

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

A. 510(k) Number:

k150403

B. Purpose for Submission:

Adding updated pediatric reference ranges and new infant reference ranges to a previously cleared assay, k083844.

C. Measurand:

Thyroid Stimulating Hormone (TSH)

D. Type of Test:

Quantitative, chemiluminescence immunoassay

E. Applicant:

Siemens Healthcare Diagnostics Inc.

F. Proprietary and Established Names:

ADVIA Centaur TSH3-Ultra

G. Regulatory Information:

1. Regulation section:

21 CFR § 862.1690, Thyroid stimulating hormone test system

2. Classification:

Class II

3. Product code:

JLW

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications(s) for use below

2. Indication(s) for use:

For in vitro diagnostic use in the quantitative determination of thyroid-stimulating hormone (TSH, thyrotropin) in serum, heparinized plasma, and EDTA plasma using the ADVIA Centaur and ADVIA Centaur XP systems. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

ADVIA Centaur and ADVIA Centaur XP systems.

I. Device Description:

ADVIA Centaur TSH3-Ultra (TSH3-UL) kit consists of the following reagents:

Ultra-Lite Reagent- bovine serum albumin (BSA) conjugated to monoclonal anti- TSH (~0.3 µg/mL) labeled with acridinium ester in HEPES buffered saline, mouse IgG, BSA, goat serum, surfactant, and preservatives.

Solid Phase Reagent - anti-fluorescein monoclonal mouse antibody covalently linked to paramagnetic particles (PMP) (~85 µg/mL) in HEPES buffered saline, BSA, goat serum, surfactant, and preservative.

Ancillary Well Reagent – Fluorescein isothiocyanate conjugated to monoclonal anti-TSH (~3 µg/mL) in HEPES buffered saline, mouse IgG, BSA, goat serum, surfactant, and preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):

ADVIA Centaur TSH3-Ultra

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

k083844

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate device ADVIA Centaur TSH3-Ultra	Predicate Device ADVIA Centaur TSH3-Ultra (k083844)
Intended Use	For in vitro diagnostic use in the quantitative determination of thyroid-stimulating hormone (TSH, thyrotropin) in serum, heparinized plasma, and EDTA plasma.	Same
Reagents	ADVIA Centaur TSH3-Ultra	Same
Analyzers	ADVIA Centaur , ADVIA Centaur XP	Same
Analytical Measuring Range (Assay Range)	0.008 – 150 μ IU/mL	Same
Infant Reference Intervals	1 month -23 months: 0.87 - 6.15 μ IU/mL	None
Children Reference Intervals	2 to 12 years: 0.67 - 4.16 μ IU/mL	2 to less than 12 years: 0.636 -6.267 μ IU/mL

Adolescents Reference Intervals	13 years – 20years: 0.48 - 4.17 μ IU/mL	12 to less than 18 years: 0.51-4.94 μ IU/mL
Adult Reference Intervals	21 years and older: 0.55– 4.78 μ IU/mL	18 years and older: 0.55– 4.78 μ IU/mL

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

Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory;
Approved Guideline - Third Edition (CLSI C28-A3).

L. Test Principle:

The ADVIA Centaur TSH3-Ultra assay is a third-generation assay that employs anti-FITC monoclonal antibody covalently bound to paramagnetic particles, and FITC-labeled anti-TSH capture monoclonal antibody, and a tracer consisting of a proprietary acridinium ester and an anti-TSH monoclonal antibody conjugated to bovine serum albumin (BSA) for chemiluminescent detection. A direct relationship exists between the amount of TSH present in the patient sample and the amount of relative light units (RLUs) detected by the system.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Provided in k083844.

b. Linearity/assay reportable range:

Provided in k083844.

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

Provided in k083844.

d. Detection limit:

Provided in k083844.

e. Analytical specificity:

Provided in k083844.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Provided in k083844.

b. Matrix comparison:

Provided in k083844.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

A pediatric reference range study using population age from 1 month old to 20 years old was conducted. Serum samples were collected at 8 U.S. sites to be representative of the U.S. population diversity. Data from a total of 442 pediatric patients (94 infants, 198 children, and 150 adolescents) from one ADVIA Centaur analyzer and three reagent lots were analyzed to establish the ADVIA Centaur TSH-3 Ultra assay reference ranges for the studied pediatric population. Results from the 2.5th to 97.5th percentile were used as the pediatric reference ranges. The reference interval for the infant group was calculated

by performing a log-transformation of the raw data followed by the application of the robust symmetric method to the transformed data. This approach was selected to be most appropriate for the smaller sample size as the data from this population was highly skewed to the right and a transformation was necessary to obtain a normal distribution. The sponsor has added language to their package insert explaining the uncertainty in the value for the upper limit of the reference range. A non- parametric approach was used to establish the reference intervals for children and adolescents based on the CLSI C28-A3 recommendation because the sample size was greater than 120. Reference ranges are summarized in the table below.

Age Range	Reference Ranges
Infants (01 – 23 months)	0.87 - 6.15 μ IU/mL
Children (02 – 12 years)	0.67 - 4.16 μ IU/mL
Adolescents (13 – 20 years)	0.48- 4.17 μ IU/mL

Confidence intervals for the limits of the infant reference range are as follows:

	Lower Limit of reference range	Upper Limit of reference range
90% confidence intervals:	0.74- 1.04 μ IU/mL	5.32 – 6.98 μ IU/mL

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.