GBI Thyroid Stimulating Hormone (TSH) EIA 510(k) Summary

K072458

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2) Device Trade or Proprietary Name: GBI TSH Neonatal Screening Kit

Device Common or Usual Name: Thyroid stimulating hormone (TSH) neonatal screening enzyme immunoassay (EIA)

Device Classification Name: Radioimmunoassay, Thyroid Stimulating Hormone

Product Code: JLW

3) Legally Marketed Predicate Device: Accuwell Thyroid Stimulating Hormone (TSH) ELISA

4) Device Description:

Summary and Explanation of the Test

Congenital hypothyroidism (CH) is one of the most common metabolic disorders resulting in permanent mental retardation if undetected or left untreated soon after birth. Newborns that have been identified and treated for CH within two weeks of birth can be expected to have normal cognitive development.

Screening programs for the disorder were developed early in 1974 and have now been established in Western Europe, North America, Japan and parts of Eastern Europe, Asia, South and Central America. The American Academy of Pediatrics first published recommendations for screening for CH in 1993. Advances in screening methods and expanded knowledge of the physiology of thyroid hormones has lead to new recommendations by the Academy in 2006.[2] In North America more than five million newborns are screened annually with over 1400 hypothyroid cases detected each year. The incidence of hypothyroidism varies among different populations and ranges from 1 in 3000 to 1 in 4000. The incidence of CH is higher in Hispanics and lower in black individuals. Females have a 2:1 greater incidence of CH than males. A higher frequency of the CH disorder has been observed in individuals with Downs Syndrome.

Thyroid stimulating hormone (TSH) is a pituitary-derived glycoprotein with a molecular weight of approximately 28 kDa. TSH is produced by the anterior lobe of the pituitary gland under the control of thyrotropin releasing hormone (TRH) which is secreted by the hypothalamus. TSH acts on the thyroid gland to release the thyroid hormones triiodothyronine (T_3) and thyroxine (T_4). Under normal thyroid function, the level of the thyroid hormones T_3 and T_4 is inversely related to the concentrations of TSH and TRH in the bloodstream via a negative feedback mechanism. As a result of this negative feedback mechanism between the thyroid gland and the pituitary, TSH is always elevated in cases of primary hypothyroidism and often to very high levels. It is

for this reason that the measurement of TSH concentration is a valuable diagnostic tool for the detection of hypothyroidism.

Thyroid hormone (TH) levels of the fetus are low during the first half of pregnancy. Maternal status of TH hormones is entirely responsible for the regulation of fetal TH, transmitted through the placenta. The fetal hypothalamic—pituitary—thyroid axis develops during the second half of gestation and is mature at time of birth. A surge of TSH concentration occurs at birth and then declines rapidly within the first few days of life, and continues to decrease more slowly to adult levels. It is recommended to perform screening for CH ideally within the 2nd to 4th days after birth or at time of discharge.

Blood samples collected before 24 hours of age, from low birth weight or ill infants can lead to elevated TSH and thus false positive results. Hypothyroid infants may be partially protected by maternal TH levels and so most infants will appear normal at birth. There have also been reported cases of transient hypothyroidism due to maternal hypothyroidism and other maternal abnormalities. Hypothyroidism can develop after birth, and in such cases will yield a normal newborn screening result.

Since the incidence of hypothyroidism and the concentrations of TSH have been shown to vary according to a variety of factors (e.g., demographics, ethnicity, the sex and age of the infant, low birth weights and premature births) it is important that each newborn screening laboratory examine its test population and determine its own normal range and cut-off values with these factors taken into consideration.

Screening algorithms vary among centers from initial TSH with confirmation via T4 measurements, to T4 initial screen with confirmation via TSH measurements, to both tests (T4 and TSH) being performed simultaneously. Regardless of method, repeated positive results on a neonate should be cause for referral for additional confirmation testing.

Principle of the Assay

The GBI TSH Neonatal Screening Kit is an enzyme immunoassay. A highly specific polyclonal goat anti-hTSH (human) antibody has been immobilized onto each well of the 96-well microplates provided. To begin the assay, sample discs punched from dried whole blood spot standards, controls and neonate specimens are added to the coated wells. An elution buffer is also added. The plate is incubated to elute TSH from the sample disc and to allow capture of the eluted TSH by the antibody immobilized onto the microplate wells. Following incubation the plates are washed to remove the sample discs as well as the eluate.

A second antibody, a ß-specific anti-hTSH monoclonal that has been conjugated to the enzyme horseradish-peroxidase (HRP), is then added to the wells and incubated. The eluted TSH of the sample already captured by the microplate-bound antibody is now also bound by the enzyme-conjugated monoclonal antibody added. An antibody-TSH-antibody bridge, or "sandwich", forms that is bound to the surface of the microplate wells. Any unbound complexes are removed with subsequent plate washings.

The final stage of the assay is the detection of the microwell-bound complexes by the addition of a color developing reagent. The enzyme (HRP) portion of the bound "sandwich" reacts with the color developer, 3, 3', 5, 5'-Tetramethylbenzidine (TMB) in the presence of hydrogen peroxide (H_2O_2). The TMB/ H_2O_2 liquid is converted from colorless to blue. The degree of color change is directly proportional to the amount of TSH antigen that is bound in the well. The color development is terminated with the addition of a color stopper that converts the blue to yellow.

The results are measured with a microplate reader at a wavelength of 450 nm. The absorbance measured is directly proportional to the concentration of TSH in the sample. A standard curve is generated by plotting the light absorbance of each standard versus its known TSH concentration. The concentrations of TSH in the unknown samples are determined by interpolation from this standard curve.

Kit Contents

Materials Supplied

	Quantity per Kit
Total Tests:	576
TSH Capture Microplate	6 X 96 wells
TSH Elution Buffer	1 x 70 ml
Anti-TSH PO Conjugate	1 x 1.4 ml
TSH Diluent Buffer	1 x 70 ml
PO Wash Buffer (20X)	1 x 100 ml
PO Color Reagent*	1 x 70 ml
PO Color Stopper	1 x 70 ml
TSH Dried Blood Standards and Controls	1 Set

*** This reagent is light sensitive. Avoid prolonged exposure to light.**

NOTE: Do NOT use reagents that are cloudy or discolored as these conditions indicate deterioration. Reagents should be stored in their original containers with the exception of the diluted wash buffer.

Do NOT exchange reagents from one kit with those of another kit.

Reagent Descriptions

TSH Capture Microplate
Goat polyclonal anti-alpha hTSH antibody coated 96-well microplates. The microplates are packaged in zipper-lock bags containing a desiccant. Store the unused microplates in zipper-lock bags with desiccant.
Storage: Dry at 2-25° C.
Expiration: Refer to the expiration date printed on the label

TSH Elution Buffer
A borate buffer containing bovine albumin, surfactant and preservatives. This buffer contains sodium azide as a preservative.
Storage: 2-8° C
Expiration: Refer to the expiration date printed on the label.

Anti-TSH PO Conjugate
A mouse monoclonal β-specific anti-hTSH antibody conjugated to horseradish peroxidase (HRP) in borate buffer containing bovine albumin, surfactant, and preservatives. This buffer contains thimerosal as a preservative; refer to "Warnings and Precautions", below. Store in the original brown container. This conjugate is concentrated and must be diluted before use.
Storage: 2-8° C
Expiration: Refer to the expiration date printed on the label.

TSH Diluent Buffer
A borate buffer containing bovine albumin, surfactant, and preservatives. This buffer contains thimerosal as a preservative.
Storage: 2-8° C
Expiration: Refer to the expiration date printed on the label.

PO Wash Buffer (20X)
A concentrated solution of phosphate buffered saline containing a surfactant and preservatives. Wash Buffer Concentrate must be diluted with deionized or distilled water before use.
Storage: 2-25° C
Expiration: Concentrate: Refer to the expiration date printed on the label.
Diluted wash buffer is stable for 1 month when stored at 2-25° C.

PO Color Reagent*
A colorless solution of 3,3′, 5,5′-Tetramethylbenzidine (TMB) and hydrogen peroxide. ***This reagent is light sensitive.** Store in the original brown container. Do not pour any of the unused Color Developer back into the original container. This reagent should remain colorless. If it has discolored, discard it.
Storage: 2-8° C **Protected from light.**
Expiration: Refer to the expiration date printed on the label.

PO Color Stopper
A solution containing < 1% hydrochloric acid.
Storage: 2-8° C.
Expiration: Refer to the expiration date printed on the label.

TSH Dried Blood Standards and Controls
Prepared from human whole blood, adjusted to a hematocrit of 55% and spotted onto Whatman 903® specimen collection paper. The six Standards contain concentrations of added TSH at approximately zero, 7.5, 15.0, 30.0, 60.0, and 120.0 µIU/ml serum equivalent. The three Controls contain approximate TSH concentrations of 15, 30 and 80 µIU/ml serum equivalent. Refer to the labels for the exact concentrations of the Standards and acceptable ranges for the Controls. Store in a zipper-lock bag containing a desiccant. Standards are referenced against WHO 3rd IRP of human TSH 81/565.
Storage: Dry at 2-8° C or below.
Expiration: Refer to the expiration date printed on the label.

Materials Required But Not Supplied

1. 1/8 inch (3 mm) diameter hole punch (sample prep)
2. Forceps or fine tweezers to pick up the punched sample discs
3. Plastic, disposable tube and screw-cap; ≥ 15 ml volume (conjugate prep)
4. Serological pipette to dispense 10 ml volumes (wash buffer prep)
5. Precision pipettes to accurately dispense 100 µl volumes (reagent adds)
6. Multi-channel pipettes to dispense 350 µl volumes or an automated plate washer (plate washes)
7. Microplate reader capable of reading at a wavelength of 450 nm
8. Plate rotator (sample & test reagent mixing)
9. Clear, adhesive sealing tape or plate sealers; solid plastic, reusable microplate covers
10. Graduated cylinders
11. Deionized or distilled water

5) Intended Use:

The GBI TSH Neonatal Screening Kit is designed for the quantitative determination of Thyroid Stimulating Hormone (TSH) concentrations in neonatal blood samples that have been collected onto Whatman 903® specimen collection paper. The results are used to screen newborns for congenital hypothyroidism.

6) Summary of Technological Characteristics:

Item #:	Characteristic:	Predicate[1,2]:	New Device:
1	Intended User	Clinical Laboratory Professionals	Clinical Laboratory Professionals
2	Target Population	Neonates only	Neonates only
3	Intended Use	The quantitative determination of Thyroid Stimulating Hormone (TSH) concentrations in neonatal blood samples that have been collected onto Whatman 903® specimen collection paper.	The quantitative determination of Thyroid Stimulating Hormone (TSH) concentrations in neonatal blood samples that have been collected onto Whatman 903® specimen collection paper.
4	Indications for Use	The screening of newborns for elevated TSH suggestive of congenital hypothyroidism.	The screening of newborns for elevated TSH suggestive of congenital hypothyroidism.
5	Assay Type	Enzyme-Linked Immunosorbent assay (ELISA)	Enzyme Immunoassay (EIA)
6	Assay Processing Method	Manual	Manual
7	Chemical Principle	Polyclonal goat anti-hTSH that is bound to the microplate captures eluted specimen TSH; after washing away free TSH, conjugated monoclonal-horseradish peroxidase is added and binds to the captured TSH thus forming an immobilized antibody+TSH+antibody-enzyme "sandwich". After washing away free enzyme, immobilized peroxidase reacts with added color developer containing hydrogen peroxide and 3,3′,5,5′-Tetramethylbenzidine (TMB). The TMB is converted from colorless to blue. The color development is terminated by the addition of a stopping reagent.	Polyclonal goat anti-hTSH that is bound to the microplate captures eluted specimen TSH; after washing away free TSH, conjugated monoclonal-horseradish peroxidase is added and binds to the captured TSH thus forming an immobilized antibody+TSH+antibody-enzyme "sandwich". After washing away free enzyme, immobilized peroxidase reacts with added color developer containing hydrogen peroxide and 3,3′,5,5′-Tetramethylbenzidine (TMB). The TMB is converted from colorless to blue. The color development is terminated by the addition of a stopping reagent that also converts the blue to yellow.
8	Detection Method	The light absorbance of the reaction endpoint is measured spectrophotometrically at a wavelength of 650nm. The degree of color development is directly proportional to the amount of TSH antigen that has been "sandwiched" onto the microwell.	The light absorbance of the reaction endpoint is measured spectrophotometrically at a wavelength of 450nm. The degree of color development is directly proportional to the amount of TSH antigen that has been "sandwiched" onto the microwell.
9	Special Instrumentation Required	Microplate Spectrophotometer (at 650 nm)	Microplate Spectrophotometer (at 450 nm)
10	Specimen Type	Neonatal whole blood collected onto Whatman 903® filter paper and dried	Neonatal whole blood collected onto Whatman 903® filter paper and dried
11	Specimen Volume Requirement	1/8 inch punch (from dried blood spot sample)	1/8 inch punch (from dried blood spot sample)
12	Calibrator (Standard) Configuration	Stripped serum, lysed cells and purified TSH analyte combined, spotted onto Whatman 903® filter paper and dried	Stripped serum, lysed cells and purified TSH analyte combined, spotted onto Whatman 903® filter paper and dried
13	Calibrator (Standard) Range of Values	0 – 160 uIU/ml serum equivalents	0 – 120 uIU/ml serum equivalents
14	Internal Control Configuration	Stripped serum, lysed cells and purified TSH analyte combined, spotted onto Whatman 903® filter paper and dried	Stripped serum, lysed cells and purified TSH analyte combined, spotted onto Whatman 903® filter paper and dried

15	Internal Control Levels	Low at ≈ 20 uIU/ml Mid at ≈ 40 uIU/ml High at ≈ 80 uIU/ml	Low at ≈ 15 uIU/ml Mid at ≈ 30 uIU/ml High at ≈ 80 uIU/ml
16	Recommended Reference Ranges	From American Academy of Pediatrics: Normal < 20 uIU/ml serum equivalent Borderline 20-40 uIU/ml serum equivalent Hypothyroid > 40 uIU/ml serum equivalent	From American Academy of Pediatrics: Normal < 20 uIU/ml serum equivalent Borderline 20-40 uIU/ml serum equivalent Hypothyroid > 40 uIU/ml serum equivalent
17	Expected Values - Normal Neonate Population	N=1040: Mean = 9.9 uIU/ml S.D. = 5.8 uIU/ml	N=902: Mean = 8.1 uIU/ml S.D. = 4.0 uIU/ml
18	Analytical Sensitivity	2.9 uIU/ml	2.4 uIU/ml
19	Precision[3]	Within Run Precision: NA NA 24.0 uIU/ml cv = 10.0 % 51.1 uIU/ml cv = 7.8 % 159.2 uIU/ml cv = 4.3 % Between Run Precision: NA NA 27.3 uIU/ml cv = 6.1 % 40.8 uIU/ml cv = 8.4 % 78.5 uIU/ml cv = 6.5 % Over-All (Within-Device) Precision: NA - Not published	Within-Run Standard Deviation (Sr): 15 uIU/ml Sr = 0.9 uIU/ml cv= 6.2% 30 uIU/ml Sr = 1.3 " cv= 4.6% 25+ uIU/ml Sr = 2.6 " cv= 8.5% 40+ uIU/ml Sr = 4.2 " cv= 9.1% 80+ uIU/ml Sr = 6.5 " cv= 7.5% Between-Day Standard Deviation (Sdd): 15 uIU/ml Sdd = 1.0 uIU/ml cv= 6.8% 30 uIU/ml Sdd = 2.3 " cv= 8.1% 25+ uIU/ml Sdd = 2.6 " cv= 8.5% 40+ uIU/ml Sdd = 1.2 " cv= 2.6% 80+ uIU/ml Sdd = 10.3 " cv= 11.9% Within-Device Standard Deviation (ST): 15 uIU/ml ST = 1.2 uIU/ml cv= 8.2% 30 uIU/ml ST = 2.5 " cv= 8.8% 25+ uIU/ml ST = 3.7 " cv= 12.1% 40+ uIU/ml ST = 4.4 " cv= 9.5% 80+ uIU/ml ST = 12.2 " cv= 14.1%
20	Interfering Substances	No Interference observed at the highest concentration tested*: Bilirubin - no interference up to 60 mg/dl* Lipids - no interference up to 1000 mg/dl* Hemoglobin - no interference up to 78 g/dl*	No Interference observed at the highest concentration tested*: Bilirubin - no interference up to 20 mg/dl* Lipids - no interference up to 1350 mg/dl* Hemoglobin - no interference up to 80 g/dl*
21	Cross Reacting Substances	No interference found at the highest concentration tested: FSH- no interference up to 500 mIU/ml LH- no interference up to 500 mIU/ml HCG- no interference up to 100,000 mIU/ml	No interference found at the highest concentration tested: FSH- no interference up to 500 mIU/ml LH- no interference up to 500 mIU/ml HCG- no interference up to 100,000 mIU/ml
22	Method Comparison	For N=995: Normal = 974/995 (97.9%) Borderline = 6/995 (0.6%) Positive = 15/995 (1.5%) For (subset) N=832: Mean = 8.1 uIU/ml; Range = 2.9 to 104 uIU/ml.	For N=995: Normal = 969/995 (97.4%) Borderline = 11/995 (1.1%) Positive = 15/995 (1.5%) For (subset) N=832: Mean = 8.9 uIU/ml; Range = 2.4 to 114 uIU/ml y (GBI TSH EIA) = 1.0695x (Predicate) + 0.2671, R^2 = 0.9185

23	CDC Controls (Enrichment Values in serum equivalents) - CDC Lot 611 – 25 uIU/ml	N = 29[4] intercept = 0.1505 slope = 1.0231 26.0 uIU/ml serum equivalent	N = 40[5] intercept = 5.2083 slope = 1.0208 30.6 uIU/ml serum equivalent
	CDC Lot 612 – 40 uIU/ml	40.7 uIU/ml serum equivalent	46.3 uIU/ml serum equivalent
	CDC Lot 613 – 80 uIU/ml	82.1 uIU/ml serum equivalent	86.8 uIU/ml serum equivalent

1 Predicate data and descriptive text were obtained from the Accuwell TSH ELISA Directions For Use (DFU) unless otherwise indicated.

2 The predicate DFU declares the use of "Schleicher & Schuell (S&S) 903™" filter paper as the sample substrate. S&S has since been purchased by Whatman and the name of the 903 filter paper has been changed to "Whatman 903®". For this reason, table references throughout use the Whatman 903® designation only, even though the predicate DFU actually refers to the paper as S&S 903™.

3 Precision data were not generated in the same way nor reported in precisely the same terms for the predicate vs the new device. The new (GBI TSH) device precision was established and reported according to NCCLS EP5-A2, "Evaluation of Precision Performance of Quantitative Measurement Methods"; Approved Guideline-Second Edition.

4 Predicate values were obtained from the CDC's Newborn Screening Quality Assurance Program (NSQAP) 2006 Annual Summary Report; Volume 24, January 2007.

5 GBI values were obtained from the same data set that was used to establish assay precision values.

7) Clinical and Non-Clinical Data:

Precision

Precision studies were conducted in accordance with NCCLS EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition.

Testing included two sample aliquots per run, one run per day, performed on 20 different days using the GBI published assay procedure. The resulting data were used to estimate repeatability, between-day and within-device precision as described by the standard. Refer to the table below.

Sources of variability included the use of different: operators, days and reagent lot numbers.

Summary Results and Estimates of Precision for GBI TSH EIA Kit

Sample ID:		C1	C2	C3	C4	C5
Precision Parameter	*Count*	*40*	*40*	*40*	*40*	*40*
	Mean	14.6	28.3	30.6	46.3	86.8
	SD	1.2	2.5	3.7	4.4	12.1
	%CV	7.9	8.7	11.9	9.4	13.9
	Min	12.5	23.5	23.3	37.5	71.4
	Max	18.0	34.0	40.4	59.1	122.5
Within-Run Standard Deviation:	Sr =	0.9	1.3	2.6	4.2	6.5
Between-Day Standard Deviation:	Sdd =	1.0	2.3	2.6	1.2	10.3
Within Device Standard Deviation:	ST =	1.2	2.5	3.7	4.4	12.2

Analytical Sensitivity

The Analytical Limit at Low Levels (limit of sensitivity) for the GBI TSH EIA Kit was determined by testing the zero standard multiple times (N=20) within a single assay. The resulting data were used to calculate the analytical limit at low levels. Refer to the table below.

The analytical sensitivity is defined as the calculated concentration that corresponds to the mean of the absorbance values of the zero standard (N=20) plus two times the standard deviation derived from those same (N=20) absorbance values.

These data are provided for example only. Each laboratory should establish appropriate working limits based upon their own patient population and/or data.

Summary Results and Analytical Limits at Low Levels for GBI TSH EIA

	GBI TSH
Count	*20*
Mean ABS	0.0354
SD	0.0063
%CV	18
Min	0.0289
Max	0.0570
Mean + (2 *S.D.) ABS:	0.0480
Analytical Limit (uIU/ml)	2.4

Linearity, Recovery and Assay Measurable (Reportable) Range

The GBI TSH EIA Kit linear range was assessed according to the NCCLS Guideline EP6-A: Evaluation of the Linearity of Quantitative Analytical Methods, 2003.

A series of dried whole blood spot samples was prepared to provide the desired range of TSH concentrations for the study (N=19; see table column "Expected Value", below).

Two one-eighth inch punches from each concentration level were tested in each of two runs. The mean of the total number of results for a level (n=4) was compared to the expected value. Results are described in the table below.

Results of Assay Linearity and % Recovery Study for GBI TSH EIA Kit

Linear Regression Analysis		**$y = 0.8997x + 0.6036$, $R^2 = 0.999$**	
Linearity Sample #	Expected Value (uIU/ml)	GBI Assay Result (Mean uIU/ml; N=4)	Recovery (%)
1	1.5	1.6	107
2	2.7	3.1	114
3	3.9	4.1	105
4	6.2	6.0	96.8
5	8.6	8.1	93.6
6	10.0	10.6	106
7	10.9	9.8	89.4
8	13.3	12.4	93.0
9	15.6	14.9	95.4
10	18.0	16.1	89.2
11	20.3	17.9	88.1
12	22.7	20.1	88.3
13	24.5	21.9	89.4
14	25.0	22.8	91.1
15	39.0	37.2	95.3
16	68.0	65.4	96.2
17	97.0	89.5	92.3
18	126.0	113.5	90.1
19	155.0	138.0	89.0
Average Recovery-Overall %			**95.2**
Minimum %			88.1
Maximum %			114

The GBI TSH EIA Kit reportable range is approximately 2.4 uIU/ml to 120 uIU/ml. The lower limit is the concentration calculated from the analytical sensitivity study (above) and the upper limit is the concentration of the highest standard of the calibration curve.

Assay results obtained outside the measuring (reportable) range should be reported as either "less than" or "greater than" the established low or high limit, respectively, as applicable to the individual result.

Specificity

Cross Reactivity

The following compounds were tested for cross-reactivity. Each compound was added at several concentrations to TSH-free whole blood which had been adjusted to a hematocrit of 55%. The samples were spotted onto Whatman 903® specimen collection paper, air-dried and assayed. Refer to the table below.

Results of a Cross-Reactivity Study of the GBI TSH EIA Screening Assay

Peptide Hormone	Cross-Reactant Concentration Added (µIU/ml)	TSH Concentration Measured (µIU/ml)
FSH (WHO 2nd IRP HMG)	125	None Detected*
	250	None Detected*
	500	None Detected*
LH (WHO 1st IRP 68/40)	125	None Detected*
	250	None Detected*
	500	None Detected*
HCG (WHO 2nd I.S. 61/6)	10,000	None Detected*
	50,000	None Detected*
	100,000	None Detected*

* "None Detected" represents values obtained that were below the limit of detection for the assay (i.e., < 2.4 uIU/ml.)

Interfering Substances

Assay interference due to the presence of hemoglobin, conjugated and unconjugated bilirubin, and lipids was studied using methods described in NCCLS EP7A: Interference Testing in Clinical Chemistry as guidance.

Testing was performed to evaluate the effects of interfering substances at the medical decision(s) concentrations using fresh whole blood. The interferents (i.e., hemoglobin, conjugated and unconjugated bilirubin, and lipids) were present in the whole blood specimens at the desired ("worst case") concentrations before specimens were spotted onto filter paper and dried. As such, the sample elution procedure was captured in the subsequent testing process. These prepared dried blood spot specimens were then assayed using the GBI TSH Kit as prescribed herein. (Results are presented below.)

An additional study was conducted that challenged the assay at a much higher hemoglobin concentration. During the initial sample elution step of the assay procedure, three different concentrations (physiologic low, mid, high) of hemoglobin were added separately to microplate wells that also separately contained the three different concentrations (physiologic low, mid, high) of a CDC TSH control sample series. The remainder of the GBI TSH assay was performed as prescribed herein. (Results are presented below.)

Interference was defined as a test value obtained that was greater than +/- 1 S.D. (within-run) of the matching control value obtained in the same assay; AND, the difference of the test value obtained from the matching control value is clinically significant at that level.

No interference with expected values of any clinical significance was observed from any substance tested, at any concentration tested.

Results of Interference Testing of the GBI TSH EIA Screening Assay

DBS Sample ID#	Interferent	Interferent Concentration	TSH uIU/ml - Expected Value	TSH uIU/ml - Observed (Mean; n=4)	Acceptance Criteria (+/- 1 SD of Control Value)
25	Lipid-Control	0 mg/dL	na	16.2	16.2 +/- 0.9
19	Lipid	1350 mg/dL	16.2	18.0	15.3 – 17.1
26	Lipid-Control	0 mg/dL	na	46.1	46.1 +/- 4.2
20	Lipid	1350 mg/dL	46.1	44.2	41.9 – 50.3
27	Lipid-Control	0 mg/dL	--	85.6	85.6 +/- 6.5
21	Lipid	1350 mg/dL	85.6	83.5	79.1 – 92.1
36	Bili-Control	0 mg/dL	na	13.6	13.6 +/- 0.9
31	Conj-Bilirubin	20 mg/dL	13.6	14.6	12.7 – 14.5
28	Un-Bilirubin	20 mg/dL	13.6	14.9	
41	Bili-Control	0 mg/dL	na	27.1	27.1 +/- 1.3
32	Conj-Bilirubin	20 mg/dL	27.1	27.4	25.8 – 28.4
29	Un-Bilirubin	20 mg/dL	27.1	28.1	
46	Bili-Control	0 mg/dL	na	68.2	68.2 +/- 5.4
33	Conj-Bilirubin	20 mg/dL	68.2	68.4	62.8 – 73.6
30	Un-Bilirubin	20 mg/dL	68.2	67.6	
36	Hb-Control	17.0 gm/dL	13.6	13.6	+/- 0.9
37	Hb	18.7 gm/dL	12.1	13.1	12.7 – 14.5
41	Hb-Control	17.0 gm/dL	27.1	27.1	+/- 1.3
42	Hb	18.7 gm/dL	24.0	25.4	25.8 – 28.4
46	Hb-Control	17.0 gm/dL	68.2	68.2	+/- 5.4
47	Hb	18.7 gm/dL	60.6	63.6	62.8 – 73.6

Results of Additional Hemoglobin Interference Testing of the GBI TSH EIA Screening Assay

DBS Sample ID#	Hemoglobin Concentration - (gm/dL)	TSH uIU/ml - Expected Value	TSH uIU/ml - Observed (Mean; n=6)	Acceptance Criteria (+/- 1 SD of Control Value)
C1+ Saline Ctrl	17	na	14.8	14.8 +/- 0.9
C1+ Lysate (Hb)	40	14.8	14.3	(13.9 - 15.7)
C1+ Lysate (Hb)	80	14.8	15.2	
C2 + Saline Ctrl	17	na	33.7	33.7 +/- 1.3
C2 + Lysate (Hb)	40	33.7	32.3	(32.4 - 35.0)
C2 + Lysate (Hb)	80	33.7	31.5	
C3 + Saline Ctrl	17	na	53.4	53.4 +/- 4.2
C3 + Lysate (Hb)	40	53.4	50.5	(49.2 - 57.6)
C3 + Lysate (Hb)	80	53.4	51.9	
C4 + Saline Ctrl	17	na	92.1	92.1 +/- 6.5
C4 + Lysate (Hb)	40	92.1	89.9	(85.6 - 98.6)
C4 + Lysate (Hb)	80	92.1	90.7	

Method Comparison

A total of 995 neonatal blood spot specimens, 980 randomly selected from a presumed normal population and 15 from patients confirmed as positive for hypothyroidism, were analyzed in-house with the GBI TSH EIA. Results were compared to those obtained using a commercially available neonatal TSH assay (Predicate). Refer to the Table below.

Comparison of Result Interpretations Obtained by the GBI TSH EIA versus a Predicate TSH EIA

Population N=995			**GBI Results**			
	Published Cut-off Ranges		Normal	Borderline	Positive	
			< 20	20 - 40	> 40	(Row) **Totals:**
Predicate Results	Normal	(<20) N=974	**967**	7	**0**	974
	Borderline	(20-40) N=6	2	**4**	**0**	**6**
	Positive	(>40) N=15	0	0	**15**	15
	(Column) **Totals:**		**969**	**11**	**15**	**995**

Of the 995 total blood spot samples tested, 163 results produced non-numeric values (either "less than the limit of sensitivity", n=153; or "greater than the highest standard", n=10) for one or both assays. These samples could not therefore be included in statistical analysis presented below and account for the observed difference in method comparison population "N" (995 - 163 = 832).

The method comparison results for the N=832 population were:

GBI TSH Mean = 8.9 uIU/ml, with a range of 2.4 to 114 uIU/ml;
Predicate TSH Mean = 8.1 uIU/ml, with a range of 2.9 to 104 uIU/ml.

The results of linear regression analysis were:

y (GBI TSH EIA) = 1.0695x (Predicate) + 0.2671, $R^2 = 0.9185$

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Golden Bridge International, Inc.
c/o Dr. Xiaoping Zhang
9700 Harbour Place, Suite 129
Mukilteo, WA 98275

APR 10 2008

Re: k072458
Trade/Device Name: GBI TSH Neonatal Screening Kit
Regulation Number: 21 CFR 862.1690
Regulation Name: Thyroid Stimulating Hormone Test System
Regulatory Class: II
Product Code: JLW
Dated: March 10, 2008
Received: March 12, 2008

Dear Dr. Zhang:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): k072458

Device Name: GBI TSH Neonatal Screening Kit

Indication For Use:

The GBI TSH Neonatal Screening Kit is designed for the quantitative determination of Thyroid Stimulating Hormone (TSH) concentrations in neonatal blood samples that have been collected onto Whatman 903 specimen collection paper. The results are used to screen newborns for congenital hypothyroidism.

Prescription Use ___X___ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k)__k072458_____