BECKMAN COULTER

CE 2797

ACCESS
Immunoassay Systems

Instructions For Use

Access Free T4
Thyroxine, Free

REF 33880

FOR PROFESSIONAL USE ONLY

For *in vitro* diagnostic use

Rx Only

For use on DxI Access Immunoassay Analyzers

PRINCIPLE

INTENDED USE

The Access Free T4 assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of free thyroxine levels in human serum and plasma (heparin) using the Access Immunoassay Systems.

SUMMARY AND EXPLANATION

The clinical importance of free T4 determination is as an aid in the diagnosis of thyroid disorders.[1,2,3,4]

The hypothalamic-pituitary-thyroid axis controls thyroid hormone synthesis, release, and action. Thyrotropin-releasing hormone (TRH) secreted from the hypothalamus stimulates the synthesis and release of thyrotropin or thyroid-stimulating hormone (TSH). TSH, in turn, stimulates the synthesis, storage, secretion, and metabolism of thyroxine (T4) and triiodothyronine (T3). Both free and bound forms of T4 and T3 are present in the blood. More than 99% of the T4 and T3 circulate in the blood bound to carrier proteins, leaving less than 1% unbound. It is this level of unbound or free hormone that correlates with the functional thyroid state in most individuals.[5,6]

Free T4 and free T3 regulate normal growth and development by maintaining body temperature and stimulating calorigenesis. In addition, free T4 and free T3 affect all aspects of carbohydrate metabolism as well as certain areas of lipid and vitamin metabolism.

Elevated free T4 levels support the clinical findings of a diagnosis of hyperthyroidism while low free T4 levels coupled with appropriate clinical findings, can establish a diagnosis of hypothyroidism. Measurement of free T4 levels along with other thyroid tests and clinical findings can establish subclinical hyperthyroid and hypothyroid diagnoses.[3,4,7]

Equilibrium dialysis RIA is considered the reference method for measuring free T4 because it allows for the separation of free T4 from protein bound T4 before direct measurement of the free T4.[6] However, this method is cumbersome, technically demanding, and not suited to routine clinical laboratory use. More recently, radioimmunoassays and enzyme immunoassays have been developed for measuring free T4. These assays employ various combinations of analog or non-analog tracers and one-step or two-step incubation procedures.

METHODOLOGY

Assay type: two-step, competitive

The Access Free T4 assay is a two-step enzyme immunoassay. Monoclonal anti-Thyroxine (T4) antibody coupled to biotin, sample, buffered protein solution, and streptavidin-coated solid phase are added to the reaction vessel. During this first incubation the anti-T4 antibody coupled to biotin binds to the solid phase and the free T4 in the sample. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials

are washed away. Next, buffered protein solution and triiodothyronine (T3)-alkaline phosphatase conjugate are added to the reaction vessel. The T3-alkaline phosphatase conjugate binds to the vacant anti-T4 antibody binding sites.

After incubation, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is inversely proportional to the concentration of analyte in the sample. Analyte concentration is automatically determined from a stored calibration.

SPECIMEN

SPECIMEN COLLECTION AND PREPARATION

1. Serum and plasma (heparin) are the recommended samples.
2. Observe the following recommendations for handling, processing, and storing blood samples:[8,9]
   - Collect all blood samples observing routine precautions for venipuncture.
   - Allow serum samples to clot completely before centrifugation.
   - Keep tubes stoppered at all times.
   - Physically separate serum or plasma from contact with cells as soon as possible.
   - Store samples tightly stoppered at room temperature (15 to 30°C) for no longer than eight hours.
   - If the assay will not be completed within eight hours, refrigerate the samples at 2 to 8°C.
   - If the assay will not be completed within 48 hours, or for shipment of samples, freeze at -20°C or colder.
   - Thaw samples only once.
3. Use the following guidelines when preparing specimens:
   - Ensure residual fibrin and cellular matter has been removed prior to analysis.
   - Follow blood collection tube manufacturer's recommendations for centrifugation.
4. Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot to lot.

REAGENTS

CONTENTS

Access Free T4 Reagent Pack

Ref. No. 33880: 100 determinations, 2 packs, 50 tests/pack

The same reagent formulation is used on all Access Immunoassay Systems.

- All antisera are polyclonal unless otherwise indicated.

Well	Contents	Ingredients
R1a:	3.25 mL	Dynabeads* paramagnetic particles coated with streptavidin in a TRIS buffer with protein (aves), surfactant, 0.125% NaN_3, and 0.125% ProClin** 300.
R1b:	13.25 mL	TRIS buffered saline with protein (aves), surfactant, < 0.1% NaN_3, and 0.1% ProClin 300.
R1c:	3.1 mL	TRIS buffered saline with protein (aves), surfactant, 0.125% NaN_3, and 0.125% ProClin 300.

Well	Contents	Ingredients
R1d:	3.1 mL	Triiodothyronine-alkaline phosphatase (bovine) conjugate in a TRIS buffer with protein (aves), surfactant, < 0.1% NaN_3, and 0.1% ProClin 300.
R1e:	3.1 mL	Mouse monoclonal anti-Thyroxine (T4) coupled to biotin in a TRIS buffer with protein (aves and murine), surfactant, 0.125% NaN_3, and 0.125% ProClin 300.

*Dynabeads is a registered trademark of Dynal A.S., Oslo, Norway.

**ProClin is a trademark of LANXESS Corp.

WARNING AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Patient samples and blood-derived products may be routinely processed with minimum risk using the procedure described. However, handle these products as potentially infectious according to universal precautions and good clinical laboratory practices, regardless of their origin, treatment, or prior certification. Use an appropriate disinfectant for decontamination. Store and dispose of these materials and their containers in accordance with local regulations and guidelines.
- For hazards presented by the product refer to the following sections: REACTIVE INGREDIENTS and GHS HAZARD CLASSIFICATION.

REACTIVE INGREDIENTS

⚠ CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).
To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.

GHS HAZARD CLASSIFICATION

PMP (Compartment R1a) WARNING

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.
P273	Avoid release to the environment.
P280	Wear protective gloves, protective clothing and eye/face protection.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before use.
	Sodium Azide < 0.18%
	reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%

Buffer 1 (Compartment R1b)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Buffer 2 (Compartment R1c)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		Sodium Azide < 0.18%
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Conjugate (Compartment R1d)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.

		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
Biotin Reagent (Compartment R1e)	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		Sodium Azide < 0.18%
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

SUPPLEMENTAL HAZARD

This product is subject to EU REACH and UK REACH Authorisation:

EUREACH/23/15/6, EUREACH/23/15/7, EUREACH/23/15/8, EUREACH/23/15/9, EUREACH/23/15/10, EUREACH/23/15/11, EUREACH/23/15/12

UKREACH/22/03/0

See Safety Data Sheet Section 15 for more details.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

1. Access Free T4 Calibrators
   Provided at zero and approximately 0.5, 1.0, 2.0, 3.0, and 6.0 ng/dL (6.4, 12.9, 25.7, 38.6, and 77.2 pmol/L).
   Ref. No. 33885
2. Quality Control (QC) materials: commercial control material.
3. Lumi-Phos PRO
   Ref. No. B96000
4. UniCel DxI Wash Buffer II
   Ref. No. A16793

REAGENT PREPARATION

Provided ready to use.

REAGENT STORAGE AND STABILITY

Stability	
Unopened at 2 to 10°C	Up to stated expiration date
After opening at 2 to 10°C	28 days

- Store upright.
- Refrigerate at 2 to 10°C for a minimum of two hours before use on the instrument.
- Signs of possible deterioration are a broken elastomeric layer on the pack or quality control values out of range.
- If the reagent pack is damaged (e.g., broken elastomer), discard the pack.

CALIBRATION

CALIBRATION INFORMATION

An active calibration is required for all tests. Calibration is required every 28 days. See calibrator Instructions For Use (IFU) for additional calibration information. Refer to the appropriate system manuals and/or Help system for information on calibration method, configuring calibrators, calibrator test request entry, and reviewing calibration data.

QUALITY CONTROL

Quality control materials are essential for monitoring the system performance. Quality controls with varying concentration ranges should be run individually at least once every 24 hours when the assay is being performed.[10] Quality control ranges should be determined by each laboratory's individual requirements. Follow applicable regulations and guidelines for quality control.

TESTING PROCEDURE(S)

PROCEDURE

1. Refer to the appropriate system manuals and/or Help system for a specific description of installation, start-up, principles of operation, system performance characteristics, operating instructions, calibration procedures, operational limitations and precautions, hazards, maintenance, and troubleshooting.
2. Refer to the appropriate system manuals and/or Help system for information on managing samples, configuring tests, requesting tests, and reviewing test results.
3. Mix contents of new (unpunctured) reagent packs by gently inverting pack several times before loading on the instrument. Do not invert open (punctured) packs.
4. Use 30 µL of sample for each determination in addition to the sample container and system dead volumes. Refer to the appropriate system manuals and/or Help system for the minimum sample volume required.
5. The system default unit of measure for sample results is ng/dL. To change sample reporting units to the International System of Units (SI units), pmol/L, refer to the appropriate system manuals and/or Help system. To manually convert concentrations to the International System, multiply ng/dL by multiplication factor 12.87.

LIMITATIONS

1. For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce human anti-animal antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other antibodies such as human anti-goat antibodies

may be present in patient samples.[11,12] Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.

2. Other potential interferences in the patient sample could be present and may cause erroneous results in immunoassays. Some examples that have been documented in literature include rheumatoid factor, endogenous alkaline phosphatase, fibrin, and proteins capable of binding to alkaline phosphatase.[13] Carefully evaluate results if the sample is suspected of having these types of interferences.
3. The results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information.
4. Samples containing thyroxine autoantibodies can be assayed in two step procedures such as the Access Free T4 assay without significant interference.[6]
5. Non-thyrometabolic disorders may cause abnormal free T4 levels. Anticonvulsant drug therapy (particularly phenytoin) may result in decreased free T4 levels due to an increased hepatic metabolism, and secondarily to displacement of hormone from binding sites.[6,14,15] Anti-inflammatory drugs such as salicylate and phenylbutazone also compete for hormone binding sites, but their effect on free T4 levels has not been clearly defined.[6,16] Patients on heparin therapy may have elevated free T4 levels due to release of non esterified fatty acids, which can alter the relationship between free and bound hormones.[15] Determination of thyroid status in patients with non-thyroidal illness (NTI) should be interpreted with caution.[6,17]In rare conditions, such as Familial Dysalbuminemic Hyperthyroxinemia (FDH), direct free hormone assays may yield erroneous results due to the extreme variations in the albumin-binding capacity for T4.

The following substances were added to euthyroid serum samples. When tested in the Free T4 assay, the observed mean percent changes in Free T4 values were as follows:

Substance	Amount Added (mg/dL)	% Change
Aspirin	60	+6.4
Sodium Salicylate	50	+9.1
Phenylbutazone	7.5	+8.48
Thiouracil	5.0	-0.6
Phenytoin	5.0	+8.0
Methimizole	0.4	+0.9

6. This assay is not significantly influenced by the presence of thyroxine hormone binding proteins. In one study, the zero calibrator, which contains normal levels of protein, was spiked with the following human source thyroxine hormone binding proteins. Below is the observed change to the assay signal response.

Substance	Amount Added	% Change
Albumin	10.0 g/dL	-7.2
Thyroxine binding globulin (TBG)	160 µg/mL	-5.6
Prealbumin	600 µg/mL	-1.3

7. This assay is susceptible to interference from high levels of biotin. The recommended daily intake for biotin is 30 µg. High doses of biotin (up to 30 mg per day) may be taken as a dietary supplement aimed at improving hair loss, nail growth, or skin condition.[18]
    - Some pharmacokinetic studies have shown that serum concentrations of biotin can reach up to 300 ng/mL when subjects taking supplements containing 20 mg biotin[19] or 1,160 ng/mL for subjects taking doses of biotin up

to 300 mg.[18] These studies were performed in apparently healthy subjects and some patients may be taking supplements with biotin at levels > 20 mg per day.

- Clearance rates of biotin may differ between patients tested with this device (e.g., patients with renal impairment), which may lead to higher than expected, or prolonged, concentrations in serum. If medically practicable, patients receiving biotin supplements should discontinue use prior to sample draws to minimize the risk of interference. Specimens with biotin concentrations ≤ 10 ng/mL demonstrated non-significant bias (≤ 10%) in results. Biotin concentrations > 10 ng/mL can lead to significant (> 10%) positive bias in Free T4 results.
- If unexpected results are obtained, and biotin interference is suspected, the Beckman Coulter TSH assay may provide a better assessment of thyroid function as it is not susceptible to biotin interference.

RESULTS INTERPRETATION

Test results are determined automatically by the system software. Test results can be reviewed using the appropriate screen. Refer to the appropriate system manuals and/or Help system for complete instructions on reviewing sample results.

REPORTING RESULTS

MEASURING INTERVAL

Approximately 0.32 - 6.0 ng/dL (4.12 - 77 pmol/L)

Samples can be accurately measured within the measuring interval defined as the lower Limit of Quantitation (LoQ) and the highest calibrator value.

1. If a sample contains less than the lower limit for the assay, report the result as less than that value.
2. If a sample contains more than the stated value of the highest calibrator, report the result as greater than that value.

SAMPLES CANNOT BE DILUTED FOR FREE T4 DETERMINATIONS

EXPECTED RESULTS

1. Each laboratory should validate or establish its own reference intervals to assure proper representation of specific populations.
2. Sera samples were obtained from a minimum of 150 males and 150 females ranging in age from 18-60 years old. The samples were collected from the east, west and central United States. Following the guidance of both the National Academy of Clinical Biochemists (NACB) Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease[20] and the American Association of Clinical Endocrinologists,[21,22,23] the following screening criteria was utilized: TSH value 0.3-3.0 µIU/mL, no known personal or family history of thyroid disease or autoimmune disease and the absence of thyroid medication. After completing the Access TSH screen, 32 samples were excluded due to TSH values outside of the 0.3-3.0 µIU/mL range.

n	95% Reference Limit (ng/dL)	95% CI for Lower Limit (ng/dL)	95% CI for Upper Limit (ng/dL)
316	0.61 - 1.12	0.54 - 0.67	1.07 - 1.24

n	95% Reference Limit (pmol/L)	95% CI for Lower Limit (pmol/L)	95% CI for Upper Limit (pmol/L)
316	7.86 - 14.41	7.00 - 8.57	13.73 - 15.96

3. Sera samples were obtained from a minimum of 120 women in the first, second and third trimester of pregnancy.

Sample Type	n	95% Reference Limit (ng/dL)	90% CI for Lower Limit (ng/dL)	90% CI Upper Limit (ng/dL)
1st Trimester	131	0.52 - 1.10	0.47 - 0.57	1.08 - 1.27
2nd Trimester	120	0.45 - 0.99	0.40 - 0.48	0.80 - 1.08
3rd Trimester	121	0.48 - 0.95	0.45 - 0.51	0.83 - 1.23

Sample Type	n	95% Reference Limit (pmol/L)	90% CI for Lower Limit (pmol/L)	90% CI Upper Limit (pmol/L)
1st Trimester	131	6.67 - 14.12	6.00 - 7.31	13.86 - 16.28
2nd Trimester	120	5.79 - 12.70	5.19 - 6.14	10.24 - 13.86
3rd Trimester	121	6.11 - 12.20	5.77 - 6.62	10.68 - 15.79

4. The Access Free T4 Assay has not been validated for dry blood spot samples.

PERFORMANCE CHARACTERISTICS

ASSAY CRITERIA AND REPRESENTATIVE DATA

Representative data is provided for illustration only. Performance obtained in individual laboratories may vary.

METHODS COMPARISON

A study based on CLSI EP09c, 3rd Edition[24] using Passing-Bablok regression and Pearson's correlation compared the Access 2 Immunoassay System and the DxI 9000 Access Immunoassay Analyzer.

N	Concentration Range* (ng/dL)	Slope	Slope 95% CI	Intercept	Intercept 95% CI	Correlation Coefficient R
113	0.35 - 4.8	1.02	0.99 - 1.04	-0.037	(-0.059) - (0.011)	1.00

*Range is Access 2 values

IMPRECISION

The assay was designed to have within-laboratory imprecision as listed below:

- < 0.06 ng/dL (0.77 pmol/L) SD at concentrations < 0.61 ng/dL (7.9 pmol/L)
- ≤ 10.0% CV at concentrations ≥ 0.61 ng/dL (7.9 pmol/L)

A study based on CLSI EP05-A3[25] performed on the DxI 9000 Access Immunoassay Analyzer tested multiple samples in duplicate in 2 runs per day for a minimum of 20 days.

ng/dL			Repeatability (Within-Run)		Between-Run		Between-Day		Within-Laboratory	
Sample	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	80	0.46	0.02	3.9	0.00	0.0	0.02	3.4	0.02	5.2
Sample 2	80	0.84	0.02	2.6	0.00	0.3	0.02	2.5	0.03	3.6
Sample 3	80	1.1	0.02	2.3	0.01	0.5	0.03	2.4	0.04	3.3

ng/dL			Repeatability (Within-Run)		Between-Run		Between-Day		Within-Laboratory	
Sample	**N**	**Mean**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sample 4	80	2.2	0.04	2.0	0.00	0.0	0.04	1.8	0.06	2.7
Sample 5	80	4.0	0.10	2.4	0.00	0.0	0.06	1.4	0.11	2.8

ANALYTICAL SPECIFICITY / INTERFERENCES

Samples containing up to 10 mg/dL (171 µmol/L) bilirubin, lipemic samples containing the equivalent of 1,800 mg/dL (20.32 mmol/L) triolein, and hemolyzed samples containing up to 1 g/dL (10 g/L) hemoglobin do not affect the concentration of free T4 assayed.

The following table describes the cross-reactivity of the antibody used in the Free T4 assay with substances which are similar in structure to T4. The antibody specificity is determined in a total thyroxine assay to avoid binding displacement of T4 by related compounds. The substances were added to an Access Free T4 calibrator pool and found to give the following results expressed by weight.

Substance	Analyte Added (µg/dL)	Cross-reactivity (%)
L-T4	5	> 100
D-T4	10	71
L-T3	500	1.7
R-T3	100	23
Tetraiodothyroacetic Acid	25	4
D-T3	500	0.7
3,3' L-T2	5,000	< 0.1
3,5 L-T2	5,000	< 0.1
3',5' L-T2	5,000	< 0.1
L-Tyrosine	5,000	< 0.01
d-Tyrosine	5,000	< 0.01
Monoiodotyrosine	5,000	< 0.01
Diiodotyrosine	5,000	< 0.01

Biotin

The following concentrations of biotin were spiked into normal serum samples at high and low Free T4 concentrations and found to give the following percent change in result response.

		Biotin (ng/mL)					
Analyte Range	**Analyte Concentration**	**10**	**25**	**100**	**300**	**600**	**1,200**
Low	0.7 - 0.9 ng/dL	6%	14%	140%	371%	545%	*
High	1.8 - 4.3 ng/dL	8%	13%	*	*	*	*

* = Result above assay measuring range

DETECTION CAPABILITY

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) studies were conducted on the DxI 9000 Access Immunoassay Analyzer following CLSI guideline EP17-A2.[26] The LoB study included multiple reagent lots and 3 instruments over a minimum of 3 days. The LoD and LoQ studies included multiple reagent lots and 3 instruments over a minimum of 5 days.

	Maximum Observed Result		Design Criteria	
	ng/dL	pmol/L	ng/dL	pmol/L
Limit of Blank (LoB)	0.18	2.34	≤ 0.25	≤ 3.22
Limit of Detection (LoD)	0.22	2.89	≤ 0.32	≤ 4.12
Limit of Quantitation (LoQ) ≤ 20% within-lab CV	0.22	2.89	≤ 0.32	≤ 4.12

ADDITIONAL INFORMATION

For a patient/user/third party in the European Union and in countries with identical regulatory regime (Regulation 2017/746/EU on In vitro Diagnostic Medical Devices); if, during the use of this device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and/or its authorized representative and to your national authority.

REVISION HISTORY

Revision A

New release of DxI Access Immunoassay Analyzer reagent IFU.

Revision B

Added Translations.

Revision C

Added Translations.

Revision D

Updated ProClin trademark statement.

Revision E

Added Translations.

Revision F

Updated "Reagents" section.

SYMBOLS KEY

Glossary of Symbols is available at beckmancoulter.com/techdocs (document number C02724).

REFERENCES

1. Esfandiari, Nazanene & Papaleontiou, Maria. (2017). Biochemical Testing in Thyroid Disorders. Endocrinology and Metabolism Clinics of North America. 46. 10.1016/ j.ecl.2017.04.002.

2. N Rifai, AR Horvath, and CT Wittwer. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 6th ed. 2018 Elsevier, St. Louis, Missouri. In Chapter 67: Thyroid Disorders. DB Freedman, D Halsall, WJ Marshall and C Ellervik. Pages 1572-1616.

3. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, et al.; American Thyroid Association Task Force on Thyroid Hormone Replacement. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. Thyroid. 2014 Dec; 24(12):1670 -751.

4. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. 2016 Oct;26(10):1343 -421.

5. Gornall, AG, Luxton, AW, Bhavnani, BR. Endocrine disorders. In Applied Biochemistry of Clinical Disorders. 1986, 305-318. Philadelphia, PA: J. B. Lippincott Co.

6. White, GH. Recent advances in routine thyroid function testing. CRC - Critical Reviews in Clinical Laboratory Sciences, 1987, 24: 315-362.

7. Lazarus J, Brown RS, Daumerie C, Hubalewska-Dydejczyk A, Negro R, Vaidya B. 2014 European thyroid association guidelines for the management of subclinical hypothyroidism in pregnancy and in children. Eur Thyroid J. 2014 Jun;3(2):76-94.

8. Approved Guideline - Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests, GP44-A4. 2010. Clinical and Laboratory Standards Institute.

9. World Health Organization. (2002). Use of Anticoagulants in Diagnostic Laboratory Investigations (WHO Standard No. WHO/DIL/LAB/99.1 Rev.2).

10. Cembrowski GS, Carey RN. Laboratory quality management: QC ⇌ QA. ASCP Press, Chicago, IL, 1989.

11. Kricka L. Interferences in immunoassays - still a threat. Clin Chem 2000; 46: 1037-1038.

12. Bjerner J, et al. Immunometric assay interference: incidence and prevention. Clin Chem 2002; 48: 613-621.

13. Lingwood D, Ballantyne JS. Alkaline phosphatase-immunoglobulin conjugate binds to lipids in vitro, independent of antibody selectivity. Journal of Immunological Methods 2006; 311: 174-177.

14. Liewendahl, K, Majuri, H, Helenius, T. Thyroid function tests in patients on long-term treatment with various anticonvulsant drugs. Clinical Endocrinology, 1978; 8: 187-191.

15. Wenzel, KW. Pharmacological interference with in vitro tests of thyroid function. Metabolis. 1981; 30(7): 717-732.

16. Wilke, TJ. Estimation of free thyroid hormone concentrations in the clinical laboratory. Clinical Chemistry. 1986; 32(4): 585-592.

17. Spencer, CA. Thyroid status: trends in testing - selective test use cuts cost. Clinical Chemistry News, November, 1989, 15(11): 9-14.

18. Piketty ML, et al. 2017. High-dose biotin therapy leading to false biochemical endocrine profiles: validation of a simple method to overcome biotin interference. Clin Chem Lab Med. 55(6):817-825.

19. Grimsey P, et al. 2017. Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and in vitro immunoassay interference. 2(4):247-256.

20. Demers, LM, Spencer, CA. Laboratory medicine practice guidelines: laboratory support for the diagnosis and monitoring of thyroid disease. Clin Endocrinol (Oxf) 2003; 58(2): 138-140.

21. Lee, SL. When is the TSH normal? New criteria for diagnosis and management. 12th Annual Meeting of the American Association of Clinical Endocrinologists (AACE), May, 2003.

22. Haugen, BR. When isn't TSH normal and why? Clinical implications and causes. 12th Annual Meeting of the American Association of Clinical Endocrinologists (AACE), May, 2003.

23. Singer, PA. Now it's normal - now it's not: food for thought from a complex case. 12th Annual Meeting of the American Association of Clinical Endocrinologists (AACE), May, 2003.

24. Approved Guideline - Measurement Procedure Comparison and Bias Estimation Using Patient Samples, EP09c, 3rd Edition. June 2018. Clinical and Laboratory Standards Institute.

25. Approved Guideline – Evaluation of Precision of Quantitative Measurement Procedures, EP05-A3. October 2014. Clinical and Laboratory Standards Institute.

26. Approved Guideline - Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, EP17-A2. June 2012. Clinical and Laboratory Standards Institute.

EC REP Beckman Coulter Ireland Inc., Lismeehan, O'Callaghan's Mills, Co. Clare, Ireland +(353) (0) 65 683 1100

Beckman Coulter, Inc., 250 S. Kraemer Blvd., Brea, CA 92821 U.S.A.
+(1) 800-854-3633
www.beckmancoulter.com