SIEMENS Healthineers

Free Thyroxine (FT4)

Current Revision and Date[a]	Rev. 06, 2023-01	
Product Name	Atellica IM Free Thyroxine (FT4)	REF 10995589 (50 tests) REF 10995588 (250 tests)
Abbreviated Product Name	Atellica IM FT4	
Test Name/ID	FT4	
Systems	Atellica CI Analyzer	
Materials Required but Not Provided	Atellica IM CAL A	REF 10995500 (2-pack) REF 10995501 (6-pack)
	Atellica IM APW1	REF 10995458
Optional Materials	Atellica IM FT4 MCM	REF 10995590
Specimen Types	Serum, EDTA plasma, heparinized plasma	
Sample Volume	25 µL	
Measuring Interval	0.10–12.00 ng/dL (1.29–154.80 pmol/L)	

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

CE

Intended Use

The Atellica® IM Free Thyroxine (FT4) assay is for *in vitro* diagnostic use in the quantitative determination of free thyroxine in human serum and plasma (EDTA and heparin), using the Atellica® CI Analyzer.

Measurements of free thyroxine are used in the diagnosis and treatment of thyroid disease.

Summary and Explanation

Thyroxine (3,5,3',5'-tetraiodothyronine, L-thyroxine or T_4) is a hormone synthesized and secreted by the thyroid gland and plays an important role in regulating metabolism. Secretion into the circulation is in response to the pituitary hormone TSH (thyroid-stimulating hormone) and is regulated by a negative feedback mechanism involving the thyroid gland, pituitary gland, and hypothalamus.[1,2]

In the circulation, 99.95% of T_4 is reversibly bound to transport proteins, primarily thyroxine-binding globulin (TBG) and to a lesser extent albumin and thyroxine-binding prealbumin (TBPA). The remaining T_4 is not bound to transport proteins, but is free in the circulation. This unbound fraction, or free T_4 (FT_4), is both metabolically active and a precursor to triiodothyronine (T_3).[1,3-5]

Free T_4 levels correlate with T_4 secretion and metabolism. In hypothyroidism and hyperthyroidism, FT_4 levels parallel changes in total T_4 levels.[4] Measuring free T_4 is useful when altered levels of total T_4 occur due to changes in T_4-binding proteins, especially TBG. TBG levels remain relatively constant in healthy individuals, but certain conditions, such as normal pregnancy and steroid therapy, can alter these levels. In these conditions, free T_4 levels are unchanged, while total T_4 levels parallel the changes in TBG.

Principles of the Procedure

The Atellica IM FT4 assay is a competitive immunoassay using direct chemiluminescent technology. FT_4 in the patient sample competes with acridinium-ester-labeled T_4 in the Lite Reagent for a limited amount of biotinylated rabbit polyclonal anti-T_4 antibody. Biotin-labeled anti-T_4 is bound to avidin that is covalently coupled to paramagnetic particles in the Solid Phase.

An inverse relationship exists between the amount of FT_4 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 FT4 ReadyPack® primary reagent pack **Lite Reagent** 5.0 mL/reagent pack T_4 labeled with acridinium ester (~0.2 µg/mL) in sodium barbital buffer (1.03%); protein stabilizers; EDTA; sodium azide (< 0.1%) **Solid Phase** 15.0 mL/reagent pack Biotinylated rabbit polyclonal anti-T_4 antibody (~0.525 µg/mL) bound to avidin covalently coupled to paramagnetic particles in sodium barbital buffer (1.03%); protein stabilizers; EDTA; sodium azide (< 0.1%)	Unopened at 2–8°C Onboard	Until expiration date on product 14 days
Atellica IM APW1 ReadyPack ancillary reagent pack[b] 25.0 mL/reagent pack 0.4 N sodium hydroxide	Unopened at 2–8°C Onboard	Until expiration date on product 14 days

[a] Refer to *Storage and Stability*.

[b] Refer to *Materials Required but Not Provided*.

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.

H290, H319, H315 P234, P264, P280, P337+P313, P390, P501	**Warning!** May be corrosive to metals. Causes serious eye irritation. Causes skin irritation. Keep only in original container. Wash hands thoroughly after handling. Wear protective gloves/protective clothing/eye protection/face protection. If eye irritation persists: Get medical advice/attention. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** sodium hydroxide (in Atellica IM APW1)

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.

Store Atellica IM APW1 in an upright position. Unopened reagents are 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

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 (EDTA and heparinized) are the recommended sample types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[6]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[7]
- Follow the instructions provided with your specimen collection device for use and processing.[8]
- Allow blood specimens to clot completely before centrifugation.[9]
- Keep tubes capped at all times.[9]

Storing the Specimen

- Do not use samples that have been stored at room temerature for longer than 8 hours.
- 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 sample is not assayed within 48 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 system online help.

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.[9]

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

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10995589	1 ReadyPack primary reagent pack containing Atellica IM FT4 Lite Reagent and Solid Phase FT4 master curve and test definition MC TDEF	50
10995588	5 ReadyPack primary reagent packs containing Atellica IM FT4 Lite Reagent and Solid Phase FT4 master curve and test definition MC TDEF	250

Materials Required but Not Provided

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

REF	Description	
	Atellica CI Analyzer[a]	
10995500	Atellica IM CAL A (calibrator)	2 x 5.0 mL low calibrator CAL L 2 x 5.0 mL high calibrator CAL H Calibrator lot-specific value sheet CAL LOT VAL
10995501	Atellica IM CAL A (calibrator)	6 x 5.0 mL low calibrator CAL L 6 x 5.0 mL high calibrator CAL H Calibrator lot-specific value sheet CAL LOT VAL
10995458	Atellica IM APW1 (probe wash)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH

[a] Additional system fluids are required to operate the system. 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	
10995590	Atellica IM FT4 MCM (master curve material)	7 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 100 µL of Lite Reagent and 300 µL of Solid Phase, then incubates for 12 minutes at 37°C.
3. Separates, aspirates, then washes the cuvette with special reagent water.

   Note For information about special reagent water requirements, refer to the system online help.
4. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
5. 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 system 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 system online help.

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 system online help.

Performing Calibration

For calibration of the Atellica IM FT4 assay, use the Atellica IM CAL A. 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	21
Pack Calibration	14
Reagent Onboard Stability	14

For information about lot calibration and pack calibration intervals, refer to the system 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 FT4 assay, use an appropriate quality control material of known analyte concentration with a minimum of two levels (low and high) at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use.

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 assigned values, 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 system determines the result using the calculation scheme described in the system online help. The system reports results in ng/dL (common units) or pmol/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: 1.0 ng/dL (common units) = 12.9 pmol/L (SI units)

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

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:

- Performance of this assay has not been established with neonatal specimens.
- The anticonvulsant drug phenytoin may interfere with total and free T_4 levels due to competition for TBG binding sites.
- Free T_4 values may be decreased in patients with non-thyroidal conditions and in patients taking carbamazepine.
- Thyroid autoantibodies in human serum may interfere and cause falsely elevated free T_4 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.[10,11]

Expected Values

The reagent formulations used on the Atellica CI Analyzer are the same as those used on the ADVIA Centaur® system and ACS:180™ system. Expected values were established using the ADVIA Centaur system or ACS:180 system and confirmed by assay comparison. Refer to *Assay Comparison*.

Data were obtained on serum samples from 388 apparently healthy individuals. Based on this population, the following reference intervals were established using the ACS:180™ system:

Clinical Condition	FT4 Range (ng/dL)	FT4 Range (pmol/L)
Euthyroid	0.89–1.76	11.5–22.7
Hypothyroid	< 0.89	< 11.5
Hyperthyroid	> 1.76	> 22.7

Based on a pediatric population (infants, children, and adolescents), reference intervals were established using the ADVIA Centaur system in accordance with the CLSI guideline C28-A3c.[12] Samples were collected prospectively from apparently healthy (euthyroid) pediatric subjects, using predefined inclusion criteria.

The reference interval for infants was calculated by a robust measure of location and spread as developed by Horn and Pesce.[13] A non-parametric approach based on the CLSI guideline was used to establish reference intervals for children and adolescents. The 2.5th and 97.5th percentiles of the distribution of values were calculated for each age group. Based on this population, the following reference intervals were established using the ADVIA Centaur system:

		Reference Intervals	
Pediatric Age Group	Number of Samples	(ng/dL)	(pmol/L)
Infants (1–23 months)	72	0.94–1.44	12.1–18.6
Children (2–12 years)	190	0.86–1.40	11.1–18.1
Adolescents (13–20 years)	129	0.83–1.43	10.7–18.4

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 CI Analyzer are the same as those used on the Atellica IM Analyzer and ADVIA Centaur system. Some performance characteristics were established using the Atellica IM Analyzer or ADVIA Centaur system.

Measuring Interval

The Atellica IM FT4 assay is linear from 0.10–12.00 ng/dL (1.29–154.80 pmol/L). The lower limit of the measuring interval is defined by the design requirement for the analytical sensitivity. Report results below the measuring interval as < 0.10 ng/dL (< 1.29 pmol/L).

Specificity

The cross-reactivity can be expressed as the ratio of:

- the amount of T_4 required to displace 50% of the maximally bound labeled T_4 from the anti-T_4 antibody, and
- the amount of the cross-reactant to give the same 50% displacement.

Cross-Reactant	Highest Amount Added (mg/dL)	% Cross-Reactivity
L-Triiodothyronine	1.00	< 0.02
Diiodotyrosine	100	< 0.02
Monoiodotyrosine	100	< 0.02
3,5-Diiodo-L-Thyronine	10.0	< 0.02
Reverse Triiodothyronine (rT3)	1.50	< 0.02

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

Detection Capability

Analytical Sensitivity	0.10 ng/dL (1.29 pmol/L)
Limit of Blank (LoB)	0.10 ng/dL (1.29 pmol/L)
Limit of Detection (LoD)	0.30 ng/dL (3.87 pmol/L)
Limit of Quantitation (LoQ)	0.30 ng/dL (3.87 pmol/L)

Analytical sensitivity is defined as the concentration of FT_4 that corresponds to the RLUs that are 2 standard deviations less than the mean RLUs of 20 replicate determinations of the FT4 zero standard. This response is an estimate of the minimum detectable concentration with 95% confidence.

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 FT_4 that can be detected with a probability of 95%.

The LoQ corresponds to the lowest amount of FT_4 in a sample at which the within laboratory CV is ≤ 20%.

Detection capability was determined in accordance with CLSI Document EP17-A2.[15]

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[16] Samples were assayed on an Atellica CI Analyzer in duplicate in 2 runs per day for 20 days. The following results are representative of the performance of the assay:

		Mean		Repeatability			Within-Laboratory Precision		
				SD[b]		CV[c]	SD		CV
Sample Type	N[a]	(ng/dL)	(pmol/L)	(ng/dL)	(pmol/L)	(%)	(ng/dL)	(pmol/L)	(%)
Serum A	80	0.37	4.77	0.010	0.129	2.7	0.023	0.297	6.3
Serum B	80	0.81	10.45	0.011	0.142	1.3	0.048	0.619	5.9
Serum C	80	4.21	54.31	0.047	0.606	1.1	0.132	1.703	3.1
Serum D	80	11.15	143.84	0.172	2.219	1.5	0.536	6.914	4.8
Control 1	80	0.89	11.48	0.012	0.155	1.3	0.032	0.413	3.6

		Mean		Repeatability			Within-Laboratory Precision		
				SD[b]		CV[c]	SD		CV
Sample Type	N[a]	(ng/dL)	(pmol/L)	(ng/dL)	(pmol/L)	(%)	(ng/dL)	(pmol/L)	(%)
Control 2	80	1.95	25.16	0.022	0.284	1.1	0.065	0.839	3.4
Control 3	80	3.43	44.25	0.076	0.980	2.2	0.144	1.858	4.2

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

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

Reproducibility

Reproducibility was determined in accordance with CLSI Document EP05-A3 using the Atellica CI Analyzer.[16] Samples were assayed in replicates of 5 with 1 run per day for 5 days using 3 instruments and 3 reagent lots (225 measurements per sample).

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

		Repeatability		Between Day		Between Lot		Between Instrument		Reproducibility	
Sample	Mean ng/dL (pmol/L)	SD ng/dL (pmol/L)	CV (%)	SD ng/dL (pmol/L)	CV (%)	SD ng/dL (pmol/L)	CV (%)	SD ng/dL (pmol/L)	CV (%)	SD ng/dL (pmol/L)	CV (%)
Serum A	0.39 (5.03)	0.015 (0.194)	3.8	0.014 (0.181)	3.6	0.008 (0.103)	2.1	0.000 (0.000)	0.0	0.022 (0.284)	5.6
Serum B	0.87 (11.22)	0.020 (0.258)	2.3	0.023 (0.297)	2.6	0.008 (0.103)	0.9	0.016 (0.206)	1.8	0.036 (0.464)	4.1
Serum C	4.34 (55.99)	0.076 (0.980)	1.8	0.084 (1.084)	1.9	0.000 (0.000)	0.0	0.054 (0.697)	1.2	0.126 (1.625)	2.9
Serum D	9.59 (123.71)	0.291 (3.754)	3.0	0.261 (3.367)	2.7	0.203 (2.619)	2.1	0.294 (3.793)	3.1	0.530 (6.837)	5.5
Control 1	0.89 (11.48)	0.019 (0.245)	2.1	0.021 (0.271)	2.4	0.000 (0.000)	0.0	0.000 (0.000)	0.0	0.029 (0.374)	3.3
Control 2	2.36 (30.44)	0.035 (0.452)	1.5	0.034 (0.439)	1.4	0.000 (0.000)	0.0	0.000 (0.000)	0.0	0.049 (0.632)	2.1
Control 3	3.53 (45.54)	0.067 (0.864)	1.9	0.033 (0.426)	0.9	0.011 (0.142)	0.3	0.038 (0.490)	1.1	0.084 (1.084)	2.4

The assay was designed to have the following reproducibility:

Concentration Interval		Reproducibility
(ng/dL)	(pmol/L)	
< 0.50	< 6.45	≤ 0.04 ng/dL SD (≤ 0.52 pmol/L SD)
0.50–1.00	6.45–12.90	≤ 8.0% CV
> 1.00	> 12.90	≤ 6.0% CV

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

Assay Comparison

Assay comparison was determined with the weighted Deming regression model in accordance with CLSI Document EP09c-ed3.[17]

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

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	Atellica IM FT4 on Atellica IM Analyzer	y = 0.97x + 0.02 ng/dL (y = 0.97x + 0.26 pmol/L)	0.43–11.51 ng/dL (5.55–148.48 pmol/L)	110	0.997
Serum	ADVIA Centaur FT4	y = 1.01x - 0.05 ng/dL (y = 1.01x - 0.65 pmol/L)	0.41–10.11 ng/dL (5.29–130.42 pmol/L)	111	0.992

[a] Number of samples tested.

[b] Correlation coefficient.

The assay is designed to have a correlation coefficient of ≥ 0.97 and a slope of 1.00 ± 0.10.

For 283 samples in the range of 0.14–11.1 ng/dL (1.81–143 pmol/L), the relationship between the ADVIA Centaur FT4 assay and the ACS:180 FrT4 assay is described using ordinary least squares regression by the following equation:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ACS:180 FrT4	y = 0.973x + 0.016 ng/dL (y = 0.973x + 0.21 pmol/L)	0.14–11.1 ng/dL (1.81–143.19 pmol/L)	283	0.995

[a] Number of samples tested.

[b] Correlation coefficient.

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

Specimen Equivalency

Specimen equivalency was determined using Deming regression. The following results were obtained:

Specimen (y)	Reference Specimen (x)	Regression Equation	Sample Interval	N[a]	r[b]
Heparin plasma	Serum	y = 0.979x + 0.06 ng/dL (y = 0.979X + 0.8 pmol/L)	0.2–11.4 ng/dL (2.6–147.1 pmol/L)	133	0.997
EDTA plasma	Serum	y = 0.967x + 0.01 ng/dL (y = 0.967x + 0.1 pmol/L)	0.2–10.0 ng/dL (2.6–129.0 pmol/L)	108	0.998

[a] Number of samples tested.

[b] Correlation coefficient.

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 EP7-A2.[18]

The following substances were added to serum samples containing different levels of FT_4. When tested against the appropriate control, the percent change was noted. The table below shows the mean percent change for each set of samples with FT_4 values in the range of 0.95–5.49 ng/dL (12.2–70.8 pmol/L).

Substance	Amount Added (mg/dL)	% Change
Propylthiouracil	4.00	-0.771
Methimazole	0.40	0.318
Phenylbutazone	15.0	6.338
Phenytoin	4.00	3.833
Sodium Salicylate	50.0	1.849
Aspirin	50.0	1.102

Hemolysis, Icterus, and Lipemia (HIL)

Serum specimens that are or that contain . . .	Have an insignificant effect on the assay up to . . .
hemolyzed	300 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	20 mg/dL of bilirubin
biotin	3500 ng/mL of biotin

Results were established using the ADVIA Centaur system, except for biotin which were established using an Atellica IM Analyzer.

Standardization

The Atellica IM FT4 assay is traceable to an internal standard manufactured using U.S.P. (United States Pharmacopeia) material. Assigned values for calibrators are traceable to this standardization.

Technical Assistance

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

siemens-healthineers.com

References

1. Kaplan MM. Thyroid function testing in patients with thyroid and non-thyroid diseases. Mono: Thyroid Testing. Emeryville, CA: Chiron Diagnostics Corporation; 1996.
2. Fisher DA. Physiological variations in thyroid hormones: physiological and pathophysiological considerations. *Clin Chem*. 1996;42(1):135-139.
3. Chen IW, Sperling MI. Thyroxine. In: Kaplan LA, Pesce AJ, eds. *Clinical Chemistry: Theory, Analysis, and Correlation*. 2nd ed. St. Louis, MO: CV Mosby; 1989:952–956.
4. Watts NB, Keffer JH. *Practical Endocrine Diagnosis*. 3rd ed. Philadelphia, PA: Lea and Febiger; 1982:1–27, 77–96.
5. Chattoraj SC, Watts NB. Endocrinology. In: Tietz NW, ed. *Fundamentals of Clinical Chemistry*. 3rd ed. Philadelphia, PA: WB Saunders; 1986:550–551.
6. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document M29-A4.

7. Clinical and Laboratory Standards Institute. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2007. CLSI Document GP41-A6.
8. 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.
9. Clinical and Laboratory Standards Institute. *Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP44-A4.
10. Kricka LJ. Human anti-animal antibody interferences in immunological assays. *Clin Chem*. 1999;45(7):942–956.
11. 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.
12. 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 (formerly C28-A3c).
13. Horn PS, Pesce AJ. *Reference Intervals: A User's Guide,* Washington, DC: AACC Press; 2005.
14. Clinical and Laboratory Standards Institute. *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2000. CLSI Document C28-A2.
15. 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.
16. 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.
17. 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; 2018. CLSI Document EP09c-ed3.
18. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP7-A2.

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		Authorized representative in Switzerland
	Catalog number		Batch code
	Consult Instructions for Use		Contains sufficient for <n> tests

Symbol	Symbol Title	Symbol	Symbol Title
<…/eifu>	Internet URL address to access the electronic instructions for use	Rev. XX	Version of Instructions for Use
IVD	*In vitro* diagnostic medical device	Rev. REVISION	Revision
RxOnly	Prescription device (US only)	UDI	Unique Device Identifier
CE XXXX	CE Marking with Notified Body	CE	CE Marking
	Temperature limit		Keep away from sunlight
	Upper limit of temperature		Lower limit of temperature
	Do not re-use		Do not freeze
	Recycle		This way up
	Biological risks		Caution
UNITS C	Common Units	UNITS SI	International System of Units
YYYY-MM-DD	Date format (year-month-day)	YYYY-MM	Date format (year-month)
	Document face up[a]		Handheld barcode scanner
	Target		Mixing of substances
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.		Interval
MATERIAL ID	Unique material identification number	MATERIAL	Material
CONTROL TYPE	Type of control	CONTROL NAME	Name of control
CONTROL LOT VAL	Quality control lot value	CAL LOT VAL	Calibrator lot value

[a] Indicates Assay-eNote

Legal Information

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591 USA

Siemens Healthineers Headquarters
Siemens Healthcare GmbH
Henkestraße 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens-healthineers.com