SIEMENS Healthineers

Insulin (IRI)

Current Revision and Date[a]	Rev. 06, 2022-11	
Product Name	Atellica IM Insulin (IRI)	REF 10995628
Abbreviated Product Name	Atellica IM IRI	
Test Name/ID	IRI	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM IRI CAL	REF 10995629
Optional Materials	Atellica IM IRI DIL	REF 10995630 (2-pack) REF 10995631 (vial)
	Atellica IM IRI MCM	REF 10995632
Specimen Types	Serum	
Sample Volume	25 µL	
Measuring Interval	0.5–300.0 mU/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 Insulin (IRI) assay is for *in vitro* diagnostic use in the quantitative determination of insulin in human serum using the Atellica® IM Analyzer. This assay can be used to aid in the diagnosis and treatment of diabetes mellitus and hypoglycemia.

Summary and Explanation

Insulin is a protein hormone that is synthesized, stored, and secreted by the beta cells located in the islets of Langerhans in the pancreas. Insulin is responsible for regulating glucose concentrations in the blood. Initially in the beta cells, insulin exists as a large molecule (MW ~12,000) called preproinsulin. Preproinsulin is a single-chain precursor consisting of 110 amino acids. A chain of 24 amino acids of preproinsulin is cleaved forming proinsulin (MW ~9000), the precursor of insulin and C-peptide.[1-3]

Proinsulin consists of 2 amino acid chains of insulin connected by disulfide bonds and a connective peptide, called C-peptide. The alpha (A) chain of insulin consists of 21 amino acids, the beta (B) chain of insulin consists of 30 amino acids, and C-peptide consists of 31 amino acids. Proinsulin is stored in the secretory granules in the Golgi apparatus of the beta cells until proinsulin undergoes proteolysis to form insulin (MW ~6000) and C-peptide (MW ~3000). At the cell membrane, insulin and C-peptide are released into the portal circulation in equimolar amounts.[1-3]

Insulin is released in response to the presence of glucose in the blood typically after the ingestion of a meal. A normal healthy individual produces 40–50 units of insulin each day. The half-life of insulin in serum or plasma is 5–10 minutes. Approximately 50% of the insulin released into the portal circulation is cleared by the liver. Insulin binds to receptor cells located on cell membranes of target tissues. The target tissues are primarily liver, fat, and muscle tissue. Insulin lowers glucose concentrations in the blood by stimulating glycogenolysis in the liver, triglyceride synthesis in adipose tissue, and protein synthesis in muscle.[1-3] Recent studies have indicated that insulin and insulin receptors may play a role in learning and memory. The interruption of insulin production and insulin receptor activity may lead to deficits in learning and memory formation.[4] Increased insulin production is common in the development of cancers.[5]

If insulin production is not stimulated, blood glucose levels will not be lowered and hyperglycemia results. Fasting hyperglycemia supports the diagnosis of diabetes mellitus. There are 2 types of diabetes mellitus: type I or insulin-dependent diabetes mellitus (IDDM) and type II or non-insulin-dependent diabetes mellitus (NIDDM). Insulin therapy is used for insulin-dependent diabetes mellitus (IDDM) patients and many non-insulin-dependent diabetes mellitus (NIDDM) patients. In type I diabetes (IDDM), there is a deficiency of insulin. This can be the result of autoimmune destruction of the beta cells or the presence of autoantibodies to insulin. Many factors can play a role in the development of type II diabetes (NIDDM). Type II diabetes (NIDDM) can result if there is a decreased biological response to circulating insulin (insulin resistance) or if there is decreased or diminished insulin secretion due to beta cell failure.[1-3]

Insulin levels are not typically used in the diagnosis or management of diabetic patients. Insulin levels can be useful in evaluating patients with fasting hypoglycemia, in determining insulin resistance in the general population, and in assessing abnormalities in beta cell secretory function. Insulin levels are used in studying the pathophysiology of diabetes.[6,7]

Principles of the Procedure

The Atellica IM IRI assay is a 2-site sandwich immunoassay using direct chemiluminescent technology which uses constant amounts of 2 antibodies. The first antibody, in the Lite Reagent, is a mouse monoclonal anti-insulin antibody labeled with acridinium ester. The second antibody, in the Solid Phase, is a mouse monoclonal anti-insulin antibody, which is covalently coupled to paramagnetic particles.

A direct relationship exists between the amount of insulin 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 IRI ReadyPack® primary reagent pack **Lite Reagent** 5.0 mL/reagent pack Mouse monoclonal anti-insulin antibody (~0.24 µg/mL) labeled with acridinium ester in buffered saline; bovine serum albumin; sodium azide (< 0.1%); preservatives **Solid Phase** 25.0 mL/reagent pack Mouse monoclonal anti-insulin antibody (~6.0 µg/mL) covalently coupled to paramagnetic particles in buffered saline; bovine serum albumin; sodium azide (< 0.1%); preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 21 days
Atellica IM IRI DIL ReadyPack ancillary reagent pack[b] 10.0 mL/pack Buffered saline; casein, potassium thiocyanate (3.89%); sodium azide (< 0.1%); preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 21 days
Atellica IM IRI DIL[b] 20.0 mL/vial Buffered saline; casein, potassium thiocyanate (3.89%); sodium azide (< 0.1%); preservatives	Unopened at 2–8°C	Until expiration date on product

[a] Refer to *Storage and Stability*.

[b] 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-healthineers.com.

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.

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 Atellica IM IRI DIL in an upright position. Atellica IM IRI DIL 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 21 days. Discard reagents at the end of the onboard stability interval.

Atellica IM IRI DIL is stable onboard the system for 21 days.

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

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.[8]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[9]
- Follow the instructions provided with your specimen collection device for use and processing.[10]
- Allow blood specimens to clot completely before centrifugation.[11]
- Keep tubes capped at all times.[11]

Storing the Specimen

- Centrifuge samples at ≥ 1000 x g for 15–20 minutes.
- Do not use samples that have been stored at room temperature for longer than 8 hours.
- Separate serum from the red blood cells before storage at 2–8°C or -20°C.
- Tightly cap and refrigerate specimens at 2–8°C if the assay is not completed within 8 hours.
- Freeze samples at ≤ -20°C if the assay is not completed within 24 hours.
- Freeze samples only 1 time and mix thoroughly after thawing.

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.

Preparing the Samples

This assay requires 25 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.

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. 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.[11]

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
10995628	1 ReadyPack primary reagent pack containing Atellica IM IRI Lite Reagent and Solid Phase Atellica IM IRI master curve and test definition MC TDEF	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]	
10995629	Atellica IM IRI CAL (calibrator)	2 x 1.0 mL low calibrator CAL L 2 x 1.0 mL high calibrator CAL H Calibrator lot-specific value sheet CAL LOT VAL

[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	
10995630	Atellica IM IRI DIL (diluent)	2 ReadyPack ancillary reagent packs containing 10.0 mL/pack DIL
10995631	Atellica IM IRI DIL (diluent)	20.0 mL/vial DIL
10995632	Atellica IM IRI MCM (master curve material)	10 x 1.0 mL levels of master curve material MCM

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 25 µL of sample into a cuvette.
2. Dispenses 50 µL of Lite Reagent, then incubates for 5 minutes at 37°C.
3. Dispenses 250 µL of Solid Phase, then incubates for 7 minutes at 37°C.

4. Separates, aspirates, then washes the cuvette with Atellica IM Wash.
5. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
6. Reports results.

Preparing the Reagents

All 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 IRI DIL 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 IRI assay, use the Atellica IM IRI CAL. Use the calibrators in accordance with the calibrator instructions for use.

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	91
Pack Calibration	14
Reagent Onboard Stability	21

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.

Performing Quality Control

For quality control of the Atellica IM IRI assay, use an appropriate quality control material of known analyte concentration with at least 2 levels (low and high) at least once during each day that samples are analyzed. For assistance in identifying a quality control material, refer to *Atellica® IM Quality Control Material Supplement* available on siemens-healthineers.com.

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 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 mU/L.

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

Dilutions

The measuring interval for serum is 0.5–300.0 mU/L. For information about dilution options, refer to the online help.

Dilute and retest serum samples with insulin levels > 300.0 mU/L to obtain accurate results.

For automated dilutions, ensure that Atellica IM IRI DIL 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 ≤ 300 mU/L.

Sample	Dilution	Sample Volume (µL)
Serum	1:2	100
Serum	1:5	40

If patient results exceed the measuring interval of the assay when using automated dilution, or if laboratory protocol requires manual dilution, manually dilute the patient sample.

For manual dilutions, perform the following actions:

- Use Atellica IM IRI DIL (vial) to prepare a manual dilution.
- For information about ordering tests for manually diluted samples, refer to the online help.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of 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:

- Insulin autoantibodies in human serum may interfere and cause discordant results.
- 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.[12,13] 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® and ACS:180™ systems. Expected values were established using the ACS:180 system and confirmed by assay comparison. Refer to *Assay Comparison*.

Serum samples were obtained from 145 apparently healthy individuals who had normal hemoglobin A1c and glucose levels after a 12-hour fast. For this population, 95% of the values were in the range of 3.0–25.0 mU/L, with an overall range of 2.6–37.6 mU/L and a median value of 6.1 mU/L.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[14] 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 and ACS:180 systems. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur or ACS:180 systems.

Measuring Interval

The Atellica IM IRI assay provides results from 0.5–300.0 mU/L. The lower end of the measuring interval is defined by the design requirement for analytical sensitivity. Report results below the measuring interval as < 0.5 mU/L. When sample results exceed the measuring interval, refer to *Dilutions*.

Specificity

Cross-reactivity was determined in accordance with CLSI Document EP7-P[15] by spiking serum samples with the following compounds at the indicated levels. The following results were obtained:

Substance	Amount Added	Mean Recovery (%)
Proinsulin	1 µg/mL	100.8
C-peptide	500 ng/mL	95.1
Gastrin-1	1 µg/mL	96.6
Glucagon	1 µg/mL	100.2
Secretin	1 µg/mL	101.6

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.[16] The assay is designed to have an analytical sensitivity ≤ 0.5 mU/L, a limit of blank (LoB) ≤ 1.0 mU/L, and a limit of detection (LoD) ≤ 2.0 mU/L.

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

Analytical sensitivity is defined as the concentration of insulin that corresponds to the RLUs that are 2 standard deviations more than the mean RLUs of 20 replicate determinations of the insulin zero standard. This response is an estimate of the minimum detectable concentration with 95% confidence. The analytical sensitivity for the Atellica IM IRI assay is 0.3 mU/L.

The LoB corresponds to the highest measurement result that is likely to be observed for a blank sample. The LoB of the Atellica IM IRI assay is 0.6 mU/L.

The LoD corresponds to the lowest measurement of insulin that can be detected with a probability of 95%. The LoD for the Atellica IM IRI assay is 0.8 mU/L and was determined using 360 determinations, with 300 blank and 60 low-level replicates, and an LoB of 0.6 mU/L.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[17] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days. The assay was designed to have within-laboratory precision of ≤ 11% CV for samples from 0.5–10.0 mU/L, ≤ 10% CV for samples from 11.0–50.0 mU/L, and ≤ 11% CV for samples from 51.0–300.0 mU/L. The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (mU/L)	SD[b] (mU/L)	CV[c] (%)	SD (mU/L)	CV (%)
Serum A	80	3.7	0.07	1.8	0.13	3.5
Serum B	80	255.7	3.65	1.4	7.15	2.8
Control 1	80	14.9	0.14	0.9	0.43	2.9
Control 2	80	52.0	0.83	1.6	1.60	3.1
Control 3	80	161.7	2.44	1.5	5.77	3.6

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

Based on internal testing on the Atellica IM Analyzer, the overall reproducibility is estimated to be ≤ 11% CV for samples tested and includes multiple reagent lots, instruments, days, and replicates. Performance of the assay at individual laboratories may vary.

Assay Comparison

The Atellica IM IRI assay is designed to have a correlation coefficient of ≥ 0.95 and a slope of 1.0 ± 0.1 when compared to the ADVIA Centaur Insulin assay. Assay comparison was determined using the weighted Deming regression model in accordance with CLSI Document EP09-A3.[18] The following results were obtained:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ADVIA Centaur Insulin	y = 0.99x + 0.06 mU/L	1.8–266.5 mU/L	142	0.99

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

The relationship between the ADVIA Centaur and ACS:180 Insulin assays is described by this equation:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ACS:180 Insulin	y = 0.99x + 0.49 mU/L	1.1–319.1 mU/L	328	0.99

[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.

Interferences

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

Serum specimens that are . . .	Demonstrate ≤ 6% change in results up to . . .
hemolyzed	125 mg/dL of hemoglobin
icteric	20 mg/dL of bilirubin
lipemic	1000 mg/dL of lipid
hyperproteinemic	12 g/dL of protein

Results were established using the ADVIA Centaur system.

Dilution Recovery

Five human serum samples in the range of 129.7–237.8 mU/L of insulin were serially diluted 1:2, 1:4, and 1:8 with Insulin Diluent and assayed for recovery and parallelism. The recoveries ranged from 84.6%–109.4% with a mean of 94.6%.

Sample	Dilution	Observed (mU/L)	Expected (mU/L)	Recovery (%)
1	—	129.7	—	—
	1:2	55.8	64.9	86.0
	1:4	27.4	32.4	84.6

Sample	Dilution	Observed (mU/L)	Expected (mU/L)	Recovery (%)
	1:8	13.9	16.2	85.8
	Mean			85.5
2	—	192.7	—	—
	1:2	105.5	96.4	109.4
	1:4	47.0	48.2	97.5
	1:8	24.1	24.1	100.0
	Mean			102.3
3	—	237.8	—	—
	1:2	127.4	118.9	107.1
	1:4	56.1	59.4	94.4
	1:8	29.2	29.7	98.3
	Mean			99.9
4	—	229.9	—	—
	1:2	114.9	114.9	100.0
	1:4	51.3	57.5	89.3
	1:8	25.2	28.7	87.8
	Mean			92.4
5	—	154.0	—	—
	1:2	74.2	77.0	96.4
	1:4	33.6	38.5	87.2
	1:8	18.2	19.3	94.3
	Mean			92.6
Mean				94.6

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

Spiking Recovery

Varying amounts of insulin were added to 6 serum samples with endogenous insulin levels ranging from 2.6–8.1 mU/L. The amount of insulin that was added varied from 25.7–51.4 mU/L. When compared to the expected value, the measured (recovered) values of insulin averaged 108.5% with a range of 103.8%–113.8%.

Sample	Amount Added (mU/L)	Observed (mU/L)	Expected (mU/L)	Recovery (%)
1	—	2.9	—	—
	25.7	30.3	28.6	105.9

Sample	Amount Added (mU/L)	Observed (mU/L)	Expected (mU/L)	Recovery (%)
2	—	2.6	—	—
	51.4	58.4	53.9	108.3
3	—	4.8	—	—
	25.7	33.2	30.5	108.9
4	—	4.3	—	—
	51.4	61.3	55.7	110.1
5	—	8.1	—	—
	25.7	35.1	33.8	103.8
6	—	7.2	—	—
	51.4	66.7	58.6	113.8
Mean				108.5

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

High-Dose Hook Effect

High insulin concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with insulin concentrations as high as 3000 mU/L will report > 300.0 mU/L. Results were established using the Atellica IM Analyzer.

Standardization

The Atellica IM IRI assay is standardized against World Health Organization (WHO) 1st IRP 66/304. Assigned values for calibrators 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.

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10. Clinical and Laboratory Standards Institute. *Tubes and Additives for Venous and Capillary Blood Specimen Collection; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP39-A6.

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13. Vaidya HC, Beatty BG. Eliminating interference from heterophilic antibodies in a two-site immunoassay for creatine kinase MB by using F(ab')2 conjugate and polyclonal mouse IgG. *Clin Chem*. 1992;38(9):1737–1742.

14. Clinical and Laboratory Standards Institute. *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document EP28-A3c.

15. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Proposed Guideline*. Wayne, PA: Clinical and Laboratory Standards Institute; 1986. NCCLS Document EP7-P.

16. Clinical and Laboratory Standards Institute. *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI Document EP17-A2.

17. Clinical and Laboratory Standards Institute. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document EP05-A3.

18. Clinical and Laboratory Standards Institute. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013. CLSI Document EP09-A3.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]	EC REP	Authorized representative in the European Community	5.1.2[a]
	Use-by date	5.1.4[a]	CH REP	Authorized representative in Switzerland	Proprietary

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
REF	Catalog number	5.1.6[a]	LOT	Batch code	5.1.5[a]
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
< .../eifu >	Internet URL address to access the electronic instructions for use	Proprietary	Rev. XX	Version of Instructions for Use	Proprietary
IVD	*In vitro* diagnostic medical device	5.5.1[a]	Rev. REVISION	Revision	Proprietary
RxOnly	Prescription device (US only)	FDA[b]	UDI	Unique Device Identifier	5.7.10[c]
CE XXXX	CE Marking with Notified Body	EU IVDR[d]	CE	CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of temperature	5.3.5[a]
	Do not re-use	5.4.2[a]		Do not freeze	Proprietary
	Recycle	1135[e]		This way up	0623[e]
	Biological risks	5.4.1[a]		Caution	5.4.4[a]
UNITS C	Common Units	Proprietary	UNITS SI	International System of Units	Proprietary
YYYY-MM-DD	Date format (year-month-day)	N/A	YYYY-MM	Date format (year-month)	N/A
	Document face up[f]	1952[e]		Handheld barcode scanner	Proprietary
	Target	Proprietary		Mixing of substances	5657[g]
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	Proprietary		Interval	Proprietary
MATERIAL ID	Unique material identification number	Proprietary	MATERIAL	Material	Proprietary

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
CONTROL TYPE	Type of control	Proprietary	CONTROL NAME	Name of control	Proprietary
CONTROL LOT VAL	Quality control lot value	Proprietary	CAL LOT VAL	Calibrator lot value	Proprietary

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.
[b] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.
[c] ISO 15223-1:2020-04
[d] IVDR REGULATION (EU) 2017/746
[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.
[f] Indicates Assay-eNote
[g] International Electrotechnical Commission (IEC). IEC 60417-1 Graphical symbols for use on equipment – Part 1: Overview and Application

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