EXPECTED NORMAL VALUES

The reference range for serum TSH concentration in normal subjects varied based upon the subject's age and the assay methods used. TSH values in normal subjects average 0.5 to 5.0 mIU/L (Daniel, GH, Martin, JB, Neuroendocrine Regulation and Diseases of the Anterior Pituitary and Hypothalamus in Wilson, JD, Braunwald, E., Isselbacher, KJ, et. al., Harrison's Princples of Internal Medicine, 12th Edition, McGraw-Hill, Inc., New York, NY, 1991, p. 1666). An elevated TSH level is a sensitive indicator of the underproduction of T4 by the thyroid gland that is primary hypothyroidism. Suspect primary hypothyroidism when TSH > 5 mIU/L.

WAIVER PERFORMANCE

A study was conducted at three geographical locations using 20 lay users at each site, for a total of 60 lay users. The lay users were given only the written instructions to perform the testing. No coaching or training was provided. The lay users had no prior experience or training in testing laboratory devices. Each lay user tested 5 pre-spiked samples for a total of 300 test results. The values for the samples were determined using the DPC Immulite 200 3rd generation TSH methodology, which is standardized to 3rd IRP (WHO) 81/656 Reference Material. The results of the study are shown in the table below.

Actual value	Expected result (n)	Accuracy of lay user
3.46 mIU/L	**Negative (60)**	**100.0%** (60/60) 95% CI: (94.0% – 100.0%)
4.19 mIU/L	**Negative (60)**	**93.3%** (59/60) 95% CI: (91.0% – 99.9%)
5.14 mIU/L	**Positive (60)**	**90.0%** (54/60) 95% CI: (79.5% – 96.2%)
5.71 mIU/L	**Positive (60)**	**98.3%** (59/60) 95% CI: (91.0% – 99.9%)
6.41 mIU/L	**Positive (60)**	**100%** (60/60) 95% CI: (94.0% – 100.0%)

The waived study with sixty (60) lay users at three (3) sites demonstrated minimal among-site imprecision. Overall Agreement = 97.7%, which was not statistically significant (p value = 1,000).

PERFORMANCE CHARACTERISTICS

Sensitivity

Sensitivity when compared to a predicate second/ third generation TSH assay = 100%. At cutoff level of 5 mIU/L +/- < 10% = 98.5% or 129/131.

Specificity

Specificity when compared to a predicate second/ third generation TSH immunoassay = 98.5%. At cutoff level of 5 mIU/L +/- < 10% = 96.9% or 127/131.

Accuracy

A correlation study was performed using 240 elevated TSH and normal TSH blood specimens assayed with the Thyrochek test and a commercially available 2nd or 3rd generation TSH assay kit.

Commercial TSH Kit	Thyrochek TSH Assay	
	>5 mIU/L	<5 mIU/L
167 (<5 mIU/L)	2	165
73 (>5 mIU/L)	72	1

Precision

The precision of the Thyrochek was determined using replicate assays of samples from three different serum pools, with kits from three different production lots. Each specimen sample was run through ten parallel assays. The data showed 100% precision for the duplicated of each sample and 100% precision from different lots.

Interference Data

Other hormones and commonly found substances were tested to show that these substances do not interfere with the Thyrochek results.

a. HCG in concentrations up to 82,500 mIU/ml
b. LH/FSH in concentrations > 25 mIU/L
c. Hematocrit between 14 – 65%
d. Azotemia with BUN up to 70 mg% and creatinine up to 8.6 mg%
e. Hyperglycemia with blood sugars up to 707 mg%
f. Hyperlipidemia with serum triglycerides up to 844 mg%

Substance	References	Concentration	TSH Negative < 5 mIU/mL	TSH Positive > 5 mIU/mL
HCG	WHO 1st IRP	200,000 mIU/mL	Negative	Positive
FSH	WHO 2nd IRP HMG	2,000 mIU/mL	Negative	Positive
IH	WHO 68/40	500 mIU/mL	Negative	Positive

Substance	Concentration	TSH Negative <5 mIU/mL	TSH Positive >5 mIU/mL
Acetaminophen	20 mg/dl	Negative	Positive
Acetylsalicyclic Acid	20 mg/dl	Negative	Positive
Ampicillin	20 mg/dl	Negative	Positive
Ascorbic Acid	20 mg/dl	Negative	Positive
Atropine	20 mg/dl	Negative	Positive
Caffeine	20 mg/dl	Negative	Positive
Gentesic Acid	20 mg/dl	Negative	Positive
Glucose	2 mg/dl	Negative	Positive
Hemoglobin	20mg/dl	Negative	Positive
Hemoatocrit Range	20-50	Negative	Positive
Tetracycline	20mg/dl	Negative	Positive

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	Do not reuse		Use by YY-MM-DD or YYYY-MM
LOT	Batch code	SN	Serial number
	Caution, consult accompanying documents	REF	Catalog number
	Manufacturer		Temperature limitation
	Contains sufficient for <n> tests		Keep away from sunlight
IVD	*In vitro* diagnostic medical device		Keep away from moisture
	Consult instructions for use	CE	CE mark
	Recycle	EC REP	Authorized representative in the European community

THYROCHEK®

Thyroid Test Rapid TSH Cassette (Whole Blood)

EC REP

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The Hague, The Netherlands

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Fax: 31-0-70-346-7299

IVD

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11578 Sorrento Valley Road
San Diego, CA 92121 USA

Tel: 1-888-882-7739 (toll-free)
Tel: 1-858-481-5031
Fax: 1-801-720-7568

Email: info@cliawaived.com
Web: www.cliawaived.com

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CLIAwaived, Inc., San Diego, CA

P.N.: THYROCHEK-120-A-KIT
Rev.: G

 Made in the U.S.A. CE

THYROCHEK®

Thyroid Test Rapid TSH Cassette (Whole Blood)

Whole Blood One-Step TSH Assay for Hypothyroidism Screening in Ambulatory Adults
For Professional Use

CLIA WAIVED FOR USE IN WAIVED AND COMPLEX LABS | **ISO CERTIFIED** CE

A certificate of waiver is required to perform the testing in a waived setting. If the laboratory does not have a certificate of waiver, the application for certification (Form CMS-116) can be obtained at www.cms.hhs.gov/clia/. The form should be mailed to the address of the local state agency of the state in which the laboratory resides (www.cms.hhs.gov/clia/ssa-map.asp). Laboratories with a certificate of waiver must follow the manufacturer's instructions for performing the test. If the laboratory modifies the instructions, the test no longer meets the requirements for waived categorization. A modified test is considered to be high complexity and subject to all CLIA requirements. Read the package insert and quality control procedures completely before using the product. Follow the instructions carefully when performing a test.

INTENDED USE

The Thyrochek Rapid TSH Cassette (Thyrochek) immunoassay for the qualitative determination of human thyroid stimulating hormone (TSH) in whole blood samples. This test is intended to detect TSH at concentrations > 5 mIU/L. It is intended for use by medical professionals to screen an ambulatory adult population for primary hypothyroidism. It is not indicated for use screening neonates for hypothyroidism.

REAGENTS AND MATERIALS PROVIDED

Before you start, review the contents of the kit and read the instructions carefully.

- Test Cassette (20 each)–An absorbent membrane cassette individually wrapped in foil pouch, containing a plastic pipette for blood sample.
- Dropper Bottle (12 mL) containing Buffer Diluent.

REQUIRED MATERIALS *NOT* PROVIDED

- Timer
- Gauze pads
- Lancets
- Alcohol wipes
- Gloves
- Positive and negative controls

STORAGE AND STABILITY

The test kit may be stored at room temperature (15–30˚C, 59–86˚F). **Do not freeze.**

Do not use the test cassette after the date printed. Keep away from moisture, heat or direct sunlight on the foil pouch.

SUMMARY AND EXPLANATION OF TEST

Thyroid stimulating hormone (TSH), or thyrotropin, is the primary regulator of the functional state of the thyroid gland. Its production and release is stimulated by the hypothalamic thyrotropin-releasing hormone (TSH) and is controlled by levels of the thyroid hormones (thyroxine and triodothyronine) at the pituitary gland and possibly the hypothalamus. Serum TSH levels are raised in cases of primary hypothyroidism. The diagnosis of hypothyroidism is made by finding a low total or free T4 value and is confirmed by a raised TSH level. Mild primary hypothyroidism may be more difficult to diagnose by just measuring the level of total and free T4, because the total and free T4 value can sometimes be within the normal range. In these cases, TSH assays are useful for diagnosis since the levels of TSH are raised. In hyperthyroidism, levels of T3 and T4 are raised and TSH level is reduced.

"There is no single level of serum TSH at which clinical action is always either indicated or contraindicated. The higher the TSH, the more compelling is the rationale for treatment. It is important to consider the individual clinical context (e.g. pregnancy, lipid profile, ATPO antibodies)," Surks et. al., JAMA 291:228, 2004.

For further information, please refer to the American Thyroid Association at www.thyroid.org and the NACB guidelines for thyroid testing available at www.nacb.org.

WARNINGS AND PRECAUTIONS

CLINICAL:

1. For *in vitro* diagnostic use.
2. A positive test must be confirmed using a quantitative laboratory TSH assay.
3. For professional use only.
4. Clinical judgment is necessary for interpreting the test results.
5. No treatment should be given based upon this qualitative TSH test result, nor should any condition or treatment be monitored using this qualitative TSH test result.
6. False positive results can occur due to heterophilic (unusual) antibodies, and certain clinical conditions such as central hypothyroidism, TSH-secreting tumors or thyroid hormone resistance.
7. A negative result does not rule out hypothyroidism as TSH > 5 mIU/L is not seen in secondary or tertiary hypothyroidism.
8. Test results cannot be used to determine hyperthyroidism.

TECHNICAL:

1. Blood specimens may be potentially infectious. Avoid contact with skin by wearing gloves and proper laboratory attire. Properly handle and discard all used test devices in an approved biohazard container.
2. Do not use test cassettes if foil pouches are opened or defective.
3. Do not use the buffer or cassette after the expiration date printed on the outside of each foil pouch.
4. Test cassettes are single use only.
5. Persons performing the test must be tested for colorblindness before performing the test.

QUALITY CONTROL

The Thyrochek contains built-in quality control features. A pink line in the Control Zone should always be seen. It shows: (1) that enough volume is added and (2) that proper flow is obtained. If this line is missing, the test was not run correctly or it failed to function correctly. The test is invalid, and testing should be repeated using a new cassette. If you are testing under CLIA-waived status, the manufacturer recommends running controls:

- Each new lot
- Each new shipment (even if from the same lot previously received)
- Each new operator (an individual who was not run the tests for at least two weeks)
- Monthly, as a continued check on storage conditions
- Whenever problems (storage, operator or other) are identified
- Other times as required by your laboratory's standard QC procedures.

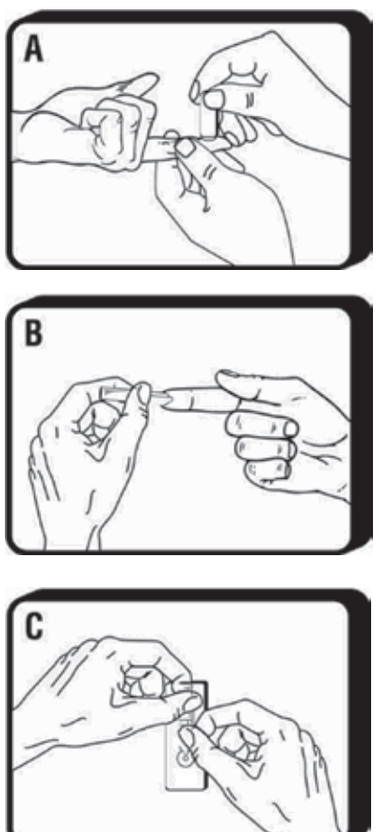
A set of positive and negative CLIAwaived, Inc. TSH Controls is available from CLIAwaived, Inc. For ordering information, please visit www.cliawaived.com.

The positive and negative controls should be run according to laboratory requirements. These controls should be run like an unknown sample. If the controls do not give expected results (positive or negative), patient results must not be reported, and the testing should be re-run.

If you are not running the Thyrochek under CLIAwaived status, or if your local or state regulations require more frequent testing of quality control material, quality control must be performed in compliance with those regulations. Each laboratory or testing site using the Thyrochek must have a CLIA Certificate of Waiver. Call your state health department for an application form.

If the test does not show any Control or Test line in the window, or a smudged or partial line, the test cassette should be discarded. Do not report the results. Run the test again with a new cassette and follow the procedures exactly. If the second test does not show lines, please contact Technical Services at 1-888-882-7739. For any other concerns regarding Thyrochek, please call 1-858-481-5031, Monday – Friday, from 8 a.m. to 5 p.m. Pacific Standard Time (PST).

SPECIMEN COLLECTION AND PREPARATION



Each Thyrochek is run with fresh whole blood. Samples should be tested immediately after collection into the pipette. If the blood appears to be clotted in the pipette, a new, fresh blood sample should be taken. If the fresh whole blood is from a venous collection, use the sample immediately and discard after use.

TO COLLECT FINGER-STICK BLOOD:

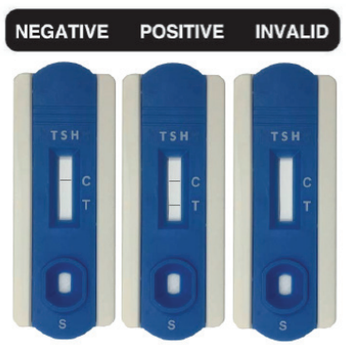
1. Rub the chosen finger toward the tip and wipe the end of the finger with an alcohol pad.
2. Let dry thoroughly. Alcohol will affect the test.
3. One drop of whole blood (50 µL) is required to perform the test.
4. Stick fingertip with lancet. Follow instructions for use. **(See Picture A.)**
5. Wipe away first drop of blood.
6. Rub the finger toward the tip for a second drop. **NOTE:** It is important to use the second drop to avoid potential interference from the alcohol.
7. Hold the pipette flat and touch end of pipette (included in pouch) to the drop of blood. **(See Picture B.)**
8. Let the blood fill to the line on the pipette, making sure that there are no air bubbles, empty spaces or gaps in the specimen. If air bubbles, empty spaces or gaps are present, collect another sample. The pipette will fill to the line by itself.
9. It may be necessary to rub the finger for an additional drop of blood to fill the line.

TO COLLECT HEPARINIZED VENOUS BLOOD: (Use within 5 minutes)

1. Draw venous whole blood sample into syringe or a vacuum collection tube containing heparin as an anticoagulant.
2. Remove tube cap and touch end of pipette included in the kit to the blood in the tube by tipping the tube and holding the pipette as horizontal as possible.
3. Let the blood fill to the line on the pipette, making sure that there are no air bubbles, empty spaces or gaps in the specimen. If air bubbles, empty spaces or gaps are present, collect another sample. The pipette will fill to the line by itself.
4. Replace cap on tube.

TEST PROCEDURE

1. Remove the test cassette and pipette from the foil pouch by tearing at notch at the corner of the pouch.
2. Place the cassette on a hard flat surface with the windows facing up.
3. Add **one drop** of whole blood directly into the specimen **well S**, located at the bottom of the cassette, with the pipette provided in the pouch. **(see Picture C.)** Discard the pipette into a waste container after use.



4. Set timer and wait for **90 seconds** before proceeding.
5. Add **four full drops** of the buffer into the Specimen **well S** located at the bottom of the cassette.
6. Set timer for **10 minutes.** Do not move the cassette during this time.
7. At the end of 10 minutes, read the line(s) in the rectangular results window of the cassette. Do not move the cassette until you have checked the lines. Do not read results after 15 minutes.

READING TEST RESULTS

NEGATIVE RESULT:
One pink line appears at C in the rectangular result window. There is no pink colored line at T in the rectangular result window. A negative result means that the TSH level is below the cut-off level of 5 mIU/L.

POSITIVE RESULT:
Two pink lines appear in the rectangular result window. (One pink line appears at C and one pink line appears at T.) A positive result means that the TSH level is above the cut-off level of 5 mIU/L.

IMPORTANT: In addition to the pink line by the control mark, any line that is seen near the test mark of the cassette at the 10-minute time is considered a positive result. The intensity of the line does not matter.

Please note: do not read after 15 minutes.

INVALID RESULT:
A pink line should always appear at C. If there is no pink line seen near C, the test is invalid. Do not report the result. In this case, the test should be repeated with a new cassette, or call 1-888-882-7739 for CLIAwaived, Inc. Technical Services.

REPORTING RESULTS

Test results should be reported to a physician for individual interpretation and symptom management.

DISCARD USED MATERIALS
After the test is completed, discard all used materials in a biological waste container.

LIMITATIONS OF THE TEST

1. Follow the directions exactly.
2. Running the test at temperatures below or above room temperature (15°- 30°C, 59°-86°F) may affect the results. Make sure the buffer and cassette are at room temperature before running the test.
3. The blood sample must be dispensed immediately after filling the pipette. If blood is clotted, collect a new sample and re-test.
4. TSH elevations have been reported concomitant to hyperthyroidism in patients with neoplasis of the pituitary.
5. As with all screening assays, results should be considered presumptive until confirmed. Results obtained from this kit should be used only as a companion to other diagnostic procedures and information available to the physician.
6. To avoid incorrect readings, do not interpret the results after 15 minutes.
7. Check the expiration date. If the test kit is expired, do not use the test cassette.