

K974551

DEC 22 1997

SeaLite Sciences, Inc.

510(k) SUMMARY

I. GENERAL INFORMATION

Trade or proprietary name - SeaLite Sciences, Inc. AquaLite® Free T₄ Assay

Common or usual name - Bioluminescent immunoassay (BIA)

Classification name - FDA has classified Free T₄ test systems intended for the measurement of free thyroxine in serum or plasma to diagnose and treat diseases of the thyroid as Class II devices. (21 C.F.R. § 862.1695)

Submitter's Name and Address: Cathryn N. Cambria, Director
Regulatory Affairs and Quality Assurance
SeaLite Sciences, Inc.
3000 Northwoods Parkway
Suite 200
Norcross, GA 30071
(800) 874-4471, ext. 227

Submission Date: December 3, 1997

Legally Marketed Device To Which Claim Substantial Equivalence: Nichols Institute Free T₄ Assay

II. INDICATIONS FOR USE

The AquaLite® Free T₄ Bioluminescent Immunoassay (BIA) Kit (or the AquaLite® Free T₄ Assay) is an *in vitro* diagnostic product intended for use in clinical laboratories for the quantitative determination of human free T₄ in serum.

III. DEVICE DESCRIPTION

The AquaLite® Free T₄ Assay is a single-site, competitive inhibition bioluminescent immunoassay kit. A T₄ carrier complex is immobilized on polystyrene tubes (solid phase). Serum samples, appropriate calibrators or controls, are pipetted (50 µL) into the pre-coated tubes. A mouse monoclonal anti-T₄ antibody covalently linked to AquaLite® (100 µL) is then added to the tubes. Free T₄ in the sample competes with immobilized T₄ for the available T₄ binding sites of the anti-T₄ antibody conjugate. Complex formation is complete after a 90-minute incubation period at room temperature on a standard orbital shaker. The tubes are then washed to remove unbound conjugate.

The washed tubes are placed in a luminometer that is capable of reading a triggered, flash-type reaction in 12 x 75 mm tubes. Injection of the calcium trigger buffer causes AquaLite® to oxidize its self-contained luciferin molecule, producing a flash of light, which is measured by the luminometer. The presence of T₄ in the sample or calibrator reduces the binding of the conjugate to the immobilized T₄ pre-coated on the tubes. The amount of signal inhibition is indirectly proportional to the Free T₄ concentration. To calculate results, the luminometer uses a cubic spline curve fit applied to a log-log transformation of the light intensity (in relative light units, RLU) of the Free T₄ calibrators versus Free T₄ concentration (in ng/dL).

IV. SUMMARY OF STUDIES AND TECHNOLOGICAL CHARACTERISTICS

Studies on the AquaLite® Free T₄ Assay were conducted at SeaLite Sciences. The results are summarized below:

Performance Characteristics

1. Sensitivity

The sensitivity or detection limit of the AquaLite® Free T₄ Assay is 0.007 ng/dL. Sensitivity is calculated by determining the Free T₄ concentration that corresponds to the 95 % confidence level of twenty replicates of the A Calibrator (0 ng/dL).

2. Specificity and Cross Reactivity

Cross reactivity of the AquaLite® Free T₄ Assay was determined by spiking Calibrator A containing Free T₄ (0 ng/dL) with the following compounds.

<u>Compound</u>	<u>Concentration</u>	<u>% Cross Reactivity</u>
Triiodo-L-thyronine	20 µg/dL	undetectable
Triiodothyroacetic acid	20 µg/dL	undetectable
Monoiodotyrosine	20 µg/dL	undetectable
Diiodo-L-tyrosine	20 µg/dL	undetectable
Methimazole	0.4 mg/mL	undetectable
6-n-Propyl-2-thiouracil	0.4 mg/mL	undetectable

3. Drift

Two patient samples were run (5 duplicates each) and assayed for reagent addition drift. The data demonstrate that the AquaLite® Free T₄ Assay does not exhibit "end of run" effect with 100 tubes.

(All measurements, in ng/dL)

<u>Sample</u>	<u>Tubes 20-30</u>	<u>Tubes 50-60</u>	<u>Tubes 90-100</u>
1	2.8	2.9	2.8
2	4.5	4.5	4.5

4. Precision and Reproducibility

- a. Intra-assay precision. Three serum controls containing Free T₄ at the following concentrations were assayed to determine intra-assay precision (n=20 per concentration level).

<u>Free T₄ Level (ng/dL)</u>	<u>% CV</u>
0.75	10.1
2.6	4.1
4.4	2.9

- b. Inter-assay precision. Three serum controls containing Free T₄ at the following concentrations were assayed in duplicate in 20 assays. A new standard curve was generated for each assay (n = 2 x 20 = 40). Inter-assay precision observed over a 2 week period for the solutions is as follows:

<u>Free T₄ Level (ng/dL)</u>	<u>% CV</u>
0.6	13.0
2.6	5.0
4.2	3.4

5. Method Comparison

Free T₄ ranging from 0.27 to 3.67 ng/dL in serum samples (n = 127) was measured using the AquaLite® Free T₄ Assay and a commercially available chemiluminescence immunometric assay kit for Free T₄. Correlation by linear regression analysis gave a slope of 1.1 with a y intercept of -0.2. The correlation coefficient was 0.92.

6. Kinetics

Three human serum samples were assayed in parallel at 60 minutes, 90 minutes and 120 minutes to demonstrate the effect of incubation times. Results indicate a 90 minute incubation is optimal.

<u>Standard ng/dL</u>	<u>1 Hour %B/Bo</u>	<u>1.5 Hours %B/Bo</u>	<u>2 Hours %B/Bo</u>
0	100.0	100.0	100.0
0.4	85.9	84.0	82.6
0.9	68.8	68.1	68.8
2	38.0	38.4	41.2
4	8.6	9.1	10.7

Sample <u>ng/dL</u>	Free T ₄ <u>ng/dL</u>	Free T ₄ <u>ng/dL</u>	Free T ₄ <u>ng/dL</u>
1	0.6	0.6	0.5
2	2.6	2.6	2.7
3	4.4	4.4	4.4

7. Recovery in Serum and Plasma

Blood samples from 7 normal subjects were prepared as sera (standard technique and SST tubes) as well as heparin and EDTA plasmas. Free T₄ was quantified using the AquaLite® Free T₄ Assay. Recovered Free T₄ was compared with the Free T₄ recovered in serum (standard technique). The data demonstrates that there are no significant differences between standard serum or serum separator tubes, nor heparin and EDTA plasmas when using the AquaLite® Free T₄ Assay.

<u>Sample</u>	<u>Serum</u>	<u>Heparin</u>	<u>EDTA</u>	<u>SST</u>
1	1.5	1.4	1.4	1.3
2	1.5	1.6	1.5	1.4
3	1.6	1.8	1.5	1.4
4	1.8	1.7	1.8	1.6
5	1.4	1.4	1.4	1.3
6	1.3	1.3	1.5	1.2
7	0.9	1.0	0.8	0.6

8. Effect of Hemolysis

Three patient samples were spiked with preparations of hemoglobin and assayed to demonstrate effect of mild, moderate and severely hemolyzed serum. The data demonstrates that the AquaLite® Free T₄ Assay is not significantly affected by hemoglobin.

<u>Sample</u>	<u>Neat</u>	<u>Mild</u>	<u>Moderate</u>	<u>Severe</u>
1	1.6	1.5	1.5	1.5
2	1.7	1.5	1.8	1.7
3	1.0	1.1	0.9	1.1

9. Effect of TBG

This experiment tested for the possible interference of the immobilized Free T₄ with purified TBG. If TBG bound to the immobilized Free T₄, there would be a reduction of binding of the anti-T₄ AquaLite® Free T₄ conjugate. This would be reflected in an apparent increase in Free T₄ concentration. At a normal TBG level (15-34 mg/L)¹⁸ there was no interference of the AquaLite® Free T₄ Assay. There was slight inhibition of the %B/Bo at 200 and 300 mg/L of TBG (5.9 and 8.8 times normal physiologic level).

<u>TBG Added</u>	<u>%B/Bo</u>
0	100%
50 mg/L	100%
75 mg/L	100%
100 mg/L	104%
200 mg/L	91%
300 mg/L	93%
600 mg/L	73%

10. Effect of Albumin

Three patient samples were spiked with 15, 25 and 75 mg/mL of albumin and assayed. The data demonstrate that the AquaLite® Free T₄ Assay is not significantly affected by albumin.

<u>Sample</u>	<u>Neat</u>	<u>Albumin</u>		
		<u>15 mg/mL</u>	<u>25 mg/mL</u>	<u>75 mg/mL</u>
1	1.8	1.6	1.5	1.9
2	1.2	1.3	1.2	1.4
3	1.3	1.4	1.3	1.6

11. Effect of Nonesterified Fatty Acids

Three patient samples were spiked with 2.5, 5 and 10 mmol/L oleic acid and assayed. The data demonstrate that the AquaLite® Free F₄ Assay is not significantly affected by oleic acid at the levels tested.

<u>Sample</u>	<u>Neat</u>	<u>Oleic Acid</u>		
		<u>2.5 mmol/L</u>	<u>5 mmol/L</u>	<u>10 mmol/L</u>
1	0.9	0.9	1.2	1.0
2	1.5	1.5	1.4	1.4
3	1.1	0.9	1.1	1.1

12. Effect of Bilirubin

Three patient samples were spiked with 10 and 20 mg/dL bilirubin and assayed. The data demonstrate that the AquaLite® Free T₄ Assay is not significantly affected by bilirubin at the levels tested.

<u>Sample</u>	<u>Neat</u>	<u>Bilirubin</u>	
		<u>10 mg/dL</u>	<u>20 mg/dL</u>
1	1.1	1.3	1.2
2	1.1	1.0	1.0
3	1.5	1.4	1.3

13. Effect of Salicylate

Three patient samples were spiked with 1, 5, 10 and 25 mg/dL salicylate and assayed. The data demonstrate that the AquaLite® Free T₄ Assay is not significantly affected by salicylate at the levels tested.

<u>Sample</u>	<u>Neat</u>	<u>Salicylate</u>			
		<u>1 mg/dL</u>	<u>5 mg/dL</u>	<u>10 mg/dL</u>	<u>25 mg/dL</u>
1	1.5	1.3	1.7	1.7	1.6
2	0.9	1.2	0.8	1.1	1.1
3	0.9	1.0	1.2	0.9	1.2

14. Effect of Phenytoin

Two patient samples were spiked with 1, 5, 10 and 25 $\mu\text{g/mL}$ phenytoin and assayed. The data demonstrate that the AquaLite[®] Free T₄ Assay is not significantly affected by phenytoin at the levels tested. *values in patients taking phenytoin should be interpreted with caution.*

<u>Sample</u>	<u>Neat</u>	<u>Phenytoin</u>			
		<u>1 $\mu\text{g/mL}$</u>	<u>5 $\mu\text{g/mL}$</u>	<u>10 $\mu\text{g/mL}$</u>	<u>25 $\mu\text{g/mL}$</u>
1	1.1	1.0	1.6	1.6	2.2
2	1.5	1.2	1.5	1.9	2.2

15. Effect of Phenylbutazone

Three patient samples were spiked with 1, 5 and 10 $\mu\text{g/mL}$ phenylbutazone and assayed. The data demonstrate that the AquaLite[®] Free T₄ Assay is not significantly affected by phenylbutazone at the levels tested.

<u>Sample</u>	<u>Neat</u>	<u>Phenylbutazone</u>		
		<u>1 $\mu\text{g/mL}$</u>	<u>5 $\mu\text{g/mL}$</u>	<u>10 $\mu\text{g/mL}$</u>
1	1.0	1.0	0.9	0.8
2	1.7	1.6	1.4	1.7
3	0.9	0.7	0.8	0.8

V. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Caution: Use Universal Precautions. No known test method can offer complete assurance that products derived from human serum are pathogen-free; therefore, handle all materials of human origin as though they were potentially infectious.

Sodium azide is used as a preservative. This preservative may react with metallic plumbing to form explosive metal azides. Flush with large volumes of water when disposing of materials containing sodium azide.

As an *in vitro* diagnostic test, there are not direct adverse effects on the health of a patient from the use of this product. However, failure of the device to perform as indicated, the contamination of reagents, the use of reagents past the labeled expiration dates, the use of improper specimens, or human error during the performance of the test may lead to erroneous results and possible improper patient management.

VI. CONCLUSIONS DRAWN FROM STUDIES

The data from the studies conducted demonstrate that the performance of SeaLite Sciences, Inc. AquaLite® Free T₄ Assay is similar and substantially equivalent to that of other commercially available assays for Free T₄.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 22 1997

Cathryn Cambria
• Director, Regulatory Affairs and
Quality Assurance
SeaLite Sciences, Inc.
3000 Northwoods Parkway, Suite 200
Norcross, Georgia 30071

Re: K974551
AquaLite® Free T4 Assay
• Regulatory Class: II
Product Code: CEC
Dated: December 3, 1997
Received: December 4, 1997

Dear Ms. Cambria:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to 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). 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.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

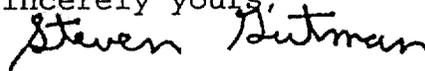
Page 2

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>".

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K974551

Device Name: AquaLite® FT4 Bioluminescent Immunoassay (BIA) Kit (or the AquaLite® FT4 Assay)

Indications for Use:

The AquaLite® FT4 Bioluminescent Immunoassay (BIA) Kit (or the AquaLite® FT4 Assay) is an *in vitro* diagnostic product intended for use in the quantitative measurement of FT4 in human serum in clinical laboratories. Free thyroxine measurements are used to diagnosis and treat diseases of the thyroid.



(Division Sign-Off)

Division of Clinical Laboratory Devices

510(k) Number K974551

(PLEASE DO NOT WRITE BELOW THIS LINE CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use

OR

Over-The-Counter Use

(Per 21 CFR 801.109)

(Optional Format 1-2-96)