

# TSH-CHECK-1

## Quantitative determination of Thyroid Stimulating Hormone in whole blood, plasma or serum samples

FOR EASY READER® AND EASY READER+® USE ONLY

Ref.: 21091 (20 tests) & Ref.: 21091-10T (10 tests)

### I- INTENDED PURPOSE

TSH-CHECK-1 is a rapid screening test for the detection of TSH in whole blood, plasma or serum samples to be used as an aid by medical healthcare professionals in assessing thyroid function. The sole measurement of TSH concentration is not sufficient to diagnose thyroid disorders nor to predict thyroiditis evolution. Determination of other thyroid secreted hormones (T3, T4...) and additional clinical investigation are necessary to confirm the diagnosis

### II- PRINCIPLE

Human thyroid stimulating hormone (TSH) is a glycoprotein secreted by the thyrotroph cells in the anterior pituitary (1).

The primary function of TSH is to regulate the release and to control the synthesis of the major thyroid hormones. When circulating thyroid hormone levels fall below normal, the pituitary secretes TSH. This in turn acts on the thyroid gland to produce and release more thyroid hormones. However, when circulating thyroid hormone levels rise above normal, the pituitary responds by releasing less TSH, causing the thyroid gland to decrease production and secretion of thyroid hormones.

Measurement of basal serum concentration of TSH is an essential test in the investigation of suspected hypothyroidism (abnormally low levels of thyroid hormones). A raised concentration of TSH confirms a primary cause of the disease, while a normal or low concentration excludes it or, more rarely, indicates a pituitary or hypothalamic cause (1, 2).

Since the development of highly sensitive TSH immunometric assays, it is widely believed that measurement of TSH in serum probably represents the best single assessment of thyroid function. As well, measurement of TSH after injection of exogenous TRH is useful in the differentiation of secondary and tertiary (hypothalamic) hypothyroidism (3, 4, 5).

The TSH-CHECK-1 is a rapid quantitative assay for the detection of TSH in serum, plasma or whole blood to be used as a screening test for **hypothyroidism diagnosis**. **Under no circumstances, TSH-CHECK-1 must be used for detection of hyperthyroidism in patient**. The method employs a unique combination of monoclonal dye conjugate and polyclonal-solid phase antibodies to identify TSH in the test samples with a high degree of specificity.

As the sample flows through the absorbent device, the labelled antibody-dye conjugate binds to the TSH forming an antibody-antigen complex. This complex binds to the anti-TSH antibody in the reaction zone (T) and produces a pink colour band. In the absence of TSH, there is no line in the reaction zone (T). The mixture continues flowing through the absorbent device past the reactive zone (T) and control zone (C). Unbound conjugate binds to the reagents in the control zone (C), producing a pink colour band and demonstrating that the reagents are functioning correctly.

### III- TSH-CHECK-1 KIT COMPONENTS

Each kit contains everything needed to perform 10 or 20 tests.

1- TSH-CHECK-1 reaction devices:	10	20
2- Disposable plastic pipettes:	10	20
3- Diluent in a dropper bottle:	2.5mL	5mL
4- Instruction leaflet:	1	1

### 5- Controls (Optional):

**Positive control (ref. V2500) and Negative control (ref. V2501):** a freeze-dried preparation of a non-infectious compound in diluted human serum, tested and found negative for anti-HIV, anti-HCV and HBs antigen, containing 0.05 % sodium azide and optionally available as a positive and negative control (1x 0.25 mL). The concentration range is indicated on the vial label.

### IV- STORAGE AND STABILITY

1- All TSH-CHECK-1 kit components should be stored at room temperature (+4°C to +30°C) in the sealed pouch.

2- **Do not freeze the test kit.**

3- The TSH-CHECK-1 kit is stable until the expiry date stated on the package label.

### V- PRECAUTIONS

1- This test is designed for *in vitro* diagnostic use and professional use only.

2- Read the instructions carefully before using this test.

3- Handle all specimens as if they contained infectious agents. When the assay procedure is completed, dispose of specimens carefully after autoclaving them for at least one hour. Alternatively, they can be treated with 0.5% to 1% solution of sodium hypochlorite for one hour before disposal.

4- Wear protective clothing such as laboratory coats and disposable gloves while assaying samples.

5- Do not eat, drink or smoke in the area where specimens and kit reagents are handled.

6- Avoid any contact between hands and eyes or nose during specimen collection and testing.

7- Do not use beyond the expiry date which appears on the package label.

8- Do not use a test from a damaged protective wrapper.

### VI- SPECIMEN COLLECTION AND PREPARATION

1- TSH-CHECK-1 test is to be performed on human serum, plasma or whole blood.

2- The specimen should be collected under standard laboratory conditions (aseptically in such a way as to avoid haemolysis).

3- Each specimen should be treated as if potentially infectious.

4- **Whole blood samples should be tested immediately (< 4 hours). Finger prick samples should be assayed just after collection.**

5- **If the test is to be run within 48 hours of collection the specimen should be stored in the refrigerator (+2°C to +8°C). If testing is delayed more than 48 hours, the specimen should be frozen. The frozen specimen must be completely thawed, thoroughly mixed and brought to room temperature prior to testing. Avoid repeated freezing and thawing.**

6- In case of cloudiness, high viscosity or presence of particulate matter into the serum specimen, it should be diluted with equal volume (V/V) of diluting buffer (not provided but available upon request) before testing.



## VII- ASSAY PROCEDURE

**IMPORTANT:** Switch the reader on and allow it to warm up for at least 30 minutes before performing any measurements.

### a) Control testing

- Wait for 15 minutes after freeze-dried dissolving.
- Add the requested volume (25µL) with **lab pipette (disposable tips)** into the sample well of the cassette and proceed in the same way as for a patient's sample.
- The concentration range (**in mIU/L**) is indicated on the vial label and obtained result must be within the specified range. The confidence range can change slightly depending on lot number.

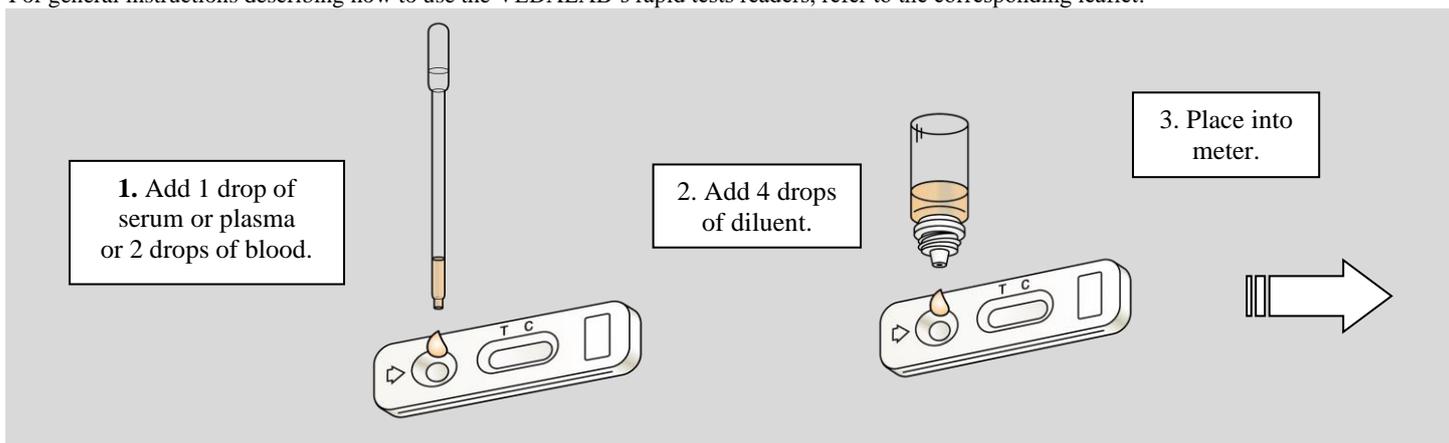
- The reconstituted vial should be kept between +2°C and +8°C and should be used within 7 days after reconstitution.

### b) Samples testing

**Follow the below instructions or refer to the picture n°1.**

- 1- Allow samples and TSH-CHECK-1 test devices to come to room temperature prior to testing.
- 2- Remove the reaction device from its protective wrapper by tearing along the split.
- 3- Label device with the patient's name or control number.
- 4- Fill the serum dropper with specimens (serum, plasma or whole blood) and by holding it vertically, dispense one drop (25 µL) into the sample well. If whole blood is used, dispense 2 drops (50 µL) into the sample well **and wait for the blood sample to be completely absorbed before adding diluent.**
- 5- Hold the dropper bottle vertically and slowly add exactly 4 drops (150µL) in the sample well of the device (▷) with an interval of 2-3 seconds between each drop.
- 6- Read the result (**in mIU/L**) after 15 minutes either using the immediate or countdown reading mode (see corresponding leaflet).

For general instructions describing how to use the VEDALAB's rapid tests readers, refer to the corresponding leaflet.



Picture n° 1

## VIII- PERFORMANCES CHARACTERISTICS

### a) Linearity

A study has been performed using serum samples obtained from dilutions of TSH W.H.O reference material (international standard n° 81/565). Covering a range of 0 to 120 mIU/L. The dose response obtained with the TSH-CHECK-1 quantitative test fits a linear regression in the range of 2 to 80 mIU/L:

$$Y = 1.0586x - 1.4226$$

Linear regression coefficient ( $R^2$ ) = 0.9971

The measuring range is 2 – 80mIU/L.

For TSH concentration below 2mIU/L, the result will be given as “< 2mIU/L”.

For TSH concentration over 80mIU/L, the result will be given as “> 80mIU/L”.

For samples whose concentration is higher than 80 mIU/L, dilute with saline and repeat the assay as per instructions of Part. VII.

### b) Accuracy

Serial dilution of TSH W.H.O reference material (International standard n°81/565) in TSH negative serum pool have been tested using TSH-CHECK-1 quantitative test.

The obtained results are summarized in Table 1.

International standard theoretical concentration	TSH concentration (mIU/L)				
	3.8	7.5	15.0	30.0	60.0
Mean of TSH-CHECK-1 results (5 replicates)	3.6	7.2	13.7	28.4	63.1
CV	10.1 %	11.2 %	10.6 %	7.5 %	6.1 %
Bias	-5.3 %	-4.0 %	-8.7 %	-5.3 %	+5.2 %

**Table 1: Accuracy**

The bias between nominal and measured values is statistically (95% t-test) non-significant and TSH concentrations determined using TSH-CHECK-1 test are accurately measured when compared to W.H.O reference material.

**c) Analytical sensitivity**

Concentrations close to 1mIU/L are detected by TSH-CHECK-1 test. In these cases, results will be rendered as “< 2 mIU/L”. Levels higher than 5mIU/L are generally considered as abnormal values (Hypothyroidism).

**d) Diagnostic sensitivity and specificity and overall correlation**

A panel of 73 human pre-assayed serum samples (Biomérieux VIDAS analyser) is assayed using the TSH-CHECK-1 quantitative test. A summary of obtained results (using VEDALAB reader) is reported in the table 1 (negative samples correspond to samples for which the TSH concentration is < 5 mIU/L and positive samples correspond to samples for which the TSH concentration is ≥ 5 mIU/L).

		VIDAS		
		Positive	Negative	Total
TSH-CHECK-1	Positive	42	0	42
	Negative	1	30	31
	Total	43	30	73

**Table 1: Summary of results**

**Diagnostic sensitivity:**

$$\frac{42}{43} \times 100 = 97.7\% \text{ (CI* 95\% [87.1 – 100.0])}$$

**Diagnostic specificity:**

$$\frac{30}{30} \times 100 = 100\% \text{ (CI* 95\% [88.0 – 100.0])}$$

**Global correlation:**

$$\frac{(42+30)}{73} \times 100 = \frac{72}{73} \times 100 = 98.6\% \text{ (CI* 95\% [92.2 – 100.0])}$$

\*CI 95%: 95% Confidence interval

On the other hand, the coefficient of correlation between quantified results of TSH-CHECK-1 test and VIDAS results is 96.7% (CI\* 95% [94.1 – 98.2]).

**e) Analytical specificity (cross-reactivity)**

There is no cross reaction when using the TSH-CHECK-1 quantitative test for the following hormones (WHO international standard concentrations):

- hCG up to a concentration of 100,000 IU/L
- LH up to a concentration of 250 mIU/mL
- FSH up to a concentration of 250 IU/L

**f) Interferences**

1- Rheumatoid factor (RF)

A serum sample having a RF concentration of 1,862 IU/mL has not shown any false positive result. Therefore, there is no interference of the TSH-CHECK-1 quantitative test up to a RF concentration of 1,862 IU/mL.

2-HAMA

A HAMA (anti-mouse human antibody) positive serum samples (type 1 or 2) have not shown any false positive results. Therefore, there is no interference of the TSH-CHECK-1 quantitative test on HAMA type 1 and type 2 positive samples.

3-Anticoagulants

Negative (0 mIU/L), weak positive (10 mIU/L) and strong positive (50 mIU/L) TSH samples, spiked with EDTA dipotassium (final concentration: 1.8 mg/mL), citrate trisodic (final concentration: 32 mg/mL) or heparin lithium (final concentration: 17 U/mL) did not show any effect on TSH-CHECK-1 quantitative test results (negative or positive).

4-Hemoglobin, bilirubin and triglycerides

Negative (0 mIU/L), weak positive (4 and 10 mIU/L) and strong positive (50 mIU/L) TSH samples, spiked with hemoglobin (final concentration: 5g/L), bilirubin (final concentration: 30 mg/L) or triglycerides (final concentration: 15 g/L) did not show any effect on TSH-CHECK-1 quantitative test results (negative or positive).

**g) Matrix effect**

Results between serum, plasma and whole blood samples show an excellent correlation. There is no matrix effect on TSH-CHECK-1 quantitative test when using plasma, serum or whole blood samples.

**h) Hook effect**

No hook effect has been observed up to 2,000 mIU/L TSH international standard concentration.

**i) Intra-lot repeatability**

Within run precision was evaluated by performing 20 replicates of three serum samples with different concentrations (0, 10 and 50 mIU/L) using TSH-CHECK-1 quantitative test and VEDALAB reader. Negative sample results obtained are all similar. Coefficients of variations obtained for 10 and 50 mIU/L positive samples are respectively 10.8% and 9.5%.

**j) Inter-lot reproducibility**

Between run reproducibility was determined by performing three samples with different concentration (0, 10 and 50 mIU/L) using three different lots of TSH-CHECK-1 quantitative test and VEDALAB reader. Negative sample results obtained are all similar. Coefficients of variations obtained for 10 and 50 mIU/L positive samples are respectively 13.6% and 9.3%.

## XI- LIMITATIONS

1- As for any diagnostic procedure, the physician should confirm the data obtained using this test by other clinical methods.

**2- TSH-CHECK-1 rapid test is designed to quantify TSH within 2 to 80 mIU/L concentration range. Therefore, TSH- CHECK-1 rapid test must only be used to detect hypothyroidism and not hyperthyroidism for which very low level of TSH (<0.1 mIU/L) must be measured. In the case that hyperthyroidism is suspected, TSH assay must be performed using a suitable specific test.**

3- Very rare cases of hypothyroidism with an associated low level of TSH or hyperthyroidism with an associated high level of TSH have been reported.

4- In early pregnancy, high level of TSH could be detected.

**5- When the test is performed with whole blood, only fresh samples should be used (< 4hours). Finger prick samples should be assayed just after collection.**

6- As it is true for any diagnostic method or for any measurements through analysers, there is a variability of the obtained result. Therefore, a confidence range of +/- 25% should be considered for the final value and for the clinical significance of the result.

7- High level of CRP (C-reactive protein) indicates inflammatory process related to infection and thus increased concentration in poly-specific antibodies that could give false positive result in some cases.

8- This format of test is to be only used with VEDALAB rapid test reader (EASY READER® or EASY READER+®).

9- If the reading time (15 minutes) is not strictly respected, wrong results will be obtained.

10- This format of test should not be used for visual reading.

**11- Do not use the reader for measurements before at least 30 minutes warm-up after having switched on.**

12- In case of doubtful results, additional T4 or T3 assays should be performed.

## X- BIBLIOGRAPHY

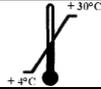
**1- Burger, HG and Patel, YC (1977).** Thyrotropin releasing hormone – TSH. Clin. Endocrin Metab, 6, 83-100.

**2- Sterling, K and Lazarus, JH (1977),** The thyroid and its control. Ann Rev Physiol 39, 349-371.

**3- Thornes, HM, Mcleod, DT and Carr D (1987),** Economy and efficiency in routine thyroid function testing : Use of a sensitive immunometric assay for thyrotropin in a general hospital laboratory. Clin Chem 33, 1635-1638.

**4- Klee, GC and Hay, ID (1987),** Assessment of sensitive thyrotropin assays for an expanded role in thyroid function testing: Proposed criteria for analytic performance and clinical utility. J Clin Endocrin Metab, 64, 461 –471.

**5- Synder, PJ and Utiger, RD (1972),** Response to thyrotropin releasing hormone (TRH) in normal man. J. Clin Endocrin Metab, 3 4, 380-385.

	Read the instructions before use		For <i>in vitro</i> diagnostic use
	Temperature limitations		Do not reuse
	Manufacturer		



Manufactured by VEDALAB – France

## CHANGES DESCRIPTION

Changes type:

- N/A	Not Applicable (creation)
- Technical change	Addition, revision and/or removal of information related to the product.
- Administrative	Implementation of non-technical changes noticeable to the end-user.

Changes type	Change description
Administrative	Addition: Ref 10 Tests, Chap I
Technical change	Modifications in Chap VIII a), b), c), d), e), f), g), h) i) and j). Addition in Chap IX limitation 11, 12

**Note:** Minor typographical, grammar, spelling and formatting changes are not reported in the change details.