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

A. 510(k) Number:

k090846

B. Purpose for Submission:

New device

C. Measurand:

Thyroid stimulating hormone (TSH)

D. Type of Test:

Quantitative Time-resolved Fluoroimmunoassay

E. Applicant:

Wallac Oy

F. Proprietary and Established Names:

GSP Instrument, GSP Neonatal hTSH kit

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JLW	II	21 CFR 862.1690 Thyroid stimulating hormone test system	Chemistry (75)
KHO	I	21 CFR 862.2560 Fluorometer for clinical use	Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See Indications for use below.

2. Indication(s) for use:
   The GSP™ instrument is a fully automated, high throughput batch analyzer for time- resolved and prompt fluorescence analysis of samples in microtitration plates. It is intended for *in vitro* quantitative / qualitative determination of analytes in body fluids.

   The GSP™ Neonatal hTSH kit is intended for the quantitative determination of human thyroid stimulating hormone (hTSH) in blood specimens dried on filter paper as an aid in screening newborns for congenital (neonatal) hypothyroidism

using the GSP instrument.

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

   The data obtained using the GSP Neonatal hTSH blood spot immunoassay should be used as an aid to other medically established procedures and results interpreted in conjunction with other clinical data available to the clinician.

   Screening for congenital hypothyroidism by measurement of hTSH concentrations requires a decision of the screening policy, definition of tiers, cut-off values and follow-up. The laboratory needs to establish its own cut-off values, which can be based on a percentile, or on the basis of a normal range[1]. Interpretation of results and the recommended follow-up algorithm for congenital hypothyroidism screening is described by American Academy of Pediatrics/American Thyroid Association.

4. Special instrument requirements:
   For use on the GSP instrument only.

I. Device Description:

- **Neonatal hTSH calibrators and Neonatal hTSH controls** - prepared from human blood with a hematocrit value of 50-55% and calibrated against the Thyroid-Stimulating Hormone, Human, for Immunoassay, Third International Standard, NIBSC Code 81/565. The six calibrators contain concentrations of added TSH at approximately 1, 10, 25, 50, 100 and 250 µU/mL blood. The two controls contain approximate TSH concentrations of 15 and 60 µU/mL blood.
- **Anti-hTSH-Eu tracer** – mouse monoclonal in Tris-HCl buffered (pH 7.8) salt solution containing bovine serum albumin, mouse IgG, and < 0.1% sodium azide as preservative.
- **Neo hTSH assay buffer** – Tris-HCl buffered (pH 7.8) salt solution containing bovine serum albumin, bovine globulin, Tween 40, polyethyleneglycol 6000, an insert red dye, and < 0.1% sodium azide as preservative.
- **Anti-hTSH Microtitration Strips** – plates coated with antibodies directed against a specific site on the beta subunit of the hTSH molecule.

  Each kit contains reagents for 1152 assays.

  All human source materials used in the preparation of kit components was tested and found to be non-reactive for the presence of HBsAg, anti-HIV 1 and 2, and HCV by FDA approved methods.

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[1] American Academy of Pediatrics (2006): Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics **117** (6), 2290–2303.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   AutoDELFIA Neonatal hTSH, AutoDELFIA instrument

2. Predicate K number(s):
   k905710, k935047

3. Comparison with predicate:

   GSP Instrument:

Similarities		
Item	Proposed Device	Predicate Device (k905710)
Intended Use/Indications for Use	The GSP™ instrument is a fully automated, high throughput batch analyzer for time resolved analysis of samples in microtitration plates. It is intended for *in vitro* quantitative / qualitative determination of analytes in body fluids.	The Wallac 1235 AutoDELFIA automatic immunoassay system is designed to automatically perform assays using the DELFIA technology. DELFIA is based on the widely used method of time-resolved fluorometry.
Test Mode	Same	Batch mode
Detection Technology	Same	Time-resolved fluoroimmunoassay

Differences		
Item	Proposed Device	Predicate Device (k905710)
Sample Type	Dried blood spots	Dried blood spots, serum, plasma
Plate Capacity	24 plates	12 plates
Reagents	Individually bar-coded reagents	Reagent information on separate barcode labels
User Interface	GSP software –MicroSoft Windows Vista embedded - touch screen	AutoDELFIA Workstation software (MicroSoft Windows – resides on external PC – keyboard, mouse
Instrument Components	Instrument (consists of plate manipulator and modules). External PC Barcode reader	Sample processor Plate processor External PC

GSP Neonatal hTSH kit:

Similarities		
Item	Proposed Device	Predicate Device (k935047)
Technology	Same	Time-resolved fluorescence
Sample Type	Same	Newborn Blood spot specimens
Number of Calibrators	Same	Six levels
Matrix for controls and calibrators	Filter paper cassettes (Whatman no.903)	Filter paper sheets (Whatman no. 903)
Calibrator Concentrations	Same	A 1 µU/mL blood B 10 µU/mL blood C 25 µU/mL blood D 50 µU/mL blood E 100 µU/mL blood F 250 µU/mL blood
Number of Controls	Same	Two levels
Control Concentrations	Same	Approx. values: C1 15 µU/mL blood C2 60 µU/mL blood
Assay Buffer	Same	Neo hTSH Assay Buffer 3 bottles, 120 mL

Differences		
Item	Proposed Device	Predicate Device (k935047)
Tracer	Anti-h-TSH-Eu solution (~5 µg/mL); 3vials, 2.8 mL The tracer is Eu-N3-labeled antibody (clone 5409)	Anti-h-TSH-Eu stock solution (~20 µg/mL); 6vials, 1.1 mL The tracer is Eu-N1-labeled antibody (clone 5403)
Plates	Anti-hTSH Microtitration Strips (Nunc); 12 plates	Anti-hTSH Microtitration Strips (Thermo Electron); 12 plates
Calculation	GSP Workstation software, X-axis LIN, Y-axis LIN; fitting algorithm spline smoothed	Multicalc, X- axis LIN, Y-axis LIN ; fitting algorithm spline smoothed
Incubation Detail	3.5 hours, 25°C	5 hours, 25°C

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

- CLSI Guideline EP5-A2: *Evaluation of Precision Performance of Quantitative Measurement Methods*
- CLSI Guideline EP 17-A: *Protocols for Determination of Limits of Detection and Limits of Quantitation*
- CLSI Guideline EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach*
- CLSI Guideline EP9-A2*: Method Comparison and Bias Estimation Using Patient Samples*
- CLSI Protocol EP7-A2: *Interference Testing in Clinical Chemistry*

L. Test Principle:

The GSP instrument is a fully automated, high throughput batch analyzer for time resolved and prompt fluorescence analysis of samples in microtitration plates. It is intended for *in vitro* quantitative and qualitative determination of analytes in body fluids.

The GSP™ Neonatal hTSH assay is a solid phase, two-site fluoroimmunometric assay based on the direct sandwich technique in which two monoclonal antibodies (derived from mice) are directed against two separate antigenic determinants on the hTSH molecule. Calibrators, controls and test specimens containing hTSH are reacted simultaneously with immobilized monoclonal antibodies directed against a specific antigenic site on the ß hTSH subunit and europium-labeled monoclonal antibodies (directed against a different antigenic site located partly on the ß subunit and partly on the a subunit) in assay buffer.
The assay buffer elutes hTSH from the dried blood spots on the filter paper disks. The complete assay requires one incubation step.
DELFIA Inducer dissociates europium ions from the labeled antibody into solution where they form highly fluorescent chelates with components of DELFIA Inducer. The fluorescence in each well is then measured. The fluorescence of each sample is proportional to the concentration of hTSH in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

   Precision was evaluated in accordance with CLIA document EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline.*

   The variation of the GSP Neonatal hTSH assay was determined using spiked dry whole blood spot samples, 3 kit lots and 3 GSP systems. The samples were dried blood spot specimens (DBS) prepared from whole blood spiked with TSH. The sample concentrations were chosen to cover the calibrator range of the GSP Neonatal hTSH kit, which is 1 - 250 µU/mL blood. Two of the samples were chosen to be as close as possible to the medical decision level (7 - 25 µU/mL blood).

Heparinized whole blood specimens were collected from four apparently healthy adults. In addition, heparinized whole blood was used for preparation of one specimen (sample 5). The hematocrit of the specimens was adjusted to correspond to the hematocrit of neonates (approximately 50-55%). The samples were spiked with four TSH concentrations. The four blood samples were used to prepare dried blood spot samples by dispensing the prepared samples onto filter paper. The filter papers were dried overnight at room temperature in a laminar flow hood and stored thereafter at -20 ºC in sealed bags with desiccant. The study was performed over 23 days in 27 runs each consisting of 2 plates with 4 replicates per sample. The analysis of variance approach was used to calculate the following:

Precision data using a full calibration curve on each plate:

Sample	Total mean value µU/mL blood	Within-run variation (% CV)	Within-lot variation (% CV)	Total variation (% CV)
1	10.5	6.8	8.9	10.1
2	23.2	5.9	8.6	8.9
3	102	6.1	8.3	8.5
4	241	6.4	8.4	8.7

Precision data using one calibration curve valid for 24 h:

Sample	Total mean value µU/mL blood	Within-run variation (% CV)	Within-lot variation (% CV)	Total variation (% CV)
1	10.6	7.0	8.7	9.9
2	23.4	6.1	8.0	8.3
3	102	6.2	7.7	7.7
4	241	6.8	7.7	7.9

b. *Linearity/assay reportable range:*

The linearity study protocol and analysis for the GSP Neonatal hTSH kit was performed in accordance with CLSI document EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach, Approved Guideline*.

The claimed measuring range for the TSH assay is 1.31 – 250 uU/mL.

Blood was drawn from one apparently healthy adult that represented a "low concentration" sample. The hematocrit of the specimen was adjusted to correspond to the hematocrit of neonates (approximately 0.5 - 0.55). A part of the specimen was separated and TSH standard was added to obtain a high concentration sample containing TSH approximately 300 µU/mL. 10 samples with intermediate concentrations were prepared by mixing the low sample with the high sample and spotted on filter paper and dried overnight. The dried blood spot samples were measured in random order in a single run with two GSP Neonatal hTSH kit lots and two GSP instruments. The samples were analyzed in three replicates per run.

A polynomial evaluation of linearity was used for the data analysis. The assumption of constant variance across all levels is not fulfilled in the GSP Neonatal hTSH kit. Rather, the variance is proportional across different measurement levels. Therefore, weighted regression models were used.

A linear regression line and second and third order polynomials were fitted to the data. The results of regression analyses were compared. The significance of the second and third order polynomials were evaluated by performing a t-test. Both the second and third order regressions have statistically significant nonlinear terms ($\beta 2$, $\beta 3$) at a 95% significance level (p-value <0.05).

For TSH concentrations over 5µU/mL blood, the maximum observed difference between the linear regression models was -5.4 %. For concentrations $\leq$ 5 µU/mL blood, the observed absolute difference between the models was 0.32 µU/mL blood. Therefore, the assay has been demonstrated to be linear over the claimed measuring range of 1.31 - 250 µU/mL.

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

Calibrators and Controls: The calibrators and controls for the GSP Neonatal hTSH are only available in the kit.

The Neonatal hTSH calibrators and Neonatal hTSH controls are dried blood spots (DBS) on filter paper in sheet format prepared from a commercial TSH standard and washed red blood cells diluted in filtered human serum (with a final hematocrit value of 50-55%). The six calibrators contain concentrations of added TSH at approximately 1, 10, 25, 50, 100 and 250 µU/mL blood. The two controls contain approximate TSH concentrations of 15 and 60 µU/mL blood. The calibrators and controls are stored at +2 - +8 °C.

TSH-WHO standard material (WHO 3rd IS for TSH 81/565) is used to prepare primary calibrators for the GSP Neonatal hTSH kit. The standard material is diluted in 1% BSA-TSA solution and the concentration of the stock solution is gravimetrically determined. The WHO stock solution is added to washed red blood cell/filtered serum suspension and dispensed as blood spots on Whatman 903 filter paper.

The primary calibrators are used to monitor the level of secondary calibrators regularly. The primary calibrators are used to draw a standard curve against

which the secondary calibrators are evaluated. The secondary calibrators are prepared identically to the kit calibrators and controls (described above). The concentration determination is done against the previous lot of the secondary calibrators. They are stored at -20°C.

Initial concentration values for the kit calibrators and the kit controls are assigned against the secondary calibrators using GSP instrument. The final, kit lot specific concentrations for the kit calibrators and kit controls are assigned in the final release test using the level calibrators and GSP instrument.

Stability:
Accelerated and real-time shelf-life stability: Study protocols, preliminary data and acceptance criteria for shelf-life stability testing were provided for the Neonatal hTSH kit components including the calibrators and controls at refrigerated (2-8°C) and elevated (35°C) temperatures and elevated humidity (RH 80%) and found to be acceptable. Based on the accelerated stability data, twelve month shelf-life stability at 4°C is claimed for the Assay kit. Real-time studies will continue to confirm and extend the dating.

In-use and on-board stability: Study protocols, preliminary data and acceptance criteria for in-use and on-board stability were provided for the Neonatal hTSH kit and found to be acceptable. Once opened, calibrators and controls can be stored for 2 weeks at +2 to +8 °C in the original bag (protected from light and moisture), and thereafter used in the hTSH assay. After opening the package, the anti-hTSH microtitration strips can be stored for 2 weeks at +2 - +8 °C in the original package or in a resealable plastic bag with desiccant (protected from light and moisture), and thereafter used in the hTSH assay. Punched anti-hTSH microtitration strips can be stored on-board in the GSP instrument plate storage magazine for 12 hours. On-board stability data supports on-board storage of Anti-hTSH-Eu-tracer and Neo hTSH Assay buffer up to 5 days.

d. Detection limit:
The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) was determined in accordance with the CLSI Guideline EP 17-A: *Protocols for Determination of Limits of Detection and Limits of Quantitation.*

Limit of Blank: Three blank pools were prepared using washed red blood cell and filtered serum. The hematocrit of the specimens was adjusted to correspond to the hematocrit of neonates (approximately 50-55%). Blank dried blood spot samples for testing were prepared and dried overnight. Repeated measurements (n = 216, n = 72 / specimen, n = 24 / specimen / kit lot) were carried out using the samples. 18 separate runs were performed using three kit lots and three GSP instruments over six days.
The LoB was estimated nonparametrically as the 95th percentile of the measurements. The LoB was determined to be 0.96 µU/mL blood.

Limit of Detection (LoD) and Limit of Quantitation (LoQ): To prepare the samples for the determination of LoD and LoQ, blood was drawn from three apparently healthy adults. In addition, heparinized whole blood was used for preparation of one specimen (sample LoD3). The hematocrit of the specimens was adjusted to correspond to the hematocrit of neonates (approximately 50-55%). Low level samples for the LoD and LoQ analyses were prepared by dispensing the different blood specimens without any addition of TSH on filter paper and dried overnight.
Repeated measurements (n = 216 / specimen) were carried out using the 4 dried blood spot specimens. The runs were performed using three different Neonatal hTSH kit lots and three different GSP instruments. Statistical analysis calculated the LoD to be 1.31 µU/mL blood.

In absence of a recognized reference method, a functional sensitivity study was used to define LoQ. LoQ is the lowest concentration of TSH that can be measured with acceptable total variation of the assay (CV% < 20%). LoQ was determined to be 1.31 µU/mL blood.

Samples that result in values below 1.31 µU/mL blood (2.91 µU/mL serum) are recommended to be reported as "<1.31µU/mL blood" or "<2.91 µU/mL serum". These results are not considered to be accurate, but can be considered screen negative for congenital hypothyroidism.

Samples that result in values above the uppermost calibrator (Cal F; approximately 250µU/mL blood or 555 µU/mL serum) are recommended to be reported as "> Cal F µU/mL blood (kit lot specific value)" or "> Cal F µU/mL serum (kit lot specific value)". The results are not recommended to be considered accurate, but can be considered screen positive for congenital hypothyroidism.

e. Analytical specificity:

Hook effect:

For the GSP Neonatal hTSH assay no hook effect was observed with TSH concentrations up to 2000 µU/mL blood.

Blood was drawn from one apparently healthy adult donor. The hematocrit was adjusted to correspond to the hematocrit of neonates (approximately 0.5 - 0.55%). This specimen represented “low concentration” sample. A part of the specimen was separated and TSH standard was added to obtain “high concentration” sample (2000 µU/mL blood). The other samples with intermediate concentrations were prepared by pooling the “low concentration” sample with the “high concentration” sample as presented. The different dilutions were used to prepare dried blood spot samples by dispensing the blood pools onto filter paper and dried overnight. The TSH concentrations of the dried blood spot samples were measured using three kit lots and one GSP

system. The samples were analyzed in four replicates in random order on a plate.

The results from the dilution series were analyzed. In this study the tested sample concentrations did not result in test results where the result came back to the calibrator curve, therefore no hook effect was seen at the concentrations tested. The highest value expected in newborns would be approximately 1000 uU/mL.

Cross-reactive substances:

Cross reactivity was determined in accordance with CLSI document EP7-A2, *Interference Testing in Clinical Chemistry*; Approved Guideline – Second Edition.

To determine the effect of the potential interferent on the measured TSH concentrations of the samples with the addition of the tested substance, the results were compared to those of the samples with no additions other than the solvent. The 95% confidence interval approach was used to evaluate the magnitude of the cross-reactivity. A bias of greater than ±1SD (from the product specifications) was considered as analytically significant cross-reactivity. Ten percent (10%) is the specification for the within-plate assay variation (CV%) at the tested TSH concentration levels.

Heparinized whole blood was used as sample. The hematocrit of the blood was adjusted to correspond to the hematocrit of neonates (approximately 0.5-0.55). The blood was spiked with two different clinically relevant TSH concentrations, 15 and 30 µU/mL blood; the tested substances were added to these blood samples. The samples without any additions except solvent (1%TSA-BSA) were used as controls. Dried blood spot samples were prepared by dispensing blood pools on filter paper and dried overnight.

The TSH responses of the dried blood spot cross-reactivity samples were analyzed with one GSP Neonatal hTSH kit lot in a single run. The samples were analyzed in 12 replicates in random order.

The tested potential cross-reacting substances and their test concentrations:

Substance	**Test concentration**
hCG	100000 U/L
hLH	250 U/L
hFSH	250 U/L

Potential crossreacting substance	TSH concen-tration	Observed interference effect (µU/mL blood)	95% Confidence interval (µU/mL blood)	Cut-off ±1SD	Interference
hFSH	Low 15 uU/mL	0.516	-0.842 – 1.87	±1.9	No
	High 30 uU/mL	0.208	-1.37 – 1.78	±3.0	No
hLH	Low 15 uU/mL	0.819	-0.283 – 1.92	±1.5	No
	High 30 uU/mL	-0.384	-1.79 – 1.02	±3.1	No
hCG	Low 15 uU/mL	-0.934	-1.73 – -0.136	±1.6	No
	High 30 uU/mL	-0.483	-1.8 – 0.836	±2.9	No

The sponsor concludes that hCG at concentration 100,000 U/L and hFSH and hLH at concentrations 250 U/L do not cross react with the measurement of TSH using the GSP Neonatal hTSH kit.

Interference:

To determine the effect of the potential interferent on the measured TSH concentrations of the samples with the addition of the tested substance, the results were compared to those of the samples with no additions other than the solvent. The 95% confidence interval approach was used to evaluate the magnitude of the interference. A bias of greater than ±1SD (from the product specifications) was considered as analytically significant interference.

Heparinized whole blood was used as sample. The hematocrit of the blood was adjusted to correspond to the hematocrit of neonates (approximately 50-55%). The blood was spiked with two different clinically relevant TSH concentrations, 15 and 30 µU/mL blood; potentially interfering substances were added to these blood samples. The pools without any additions except solvent were used as controls. Dried blood spot samples were prepared by dispensing the blood samples onto filter paper and dried overnight.

The TSH responses of the dried blood spot interference samples were analyzed with one GSP Neonatal hTSH kit lot in a single run. The samples were analyzed in 12 replicates in random order.

Potential interfering substance	TSH concen-tration	Mean control pool value (µU/mL blood)	Observed inter-ference effect (µU/mL blood)	95% Confidence interval (µU/mL blood)	Cut-off ±1SD	Inter-ference
Un-conjugated bilirubin 20 mg/dL	Low 15 uU/mL	14.5	1.39	0.51-2.27	±2.3	No
	High 30 uU/mL	30	1.73	0.30 – 3.17	±4.7	No
Conjugated bilirubin 20 mg/dL	Low 15 uU/mL	13.7	0.34	-0.53 – 1.21	±2.1	No
	High 30 uU/mL	28.6	2.96	1.64 – 4.27	±4.5	No
Lipemia, Intralipid 30 mg/mL	Low 15 uU/mL	15.7	0.34	-0.54 – 1.22	±2.5	No
	High 30 uU/mL	32.1	2.24	0.85 – 3.63	±5.1	No
Hemoglobin 15 g/L	Low 15 uU/mL	14.9	0.88	0.12 – 1.65	±2.3	No
	High 30 uU/mL	28.6	1.83	0.24 - 3.4	±4.5	No

The sponsor concludes that icteric (unconjugated bilirubin </= 342 µmol/L, equivalent to 20 mg/dL in blood, and conjugated bilirubin </= 237 µmol/L, equivalent to 20 mg/dL in blood) and lipemic samples (Intralipid solution 30 mg/mL in serum) do not interfere with the assay. Additional hemoglobin up to 15 g/L do not interfere with the assay.

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted internally. 162 samples consisting of routine newborn screening samples and blood samples spiked with TSH were assayed on the predicate and proposed devices. The TSH concentration in the samples tested ranged 1.31 to 238 µU/mL blood. Weighted Deming regression analysis of the data provides:

Regression equation	95% confidence interval
y = 0.97x - 0.21	Slope: (0.94, 1.00); Intercept: (-0.34, -0.09)

b. Matrix comparison: Not applicable. This assay uses neonatal dried blood spots only.

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):

Clinical data from newborn screening specimens tested at two U.S. state laboratories are presented below. At both sites, the routine screening samples were obtained from the samples submitted to the laboratories for testing by order of a physician. The confirmed positive samples were acquired from retrospective, banked samples in the possession of the laboratories.

Screening cut-offs used for classifying test results from both devices at both external sites were those found in the table below, based on the American Association of Pediatrics recommendations[1]:

Screening negative	Borderline	Screening positive
<9 uU/mL blood <20 uU/mL serum	9-18 uU/mL blood 20-40 uU/mL serum	>18 uU/mL blood >40 uU/mL serum

Study 1: 2053 routine left-over neonatal DBS specimens were assayed in the study and used in the analysis. Of the 2053 there were 20 retrospective samples from diagnosed hypothyroid babies and 2 samples found during the testing of the routine left-over specimens were screening positive.

Screening performance:

		AutoDELFIA (predicate)			
		Screening negative	Borderline	Screening positive	Total
GSP	Screening negative	1958	20	0	1978
	Borderline	12	41	0	53
	Screening positive	0	0	22	22
	Total	1970	61	22	2053

Classification of diagnosed positive samples:

	Normal < 20 µU/mL serum	**Borderline 20-40 µU/mL serum**	**Hypothyroid > 40 µU/mL serum**
GSP	0	0	20
AutoDELFIA	0	0	20

Study 2: A total of 2180 routine left-over neonatal DBS specimens were assayed in the study, of which 2104 were included in the analysis. Of the 2104 there were included 23 retrospective samples from diagnosed hypothyroid newborns. During the evaluation 3 routine left-over specimens were confirmed to be from hypothyroid newborns and therefore the total number of hypothyroid specimens is 26 of the 2104 specimens.

		AutoDELFIA (predicate)			
		Screening negative	Borderline	Screening positive	Total
GSP	Screening negative	2000	22	1*	2023
	Borderline	11	45	0	56
	Screening positive	0	0	25	25
	Total	2011	67	26	2104

* Initial patient screening result at the state laboratory was screen normal; GSP result matches the state laboratory result but does not agree with the result given by the predicate device in this study.

Classification of diagnosed positive samples:

	Normal < 20µU/mL serum	**Borderline 20-40 µU/mL serum**	**Hypothyroid > 40µU/mL serum**
GSP	0	1*	25
AutoDELFIA	0	1*	25

* Initial patient screening result at the state laboratory also was borderline but upon follow-up, infant was eventually diagnosed with primary hypothyroidism.

4. Clinical cut-off**:**
   Screening for congenital hypothyroidism by measurement of hTSH concentrations requires a decision of the screening policy, definition of tiers, cut-off values and follow-up[1]. The laboratory needs to establish its own cut-off values, which can be based on a percentile, or on the basis of a normal range. Cut-off values should be monitored and reassessed when necessary.

5. Expected values/Reference range:
   hTSH patient values by percentile from the testing completed with the Neonatal hTSH kit at the two U.S. state laboratories described above (3c):

Study	n	hTSH µU/mL blood		hTSH µU/mL serum	
		Mean	Median	Mean	Median
1	2081	4.0	3.2	8.8	7.0
2	2033	4.1	3.6	9.1	8.0

		Percentiles									
Study	n	hTSH µU/mL blood					hTSH µU/mL serum				
		95th	97th	98th	99th	99.5th	95th	97th	98th	99th	99.5th
1	2081	7.9	8.8	9.5	10.7	11.6	17.6	19.6	21.1	23.7	25.8
2	2033	7.8	8.8	9.5	11.5	13.0	17.4	19.6	21.1	25.4	29.0

   It should, however, be remembered that cut-off values of hTSH in dry blood spots may vary between different tests and different populations. Therefore, it is recommended that each laboratory establishes its own reference range and cut-off limit from a representative sample population.

N. Instrument Name:
The GSP Instrument

O. System Descriptions:

1. Modes of Operation:
   The GSP instrument is a fully automated, high throughput, batch mode analyzer.

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:
   The sample format for the GSP is dried blood spots. If the dried blood spots are prepared via an external puncher such as the Wallac DBS Puncher, Wallac MultiPuncher or Wallac AutoPuncher a worklist of the samples is transmitted directly to the GSP database in the instrument. If the dried blood spots are prepared manually then GSP Workstation is used to enter worklists into the

database. When the plate barcode is read, the GSP software accesses the worklist information from the database.
The GSP sends the sample results to GSP Workstation. Before it sends them, results are stored in GSP.
Each GSP plate is barcoded with a unique identifier that is read by the barcode reader resident on the GSP instrument.

4. Specimen Sampling and Handling:
   The GSP instrument specimens are dried blood spot format and no mixing of the sample is required to prepare it prior to analysis on the instrument. Either through manual punching or auto punching the dried blood spots are prepared and added to the plate wells. The plates are loaded into a removable plate magazine. Up to 24 plates may be loaded into the plate magazine. The plate magazine is there loaded into the stacker on the GSP instrument and the door closed. The GSP instrument will then present each plate to the barcode scanner for identification and matching to the plate work list.

5. Calibration:
   The six levels of calibrators, calibration curve, must be run in duplicate for each kit lot and DELFIA Inducer lot. Thereafter the calibration curve is valid for up to 24 hours, or until a new calibration curve is run.

6. Quality Control:
   Controls are provided in the kit. Controls should always be used to assure the day-to-day validity of results. The controls should be run in the same way as the samples. Controls at different levels are included in the kit and may number from 2 to 3 levels. These controls should be run in each assay; if the assay includes more than one plate, controls should be run on each plate. Each laboratory should establish its own mean and acceptable range for the controls. The established mean should be within +/- 20% of the values stated on the quality control certificate provided with the kit. It is recommended that the laboratories establish their own controls at different levels in addition to the controls included in the kit. Samples results should only be reported if control results for the assay meet the laboratory's established criteria for acceptability.

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

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.