development of existing assays and new assays.
3. Calibration.
4. Application of incidence assays.

To achieve objective 1, a number of short-term tasks were agreed upon, a lead person assigned and associated timeline for completion.

Tasks 1: Short term task, 6 months - 1 year

Task	Lead Person	Time-line
Draft project planning and time line (Gantt chart) into the long term (approx. 3 years)	WHO	End of April 2008
Desirable characteristics of HIV incidence assays	Gary Murphy	End of March 2008
Potential uses and challenges of HIV incidence assays for different applications	Stephane Le Vu, Robert Remis, Thomas Rehle	March 2008
Finalize literature review • Disseminate and publish • Two separate publications to be prepared	Rebecca Guy, John Kaldor	RG to send a revised version in 7 working days (11 Feb 08) and then 2 weeks to submit final comments (25 Feb 08)
Define assay assessment pathway	Connie Sexton, Niel Constantine, Gary Murphy	April 2008
Finalize validation protocol • Incorporation of comments from meeting • Circulate by email for additional comments	A Kim to incorporate comments from this WG and email for comment	May 2008
Organize working group on statistical approaches Finalize window period estimation protocol (statistics) Finalize window period estimation protocol (statistics)	Chris Archibald, John Hargrove, Meade Morgan, Tim Green, Mike Busch, Andrea Kim, Stephane Le Vu	May 2008
Define characteristics of specimens consistent with the needs of the assessment pathway	Bharat Parekh, Niel Constantine, Liz Dax	April 2008
Submit joint funding request for a WG meeting in Mexico City (WHO)	WHO	March 2008
Brief meeting report to be prepared	WHO	February 2008
Develop funding proposal to support further work Sub-group to be convened to further discuss after Mexico?	WHO,	August 2008

Next Steps

Next meeting

A meeting of the working group to be held on Saturday 2nd & Sunday 3rd August, adjunct to the IAS AIDS 2008 in Mexico City with the objective to move outstanding tasks forward. This would include workflow management for process of acquiring appropriate specimen panels.

Criteria for membership of WHO Working Group on HIV Incidence Assays

- Geographical representation.
- Exclude those with active assay development in place for validation of assays.
- Lab experts.
- Epidemiologist.

Annex 1

Programme of Work

Day 1

Monday 28 January 2008

Session 1		Presenter	Chair
08:30 - 09:00	Registration of participants		
09:00 - 09:15	Opening of meeting	WHO/HIV, Dr K De Cock WHO/EHT, Dr G Vercauteren	
09:15 - 9:30	Introduction to objectives and expected results for the meeting	WHO, Dr J Garcia Calleja, Dr G Vercauteren	
	Review agenda	Mr J Kaldor	
9:30 - 10: 30	Presentation of the literature review on HIV incidence assays	Mr J Kaldor	
	Discussion		
10:30 - 10:45	<i>Coffee/Tea Break</i>		
10:45- 12:30	New developments on incidence assays (recent, unpublished data)	Dr J Parry Dr N Constantine Dr B Parekh	
12:30 - 14:00	<i>Lunch</i>		
Session 2		Presenter	Chair
14:00 - 17:15	Update on existing HIV incidence assays	See below	
14:00 - 14:30	LS-EIA (detuned assay)	Dr M Busch	
14:30 - 15:00	IgG capture BED-EIA	Dr B Parekh	
15:00 - 15:30	3-well EIA for gp41-IDR, V3 loop, p31	Dr S Le Vu	
15:30 - 15:45	<i>Coffee/Tea Break</i>		

15:45 - 16:15	Avidity Index Assay	Dr B Suligo
16:15 - 16:45	Anti-p24 IgG3 Antibody Assay	Dr E Dax
16:45- 17:15	New data from South Africa and long term specificity for BED	Dr J Hargrove
17: 15- 17:45	Discussion on the specifications for HIV incidence assays	

Day 2

Tuesday 29 January 2008

Session 3

		Presenter	Chair
09:00 - 09:30	Presentation of the draft protocol for validation of existing and future HIV incidence assays	Dr A Kim	
09:30 - 10:30	Discussion on the protocol		
10:30 - 10:45	<i>Coffee/Tea Break</i>		
10:45 - 12:30	Working groups on issues related to the draft protocol		
12:30- 14:00	<i>Lunch</i>		

Session 4

		Presenter	Chair
14:00 - 15:30	Report back from working groups	Rapporteur	
	Discussion of draft protocol		
15:30 - 15:45	<i>Coffee/Tea Break</i>		
15:45 - 16:00	Procedures for specimen collection for validation of incidence assays	Group Discussion	
16:00 - 17:00	Discussion		

Day 3

Wednesday 30 January 2008

Session 5

		Presenter	Chair
09:00 - 10:30	Confirmation of working group on HIV incidence assays: members, responsibilities	Group Discussion	
	Other issues for the Working Group		
10:30 - 10:45	<i>Coffee/Tea Break</i>		
10:45 - 12:00	Next steps		
12:00 - 12:30	Meeting closure and thanks	WHO	



**WHO Working Group on Protocol for Validation of HIV Incidence Assays
WHO/HQ, Room D46031 (D-Bldg) Geneva, Switzerland
28-30 January 2008**

PROVISIONAL LIST OF PARTICIPANTS

Dr Chris ARCHIBALD	Director Surveillance and Risk Assessment Division Public Health Agency of Canada Room 2354 - LCDC building 100 Eglantine Driveway Ottawa, Ontario Canada K1A 0K9 Tel: +1 613 941 3155 E-mail: chris_archibald@phac-aspc.gc.ca
Dr Michael BUSCH	Blood Systems Research Institute 270 Masonic Avenue San Francisco, California 94118 USA Tel: +1 415 749 6615 Fax: +1 415 775 3859 E-mail: MBusch@bloodsystems.org
Dr Andre CHARLETT	Health Protection Agency Centre for Infections Virus Reference Department 61 Colindale Avenue London NW9 5HT United Kingdom E-mail: Andre.Charlett@hpa.org.uk
Dr Niel CONSTANTINE	Professor of Pathology University of Maryland School of Medicine Institute of Human Virology 725 W. Lombard St. Baltimore, MD 21201 USA Tel: +1 410 706 2788 Fax: +1 410 706 2789 E-mail: Nconstantine@hiv.umaryland.edu

Dr Elizabeth DAX

Director
National Serology Reference Laboratory, Australia
4th Floor, Healy Building
41 Victoria Parade
Fitzroy 3065, Victoria
Australia
Tel: +61 3 9418 1111
Fax: +61 3 9418 1155
E-mail: liz@nrl.gov.au

Ms Rebecca GUY

Epidemiologist
Centre for Epidemiology and Population Health
Research (CEPHR)
The Macfarlane Burnet Institute
for Medical Research and Public Health
85 Commercial Road
Melbourne, Victoria 3181
Australia
Tel: +61 3 9282 2290
E-mail: Rebecca.Guy@burnet.edu.au

Dr Magid HERIDA
(unable to attend)

European Centre for Disease Prevention and Control
(ECDC)
SE-171 83 Stockholm, Sweden
Visiting address: Tomtebodavagen 11A
Tel: +46 858 60 12 16
Mobile: +46 76 101 0713
Fax: +46 8 30 00 57
E-mail: Magid.Herida@ecdc.europa.eu

Prof John HARGROVE

Director
SACEMA
DST/NRF Centre of Excellence in Epidemiological
Modelling and Analysis
c/o STIAS, 19 Jonkershoekweg
Stellenbosch 7600, Cape Province
South Africa
Tel: +27 21 808 2589
Fax: +27 21 808 2586
E-mail: jhargrove@sun.ac.za

Prof John KALDOR

Deputy Director and Professor of Epidemiology
National Centre in HIV Epidemiology
and Clinical Research
Level 2, 376 Victoria Street
Darlinghurst, NSW 2010
Australia
Tel: +61 2 9385 0900
E-mail: jkaldor@nchechr.unsw.edu.au

Dr Stephane LE VU

Infectious Disease Department
Institut de Veille Sanitaire
Département des maladies infectieuses
94415 Saint-Maurice
France
Tel: +33 1 41 79 68 30
E-mail: s.levu@invs.sante.fr

Dr Gary MURPHY

Health Protection Agency
Centre for Infections
Virus Reference Department
61 Colindale Avenue
London NW9 5HT
United Kingdom
Tel: +44 20 8327 6935
E-mail: Gary.Murphy@hpa.org.uk

Prof John PARRY

Deputy Director
Health Protection Agency
Centre for Infections
Virus Reference Department
61 Colindale Avenue
London NW9 5HT
United Kingdom
Tel: +44 20 8327 6208
Fax: +44 20 8200 1569
E-mail: john.parry@hpa.org.uk

Dr Josiane PILLONEL
(unable to attend)

Epidemiologist
Infectious Disease Department
Institut de Veille Sanitaire
Saint-Maurice
France 94215
Tel: +33 1 41 79 67 47
E-mail: j.pillonel@invs.sante.fr

Prof Thomas REHLE

Director
Social Aspects of HIV/AIDS and Health
Human Sciences Research Council
Private Bag X9182, Cape Town 8000, South Africa
Tel: +27 21 466 7938/7844
Fax: +27 21 461 0299
E-mail: trehle@hsrc.ac.za

Dr Robert REMIS

Professor, Public Health Sciences
University of Toronto
155 College Street
Toronto, Ontario
Canada M5T 3M7
Tel: +1 416 946 3250
E-mail: rs.remis@utoronto.ca

Dr Renee RIDZON

Bill and Melinda Gates Foundation
1551 Eastlake Avenue East
Seattle, WA 98102-3706
USA
E-mail: renee.ridzon@gatesfoundation.org

Dr Connie SEXTON

Global Research Services
Family Health International
Research Triangle Park
NC 27709, USA
Tel: +1 919 544 7040 x551
E-mail: CSexton@fhi.org

Dr Barbara SULIGOI

Director
Centro Operativo AIDS
Istituto Superiore di Sanità
Viale Regina Elena 299
00161 Roma
Italy
Tel: 06 49906125
Fax: 06 49902755
E-mail: barbara.suligo@iss.it

OTHER PARTNER AGENCIES

CDC

Dr Bernard BRANSON

Associate Director
Laboratory Diagnostics
Division of HIV/AIDS Prevention
Centers for Disease Control and Prevention
1600 Clifton Road, D-21
Atlanta, Georgia 30345
USA
Tel: +1 404 639 6166
E-mail: BBranson@cdc.gov

Dr Andrea KIM

Centers for Disease Control and Prevention
Global AIDS Program, Surveillance Team
1600 Clifton Road, D-21
Atlanta, Georgia 30345
USA
E-mail: bwd2@cdc.gov

Dr Bharat PAREKH

Chief, Serology/Incidence and Diagnostics Team
GAP International Laboratory Branch
Centers for Disease Control and Prevention
Atlanta, GA 30333
USA
Tel: +1 404 639 3647
E-mail: bsp1@cdc.gov

Dr Meade MORGAN (unable to attend)

Centers for Disease Control and Prevention
Atlanta, GA 30333
USA
E-mail: wmm1@cdc.gov

UNAIDS

Ms Eleanor GOUWS

Epidemic and Impact Monitoring
Tel: +41 22 791 4237
E-mail: gouwse@unaids.org

WHO/HQ SECRETARIAT

Dr Jesus Maria GARCIA CALLEJA	Department of HIV/AIDS Strategic Information E-mail: callejaj@who.int
Dr Charlie GILKS	Department of HIV/AIDS ART and HIV Care E-mail: gilksc@who.int
Dr Yves SOUTEYRAND	Department of HIV/AIDS Strategic Information E-mail: souteyrandy@who.int
Ms Mercedes PEREZ GONZALEZ	Department of Essential Health Technologies Health Systems and Services E-mail: perezgonzalezm@who.int
Ms Anita SANDS	Department of Essential Health Technologies Health Systems and Services Tel: +4122 791 1691 E-mail: sandsa@who.int
Dr Gaby VERCAUTEREN	Department of Essential Health Technologies Health Systems and Services E-mail: vercautereng@who.int

