

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

A. 510(k) Number:

k033454

B. Analyte:

Thyrotropin/Thyroid-stimulating hormone (TSH) Receptor Antibody

C. Type of Test:

Quantitative luminescence receptor assay

D. Applicant:

BRAHMS Diagnostica, LLC.

E. Proprietary and Established Names:

BRAHMS LUMItest® TRAK human

F. Regulatory Information:

1. Regulation section:
21 CFR § 866.5870 Thyroid Autoantibody Immunological Test System
2. Classification:
Class II
3. Product Code:
JZO System, Test, Thyroid Autoantibody
4. Panel:
Immunology 82

G. Intended Use:

1. Intended use(s):
LUMItest TRAK human is a luminescence receptor assay (LRA) for the quantitative determination of antibodies to the human thyrotropin (TSH) receptor. The measurement of TSH receptor autoantibodies is used in the assessment of patients with suspect Graves' disease (autoimmune hyperthyroidism).
2. Indication(s) for use:
LUMItest TRAK human is a luminescence receptor assay (LRA) for the quantitative determination of antibodies against the human thyrotropin (TSH) receptor. The measurement of TSH receptor autoantibodies is used in the assessment of patients with suspect Graves' disease (autoimmune hyperthyroidism).
3. Special condition for use statement(s):
The device is for prescription use only.
4. Special instrument Requirements:
Luminometer with two injectors

H. Device Description:

The LUMItest TRAK human assay consists of tracer A, luminescence-labeled (acridinium derivative) bovine TSH (lyophilized); sample incubation buffer; tubes coated with recombinant human TSH receptor; buffer for reconstitution of tracer A; washing solution, concentrate; TRAK standards (human serum) in concentrations: 0, 1, 2, 4, 16, 40 IU/L; and TRAK controls I (negative, indeterminate) and II (positive) human serum.

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	Aid in the confirmation and differential diagnosis of Graves' disease
Analyte	TSH receptor antibodies	Same
Sample matrix	Serum	Same
Differences		
Item	Device	Predicate
Assay principle	Luminescence receptor assay	Radio-receptor immuno-inhibition assay
Solid phase	Human recombinant TSH receptor pre-coated tubes	Porcine TSH receptor reagent added manually to test tubes
Tracer	Luminescence-labeled (acridinium derivative) bovine TSH	I ¹²⁵ TSH
Calibration	WHO TSAb Standard 90/672	LATS Standard B (NIBSC 65/122)
Detection	Luminometer	Gamma counter
Units	IU/L	U/L
Cut-off	Positive: >2 IU/L Equivocal: 1 - 2 IU/L Negative: <1.0 IU/L	Positive: > 15 U/L (15% inhibition) Equivocal: 11-15 U/L (11-15% inhibition) Negative: <= 10 (10% inhibition)
Reportable range	0.9 - 40 IU/L	0 - 405 U/L

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

None referenced.

K. Test Principle:

Detection is based on the ability of TRAb in patients' serum to prevent the binding of labeled TSH to the TSH receptor bound to the solid phase (test tube). In the first step of the assay, the patient sample containing an unknown TRAb concentration and the standards with known TRAb concentrations are incubated in test tubes coated with recombinant human TSH receptor. After an initial wash, labeled bovine TSH is measured in a luminescence reader. The measured signal, reported as relative light units (RLU), is inversely proportional to the quantity of TRAb in the test sample. The TRAb concentration in the patients' sample can be calculated from the standard curve which is constructed by measuring the known TRAb concentration in the standards.

L. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*Inter-assay precision:

The inter-assay precision testing was carried out by running duplicate determinations of 9 samples in 10 separate assays. The sample means ranged from 0.6 IU/L to 20.3 U/L. The resulting %CV ranged from 4.1 to 35.1%.

Intra-assay precision:

To assess the intra-assay precision, testing was carried out on 10 samples, 10 replicates each, ranging from 0.9 IU/L to 101.7 IU/L (4 samples at the cut-off for positive). The %CV ranged from 2.3 to 24.2%.

b. *Linearity/assay reportable range:*Dilution/recovery studies:

Two patient samples with levels of autoantibody to TSH receptor (ranging from 6.9 and 14.4 IU/L were serially diluted with TRAb-free human serum. The recoveries ranged from 88.2% to 105.6%. The reportable range is 0 to 40 IU/L.

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

The calibrators were standardized against the WHO 1st International reference material, 90/672 for Thyroid Stimulating Hormone Antibody.

d. *Detection limit:*

The analytical sensitivity of the assay was determined to be 0.4 IU/L which corresponds to 2 standard deviations from 10 replicate determinations of the zero standard. The functional sensitivity of 0.9 IU/L was determined by running 29 control samples in 10 separate assays. Precision was calculated over two concentration ranges, 0-25 IU/L and 0-5 IU/L.

e. *Analytical specificity:*

Studies were performed with potential interferants:

Hemoglobin:

Two control samples were diluted in three steps with plasma plus red blood cells and plasma neat as reference. Recovery ranged from 100-125%.

Bilirubin:

Concentrations of bilirubin (0.625, 1.25, 2.5, 5, 10 and 20 mg/dL) were added to two different control samples. Recovery ranged from 91-100%.

Lipids:

A TRAK positive control sample was diluted serially with lipemic serum (634 mg/dL triglycerides). Serial dilutions of the sample with a non-lipemic serum served as referee. Recovery ranged from 76-100%.

Hormones and other autoantibodies (crossreactivity):

A sample containing undetectable TRAb was spiked with concentrations of LH (9000 U/L), TSH (1000 U/L), FSH (15000 U/L), anti-TPO antibodies (3000U/mL) and Anti-Tg antibodies (2000 U/mL). No significant interference was observed at these levels.

f. Assay cut-off:

In a study of 282 healthy individuals, an upper limit of 1.0 IU/L was determined. The cut-off was challenged with 86 patients with untreated Graves' disease. A sensitivity of 98.8% and a specificity of 99.6% were demonstrated using this cut-off. Values <1 IU/L are considered negative for TSH receptor autoantibodies, values between 1.0-2.0 IU/L are considered equivocal and >2.0 IU/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 LUMItest TRAK assay. Fifty-two (52) serum samples obtained from either confirmed Graves' disease patients or patients with non-Graves thyroid disease were tested in parallel. Overall agreement between the two assays was 75.0%.

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:

Based on information in the submission, the BRAHMS LUMItest® TRAK human assay is recommended as substantially equivalent to other devices regulated under 21 CFR § 866.5870, Thyroid autoantibody immunological test system (Class II, product code – JZO, product name – Thyroid autoantibody test system).