

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

k052308

B. Purpose for Submission:

New Devices

C. Measurand:

Anti-Tg Autoantibodies

D. Type of Test:

Quantitative Chemiluminescent Microparticle Immunoassay

E. Applicant:

Fisher Diagnostics

F. Proprietary and Established Names:

ARCHITECT[®] Anti-Tg Immunoassay Reagents

ARCHITECT[®] Anti-Tg Calibrators

ARCHITECT[®] Anti-Tg Controls

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5870, Thyroid Autoantibody Immunological Test System

21 CFR 862.1660, Quality Control Material (Assayed and Unassayed)

21 CFR 862.1150, Calibrator

2. Classification:

Class II

3. Product code:

JZO- System. Test, Thyroid Antibody

JJX- Single (Specified) Analyte Controls (Assayed and Unassayed)

JIT- Calibrator, Secondary

4. Panel:

Immunology 82

Clinical Chemistry 75

H. Intended Use:

1. Intended use(s):

ARCHITECT[®] Anti-Tg is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of the IgG class of thyroglobulin autoantibodies (anti-Tg) in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT Anti-Tg assay is intended for use as an aid in the diagnosis of thyroid disease.

The ARCHITECT[®] Anti-Tg Calibrators are for the calibration of the ARCHITECT[®] *i* System when used for the quantitative determination of IgG class of thyroglobulin autoantibodies (anti-Tg) in human serum and plasma.

The ARCHITECT[®] Anti-Tg Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT[®] *i* System (reagents, calibrators and instrument) when used for the quantitative determination of IgG class of thyroglobulin autoantibodies (anti-Tg) in human

- serum and plasma.
2. Indication(s) for use:
Same as Intended Use.
 3. Special conditions for use statement(s):
For prescription use only.
 4. Special instrument requirements:
ARCHITECT *i* 2000 System and ARCHITECT *i* 2000_{SR} System

I. Device Description:

The ARCHITECT Anti-Tg assay, including Calibrators and Controls are designed to be used on the ARCHITECT *i* System. Each reagent kit contains microparticles, conjugate, assay diluent, pre-trigger solution, trigger solution and wash buffer. In addition, 6 calibrators (calibrators A-F) and a positive and negative control are provided. A CD-ROM containing the assay files to be installed in the ARCHITECT *i* System is also included.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Nichols Advantage Thyroglobulin Autoantibodies Assay
Nichols Advantage Chemiluminescence Tri-Level Controls
2. Predicate 510(k) number(s):
k983992
k972070
3. Comparison with predicate:

Similarities		
Item	New Device	Predicate Device
Intended use	To aid in the diagnosis of autoimmune thyroid disease.	Same
Technology	Microparticle Immunoassay	Same
Assay Format	Quantitative	Same
Preservatives	Anti-microbial agent	Same
Solid Support	Magnetic Microparticles	Same
Detection Method	Chemiluminescence	Same

Differences		
Item	Device	Predicate
Sample Type	Serum and Plasma	Serum
Magnetic Microparticles	Human thyroglobulin coated microparticles in MES buffer with protein (goat) stabilizer.	Streptavidin coated magnetic particles in a buffer containing goat, rabbit and mouse gamma globulins.
Conjugate	Anti-human IgG (mouse monoclonal) acridinium labeled conjugate in MES buffer with protein (bovine)	Acridinium labeled Tg protein based buffer

Differences		
Item	Device	Predicate
	stabilizer	
Assay Diluent	Caprine based Assay Diluent in MES buffer Preservative: Antimicrobial agent	Contains human serum based Assay Diluent Preservative: Sodium Azide

K. Standard/Guidance Document Referenced (if applicable):

None referenced.

L. Test Principle:

The ARCHITECT Anti-Tg assay is a two-step immunoassay for the quantitative determination of the IgG class of thyroglobulin autoantibodies (anti-Tg) in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex®. In the first step, sample, assay diluent and Tg coated paramagnetic microparticles are combined and incubated. Anti-Tg present in the sample binds to the Tg coated microparticles. After washing, anti-human IgG acridinium labeled conjugate is added in the second step. Following another incubation and wash, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-Tg in the sample and the RLUs detected by the ARCHITECT *i** system optics.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The ARCHITECT Anti-Tg assay was design to have an assay precision of $\leq 10\%$ CV for samples ≥ 4.0 IU/ml. ARCHITECT Anti-Tg positive control and four human panels (covering the analytical range) were assayed using three lots of reagents in replicates of two at two separate times per day for 20 days in 3 instruments (n=5). Each reagent lot used a single calibration curve throughout the study. Samples concentrations are described below:

Control = ~ 150 IU/ml

Panel 1 = ~ 4 IU/ml

Panel 2 = ~ 17 IU/ml

Panel 5 = ~ 400 IU/ml

Panel 6 = ~ 750 IU/ml

The replicate measurements statistically determine the product's precision of reproducibility and repeatability: total and within-run precision statistics for the assays label claim. The values for within-run % CV were 2%-6% and for the Total % CV values were 2.8%-6.1%. The results indicated that all three reagent lots on each instrument performed within the acceptance criteria on assay precision of $\leq 10\%$ CV.

b. *Linearity/assay reportable range:*

Three high sample pools (1000, 300, and 30 IU/mL) were each combined with a low pool (ARCHITECT Anti-Tg Calibrator A) to prepare nine sets of test dilutions extending to 1/10th the starting concentration. All of these dilutions

were analyzed with the ARCHITECT Anti-Tg assay using a single reagent lot. Based on this study, the ARCHITECT Anti-Tg assay is linear between 3.0 and 1000.0 IU/mL.

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The ARCHITECT Anti-TG Calibrators are standardized to the NIBSC 65/093 reference preparation. The ARCHITECT Anti-TG Primary Reference Calibrator was produced by gravimetric dilutions of NIBSC 65/093. The Anti-Tg Stock Concentrate with an assigned NIBSC value is used to produce the ARCHITECT Anti-Tg Master Calibrator.
- d. *Detection limit:*
The ARCHITECT Anti-Tg assay is designed to have an analytical sensitivity of ≤ 1.0 IU/mL. The analytical sensitivity of the ARCHITECT Anti-Tg assay, defined as the concentration at two standard deviations above the ARCHITECT Anti-Tg Calibrator A (0.0 IU/mL) was calculated to be 0.07 IU/mL at the 95% level of confidence (n=48 runs, 10 replicates of Calibrator A and 4 replicates of Calibrator B per run).
- e. *Analytical specificity:*

Interference

Interference from elevated levels of bilirubin, hemoglobin, triglycerides, and total protein in the ARCHITECT Anti-Tg assay is designed to be $\leq 15\%$ at the levels indicated. Specimens with anti-Tg levels between 53.41 and 320.25 IU/mL were supplemented with the potentially interfering compounds described below. The average amount of interference observed during the study ranged from 3.8% to +1.7%.

Potentially Interfering Substance	Potentially Interfering Substance Concentration
Bilirubin	20 mg/dL
Hemoglobin	1000 mg/dL
Total Protein (Low)	4 g/dL
Total Protein (High)	10 g/dL
Triglycerides	2000 mg/dL

* Representative data; results in individual laboratories may vary from these data.

Potential interference from autoimmune disease specimens and high titer IgG samples in the ARCHITECT Anti-Tg assay is designed to be $\leq 20\%$. In a study, the ARCHITECT Anti-Tg assay was evaluated by testing specimens with known autoimmune diseases and elevated IgG. Specimens were evaluated with anti-Tg levels spiked between 175.58 and 235.86 IU/mL. Mean absolute % interference is summarized in the following table:

Clinical Condition	Mean Absolute % Interference
Anti-Nuclear Antibody (ANA)	1.2
Rheumatoid Arthritis (RA)	1.8
Systemic Lupus Erythematosus (SLE)	2.1
Insulin Dependent Diabetes Mellitus (IDDM)	3.0
Crohn's Disease	2.5
Multiple Sclerosis	3.6
Ulcerative Colitis	2.6
Hyperglobulinemia (high IgG)	4.5

* Representative data; results in individual laboratories may vary from these data.

f. Assay cut-off:

A cut-off value of 4.11 was observed for ARCHITECT as established in the Normal Range Study.

2. Comparison studies:

a. Method comparison with predicate device:

This specimen data (n=204) along with data from 30 specimens above 1000 IU/mL are the basis for the Concordance table summarized in the proposed Package Insert. The agreement between the new device and the predicate is 97.0%. The Concordance Table conveys the relationship between the ARCHITECT anti-Tg and the Nichols.

		Nichols		
		Negative	Positive	Total
ARCHITECT	Negative	111	6	117
	Positive	11	106	117
	Total	122	112	234

% Overall Agreement=217/234=92.7%

b. Matrix comparison:

The new device and the predicate were compared using serum as the matrix. However, the new device can also use plasma.

Serum vs. Plasma Anticoagulant Studies

Plasma samples were collected in different anticoagulants in either glass or plastic collection tubes (glass and plastic) and compared to matched serum samples from the same donor. Twenty-Two donors were evaluated in each of the nine listed tube types:

- EDTA Glass Tube vs. Serum Uncoated Tube
- EDTA Plastic Tube vs. Serum Uncoated Tube
- Lithium Heparin Glass Tube vs. Serum Uncoated Tube
- Lithium Heparin Plastic Tube vs. Serum Uncoated Tube
- Plasma Separator Lithium Heparin Glass Tube vs. Serum Uncoated Tube
- Plasma Separator Lithium Heparin Plastic Tube vs. Serum Uncoated Tube
- Sodium Heparin Glass Tube vs. Serum Uncoated Tube
- Sodium Heparin Plastic Tube vs. Serum Uncoated Tube.

The mean percentage interference was less than 10% for all anticoagulant collection tube types when compared to glass serum tubes. The average absolute interference of the individual specimens across all anticoagulants ranged from 1.1 to 1.9% for all twenty-one-donor specimens within the assay

range. One donor produced values that exceeded the upper end of the assay range (>1000 IU/mL) and was eliminated from further analysis. The actual interference with anticoagulants ranged from -5.1% to 4.0% for all 21 donor specimens within the assay range.

3. Clinical studies:

a. *Clinical Sensitivity and Clinical Specificity:*

Two hundred and thirty four serum samples from individuals with Grave's disease (n=85) and Hashimoto's disease (n=68), including 81 serum samples from apparently normal individuals were tested with both the ARCHITECT Anti-Tg assay and the Nichols Advantage Thyroglobulin Autoantibodies Assay. Using a cutoff of 4.11 IU/ml for the ARCHITECT and 1 IU/ml for the Nichols Advantage, the following clinical sensitivities and specificities were found:

	Normal Individuals		Graves' disease		Hashimoto's disease	
Assay Platform	ARCHITECT	Nichols	ARCHITECT	Nichols	ARCHITECT	Nichols
N	81	81	85	85	68	68
Clinical Sensitivity	-	-	75.3%	68.2%	75%	77.9%
95% CI Clinical Sensitivity	-	-	66.4-82.8%	57.2-77.9%	63.0-84.7%	66.2-87.1%
Clinical Specificity	97.5%	98.8%				
95% CI Clinical Specificity	91.4-99.7%	93.3-100%				

To determine the Clinical Specificity 81 serum samples from normal individuals were tested in the ARCHITECT. The results indicated that the Clinical Specificity of the ARCHITECT Anti-Tg assay is 97.5%.

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

Not applicable.

4. Clinical cut-off:

Same as assay cut-off.

5. Expected values/Reference range:

Human serum specimens were collected from a population of 234 apparently healthy individuals. All specimens delivered TSH values within the normal reference range. Of this study population, 6 specimens delivered positive results on a commercially available anti-Tg assay device and were excluded from further analysis. The 97.5 percentile concentration of the remaining population was 4.11 IU/mL. On the basis of this study population, the expected normal range is <4.11 IU/mL. A total of 97.8% (223/228) of the population gave values within this expected normal range. This normal range is suggested as a guideline and each laboratory should establish a normal range appropriate to their patient populations, giving due consideration to age, gender, geographical location and their clinical practice.

N. Proposed Labeling:

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

O. Conclusion:

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