SIEMENS Healthineers

Free Beta Human Chorionic Gonadotropin (FBHCG)

Current Revision and Date[a]	Rev. 05, 2022-05	
Product Name	Atellica IM Free Beta Human Chorionic Gonadotropin (FBHCG)	REF 10733009 (100 tests) REF 10733010 (500 tests)
Abbreviated Product Name	Atellica IM FBHCG	
Test Name/ID	FBHCG	
Systems	Atellica IM Analyzer	
Optional Materials	Atellica IM Multi-Diluent 13	REF 10995643
Specimen Types	Serum	
Sample Volume	20 µL	
Measuring Interval	0.14–200.00 IU/L	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

CE 0197

Intended Use

The Atellica® IM Free Beta Human Chorionic Gonadotropin (FBHCG) assay is for *in vitro* diagnostic use in the quantitative determination of the free beta subunit of chorionic gonadotropin in human serum using the Atellica® IM Analyzer.

The Atellica IM FBHCG assay is intended for use as one component in combination with other parameters to evaluate the risk of Trisomy 21 (Down syndrome) during the first trimester of pregnancy. Further testing is required for diagnosis of chromosomal aberrations.

Summary and Explanation

Human chorionic gonadotropin (HCG) is a glycoprotein hormone normally found in blood and urine only during pregnancy. It is secreted by placental tissue, beginning with the primitive trophoblast, almost from the time of implantation, and serves to support the corpus luteum during the early weeks of pregnancy. HCG or HCG-like material is also produced by a variety of trophoblastic and nontrophoblastic neoplasia.[1–4]

Intact HCG is a 39,500 Dalton molecule composed of two nonidentical subunits, alpha and beta, that are bound to each other in a noncovalent manner. These subunits can also occur in a free, or unbound, form.[5,6] Only intact HCG has biological activity. The HCG alpha subunit is structurally identical to the alpha subunit of the homologous pituitary glycoprotein hormones, luteinizing hormone, follicle-stimulating hormone and thyroid-stimulating hormone. The beta subunit is specific for each of these hormones, and confers upon them their differing biological activities. The beta subunits of HCG and luteinizing hormone, however, are structurally quite similar, accounting for the essentially identical biological activities of these two hormones.[5]

Measurements of free beta HCG levels have been found to aid in the diagnosis and monitoring of trophoblastic diseases (moles, choriocarcinoma) and certain testicular tumors, where the ratios of the free beta subunit to intact HCG can be quite high. Occasionally, tumors are found to secrete only free beta HCG subunit, and virtually no intact HCG can be detected.[7–9] Application in diagnosis and monitoring of tumor recurrence requires high sensitivity in the assay's low end, and careful interpretation is required (see *Limitations*). The Atellica IM FBHCG assay is not applicable for this clinical utility. Measurements of free beta HCG levels may also have value in the early monitoring of the outcome of *in vitro* fertilization procedures.[10]

Maternal serum free beta HCG assessment is reported to have significant utility in first- and second-trimester prenatal screening for Down syndrome and other chromosomal anomalies. The efficiency of prenatal screening in the first trimester might be substantially improved by using the combination of serum pregnancy-associated plasma protein-A (PAPP-A) and serum free beta HCG measurements, and maternal age and fetal nuchal translucency (NT) measurements. Using this approach, various investigators have reported detection rates for Down syndrome of 85% to 90% at a 5% false-positive rate.[11–13]

PRISCA Software for Use in Maternal Screening

PRISCA™ is a software program that provides statistical risk assessment for fetal chromosomal abnormalities, relying on maternal and gestational age, medical history, and the results of biochemical and echographic maternal screening markers.[14,15] It compares the subject's serum result for each marker with the established median for the gestational age. The software expresses the result of the comparison as a multiple of the median (MoM) for PAPP-A and free beta HCG during the first trimester.

The software provides MoMs based on gestational age and the related median, and corrects them for maternal weight, ethnicity, smoking, twin pregnancy, diabetes, and *in vitro* fertilization procedures, along with maternal age to yield a final risk assessment. It operates in MICROSOFT WINDOWS, either on a single computer or in a computer network. It features a statistical module in which users can update medians and create a quality control program for monitoring any of the relevant maternal screening components (for example: MoMs, detection rates, false-positive rates, and population parameters, among others).

PRISCA software is configured for use with Atellica IM FBHCG and Atellica IM Pregnancy-Associated Plasma Protein-A (PAPP-A) assays.

Principles of the Procedure

The Atellica IM FBHCG assay is a fully automated, 2-step sandwich immunoassay using direct chemiluminescent technology. The assay utilizes an acridinium ester-labeled anti-free beta HCG monoclonal antibody as the Lite Reagent. The Solid Phase consists of anti-free beta HCG monoclonal antibody-coated paramagnetic microparticles.

A direct relationship exists between the amount of free beta HCG present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Reagents

Material Description	Storage	Stability[a]
Atellica IM FBHCG ReadyPack® primary reagent pack **Lite Reagent** 17.0 mL/reagent pack (8.5 mL in each of 2 reagent wells) Anti-free beta HCG mouse monoclonal antibody labeled with acridinium ester in buffer; bovine serum albumin (BSA); surfactant; sodium azide (< 0.1%); preservative **Solid Phase** 25.0 mL/reagent pack Anti-free beta HCG mouse monoclonal antibody-coated paramagnetic microparticles (0.75 mg/mL); buffer; BSA; surfactant; preservative	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM FBHCG CAL 2.0 mL/vial; lyophilized After reconstitution, human free beta HCG; BSA; bovine serum; preservative	Lyophilized at 2–8°C Reconstituted at 2–8°C Reconstituted at room temperature Atellica® Sample Handler[b]	Until expiration date on product 30 days 8 hours
Atellica IM Multi-Diluent 13 ReadyPack ancillary reagent pack[c] 10 mL/pack Buffer; surfactant; sodium azide (< 0.1%)	Unopened at 2–8°C Onboard	Until expiration date on product 28 days

[a] Refer to *Storage and Stability*.
[b] Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.
[c] Refer to *Optional Materials*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens.com/healthineers.

H319, H315, H317, H412	**Warning!** Causes serious eye irritation. Causes skin irritation. May cause an allergic skin reaction. Harmful to aquatic life with long lasting effects.
P264, P272, P280, P273, P305+P351+P338, P337+P313, P302+P352, P333+P313, P363, P501	Wash hands thoroughly after handling. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/protective clothing/eye protection/face protection. Avoid release into the environment. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional and national regulations. **Contains:** reaction mass of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1); (in Atellica IM FBHCG CAL).

H317	**Warning!**
P280, P272, P302+P352, P333+P313, P363, P501	May cause an allergic skin reaction. Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of container in accordance with all local, regional, and national regulations. **Contains:** reaction mass of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1); (in Atellica IM FBHCG ReadyPack).

CAUTION POTENTIAL BIOHAZARD

Contains human urine-sourced material. This material should be handled using good laboratory practices and universal precautions.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Note For information about calibrator preparation, refer to *Preparing the Calibrators.*

Storage and Stability

Store reagents in an upright position. Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

Store calibrators in an upright position. Lyophilized calibrators are stable until the expiration date on the product when stored at 2–8°C. Reconstituted calibrators are stable for 30 days at 2–8°C, or for 8 hours at room temperature.

Store Atellica IM Multi-Diluent 13 in an upright position. Unopened Atellica IM Multi-Diluent 13 is stable until the expiration date on the product when stored at 2–8°C.

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 28 days. Discard reagents at the end of the onboard stability interval.

Note Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

Atellica IM Multi-Diluent 13 is stable onboard the system for 28 days.

Do not use products beyond the expiration date printed on the product.

Specimen Collection and Handling

Serum is the recommended sample type for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[16]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[17]
- Follow the instructions provided with your specimen collection device for use and processing.[18]
- Allow blood specimens to clot completely before centrifugation.[19] Separate promptly from the clot.
- Keep tubes capped at all times.[19]
- Test samples as soon as possible after collecting.

Storing the Specimen

Separated specimens are stable for up to 24 hours at room temperature, and for up to 6 days at 2–8°C. For longer storage, specimens may be frozen for up to 6 months at -20°C.[20] Avoid more than 1 freeze/thaw cycle. Do not store in a frost-free freezer.

Thoroughly mix all thawed samples and centrifuge before using. Collect the supernatant into a clean vial.

The handling and storage information provided here is based on data or references maintained by the manufacturer. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Store specimens at ≤ -20°C upon arrival.

Ship specimens frozen.

Preparing the Samples

This assay requires 20 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

If automatic dilution of a sample is required, load Atellica IM Multi-Diluent 13 in the reagent compartment. Refer to *Dilutions*.

Note Do not use specimens with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[19]

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10733009	1 ReadyPack primary reagent pack containing Atellica IM FBHCG Lite Reagent and Solid Phase	100
	Atellica IM FBHCG master curve and test definition MC TDEF	
	1 vial Atellica IM FBHCG CAL low calibrator CAL L	
	1 vial Atellica IM FBHCG CAL high calibrator CAL H	
	Atellica IM FBHCG calibrator lot-specific value sheet CAL LOT VAL	
10733010	5 ReadyPack primary reagent packs containing Atellica IM FBHCG Lite Reagent and Solid Phase	500
	Atellica IM FBHCG master curve and test definition MC TDEF	
	2 vials Atellica IM FBHCG CAL low calibrator CAL L	
	2 vials Atellica IM FBHCG CAL high calibrator CAL H	
	Atellica IM FBHCG calibrator lot-specific value sheet CAL LOT VAL	

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description
	Atellica IM Analyzer[a]

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Optional Materials

The following materials may be used to perform this assay, but are not provided:

REF	Description	
10995643	Atellica IM Multi-Diluent 13 (diluent)	2 ReadyPack ancillary reagent packs containing 10.0 mL/pack DIL

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 20 µL of sample into a cuvette.
2. Dispenses 250 µL of Solid Phase reagent, then incubates for 17 minutes at 37°C.
3. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
4. Resuspends the particles in Atellica IM Wash.
5. Dispenses 170 µL of Lite Reagent (85 µL from each of 2 wells in the ReadyPack), then incubates the mixture for 18 minutes at 37°C.
6. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
7. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
8. Reports results.

Preparing the Reagents

The ReadyPack primary reagents are liquid and ready to use. Before loading primary reagent packs onto the system, mix them by hand and visually inspect the bottom of the reagent pack to ensure that all particles are resuspended. For information about preparing the reagents for use, refer to the online help.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. The system automatically mixes reagent packs to maintain homogeneous suspension of the reagents. For information about loading reagent packs, refer to the online help.

For automated dilutions, ensure that Atellica IM Multi-Diluent 13 is loaded in the reagent compartment.

Master Curve Definition

Before initiating calibration on each new lot of reagent, load the assay master curve and test definition values by scanning the MC TDEF 2D barcodes. For loading instructions, refer to the online help.

Performing Calibration

For calibration of the Atellica IM FBHCG assay, use the calibrators provided with each kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	28
Pack Calibration	14
Reagent Onboard Stability	28

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Prepare calibrators using the following steps:

1. Add 2.0 mL of special reagent water into each vial using a precision pipet. Replace cap.

   Note For information about special reagent water requirements, refer to the online help.
2. Invert the vial 5 times and let the vials stand for 30 minutes at room temperature to allow the lyophilized material to dissolve.
3. Gently mix and invert the vials to ensure homogeneity of the material. Do not vortex.
4. Aliquots of reconstituted calibrators may be stored at 2–8°C for storage information refer to *Storage and Stability*.

Note Use calibrators within the stability limits specified in *Storage and Stability* and discard any remaining material.

Calibration Procedure

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the online help.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet MC TDEF provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit with reagents from a different assay kit lot.

- For the calibrator definitions, refer to the lot-specific value sheet CAL LOT VAL provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the online help.

Performing Quality Control

For quality control of the Atellica IM FBHCG assay, use an appropriate quality control material of known analyte concentration at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use.

A satisfactory level of performance is achieved when the analyte values obtained are within the expected control interval for the system or within your interval, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Test quality control samples after a successful calibration.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help. The system reports results in IU/L. The assay results can be converted to ng/mL or mIU/mL.

Conversion formula: 1 IU/L = 1 ng/mL or 1 mIU/mL

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Dilutions

The measuring interval for serum is 0.14–200.00 IU/L (ng/mL). For information about dilution options, refer to the online help.

Dilute and retest serum samples with free beta HCG levels > 200.00 IU/L (ng/mL) to obtain accurate results.

For automated dilutions, ensure that Atellica IM Multi-Diluent 13 is loaded in the reagent compartment. Ensure that sufficient sample volume is available to perform the dilution and that the appropriate dilution factor is selected when scheduling the test, as indicated in the table below.

For automatic dilutions, enter a dilution setpoint ≤ 200 IU/L (ng/mL).

Sample	Dilution	Sample Volume (µL)
Serum	1:10	20

Interpretation of Results

Do not use Atellica IM FBHCG test results interchangeably with test results from other free beta HCG assays.

Note If the controls are out of range, the sample results are invalid. Do not report results.

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

The following information pertains to limitations of the assay:

- This assay is not intended for use in monitoring or detecting trophoblastic and testicular tumors.
- The performance of the assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum, such as saliva, urine, amniotic fluid, or pleural fluid.
- The performance of the assay has not been established for populations of immunocompromised or immunosuppressed patients.
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[21,22] Additional information may be required for diagnosis.

Expected Values

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur® system. Expected values were established using the ADVIA Centaur system and confirmed by assay comparison. Refer to *Assay Comparison*.

Results were obtained on 260 apparently healthy non-pregnant females. The age ranges were 18–50 years (n = 130) and 51–86 years (n = 130). The median free beta HCG concentration for the group was established at < 0.28 IU/L (ng/mL) according to CLSI Document EP28-A3c.[23]

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[23] Consider these values as guidance only.

Performance Characteristics

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur system. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur system.

Measuring Interval

The Atellica IM FBHCG assay provides results from 0.14–200.00 IU/L (ng/mL). The lower end of the measuring interval is defined by the limit of quantitation (LoQ). Report results below the measuring interval as < 0.14 IU/L (ng/mL).

When sample results exceed the measuring interval, refer to *Dilutions*.

Specificity

Specificity was determined in accordance with CLSI Document EP07-A2.[24] The following substances were evaluated for cross-reactivity and do not interfere with the Atellica IM FBHCG assay when present in serum at the concentrations indicated. Cross reactivity was tested in the presence of free beta HCG at concentrations in the range of 7–9 IU/L (ng/mL) and in the absence of free beta HCG.

Percent cross-reactivity is calculated as:

$$\% \text{ cross-reactivity} = \frac{(\text{concentration of spiked sample - concentration of unspiked sample})}{\text{concentration of cross-reactant}} \times 100$$

The following results were obtained:

Substance	Substance Test Concentration	Cross-reactivity (%)
Follicle-stimulating hormone	1000 IU/L	ND[a]
Intact human chorionic gonadotropin	100,000 IU/L	0.062%
Luteinizing hormone	1000 IU/L	ND
Thyroid-stimulating hormone	2500 mIU/L	ND

[a] ND = not detected

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[25] The assay is designed to have a limit of detection (LoD) ≤ 0.50 IU/L (ng/mL), and an LOQ ≤ 1.00 IU/L (ng/mL).

Representative detection capability data are shown below. Assay results obtained at individual laboratories may vary from the data presented.

The limit of blank (LoB) corresponds to the highest measurement result that is likely to be observed for a blank sample. The LoD corresponds to the lowest concentration of free beta HCG that can be detected with a probability of 95%. The LoD for the Atellica IM FBHCG assay is 0.11 IU/L (ng/mL), and was determined using 135 determinations and an LoB of 0.07 IU/L (ng/mL).

The LoQ is determined by the functional sensitivity. The functional sensitivity corresponds to the lowest amount of free beta HCG in a sample at which the total CV is ≤ 20%. The LoQ of the Atellica IM FBHCG assay is 0.14 IU/L (ng/mL), and was determined using multiple patient samples in the interval 0.14–1.23 IU/L (ng/mL). All samples were assayed in replicates of 5 in 1 run per day using 3 reagent lots, over a period of 3 days.

Clinical Sensitivity and Specificity

Normal Subjects (Non-Pregnant)

The ADVIA Centaur FBHCG assay results were obtained on 260 apparently healthy non-pregnant female subjects. The age range was 18–86 years. All of the samples (100%) reported concentrations below the LoQ of the assay.

Normal Values During 1st Trimester of Pregnancy

The ADVIA Centaur FBHCG assay results were obtained on 842 serum samples from first trimester pregnant female subjects. All samples were obtained from routine pregnancy screening at the Fetal Medicine Research Institute in the United Kingdom.

The median values for free beta HCG at each completed week of gestation in the first trimester are shown below. The population tested consisted of Caucasian pregnant women. Twin pregnancies, women who were smokers, and women with ethnic origins other than Caucasian were removed from the database before the medians were determined.

The following results were determined at gestational weeks 8–13 using the ADVIA Centaur FBHCG assay as shown in the following table:

Completed Week of Gestation	Median of Gestational Week	N	5th Percentile (IU/L; ng/mL)	Median (IU/L; ng/mL)	95th Percentile (IU/L; ng/mL)
8	8.71	78	39.79	79.51	174.28
9	9.43	109	26.60	67.08	169.39
10	10.43	139	23.69	58.08	169.40
11	11.71	177	16.18	44.11	131.86
12	12.57	174	13.41	36.02	95.06
13	13.29	165	11.46	28.40	81.93

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[23] Consider these values as guidance only.

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Affected Population

The ADVIA Centaur FBHCG assay results were obtained on 60 maternal serum samples from known Trisomy 21 pregnancies.

The medians established are shown in the following table:

Affected Population	N	Gestational Week (Week + Days)	5th Percentile (IU/L; ng/mL)	Median (IU/L; ng/mL)	95th Percentile (IU/L; ng/mL)
Trisomy 21	30	11+0–12+6	35.13	93.17	198.99
	30	13+0–13+6	24.75	79.95	184.27

When used together in risk modeling, the ADVIA Centaur FBHCG and ADVIA Centaur PAPP-A assays resulted in a detection rate of 85% of Trisomy 21 cases with a 5% false positive rate.

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Risk Calculation

The individual risk for chromosomal abnormalities is calculated by including all parameters in an algorithm that applies the mathematical calculations for Gaussian multivariate distribution.[26-29]

Offline software packages are available to perform these calculations.[15]

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[30] Samples were assayed on an Atellica IM Analyzer, in 2 runs per day, using 3 lots of reagent, for 20 days, yielding 240 observations per sample.

The assay was designed to have repeatability of ≤ 4% CV for samples from ≥ 7–< 18 IU/L (ng/mL) and ≤ 3% CV for samples from ≥ 18–95 IU/L (ng/mL).

The assay was designed to have within-laboratory precision of ≤ 6% CV for samples from ≥ 7–< 18 IU/L (ng/mL) and ≤ 5% CV for samples from ≥ 18–95 IU/L (ng/mL).

Representative data from the study is shown in the following table:

			Repeatability		Within-Laboratory Precision	
Specimen Type	**N[a]**	**Mean (IU/L; ng/mL)**	**SD[b] (IU/L; ng/mL)**	**CV[c] (%)**	**SD (IU/L; ng/mL)**	**CV (%)**
Serum A	240	8.31	0.12	1.5	0.19	2.3
Serum B	240	20.03	0.31	1.5	0.51	2.5
Serum C	240	81.17	1.05	1.3	2.11	2.6
Serum D	240	177.70	2.30	1.3	4.02	2.3

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.

Assay results obtained at individual laboratories may vary from the data presented.

Assay Comparison

The Atellica IM FBHCG assay is designed to have a correlation coefficient of (r) ≥ 0.95 and a slope of 1.0 ± 0.05 compared to the ADVIA Centaur FBHCG assay. Assay comparison was determined using the Passing-Bablok regression model in accordance with CLSI Document EP09-A3.[31] The following results were obtained:

Specimen	**Comparative Assay (x)**	**Regression Equation**	**Sample Interval**	**N[a]**	**r[b]**
Serum	ADVIA Centaur FBHCG	y = 0.95x - 0.98 IU/L (ng/mL)	0.29–184.47 IU/L (ng/mL)	131	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

Agreement of the assays may vary depending on the study design, comparative assay, and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Specimen Equivalency

Specimen equivalency was determined using the Passing-Bablok regression model in accordance with CLSI Document EP09-A3.[31] The following results were obtained:

Specimen (y)	Reference Specimen (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum gel-barrier tube	Plain serum tube	y = 1.01x - 0.15 IU/L (ng/mL)	9.51–157.55 IU/L (ng/mL)	65	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

Agreement of the specimen types may vary depending on the study design and sample population used. Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2.[24]

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

The assay is designed to have ≤ 10% interference from hemoglobin, bilirubin, and lipemia at free beta HCG concentrations of 7–9 IU/L (ng/mL) and 75–95 IU/L (ng/mL). Interfering substances at the levels indicated in the table below were tested in accordance with CLSI Document EP07-A2.[24]

Bias is the difference in the results between the control sample (does not contain the interferent) and the test sample (contains the interferent) expressed in percent. Analyte results should not be corrected based on this bias.

Substance	Substance Test Concentration Common Units (SI Units)	Analyte Concentration (IU/L; ng/mL)	Bias (%)
Hemoglobin	500 mg/dL (0.31 mmol/L)	7–9 75–95	-3 -3
Bilirubin, conjugated	40 mg/dL (684 µmol/L)	7–9 75–95	-2 -1
Bilirubin, unconjugated	60 mg/dL (1026 µmol/L)	7–9 75–95	2 -1
Lipemia (triglycerides)	1000 mg/dL (11.3 mmol/L)	7–9 75–95	4 5

Assay results obtained at individual laboratories may vary from the data presented.

The following substances do not interfere with the assay when present in serum at the concentrations indicated in the table below. Bias due to these substances is ≤ 10% at an analyte concentration of 7–9 IU/L (ng/mL) and 75–95 IU/L (ng/mL).

Substance	Substance Test Concentration Common Units (SI Units)	Analyte Concentration (IU/L; ng/mL)	Bias (%)
Biotin	1500 ng/mL (6140 nmol/L)	7–9 75–95	-1 -2
Cholesterol	500 mg/dL (12.95 mmol/L)	7–9 75–95	3 -2
Protein albumin (human)	6 g/dL (60 g/L)	7–9 75–95	-7 -4
Protein gamma globulin (human)	6 g/dL (60 g/L)	7–9 75–95	-5 -10
Rheumatoid factor	200 IU/mL	7–9 75–95	-4 -1

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Dilution Recovery

Five samples containing high levels of free beta HCG (160.70–207.35 IU/L (ng/mL)) were diluted 1:10 with Atellica IM Multi-Diluent 13 and assayed for recovery. The following results were obtained:

Sample	Dilution	Observed (IU/L)	Expected (IU/L)	Recovery (%)
Sample 1	1:10	150.71	162.61	93
Sample 2	1:10	160.81	160.70	100
Sample 3	1:10	175.11	194.19	90
Sample 4	1:10	157.34	175.20	90
Sample 5	1:10	196.71	207.34	95

Results were established using the Atellica IM Analyzer. Assay results obtained at individual laboratories may vary from the data presented.

High-Dose Hook Effect

High free beta HCG concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with free beta HCG concentrations above the measuring interval and as high as 78,940 IU/L (ng/mL) will report > 200.00 IU/L. Results were established using the Atellica IM Analyzer.

Standardization

The Atellica IM FBHCG assay is traceable to the World Health Organization (WHO) 1st International Reference Preparation of Chorionic Gonadotrophin Beta Subunit Human; NIBSC code: 75/551. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens.com/healthineers

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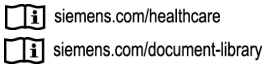
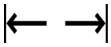
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
	Revision
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.
	Corrosive
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.

Symbol	Symbol Title and Description
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner
IVD	*In vitro* diagnostic medical device
Σ (n)	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.
	Mixing of substances Mix product before use.
g mL	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
PRINTED WITH SOY INK	Printed with soy ink
CE	CE Mark
CE 0088	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year month day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.

Symbol	Symbol Title and Description
UNITS C	Common Units
UNITS SI	International System of Units
MATERIAL	Material
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

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