

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

A. 510(k) Number:

k060090

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Thyrotropin (TSH)

D. Type of Test:

Quantitative Chemiluminescence Immunoassay

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista™ Thyroid Stimulating Hormone (TSH) Flex® reagent cartridge

G. Regulatory Information:

1. Regulation section:

21 CFR § 862.1690, Thyroid stimulating hormone test system

2. Classification:

Class II

3. Product code:

JLW, Radioimmunoassay, thyroid-stimulating hormone

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indication(s) for use below

2. Indication(s) for use:

The Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridge (TSH) is a device intended to measure thyroid stimulating hormone, also known as thyrotrophin and thyrotrophic hormone, in serum and plasma. 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:
Dade Behring Dimension Vista™ System

I. Device Description:

The TSH method is a homogeneous, sandwich chemiluminescent immunoassay based on Luminescent Oxygen Channeling Immunoassay (LOCI™) technology. The LOCI™ reagents include two latex bead reagents and a biotinylated anti-TSH monoclonal antibody fragment. The first bead reagent (Sensibeads) is coated with streptavidin and contains photosensitizer dye. The second bead reagent (Chemibeads) is coated with a second anti-TSH monoclonal antibody and contains chemiluminescent dye. Sample is incubated with biotinylated antibody and Chemibeads to form bead-TSH-biotinylated antibody sandwiches. Sensibeads are added to bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direct function of the TSH concentration in the sample.

J. Substantial Equivalence Information:

1. Predicate device name(s):
ADVIA Centaur TSH-3 assay
2. Predicate 510(k) number(s):
k981312
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For the <i>in vitro</i> quantitative measurement of thyroid-stimulating hormone (TSH) in human serum and plasma.	For the <i>in vitro</i> quantitative determination of thyroid-stimulating hormone (TSH) in human serum.
Detection	Chemiluminescence	Chemiluminescence
Assay Methodology	Sandwich immunoassay	Sandwich immunoassay

Differences		
Item	Device	Predicate
Intended Use	For the <i>in vitro</i> quantitative measurement of thyroid-stimulating	For the <i>in vitro</i> quantitative determination of thyroid-

Differences		
Item	Device	Predicate
	hormone (TSH) in human serum and plasma.	stimulating hormone (TSH) in human serum.
Sample Type	Plasma and Serum	Serum
Antibody	Two anti – TSH mouse monoclonals (one whole antibody and one fragment.	Monoclonal mouse anti-TSH and polyclonal sheep anti-TSH.
Solid Phase	Latex Microparticles	Paramagnetic Particles
Instrument Required	Dimension Vista™ System	ADVIA Centaur

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

NCCLS EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods
 NCCLS EP7-A, Interference Testing in Clinical Chemistry
 NCCLS EP9-A2, Evaluation of Precision Performance of Quantitative Measurement Methods

L. Test Principle:

See Device Description above.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Two patient serum pools and three control materials were assayed. During each day of testing, two separate runs, with two test samples, for each test material were analyzed for 20 days. The assays were run on a single analyzer using one lot of reagent. Results for precision are summarized below.

	Control Level 1	Control Level 2	Control Level 3	Serum Pool 1	Serum Pool 2
Mean, μ IU/mL	0.391	6.31	38.3	4.05	76.5
	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)
Repeatability	0.007(1.69)	0.09(1.47)	0.7(1.76)	0.07(1.63)	1.3(1.70)
Between Run	0.000(0.00)	0.00(0.00)	0.4(0.98)	0.00(0.00)	1.4(1.84)
Between Day	0.008(2.01)	0.11(1.76)	0.6(1.66)	0.08(1.93)	1.3(1.75)
Within Lab	0.010(2.62)	0.14(2.30)	1.0(2.61)	0.10(2.53)	2.3(3.06)

b. *Linearity/assay reportable range:*

The linear range of the Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridge was confirmed by assaying samples prepared from dilutions of the Level C calibrator. The TSH concentrations observed in the samples ranged from 0.008 to 102.9 µIU/mL. The means of the observed values for each sample were plotted versus the expected values. The linear relationship appeared acceptable by visual examination. Results are summarized below.

Sample	Expected Value, µIU/mL	Observed Value, µIU/mL
1	0.000	0.008
2	26.4	25.2
3	52.9	51.0
4	79.3	77.7
5	105.7	102.9

Least squares regression analysis gave the following: Observed = 0.98(Expected) – 0.32; r = 0.9999

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

The LOCI I calibrator (k053531), is used to calibrate the Dimension Vista™ flex® reagent cartridge. The calibrator is referenced to the WHO 2nd IRP 80/558 standard. See k053531 for more information.

Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridges were stored in a controlled environment at 2-8°C. QC materials (3 levels of Bio-Rad Lyphochek Immunoassay Plus Control, lot 40150) and a human serum pool were aliquotted and frozen at -70°C. On each measuring day, one aliquot was thawed, the Dimension Vista TSH method was calibrated, and the QC material and serum pool run in 5 replicates. The analyte values obtained on each day were averaged over the replicates. At the end of the study, the mean values for each day were graphed against the day, inspected visually, and analyzed by linear regression. The Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridge was shown to be stable up to 366 days.

d. *Detection limit:*

Functional sensitivity was determined by measuring eight serum pools ranging in concentration from 0.004 to 0.021 µIU/mL. Each sample was tested twice a week for approximately six weeks. The concentration at which assay imprecision was calculated to be 20 % CV (by interpolation) is 0.005 µIU/mL.

e. *Analytical specificity:*

To test the crossreactivity of this device to similar endogenous analytes, serum samples were spiked with hCG, LH, and FSH at 200000, 1000, and 1000 mIU/mL, respectively, and compared to a non-spiked base pool. No analytes tested significantly cross-reacted in this analysis.

A patient serum sample was spiked with specific concentrations of potential interfering substances, and the TSH values were obtained using the Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridge then compared to a non-spiked control sample. Bias exceeding 10% is considered interference. No interference was found. Results are summarized below.

Substance	Amount	[TSH] μIU/mL	Bias
Hemoglobin (hemolysate)	1000 mg/dL	4.32	-8.2
Bilirubin (unconjugated)	60 mg/dL	4.32	-2.6
Bilirubin (conjugated)	60 mg/dL	4.32	-4.0
Lipemia (Intralipid®)	3000 mg/dL	4.32	5.0
Biotin	500 ng/mL	4.32	-4.9
Dextran 40	3 g/dL	4.32	9.4

The potential for a high dose hook effect was evaluated for this assay by spiking a human serum pool that was initially 0.80 μIU/mL TSH to 30,000 μIU/mL TSH. The spiked pool was serially diluted into the assay range. Data shows no overlap in instrument response demonstrating that there is no high dose hook effect up to 30,000 μIU/mL.

f. *Assay cut-off:* N/A
N/A

2. Comparison studies:

a. *Method comparison with predicate device:*

Clinical samples (n=189 commercially purchased serum samples) were tested using the device and the predicate and compared. Results were determined using linear regression and are summarized below.

$$\text{Device} = 0.95(\text{Predicate}) + 0.21; r = 0.997$$

b. *Matrix comparison:*

Samples from 55 patients were then used to compare serum results to sodium heparin plasma (with TSH levels ranging from 0.299-97.0 μ IU/mL), lithium heparin plasma (with TSH levels ranging from 0.266-97.0 μ IU/mL), and EDTA plasma samples (with TSH levels ranging from 0.259-97.0 μ IU/mL) in order to demonstrate that serum results match plasma results. Results are summarized below.

Comparison	Slope	Y-Intercept	<i>r</i>
Serum vs Na heparin plasma	1.01	0.36	0.997
Serum vs Li heparin plasma	1.02	0.19	0.998
Serum vs EDTA plasma	0.99	0.05	0.999

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable (NA)

b. *Clinical specificity:*

NA

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

NA

4. Clinical cut-off:

NA

5. Expected values/Reference range:

Serum samples from 297 apparent healthy adult blood bank donors (187 males and 110 females, ages 18 to 65) were commercially purchased and assayed with the Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridge. The expected normal range for the Dimension Vista™ Thyroid Stimulating Hormone Flex® reagent cartridge was found to be 0.358-3.74 μ IU/mL based on the central 95% of the frequency distribution.

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.