

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k060578

B. Purpose for Submission:

Clearance to market a calcitonin assay.

C. Measurand:

Calcitonin

D. Type of Test:

Quantitative immunoassay

E. Applicant:

Scantibodies Laboratory Inc.

F. Proprietary and Established Names:

Calcitonin Immunoradiometric Assay (IRMA) (Coated Tube Version)

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1140: Calcitonin test system.

2. Classification:

Class II

3. Product code:

JKR

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

Please see indications for use.

2. Indication(s) for use:

The Scantibodies Laboratory Inc. Calcitonin test system is a device intended to measure the thyroid hormone calcitonin (thyrocalcitonin) levels in serum. Calcitonin measurements are used in the diagnosis and treatment of diseases involving the thyroid and parathyroid glands, including carcinoma and hyperparathyroidism (excessive activity of the parathyroid gland).

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

This manual assay does require the use of a gamma scintillation counter.

I. Device Description:

The Calcitonin Immunoradiometric Assay (IRMA) (Coated Tube Version) is a two site immunoassay where the concentration of the sandwich complex is determined by its activity. As supplied by the company, the kit contains 6 vials of lyophilized human serum used for calibration, 2 vials of lyophilized human serum as control material, a bottle of concentrated wash solution, 50 coated tubes, and 2 vials of labeled antibodies.

The tubes are coated with polyclonal antibodies derived from goats and specific to N terminal end of the Calcitonin peptide. The labeled antibodies are polyclonal material derived from goat and specific to the C terminal end of the Calcitonin peptide. The C terminal specific antibodies are labeled with ¹²⁵I. The 2 vials of labeled antibodies are the only radioactive components of the kit.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Calcitonin IRMA Kit (Coated Bead Version)

2. Predicate 510(k) number(s):

k961043

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Assay to detect human calcitonin in serum	Same
Assay Principle	Immunoradiometric Assay (sandwich)	Same
Matrix	Serum	Same

Differences		
Item	Device	Predicate
Capture Phase	Antibody Coated Tubes	Antibody Coated Beads

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

CLSI C28-A2: How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline—Second Edition

L. Test Principle:

Scantibodies' Calcitonin Coated Tube kit is an immunoradiometric assay (IRMA) utilizing two polyclonal goat antibodies. The capture antibody, coating the inside of the tubes supplied with the kit, is specific to the N terminal region of the Calcitonin peptide. Calcitonin in patient serum is captured by this bound antibody. An ^{125}I C-terminal specific antibody is added to the tube with the sample serum. After extended incubation, the solution in the tube is removed and the tube is rinsed repeatedly with the wash buffer provided with the kit.

The concentration of calcitonin in the patient sample is proportional to the activity of the rinsed tube. Users calibrate their measurements by comparison to samples of known calcitonin concentration provided with the kit and run in parallel with the clinical sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The company assessed the inter-assay variation of their device by measuring clinical samples at 3 different concentrations twice a day for 20 days. The company used 3 different lots of kits in this study. The measurement session extended beyond a day due to the long incubation time (16-24 hours) noted in

the Steps section of the product insert. For their inter-assay precision, the company found:

Kit	Mean [Calcitonin], (pg/ml)	Std. Dev., (pg/ml)	%CV
E1	19.73	1.81	9.18
	188.09	14.05	7.47
	487.73	32.19	6.6
E2	16.48	0.38	2.33
	178.78	6.44	3.6
	466.79	18.27	3.91
E3	17.31	1.68	9.72
	180.97	7.69	4.25
	483.93	18.71	3.87

The company assessed the intra-assay variation of their device by measuring clinical samples at 3 different concentrations of calcitonin 20 times at each concentration during one measurement session. The measurement session extended beyond a day due to the long incubation time (16-24 hours) noted in the Steps section of the product insert. For their intra-assay precision, the company found:

Kit	Mean [Calcitonin], (pg/ml)	Std. Dev., (pg/ml)	%CV
E1	19.58	0.68	3.48
	189.37	3.33	1.76
	504.61	10.44	2.07
E2	16.93	0.37	2.17
	186.97	3.35	1.79
	511.59	9.10	1.78
E3	15.72	1.45	9.24
	178.52	8.93	5.00
	475.11	12.20	2.57

The company performed additional precision studies at the end of the claimed shelf life of their kit to determine their “end of run” precision. The company determined that a loss of precision due to isotope decay led to less than a 10% loss in precision.

b. *Linearity/assay reportable range:*

The company demonstrated their ability to measure calcitonin across a range of concentrations using a series of recovery and dilution experiments. For the addition studies, three serum samples containing endogenous calcitonin were spiked with known quantities of calcitonin for a total of 9 different calcitonin concentrations ranging from 33 – 679 pg/ml. Measured vs. expected calcitonin concentrations varied from 96% to 109%. These measurements met the company's acceptance criterion that an average of all measurements falls within 80% and 120% of the expected value.

For their dilution studies, the company diluted clinical serum samples with initial calcitonin concentrations ranging from 41 pg/ml to 785 pg/ml. A total of 28 calcitonin concentrations were measured. The measured vs. expected calcitonin concentrations varied from 88% to 149%. The company's measurements met their acceptance criteria that an average of all measurements falls within 80% and 120% of the expected value.

In their product insert, the company noted that for samples over 500 pg/ml, individual errors in measurement ranged from a low of 12% to 40%.

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

Calibrators and controls for use with this device were previously cleared with the predicate.

Studies performed by the company indicated that their unlabeled antibodies were stable for in excess of a year when properly stored. The shelf life of the kit was dictated by the half life of the ¹²⁵I isotope, 60.2 days. The company claims a shelf life of 56 days from the date of manufacture for this device. End of run precision studies supplied by the company support their claim for a 56 day shelf life.

d. *Detection limit:*

The company defined the detection limit of their assay as two standard deviations above the mean value of their zero concentration calibrator. The company determined this limit using 20 measurements on their zero calibrator made on the same day with the same assay. The company determined that their claimed lower limit of detection – a limit of the blank – was 1 pg/mL.

e. *Analytical specificity:*

The company challenged the specificity of their antibodies with proteins often associated with high concentrations of calcitonin in diseased individuals. In addition, they challenged their assay with several human calcitonin analogues used in patient treatment. The company found:

Crossreactant	[Crossreactant]	Δ [Calcitonin], pg/ml	% Change, [Calcitonin]
PTH	100,000 pg/ml	3.97	1.10
	25,000 pg/ml	-9.58	-2.67
	10,000 pg/ml	-8.59	-2.39
TSH	5,000 μ IU/ml	-5.12	-1.42
	500 μ IU/ml	0.62	0.17
	50 μ IU/ml	0.14	0.04
Calcitonin Gene Related Peptide	1,000,000 pg/ml	-6.1	-1.70
	100,000 pg/ml	3.7	1.03
Porcine Calcitonin	1,000,000 pg/ml	-9.21	-2.56
	100,000 pg/ml	5.95	1.66
Salmon Calcitonin	1,000,000 pg/ml	-47.76	-13.29
	100,000 pg/ml	-9.58	-2.67

All testing was done with test samples with a calcitonin concentration of 359.4 pg/ml.

The company determined that concentrations of triglycerides to 250 mg/dL, hemoglobin to 15 mg/dL, and bilirubin to 15 mg/dL did not impact the clinical utility of the assay. The company did not note a high dose Hook effect below 1000 pg/ml.

f. Assay cut-off:

Not applicable to this submission.

2. Comparison studies:

a. Method comparison with predicate device:

The company compared their proposed device to their legally marketed predicate using 250 serum samples. The company spiked some samples with calcitonin to cover the full range of both assays. Measurements were performed on the same day using both devices. The company obtained a slope of 1.08 when fitting a line to their proposed vs. predicate data. They reported a correlation coefficient of 0.98 for their line fit and an intercept of -2.75.

b. Matrix comparison:

Not applicable to this submission.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable to this submission.

b. Clinical specificity:

Not applicable to this submission.

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

Not applicable to this submission.

4. Clinical cut-off:

Not applicable to this submission.

5. Expected values/Reference range:

The company followed CLSI C28-A “How to Define and Determine Reference Intervals in the Clinical Laboratory” in determining their reference intervals for calcitonin. The company measured calcitonin in serum from 125 apparently healthy (self-reported) adults using the proposed Scantibodies Calcitonin RadioImmunoassay. The study consisted of 72 female and 53 males. Using their proposed device, the company determined the normal range for males was 3 - 21 pg/mL. For females, the company determined the normal concentration for calcitonin was 1 - 8 pg/mL

In their product insert, the company recommends that laboratories establish their own reference range.

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.