

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

A. 510(k) Number:

k032134

B. Analyte:

Thyroid-stimulating hormone (TSH) Receptor Antibody

C. Type of Test:

Qualitative or quantitative radioimmunoassay

D. Applicant:

KRONUS Market Development Associates

E. Proprietary and Established Names:

KRONUS TSH Receptor Antibody (TRAb) Coated Tube (CT) Assay Kit

F. Regulatory Information:

1. Regulation section:
21 CFR § 866.5870
Thyroid Autoantibody Immunological Test System
2. Classification:
Class II
3. Product Code:
JZO
4. Panel:
IM82

G. Intended Use:

1. Intended use(s):
KRONUS TSH Receptor Antibody (TRAb) Coated Tube (CT) Assay Kit is designed to measure human serum autoantibodies to the thyroid stimulating hormone (TSH or thyrotropin) receptor. The TRAb CT kit is useful as an aid in the differential diagnosis of Graves' Disease.
2. Indication(s) for use:
KRONUS TSH Receptor Antibody (TRAb) Coated Tube (CT) Assay Kit is for the quantitative or qualitative determination of thyroid stimulating hormone receptor antibody in human serum. The TRAb CT Assay Kit is useful as an aid in the differential diagnosis of Graves' disease.
3. Special condition for use statement(s):
The device is for prescription use only.
4. Special instrument Requirements:
Gamma counter set for ¹²⁵I

H. Device Description:

The assay is a radioimmunoassay (RIA) in which TSH receptor autoantibodies (TRAb), if present in a patient's serum, are allowed to interact with TSH receptor coated onto plastic tubes and fluid-phase radiolabeled TSH. Bound TRAb are detected by their ability to inhibit the binding of ¹²⁵I-labeled TSH to the receptor coated tubes. TRAb levels are then expressed as an inhibition of TSH binding index

or read off a standard curve. The assay consists of the following components: TSH receptor coated plastic tubes, ¹²⁵I-labeled TSH, start buffer (1% Triton X-100 and 0.2 mg/mL normal mouse IgG), wash buffer, calibrators (1, 2, 8, and 40 U/L), and controls (positive and negative).

I. Substantial Equivalence Information:

1. Predicate device name(s):
KRONUS TSH Receptor Antibody (TRAb) Kit
2. Predicate K number(s):
k863006
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For measurement of TRAb as an aid in the diagnosis of Graves' disease	Same
Assay principle	Radio-receptor inhibition immunoassay	Same
Analyte	TSH receptor antibodies	Same
Sample matrix	Serum	Same
Differences		
Item	Device	Predicate
Trade name	KRONUS TSH Receptor Antibody (TRAb) Coated Tube Assay	KRONUS TSH Radio-receptor Antibody (TRAb) Assay Kit
Solid phase	TSH receptor reagent coated tubes - "ready to use"	Uncoated tubes - TSH receptor reagent must be manually added to test tube
Calibration	NIBSC Standard 90/672	LATS Standard B (NIBSC 65/122)
Cut-off	Positive: >1.5 U/L (15% inhibition) Equivocal: 1.1-1.5 U/L (11-15% inhibition) Negative: <= 1.0 U/L (10% inhibition)	Positive: > 15 U/L (15% inhibition) Equivocal: 11-15 U/L (11-15% inhibition) Negative: <= 10 (10% inhibition)

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

"Review Criteria for In Vitro Diagnostic Devices for the Assessment of Thyroid Autoantibodies Using Direct Immunofluorescence Assay (IFA), Indirect Hemagglutination (IHA), Radioimmunoassay (RIA), and Enzyme Linked-Immunesorbent Assay (ELISA)."

K. Test Principle:

Radioimmunoassay (RIA) technology is a well established methodology.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Inter-assay precision:

To assess the inter-assay precision, testing was carried out on 4 samples (n = 9, 9, 24 and 25 repeats) ranging from 0.83 U/L to 21.6 U/L which resulted in a range of CVs from 7.2 to 18.8%.

Intra-assay precision:

The intra-assay precision testing was carried out on 5 samples ranging from 0.8 U/L to 4.5 U/L in replicates of either 25 or 27 which resulted in a range of CVs from 4.7 to 16.0%.

b. *Linearity/assay reportable range:*

Dilution/recovery studies:

Eleven serum samples of varying levels of autoantibody to TSH (ranging from 0.0 to 38.7 U/L) were diluted as follows: 400 uL of sample + 100 uL of calibrator 3 (8 U/L). The recoveries ranged from 94% to 111% with a mean recovery across samples of 102%.

Hook effect:

Three elevated serum samples were serially diluted in kit negative control to determine if there was any hook effect. None was observed.

c. *Traceability (controls, calibrators, or method):*

The calibrators were standardized against the National Institute for Biological Standards and Control (NIBSC) 90/672, Thyroid Stimulating Hormone Antibody.

d. *Detection limit:*

The lower detection limit of the assay was determined by sequentially testing the negative control included with the kit 20 times. A calibration curve of %B/Bo versus concentration was constructed. The mean and SD for the %B/Bo of the negative were calculated and the mean +2SD and the mean +3SD were read off the calibration curve to give a U/L value for the lower detection limit. The limit was computed to be 0.3 U/L which is the mean of 20 determinations plus 2SD.

e. *Analytical specificity:*

Studies were performed with potential interferants:

Hemoglobin:

Samples from both patients positive for autoantibodies to TSH receptor and normal healthy blood donors spiked with hemoglobin were analyzed. Thirteen samples were spiked with 50 mg/dL and 500 mg/dL. Another study included 2 samples spiked with varying concentrations of hemoglobin. There was a positive effect on TSH receptor results with hemoglobin concentrations above 50 mg/dL.

Bilirubin:

Samples from patients positive for TSH receptor antibodies and from healthy blood donors were spiked with 20 mg/dL of bilirubin. No significant interference was noted at this level.

Lipids:

Samples from patients positive for TSH receptor antibodies and from healthy blood donors were spiked with 3000 mg/dL and 1000 mg/dL of a lipid containing substance. Interference was noted in samples spiked with 3000 mg/dL causing generally reduced levels but not in those containing 1000 mg/dL.

Hormones (crossreactivity):

A sample negative for TRAb was spiked with varying concentrations of LH, hCG, TSH and FSH. No significant interference was observed at the highest level of all interferants tested, with the exception of TSH where interference was noted at concentrations above 3.350 mU/mL.

f. Assay cut-off:

To validate the appropriateness of the cut-off point (<1 U/L), 242 human blood donor serum specimens were tested. Of the 242 sera tested, 240 (99.2%) yielded inhibition of less than 1 U/L. Two samples reported 1.03 U/L and 1.1 U/L respectively. Given these results and taking into account the analytical sensitivity of the assay, values <1 U/L are considered negative for TSH receptor autoantibodies, values between 1.1-1.5 U/L are considered equivocal and > 1.5 U/L are considered positive.

2. Comparison studies:

a. Method comparison with predicate device:

A correlation study was performed between the predicate KRONUS TRAb assay and the proposed KRONUS TRAb assay. Sixty-two (62) serum samples obtained from either confirmed Graves' disease patients or patients presumptively diagnosed with Graves' disease were tested in parallel. Overall agreement between the two assays was 92.3%.

b. Matrix comparison:

Not applicable - both assays use serum.

3. Clinical studies:

a. Clinical sensitivity:

Not provided

b. Clinical specificity:

Not provided

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

4. Clinical cut-off:

See assay cut-off

5. Expected values/Reference range:

See assay cut-off

M. Conclusion:

KRONUS TSH Receptor Antibody (TRAb) Coated Tube (CT) Assay Kit is substantially equivalent to other devices regulated under 21 CFR § 866.5870, product code JZO.