Elecsys HIV Duo

cobas®

REF		Σ	SYSTEM
08836973160	08836973503	300	**cobas e** 402 **cobas e** 801

English

For use in the USA only

System information

Short name	Assay type	To be used for	ACN (application code number)
HIVDUO	**cobas e** flow	HIV Duo	12016
HIVDUOR	**cobas e** flow	HIV Duo duplicate repeat	12030
HIVAG[a)]	HIV Antigen (HIV Ag) embedded application	HIV Duo **cobas e** flow	11014
AHIV[a)]	Anti-HIV embedded application	HIV Duo **cobas e** flow	11013

a) Embedded application within HIV Duo

Intended use

Elecsys HIV Duo is an immunoassay intended for the in vitro simultaneous qualitative detection and differentiation of HIV-1 p24 antigen and antibodies to HIV, HIV-1 (groups M and O) and HIV-2 in human serum and plasma. Elecsys HIV Duo assay is intended to be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1/HIV-2 infection in subjects greater than 2 years of age and in pregnant women. Elecsys HIV Duo is not intended for the screening of donors of blood and blood products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).

Elecsys HIV Duo is an **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" intended for use on the **cobas e** 402 and **cobas e** 801 immunoassay analyzers.

Summary

The human immunodeficiency virus (HIV), the causative agent of Acquired ImmunoDeficiency Syndrome (AIDS), belongs to the family of retroviruses. HIV can be transmitted through sexual contact, contaminated blood and blood products or from an HIV-infected mother to her child before, during and after birth.
Two types of HIV, called HIV-1 and HIV-2, have been identified to date.[1,2,3,4] HIV-1 can be divided into 4 distantly related groups: group M (for main), group N (for non-M, non-O), group O (for outlier) and group P (Plantier).[5,6,7] Based on their genetic relationship, 10 different subtypes (A to D, F to H, J, K and L) as well as several circulating recombinant forms (CRFs) have been identified within HIV-1 group M.[8,9] The large majority of HIV-1 infections are caused by viruses belonging to group M, while geographical distribution of subtypes and CRFs within this group varies strongly.[10] Due to differences in the sequence of immunodominant epitopes, especially in the envelope proteins of HIV-1 group M, HIV-1 group O and HIV-2, specific antigens are necessary to avoid failure in the detection of an HIV infection by immunoassays.[11,12]

HIV p24 antigen in blood specimens of recently infected patients can be detected as early as 2-3 weeks after infection.[13,14] Anti-HIV antibodies are detectable in serum from around 4 weeks post infection.[13,15] The combined detection of HIV p24 antigen and anti-HIV antibodies in 4th generation HIV screening assays leads to improved sensitivity and therefore a shorter diagnostic window compared to traditional anti-HIV assays.[16,17]

With the Elecsys HIV Duo assay, HIV-1 p24 antigen (HIV Ag), as well as antibodies to HIV-1 and HIV-2 (anti-HIV) can be detected in parallel with two separate determinations. On the basis of these determinations, the Elecsys HIV Duo main result is subsequently calculated automatically by the analyzer. The subresults HIV Ag and anti-HIV can be used as an aid in the selection of the confirmation algorithm for reactive samples. The Elecsys HIV Duo assay uses monoclonal antibodies to detect the HIV Ag and recombinant antigens derived from the Env- and Pol-region of HIV-1 (including group O) and HIV-2 to detect anti-HIV antibodies. Repeatedly reactive samples must be confirmed according to recommended confirmatory algorithms.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: For HIV Ag detection (HIVAG), 30 µL of sample react with biotinylated monoclonal anti-p24 antibodies and ruthenylated[b)] monoclonal anti-p24 antibodies, to form a sandwich complex. For anti-HIV detection (AHIV), 30 µL of sample react with biotinylated HIV-specific recombinant antigens/peptides and ruthenylated[b)] HIV-specific recombinant antigens/peptides, to form a sandwich complex. The incubations are performed in parallel in separate vessels.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined automatically by the software by comparing the electrochemiluminescence signal obtained from the sample with the cutoff value obtained by HIV Ag embedded and anti-HIV embedded calibrations. The Elecsys HIV Duo result is calculated automatically based on signal to cutoff ratios (cutoff index, COI) from HIV Ag and anti-HIV.

b) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The **cobas e** pack HIV Ag (M, R1, R2) is labeled as HIVAG.

The **cobas e** pack Anti-HIV (M, R1, R2) is labeled as AHIV.

HIVAG

M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-HIV p24-Ab~biotin, 1 bottle, 14.8 mL:
Biotinylated monoclonal anti-HIV p24 antibodies (mouse) approximately 0.75 mg/L; MES[c)] buffer 50 mmol/L, pH 6.5; preservative.

R2 Anti-HIV p24-Ab~$Ru(bpy)_3^{2+}$, 1 bottle, 14.8 mL:
Monoclonal anti-p24 antibodies (mouse) labeled with ruthenium complex approximately 0.75 mg/L; MES[c)] buffer 50 mmol/L, pH 6.5; preservative.

c) MES = 2-morpholino-ethane sulfonic acid

HIVDUO Cal1 Negative calibrator (lyophilized), 1 bottle for 1.0 mL:
Human serum, non-reactive for anti-HIV-1 and anti-HIV-2.

HIVDUO Cal2 Positive calibrator (lyophilized), 1 bottle for 1.0 mL:
HIV p24 antigen (E. coli, rDNA) in human serum, non-reactive for anti-HIV-1 and anti-HIV-2.

AHIV

M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 HIV-1/2-specific recombinant antigens (E. coli)~biotin, HIV-1/2-specific synthetic peptides~biotin, 1 bottle, 14.8 mL:
Biotinylated HIV-1/2-specific recombinant antigens (E. coli) and biotinylated HIV-1/2 specific synthetic peptides approximately 0.63 mg/L; TES[d)] buffer 40 mmol/L, pH 7.3; preservative.

Elecsys HIV Duo

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R2 HIV-1/2-specific recombinant antigens (E. coli)~Ru(bpy)$_3^{2+}$, HIV-1/2-specific synthetic peptides~Ru(bpy)$_3^{2+}$, 1 bottle, 14.8 mL: HIV-1/2-specific recombinant antigens (E. coli) and HIV-1/2-specific synthetic peptides labeled with ruthenium complex approximately 1.22 mg/L; TES[d)] buffer 40 mmol/L, pH 7.3; preservative.

d) TES = 2-[[1,3-dihydroxy-2-(hydroxymethyl)propane-2-yl]amino]ethanesulfonic acid

HIVDUO Cal3 Negative calibrator (lyophilized), 1 bottle for 1.0 mL: Human serum, non-reactive for anti-HIV-1 and anti-HIV-2.

HIVDUO Cal4 Positive calibrator (lyophilized), 1 bottle for 1.0 mL: Anti-HIV-1 positive human serum (inactivated) in human serum negative for anti-HIV-1 and anti-HIV-2.

Precautions and warnings

For in vitro diagnostic use. This test is prescription use only by healthcare professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317 May cause an allergic skin reaction.

H412 Harmful to aquatic life with long lasting effects.

Prevention:

P261 Avoid breathing dust.

P273 Avoid release to the environment.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

All human material should be considered potentially infectious.

The negative calibrators (HIVDUO Cal1 and HIVDUO Cal3) as well as the HIV Ag positive calibrator (HIVDUO Cal2) have been prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.

The serum containing anti-HIV-1 (HIVDUO Cal4) was inactivated using β-propiolactone and UV-radiation.

However, as no inactivation or testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[18,19]

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagents (M, R1, R2) in the kit are ready-for-use and are supplied in **cobas e** packs.

Calibrators

Carefully dissolve the contents of one bottle by adding exactly 1.0 mL of distilled or deionized water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding foam formation.

Transfer the reconstituted calibrators into the supplied empty labeled snap-cap bottles.

Unless the entire volume is necessary for calibration on the analyzer, transfer aliquots of the freshly reconstituted calibrators into empty snap-cap bottles (CalSet Vials). Attach the supplied labels to these additional bottles. Store the aliquots at 2-8 °C or -20 °C (± 5 °C) for later use.

Perform **only one** calibration procedure per aliquot.

All information required for correct operation is available via the **cobas** link.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability of the **cobas e** pack:	
unopened at 2-8 °C	up to the stated expiration date
on the **cobas e** 402 and **cobas e** 801 analyzers	16 weeks

Stability of the calibrators:	
lyophilized	up to the stated expiration date
reconstituted at 2-8 °C	3 days
reconstituted at - 20 °C (± 5 °C)	16 weeks (may be frozen 3 times)
on the **cobas e** 402 and **cobas e** 801 analyzers	use only once

Store calibrators **upright** in order to prevent the calibrator solution from adhering to the snap-cap.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, ACD, CPD, CP2D, CPDA, potassium oxalate and Na-citrate plasma.

Li-heparin plasma tubes containing separating gel can be used.

Criterion: Correct assignment of negative and positive samples within a recovery of ± 0.2 COI for negative and 80-120 % for positive samples.

Stable for 7 days at 20-25 °C, 4 weeks at 2-8 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen up to 5 times.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower COI values for individual patient specimens. In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions.

The sample types listed were tested with a selection of sample collection tubes or systems that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in

primary tubes (sample collection systems), follow the instructions of the tube/collection system manufacturer.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples and calibrators are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples and calibrators on the analyzers should be analyzed/measured within 2 hours.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

The performance of the Elecsys HIV Duo assay has not been established with body fluids other than serum and plasma.

Materials provided

See "Reagents – working solutions" section for reagents.

- 4 bottle labels
- 4 empty labeled snap-cap bottles

Materials required (but not provided)

- REF 06924107160, PreciControl HIV Gen II, for 6 x 2.0 mL
- REF 06924115160, PreciControl HIV; HIV-2+GrpO, for 4 x 2.0 mL
- REF 11776576322, CalSet Vials, 2 x 56 empty bottles with snap-caps
- General laboratory equipment
- **cobas e** 402 or **cobas e** 801 analyzer
- Distilled or deionized water

Additional materials for **cobas e** 402 and **cobas e** 801 analyzers:

- REF 06908799190, ProCell II M, 2 x 2 L system solution
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- REF 06908853190, PreClean II M, 2 x 2 L wash solution
- REF 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- REF 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- REF 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- REF 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

Calibrators:

Place the reconstituted calibrators in the sample zone.

Read in all the information necessary for calibrating the assay.

Calibration

Traceability:

HIVAG: This method has been standardized against the WHO International Standard HIV-1 p24 Antigen, NIBSC (National Institute for Biological Standards and Control) code 90/636.

AHIV: No internationally accepted standard for anti-HIV-1 and anti-HIV-2 exists.

Calibration frequency: Calibration must be performed once per reagent lot using HIVDUO Cal1, HIVDUO Cal2, HIVDUO Cal3, HIVDUO Cal4 and fresh reagent (i.e. not more than 24 hours since the **cobas e** pack was registered on the analyzer).

Recalibration is recommended as follows:

- after 12 weeks when using the same reagent lot
- after 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl HIV Gen II and PreciControl HIV; HIV-2+GrpO.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

The analyzer automatically calculates the cutoff based on the measurement of HIVDUO Cal1 and HIVDUO Cal2 for the HIVAG module, and HIVDUO Cal3 and HIVDUO Cal4 for the AHIV module.

The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index (signal sample/cutoff).

The following formula is used to calculate the main Elecsys HIV Duo result based on the HIVAG and AHIV subresults:

$$\text{HIVDUO (COI)} = \sqrt{(\text{HIVAG [COI]})^2 + (\text{AHIV [COI]})^2}$$

Interpretation of the results (HIVDUO or HIVDUOR)

Initial main result

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Negative for HIV-1 Ag and negative for anti-HIV-1/2 antibodies. No further testing needed.
COI ≥ 1.00	Reactive	Reactive in the Elecsys HIV Duo assay. All initially reactive samples should be redetermined in duplicate with the Elecsys HIV Duo assay. Redetermination of samples with an initial COI ≥ 1.00 can be performed automatically (see section **cobas e** flow).

Subresult HIVAG

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Negative for HIV-1 p24 antigen.
COI ≥ 1.00	Reactive	Reactive in the HIV-1 Ag module.

Subresult AHIV

Numeric result	Result	Interpretation
COI < 1.00	Non-reactive	Negative for anti-HIV-1/2 antibodies.
COI ≥ 1.00	Reactive	Reactive in the anti-HIV module.

Elecsys HIV Duo

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Repeat main result

Numeric result	Result	Interpretation
Both of the duplicate retests have a COI < 1.00	Non-reactive	Negative for HIV-1 Ag and negative for anti-HIV-1/2 antibodies. No further testing needed.
One or both of the duplicate retests have a COI ≥ 1.00	Repeatedly reactive	Repeatedly reactive samples must be confirmed according to CDC recommended confirmatory algorithms. The subresults for either HIVAG or AHIV can be used as an aid in the selection of the confirmation algorithm for reactive samples.

Please note: In case the HIVAG and AHIV results are both negative though elevated, the formula may result in Elecsys HIV Duo result as reactive with a COI ≥ 1.00 and reported as reactive. These results will be flagged as "Antigen test negative, Antibody test negative".

cobas e flow

A **cobas e** flow is a procedure programmed into the system to enable a fully automated sequence of measurements and the calculation of assay combinations to perform decision algorithms.
The HIVDUO **cobas e** flow is required to enable simultaneous separate measurement of HIVAG and AHIV with subsequent calculation of the main result.
A second HIV **cobas e** flow is available to perform a repetition of measurements in duplicate automatically for samples with an initial cutoff index ≥ 1.00 (short name HIVDUOR). Both subresults and the overall result message will be reported.

Limitations of the test

- Elecsys HIV Duo is for in vitro diagnostic use only.
- This assay is not for the screening of donors of blood or blood components, or human cells, tissues, or cellular and tissue-based products (HCT/Ps).
- This test is not intended to be used to monitor individuals who are undergoing treatment for HIV infection.
- Elecsys HIV Duo is limited to the detection of HIV-1 p24 antigen and antibodies to HIV, HIV-1 (Groups M and O) and/or HIV-2 in human serum and plasma; other specimen types may result in inaccurate test results.
- The performance of the Elecsys HIV Duo assay has not been established with cord blood, neonatal specimens, cadaveric specimens, heat-inactivated specimens, or body fluids other than serum and plasma such as saliva, urine and amniotic or pleural fluids.
- Heat-inactivated specimens and specimens stabilized with azide should not be used. Specimens should be at 20-25 °C prior to use with the assay.
- Due to possible evaporation effects, specimens placed on the analyzers should be measured within 2 hours.
- The reported antigen and/or antibody level cannot be correlated to an endpoint titer. The calculated values for the anti-HIV and/or p24 antigen in a given specimen as determined by assays from different manufacturers can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay used. Values obtained with different assay methods cannot be used interchangeably.
- All test results should be interpreted in conjunction with the individual's clinical presentation, history, and other laboratory results.
- A specimen with a reactive result should be investigated further following current guidelines.
- Heterophilic and Human Antibodies to Mouse Antigens (HAMA) in human specimens can react with reagent antibodies, interfering with in vitro immunoassays. Specific test design has been applied, but patients routinely exposed to animals or animal serum products for diagnosis or therapies can be prone to this interference and anomalous values may be observed. Specimens from patients who have received mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies and may interfere in assays that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.
- Elecsys HIV Duo may not detect all infected individuals. A negative test does not exclude the possibility of exposure to or infection with HIV. HIV antibodies and/or p24 antigen may be undetectable in some stages of infection and in some clinical conditions.
- A person who has antigen or antibodies to HIV is presumed to be infected with the virus. However, a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.
- Individuals undergoing antiretroviral therapy (ART) or taking pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) may produce non-reactive results.
- The claims, including those pertaining to sample stability made in the labeling of the cleared/approved reagents of Roche Diagnostics are part of the clearance/approval of the overall IVD test system (assay). Sample stability was tested only for the temperatures/time frame as claimed by the manufacturer under the conditions claimed in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 1129 µmol/L or ≤ 66 mg/dL
Hemoglobin	≤ 0.311 mmol/L or ≤ 500 mg/dL
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Human Serum Albumin	≤ 7.0 g/dL

Criterion: Correct assignment of negative and positive samples within a recovery of ± 0.15 COI for negative samples and 80-120 % for positive samples.

This assay has no biotin interference in serum concentrations up to 1200 ng/mL. Pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 355 ng/mL within the first hour after biotin ingestion for subjects consuming supplements of 20 mg biotin per day[20] and up to 1160 ng/mL for subjects after a single dose of 300 mg biotin.[21]

No false negative result due to high-dose hook effect was found with the Elecsys HIV Duo assay.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

A negative test result does not completely rule out the possibility of an infection with HIV. Serum or plasma samples from the very early (pre-seroconversion) phase or the late phase of HIV infection can occasionally yield negative findings. Yet unknown HIV variants can also lead to a negative HIV finding. The presence of antibodies to HIV is not a diagnosis of AIDS.

Drug interferences

In vitro tests were performed on 16 commonly used pharmaceuticals to determine the interference by therapeutic drugs with Elecsys HIV Duo

according to CLSI EP07-A2. 16 common therapeutic drugs were tested for potential interference (see table below for the drugs tested and the maximum concentration tested). Each drug was spiked into 1 negative, 1 anti-HIV antibody positive (s/co 1.5 - 4) and 1 HIV antigen positive sample (s/co 1.5 - 4). The spiked samples were evaluated at a concentration "x" times the maximum daily dosage. Each drug was found to be non-interfering at the claimed concentration.

Compound	Concentration tested mg/L
Acetylcysteine	553
Ampicillin-Na	1000
Ascorbic acid	300
Cyclosporine	5
Cefoxitin	2500
Heparin	5000 U/L
Levodopa	20
Methyldopa	20
Metronidazole	200
Phenylbutazone	400
Doxycycline	50
Acetylsalicylic acid	1000
Rifampicin	60
Acetaminophen	200
Ibuprofen	500
Theophylline	100

Specific performance data

Representative performance data on the **cobas e** 801 analyzer, as a member of the Elecsys instrument family of analyzers, is given below. Results obtained in individual laboratories may differ.

System Equivalency: The system equivalency between the **cobas e** 402 analyzer and the **cobas e** 801 analyzer was demonstrated by evaluating the analytical performance and method comparison study.

Precision and reproducibility

Precision and reproducibility were determined at 3 external sites on the **cobas e** 801 immunoassay analyzer using 3 lots of reagent and 1 lot of control for each of PreciControl HIV Gen II and PreciControl HIV; HIV-2+GrpO. Sample pools for precision testing included PreciControl HIV levels 1-5 and 8 spiked human serum pools in accordance with CLSI EP05-A3 guidelines (n = 270). The precision and reproducibility for the Elecsys HIV Duo assay and the subresults for the HIVAG module and the AHIV module are presented respectively in the following tables.

Overall repeatability and reproducibility for Elecsys HIV Duo

		Repeatability		Inter-run		Inter-day	
Sample	Mean	SD	CV (%)	SD	CV (%)	SD	CV (%)
HSP06[e)]	3.00	0.046	1.5	0.033	1.1	0.030	1.0
HSP07	63.9	0.921	1.4	0.555	0.9	0.591	0.9
HSP08	3.40	0.075	2.2	0.036	1.1	0.030	0.9
HSP09	57.8	0.852	1.5	0.856	1.5	0.775	1.3
HSP10	4.42	0.074	1.7	0.076	1.7	0.050	1.1
HSP11	50.2	0.579	1.2	0.668	1.3	0.522	1.0
HSP12	55.6	1.00	1.8	0.816	1.5	0.479	0.9
HSP13	0.165	0.008	4.7	0.003	2.0	0.004	2.6
PC[f)] HIV1	0.185	0.008	4.3	0.003	1.7	0.005	2.7
PC HIV2	2.98	0.041	1.4	0.026	0.9	0.026	0.9
PC HIV3	7.83	0.089	1.1	0.061	0.8	0.073	0.9
PC HIV4	3.93	0.060	1.5	0.059	1.5	0.066	1.7
PC HIV5	5.47	0.097	1.8	0.077	1.4	0.089	1.6

e) HSP = human serum pool

f) PC = PreciControl

Overall repeatability and reproducibility for Elecsys HIV Duo

		Inter-site x Lot		Inter-lot	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP06	3.00	0.053	1.8	0.063	2.1
HSP07	63.9	1.16	1.8	1.56	2.4
HSP08	3.40	0.026	0.8	0.043	1.3
HSP09	57.8	0.334	0.6	0.995	1.7
HSP10	4.42	0.068	1.5	0.066	1.5
HSP11	50.2	0.794	1.6	0.000	0.0
HSP12	55.6	1.01	1.8	0.882	1.6
HSP13	0.165	0.001	0.6	0.011	6.6
PC HIV1	0.185	0.004	2.1	0.020	10.8
PC HIV2	2.98	0.059	2.0	0.142	4.8
PC HIV3	7.83	0.069	0.9	0.155	2.0
PC HIV4	3.93	0.061	1.6	0.000	0.0
PC HIV5	5.47	0.109	2.0	0.045	0.8

Overall repeatability and reproducibility for Elecsys HIV Duo

		Inter-site		Reproducibility	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP06	3.00	0.029	1.0	0.108	3.6
HSP07	63.9	1.26	2.0	2.62	4.1
HSP08	3.40	0.077	2.3	0.127	3.7
HSP09	57.8	0.487	0.8	1.84	3.2
HSP10	4.42	0.000	0.0	0.151	3.4
HSP11	50.2	0.462	0.9	1.38	2.7
HSP12	55.6	0.000	0.0	1.93	3.5
HSP13	0.165	0.000	0.0	0.014	8.8
PC HIV1	0.185	0.000	0.0	0.023	12.2
PC HIV2	2.98	0.029	1.0	0.166	5.6
PC HIV3	7.83	0.000	0.0	0.214	2.7
PC HIV4	3.93	0.037	0.9	0.128	3.3
PC HIV5	5.47	0.055	1.0	0.200	3.7

Overall repeatability and reproducibility for Elecsys HIV Duo - HIVAG module

		Repeatability		Inter-run		Inter-day	
Sample	Mean	SD	CV (%)	SD	CV (%)	SD	CV (%)
HSP06	0.169	0.009	5.0	0.005	3.1	0.002	1.4
HSP07	0.127	0.008	6.4	0.003	2.5	0.004	3.4

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		Repeatability		Inter-run		Inter-day	
Sample	Mean	SD	CV (%)	SD	CV (%)	SD	CV (%)
HSP08	3.40	0.075	2.2	0.036	1.1	0.030	0.9
HSP09	57.8	0.852	1.5	0.856	1.5	0.775	1.3
HSP10	0.162	0.008	4.8	0.006	3.5	0.001	0.8
HSP11	0.165	0.074	44.9	0.000	0.0	0.000	0.0
HSP12	0.172	0.008	4.6	0.004	2.1	0.005	2.7
HSP13	0.147	0.008	5.7	0.004	2.7	0.004	2.8
PC HIV1	0.171	0.008	4.9	0.004	2.3	0.005	3.0
PC HIV2	0.171	0.008	4.8	0.003	1.9	0.004	2.3
PC HIV3	7.83	0.089	1.1	0.061	0.8	0.073	0.9
PC HIV4	0.171	0.009	5.0	0.002	1.3	0.005	3.0
PC HIV5	0.173	0.027	15.9	0.000	0.0	0.000	0.0

Overall repeatability and reproducibility for Elecsys HIV Duo - HIVAG module

		Inter-site x Lot		Inter-lot	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP06	0.169	0.002	0.9	0.017	10.0
HSP07	0.127	0.000	0.0	0.008	6.1
HSP08	3.40	0.026	0.8	0.043	1.3
HSP09	57.8	0.334	0.6	0.995	1.7
HSP10	0.162	0.002	1.5	0.014	8.9
HSP11	0.165	0.002	1.4	0.024	14.5
HSP12	0.172	0.001	0.7	0.014	8.2
HSP13	0.147	0.000	0.0	0.010	6.7
PC HIV1	0.171	0.003	1.6	0.020	11.7
PC HIV2	0.171	0.000	0.0	0.019	11.3
PC HIV3	7.83	0.069	0.9	0.155	2.0
PC HIV4	0.171	0.000	0.0	0.020	11.7
PC HIV5	0.173	0.002	1.3	0.017	9.8

Overall repeatability and reproducibility for Elecsys HIV Duo - HIVAG module

		Inter-site		Reproducibility	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP06	0.169	0.002	1.2	0.020	11.8
HSP07	0.127	0.000	0.0	0.013	9.8
HSP08	3.40	0.077	2.3	0.127	3.7
HSP09	57.8	0.487	0.8	1.84	3.2
HSP10	0.162	0.001	0.8	0.018	10.8
HSP11	0.165	0.000	0.0	0.078	47.2
HSP12	0.172	0.000	0.0	0.017	10.1
HSP13	0.147	0.000	0.0	0.014	9.7
PC HIV1	0.171	0.000	0.0	0.023	13.3
PC HIV2	0.171	0.000	0.0	0.022	12.6
PC HIV3	7.83	0.000	0.0	0.214	2.7
PC HIV4	0.171	0.000	0.0	0.022	13.1
PC HIV5	0.173	0.000	0.0	0.032	18.7

Overall repeatability and reproducibility for Elecsys HIV Duo - AHIV module

		Repeatability		Inter-run		Inter-day	
Sample	Mean	SD	CV (%)	SD	CV (%)	SD	CV (%)
HSP06	3.00	0.046	1.5	0.033	1.1	0.030	1.0
HSP07	63.9	0.921	1.4	0.555	0.9	0.591	0.9
HSP08	0.088	0.003	3.8	0.001	1.6	0.000	0.0
HSP09	0.077	0.003	4.3	0.001	2.0	0.000	0.0
HSP10	4.42	0.074	1.7	0.076	1.7	0.050	1.1
HSP11	50.2	0.579	1.2	0.668	1.3	0.522	1.0
HSP12	55.6	1.00	1.8	0.816	1.5	0.479	0.9
HSP13	0.076	0.003	4.5	0.001	2.0	0.000	0.0
PC HIV1	0.070	0.003	4.5	0.002	2.2	0.000	0.0
PC HIV2	2.98	0.042	1.4	0.027	0.9	0.025	0.9
PC HIV3	0.070	0.003	4.6	0.001	0.9	0.001	1.2
PC HIV4	3.93	0.060	1.5	0.059	1.5	0.066	1.7
PC HIV5	5.47	0.096	1.8	0.077	1.4	0.089	1.6

Overall repeatability and reproducibility for Elecsys HIV Duo - AHIV module

		Inter-site x Lot		Inter-lot	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP06	3.00	0.053	1.8	0.059	2.0
HSP07	63.9	1.16	1.8	1.56	2.4
HSP08	0.088	0.004	4.3	0.003	3.0
HSP09	0.077	0.003	4.2	0.004	4.7
HSP10	4.42	0.068	1.5	0.066	1.5
HSP11	50.2	0.794	1.6	0.000	0.0
HSP12	55.6	1.01	1.8	0.882	1.6
HSP13	0.076	0.003	4.0	0.004	5.5
PC HIV1	0.070	0.003	4.5	0.004	5.5
PC HIV2	2.98	0.059	2.0	0.138	4.6
PC HIV3	0.070	0.003	4.5	0.004	5.7
PC HIV4	3.93	0.061	1.6	0.000	0.0
PC HIV5	5.47	0.109	2.0	0.045	0.8

Overall repeatability and reproducibility for Elecsys HIV Duo - AHIV module

		Inter-site		Reproducibility	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP06	3.00	0.029	1.0	0.106	3.5
HSP07	63.9	1.26	2.0	2.62	4.1
HSP08	0.088	0.003	2.9	0.006	7.3
HSP09	0.077	0.003	3.4	0.007	8.6

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		Inter-site		Reproducibility	
Sample	Mean	SD	CV (%)	SD	CV (%)
HSP10	4.42	0.000	0.0	0.151	3.4
HSP11	50.2	0.462	0.9	1.38	2.7
HSP12	55.6	0.000	0.0	1.93	3.5
HSP13	0.076	0.003	3.5	0.007	9.1
PC HIV1	0.070	0.002	3.1	0.007	9.2
PC HIV2	2.98	0.029	1.0	0.163	5.5
PC HIV3	0.070	0.003	3.7	0.007	9.5
PC HIV4	3.93	0.037	0.9	0.128	3.3
PC HIV5	5.47	0.055	1.0	0.200	3.7

Results: The precision and reproducibility of Elecsys HIV Duo and the subresults for the HIVAG and AHIV modules demonstrated minor variability from run to run, day to day and between reagent lots.

Effects on Elecsys HIV Duo - neat and spiked samples

356 subjects with other infectious agents or medical conditions were tested with the Elecsys HIV Duo assay comprising specimens:

- containing antibodies against HAV, HBV, HCV, HTLV I/II, CMV, EBV, HSV-1, HSV-2, Rubella, Rotavirus, Smallpox, VZV
- containing autoantibodies and elevated titers of rheumatoid factor
- positive for Candida, E. coli, Plasmodium falciparum/vivax, Mycobacterium tuberculosis, Chlamydia, Treponema pallidum (syphilis)
- after vaccination against HAV, HBV and influenza
- from patients with monoclonal gammopathy and multiple myeloma/lymphoma, common cold, Graves' disease, Crohn's disease

Testing was conducted with neat specimens and aliquots individually spiked with HIV-1 antibody, HIV-2 antibody and HIV-1 p24 antigen. Results showed no interference from the above agents.

Effect of potentially interfering medical conditions on specificity/ sensitivity of Elecsys HIV Duo

Clinical category	Number tested	Effect on Elecsys HIV Duo results
ANA	10	0/10
Candida	10	0/10
CMV	10	0/10
EBV	10	0/10
E. coli	10	0/10
Influenza vaccination	10	0/10
HAV	10	0/10
HAV HBV vaccination	8	0/8
HBV	10	0/10
HCV	10	0/10
HSV	10	0/10
HTLV	10	0/10
Lymphoma	10	0/10
Malaria	10	0/10
Monoclonal gammopathy	10	0/10
Pregnant 1st trimester	30	0/30
Pregnant 2nd trimester	30	0/30
Pregnant 3rd trimester	30	0/30
Rheumatoid factor	10	0/10
Rubella	10	0/10
Syphilis	10	0/10
Tuberculosis	10	0/10
Rotavirus	10	0/10
Chlamydia	10	0/10
Common cold	10	0/10
Smallpox	10	0/10
VZV	9	0/9
Multiparous pregnancies	10	0/10
Graves' disease	9	0/9
Crohn's disease	10	0/10

Analytical sensitivity

Analytical sensitivity of Elecsys HIV Duo for detection of HIV-1 p24 antigen was evaluated using the WHO International Standard HIV-1 p24 antigen, NIBSC code 90/636. HIV-1 p24 antigen was diluted with HIV negative serum and measured with Elecsys HIV Duo. 7 dilution steps of each standard were prepared and measured. Sensitivity was calculated using the mean of 3 lots tested by reading off the concentration at the cutoff from the HIV-Ag reference standard curve. The analytical antigen sensitivity of Elecsys HIV Duo as measured by WHO International Standard HIV-1 p24 antigen, NIBSC code 90/636 was shown to be ≤ 1 IU/mL. Using 3 reagent lots of Elecsys HIV Duo, results were 0.393, 0.395 and 0.389 IU/mL (average 0.392 IU/mL).

Seroconversion panels

Seroconversion sensitivity of the Elecsys HIV Duo assay was shown by testing 50 commercially available seroconversion panels with a total of 452 samples and comparing Elecsys HIV Duo results to the reference assay. Seroconversion testing results show equivalent performance in 444 of the 452 total bleeds tested. In 7 panels Elecsys HIV Duo was able to detect seroconversion earlier than the reference assay and in 1 panel Elecsys HIV Duo detected seroconversion later than the reference assay.

Elecsys HIV Duo assay reactivity in seroconversion panels

Panel ID	Difference in days	Elecsys HIV Duo first reactive result	Reference method first reactive result
HIV 6243 / 62238	0	Day 25	Day 25
HIV 6247 / 63602	+ 2	Day 21	Day 23
HIV 6248 / 63331	0	Day 18	Day 18
HIV 9011 / 64954	0	Day 36	Day 36
HIV 9012 / 65389	+ 2	Day 14	Day 16
HIV 9013 / 65404	+ 2	Day 23	Day 25
HIV 9014 / 65522	0	Day 10	Day 10
HIV 9016 / 65790	0	Day 30	Day 30
HIV 9017 / 65907	- 3	Day 24	Day 21
HIV 9018 / 66575	+ 3	Day 25	Day 28
HIV 9019 / 65685	0	Day 38	Day 38
HIV 9021 / 67485	0	Day 47	Day 47
HIV 9022 / 64578	0	Day 23	Day 25[g)]
HIV 9023 / 67706	0	Day 78	Day 78
HIV 9024 / 64469	0	Day 53	Day 53
HIV 9025 / 67996	0	Day 85	Day 85
HIV 9026 / 68205	0	Day 44	Day 44
HIV 9027 / 65633	0	Day 14	Day 14

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Panel ID	Difference in days	Elecsys HIV Duo first reactive result	Reference method first reactive result
HIV 9028 / 67860	0	Day 53	Day 53
HIV 9029 / 68262	0	Day 45	Day 45
HIV 9030 / 68582	0	Day 47	Day 47
HIV 9032 / 68106	+ 2	Day 22	Day 24
HIV 9033 / 66686	0	Day 82	Day 82
HIV 9034 / 66632	0	Day 46	Day 46
HIV 9075 / 62216	0	Day 22	Day 22
HIV 9076 / 63753	0	Day 66	Day 66
HIV 9079 / 75062	0	Day 40	Day 40
HIV 9081 / 63215	0	Day 24	Day 24
HIV 9089 / 65376	0	Day 16	Day 16
HIV 12007 / 73695	0	Day 117	Day 117
PRB939-AN	0	Day 16	Day 16
PRB944-AT	+ 5	Day 2	Day 7
PRB960	0	Day 28	Day 28
PRB961	0	Day 27	Day 27
PRB962	0	Day 14	Day 14
PRB963	0	Day 17	Day 17
PRB964	0	Day 22	Day 22
PRB965	0	Day 5	Day 5
PRB966	0	Day 44	Day 44
PRB967	0	Day 17	Day 17
PRB968	0	Day 26	Day 26
PRB969	0	Day 63	Day 63
PRB971	0	Day 7	Day 7
PRB972	0	Day 18	Day 18
PRB973	0	Day 7	Day 7
PRB974	0	Day 9	Day 9
PRB975	0	Day 14	Day 14
PRB976	+ 5	Day 2	Day 7
PRB977	0	Day 13	Day 13
PRB978	0	Day 33	Day 33

g) Insufficient volume to test on day 23; day 25 reactive for reference method

Summary of clinical studies

A multi-site clinical study was performed to assess the performance of Elecsys HIV Duo in 10121 subjects. Samples were from the United States and outside the United States, including the HIV-2 endemic areas of the Ivory Coast, Cameroon, Senegal, Africa and Bolivia. Samples were approximately equally divided between serum (47 %) and plasma (53 %). Of the 10121 subjects tested,1977 had a final HIV status of "HIV Positive", 8142 subjects had a final HIV status of "HIV Negative" and 2 subjects had a final HIV status of "Inconclusive". The sample population consisted of 6108 low-risk adults, 506 high-risk adults, 1249 HIV-1 confirmed positive adults (1049 US and 200 non-US), 603 low-risk pediatrics, 200 high-risk pedriatrics (4 were positive), 51 HIV-1 confirmed positive pediatrics (34 US and 17 non-US), 59 HIV positive pregnant women (49 US and 10 non-US), 204 pregnant women at high risk for HIV (15 were positive), 199 pregnant women negative for HIV, 500 from an HIV-2 endemic area, 200 HIV-2 confirmed positive adults, 50 native HIV-1 Group O specimens, 90 HIV-1 group M subtype, 50 HIV-1 antigen positive/antibody positive and 52 HIV-1 antigen positive/antibody negative specimens.

Of those 10121 subjects, 46 (0.45 %) were in the age group of ≥ 2 to < 6 years, 93 (0.92 %) were in the age group of ≥ 6 to < 11 years, 127 (1.25 %) were in the age group of ≥ 11 to < 16 years, 637 (6.29 %) were in the age group of ≥ 16 to < 22 years, 1786 (17.65 %) were in the age group of ≥ 22 to < 31 years, 1675 (16.55 %) were in the age group of ≥ 31 to < 41 years, 1853 (18.31 %) were in the age group of ≥ 41 to < 51 years, 2035 (20.11 %) were in the age group of ≥ 51 to < 61 years, 1268 (12.53 %) were in the age group of ≥ 61 to < 71 years, 448 (4.43 %) were in the age group of ≥ 71 to < 81 years, 88 (0.87 %) were in the age group ≥ 81 to < 91 years, 7 (0.07 %) were in the age group of ≥ 91 to < 101 years, and 58 (0.57 %) were missing age (not reported).

Of those 10121 subjects, 5474 (54.09 %) reported ethnicity as Hispanic or Latino, 4313 (42.61 %) reported ethnicity as not Hispanic and not Latino, 84 (0.83 %) reported ethnicity as unknown, and 250 (2.47 %) were missing (not reported). For serum specimens, 2684 (56.30 %) reported ethnicity as Hispanic or Latino, 2033 (42.65 %) reported ethnicity as not Hispanic and not Latino, 6 (0.13 %) reported ethnicity as unknown, and 44 (0.92 %) were missing (not reported). For plasma specimens, 2790 (52.11 %) reported ethnicity as Hispanic or Latino, 2280 (42.58 %) reported ethnicity as not Hispanic and not Latino, 78 (1.46 %) reported ethnicity as unknown, and 206 (3.85 %) were missing (not reported).

All subjects were tested with Elecsys HIV Duo and were compared against an FDA-approved HIV-1/HIV-2 antigen and antibody reference assay followed by additional confirmatory testing as needed to determine a final HIV status. Confirmatory testing included an FDA-approved HIV assay with HIV-antigen and antibody detection and differentiation between HIV-1 and HIV-2, as well as 2 reverse transcription-polymerase chain reaction (RT-PCR) assays. The first PCR method was used to verify the potential presence of HIV-1 RNA. The second PCR method, which can differentiate between HIV-1 RNA and HIV-2 RNA, was used to verify the potential presence of HIV-2 RNA within the HIV-2 confirmed positive and the HIV-2 endemic area cohorts. To determine the clinical sensitivity of Elecsys HIV Duo, the data from all HIV positive subjects confirmed with a reactive result on the FDA-approved confirmatory test for HIV antigen and antibody differentiation and/or a reactive HIV NAT were compared to the Elecsys HIV Duo results. The clinical specificity was determined from all subjects at low risk for HIV or negative for HIV.

Clinical sensitivity

A multi-site clinical study was performed to determine the sensitivity of Elecsys HIV Duo compared to an FDA-approved HIV assay. Testing of all subjects included a comparison against the FDA-approved HIV-1/HIV-2 antigen and antibody reference assay. Confirmation of repeatedly reactive samples followed CDC recommendations to determine a final HIV status. Confirmatory testing included an FDA-approved HIV assay with HIV-antigen and antibody detection and differentiation between HIV-1 and HIV-2 as well as 2 reverse transcription-polymerase chain reaction (RT-PCR) assays. The clinical sensitivity for US and non-US samples used in this study was determined by comparing the Elecsys HIV Duo results to the positive subjects confirmed with a reactive result on the FDA-approved confirmatory test for HIV antigen and antibody differentiation and/or a reactive HIV NAT.

Reactivity in individuals known to be positive for antibodies to HIV-1

The sensitivity of Elecsys HIV Duo for individuals known to be positive for antibodies to HIV-1 was determined using a total of 1549 subjects and included 1249 HIV-1 confirmed positive adult subjects (1049 US and 200 non-US), 51 HIV-1 confirmed positive pediatric subjects (34 US and 17 non-US; ≥ 2 years of age), 59 HIV-1 confirmed positive pregnant women subjects (49 US and 10 non-US), 90 HIV-1 group M subtype specimens, 50 HIV-1 group O specimens and 50 HIV-1 p24 antigen positive/antibody positive specimens.

The overall summary of the comparison of Elecsys HIV Duo compared to the reference assay for all US and non-US samples known to be positive for antibodies to HIV-1 based on each subject cohort is as follows:

		Elecsys HIV Duo (Main Result)			FDA-approved reference assay		
Specimen population	Number tested	NR	IR	RR	NR	IR	RR
US HIV-1 confirmed positive adults	1049	0	1049	1049	0	1049	1049
HIV-1 confirmed positive pediatrics	51	0	51	51	1	50	50

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		Elecsys HIV Duo (Main Result)			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
US HIV positive pregnant women	49	0	49	49	0	49	49
Non-US HIV positive pregnant women	10	0	10	10	0	10	10
Non-US HIV-1 confirmed positive adults	200	0	200	200	0	200	200
HIV-1 group O	50	0	50	50	0	50	50
HIV-1 group M subtypes	90	0	90	90	0	90	90
HIV-1 antigen positive/antibody positive	50	0	50	50	0	50	50
Total	1549	0	1549	1549	1	1548	1548

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
US HIV-1 confirmed positive adults	1049	1049	NT[h)]	NT
HIV-1 confirmed positive pediatrics	51	51	NT	NT
US HIV positive pregnant women	49	49	NT	NT
Non-US HIV positive pregnant women	10	10	NT	NT
Non-US HIV-1 confirmed positive adults	200	200	NT	NT
HIV-1 group O	50	49[i)]	NT	NT
HIV-1 group M subtypes	90	90	NT	NT
HIV-1 antigen positive/antibody positive	50	50	NT	NT
Total	1549	1548	n/a	n/a

h) not tested through the algorithm

i) 1 subject had insufficient volume for confirmatory testing

Results: The sensitivity of Elecsys HIV Duo for all subjects and specimens known to be positive for antibodies to HIV-1 was determined using 1549 samples and specimens. All 1549 subjects and/or specimens had a final HIV status of "HIV Positive". The sensitivity of Elecsys HIV Duo for all subjects and specimens known to be positive for antibodies to HIV-1 is 100 % (1549/1549) with a 95th percentile confidence interval of 99.75 % to 100 %.

Reactivity in individuals known to be positive for antibodies to HIV-2

The sensitivity of Elecsys HIV Duo for individuals known to be positive for antibodies to HIV-2 was determined using a total of 200 HIV-2 confirmed positive subjects from Ivory Coast, Cameroon, Senegal or Bolivia. All subjects tested were confirmed to be HIV-2 positive based on a Certificate of Analysis and/or genetic sequencing prior to enrollment.

The overall summary of the comparison of Elecsys HIV Duo compared to the reference assay for all samples known to be positive for antibodies to HIV-2 is as follows:

		Elecsys HIV Duo (Main result)			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
HIV-2 confirmed positive	200	0	200	200	0	200	200
Total	200	0	200	200	0	200	200

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
HIV-2 confirmed positive	200	200	0	98[j)]
Total	200	200	0	98

j) 1 subject had insufficient volume for confirmatory testing

Results: The sensitivity of Elecsys HIV Duo for all subjects known to be positive for antibodies to HIV-2 was determined using 200 subjects. All 200 subjects had a final HIV status of "HIV Positive". The sensitivity of Elecsys HIV Duo for all subjects known to be positive for antibodies to HIV-2 is 100 % (200/200) with a 95th percent confidence interval of 98.12 % to 100 %.

Reactivity in individuals known to be positive for HIV-1 antigen

The sensitivity of Elecsys HIV Duo for HIV-1 p24 antigen was determined using a total of 102 archived specimens that were known to be positive for HIV-1 antigen and included 50 specimens that were HIV-1 antigen positive/antibody positive and 52 specimens that were HIV-1 antigen positive/antibody negative. All specimens were confirmed to be positive for HIV-1 antigen based on a Certificate of Analysis.

The overall summary of the comparison of Elecsys HIV Duo against an FDA-approved reference assay is as follows:

		Elecsys HIV Duo			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
HIV-1 antigen positive/ antibody positive	50	0	50	50	0	50	50
HIV-1 antigen positive/ antibody negative	52	0	52	52	0	52	52
Total	102	0	102	102	0	102	102

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

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		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
HIV-1 antigen positive/ antibody positive	50	50	NT	NT
HIV-1 antigen positive/ antibody negative	52	51[k)]	NT	NT
Total	102	101	n/a	n/a

k) 1 sample did not have sufficient volume for testing so the Certificate of Analysis was used to provide objective evidence of HIV infection

Results: The HIV-1 antigen positive cohorts consisted of 102 archived specimens. All 102 specimens had a final HIV status of "HIV Positive" and were congruent reactive on the Elecsys HIV Duo assay and the FDA-approved reference assay. The sensitivity for Elecsys HIV Duo with specimens known to be positive for HIV-1 antigen was 100 % (102/102) with a 95th percent confidence interval of 96.37 % to 100 %.

Reactivity with pediatric individuals

The sensitivity of Elecsys HIV Duo in pediatric individuals was determined using a total of 854 subjects and included 603 at low risk for HIV, 200 at high risk for HIV and 51 confirmed positive for HIV (34 US and 17 non-US). The pediatric population was broken down into the following age groups:

Age range	Number of samples
2 - < 6 years	46
6 - < 11 years	93
11 - < 16 years	127
16 - < 22 years	588[l)]

l) only includes pediatric subjects from the low and high-risk pediatric and HIV confirmed positive pediatric cohorts

		Elecsys HIV Duo			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
Low-risk pediatric	603	601	2	2	600	3	3
High-risk pediatric	200	195	5	5	196	5	4
Pediatric HIV positive	51	0	51	51	1	50	50
Total	854	796	58	58	797	58	57

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
Low-risk pediatric	603	1	0	NT
High-risk pediatric	200	4	0	NT
Pediatric HIV positive	51	51	0	NT
Total	854	56	0	n/a

Results: The sensitivity of Elecsys HIV Duo in pediatric individuals was determined using a total of 854 subjects. 56 subjects had a final HIV status of "HIV positive" and 798 subjects had a final HIV status of "HIV Negative" resulting in 2 false positives for Elecsys HIV Duo. The sensitivity of Elecsys HIV Duo in pediatric individuals was 100 % (56/56) with a 95th percentile confidence limit of 93.58 % to 100 %.

Reactivity with pregnant women

The sensitivity of Elecsys HIV Duo in pregnant women was determined using a total of 588 subjects including 59 confirmed positive pregnant women (49 US and 10 non-US), 204 pregnant women at high risk for HIV and 325 pregnant women negative or at low risk for HIV (199 negative for HIV and 126 low risk for HIV). The following tables show the sensitivity of Elecsys HIV Duo in US and non-US pregnant women.

		Elecsys HIV Duo			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
HIV-1 positive pregnant	59	0	59	59	0	59	59
High-risk pregnant	204	188	16	16	189	15	15
Pregnant women negative or low-risk[m)]	325	324	1	1	324	1	1
Total	588	512	76	76	513	75	75

m) 126 subjects from low-risk population

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
HIV-1 positive pregnant	59	59	NT	NT
High-risk pregnant	204	15	0	NT
Pregnant women negative or low risk	325	1	NT	NT
Total	588	75	0	n/a

Results: The sensitivity of Elecsys HIV Duo in pregnant women was determined using a total of 588 subjects. 75 subjects had a final HIV status of "HIV Positive" and 513 subjects had a final HIV status of "HIV Negative" resulting in 1 false positive for Elecsys HIV Duo. The sensitivity of Elecsys HIV Duo in pregnant women was 100 % (75/75) with a 95th percentile confidence limit of 95.13 % to 100 %.

Reactivity with samples from individuals at high risk for HIV

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The sensitivity of Elecsys HIV Duo in individuals at high risk for HIV was determined using a total of 1410 subjects and included 506 adults, 200 pediatrics, 204 pregnant women and 500 from an HIV-2 endemic area.

		Elecsys HIV Duo			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
Adults	506	494	12	12	494	12	12
Pediatrics	200	195	5	5	196	5	4
Pregnant women	204	188	16	16	189	15	15
HIV-2 endemic	500	365	135	135	369	131	131
Total	1410	1242	168	168	1248	163	162

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

Elecsys HIV Duo

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		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
Adults	506	12	NT	NT
Pediatric	200	4	0	NT
Pregnant women	204	15	0	NT
HIV-2 endemic	500	131	25[n)]	54
Total	1410	162	25	54

n) 25 reactive HIV-2 endemic were determined by the 2nd PCR method

Results: The sensitivity of Elecsys HIV Duo in individuals at high risk for HIV was determined using a total of 1410 subjects. 162 subjects had a final HIV status of "HIV Positive" and 1248 subjects had a final HIV status of "HIV Negative" resulting in 6 false positives for Elecsys HIV Duo. The sensitivity of Elecsys HIV Duo in individuals at high risk for HIV was 100 % (162/162) with a 95th percentile confidence limit of 97.68 % to 100 %.

High-risk pediatric specimens categorized by age range and gender

The sensitivity of Elecsys HIV Duo in pediatric individuals at high risk for HIV was determined using a total of 200 subjects. All 200 subjects were further analyzed by gender and age range, respectively. The overall summary of the comparison of Elecsys HIV Duo against an FDA-approved reference assay is as follows:

			Elecsys HIV Duo			FDA-approved reference assay		
Age (years)	**Sex**	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
2 - < 6	Female	0	0	0	0	0	0	0
	Male	0	0	0	0	0	0	0
6 - < 11	Female	2	2	0	0	2	0	0
	Male	2	2	0	0	2	0	0
11 - < 16	Female	2	2	0	0	2	0	0
	Male	4	4	0	0	4	0	0
16 - < 22	Female	99	95	4	4	96	3	3
	Male	91	90	1	1	90	2	1
Total		200	195	5	5	196	5	4

			Repeatedly reactive specimens (Number reactive/positive by method)		
Age (years)	**Sex**	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
2 - < 6	Female	0	NT	NT	NT
	Male	0	NT	NT	NT
6 - < 11	Female	2	NT	NT	NT
	Male	2	NT	NT	NT
11 - < 16	Female	2	NT	NT	NT
	Male	4	NT	NT	NT
16 - < 22	Female	99	3	0	NT
	Male	91	1	NT	NT
Total		200	4	0	n/a

Results: The sensitivity of Elecsys HIV Duo in pediatric individuals at high risk for HIV was determined using a total of 200 subjects. 4 subjects had a final HIV status of "HIV Positive" and 196 subjects had a final HIV status of "HIV Negative" resulting in 1 false positive for Elecsys HIV Duo. The sensitivity of Elecsys HIV Duo in pedriatric individuals at high risk for HIV was 100 % (4/4) with 95th percentile confidence limit of 51.01 % to 100 %.

Reactivity with samples from pregnant women at high risk for HIV

The sensitivity of Elecsys HIV Duo in pregnant women at high risk for HIV was determined using a total of 204 subjects. All 204 subjects were further analyzed by their respective trimester. The overall summary of the comparison of Elecsys HIV Duo against an FDA-approved reference assay is as follows:

		Elecsys HIV Duo			FDA-approved HIV assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
First trimester	55	48	7	7	49	6	6
Second trimester	63	57	6	6	57	6	6
Third trimester	86	83	3	3	83	3	3
Total	204	188	16	16	189	15	15

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
First trimester	55	6	0	NT
Second trimester	63	6	NT	NT
Third trimester	86	3	NT	NT
Total	204	15	0	n/a

Results: The sensitivity of Elecsys HIV Duo in pregnant women at high risk for HIV was determined using a total of 204 subjects. 15 subjects had a final HIV status of "HIV Positive" and 189 subjects had a final HIV status of "HIV Negative" resulting in 1 false positive for Elecsys HIV Duo. The sensitivity of Elecsys HIV Duo in pregnant women at high risk for HIV was 100 % (15/15) with a 95th percentile confidence limit of 79.61 % to 100 %.

Reactivity with HIV-1 group M subtypes

The sensitivity of Elecsys HIV Duo for the HIV-1 group M subtypes was determined using a total of 90 specimens. All specimens tested were confirmed to be HIV-1 group M positive based on a Certificate of Analysis and/or genetic sequencing prior to enrollment. The HIV-1 group M cohort contained 6 different subtypes: A, B, C, D, CRF01_AE and CRF02_AG. Each subtype contained 15 samples with a total of 90 samples tested as shown in the following table:

Subtype	**Number tested**	**Elecsys HIV Duo**	**FDA-approved reference assay**
A	15	15/15	15/15
B	15	15/15	15/15
C	15	15/15	15/15
D	15	15/15	15/15
CRF01_AE	15	15/15	15/15
CRF02_AG	15	15/15	15/15
Total	90	90/90	90/90

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		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
A	15	15	NT	NT
B	15	15	NT	NT
C	15	15	NT	NT
D	15	15	NT	NT
CRF01_AE	15	15	NT	NT
CRF02_AG	15	15	NT	NT
Total	90	90	n/a	n/a

Results: The sensitivity of Elecsys HIV Duo for the HIV-1 group M subtypes was determined using 90 specimens. All 90 specimens had a final HIV status of "HIV Positive". The sensitivity of Elecsys HIV Duo for the HIV-1 group M cohort is 100 % (90/90) with a 95th percentile confidence limit of 95.91 % to 100 %.

Reactivity with HIV-1 group O

The sensitivity of Elecsys HIV Duo for the HIV-1 group O cohort was determined using a total of 50 native specimens from either Cameroon, Africa or Germany. All specimens tested were confirmed to be HIV-1 group O positive based on a Certificate of Analysis and/or genetic sequencing prior to enrollment. The overall summary of the comparison of Elecsys HIV Duo against an FDA-approved reference assay is as follows:

		Elecsys HIV Duo			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
Group O	50	0	50	50	0	50	50
Total	50	0	50	50	0	50	50

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
Group O	50	49[o)]	0	NT
Total	50	49[o)]	0	n/a

o) 1 subject had insufficient volume for confirmatory testing so the Certificate of Analysis was used to provide objective evidence of HIV infection

Results: The sensitivity of Elecsys HIV Duo for the HIV-1 group O cohort was determined using 50 native specimens. All 50 specimens had a final HIV status of "HIV Positive". The sensitivity of Elecsys HIV Duo for the HIV-1 group O cohort was 100 % (50/50) with a 95th percentile confidence limit of 92.87 % to 100 %.

Clinical specificity

A multi-site clinical study was performed to determine the specificity of Elecsys HIV Duo. Clinical specificity was determined using 6910 samples from individuals at low risk or negative for HIV. Testing of the 6910 samples included a comparison against the FDA-approved HIV-1/HIV-2 antigen and antibody reference assay. Confirmation of repeatedly reactive samples followed CDC recommendations to determine a final HIV status. Confirmatory testing included an FDA-approved HIV assay with HIV-antigen and antibody detection and differentiation between HIV-1 and HIV-2 antibodies as well as 2 reverse transcription-polymerase chain reaction (RT-PCR) assays.

Reactivity with samples from low risk and HIV negative individuals

The specificity of Elecsys HIV Duo was determined in individuals who were at low risk for HIV or negative for HIV. A total of 6910 subjects were tested and included 6108 low-risk adults, 603 low-risk pediatrics and 199 pregnant women negative for HIV. The overall summary of the comparison of Elecsys HIV Duo against an FDA-approved reference assay is as follows:

		Elecsys HIV Duo			FDA-approved reference assay		
Specimen population	**Number tested**	**NR**	**IR**	**RR**	**NR**	**IR**	**RR**
Low-risk adult	6108	6089	19	19	6091	18	17
Low-risk pediatrics	603	601	2	2	600	3	3
Pregnant women negative for HIV	199	199	0	0	199	0	0
Total	6910	6889	21	21	6890	21	20

NR = non-reactive, IR = initially reactive, RR = repeatedly reactive

		Repeatedly reactive specimens (Number reactive/positive by method)		
Specimen population	**Number tested**	**FDA-approved reference assay HIV-Ag/Ab with HIV-1 and HIV-2 differentiation**	**HIV-1 NAT**	**HIV-2 NAT**
Low-risk adults	6108	14[p)]	0	NT
Low-risk pediatrics	603	1	0	NT
Pregnant women negative for HIV	199	NT	NT	NT
Total	6910	15[p)]	0	n/a

p) 1 subject was inconclusive due to insufficient volume to complete testing algorithm

Results: The specificity of Elecsys HIV Duo was determined using 6910 specimens from individuals at low risk for HIV or negative for HIV. 14 subjects had a final HIV status of "HIV Positive", 6894 subjects had a final HIV status of "HIV Negative", and 2 subjects had a final HIV status of "Inconclusive". Based on the data, 6887/6894 were non-reactive on Elecsys HIV Duo resulting in 7 false positives. The specificity of Elecsys HIV Duo in individuals at low risk for HIV or negative for HIV is 99.90 % (6887/6894) with 95th percentile confidence limit of 99.79 % to 99.95 %.

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets and the Method Sheets of all necessary components (if available in your country).

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

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CONTENT	Contents of kit
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CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number

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