HIV 1/2 Rapid Test Kit

CE 0843

Principle of Dr. Drop HIV-1/2 Rapid test

Immuno-chromatographic assay for qualitative detection of the all isotype (IgG, IgM, IgA) antibodies specific to HIV-1 including subtype O and HIV-2.

- The 3rd Generation Method (Direct Sandwich System, Ag-Ab-Ag)
- Simple, Easy to use/ Fast, Accurate result
- Capture Ag : HIV-1 (p24, gp41), HIV-2 (gp36)Ag, Subtype “O” Detectable
- Serum/Plasma/Whole Blood Specimen
- Sensitivity : 100%, Specificity : 99.8%

Evaluation results

Reference		Dr. Drop HIV-1/2 Rapid Test*		Total results
Method	Result	Positive	Negative	
Commercial ELISA	Positive	1109	0	1109
	Negative	7	3821	3828
Total results		1116	3821	4937

*Results from OEM supplier's files

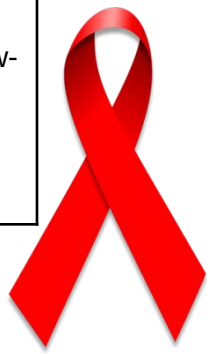
Types of human immunodeficiency virus (HIV) antibody testing

- Enzyme immunoassays (EIA), Enzyme-linked immunoassay (ELISA) for the screening of donated blood
- Western blot or immunofluorescence assay as a supplemental test, to confirm HIV positively
- Rapid tests : feasible for small laboratories or POC (Point of Care) testing

Rapid tests are useful in settings where EIAs are not feasible or practical and in geographical areas with limited laboratory infrastructure. Rapid tests may be appropriate for hard-to-reach populations (e.g. IDUS, female sex workers, MSM) or geographically remote populations for whom HIV test results may need to be provided on site on the same day as specimen collection.

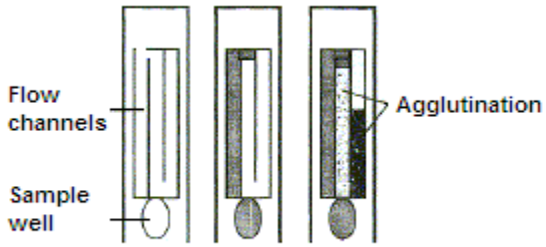
Comparison of HIV testing technologies: enzyme immunoassays and rapid tests

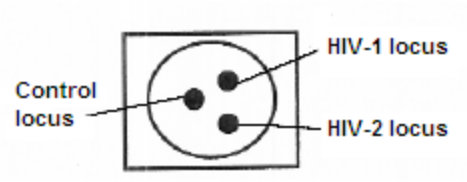
HIV testing technology	Specimens	Advantages	Limitations	Complexity (from 1 [simple] to 4 [highly complex])
Enzyme immunoassays (EIA)	Serum Plasma Dried blood spots Oral fluid	•Can be batched: good for >=90 specimens at a time •Can be automated •QC; easier to control •Identifies seroconverters earlier: highly sensitive, reduces window period if fourth-generation EIA	•Requires skilled, trained technicians to perform testing and calculate results •Can take +2 hours •Requires special equipment •Requires maintenance of equipment •Kits require refrigeration	4
Rapid test	Serum Plasma Whole blood Oral fluid	•Requires minimal equipment and reagents •Can be performed outside a laboratory (on-site testing) •Test results easy to interpret •Results in 30 min or less •Most kits can be stored at up to 30° C	•Not suitable for large numbers of specimens •Positive and negative control specimens often not included in the kit •May cost more per test than EIA	For tests based on: Immuno-chromatography 1 Dipstick and flow-through devices 1–2 Agglutination 2



Rapid Tests

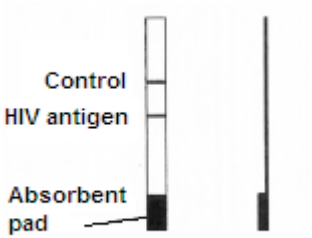
Classified by test type (Assay formats)

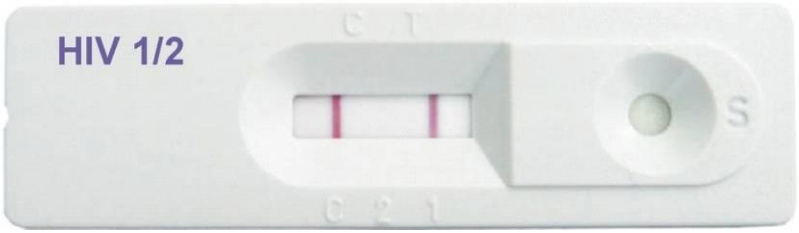




Agglutination Device

Flow through (Immuno-concentration)



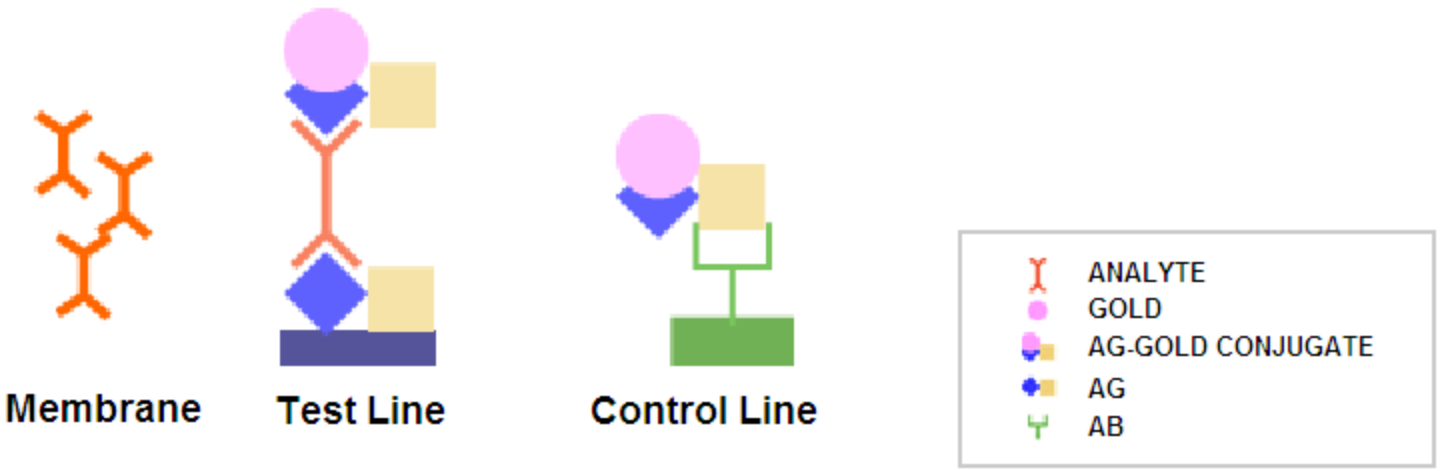


Lateral-Flow Device (Immuno-chromatography)

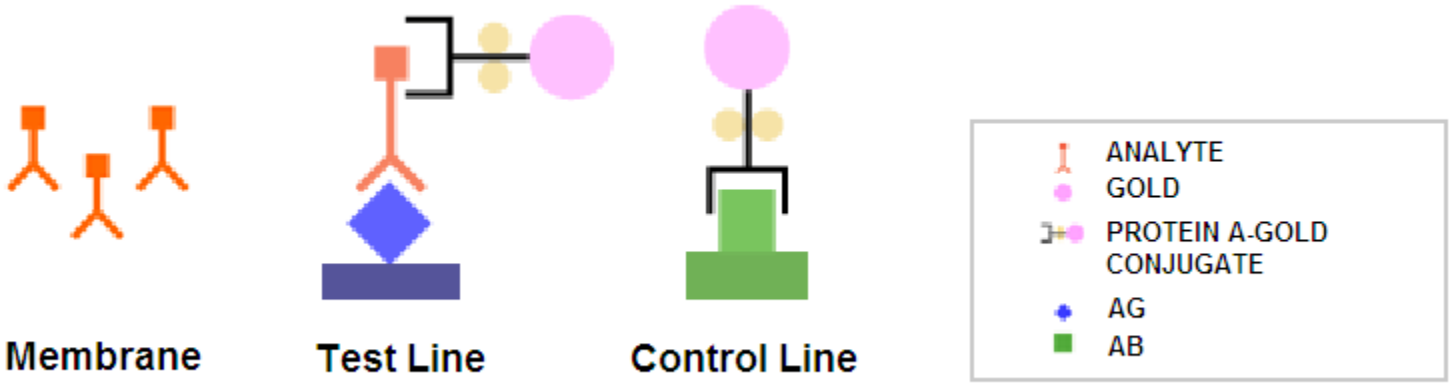
Principle of Immuno assay:

Antigen, Antibody, Conjugate binding

1. Direct sandwich System : *Early antibody (IgM) detectable*



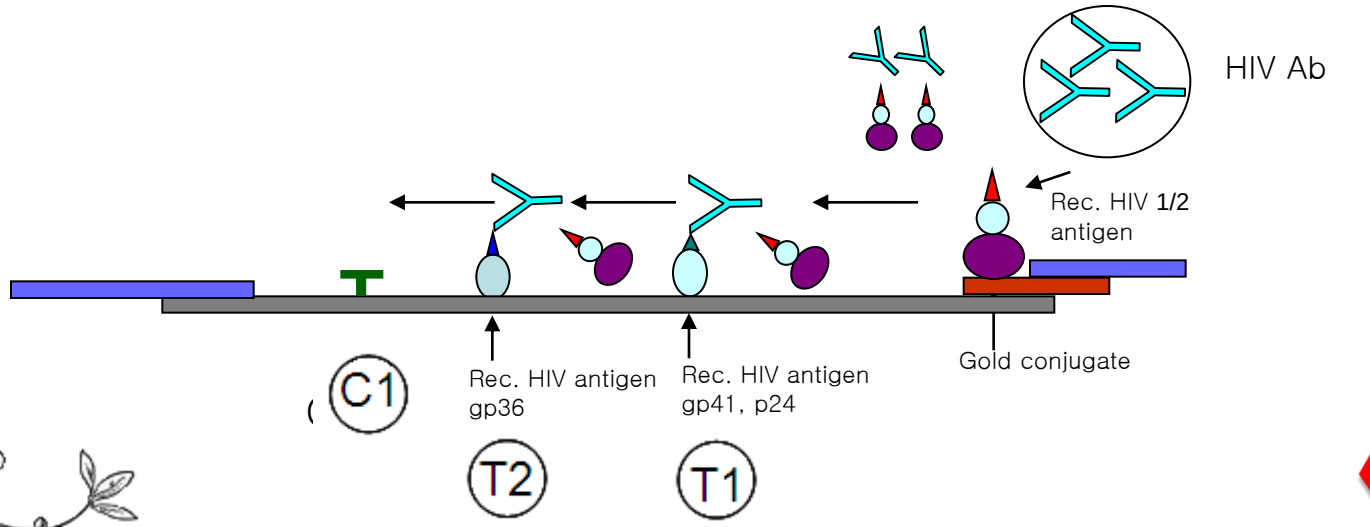
2. Indirect sandwich System:



Specialities of Dr. Drop HIV 1/2 Rapid Test

Special direct sandwich system

- Capture : Test line 1 (Rec. HIV antigen gp41, p24)
- Test line 2 (Rec. HIV antigen gp36)
- Detector : Rec. HIV 1/2 antigen gold (instead of enzyme) conjugate
- Target protein : Antibody to HIV in specimen



CE marked Dr. Drop HIV 1/2 Rapid Test

Certified by UL International (UK) Ltd.

UL International (UK) Ltd

An affiliate of Underwriters Laboratories Inc.

EC Design – Examination Certificate

(Annex IV section 4 of the Directive 98/79/EC on In Vitro Diagnostic Medical Devices)

Manufacturer

Drop Test s.r.o.
Dunajské nábrežie č. 4726
SK- 945 01
Komárno
Slovakia

Authorised Representative

Not applicable

Model Type: Dr. Drop HIV 1/2 Rapid Diagnostic Test (DRD HIV 1/2 P1)

We hereby declare that a design examination has been carried out on the device(s) listed following the requirements of the national legislation to which the undersigned is subject, transposing Annex IV section 4 of the Directive 98/79/EC on In Vitro Diagnostic Medical Devices. We certify that the design of the device(s) listed conforms with the relevant provisions of Annex IV section 4 of the directive 98/79/EC on In Vitro Diagnostic Medical Devices as transposed into national legislation.

Certificate issued by:

Certification Manager
For UL International (UK) Ltd

UL International (UK) Ltd
Wonersh House
The Guildway
Old Portsmouth Road
Guildford, Surrey GU3 1LR
United Kingdom
+44 (0)1483 302130

Certificate no: 647
Original certificate: 08 February 2011
Current certificate: 08 February 2011
Certificate expiry: 06 October 2013

Notified Body No.
0843

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CE
0843

UL International (UK) Ltd

An affiliate of Underwriters Laboratories Inc.

EC Certificate - Full Quality Assurance System Approval Certificate

(Annex IV, section 3 of the Directive 98/79/EC on In Vitro Diagnostic Medical Devices)

Manufacturer

Drop Test s.r.o.
Dunajské nábrežie č. 4726
SK- 945 01
Komárno
Slovakia

Authorised Representative

Not applicable

Scope of Certificate: Supply of Rapid Diagnostic Test Products

Device Classifications: Annex II, List A

Device descriptions: Dr. Drop HIV 1/2 Rapid Diagnostic Test (DRD HIV 1/2 P1)

We hereby declare that an examination of the full quality assurance system has been carried out following the requirements of the national legislation to which the undersigned is subject, transposing Annex IV (with the exemption of sections 4 and 6) of the Directive 98/79/EC on In Vitro Diagnostic Medical Devices. We certify that the full quality assurance system conforms with the relevant provisions of the aforementioned directive.

Certificate issued by:

Certification Manager
For UL International (UK) Ltd

UL International (UK) Ltd
Wonersh House
The Guildway
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United Kingdom
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Certificate no: 646
Original certificate: 08 February 2011
Current certificate: 08 February 2011
Certificate expiry: 17 October 2014

Notified Body No.
0843

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CE 0843

CE mark:

In vitro diagnostic medical devices bearing CE marking means that the product **meets the requirements of all relevant European Directives** 98/79/EC on in vitro diagnostic medical devices. CE Marking is a legal requirement for medical devices to enter and place on the European market.

Evaluation in EU market:

Directive 98/79/EC sets out the essential requirements that in vitro diagnostic medical devices must meet when they are placed on the market. According to these requirements, the Common Technical Specifications (CTS) for in vitro diagnostic medical devices in List A of Annex II to Directive 98/79/EC. To meet the CTS, the OEM supplier of Drop Test s.r.o. had performance evaluation at **Paul Ehrlich Institute (PEI) in Germany**.
There are specific principles and requirements as follows.
The results show that Dr. Drop HIV-1/2 was equivalent sensitive in detection of anti-HIV 1/2 with the CE-marked anti-HIV 1/2 screening assay.

Common Technical Specifications (CTS) for Anti HIV 1/2 Rapid tests

Diagnostic sensitivity	Positive specimens	400 HIV-1 100 HIV-2 including 40 non-B subtypes, all available HIV/1 subtypes should be represented by at least 3 samples per subtype
	Sero-conversion panels	20 panels 10 further panels (at Notified Body or manufacturer)
Diagnostic specificity	Negative specimens	1 000 blood donations 200 clinical specimens 200 samples from pregnant women 100 potentially interfering samples

Performance tests results*

*All tests results extracted from OEM supplier’s files

Terminology

Sensitivity, specificity and predictive value of HIV serological tests

		True HIV status		
		+	-	
Results of assay under evaluation	+	**a True-positives**	b False positives	a+b
	-	c False-negatives	**d True-negatives**	c+d
		a+c	b+d	

Sensitivity = a/(a+c) **Positive predictive value** = a/(a+b)

Specificity = d/(b+d) **Negative predictive value** = d/(c+d)

Sensitivity:

It is the ability of the assay under evaluation to detect correctly sera that contain antibody to HIV (reference assays positive). Thus sensitivity is the number of true positive sera identified by the assay under evaluation as positive (a), divided by the number of sera identified by the reference assays as positive (a+c), expressed as a percentage.

Specificity:

It is the ability of the assay under evaluation to detect correctly sera that do not contain antibody to HIV (reference assays negative). Thus specificity is the number of true negative sera identified by the assay under evaluation as negative (d), divided by the number of sera identified by the reference assays as negative (b+d), expressed as a percentage.

Sensitivity
of Dr. Drop HIV-1/2 Rapid Test

	IR	RT	RR
Clinical samples university Frankfurt/Germany			
n tested	400		400
n positive	398		400
n +/-	2	2	0
n negative	0		0
Sensitivity	100%		100%
Sensitivity final			**RR**
n tested			400
n positive			400
n +/-			0
n negative			0
Sensitivity			100%

IR = initial reactive rate
RT = repetition test
RR = repeat reactive rate

Specificity
of Dr. Drop HIV-1/2 Rapid Test

	IR	RT	RR
N samples tested	500	0	500
N negatives	500	0	500
N positives	0	0	0
Specificity	**100,00%**	**100,00%**	**100,00%**

IR = initial reactive rate
RT = repetition test
RR = repeat reactive rate

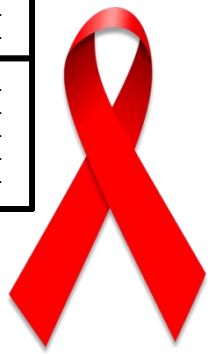
Range of assays compared with Dr. Drop HIV 1/2 Rapid Test

	Test name [1]	Category	Cat. no.	Manufacturer
1.	Access HIV Ab New	[2]	34020	Biorad SDP GmbH
2.	Advia Centaur HIV 1/O/2	[2]	03717761	Bayer HealthCare LLC
3.	Anti-HIV Tetra	[2]	807007	Biotest AG
4.	Architect HIV Ag/Ab Combo	[3]	4J27	Abbott GmbH & Co. KG
5.	AxSYM HIV 1/2 gO	[2]	3D41-22	Abbott GmbH & Co. KG
6.	AxSYM HIV Ag/Ab Combo	[3]	2G83-20	Abbott GmbH & Co. KG
7.	Determine HIV 1/2	[2]	7D2346	Unipath Ltd.
8.	Elecsys HIV Ag	[2]	11971611	Roche Diagnostics GmbH
9.	Elecsys HIV combi	[3]	03599604	Roche Diagnostics GmbH
10.	Enzygnost Anti-HIV 1/2 Plus	[2]	OQFK	Dade Behring Marburg GmbH
11.	Enzygnost HIV Integral	[2]	OQTO	Dade Behring Marburg GmbH
12.	Enzygnost HIV Integral II	[3]	OPAA	Dade Behring Marburg GmbH
13.	Genscreen HIV 1/2 Vers. 2	[2]	72278	BioRad SDP GmbH
14.	GenScreen Ultra HIV Ag-Ab	[2]	72386	BioRad SDP GmbH
15.	IMx HIV-1/HIV-2 III PLUS	[2]	8C98-20	Abbott GmbH & Co. KG
16.	Murex HIV Ag/Ab Combination	[3]	7G79	Murex Biotech Ltd.
17.	Murex HIV 1.2.O	[2]	GE94/95	Murex Biotech Ltd.
18.	Ortho HIV-1/HIV-2 Ab-Capture ELISA	[2]	932360	Ortho Clinical Diagnostics, Inc.
19.	Ortho Vitros ECI HIV	[2]	1241850	Ortho Clinical Diagnostics, Inc.
20.	PRISM HIV Ag/Ab Combo	[3]	7G46-48	Abbott GmbH & Co. KG
21.	PRISM HIV O Plus	[2]	3D34-48	Abbott GmbH & Co. KG
22.	SFD HIV PA	[4]	71110	Biorad Fujirebio
23.	Vidas HIV Duo	[2]	30114	bioMérieux S.A.
24.	Vironostika Uni-Form II Ag/Ab	[2]	285047	bioMérieux S.A.
25.	Vironostika Uniform II Plus O	[2]	84017	bioMérieux S.A.

Result of Seroconversion panel

Panel	Days since 1st bleed	HIV AG[1] S/CO	Assays under evaluation					Enzygnost Anti-HIV 1/2 Plus[2] OD/CO	Vironostika HIV Uniform II Plus O[2] OD/CO	INNO-LIA HIV Confirmation[2]							
			SR 1	SR 2[3]	SR 3	SR 4	SR 5[3]			Result	Sgp120	gp41	p31	p24	p17	sgp105	gp36
PRB910-01	0	0.4	neg	neg	neg	neg	neg	0.1	0.4	neg	-	-	-	-	-	-	-
PRB910-02	14	5.7	neg	neg	neg	neg	neg	0.1	0.4	neg	-	-	-	-	-	-	-
PRB910-03	26	0.6	pos	pos	pos	pos	pos	>6,7	8.9	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-04	28	0.5	pos	pos	pos	pos	pos	>6,7	8.9	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-05	32	0.4	pos	pos	pos	pos	pos	>6,7	8.3	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-06	35	0.4	pos	pos	pos	pos	pos	>6,7	8.4	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-07	40	0.4	pos	pos	pos	pos	pos	>6,7	8.6	HIV-1	2+	3+	-	2+	2+	-	-
PRB912-01	0	10.2	neg	neg	neg	neg	pos	1.8	0.9	neg	-	-	-	-	-	-	-
PRB912-02	9	24.9	pos	pos	pos	pos	pos	>6,7	5.4	HIV-1	-	3+	-	2+	2+	-	-
PRB912-03	14	10.6	pos	pos	pos	pos	pos	>6,7	6.8	HIV-1	-	3+	-	2+	2+	-	-
PRB912-04	16	3.2	pos	pos	pos	pos	pos	>6,7	7.7	HIV-1	-	3+	-	2+	2+	-	-
PRB912-05	28	0.5	pos	pos	pos	pos	pos	>6,7	10.7	HIV-1	-	3+	-	2+	2+	-	-
PRB912-06	30	0.5	pos	pos	pos	pos	pos	>6,7	11.9	HIV-1	-	3+	-	2+	2+	-	-
PRB914-01	0	0.4	pos	pos	neg	neg	pos	>6,7	4.9	HIV-1	1+	2+	-	+/-	-	-	-
PRB914-02	4	0.5	pos	pos	neg	neg	pos	>6,7	6.5	HIV-1	1+	2+	-	1+	-	-	-
PRB914-03	7	0.5	pos	pos	neg	neg	pos	>6,7	7.8	HIV-1	1+	2+	-	2+	1+	-	-
PRB914-04	25	0.4	pos	pos	neg	neg	pos	>6,7	13.8	HIV-1	2+	2+	-	2+	2+	-	-
PRB914-05	31	0.4	pos	pos	pos	pos	pos	>6,7	14.0	HIV-1	2+	2+	-	2+	2+	-	-
PRB917-01	0	0.4	neg	neg	neg	neg	neg	0.6	0.7	neg	-	-	-	-	-	-	-
PRB917-02	53	3.9	neg	neg	neg	neg	neg	0.1	0.3	neg	-	-	-	-	-	-	-
PRB917-03	57	21.6	neg	neg	neg	neg	neg	0.2	0.4	neg	-	-	-	-	-	-	-
PRB917-05	65	2.4	pos	pos	pos	pos	pos	>6,7	5.7	HIV-1	1+	2+	-	+/-	-	-	-
PRB917-06	67	1.6	pos	pos	pos	pos	pos	>6,7	6.8	HIV-1	1+	2+	-	1+	-	-	-
PRB927-01	0	0.6	neg	neg	neg	neg	neg	0.1	0.3	neg	-	-	-	-	-	-	-
PRB927-02	28	>22.7	neg	neg	neg	neg	neg	2.2	1.8	neg	-	-	-	-	-	-	-
PRB927-03	33	10.2	pos	pos	pos	neg	pos	>6,7	8.3	ind	-	2+	-	-	-	-	-
PRB927-04	35	2.6	pos	pos	pos	pos	pos	>6,7	5.5	HIV-1	1+	2+	-	-	-	-	-
PRB927-05	40	1.3	pos	pos	pos	pos	pos	>6,7	6.2	HIV-1	2+	3+	-	2+	2+	-	-

SR 5: Results of OEM Supplier of Dr. Drop HIV 1/2 Rapid Test



Supplementary Clinical evaluation studies

	No. of samples	Result
Early seroconversion panel	**48**	**As sensitive as the CE-Marked HIV assays**
Serum to whole blood equivalency study	**75**	**100% (150 negative/150)**
- ***Serum***	***25***	***25/25***
- ***Venous blood***	***25***	***25/25***
- ***Fingerstick blood***	***25***	***25/25***
Serum to plasma equivalency study	**100**	**100% (200 negative/200)**
- ***Serum***	***25***	***25/25***
- ***Plasma (heparin)***	***25***	***25/25***
- ***Plasma (EDTA)***	***25***	***25/25***
- ***Plasma (citrate)***	***25***	***25/25***

In conclusion, we found that the performance of the evaluated rapid test corresponds to the criteria set by the revised CTS for IVD (2009/886/EC) and it is suitable for the analysis of fingerstick blood, serum, whole blood and plasma (containing heparin, EDTA or citrate) samples.

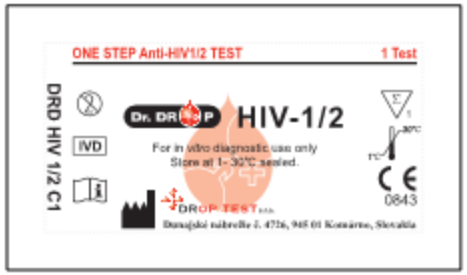
Test Procedure

Packaging: Individual kit or Multipackage for medical facilities

The Dr. Drop HIV 1/2 Rapid Test kit contains the following items:

1. Test device individually foil pouched with a desiccant
2. Assay diluents
3. Lancets
4. 20 $\mu\ell$ capillary pipettes,
5. Instruction for use

1



2

Assay diluent in vial

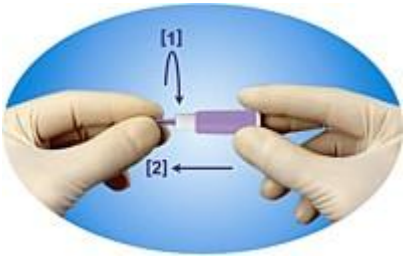
3

1) Lancet

2) 20$\mu\ell$ Capillary Pipette

When using samples of *Fingerstick blood*

An adequate blood sample can be obtained with a three step procedure.

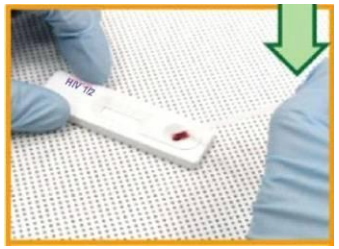


Twist off blue (purple, green or yellow) protective lancet cap and then pull it out.

Press the Medlance body firmly against the puncture site to activate the lancet.

Gently apply intermittent pressure near the puncture site to obtain the required blood volume.

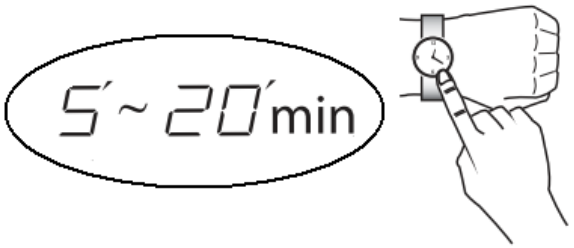
Take a 20 ㎕ capillary pipette provided, immerse the open end in the blood drop and then release the pressure to draw blood into the capillary pipette to black line.

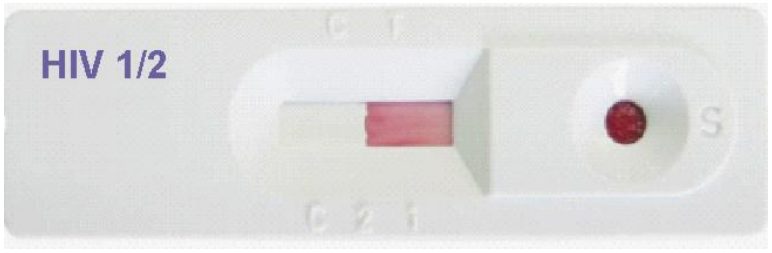


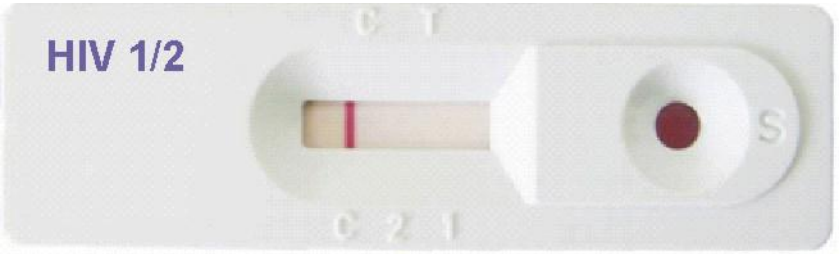
Add 20 ㎕ of drawn blood specimen with a 20 ㎕ capillary pipette into the sample well (s).

Add 4 drops of assay diluent into sample well(s).
Exactly, 4 drops should be added.

Interpret test results in 5~20 minutes.
First reading : After 5 minutes
Final reading : In or around 20 minutes
※ Do NOT read after 20 minutes!



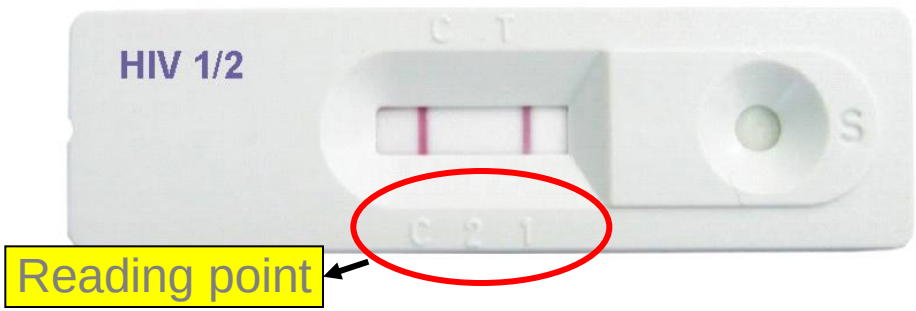




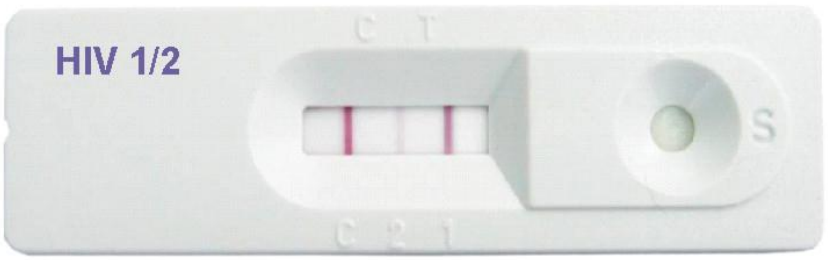
Migration Start

Migration Completed

Interpretation - I



HIV-1 positive
("C", "1" line)



HIV-1 positive
("C", "1", faint "2" line)

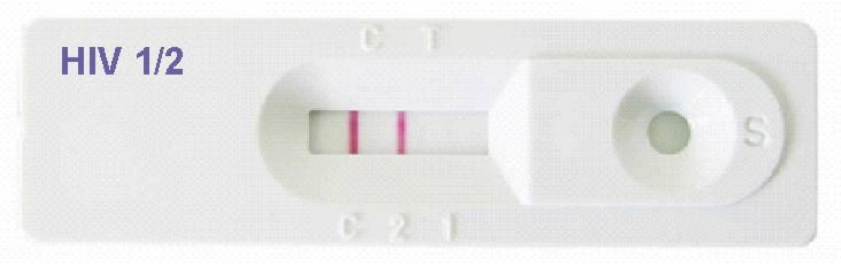
Notes:

1) If the color intensity of line "1" is darker than line "2", you can interpret the result as HIV-1 positive

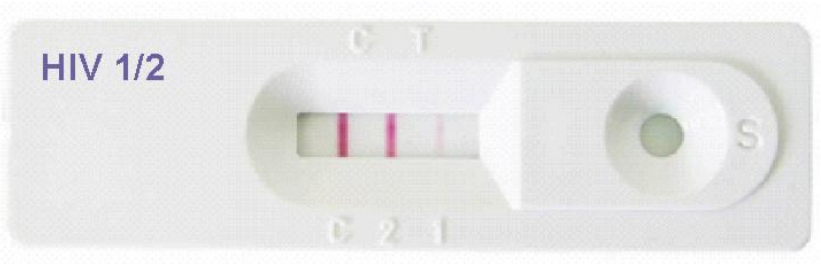
2) If the bands thickness are very similar, very rarely, positive result for HIV-1 and 2 in one patient is possible as there can be an homology in the amino acid sequence of HIV Type-1 and Type-2. In this case, confirm test using Western Blot is recommended to know exact virus type.

★ Do NOT read after 20 minutes!! ★

Interpretation - II



HIV-2 positive
("C", "2" line)



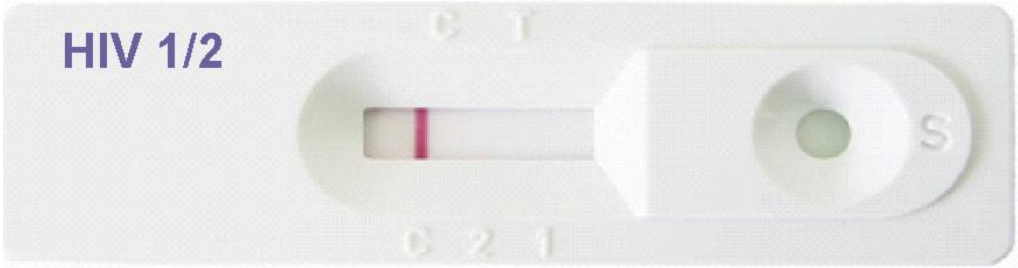
HIV-2 positive
("C, "2", faint "1" line)

Notes

- If the color intensity of line "2" is darker than line "1", you can interpret the result as HIV-2 positive.
- If the bands intensity are very similar, very rarely, both positive result for HIV-1 and 2 in one patient is may possible as there can be an homology in the amino acid sequence of HIV Type-1 and Type-2. In this case, confirm test using Western Blot is recommended to know exact virus type

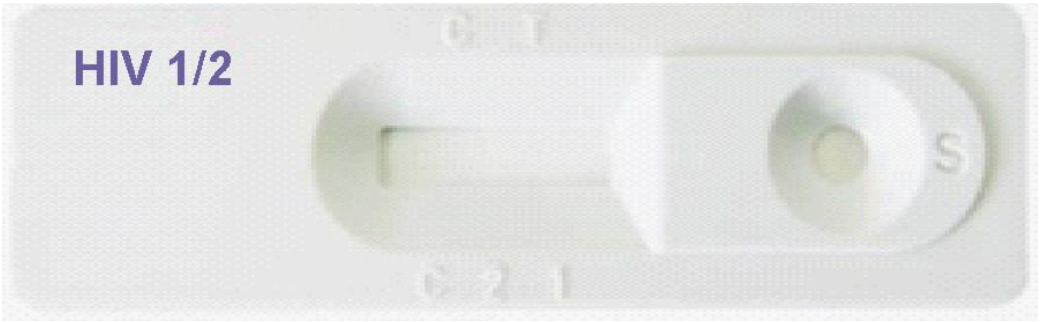
★ Do NOT read after 20 minutes!! ★

Interpretation - III



Negative

(“C” line only)



Invalid

(No line)

Why rapid test?

✓ Bedside rapid tests to detect HIV antibodies are now an equivalent alternative to the conventional antibody screening tests, as their sensitivity (98% to 100%) and specificity (86% to 100%, one outlier 75%) are comparable to the values found with the enzyme immunoassays (EIAs) performed in the laboratory.

✓ They are particularly useful in areas with little access to laboratories (e.g. Africa), in people who are difficult to reach (e.g. drug addicts or the homeless), for the critical period in which a decision has to be made about prophylaxis after exposure, and after a birth where the HIV status of the mother is uncertain.

✓ Even though the specificity is 99% to 100% in some studies, a rapid test can always in principle give a false positive result. Although current experience suggests that the problem is less severe in practice than had been expected, it is essential that positive rapid test results should be confirmed by an alternate rapid test (if resources are limited) or by a conventional test (e.g. Western blot).

Advantages and disadvantages of rapid tests

Advantages	Disadvantages
• Immediate initiation of specific antibiotic therapy is possible • Reduction in unnecessary antibiotic consumption • Reduction in selection pressure • Immediate recognition of infection chains • Reduction in pre-analytical interference • Extension of diagnostic instrumentarium; independent of culture • Better compliance with patients who are difficult to reach	• Older POCT systems perform more poorly (before. the introduction of immunochromatographic techniques) • Lack of data on pathogen sensitivity • Increased risk of operator becoming infected • Operator's qualifications may be inadequate. • Double or multiple infections are more likely to be overlooked than in culture. • Necessity of performing measures for quality control

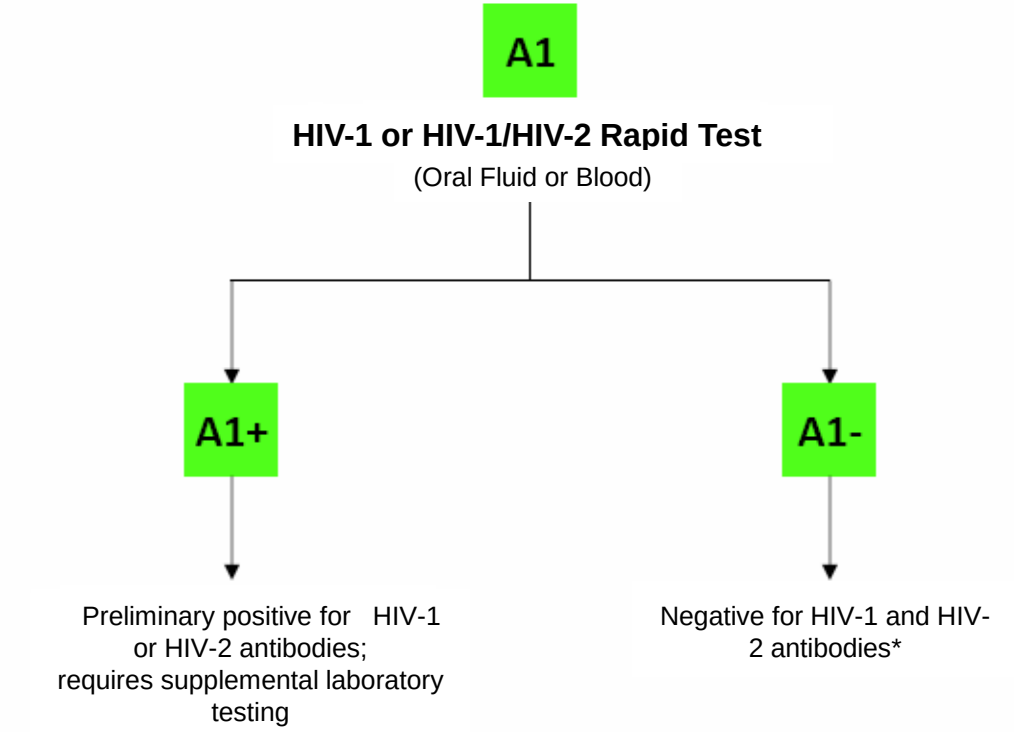
Conclusions

In general, it may be concluded that immunochromatography test strips to detect infectious pathogens are technically fully developed and that they exhibit a series of specific advantages, but also disadvantages. With modern immunochromatography tests, investigations can be performed rapidly and simply, without requiring special instruments or expertise in the method. As the sensitivity and specificity of many test procedures are now really high, rapid tests can be extraordinarily useful in answering specific questions and thus in helping to orientate diagnosis, uncovering chains of infection, and in deciding to start early specific antimicrobial therapy or drug prophylaxis. The precondition of the proper use of these tests is that they should be properly handled by medical personnel, that quality assurance measures should be in place and that the interpretation of the results should consider the severity of the clinical presentation and the epidemiological situation.

HIV Testing Algorithms

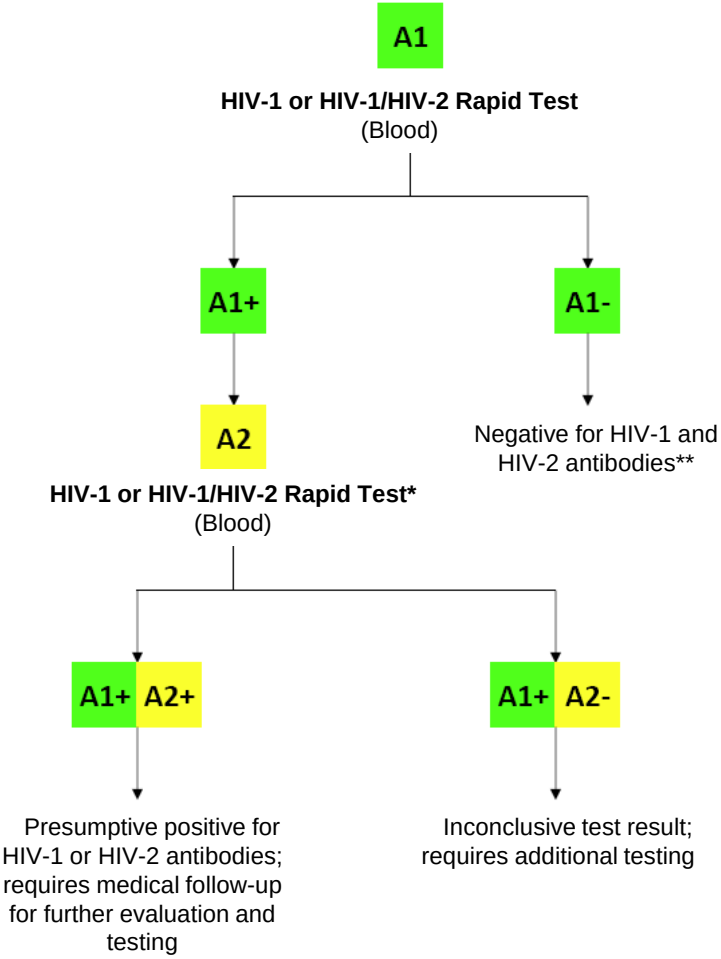
PROPOSED TESTING STRATEGIES FOR POC RAPID HIV TESTING

Algorithm 1: Single Rapid Test (A1) for HIV Screening



•If using an HIV-1 only rapid test, this result is negative **only** for HIV-1 antibodies

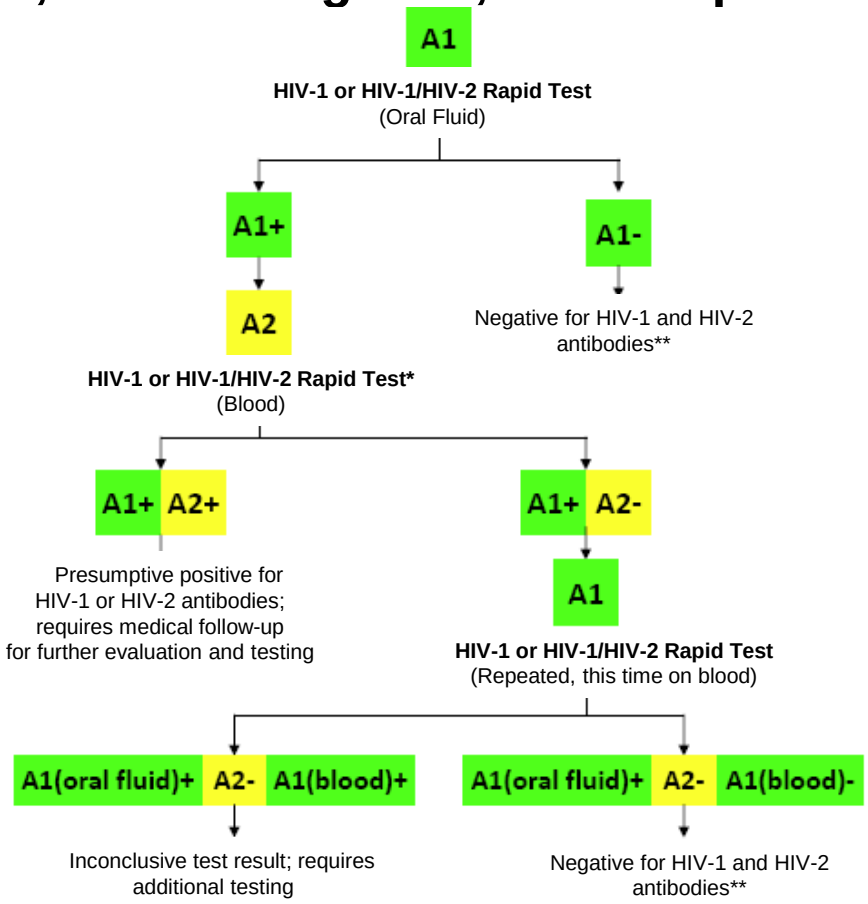
Algorithm 2: Two Rapid Tests (A1/A2) Performed in Sequence on Blood



* Test must be from a different manufacturer

****** If using an HIV-1 only rapid test, this result is negative **only** for HIV-1 antibodies

Algorithm 3: Two Rapid HIV Tests (A1 oral/A2 blood) Performed in Sequence; If A2 Is Negative, A1 Is Repeated on Blood

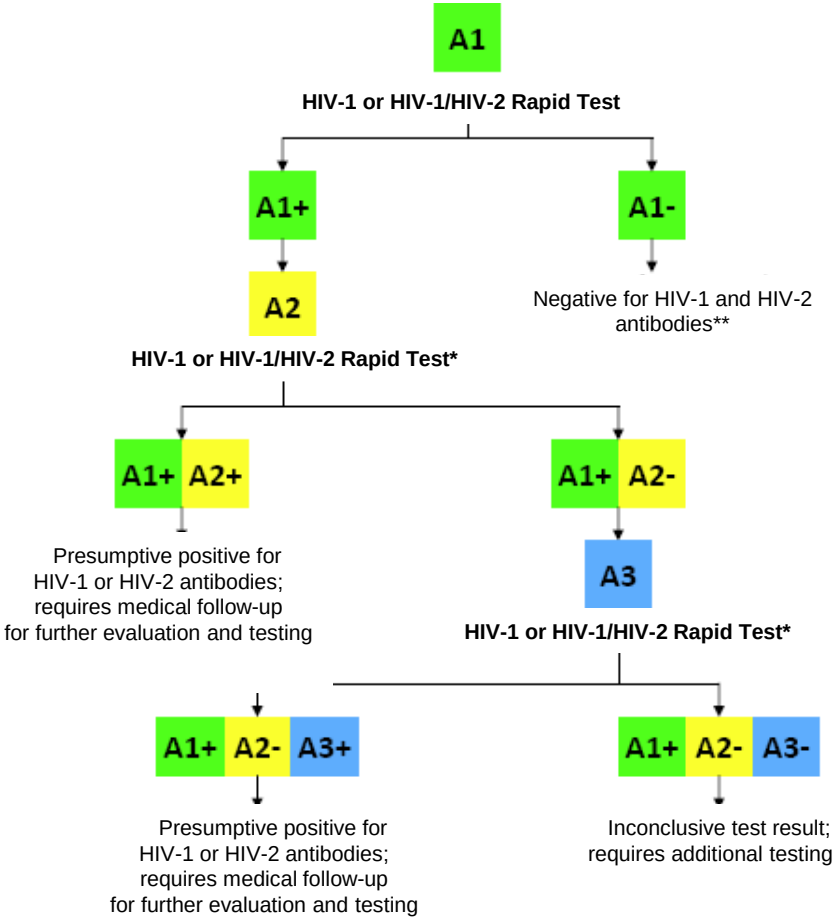


•Test must be from a different manufacturer

****** If using an HIV-1 only rapid test, this result is negative **only** for HIV-1 antibodies

\+ This algorithm may only be used when the same test is available for both oral fluid and blood

Algorithm 4: Three Rapid HIV Tests (A1/A2/A3) Performed in Sequence on Blood. (A1, A2 and A3 must be different rapid tests.)



* Test must be from a different manufacturer

****** If using an HIV-1 only rapid test, this result is negative **only** for HIV-1 antibodies