



Food and Drug Administration
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NANOENTEK USA INC
% MAUREEN GARNER
NEW WORLD REGULATORY SOLUTIONS, INC.
1983 HAZELWOOD ROAD
TOMS RIVER, NJ 08753

February 18, 2016

Re: K152422
Trade/Device Name: FREND™ Free T4 Test System
Regulation Number: 21 CFR 862.1695
Regulation Name: Free thyroxine test system
Regulatory Class: II
Product Code: CEC
Dated: December 31, 2015
Received: January 04, 2016

Dear Maureen Garner:

This letter corrects our substantially equivalent letter of February 17, 2016.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,


Katherine Serrano -S

FOR: Courtney H.Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

Indications for Use

510(k) Number (if known)

k152422

Device Name

FREND™ Free T4 Test System

Indications for Use (Describe)

The FREND™ Free T4 Test System is a rapid indirect competitive immunoassay for the quantitative determination of free thyroxine (FT4) in human serum and lithium heparinized plasma specimens using the FREND™ Free T4 system. Measurements of free thyroxine (FT4) are used in the diagnosis of thyroid disorders. The FREND™ Free T4 Test System is intended for use in clinical laboratories. For in vitro diagnostic use only. The test is not intended for point-of-care facilities.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

As required by the Safe Medical Devices Act (SMDA) of 1990 and in accordance with 21 CFR §807.92, a 510(k) summary is provided.

A. Applicant

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B. 510(k) Preparer Information (Contact Person)

Company Name: New World Regulatory Solutions, Inc.
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Contact Person: Maureen Garner
Phone Number: (732) 779-7422
Facsimile Number: (732) 270-4829
Email: NWRSinc@gmail.com

C. Purpose for Submission:

New Analyte on FRENDS™ System

D. Measurand:

Free thyroxine

E. Type of Test:

Quantitative, Fluorescence Immunoassay

F. Proprietary and Established Device Name:

FRENDS™ Free T4 Test System

G. Regulatory Information:

Common Name: FRENDS™ Free T4 (reagent cartridge)
Generic Name: Competitive Immunoassay, Free T4
Regulation Number: 21 CFR §862.1695
Product Code: CEC
Classification: Class II
Classification Name: Free thyroxine test system
Panel: Chemistry (75)

H. Intended Use:

1. Intended use:
See indications for use below:

2. Indication(s) for use:

The FREND™ Free T4 Test System, is a rapid indirect fluorescence immunoassay for the quantitative determination of free thyroxine (Free T4) in human serum and lithium heparinized plasma specimens using the FREND™ System. Measurements of free thyroxine (Free T4) are used in the diagnosis of thyroid disorders. The FREND™ Free T4 Test System is intended for use in clinical laboratories. For *in vitro* diagnostic use only. This test is not intended for point-of-care facilities.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

NanoEnTek FREND™ System

I. Device Description

The FREND™ Free T4 is a rapid fluorescence immunoassay that measures Free T4 in human serum and in lithium heparinized plasma using the FREND™ Free T4 Test System.

The FREND™ Free T4 is a single use fluorescence immunoassay designed to quantify the concentration of free thyroxine in serum and lithium heparinized plasma samples. The FREND™ Free T4 test is a two-step competitive immunoassay with gold nanoparticles labeled with T4-specific monoclonal anti-T4- antibody (mouse), T3-BSA labeled with fluorescent nanoparticles, and fluorescence detection by the FREND™ System.

The FREND™ Free T4 Test utilizes microfluidic technology and detects immune-complexes bound to Free T4. A 70µl Sample is first incubated during Step 1 for five minutes at 37 degrees C in the Free T4 Gold AB Tube with monoclonal anti-T4 antibody conjugated with gold nanoparticles. In Step 2, 35 µl of the mixture from Step 1 is manually loaded into the inlet of the cartridge, where it hydrates a T3-BSA fluorescent bead conjugate and migrates along the test strip. During migration the bound Free T4 in the sample and the fluorescent bead conjugates of T3-BSA compete to form antigen-antibody complex in the test zone. Unbound T3-BSA fluorescent conjugates flow through and bind to the anti-T4 antibody that is fixed on the surface in the reference zone. Step 2 takes approximately four minutes after which the fluorescent signals in the test and reference zones are measured.

Free T4 quantification is based upon the ratio of the intensity of the test and reference zones. A lower ratio of fluorescence is indicative of a higher Free T4 concentration, in other words, the magnitude of the fluorescence ratio is inversely proportional to the amount of Free T4 in the sample.

The free T4 detection range of the FREND™ Free T4 Test System is 0.4 to 6.0 ng/dL. Results are determined via a lot-specific calibration curve which is generated by the manufacturer using a six-point calibration determined from values averaged from five replicates at each level. The established curve is uploaded to the FREND™ System via the Free T4 Code-chip and is valid until the lot expiration date. The established curve is saved in the code-chip and valid until the expiration date of the test cartridge lot.

The FREND™ Free T4 Test cartridge is a disposable plastic device that houses the reagents and contains a port or opening (inlet) where the sample is applied. Once the sample is applied, it will mix with the reagents and travel towards the detection area via capillary action.

The FREND™ System is a portable, automated FREND™ cartridge reader. The FREND™ System is based on quantitative immunoassay technology capable of quantifying single or multiple analytes by measuring laser-induced fluorescence in a single-use disposable reagent cartridge. The FREND™ cartridge utilizes micro-fluidics lateral flow technology where the analyte of interest in the sample forms immune complexes while moving through the fluidics pathway in the cartridge. The concentration of the analyte of interest in an unknown sample is calculated using the ratio of the fluorescent intensity of the test zone and the reference zone.

The FREND™ System is a bench top fluorescence reader containing a touch screen user interface. The System has a slot that accepts the FREND™ Free T4 Test Cartridge (which contains the reagents and sample), and is programmed to analyze the Test when the sample has fully reacted with the on-board in-cartridge reagents. Results of the test are displayed on the screen and can be printed on an optional printer.

The FREND™ System software controls the graphical user interface, communication with hardware, database management and data analysis. The software also controls the functions of the mechanical components including the motor, laser, printer control and acquisition of data from the sensor. The user can set the time and date and enter patient ID through the graphic user interface. The user cannot make any changes to the software.

The FREND™ Free T4 Test System includes the following in the kit:

- 20 FREND™ Free T4 cartridges
- 20 Gold-T4 antibody tubes
- Disposable pipette tips
- 1 FREND™ Free T4 Code Chip
- 1 FREND™ Free T4 Package Insert

The FREND™ System (previously cleared in K124056 (FREND™ PSA) and K131928 (FREND™ PSA)) is not provided with the kit but is required for the use of the FREND™ Free T4 test cartridge.

J. Substantial Equivalence Information:

A general comparison of the similarities and differences of the assays is presented in the table below:

Similarities		
Item	FREND™ Free T4 Test System	Abbott ARCHITECT Free T4 (K123379)
Intended Use	The FREND™ Free T4 Test System is a rapid indirect competitive fluorescence immunoassay for the quantitative determination of free thyroxine (FT4) in human serum and lithium heparinized plasma specimens using the FREND™ system. Measurements of free thyroxine (FT4) are used in the diagnosis of thyroid disorders. The FREND™ Free T4 Test System is intended for use in clinical laboratories. For <i>in vitro</i> diagnostic use only. The test is not intended for use in point-of-care facilities.	<p>The ARCHITECT Free T4 (FT4) is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of free thyroxine (Free T4) in human serum and plasma. The ARCHITECT Free T4 assay is to be used as an aid in the assessment of thyroid status.</p> <p>The ARCHITECT Free T4 Calibrators are for the calibration of the ARCHITECT i System when used for the quantitative determination of free thyroxine (FreeT4) in human serum and plasma when using the ARCHITECT Free T4 Reagent Kit.</p> <p>The ARCHITECT Free T4 Controls are for the verification of the accuracy and precision of the ARCHITECT i System when used for the quantitative determination of free thyroxine (Free T4) in human serum and plasma when using the ARCHITECT Free T4 Reagent Kit.</p> <p>For <i>in vitro</i> diagnostic use only.</p>
Sample Type	Human serum and lithium heparinized plasma	Same
Analyte	Free thyroxine	Same
Type of Test	Fluorescent immunoassay determination of FT4	Chemiluminescent immunoassay determination of FT4
Quality Control	Internal procedural/instrument quality controls; External positive and negative assay controls	Same
Interpretation of Results	Interpolation from a lot-specific calibration curve	Same
Measuring Range	0.40- 6.00 ng/dL	Same

Differences		
Item	FREND™ Free T4 Test System	Abbott ARCHITECT Free T4 (K123379)
Sample Size	70µL for the incubation step and 35 µL for the running of the test	95 µL for the first Free T4 test plus 45 µL for each additional Free T4 from the same test cup
Test Cartridge	Disposable single-use cartridge	No single-use cartridge
Random Access/Degree of Automation	No random access, manual manipulation	Random access, semi-automated

K. Performance Characteristics (if/when applicable)

1. Analytical performance:

a. Precision/Reproducibility:

A single lot imprecision study was performed at the NanoEnTek laboratory as described in the CLSI protocol EP5-A3. Three serum pools with low, intermediate and high Free T4 levels were assayed in duplicate twice per day for 20 days (80 total measurements). The results are summarized below:

FREND™ Free T4 Single Site Single Lot Precision

Sample Pool	Mean Free T4 Conc. (ng/dL)	Repeatability		Between-run		Between-day		Within-laboratory	
		SD	CV%	SD	CV%	SD	CV%	SD	CV%
1	0.917	0.067	7.3	0.000	0.0	0.032	3.5	0.074	8.1
2	1.850	0.103	5.6	0.000	0.0	0.069	3.7	0.124	6.7
3	3.979	0.186	4.7	0.152	3.8	0.093	2.3	0.258	6.5

b. Linearity/assay reportable range:

To demonstrate the linearity of the assay, a serum base pool with an elevated free thyroxine (7.5 ng/dL) was diluted to a total of 11 levels according to the dilution protocol outlined in CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach*. At each dilution level, the samples were measured in duplicate to determine the experimental value of free thyroxine. The FREND™ Free T4 Test System was determined to have acceptable linearity across a free T4 range of 0.11 ~ 7.5 ng/dL, (Slope = 0.978, Intercept = -0.0881, $R^2 = 0.9938$). The measuring range of the FREND™ Free T4 is 0.4 ~ 6 ng/dL, which is within the linearity range.

c. Traceability, Stability, Expected values (controls, calibrators or methods):

The standards/calibrators are internally prepared according to the guideline of CLSI (Clinical Laboratory and Standards Institute), C45-A Measurement of Free Thyroid Hormones; Approved Guideline – first Edition. This internal standard is manufactured by gravimetric methods based on the L-Thyroxine (Sigma T1775, Cell culture grade). At each concentration level, the free T4 levels of calibrators are confirmed by measurement on ARCHITECT i free T4 assay (K123379). There is no need for calibration by the operator as the calibration information is coded in the individual cartridge.

d. Stability

Real-time stability testing for the Free T4 reagent kit was performed according to CLSI EP25-A, *Evaluation of Stability of In Vitro Diagnostic Reagents*. Reagent stability studies based on procedures and criteria in the NanoEnTek quality system showed that the cartridges for FREND™ Free T4 are good for at least one year from the date of manufacturer if stored refrigerated appropriately as directed.

e. Detection Limit:

The Limit of Detection (LoD) and Limit of Quantitation (LoQ) for the FREND™ Free T4 were established according to the CLSI EP17-A2 protocol and found to be 0.32 ng/dL and 0.36 ng/dL, respectively.

f. Analytical specificity:

Interference Studies

Recovery between 90% to 110% of the expected Free T4, in the presence of interferents, is considered acceptable performance. The interference studies were performed with two levels of free T4 using the recommendations in the CLSI EP07-A2 protocol. Results are summarized in the table below.

	Interferent (Concentration tested)	%Recovery Free T4 Low	%Recovery Free T4 High
Endogenous substances	Hemoglobin (500 mg/dL)	109.5	106.3
	Bilirubin conjugated (20 mg/dL)	90.5	101.5
	Bilirubin unconjugated (20 mg/dL)	103.0	101.0
	Triglyceride (3 g/dL)	108.1	105.5
	Total protein (12 g/dL)	107.7	103.6
	Biotin (2.5 µ/mL)	101.5	94.0
	IgG (2.5 mg/mL)	102.9	101.7
	IgA (60 µg/mL)	100.7	95.8
	IgM (45 µ/mL)	106.2	94.7
Pharmaceuticals	Acetaminophen (200 µ/mL)	104.4	100.3
	Erythromycin (60 µ/mL)	102.7	100.2
	Diltiazem (6.24 µ/mL)	109.5	91.1
	Verapamil (2 µ/mL)	108.2	90.5
	Acetylcysteine (415 µ/mL)	102.7	109.4
	Acetylsalicylic acid (250 µ/mL)	96.5	98.3
	Amiodarone (6 µ/mL)	105.0	99.1
	Ampicillin-Na (50.3 µ/mL)	99.7	91.8
	Ascorbic acid (60 µ/mL)	100.0	91.9
	Carbimazole (500 ng/mL)	90.5	91.2
	Cefoxitin (66 µ/mL)	93.5	92.7
	Cyclosporine (3 µ/mL)	103.8	96.2
	Doxycycline (30 µ/mL)	104.8	95.1
	Fluocortolone (400 µ/mL)	90.1	99.5
	Furosemide (12.5 µ/mL)	100.3	101.4
	Heparin (3,000 U/L)	102.2	91.2
	Hydrocortisone (1.8 µ/mL)	96.9	90.1
	Ibuprofen (250 µ/mL)	98.6	109.0
	Iodide (380 µ/mL)	98.0	86.8
	Levodopa (4 mg/mL)	99.2	103.9
	Methyldopa (15 µ/mL)	100.0	90.0
	Metronidazole (120 µ/mL)	99.0	92.9
	Octreotide (2 ng/mL)	101.7	90.8
	Perchlorate (16 ng/mL)	99.0	91.6
	Prednisolone (3 µ/mL)	98.6	91.6
	Propranolol (2 µ/mL)	96.9	90.0
	Propylthiouracil (10 µ/mL)	90.5	90.8
	Rifampicin (640 µ/mL)	91.5	93.9
	Theophylline (400 µ/mL)	107.1	94.5
	Thiamazole/Methimazole (500 µ/mL)	102.0	90.7
	Avidin (5 µg/mL)	107.7	90.4
	Au-nanoparticles (5 µg/mL)	103.4	97.4
	Heterophilic Antibodies	RF (1075 IU/mL)	109.2
HAMA (70 ng/mL)		104.4	96.5

Cross Reactivity

The following substances were evaluated for potential cross-reactivity with the FREND™ Free T4 at two concentrations. Testing was done according to the CLSI protocol EP07-A2. No significant cross-reactivity was found except for the L-Thyroxine (Levothyroxine) itself.

Cross-reactant	Cross-reactant Concentration (ng/dL)	% Cross-reactivity	
		Free T4 Low	Free T4 High
Levothyroxine, T4 (1 µg/dL)	1,000	99.44	99.57
Diiodothyronine, T2 (5 µg/dL)	5,000	0.0001	0.0006
Tetraiodothyroacetic Acid (10 µg/dL)	10,000	0.0005	0.0005
Triiodothyroacetic Acid (1 µg/dL)	1,000	0.004	0.0157
Triiodothyropropionic Acid (5 µg/dL)	5,000	0.0019	0.0055
Diiodotyrosine, DIT (1 µg/dL)	1,000,000	1E-06	2E-06
L-Triiodothyronine, T3 (1 µg/dL)	1,000	0.0037	0.026
Monoiodotyrosine (1 µg/dL)	1,000,000	1E-06	0.000019
Reverse T3 (10 µg/dL)	10,000	0.0009	0.0022

% Cross-reactivity = $100 \times ((\text{Measured value} - \text{true value}) / \text{interferent concentration})$, as absolute value

g. *Assay cut-off:*

Not applicable

2. Comparison studies

a. *Method comparison with predicate device:*

Comparison studies were performed in a CLIA-certified laboratory testing facility at the time the clinical samples were evaluated. If the predicate device and the FREND™ system could be run at the same time, samples were validated simultaneously using the same aliquot of sample. If that was not practical, two separate aliquots of each sample, freshly defrosted prior to analysis, were used – one for each method. The instrument reagent system used as the predicate device was the Abbott ARCHITECT Free T4 Assay (K123379) run on the Abbott ARCHITECT *i* System. All samples (358) used in the clinical testing were analyzed by both the predicate and the subject device.

Results generated using the FREND™ Free T4 on the FREND™ System (y) were compared to those obtained using a previously FDA cleared ARCHITECT free T4 assay (x) by Ordinary least square fit method. Results of this study are shown in the table below:

Slope: 1.010 (95% CI: 0.992 to 1.028)	y-Intercept: 0.057 (95% CI: 0.021 to 0.094)
Number of Samples: 358	Range Tested: 0.43 ~ 5.99 ng/dL
r: 0.986	

Comparability using CLSI guideline EP09-A3, shows that the difference between the concentrations measured by the test device and the predicate device is less than the allowable difference and the two methods compare favorably.

b. *Matrix comparison:*

The matrix comparison study was performed at the NanoEnTek laboratory according to CLSI EP14-A3. Free T4 concentrations in 48 paired serum and lithium heparin samples were measured using the FREND™ Free T4. Passing-Bablok regression analysis of serum results (x) compared to lithium heparin plasma results (y) yielded the following regression, indicating that FREND™ Free T4 can be measured equally well in serum and lithium heparin plasma.

Slope: 1.017 (95% CI: 0.991 to 1.044)	y-Intercept: -0.008 (95% CI: -0.055 to 0.0451)
Number of Samples: 48	Range Tested: 0.44 ~ 5.63 ng/dL

3. Clinical studies:

a. *Clinical Sensitivity*
Not applicable

b. *Clinical Specificity*
Not applicable

c. *Other clinical supportive data (when a. and b. are not applicable)*
Not applicable

4. Clinical cut-off:
Not applicable

5. Expected values/Reference range:

Serum samples from a total of 196 normal, apparently healthy adult individuals were assayed on 3 lots of the FRENTM Free T4 assay using a single FRENTM System. The reference interval for the FRENTM Free T4 Test System, determined according to CLSI C28-A3 guidelines, was found to be 0.83-1.60 ng/dL.

L. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR §809.10.

M. Conclusion

The submitted information in this premarket notification is complete and supports a substantial equivalence determination.