SIEMENS Healthineers

Placental Growth Factor (PlGF)

Current Revision and Date[a]	Rev. 01, 2021-12	
Product Name	Atellica IM Placental Growth Factor (PlGF)	REF 11200232 (100 tests)
Abbreviated Product Name	Atellica IM PlGF	
Test Name/ID	PlGF	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM PlGF Quality Control (PlGF QC)	REF 11200234 (4-pack)
Optional Materials	Atellica IM PlGF Master Curve Material (PlGF MCM)	REF 11200233
Specimen Types	Serum and dipotassium EDTA plasma	
Sample Volume	50 µL	
Measuring Interval	9–10,000 pg/mL	

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

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Intended Use

The Atellica® IM Placental Growth Factor (PlGF) assay is for *in vitro* diagnostic use in the quantitative determination of placental growth factor in human serum and plasma (dipotassium EDTA) using the Atellica® IM Analyzer. The Atellica IM PlGF assay is used in combination with the Atellica® IM sFlt-1 assay to determine the sFlt-1/PlGF ratio (PE ratio).

The PE ratio is intended for use in the prognosis of preterm delivery and adverse outcomes in women presenting with signs and symptoms of preeclampsia.

Summary and Explanation

Preeclampsia (PE), which occurs in between 6–8% of pregnancies, is a potentially serious complication that contributes to significant fetal, neonatal, and maternal morbidity and mortality.[1] In 2000 the American College of Obstetrics and Gynecology (ACOG) noted that preeclampsia and its associated sequelae accounted for 15% of US perinatal deaths, making it the second leading cause of maternal mortality,[2] and the US incidence of PE has increased by 25% since the 1990's.[3] When early delivery is used to safeguard the mother's health and welfare, significant neonatal morbidity and mortality, developmental delays, and life-long disability associated with prematurity can result.

PE is defined as the development of new-onset hypertension (HT) (≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic) after 20 weeks of gestation, in addition to other criteria such as proteinuria. In the absence of proteinuria, PE can be diagnosed if other hepatic, renal, or neurologic symptoms accompany HT.[2] If these other symptoms are not present, however, it can be difficult to differentiate PE from the less serious transitory gestational HT, and it can also be difficult to determine if PE has become superimposed on pre-existing chronic hypertension. Once the disease has been diagnosed, determining severity and prognosis can also be challenging as the currently available methods lack sufficient prognostic sensitivity or specificity.[2,4,5] Several studies have identified a relationship between PE, the sFlt-1 and PlGF markers, and their ratio.[6-20]

The pathophysiology of PE is conjectured to occur as a two phase process. In the initial phase (in the first 20 weeks gestation), insufficient advancement of placental cytotrophoblasts into the maternal uterine decidua prevents remodeling of maternal spiral artery endothelium. As a result, instead of thinning out to become low-resistance, high-volume vessels, the spiral arteries retain high-resistance, low-volume characteristics. As blood supply to the placenta increases to support the growing fetus, these high-resistance vessels trigger a hypertensive response (usually after 20 weeks gestation).[6] Placental growth factor (PlGF), a member of the vascular epidermal growth factor (VEGF) family, supports cytotrophoblast invasion, pseudovasculogenesis, and angiogenesis. In normal placentation, PlGF binds to the fms-like tyrosinase-1 receptor (Flt-1 or VEGFR1).

sFlt-1 availability appears to be regulated by a soluble mimic of the receptor-soluble fms-like tyrosinase-1 (sFlt-1) as binding of PlGF to sFlt-1 prevents binding to the cellular-bound Flt-1 receptor. High serum levels of sFlt-1 and low levels of free PlGF have been observed in PE patients.[6-9]

As has been observed in several other studies, sFlt-1 levels followed an upward curve from 10 weeks on. In preeclamptic women, the mean serum concentration of sFlt-1 was significantly higher, the mean PlGF concentration was significantly lower, and the sFlt-1/PlGF ratio was significantly higher. This is in alignment with observations made in multiple other studies, although (as would be expected) the exact values are not identical.[8,10,12-17]

Principles of the Procedure

The Atellica IM PlGF assay is a fully automated 1-step sandwich immunoassay using acridinium ester chemiluminescent technology incorporating 2 monoclonal antibodies. The first antibody, in the Lite Reagent, is a rat monoclonal anti-human PlGF antibody labeled with acridinium ester that binds to PlGF antigen in the sample. The Solid Phase, which consists of streptavidin-coated paramagnetic latex particles coated with biotinylated mouse monoclonal anti-human PlGF antibody, captures the PlGF antigen, forming a complex with the AE-labeled antibody. After a predetermined reaction time at 37°C, the particles are magnetically separated from the buffer and washed. Acid and base are added to initiate a chemiluminescent reaction.

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

Reagents

Material Description	Storage	Stability
Atellica IM PlGF ReadyPack® primary reagent pack[a, b] **Lite Reagent** 5.0 mL/reagent pack Rat monoclonal anti-human PlGF antibody (2.5 µg/mL) labeled with acridinium ester in buffer; goat serum; bovine serum albumin (BSA); mouse IgG; stabilizers; preservatives **Solid Phase** 25.0 mL/reagent pack Streptavidin-coated paramagnetic latex particles (0.25 mg/mL) with biotinylated mouse monoclonal anti-human PlGF antibody (10 µg/mg) in buffer; goat serum; BSA; mouse IgG; stabilizers; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM PlGF CAL[a] 1.0 mL/vial After reconstitution, low and high levels of PlGF antigen in buffer; equine serum; sodium azide (< 0.1%)	Lyophilized at 2–8°C Reconstituted at ≤ -20°C Reconstituted at room temperature	Until expiration date on product 30 days; thaw only once 2 hours

[a] Store in an upright position.

[b] Prevent exposure to sunlight and heat.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

For Prescription Use Only.

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-healthineers.com.

H311, H302, H412
P264, P273, P280, P312, P361+P364, P501

Danger!
Toxic in contact with skin. Harmful if swallowed. Harmful to aquatic life with long lasting effects.
Wash hands thoroughly after handling. Avoid release to the environment. Wear protective gloves/protective clothing/eye protection/face protection. Call a POISON CENTER or doctor/physician if you feel unwell. Take off immediately all contaminated clothing and wash it before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium azide (Atellica IM PlGF CAL).

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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

Specimen Collection and Handling

Serum and plasma (dipotassium EDTA) are the recommended specimen types for this assay.

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.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[21]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[22]
- Follow the instructions provided with your specimen collection device for use and processing.[23]
- Allow blood specimens to clot completely before centrifugation.[24]
- Keep tubes capped at all times.[24]

Storing the Specimen

- Separated samples are stable for up to 24 hours at room temperature, and for up to 7 days at 2–8°C.
- Separated samples are stable at ≤ -20°C for up to 30 days. Separated samples are stable at ≤ -70°C for up to 2 years. Avoid more than 1 freeze-thaw cycle. Do not store in a frost-free freezer. Thoroughly mix thawed samples and centrifuge them before using.

Transporting the Specimen

Ship specimens frozen.

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

Preparing the Samples

This assay requires 50 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 a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

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

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

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[24]

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11200232	1 ReadyPack primary reagent pack containing Atellica IM PlGF Lite Reagent and Solid Phase Atellica IM PlGF master curve and test definition MC TDEF 1 vial Atellica IM PlGF CAL low calibrator CAL L 1 vial Atellica IM PlGF CAL high calibrator CAL H Atellica IM PlGF CAL calibrator lot-specific value sheet CAL LOT VAL	100

Materials Required but Not Provided

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

REF	Description
	Atellica IM Analyzer[a]
11200234	Atellica IM PlGF QC (quality control material)

[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
11200233	Atellica IM PlGF MCM (master curve material)

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 250 µL of Solid Phase and 50 µL of Lite Reagent, then incubates for 24 minutes at 37°C.
3. Performs a wash sequence using Atellica IM Wash.
4. Dispenses 300 µL each of Atellica IM Acid Reagent and Atellica IM Base Reagent to initiate the chemiluminescent reaction.
5. Reports results.

Defining the Preeclampsia Ratio

The PE Ratio is the sFlt-1 concentration divided by the PlGF concentration (both expressed in the same units, pg/mL). The ratio is a unitless whole number. This calculation can be performed on the immunoassay system or on the laboratory information system (LIS).

When defining the ratio test definition, enter the following parameters:

Ratio test name	PE
Unit for the calculated ratio result	Ratio
Decimal places	0
Ratio test equation	sFlt-1/PlGF

For information about defining the ratio test definition, refer to the system online help.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve and test definition by scanning the MC TDEF 2D barcodes. For information about entering the master curve and test definition, refer to the system online help.

Performing Calibration

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

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same 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.

Note When loading a new primary reagent pack, a calibration is not required if there is a valid lot calibration. For information about lot calibration and pack calibration, refer to the system online help.

Stability Interval	Days
Lot Calibration	90
Pack Calibration	14
Reagent Onboard Stability	28

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 1.0 mL of special reagent water into each vial. Replace cap.

   Note For information about special reagent water requirements, refer to the system online help.

2. Let the vials stand for 15–20 minutes at room temperature to allow the lyophilized material to dissolve.
3. Gently mix and invert the vials to ensure homogeneity of the material.
4. For extended storage, aliquot and seal tightly. Store reconstituted material according to stability limits specified in *Reagents*. Do not store in a frost-free freezer.

   Note Before using frozen calibrators, allow the material to thaw completely. Gently mix and invert the vials to ensure homogeneity of the material.

Note Use calibrators within the stability limits specified in *Reagents* 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 system 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 lot with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the calibrator assigned 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 system online help.

Performing Quality Control

For quality control of the Atellica IM PlGF assay, use the Atellica IM PlGF QC at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use. For the assigned values, refer to the quality control assigned value sheet provided.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

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

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

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 system online help.

Taking Corrective Action

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

Results

Calculation of Results

The PE ratio is calculated using the sFlt-1 and PlGF results. The system reports individual assay results in pg/mL and the PE ratio as a unitless numerical value. To define the ratio test definition, refer to *Defining the Preeclampsia Ratio*. For additional information about setting up ratios, refer to the system online help.

To calculate the PE Ratio manually, obtain results for the system sFlt-1 and PlGF assays and use the equation below. The ratio should be reported to the nearest whole number.

$$\text{PE Ratio} = \frac{\text{sFlt-1 result (pg/mL)}}{\text{PlGF result (pg/mL)}}$$

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

Interpretation of Results

The system reports the result as a PE ratio and as individual assay results. Results of individual assays are for use in determining the PE ratio score. Do not release individual PlGF or sFlt-1 patient results.

The cut-off value for the PE ratio was verified based on clinical agreement of results generated from clinical studies.

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.

Prognosis of Preterm Delivery and Adverse Outcomes

sFlt-1/PlGF Cut-off Ratio	Gestational Age	Interpretation
≥ 38	20+0–35+6 (weeks + days)	At increased risk for developing adverse maternal/fetal outcomes or preterm delivery within 2 weeks

Limitations

The following information pertains to limitations of the assay:

- The performance of the assay has not been established with specimen types other than those defined in the Intended Use.
- Results obtained with the assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[25,26] 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 systems. Expected values were established using the ADVIA Centaur XP system and confirmed by assay comparison. Refer to *Assay Comparison*.

A reference interval for an apparently healthy pregnant population was established in accordance with CLSI Document EP28-A3c.[27] The reference interval was determined by calculating the 5th and 95th percentiles of the distribution of values.

Note The PE Ratio was calculated using the following equation:

$$\text{PE Ratio} = \frac{\text{sFlt -1 result (pg/mL)}}{\text{PlGF result (pg/mL)}}$$

sFlt-1 Reference Interval Results

Group Gestational Age (Week + Days)	N[a]	Median (pg/mL)	Central 90th Reference Interval	
			5th (pg/mL)	95th (pg/mL)
(10+0/7)–(14+6/7)	122	1171	533	3158
(15+0/7)–(19+6/7)	121	1083	390	3341
(20+0/7)–(23+6/7)	121	1152	464	3143
(24+0/7)–(28+6/7)	120	1059	491	3308
(29+0/7)–(33+6/7)	120	1531	556	5123
(34+0/7)–(36+6/7)	120	2399	983	9888
(37+0/7)–delivery	120	3168	665	13,388

[a] Number of samples tested.

PlGF Reference Interval Results

Group Gestational Age (Week + Days)	N[a]	Median (pg/mL)	Central 90th Reference Interval	
			5th (pg/mL)	95th (pg/mL)
(10+0/7)–(14+6/7)	122	40.1	15.6	123
(15+0/7)–(19+6/7)	121	115	52.3	422
(20+0/7)–(23+6/7)	121	292	87.6	787
(24+0/7)–(28+6/7)	120	521	176	1793
(29+0/7)–(33+6/7)	120	628	62.1	2569
(34+0/7)–(36+6/7)	120	324	60.3	2037
(37+0/7)–delivery	120	260	17.5	1545

[a] Number of samples tested.

PE Ratio Reference Interval Results

Group Gestational Age (Week + Days)	N[a]	Median (Ratio)	Central 90th Reference Interval (Ratio)	
			5th (pg/mL)	95th (pg/mL)
(10+0/7)–(14+6/7)	122	31.4	9.52	77.2
(15+0/7)–(19+6/7)	121	8.75	2.35	31.2
(20+0/7)–(23+6/7)	121	3.81	1.05	15.8
(24+0/7)–(28+6/7)	120	1.99	0.58	7.26
(29+0/7)–(33+6/7)	120	2.15	0.49	72.5
(34+0/7)–(36+6/7)	120	6.90	0.70	60.3
(37+0/7)–delivery	120	16.5	1.29	221

[a] Number of samples tested.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[27] 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

9–10,000 pg/mL

The lower limit of the measuring interval is defined by the limit of detection (LoD). Report results below the measuring interval as < 9 pg/mL.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.14[28]

Limit of Blank (LoB)	3 pg/mL
Limit of Detection (LoD)	6 pg/mL
Limit of Quantitation (LoQ)	10 pg/mL

Note All values are representative data.

The LoB corresponds to the highest measurement result likely to be observed for a blank sample with a probability of 95%.

The LoD corresponds to the lowest concentration of PlGF that can be detected with a probability of 95%. The assay is designed to have an LoD of 9 pg/mL.

The LoQ corresponds to the lowest amount of PlGF in a sample at which the within laboratory CV is = 20%.

Clinical Sensitivity and Specificity

Clinical performance was evaluated using the ADVIA Centaur XP system and confirmed by assay comparison. Refer to *Assay Comparison*.

Prognosis of Preterm Delivery and Adverse Outcomes

A total of 338 specimens collected from 24 sites were tested at 1 clinical testing site using an ADVIA Centaur XP system. Specimens were from individuals with singleton pregnancies between gestational weeks 20+0 days and 35+6 days with signs and symptoms of preeclampsia.

The clinical performance of the PE ratio was evaluated for the prognosis of preterm delivery and adverse outcomes within 2 weeks using a cut-off value of 38. Of the 338 subjects, 95 subjects experienced preterm delivery or an adverse outcome within 2 weeks of presentation.

Gestational Age 20+0–35+6 (weeks + days)

sFlt-1/PlGF Cut-off Ratio	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
≥ 38	88.42% (84/95) 95% CI: (81.99%–94.86%)	87.65% (213/243) 95% CI: (83.52%–91.79%)	73.68% (84/114) 95% CI: (65.60%–81.77%)	95.09% (213/224) 95% CI: (92.26%–97.92%)

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[29] Samples were assayed in duplicate in 2 runs per day for 20 days.

The following results are representative of the performance of the assay:

			Repeatability		Within-Laboratory Precision	
Specimen Type	N[a]	Mean pg/mL	SD[b] pg/mL	CV[c] (%)	SD pg/mL	CV (%)
Serum A	80	67.7	1.60	2.4	2.72	4.0
Serum B	80	209	3.2	1.5	6.2	2.9
Serum C	80	7978	75.8	0.9	263.6	3.3

Specimen Type	N[a]	Mean pg/mL	Repeatability SD[b] pg/mL	Repeatability CV[c] (%)	Within-Laboratory Precision SD pg/mL	Within-Laboratory Precision CV (%)
Control 1	80	102	2.0	2.0	4.9	4.8
Control 2	80	2094	26.6	1.3	67.3	3.2

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

The assay was designed to have the following precision.

Concentration Interval	Precision	
pg/mL	Repeatability (Within-Run)	Within-Laboratory (Total Precision)
< 40	≤ 5.0 pg/mL SD	≤ 6.0 pg/mL SD
≥ 40–10,000	≤ 7.0% CV	≤ 8.0% CV

Assay Comparison

Assay comparison was determined with the weighted Deming regression model in accordance with CLSI Document EP09-A3.[30]

Agreement of the assays may vary depending on the study design, comparative assay, and population tested.

Specimen Type	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ADVIA Centaur PlGF assay using the ADVIA Centaur XP system	y = 1.06x + 2 pg/mL	13–6065 pg/mL	316	0.999

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

The assay is designed to have a correlation coefficient of ≥ 0.900, a slope of 1.00 ± 0.10, and an intercept of ± 30 pg/mL.

Specimen Equivalency

Specimen equivalency was determined with the Passing-Bablok regression model using the ADVIA Centaur XP system in accordance with CLSI Document EP09-A3.[30]

Agreement of the specimen types may vary depending on the study design and population tested.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Plasma, dipotassium EDTA	y = 0.99x - 3 pg/mL	53–1734 pg/mL	50	1.000
Gel-barrier tube (serum)	y = 1.00x - 1 pg/mL	53–1734 pg/mL	50	1.000

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

The assay is designed to have a correlation coefficient of ≥ 0.950, a slope of 1.00 ± 0.05, and an intercept of ± 10 pg/mL.

Interferences

Hemolysis, Icterus, Lipemia (HIL)

Interference testing was performed using the ADVIA Centaur XP system in accordance with CLSI Document EP07-A2.[31]

The following substances do not interfere with the assay when present in serum at the concentrations indicated. Bias due to these substances does not exceed 10% at an PlGF concentration of 89–110 pg/mL and 282–342 pg/mL.

Substance	Substance Test Concentration
Hemoglobin	500 mg/dL
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	60 mg/dL
Lipemia (Intralipid)	3000 mg/dL

Other Substances

Interference testing was performed using the ADVIA Centaur XP system in accordance with CLSI Document EP07-A2.[31]

The following substances do not interfere with the assay when present in serum at the concentrations indicated. Bias due to these substances does not exceed 10% at an PlGF concentration of 84–113 pg/mL and 273–367 pg/mL.

Substance	Substance Test Concentration
Biotin	3510 ng/mL
Protein	12 g/dL

Cross-Reactivity

Cross-reactivity was determined using the ADVIA Centaur XP system in accordance with CLSI Document EP07-A2.[31]

Cross-reactants were tested at PlGF concentrations of 0–9 pg/mL, 62–113 pg/mL, and 207–379 pg/mL.

	(ng/mL)	Cross-reactivity (%)
VEGF 165	10	≤ 0.100 ≤ 0.100 ≤ 0.100
VEGF/PlGF Heterodimer	10	≤ 4.00 ≤ 4.00 ≤ 4.00
VEGF-B	10	≤ 0.100 ≤ 0.100 ≤ 0.100
Glycosylated rhPlGF-2	5	< 28.0 < 28.0 < 28.0

Linearity

Linearity testing was performed in accordance with CLSI Document EP06-A.[32]

Linearity was evaluated using a sample that contained a high level of PlGF, mixed in various proportions with a sample that contained a low level of PlGF. The resulting sample mixtures (9 combinations) were assayed for PlGF.

The Atellica IM PlGF assay is linear for the measuring interval of 9–10,000 pg/mL.

High-Dose Hook Effect

High PlGF concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with PlGF concentrations above the measuring interval and as high as 100,000 pg/mL will report > 10,000 pg/mL.

Standardization

The Atellica IM PlGF assay is traceable to an internal standard value assigned through the 09/272 NIBSC International Reference Standard. Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.

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

siemens-healthineers.com

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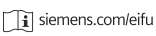
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Symbol	Symbol Title
	Manufacturer		Authorized representative in the European Community
	Use-by date		Batch code
	Catalog number		Contains sufficient for <n> tests
	Consult Instructions for Use		Version of Instructions for Use
	Internet URL address to access the electronic instructions for use		Revision
	*In vitro* diagnostic medical device		Unique Device Identifier
	Prescription device (US only)		CE Marking
	CE Marking with Notified Body		Keep away from sunlight
	Temperature limit		Lower limit of temperature
	Upper limit of temperature		Do not freeze
	Do not re-use		This way up

Symbol	Symbol Title	Symbol	Symbol Title
	Recycle		Caution
	Biological risks		Document face up[a]
UNITS C	Common Units	UNITS SI	International System of Units
YYYY-MM-DD	Date format (year-month-day)	YYYY-MM	Date format (year-month)
	Handheld barcode scanner		Mixing of substances
	Target		Interval
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	MATERIAL	Material
MATERIAL ID	Unique material identification number	CONTROL NAME	Name of control
CONTROL TYPE	Type of control	CAL LOT VAL	Calibrator lot value
CONTROL LOT VAL	Quality control lot value		

[a] Indicates Assay-eNote

Legal Information

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