05022525001© - 0207 - 2.Kn

Roche Diagnostics GmbH
D-68298 Mannheim
Germany
www.roche-diagnostics.com

Roche Diagnostics

cobas®

Life needs answers

HIV testing

Going straight for the answer

Roche Diagnostics

cobas® brand

Roche Diagnostics introduces the **cobas®** brand as the umbrella for products used to complete or expand the screening, diagnostic and monitoring applications of the professional laboratory.

cobas brand includes:

- serum work area with clinical chemistry and immunochemistry
- data management and preanalytical solutions
- products for coagulation analysis and urinalysis
- instruments for rapid blood and cardiovascular testing
- PCR-based applications for virology and women's health testing

Elecsys® HIV assays

Going straight for the answer

Roche Diagnostics has developed an automated HIV immunoassay for the combined detection of HIV antigen and antibodies. Innovative developments have included the use of electroluminescence technology and the sophisticated design of recombinant antigens leading to Elecsys® HIV combi.

The assay provides an early detection of HIV infection and a broad recognition of HIV variants.

Content

From challenges...

Closing gaps in HIV diagnosis

The major challenges in state of the art HIV serodiagnosis are the early detection of infection and the reliable recognition of all HIV variants. Addressing these two issues contributes to

- improvements in the safety of blood and blood products
- an earlier diagnosis to prevent the further spread of HIV infection
- a reduced response time for individual HIV testing after exposure e.g. needlestick injury
- a reliable diagnosis even when new variants are emerging in the virus population

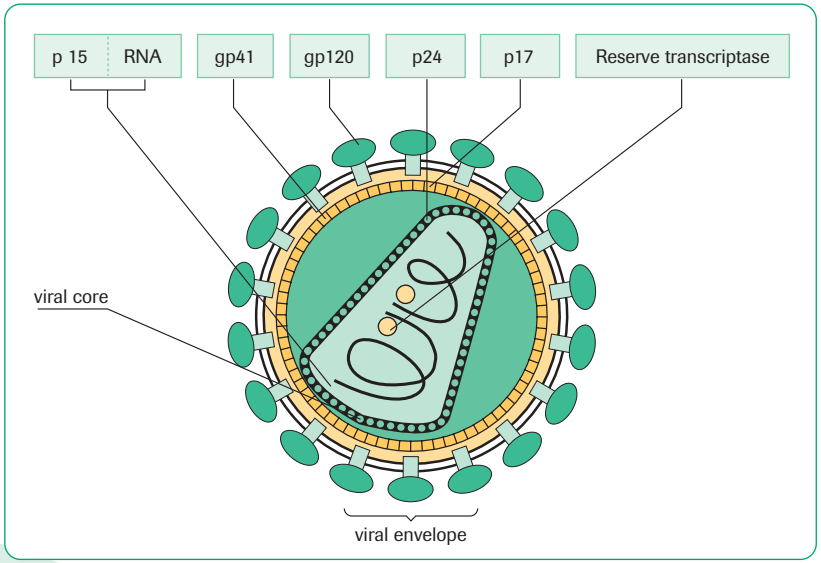


Fig. 1: Morphological Structure of HIV-1 (adapted from Fields et al [1])

...to solutions

Elecsys® HIV combi

the 4th generation HIV assay to achieve high security for diagnosis

- closing gaps in the early detection of HIV infection:
  reducing the diagnostic window period
- closing gaps in the late stage of HIV infection:
  improved identification of infected patients who have antigenemia and impaired synthesis of HIV antibody
- closing gaps in the recognition of HIV variants:
  reliable detection of all HIV-1 groups and subtypes including the highly divergent group O
- closing gaps and maintaining high specificity:
  dedicated for a short response time

Assay features	Benefits
4th generation assay format: combined detection of HIV antibodies and antigen	excellent sensitivity for the early detection of HIV infection
recognition of all major HIV-1 groups and subtypes including the highly divergent group O and HIV-2	reliable detection of HIV infection
high clinical specificity	less retesting
short total assay time: 18 min	fast response time
ready-to-use reagents	reduces possiblility of errors and saves staff time
one assay for Elecsys® 2010 and **MODULAR**® *ANALYTICS* <E>	excellent comparability of results
high throughput (up to 170 tests/h)	rapid results, shorter daily shifts

Closing gaps
in the early detection of HIV infection

reducing the diagnostic window with the 4th generation assay format

- 4th generation test principle means the simultaneous detection of HIV antibodies and antigen
- the recognition of IgG and IgM antibodies is enhanced by multivalent binding
- monoclonal anti-p24 antibodies are used for the detection of HIV-1 antigen
- recombinant antigens are used to provide optimal sensitivity

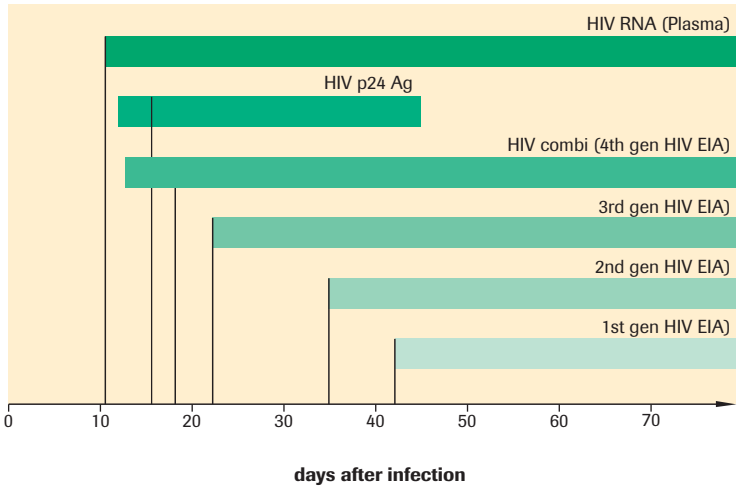


Fig. 2: Early detection of HIV infection (adapted from Weber et al. [2])

Closing gaps
in the late stage of HIV infection

improved detection in the late stage of the disease

- the combination of antigen and antibody detection within one assay leads to a higher sensitivity in the early seroconversion phase
- in addition, it permits an improved identification of infected patients during the late stage of disease who have antigenemia and impaired synthesis of HIV antibody

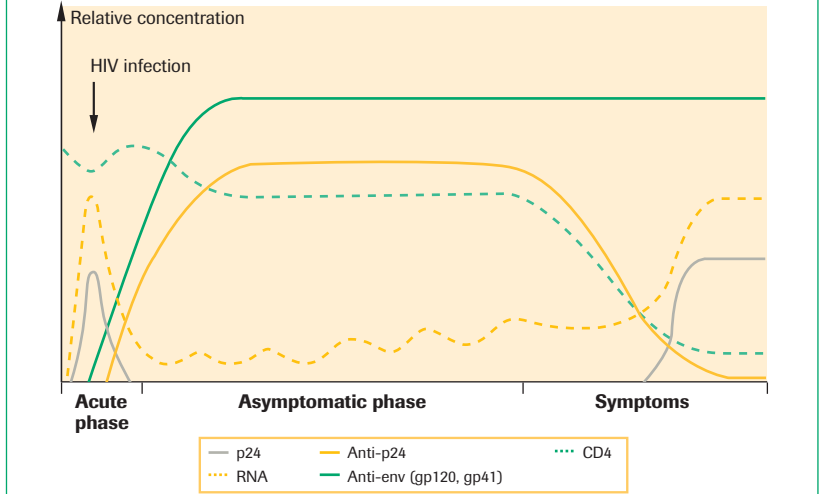


Fig. 3: Time course of HIV infection (adapted from Busch et al, [3])

Closing gaps
in the recognition of HIV variants

reliable recognition of all HIV variants

- the genetic variability of HIV represents a major challenge for the reliable detection of HIV infection
- it is mandatory to recognize all HIV-1 groups and subtypes which are distributed all over the world including the highly divergent group O [4] and emerging CRF's [5]
- a combination of recombinant envelope and reverse transcriptase antigens from highly conserved regions enhances the detection of HIV type 1 and 2

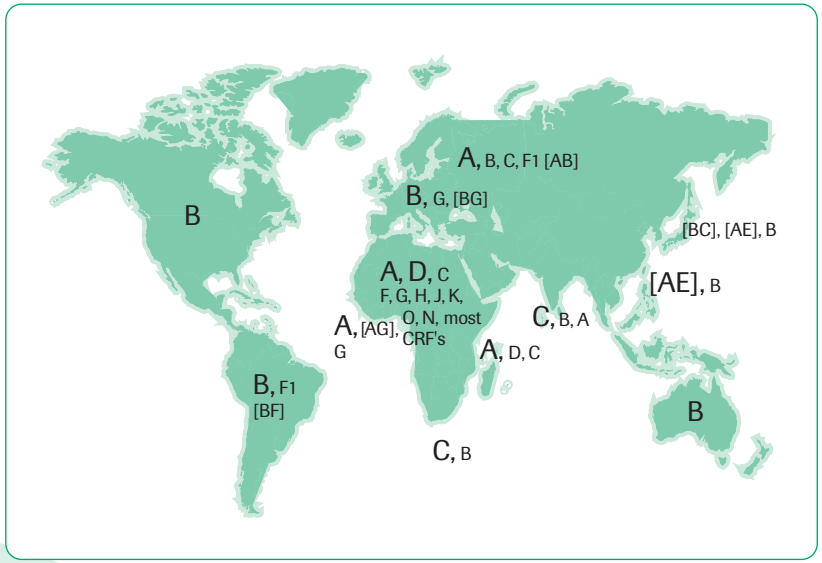


Fig. 4: Worldwide distribution of HIV-1 groups and subtypes (adapted from Thomson et al, [5]) CRF's = Circulating Recombinant Forms in brackets])

Closing gaps
using recombinant antigens

tailormade recombinant antigens for enhanced HIV detection

1) gp 41/gp 36 module:

- native-like folded antigens are derived from the envelope protein of HIV-1 (gp 41) and HIV-2 (gp 36) [13]
- specific group O antigens from an immunodominant region of the HIV-1 assure the reliable and broad detection of antibodies to group O

2) Reverse transcriptase (RT) module:

- recombinant RT from HIV-1 and HIV-2 is included in the assay
- this antigen is highly conserved in HIV variants and induces a cross-reactive antibody response to enable a reliable detection [6]

"Assays that use large recombinant antigens with multiple antibody binding sites have a higher sensitivity than those using short peptides."
Weber B., J Clin Microbiol 2002, 40:4402-4404 [8]

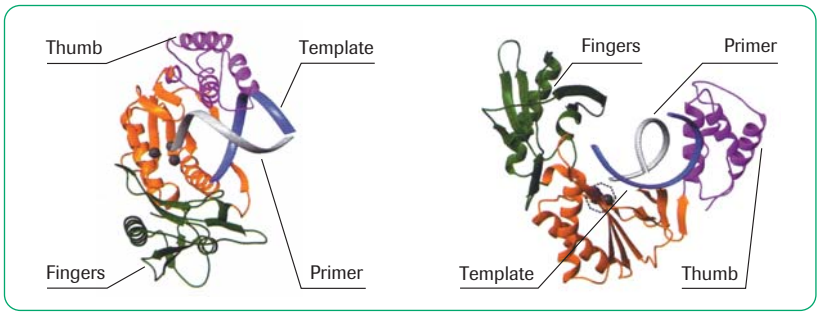


Fig. 5: Reverse Transcriptase structure model, adapted from [7]

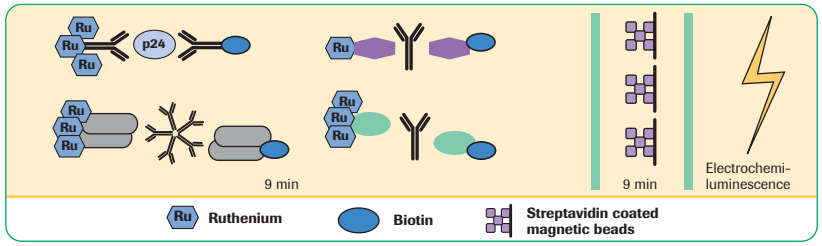
Elecsys® HIV combi

Order number 04 860 446

Test application
Immunoassay for the in-vitro qualitative detection of HIV-1 p24 antigen (group M and group O) and antibodies (IgG and IgM) to HIV-1 (group M and group O) and HIV-2 in human serum and plasma

Clinical utility
Identification of HIV infections
- in HIV-infected individuals
- in blood and blood products containing HIV

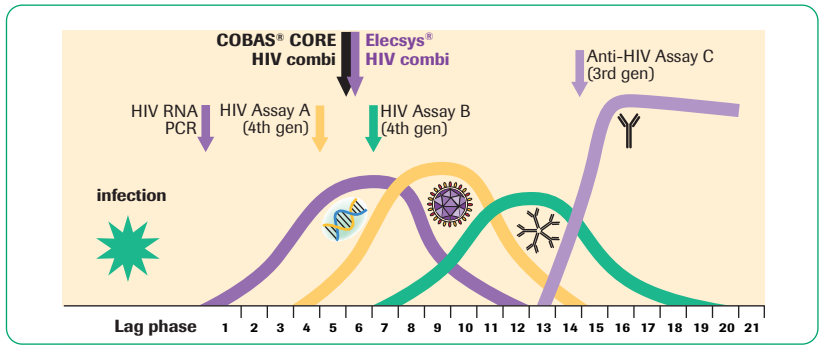
Test principle
Double antigen/antibody immunoassay
HIV specific antibodies and HIV antigen are detected within one determination (4th generation HIV assay):
- detection of HIV-1 p24 antigen using monoclonal antibodies
- detection of total anti-HIV antibodies (IgG and IgM) using recombinant antigens: gp41 including group O, gp36, reverse transcriptase (RT)

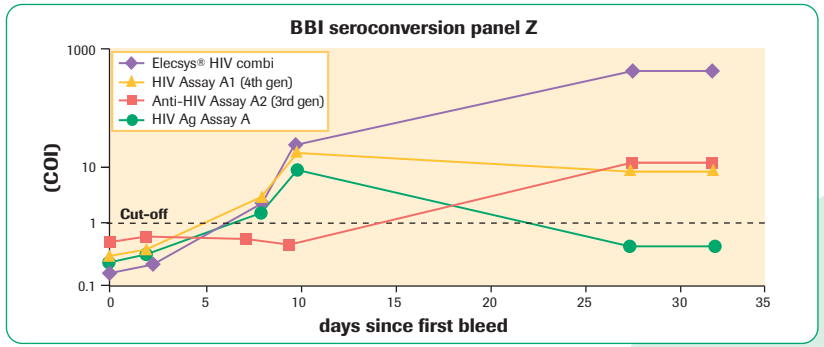


Test features
- high sensitivity
  - combined detection of HIV antigen and antibody leading to excellent seroconversion sensitivity and enhanced detection of patients during late phase of HIV infection
  - very sensitive HIV Ag detection (≤ 6 U/ml)
  - recognition of all known HIV-1 subtypes and HIV-1 group O
- high clinical and analytical specificity (99.76 % in blood donors)
- fully automated, ready to use reagents and short total assay time (18 min)
- excellent comparability between Elecsys® 2010 and **MODULAR®** *ANALYTICS* <E>

Performance data

Primary infection
Commercially available seroconversion panels (n=23) were tested with Elecsys® HIV combi in comparison to anti-HIV assays (3rd generation) and anti-HIV/HIV Ag combined assays (4th generation), e.g. COBAS® CORE HIV combi [9, 10]. Compared to 3rd and other 4th generation HIV assays, Elecsys HIV combi showed a superior or comparable sensitivity, respectively [9, 10].

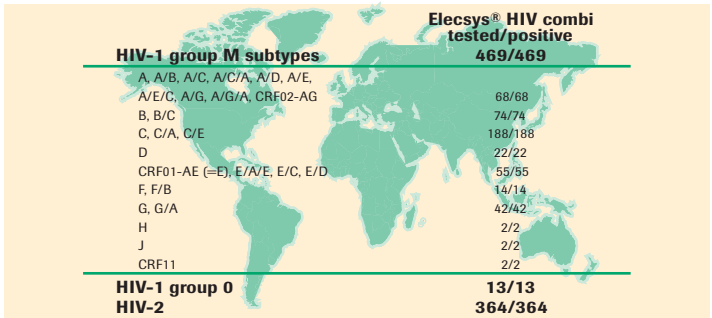




Different stages of the disease
Of 1509 samples from HIV infected patients in different stages of the disease and infected with HIV-1 groups M, O and HIV-2, 1509 were found to be repeatedly reactive with Elecsys HIV combi. The sensitivity of Elecsys HIV combi in this study was 100 % [9, 10].

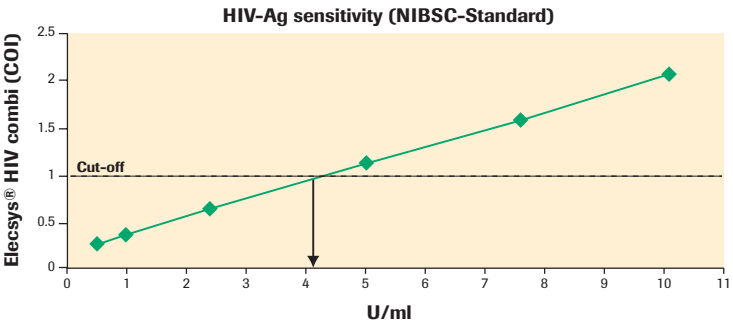
Infection with different HIV variants

846 antibody positive samples from infections with different subtypes of HIV-1 group M and group O and HIV type 2 were tested and were found positive with Elecsys® HIV combi [9, 10].



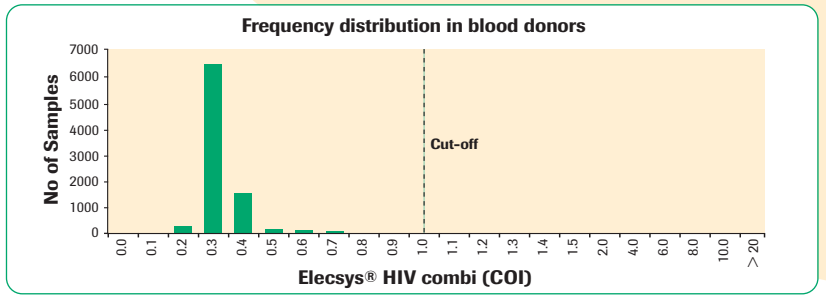
Analytical sensitivity

The HIV Ag sensitivity of Elecsys HIV combi was determined using the proposed WHO 1st International Reference Reagent for HIV-1 p24 antigen [9].



Clinical Specificity

8406 samples from blood donors were tested with Elecsys HIV combi at different evaluation sites in Europe and Asia [9, 10].
The clinical specificity was found to be 99.76 %.

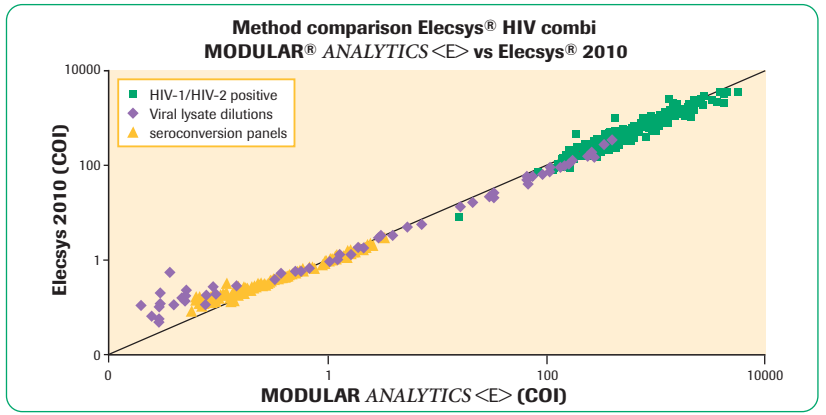


4389 samples from daily routine, from dialysis patients and from pregnant women were tested. The specificity in these clinical samples was 99.63 % [9].

	No of samples	Elecsys® HIV combi initially reactive COI ≥ 1	Elecsys HIV combi repeatedly reactive COI ≥ 1	WB confirmed positive/ Indeterminate
Blood donors	8406	31	29	6/4
Unselected samples from daily routine	3810	33	34	17/3
Dialysis patients	242	2	2	0
Pregnant women	337	1	1	0

Comparability between Elecsys® 2010 and MODULAR® *ANALYTICS* <E>

An excellent comparability of results could be shown in a method comparison with HIV positive samples, diluted viral lysates, and seroconversion panels (n=429 samples, [9]).



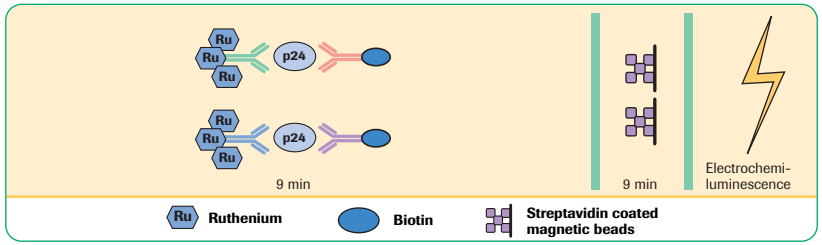
Elecsys® HIV Ag

Order number 01 971 611

Test application
Immunoassay for the in-vitro qualitative detection of the p24 antigen of HIV-1 (group M and group O) in human serum and plasma or in cell culture supernatants

Clinical utility
Identification of HIV infections
- in individuals with a known risk of HIV infection when used in combination with the HIV screening test
- in infants born to HIV-infected mothers
- to support monitoring during antiviral therapy

Test principle
Sandwich assay using monoclonal antibodies for the detection of p24 antigen of HIV-1.



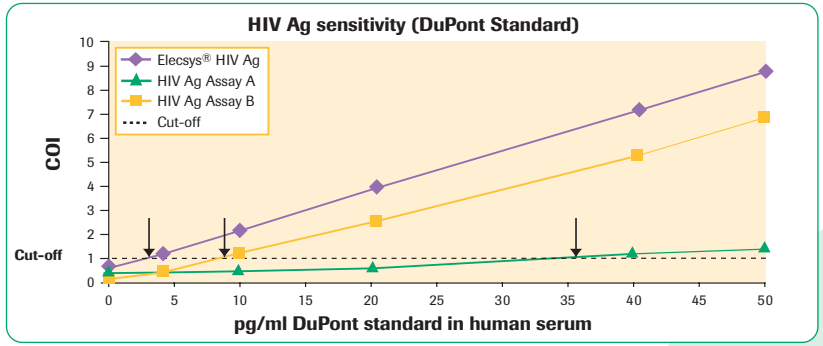
Test features
- high sensitivity in the early phase of infection
- superior analytical sensitivity: ≤ 4 pg/ml (DuPont Standard)
- recognition of all known HIV-1 subtypes and HIV-1 group O
- excellent clinical and analytical specificity
- fully automated, ready to use reagents and short total assay time (18 min)
- available on Elecsys® 2010, **MODULAR**® *ANALYTICS* <E> (**cobas**® 6000 <601> analyzer) up to 170 tests/h
- confirmation of positive results with Elecsys® HIV Ag Confirmatory Assay

Performance data

Primary infection
Commercially available seroconversion panels were tested in comparison to other HIV Ag assays. The Elecsys® HIV Ag detected seroconversions on average 1 day earlier as compared to HIV Ag assay A (internal and published results [9, 11]).

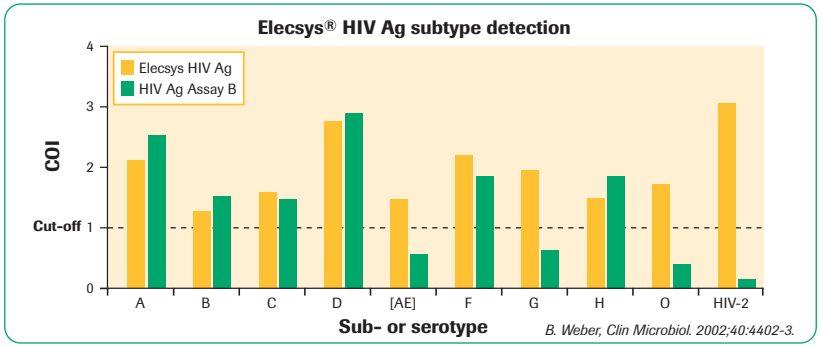
	HIV Ag Assay A	COBAS® CORE HIV Ag EIA	HIV Ag Assay B	Elecsys® HIV Ag
Number of panels	79	79	59	30
Sum of delay in first positive detection (in days)	0	-79	-81	-36
Average delay in first positive detection per seroconversion panel (in days)	0	-1.0	-1.2	-1.2

Analytical sensitivity
The analytical sensitivity of Elecsys HIV Ag was determined using standard material which was standardized against DuPont Standard [9].



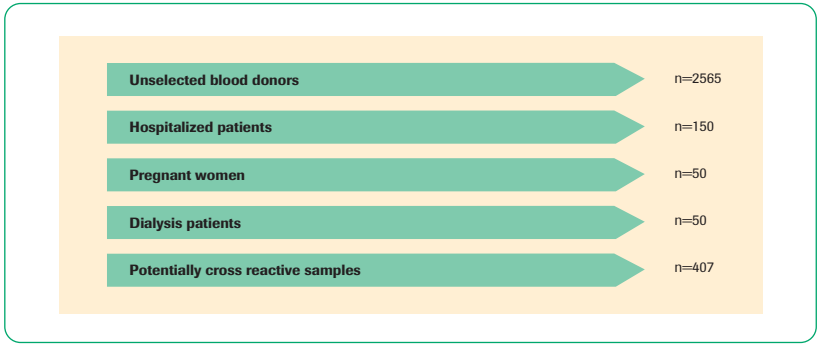
Subtype detection

The sensitivity for HIV Ag detection was evaluated by testing virus stocks of different HIV-1 group M subtypes, group O, and HIV-2 diluted in HIV negative serum adjusted to concentrations ranging between 5 and 15 pg of p24 Ag per ml according to the Dupont Standard [8].



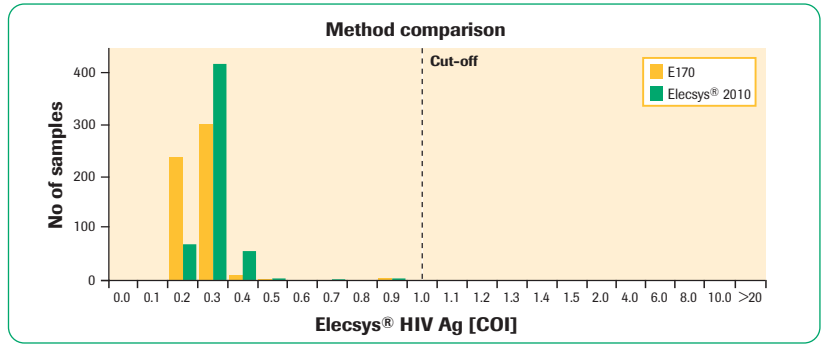
Clinical specificity

Over 3000 samples from blood donors, different patient groups and routine samples were tested with Elecsys® HIV Ag resulting in a clinical specificity of 99.8 %. In combination with the Elecsys HIV Ag confirmatory assay, the specificity reached 100 % [9, 12].



Comparability between Elecsys® 2010 and **MODULAR**® *ANALYTICS* <E>

549 fresh samples from daily routine and hospitalized patients were tested with Elecsys® HIV Ag on Elecsys 2010 and E170. No false positive result was found resulting in a specificity of 100 % (IR and RR) for both systems [9]. The frequency distribution on both systems is shown below.



Roche Diagnostics reagent portfolio for Infectious Disease testing

		Immunoassays		Molecular Diagnostics	
Indication	**Test**	Elecsys® 2010 (**cobas e** 411)	**MODULAR®** *ANALYTICS* <E> (**cobas e** 601)	COBAS AMPLICOR	COBAS Taqman/ Taqman 48
Hepatitis B	HBsAg	●	●		
	HBsAg confirmatory	●	●		
	Anti-HBs	●	●		
	Anti-HBc	●	●		
	Anti-HBc IgM	●	●		
	HBeAg	●	●		
	Anti-HBe	●	●		
	HBV DNA			●	●
Hepatitis A	Anti-HAV	●	●		
	Anti-HAV IgM	●	●		
Hepatitis C	HCV RNA			●	●
HIV	HIV combi	●	●		
	HIV Ag	●	●		
	HIV Ag confirmatory	●	●		
	HIV RNA			●	●
TORCH	Toxo IgM	●	●		
	Toxo IgG	●	●		
	Rubella IgM	●	●		
	Rubella IgG	●	●		
	CMV IgM	■	■		
	CMV IgG	■	■		
	CMV DNA			●	
Others	HPV DNA			●	■
	Mycobacterium			●	
	Chlamydia			●	

● *available*
■ *in development*
Not all products are available in all countries

Consolidated Workstations

Clinical chemistry analyzers

COBAS INTEGRA® Systems
Designed to consolidate testing and increase efficiency while reducing total running costs of the laboratory.
The broad reagent portfolio and the innovative COBAS INTEGRA reagent cassette are combined with four proven measurement technologies and sophisticated, easy to use software.
COBAS INTEGRA systems are the right choice for workflow consolidation in the small to medium workload laboratory and special chemistry testing in high volume sites. COBAS INTEGRA® 800 allows the use of Roche/Hitachi 5-position sample racks for improved pre-analytical sample flow.

Roche/Hitachi Systems
Reliability, quality and convenience make these analyzers the clinical chemistry workhorse systems for routine test consolidation. The broad reagent portfolio includes more than 100 applications.
The combination of throughput and automation delivers high productivity for the laboratory.

Immunochemistry analyzer

Elecsys® Systems
The Elecsys systems family includes a range of immunochemistry analyzers, meeting automation requirements of nearly all sizes of clinical laboratories.
Dedicated STAT ports allow priority handling of emergency samples.
The Elecsys systems family allows the use of Roche/Hitachi 5-position sample racks for improved pre-analytical sample flow.

Serum Work Area solutions

MODULAR® ***ANALYTICS*** **SWA cobas® 6000 system***
Roche serum work area solutions offer one-touch sample processing with fully automated rack transport between the individual modules. Rack traffic and sample throughput of the clinical chemistry and immunoassay modules are tailored to fulfil the turnaround time (TAT) requirements for your routine and emergency samples.
Reflex testing capabilities enable the laboratory to apply indication oriented testing cascades efficiently.

*** cobas 6000 is the first member of the Roche 2nd generation of serum work area solutions.**

Scientific References

[1] Fields BN et al. Virology. 2nd edition, pages 1529-157, *Raven Press Limited, New York 1990.*

[2] Weber B et al. Labordiagnose der HIV-Infektion: Stellenwert kombinierter HIV p24 Ag und Antikörpertests. *Journal of Laboratory Medicine 2001, 25: 226-231.*

[3] Busch MP, Satten GA.Time course of viremia and antibody seroconversion following HIV exposure. *Am J Med 1997, 102:117-24.*

[4] Gürtler LG et al. HIV-1 subtype O: Epidemiology, pathogenesis, diagnosis, and perspectives of the evolution of HIV. *Arch Virol 1996, 11: 195-202.*

[5] Thomson MM et al. Molecular epidemiology of HIV-1 genetic forms and its significance for vaccine development and therapy. *The Lancet 2002, 2: 461-71.*

[6] Gürtler LG et al. Reduction of the diagnostic window with a new combined p24 antigen and HIV antibody screening assay. *J Virol Methods 1998, 75: 27-38.*

[7] Jacobo-Molina A et al. Crystal structure of HIV-1 reverse transcriptase complexed with double-stranded DNA at 3.0 A resolution shows bent DNA. *Proc Natl Acad Sci USA 1993, 90: 6320-4.*

[8] Weber B. HIV antigen-antibody combination assays: evaluation of HIV seroconversion sensitivity and subtype detection. *Clin Microbiol 2002, 40: 4402-4.*

[9] Data on file at Roche Diagnostics. *Details on request.*

[10] Weber B. Multicenter evaluation of a new 4th generation HIV screening assay Elecsys® HIV combi. *Clin Lab 2006, 52: 463-73.*

[11] Weber B et al. Multicenter evaluation of a new automated fourth-generation HIV screening assay with a sensitive antigen detection module and high specificity. *J Clin Microbiol. 2002, 40: 1938-46.*

[12] Weber B et al. Multicenter evaluation of a new rapid automated HIV Ag detection assay. *J. Virol. Meth. 1999, 78: 61-70.*

[13] Scholz C et al. Functional solubilization of aggregation-prone HIV envelope proteins by covalent fusion with chaperone modules. *J. Mol. Biol. 2005, 345: 1229-41.*

Notes

Notes