510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:
k110761

B. Purpose for Submission:
New device

C. Measurand:
Thyroid-stimulating hormone (TSH)

D. Type of Test:
Quantitative magnetic lateral flow immunoassay

E. Applicant:
MagnaBioSciences LLC

F. Proprietary and Established Names:
MICT® TSH, MICT® Instrument

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1690 Thyroid Stimulating Hormone Test System
   21 CFR § 862.1315 Colorimeter, Photometer, Spectrophotometer for Clinical Use
2. Classification:
   Class II (assay), Class I (instrument)
3. Product code:
   JLW, JJQ
4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See "Indication(s) for use" below

2. Indication(s) for use:
   The MICT TSH is a magnetic lateral flow immunoassay for the in vitro quantitative determination of TSH in human serum. The measurements of thyroid stimulating hormone (TSH) produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders. The MICT System is intended for use in clinical laboratories.

   The MICT Instrument is intended for use with the MICT (Magnetic Immuno-

Chromatographic Test) lateral flow assays. The instrument measures the test signal, calculates, and reports results.

3. Special conditions for use statement(s):
   For prescription use only

4. Special instrument requirements:
   MICT instrument

I. Device Description:

The device consists of the MICT instrument and the MICT TSH in vitro diagnostic test cassettes. The cassettes contain:

1. Solid phase nitrocellulose membrane cassette with two detection zones
   a. Control line region containing a polyclonal goat anti-rabbit IgG antibody, and
   b. Test line region containing a murine monoclonal anti-TSH antibody
2. Lyophilized conjugate containing rabbit monoclonal anti-TSH antibody covalently coupled to 300 nm super paramagnetic particles.

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J. Substantial Equivalence Information:

1. Predicate device name(s):
   Qualigen FastPack TSH Immunoassay

2. Predicate 510(k) number(s):
   k052301

3. Comparison with predicate:

Similarities		
Item	**MICT® TSH**	**FastPack® TSH**
Intended Use	immunoassay for the in vitro quantitative determination of TSH in human serum. The measurements of thyroid stimulating hormone (TSH) produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.	same
Assay Methodology	Sandwich immunoassay	Same
Data analysis	Internal data reduction via microcomputer	Same
Test processing	Semi-automated	Same
Assay Range	0.13 – 100 uIU/mL	Same
Sample volume	100 µL	Same

Similarities		
Item	**MICT® TSH**	**FastPack® TSH**
Detection Antibody	Monoclonal (mouse)	Same
Throughput	Single sample	Same

Differences		
Item	**MICT TSH**	**FastPack TSH**
Storage condition	1-30 °C	2 – 8 °C
Sample type	Serum	Plasma
Detector	Magnetic instrument	Photomultiplier tube
Label	Super Magnetic Particles	Alkaline Phosphatase – Lucegine
Instrument required	MICT Magnetic instrument	FastPact system
Solid phase	Nitrocellulose membrane	Magnetic particles
Control Antibody	Polyclonal (goat anti-rabbit)	Monoclonal
Detection	Magnetic moment	Chemiluminescence
Calibration	Factory generated master curve; stable until expiration date of assay lot	Factory generated calibration curve using 6 standards; requires monthly recalibration
Calibration frequency	Factory calibration	Every 14 days by user
Time to result	30 minutes	15 minutes
Reagents supplied	Box of 20 reagent cassettes with lyophilized conjugate tubes	Box of 50 individual tests

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

a. EN61010-1 – Safety requirements for electrical equipment for measurement, control, and laboratory use (2nd edition)
b. EN 61326 – Electrical equipment for measurement, control and laboratory use, EMC requirements (Version 04: 1997+A1; Version 06: 1998+A2)
c. CLSI EP5-A2 – Evaluation of precision Performance of Quantitative Measurement Methods (2nd edition)
d. CLSI EP9-A2-IR – Method Comparison and Bias Estimation Using Patient Samples (2nd edition)
e. CLSI EP6-A – Evaluation of Linearity of Quantitative Measurement Procedures: A Statistical Approach (1st edition)
f. CLSI EP17-A – Protocols for the Determination of Limits of Detection and Limits of Quantitation (1st edition)

L. Test Principle:

MICT TSH is a magnetic immuno-chromatographic test (MICT) using Super Paramagnetic particles (SPMPs) as the labeling agent. The SPMP magnetic field is quantified by a MICT instrument.

MICT TSH is based on the principle of capillary flow and separation of immune complexes bound to SPMPs within a porous matrix. In the test device, TSH antibody (Ab) – antigen (Ag) immune reactions occur on a narrow strip of capillary membrane. The narrow strip is housed in a disposable plastic cassette to form a test device.

The specimen containing the TSH antigens is mixed with a lyophilized conjugate pellet and added into the sample well of the MICT cassette. As the TSH Ab-Ag, SPMP immune complexes migrate through the test device, they are captured by the second antibodies at the test line. A control line is formed by the control SPMP immune complexes. The MICT instrument is used to analyze the quantity of magnetic particles captured on both control and test lines. A visible line is not necessary for interpreting the MICT test result. The TSH concentration is directly proportional to the magnetic signal and is reported based on the predetermined test algorithms that are embedded in the cassette barcode labels.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   The precision was determined using the CLSI EP5-A2 protocol as a guide. The study was conducted at three external sites. Each site was supplied with three levels (low, medium, high) of human serum samples. The high TSH sample was prepared by spiking purified TSH antigen into pooled serum. The data was collected over 20 days in duplicate with 2 runs per day with a total of 80 samples analyzed per level at each site. The results are summarized below:

   Low Concentration #1 with observed mean = 0.19 uIU/mL

	Site 1	**Site 2**	**Site 3**
Mean, μIU/mL	0.19	0.19	0.18
Repeatability, %CV	12.1	13.3	14.4
Between-run, %CV	6.2	0	0
Between-day, %CV	3.8	7.0	3.7
Within-laboratory, %CV	14.1	15.0	14.4

   Low Concentration #1 with observed mean = 0.29 uIU/mL

	Site 1	**Site 2**	**Site 3**
Mean, uIU/mL	0.29	0.29	0.29

Repeatability, %CV	8.5	8.9	8.8
Between-run, %CV	0	0	0
Between-day, %CV	4.1	4.8	3.7
Within-laboratory, %CV	9.4	10.1	9.5

Low Concentration #2 with observed mean = 0. 86 µIU/mL

	Site 1	**Site 2**	**Site 3**
Mean, uIU/mL	0.83	0.87	0.87
Repeatability, %CV	8.3	6.0	5.8
Between-run, %CV	4.2	3.3	5.0
Between-day, %CV	0.0	3.8	0.0
Within-laboratory, %CV	9.4	7.8	7.6

Mid Concentration with observed mean = 3.92 µIU/mL

	Site 1	**Site 2**	**Site 3**
Mean, uIU/mL	3.7	4.1	3.95
Repeatability, %CV	7.3	7.7	8.2
Between-run, %CV	4.2	3.8	1.9
Between-day, %CV	2.9	3.0	3.5
Within-laboratory, %CV	8.9	9.1	9.1

High Concentration with observed mean = 47.24 µIU/mL

	Site 1	**Site 2**	**Site 3**
Mean, uIU/mL	46.71	46.63	48.39
Repeatability, %CV	6.6	5.8	6.6
Between-run, %CV	2.9	7.5	2.1
Between-day, %CV	5.1	0.0	2.9
Within-laboratory, %CV	8.8	9.5	7.5

b. Linearity/assay reportable range:

The linearity of the MICT TSH method was determined following the CLSI EP6-A procedure. Two samples were identified having TSH concentrations covering the reportable range. A series of intermediate serum samples were prepared by diluting the high level sample (126 µIU/mL) with the low level sample (0 µIU/mL). Sample 7 was mixed with the low level sample to generate samples with TSH < 8 µIU/mL (samples 2 to 6).

The samples were then analyzed using the MICT TSH system. The MICT TSH assay is linear within the reportable range, 0.13 – 100 μIU/mL.

[TSH] μIU/mL.

Sample Number	Replicate 1	Replicate 2	Observed Average	Expected
1	0	0	0.00	0.00
2	0.12	0.14	0.13	0.11
3	0.33	0.35	0.34	0.35
4	0.87	0.94	0.91	0.89
5	3.73	3.55	3.64	3.54
6	6.21	7.78	7.00	7.09
7	10.88	10.63	10.76	10.62
8	20.5	21.4	20.95	21.00
9	40.09	41.6	40.85	42.00
10	68.7	70.2	69.45	63.00
11	85.28	82.13	83.71	84.00
12	107.4	107.8	107.6	105.00
13	124.3	129.3	126.8	126.00

The analysis yields the following relationship:

Observed = 1.017 (Expected) +.0494, $R^2 = 0.9985$

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

A master file of the standard curve is generated for each lot of MICT TSH using master calibrators referenced to the WHO 2nd IRP 80/558 standard. The master file information is transferred to the MICT Instrument through the barcode label on the test cassette. Each lot of MICT TSH device with dry reagent is calibrated at the manufacturing site. The reagent is stable throughout the stated product shelf life.

For accelerated stability testing, two lots of the MICT TSH reagent devices were heat-stressed at 40 °C for varying time periods. For real-time testing, one lot was tested over a 14-month period. Based on accelerated and real-time stability testing, the shelf-life for the MICT TSH test is 14 months when stored at room temperature (22 °C).

d. *Detection limit:*

Five low TSH level human serum samples from different individuals were tested using two MICT instruments and one reagent lot over a period of three days, two runs per day following CLSI EP17-A guidelines. The TSH concentrations of the LoD samples were verified by ADVIA Centaur CP TSH3-Ultra assay, which is traceable to the WHO 3rd International Standard for human TSH (IRP 81/565). The LoD was

estimated to be 0.077 µIU/mL.

The bias of each of the five low concentration samples was estimated as the mean MICT measured concentration of each sample minus its value as determined by the ADVIA Centaur CP TSH3-Ultra. The bias of the lowest concentration sample was used as an estimate of the bias of the LoQ since this concentration was closest to LoQ. The total error was calculated to be smaller than the allowable error. The LoQ therefore = LoD = 0.077 µIU/mL. The sponsor chose the reportable range to be 0.13 to 100 µIU/mL.

Hook effect: TSH was spiked into a human serum depleted of TSH standard that had been completely depleted of TSH at 25, 50, 100, 150, 200, 250, 500, 1000, and 20000 µIU/mL. No hook effect was observed at TSH concentrations up to 2000 µIU/mL.

e. Analytical specificity:

Interference

The study was conducted using bilirubin, hemoglobin, phospholipids, and triglycerides. Human serum samples with various TSH concentrations were spiked with potential interfering substances and tested using the MICT TSH System. Controls were prepared by spiking the samples with equal volumes of the solvents that were used to dissolve the interfering substances. The concentrations of spiked and control samples were recorded, and recovery rates were calculated. Bilirubin was dissolved in DMSO plus 40 mM NaOH. Lyophilized hemoglobin and phopholipids stabilized in triglycerides were weighed out and mixed with serum samples directly. No significant interference as defined by the sponsor as ±10% was found for bilirubin, hemoglobin, phospholipids, and triglycerides at the concentrations presented in the table below.

Interfering Substance	**Sample ID**	**Control (µIU/mL)**	**AVE(control)**	**with interfering substance (µIU/mL)**	**AVE (interfering)**	**Recovery Rate %**
Bilirubin (40 mg/dL)	4	0.3	0.27	0.31	0.295	109
		0.24		0.28		
	1	0.30	0.35	0.35	0.33	94
		0.40		0.31		
	2	4.07	4.97	4.92	5.02	101
		5.86		5.11		
	3	6.71	7.38	7.53	7.31	99
		8.04		7.08		
	4	0.16	0.135	0.13	0.145	107
		0.11		0.16		

Hemoglobin (1000 mg/dL)	1	0.41	0.485	0.52	0.525	108
		0.56		0.53		
	2	4.08	3.925	3.66	3.795	97
		3.77		3.93		
	3	8.63	8.07	8.27	7.94	99
		7.45		7.61		
Phospholipid (800 mg/dL)	4	0.29	0.27	0.30	0.285	105
		0.25		0.27		
	3	0.32	0.36	0.36	0.36	100
		0.40		0.36		
Triglyceride 1 (3,200 mg/dL)	2	4.66	4.42	4.35	4.68	106
		4.18		5.00		
	3	8.53	9.26	9.05	8.68	94
		9.99		8.31		

The effects of rheumatoid factor (Rf) and human anti-mouse antibodies (HAMA) on the MICT TSH assay were evaluated. Individual patient serum samples were mixed with equal volume of HAMA or Rf positive samples. The final concentrations of Rf and HAMA in these samples were 1,000 IU/mL and 400 ng/mL, respectively. The mixed samples were analyzed in duplicate using the MICT system. The MICT TSH assay shows no detectable interference within the sponsor's acceptable limits (±10%) with rheumatoid factor and HAMA.

The results are presented in the table below:

Rf Samples (1000 uIU/mL)

Patient Sample (TSH, µIU/mL)	Rf Sample (TSH, µIU/mL)	Mixed RF Positive Sample (TSH, µIU/mL)				
		Expected Value	Replicate 1	Replicate 2	Average	% Recovery
0.41	0.25	0.33	0.36	0.29	0.325	98
1.7	1.3	1.5	1.47	1.46	1.46	97
17.0	1.3	9.13	8.56	8.48	8.52	93
10.9	1.3	6.14	5.74	5.93	5.84	95

HAMA Samples (400 ng/mL)

Patient Sample (TSH, µIU/mL)	HAMA Sample (TSH, µIU/mL)	Mixed HAMA Positive Sample (TSH, µIU/mL)				
		Expected Value	Replicate 1	Replicate 2	Average	% Recovery
0.16	0.42	0.29	0.26	0.28	0.27	92
1.94	1.3	1.62	1.59	1.76	1.68	104

8.13	1.3	4.72	4.59	4.23	4.41	93
1.74	1.3	1.52	1.43	1.38	1.41	93

Cross reactivity

Human serum samples with various TSH concentrations were spiked with potential cross reactants FSH, LH, and hCG dissolved in PBS with 1% BSA and tested in MICT TSH system. Controls were prepared by spiking samples with equal volumes of the PBS-BSA solution used in dissolving the FSH, LH, and hCG. The concentrations of spiked and control samples were recorded, and recovery rates were calculated. None of the analytes tested significantly cross-reacted with stated cross-reactants as recovery rates were within ±10%.

Cross Reactant	Sample ID	Control (μIU/mL)	AVE (control)	with cross reactant (μIU/mL)	AVE (interfering)	Recovery Rate
LH (500 mIU/mL)	1	1.66	1.57	1.69	1.69	108%
		1.48		1.69		
	2	7.27	7.29	7.38	7.46	102%
		7.31		7.54		
FSH (500 mIU/mL)	1	2.57	2.62	2.45	2.49	95%
		2.68		2.53		
	2	16.39	16.44	17.95	17.99	109%
		16.50		18.02		
hCG (200 IU/mL)	1	2.50	2.37	2.27	2.16	91%
		2.23		2.05		
	2	14.90	14.60	14.63	15.76	108%
		14.30		16.89		

f. Assay cut-off:

N/A

2. Comparison studies:

a. Method comparison with predicate device:

Patient serum samples (n=204) with TSH values ranging from 0.13 – 93.6 μIU/mL were collected and evaluated. Linear regression was used to correlate the MICT TSH assay to the Qualigen FastPack TSH assay. The results yielded the following linear regression equation: Y = 0.96X - 0.1, R =0.99

b. Matrix comparison:

Not applicable. Serum is the only sample type indicated.

3. Clinical studies:

a. Clinical Sensitivity:

N/A

b. Clinical specificity:

N/A

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

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

Serum samples from 147 normal, apparently healthy individuals, consisting of 97 females and 50 males were assayed on three lots of MICT TSH devices using two MICT Readers. The reference range was determined using the procedure in CLSI C28-A3. The expected normal range for the MICT TSH is 0.49 – 3.71 μIU/mL based on the central 95% of the frequency distribution.

N. Instrument Name:

MICT TSH Instrument

O. System Descriptions:

1. Modes of Operation:

Automatic

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes ____x____ or No _____

3. Specimen Identification:

   Barcode

4. Specimen Sampling and Handling:

   Patient samples are pipetted into the conjugate tube, mixed then manually transferred into the sample well of the assay cassette.

5. Calibration:

   Calibration of the assay is performed at the manufacturer's site. The test kits are stable up to the expiration date. All instruments are calibrated against a known magnetic standard by the manufacturer. Each system is standardized to read the magnetic material within 2%.

6. Quality Control:

   The sponsor recommends the use of commercially available external control materials for use with the MICT System. In the labeling the sponsor recommends that the quality control material be run each day the system is used to report patient results. Also the sponsor recommends that each day the MICT system is used to test patient samples the user tests the verification cassette to assess the operational status of the MICT instrument.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

N/A

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.