FREND™ TSH
Thyroid Stimulating Hormone

Intended use

FREND™ TSH is designed for *in vitro* DIAGNOSTIC USE ONLY for the quantitative measurement of Thyroid Stimulating Hormone (thyrotropin or TSH) in human serum and lithium heparin plasma using the FREND™ System.

FREND™ TSH is indicated for use in clinical laboratories upon prescription by the attending physician as an aid to clinicians in the diagnosis of thyroid disease.

Summary and explanation of test

Human Thyroid Stimulating Hormone (hTSH) or thyrotropin stimulates the secretion of thyroxine (T4) and triiodothyronine (T3) by the thyroid gland[1]. T3 and T4 are known to have diverse functions in regulating basal metabolic rate, bone growth, neuronal development, and sex maturation[2]. Underproduction of T3 and/or T4 can result in hypothyroidism, while overproduction of these hormones can result in hyperthyroidism[3]. Because of a negative feedback mechanism, elevation of T3 and T4 suppress the production of TSH[4]. TSH itself is stimulated by thyrotropin releasing hormone (TRH), a tri-peptide produced in the hypothalamus[5].

Primary hypothyroidism occurs when TSH levels are elevated while T3 and/or T4 are under- produced[6, 7]. Secondary or tertiary hypothyroidism can occur with abnormal response of TSH to TRH, while central hypothyroidism occurs from pituitary dysfunction[8, 9]. Primary hyperthyroidism is marked by low levels of TSH and high levels of T3 and/or T4[6]. Anomalies to these types classification exist, but TSH testing can (with the aid of other thyroid tests) help a clinician determine the presence of thyroid dysfunction[10~12].

Principle of the Assay

The FREND™ TSH test cartridge is a rapid quantitative "sandwich" immunoassay utilizing fluorescent nanoparticles in microfluidic flow to capture and quantify TSH in serum and lithium heparin plasma. TSH is a glycoprotein (molecular weight approximately 28,000 daltons) that is composed of alpha- and beta-subunits. The alpha-subunit is shared with other hormones and is a potential cause of cross-reactivity: human chorionic gonadotropin (hCG), follicle stimulating hormone (FSH), and luteinizing hormone (LH)[1]. The beta-subunit is unique to each of these hormones and this beta-subunit is targeted by capture antibodies in the FREND™ TSH.

A 35 µL drop of patient serum or lithium heparin plasma is placed in the FREND™ TSH cartridge inlet port, where the sample interacts with a proprietary mix of dry-loaded reagents. One of these reagents includes antibody-conjugated fluorescent nanoparticles, forming immune complexes with TSH in the patient sample. Capillary action moves the sample to the detection region, where capture antibodies grab the TSH-nanoparticle. The concentration of TSH is calculated by the FREND™ System when the ratio of Test/Reference fluorescence in an unknown is compared to that same ratio for standards of known concentration. The result is calculated using information stored on the lot specific FREND™ TSH Code chip and then is displayed on the FREND™ System screen. A hard copy printout can be obtained if desired. A ratio calculated between the Reference zone and the Test zone corrects for test-to-test variations.

Total TSH concentration in a sample analyzed with the FREND™ TSH on the FREND ™ System correlates directly with the fluorescence intensity - the higher the TSH concentration, the greater the fluorescence ratio. The FREND™ TSH has a measuring range determined as 0.06 mIU/L (or µIU/mL) to 25.0 mIU/L.

The FREND™ TSH uses single-use transparent plastic cartridges in which all required reagents are stored within the cartridge itself. All that is added by the user is a 35 µL test sample. The cartridge is inserted into the FREND™ System in a prescribed fashion indicated with a black arrow on the cartridge. The reaction is read multiple times as the sample moves via capillary action through the cartridge. This type of assay system is sometimes referred to as one which incorporates laminar flow.

Material provided (FREND™ TSH)

* Catalog number : FRTS 025

FREND™ TSH cartridges	25
Disposable pipette tips	30
FREND™ TSH Code chip	1
FREND™ TSH package insert	1

One cartridge contains:

Mouse Monoclonal anti-Human Beta-TSH*	450 ± 45 ng
Goat Polyclonal anti-Human-Beta-TSH**	48 ± 4.8 ng
Fluorescent particles	3.96 ± 0.39 µg

*BioCheck, Inc. (Foster City, CA) Cat #: 70204(BC-183)

**BioCheck, Inc. (Foster City, CA) Cat #: 70342(G-7003)

Materials required but not provided

The following materials are not provided with the reagent but are required to perform TSH analysis using the FREND™ TSH cartridges on the FREND™ System. They are available separately from NanoEnTek.

Materials	Cat. No.
FREND™ System	F10
Micro-pipette capable of delivering 35 µL	External Source

Warnings and precautions

- The FREND™ TSH cartridges are intended for *in vitro* diagnostic use only.
- TSH cartridges are only to be used on the NanoEnTek FREND™ System.
- Allow cartridges to come to room temperature for 15 ~ 30 minutes prior to use.
- Assure the humidity is within the specifications listed in the FREND™ System User Manual (10 ~ 80%).
- Assure the room temperature remains in the range of 22~30°C when tests are run.
- Avoid cross-contamination between samples by using a new pipette tip for each new specimen.
- Avoid high humidity, direct sunlight or heat in the area used for cartridge storage.
- Inaccurate results are possible if the sample used is contaminated in any way.
- Using specimens containing clotted fibrin could result in erroneous results.
- Over or under loading the cartridge with sample may result in inaccurate results.
- Cartridges should not be frozen.
- Human specimens are not used in the preparation of this product, however, since human specimens will be used for samples and other quality control products in the lab may be derived from human materials, please use standard laboratory safety procedures when handling all specimens and controls.
- Do not use the cartridges beyond the expiration date on the pouch.
- Do not use the cartridge if the pouch is damaged or the seal is broken.
- Perform testing as specified in the Package Insert and User Manual.
- TSH cartridges are disposable, single use devices. Do not reuse them under any circumstances.
- Keep the cartridge sealed in the pouch until just ready for use.
- Use the cartridge immediately after opening its pouch.
- Wear disposable gloves when handling the cartridges and the samples.
- Wash hands thoroughly and often after handling reagent cartridges or samples.
- Do not use the silica gel pouch in the cartridge for human consumption.
- TSH has been designed so that the high dose “hook effect” is not a problem for the vast majority of samples. Samples with TSH concentrations between 25 and 2,500 mIU/L will read > 25 mIU/L. The “hook effect” phenomenon may occur only at TSH concentrations > 2,500 mIU/L. Values this high are not seen clinically.
- Handle specimens in accordance with the OSHA Standard on Bloodborne Pathogens.

Storage and Stability

All unopened materials are stable until the expiration date on the label when stored at the specified temperature. Cartridge stability has been demonstrated for twenty four months from the date of manufacture.

The expiration date is clearly indicated on the product box and the cartridges.

Materials	Cat. No.
Refrigerator temperature (2 ~ 8° C) : TSH cartridges	FRTS 025
Room temperature (18 ~ 25° C): Pipette Tips	None

Specimen collection and handling

Serum or lithium heparinized plasma is required for the assay.

No special patient preparation is necessary. To use serum, a blood sample is collected aseptically without additives by venous puncture. After allowing the sample to clot for 30 minutes at room temperature, the collection tube should be centrifuged for 10 minutes at 3,000 rpm.

For lithium heparinized plasma, a venous blood sample is collected aseptically with the designated additive. The plasma should be separated from the packed cells as soon as possible.

Samples may be stored at 2~8 ℃ for up to 6 hours prior to analysis. If the analysis is scheduled to be done at some later time, the sample should be stored frozen at -20 ℃ or below for future use.

Repeated freeze-thaw cycles should be avoided. Turbid serum samples or samples containing particulate matter such as fibrin clots or strands should be centrifuged before being tested. Prior to assay, slowly bring frozen samples to room temperature (18~25 ℃) and mix gently but thoroughly before testing.

The sample required is 35 µL.

Procedure

Reagent preparation

There is no reagent preparation required to measure TSH using the FREND™ TSH cartridge on the FREND™ System. However, the cartridges needed for a particular run should be removed from the refrigerator and allowed to reach room temperature for 15~30 minutes before they are used.

Calibration

The calibrators used during the reagent manufacture process to create the information placed electronically on the FREND™ TSH Code chip are prepared gravimetrically and are compared to international reference standards (WHO International Thyroid Stimulating Hormone, human for Immunoassay, NIBSC code: 81/565). However, for the end user, there is no need for calibration as is generally performed on other automated laboratory equipment. All calibration statistics and information have been electronically stored on the FREND™ TSH Code chip included in each box of FREND™ TSH. The FREND™ TSH Code chip is specific for that manufactured lot of FREND™ TSH cartridges.

The appropriateness of the calibration information should always be checked by running sufficient external quality control materials as samples to verify that the results obtained for TSH on the FREND™ System using the FREND™ TSH cartridges of a particular lot meet the laboratory criterion for acceptability.

FREND™ TSH Code chip installation

Please refer to the FREND™ System user manual for more detailed instructions relative to the Code chip installation. Abbreviated instructions follow here:

(1) Insert the FREND™ System electrical cord into an appropriate outlet.
(2) Insert the Code chip into the Code chip slot at the rear of the FREND™ System following the arrows.
(3) Press the 'Setup' button on the 'Main' screen.
(4) Press the 'Code chip' button on the 'Setup' screen.
(5) The information embedded on the FREND™ TSH Code chip is automatically saved on the FREND™ System.
(6) When the Code chip installation is completed, press the 'OK' button to go to the 'Setup' screen.
(7) Press the 'Item' button on the 'Setup' screen.
(8) Check the FREND™ TSH cartridge lot number and the installation date of the Code chip.
(9) Press the 'Home' button to go to the 'Main' screen to begin running external quality control and patient samples.

Quality control

- **FREND™ System QC cartridge**

FREND™ QC Cartridge contains multiple controls to check optic part of the system. By testing QC Cartridge, part of analytical components of the system of (1) laser power, (2) alignment, and (3) mechanical integrity are confirmed.
For each day of patient testing, perform QC Cartridge testing. Refer to the quality control procedures section in the User Manual of FREND™ System. In brief, perform QC cartridge testing for the following conditions:

(1) Upon initial setup of the system,
(2) Each day of patient testing,
(3) When the system has been transported or moved,
(4) Whenever there is uncertainty about the performance of the system,
(5) Whenever required by your laboratory's quality control requirements.

- **Internal procedural controls**

FREND™ TSH test cartridge contains built-in control features. Fluorescence signal in the reference zone of each cartridge shows: (1) that enough volume is added, (2) that proper flow is obtained, and (3) that the antibody is reactive. If this reference zone signal is missing or lower than threshold, the FREND™ System consider it as an incorrect or failed test, not producing a test result but an error message. In addition, with each cartridge run, the system monitors, in part, for (1) flow of sample, (2) speed of sample flow, (3) shelf-life of cartridge components, (4) function of internal barcode scanner, and (5) function of scanner's mechanical components.

(1) Each new lot,
(2) Each new shipment (even if from the same lot previously received),
(3) Each new operator (an individual who has not run the tests for at least two weeks),
(4) Monthly, as a continued check on storage conditions,
(5) Whenever required by your laboratory's quality control requirements.
(6) Or other times as required by your laboratory's standard QC procedures.

Individual laboratory policy will dictate exactly which control materials and lot numbers should be run, the frequency with which controls are to be tested, criteria for acceptance of the results and required corrective action to be taken if results do not meet laboratory criteria. If any external quality control sample values are out of the acceptable range, it will be necessary to investigate the problem before reporting patient results to assure there is not an instrument or software malfunction. Do not assay patient samples on the FREND™ System using the FREND™ TSH if quality control results do not give expected values. Refer to your laboratory policies on how to determine acceptability of external control material results. Each laboratory operates under a different set of regulations. Every laboratory must follow the standardized procedures acceptable to the regulatory agencies to which the laboratory is responsible.

In the United States, please comply with all federal, state, and local regulations regarding the frequency and extent of external quality control testing.

Specimen Processing

- **Preparation**

Remove from the refrigerator sufficient cartridges of FREND™ TSH to test the number of patient samples and required external quality control materials. Allow the cartridges to come to room temperature for 15~30 minutes prior to the start of the testing sequence. For consistent results, all testing should be done when room temperature is 22~30 ℃.

If using refrigerated patient samples, remove those from the refrigerator and allow to them to come to room temperature prior to testing. If frozen samples will be utilized, be sure these are removed from the freezer, thawed naturally and then mixed gently but thoroughly prior to testing. Testing should not begin on these previously frozen samples until they have reached room temperature.

There are no other reagents or sample preparations necessary.

- **Assay Procedure**

(1) Prepare the FREND™ TSH cartridge and specimen.
(2) Record the Sample ID on the cartridge in the designated area.
(3) Drop the sample (35 µL) into the sample inlet on the cartridge using a suitable micro-pipette equipped with a fresh pipette tip.
(4) Press the 'Test' button on the 'Main' screen of the FREND™ System.
(5) The system moves to the Patient ID screen automatically.
(6) Type the Patient ID and press the 'Enter' button to begin the test.
(7) Insert the cartridge into the cartridge slot using the cartridge arrows as a guide.
⚠ ***Caution: Please check the direction of the cartridge before insertion and assure the insertion is complete.***
(8) When the reaction in the cartridge is complete, the FREND™ System will automatically begin the reading process.
(9) When the measurements are completed, the cartridge will automatically be expelled and the results displayed.
⚠ ***Caution: Do not remove power from the FREND™ System while a cartridge is inthe reading chamber. This may cause a system error.***
(10) If the FREND™ System is connected to the optional printer, press the 'Print' button and the results will be output on the printer paper.
(11) For more detailed instructions, please refer to the FREND™ System User Manual.

Procedural Notes

If a specimen Thyroid Stimulating Hormone (TSH) concentration is found to be greater than the linearity limit of the assay of 25 mIU/L and a definitive result is required, the specimen should be manually diluted with a serum/plasma sample or serum/plasma pool that has been previously measured on the FREND™ TSH and found to contain a TSH concentration of < 0.06 mIU/L and then re-assayed according to the assay procedure. The exact dilution will depend upon the original value but we suggest that one begin with a 1:5 and a 1:10 dilution. If the result of the 1:10 dilution is still outside the linear limits, a 1:20 and 1:50 dilution should be made and these dilutions re-assayed. It is desirable to dilute the sample so that the diluted sample reads between 2 and 20 mIU/L. Once a TSH result is obtained within the assay linearity, the original concentration of the unknown can be easily manually calculated.

Below is an example using a final dilted sample result of 12.6 mIU/L, a 1 : 20 dilution and a diluent sample concentration of 0.25 mIU/L where "X" equals the original concentration of the unknown sample and * indicated multiplication.

$$12.6\ \text{mIU/L} = \frac{(1 * X\ \text{mIU/L}) + (19 * 0.25\ \text{mIU/L})}{20}$$

$$12.6\ \text{mIU/L} = \frac{X\ \text{mIU/L} + 4.75\ \text{mIU/L}}{20}$$

$$(20) * (12.6)\ \text{mIU/L} = X\ \text{mIU/L} + 4.75\ \text{mIU/L}$$

$$252.0\ \text{mIU/L} = X\ \text{mIU/L} + 4.75\ \text{mIU/L}$$

$$252.0\ \text{mIU/L} - 4.75\ \text{mIU/L} = X\ \text{mIU/L}$$

$$247.25\ \text{mIU/L} = X\ \text{mIU/L}$$

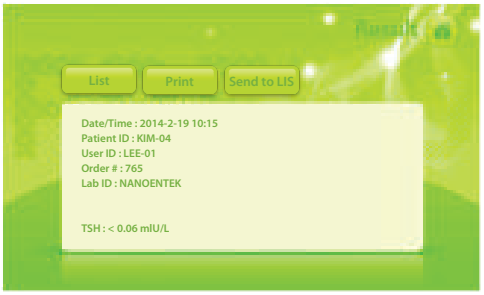
Original unknown concentration of TSH equals 247.25 mIU/L

To use this formula to calculate the original concentration of any unknown sample TSH which exceeds the assay linearity and is diluted with another sample previously measured with the FREND™ TSH, just substitute the appropriate measured result on the diluted sample, the dilution factor and the diluent TSH concentration for those used above in the example. To do a quick check on your result, the original concentration for the unknown should always be just slightly less than the diluted result multiplied by the dilution factor without taking into consideration the TSH value of the sample used as the diluent.

Calculation of Results

The FREND™ System performs all sample and reagent handling operations automatically within the cartridge once the sample has been manually loaded to the sample inlet in the cartridge and the cartridge placed into the FREND™ System. The rate of fluorescence produced by the reaction is read at various intervals during the analysis process, blank readings are subtracted after which the net rate is automatically converted to Thyroid Stimulating Hormone (TSH) concentration in mIU/L based upon information stored on the TSH Code chip. This result is then output on the screen and to the optional printer. It is also stored in memory on the FREND™ System.

Screen displays for various concentration scenarios

Displayed result	Description
	TSH concentration Less than 0.06 mIU/L (μIU/mL)
	TSH concentration Not less than 0.06 mIU/L (μIU/mL) and not higher than 25.00 mIU/L (μIU/mL)
	TSH concentration Higher than 25.00 mIU/L (μIU/mL)

Limitations of the procedure

When used for diagnostic purposes, the results obtained from this assay should be used in conjunction with other data (e.g., symptoms, results of other tests, clinical impressions, medical history, therapy, etc).

The FREND™ System paired with a FREND™ TSH cartridge, is programmed to report 25.0 mIU/L as the highest concentration of TSH measurable without dilution. The lowest measurable concentration is 0.06 mIU/L – the assay sensitivity limit.

Specimens from patients with heterophilic antibodies, such as anti-mouse (HAMA), anti-goat (HAGA), or anti-rabbit (HARA) antibodies, or those with Rheumatoid Factor (RF) may show falsely elevated or depressed values or may result in the error message "Incomplete Test"[13, 14]. Patients routinely exposed to animals or animal serum products or with rheumatoid arthritis can be prone to these types of interferences. If the TSH level is inconsistent with clinical evidence, additional TSH or other thyroid testing is suggested to confirm the results. HAMA has been shown to significantly interfere at concentrations >52.5 ng/mL. RF interference was detected above 53.8 IU/mL.

Although hemolysis has an insignificant effect on the assay, hemolyzed samples may indicate mistreatment of a specimen prior to assay and results should be interpreted with caution.

Lipemia has an insignificant effect on the assay except in the case of gross lipemia where interference with the lateral flow of the sample in the cartridge may occur.

Potential interference of the following drugs were tested at the indicated concentrations and showed no significant interference: Acetaminophen (1,324 µM), Diltiazem (15.0 µM), Erythromycin (81.6 µM) and Verapamil (4.4 µM). However, some medications may interfere with assay performance for a variety of reasons. All results should be interpreted with respect to the clinical picture of the patient.

The concentration of TSH in a given sample determined with assays from different manufacturers can vary due to differences in assay methods, calibration, and antibody specificity.

Please refer to the specimen collection and handling, warnings and precautions, storage and stability, and procedural Notes sections in this insert sheet.

FREND™ TSH has not been validated in point-of-care settings.

Performance of this assay has not been established with neonatal specimens or specimens from pregnant women.

FREND™ TSH is to be used in licensed clinical laboratories with trained technologists.

Expected values

As with every clinical diagnostic test, a reference interval corresponding to the characteristics of the population being tested should be determined by each laboratory. Historically, It has been shown that there are neither racial differences nor gender differences in the reference interval for TSH so creating a single adult reference interval is reasonable and justified.

During a clinical study, performed to support the FREND™ TSH substantial equivalence to a marketed product with the same indication, TSH measurements were determined on the serum of 385 apparently healthy ambulatory adults (195 males and 190 females ages 18~71) who stated they had no known thyroid conditions. All samples were assayed in singlicate on the FREND™ TSH and the predicate device. A single value, determined as an outlier in both the test and the predicate devices, was removed from the data set after which a non-parametric reference interval encompassing the central 95% of the results was determined. There was no significant difference in TSH reference interval between adult males and adult females.

Adult reference interval was calculated to be 0.49 ~ 3.82 mIU/L.

As in all *in vitro* diagnostic testing, a TSH result generated using the FREND™ TSH on the FREND™ System should be interpreted in the light of other clinical findings and diagnostic procedures. Any TSH results not correlating with the clinical condition should be repeated and other testing performed to clarify the situation.

Performance characteristics

Performance characteristics were evaluated for the FREND™ TSH as follows:

Accuracy

- **Dilution linearity**

Specimens from a high TSH concentration pool were diluted with a low TSH concentration pool following instructions in the CLSI EP06-A document. Linearity was demonstrated from <0.06 mIU/L to 25.54 mIU/L. Correlation with the expected values was excellent showing less than the allowable non-linearity (slope = 0.977, y-intercept = 0.17). Performance requirement was verified over the measurement interval per CLSI recommendations.

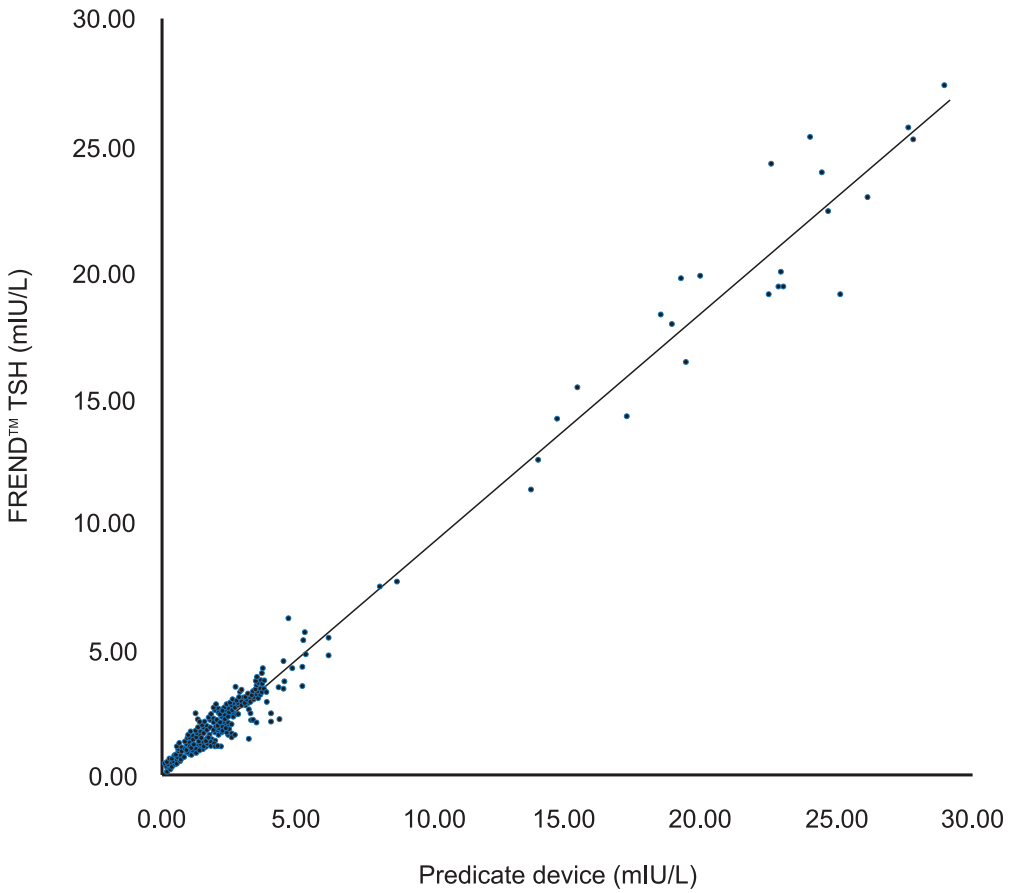
FREND™ TSH is linear from 0.06 ~ 25.0 mIU/L

FREND™ TSH Linearity

% Level	Rep. 1	Rep. 2	Rep. 3	Mean	Linear Fit
0	0.01	0.01	0.03	0.017	0.173
10	2.85	2.78	2.78	2.803	2.714
20	5.61	5.37	5.47	5.483	5.255
30	8.47	7.80	8.53	8.267	7.796
40	9.60	9.43	10.62	9.883	10.337
50	12.2 0	13.17	12.51	12.627	12.878
60	15.63	15.64	14.27	15.180	15.418
70	18.72	17.43	17.63	17.927	17.959
80	21.88	20.09	20.37	20.780	20.500
90	22.38	23.37	23.68	23.143	23.041
100	25.91	25.32	25.40	25.543	25.582

- **Comparative analysis**

In a clinical study, 438 serum samples obtained from subjects both apparently normal and with thyroid conditions as well as other undisclosed diseases and conditions and stored at -70° C under monitored conditions for less than one year, were analyzed using both the FREND™ TSH and another commercially available TSH fluorescent immunoassay. Results generated using the FREND™ TSH on the FREND™ System (y) were compared to those obtained using a previously FDA cleared TSH assay (x). Results of this study are shown below with a measuring range of 0.09~24.96 mIU/L:



Comparability using CLSI guideline EP09-A2-IR Section 7 shows that the difference in concentration between what was measured and what was expected is acceptable and that the two methods compare favorably.

Precision

- **Precision testing single lot and single site**

Precision was determined as described in the CLSI protocol EP05-A2. Four clinical samples were assayed in replicates of two at two separate times per day for twenty days using a single lot of FREND™ TSH cartridge. The findings follow showing repeatability, between-run,between-day and within-laboratory precision data.

Sample	Mean TSH	Repeatability		Between-run		Between-day		Within-laboratory	
	(mIU/L)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
1	0.496	0.043	8.6	0.012	2.4	0.017	3.4	0.047	9.6
2	5.948	0.353	5.9	0.082	1.4	0.031	0.5	0.364	6.1
3	11.989	0.555	4.6	0.375	3.1	0.156	1.3	0.688	5.7
4	23.763	0.846	3.6	0.478	2.0	0.000	0.0	0.972	4.1

Specificity

The α- subunits of luteinizing hormone (LH), follicle stimulating hormone (FSH), human chorionic gonadotropin (hCG) and thyroid stimulating hormone (TSH) are all very similar though their β- subunits are not. Because of the structural similarities, the specificity of the FREND™ TSH must be examined in the presence of large amounts of these possible cross-reactants. The following substances were evaluated for potential cross-reactivity with the FREND™ TSH at the concentrations indicated below. Testing was done according to the instructions recommended in CLSI protocol EP07-A. No significant cross-reactivity was found.

Specificity of FREND™ TSH

Sample TSH Conc. (ml/L)	Interferent	Material added	% Cross Reactivity
0.49	hCG	200,000 mIU/mL	2×10^{-8}
0.55	LH	500 mIU/mL	2×10^{-4}
0.55	FSH	500 mIU/mL	-5×10^{-6}
6.22	hCG	200,000 mIU/mL	3×10^{-7}
6.06	LH	500 mIU/mL	3×10^{-5}
6.06	FSH	500 mIU/mL	1×10^{-4}

Analytical sensitivity

The Limit of Detection (LoD) for the FREND™ TSH was determined using the CLSI EP17-A protocol. The analytical sensitivity of the FREND™ TSH was determined to be 0.06 mIU/L.

Interference

Interference is defined, for purposes of this claim, to be recovery outside ± 10% of the known mean concentration. In other words, recovery from 90% to 110% of the expected is considered acceptable performance in interference studies as listed below:

• **Endogenous interferents**
These interference studies on endogenous substances were performed using the FREND™ TSH on the FREND™ System according to the recommendations in the CLSI protocol EP07-A:

- Added hemoglobin (up to 500 mg/dL) does not interfere with the assay. Average recovery when added to serum containing TSH at 0.3 and 8 mIU/L was 98.8%.

- Added conjugated bilirubin (up to 20 mg/dL) does not interfere with the assay. Average recovery when added to serum containing TSH at 0.3 and 8 mIU/L was 100.0%.

- Added total protein up to 12.0 g/dL does not interfere with the assay. Average recovery when added to serum containing TSH at 0.3 and 8 mIU/L was 100.4%.

- Added triglyceride up to 3 g/dL does not interfere with this assay. Average recovery when added to serum containing TSH at 0.3 and 8 mIU/L was 101.6%.

- **Pharmaceutical interferents**

A variety of common medications were tested for interference with the FREND™ TSH. The testing showed there was no significant interference (<10%) from the tested drugs that would affect the interpretation of a TSH result as assayed on the FREND™ TSH.

Interference Study Results for FREND™ TSH

Tested drug	Concentration tested (µM)
Acetaminophen	1,324.0
Diltiazem	15.0
Erythromycin	81.6
Verapamil	4.4

Matrix study

Forty (40) serum/lithium heparin plasma sample pairs collected at the same time from a variety of patients were tested using the FREND™ TSH over a period of five different days with three different lots of FREND™ TSH reagent. Results covered the reporting range of the assay. Linear regression analysis (x = serum, y = lithium heparin plasma) was performed with the following results:

n	Slope	Intercept	Correration coefficient(r)	Correration coefficient(r^2)
40	0.995	-0.32	0.992	0.985

References

1) Pierce, J.G. The subunits of pituitary thyrotrophin – their relationship to other glycoprotein hormones. ***Journal of Endocrinology*** *19*71, 89, 1331-1344.
2) Smith, B.R., Pyle, G.A., Peterson, V.B, Hall, R. Interaction of thyrotrophin with the human thyrotrophin receptor. ***Journal of Endocrinology***. 1977, 75, 391-400.
3) Sterling, K., Lazarus, J.H. The thyroid and its control. ***Ann. Rev. Physiol.*** 1977, 39, 349-371.
4) Patel, Y.C., Alford, F.P., Burger, H.G. The 24-hour plasma thyrotrophin profile. ***Clinical Science.*** 1972, 43, 71-77.
5) Morley, J.E. Neuroendorine control of thyrotrophin secretion. ***Endocrine Review.*** 1981, 2, 396-436.
6) Wehmann, R.E., Rubenstein, H.A., Pugeat, M.M., Nisula, B.C. Extended clinical utility of a sensitivity and reliable radioimmunoassay of Thyroid-Stimulating Hormone. ***Southern Medical Journal.*** 1983, 76, 969-976.
7) Burger, H.G., Patel, Y.C. The value of serum thyrotrophin measurement in the diagnosis and management of hypothyroidism. ***Med. J. Aust.*** 1972, 2, 293-297.
8) Petersen, V.B., McGregor, A.M. Belchetz, P.E., Elkeles, R.S., Hall, R. The secretion of thyrotrophin with impaired biological activity in patients with hypothalamic -pituitary disease. ***Clinical Endocrinology.*** 1978, 8, 397-402.
9) Beck-Peccoz, P., Amr, S., Menezes-Ferreira, M.M., Faglia, G., Weintraub, B,D. Decreased receptor binding of biologically inactive tyhyrotrophin in central hypothyroidism. ***New England Journal of Medicine.*** 1985, 312, 1085-1090.
10) Hay, I.D., Bayer, M.F., Kaplan, M.M., Klee, G.G., Larson, P.R., Spencer, C.A. American Thyroid Association Assessment of current free thyroid hormone and thyrotrophin measurements and guidelines for future clinical assays. ***Clinical Chemistry.*** 1991, 37, 2002-2008.
11) Demers, L.M., Spencer, C.A. Laboratory medicine practice guidelines: Laboratory support for the diagnosis and monitoring of thyroid disease. ***The National Academy of Clinical Biochemistry,*** 1996.
12) Beastall, G.H., Beckett, G.J., Franklyn, J., Frasier, W.D., Kichey, J., John, R., Kendall0Taylor, P, Nevens, B., Vanderpump, M. UK Guidelines for the use of thyroid function tests. ***The association for Clinical Biochemistry,*** 2006.
13) Schroff, R.W., Foon, K.A., Beatty, S.M., Oldham, R.K., Morgan, A.C. Human Anti-Murine ImmunoglobulinResponses in Patients Receiving Monoclonal Antibody Therapy. ***Cancer Research.*** 1985, 879-885.
14) Boscato, L.M., Stuart, M.C. Heterophilic Antibodies: A Problem for All Immunoassays. ***Clinical Chemistry.*** 1988, 27.

Glossary of Symbols

	Do not reuse
	Use by YYYY-MM-DD
	Lot number
	Catalog number
	Warning or Caution
	Manufactured by
	Authorized representative in the Europe Community
	*In vitro* diagnostic medical device
	Temperature limitation
	Contains sufficient for <n> tests

NanoEnTek

ivdst@nanoentek.com
www.nanoentek.com

Manufactured by

NanoEnTek, Inc.
851-14, Seohae-ro, Paltan-myeon, Hwaseong-si, Gyeonggi-do, 18531, Korea
Tel : +82-2-6220-7942 Fax : +82-2-6220-7999

EC REP

MT Promedt Consulting GmbH
Altenhofstrasse 80, 66386 St. Ingbert, Germany

NanoEnTek, Inc. (USA)
240 Bear Hill Road, Suite 101, Waltham, MA 02451, USA
Tel: +1-781-472-2558 Fax: +1-781-790-5649
www.nanoentek.com

Revised on 2017.12.07