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

A. 510(k) Number:

k102643

B. Purpose for Submission:

New device

C. Measurand:

Galactose-1-phosphate uridyl transferase (GALT) activity

D. Type of Test:

Quantitative colorimetric enzyme assay

E. Applicant:

Astoria-Pacific, Inc.

F. Proprietary and Established Names:

SPOTCHECK® Neonatal GALT Microplate Reagent Kit

SPOTCHECK® Pro

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
KQP	II	21 CFR §862.1315 – Galactose-1-Phosphate Uridyl Transferase test system	Chemistry (75)
JJQ	I	21 CFR §862.2300 - Colorimeter, photometer, or spectrophotometer for clinical use	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The SPOTCHECK Neonatal GALT Microplate Reagent Kit is for the semiquantitative determination of galactose-1-phosphate uridyl transferase, EC 2.7.7.12 (GALT), activity in whole blood saturated filter paper disks, using a microplate absorbance reader. Measurements of galactose-1-phosphate uridyltransferase are used primarily in the diagnosis and treatment of the hereditary disease galactosemia. This method is intended for in vitro diagnostic

use as an aid in newborn screening for decreased levels of GALT enzyme activity, and not for monitoring purposes.

The SPOTCHECK Pro is used for automated sample processing in the application of *in vitro* diagnostic assays. Specimens containing patient bodily substances are introduced and analyzed in microtiter plates using qualitative/quantitative determination through absorbance measurements.

This device and assays are intended for use by trained, qualified laboratory personnel.

3. Special conditions for use statement(s):

   Specimens producing deficient (presumed positive for galactosemia) or unexpected responses require confirmation or follow-up testing according to local, state and federal requirements.

   Each laboratory must determine its range of normal and deficient levels of GALT activity, based on its patient population and analytical variables.

   Specimens incompletely dried, exposed to moisture after drying, or exposed to heat above 50°C may exhibit no GALT activity. This test cannot be used to screen for galactosemia in patients who have received a transfusion. Filter paper other than Whatman (formerly S&S®) 903™ or equivalent may not yield equal results.

4. Special instrument requirements:

   Astoria-Pacific, Inc. SPOTCHECK Pro (automated method) or a manual method using a microplate reader that can measure absorbance at 600 and 750 nm (data for the manual method in this submission was generated using the BioTek ELx808 microplate reader).

I. Device Description:

The kit includes sufficient in vitro diagnostic reagent for the analysis of 60 plates.

The kit includes: 1 vial of Color Reagent (containing MTT and Diaphorase), 2 bottles of Substrate (each containing NADP, Gal-1-Phosphate, UDP-Glucose, G6PD and PGluM), 1 vial of NADH Stock Standard (reconstituted and diluted by the user to create calibrators), and 1 bottle of TRIS Buffer.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Bio-Rad Quantase™ Neonatal GALT Test,

   BioTek ELx808 Automated Microplate Reader

2. Predicate K number(s):

   k990827, k953710

3. Comparison with predicate:

Assay:

Similarities		
Item	Proposed device	Predicate device (k990827)
Indications for use	For the quantitative determination of galactose-1-phosphate uridyl transferase activity in dried blood spots. Measurements of galactose-1-phosphate uridyltransferase are used primarily in the diagnosis and treatment of the hereditary disease galactosemia.	Same
Specimen collection, handling, storage	Use standardized blood spot collection cards; follow protocol in *CLSI LA4-A5*	Same
Sample size	1 x 1/8" punched dried blood spot	Same
Incubation temperature	37˚C	Same

Differences		
Item	Proposed device	Predicate device (k990827)
Incubation time	2 hours	3 hours
Substrate reagent	Buffered NADP + Gal-1-P + UDP-Glu + G6PD + PGluM	Buffered NADP + tetrazolium salt + Gal-1-P + UDP-Glu + glucose-1,6- diphosphate
Color reagent	Buffered MTT + diaphorase	Buffered diaphorase
Absorbance measurements	600 nm (750 nm reference)	550 or 570 nm
Calibration	Liquid NADH standards	Factor multiplication
Limit of Quantitation	0.3 U/g Hb	0.64 U/g Hb

Instrument: Both the proposed and predicate devices are automated to perform incubation/shaking, filtering, absorbance measurements and data processing. The proposed device also performs automatic liquid handling (pipetting) and robotic sample plate manipulation that the predicate device does not.

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:

Four enzyme mediated reactions are employed in the determination of GALT activity by the SPOTCHECK Neonatal GALT Microplate Reagent Kit. The GALT enzyme catalyzes the conversion of galactose-1-phosphate to glucose-1- phosphate and concurrently the conversion of UDP-glucose to UDP-galactose. Then, glucose-1-phosphate is converted to glucose-6-phosphate catalyzed by the enzyme phosphoglucomutase. Next, glucose-6-phosphate is oxidized to 6-phosphogluconate with the concurrent reduction of NADP to NADPH, catalyzed by glucose-6-phosphate dehydrogenase. Finally, a tetrazolium salt (MTT), catalyzed by diaphorase, reacts with the NADPH to form the product that is measured to yield GALT activity.

$$\text{Gal-1-P + UDP-Glu} \xrightarrow{\text{GALT}} \text{Glu-1-P + UDP-Gal}$$

$$\text{Glu-1-P} \xrightarrow{\text{PGluM}} \text{Glu-6-P}$$

$$\text{Glu-6-P + NADP} \xrightarrow[\text{Mg}]{\text{G6PD}} \text{6-PG + NADPH}$$

$$\text{MTT + NADPH} \xrightarrow{\text{Diaphorase}} \text{Colored Formazan + NADP}$$

Gal-1-P = Galactose-1-phosphate
UDP-Glu= Uridine 5'-diphosphoglucose
GALT = Galactose-1-phosphate uridyl transferase
Glu-1-P = Glucose-1-phosphate
UDP-Gal= Uridine diphosphogalactose
PGluM = Phosphoglucomutase
Glu-6-P = Glucose-6-phosphate
NADP = Nicotinamide adenine dinucleotide phosphate
G6PD = Glucose-6-phosphate dehydrogenase
6-PG = 6-phosphogluconate
NADPH = Nicotinamide adenine dinucleotide phosphate (reduced)
MTT = 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide

GALT activity is determined by measuring the colored formazan produced by the addition of the color reagent to the incubated blood/substrate mixture.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-run and total precision for the SPOTCHECK® Neonatal GALT Microplate Reagent Kit were determined by a modified protocol from the CLSI EP5-A2: *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline — Second Edition*. For each method (automated and manual), samples at 4 different levels of GALT activity were analyzed using 16 replicates on 1 run per day for 5 days (2 distinct calibration curves on 2 plates); a total of 80 data points at each level were collected.

Performance of the SPOTCHECK® Neonatal GALT Microplate Reagent Kit using the manual method:

Activity (U/g Hb)	Deficient	Partial	Near cutoff	Normal
Mean	0.45	1.3	2.4	6.7
S.D.	0.037	0.087	0.20	0.55
C.V.	8.1%	6.5%	8.3%	8.2%

Performance of the SPOTCHECK® Neonatal GALT Microplate Reagent Kit on the SPOTCHECK Pro:

Activity (U/g Hb)	Deficient	Partial	Near cutoff	Normal
Mean	0.60	1.3	2.4	6.1
S.D.	0.046	0.081	0.16	0.40
C.V.	7.8%	6.2%	6.7%	6.6%

b. Linearity/assay reportable range:

The claimed measuring range for the SPOTCHECK® Neonatal GALT Microplate Reagent Kit is 0.3 – 15.0 U/g Hb based on the Limit of Quantitation (see d. below) and Linearity studies.

In order to evaluate the linearity of the assay, a blood spot control specimen, manufactured with deficient GALT (galactose-1-phosphate uridyl transferase) activity and a hematocrit of 55% was proportionately mixed with increasing levels of GALT enzyme to provide 21 concentrations at equally spaced intervals. Four replicates at each level were analyzed in a single run to provide data to determine linearity according to CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*.

The absolute values of the differences between each replicate were calculated for each level, followed by the mean difference. Next, the sum of the squared differences and its mean were calculated as well as the sum of the squared percent differences and its mean. Finally, first, second and third order regressions of the data were performed to evaluate whether any non-linear terms were significant.

Sample (n = 4)	Actual Mean (U/g Hb)	Predicted 2nd Order Value (U/g Hb)	Difference in Predicted Values	% Difference
L1	0.25	0.26	0.011	4.4
L2	1.1	1.0	-0.083	-8.2
L3	1.7	1.7	-0.045	-2.6
L4	2.4	2.4	0.011	0.44
L5	3.1	3.1	-0.009	-0.29
L6	3.8	3.9	0.029	0.75
L7	4.5	4.6	0.053	1.2
L8	5.3	5.3	0.013	0.25
L9	6.0	6.1	0.103	1.7
L10	6.7	6.8	0.117	1.7
L11	7.5	7.6	0.056	0.74
L12	8.4	8.3	-0.075	-0.89
L13	9.1	9.1	-0.031	-0.35
L14	9.8	9.8	-0.005	-0.05
L15	10.7	10.6	-0.064	-0.60
L16	11.5	11.4	-0.108	-0.94
L17	12.2	12.1	-0.016	-0.13
L18	13.0	12.9	-0.071	-0.55
L19	13.7	13.7	-0.013	-0.09
L20	14.6	14.5	-0.113	-0.78
L21	15.0	15.3	0.241	1.6

Order	Coefficient	Value	Standard Error of the Regression	Degrees of Freedom	t-Test
First	b_0	-0.626			
First	b_1 (x term)	0.752	0.190	82	
Second	b_o	-0.449			
Second	b_1 (x term)	0.705			
Second	b_2 (x^2 term)	0.002	0.177	81	3.555
Third	b_o	-0.285			
Third	b_1 (x term)	0.625			
Third	b_2 (x^2 term)	0.011			
Third	b_3 (x^3 term)	0.000	0.172	80	-1.474 *

* Does not exceed the limits in the table for the "Students t" distribution at the 95% level. The x^3 term is therefore not significant.

The results of the t-test for b_2 (x^2 term) on the second order regression analysis show that the x^2 term is significant. The t-test for b_3 (x^3 term) on the third order regression analysis shows that the x^3 term is not significant. There are no concentrations at which the difference between the actual values and the predicted second order values exceed the ± 10% goal for percent difference. Additionally, there are no concentrations where the difference between the first and second order or the second and third order predicted models exceed the ± 0.15 U/g Hb goal for absolute difference.

The system is judged to be 2nd order over the claimed measuring range of 0.30 to 15.0 U/g Hb.

Uridyltransferase is inhibited by UDP-galactose, with a K_i of 0.2 mM, which is the cause of the 2nd order calibration curve and blood spot response.

Samples with values above 15.0 U/g Hb should be reported as > 15.0 U/g Hb.

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

Value assignment**:** NADH is used as a calibrator (NADH Stock Standard) because it mimics the NADPH formed during the reactions as part of the assay.

For a new lot of NADH stock standard, the spectrophotometric absorbance of the NADH standard at 340 nm is compared against that of a current accepted lot. Six replicates of each lot number are used in the testing protocol. The spectrophotometric response is verified against the analysis of standardized potassium dichromate solutions. The absorbance of the standardized potassium dichromate solutions must fall in the ranges stated on the quality control work instruction document. The average absorbance of both the new and existing lots of NADH must fall in the range stated on the quality control work instruction document. The percent relative standard deviation (%RSD) of the six replicates of each lot of stock standard must be less than 5%. The relative percent difference (RPD) between the new and existing lot of stock standard must also be 2% or less. A comparison analysis with the Neonatal GALT Microplate Reagent Kit is then carried out. The six replicates of each lot of stock standard are used to prepare standards with an identical value that falls in the range of the standard curve and run on a microplate using current lots of GALT substrate and color reagent. A calibration curve is constructed from both lots according to the instructions in the GALT Kit package insert. The RPD between the new and existing lots of stock standard must be 2% or less.

Accelerated and real-time shelf-life stability: Study protocols, preliminary data and acceptance criteria for shelf-life stability testing were provided for the SPOTCHECK® Neonatal GALT Microplate Reagent Kit components (unreconstituted/unprepared) at the recommended storage temperature (+2 - +8°C for kit reagents and calibrators) and at elevated temperatures (35.5°C for kit reagents and calibrators) and found to be acceptable. Based on the accelerated stability data, twenty four months of shelf-life stability at the recommended storage temperature is claimed for the calibrators and kit reagents. Real-time studies will continue to confirm and extend the dating.

In-use stability: Study protocols, preliminary data and acceptance criteria for in-use stability were provided for the SPOTCHECK® Neonatal GALT Microplate Reagent Kit and found to be acceptable. Once reconstituted or prepared by the laboratory, calibrators and color reagent can be stored for 14 days at +2 to +8 °C; substrate is stable for 7 days at +2 to +8 °C.

d. Detection limit:

A study was performed to evaluate the Limit of Detection and Limit of Quantitation of the Astoria-Pacific, Inc. SPOTCHECK® Neonatal GALT Microplate Reagent Kit test system. The studies were conducted in duplicate (one using the SPOTCHECK Pro™ automated option, the other manually) and according to CLSI EP17-A: *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.*

Blank NADH standards were analyzed 12 times per plate on 5 separate plates for a total of 60 blank observations.

Three low GALT activity samples were analyzed 8 times per plate on 10 separate plates for a total of 2401 low-level measurements. Each plate employed its own distinct calibration curve. Samples with low activity (in the deficient range) were prepared to simulate neonatal blood and spotted on Whatman 903A® absorbent filter paper.

The results are expressed as units of GALT enzyme activity per gram of hemoglobin or U/g Hb. A unit is defined as the quantity of GALT enzyme that catalyzes the formation of one micromole of UDP-galactose per minute at 37ºC.

GALT, blank	SPOTCHECK Pro (automated)	Manual
Number of Observations (N)	60	60
Mean (μ)	-0.0127	0.0330 U/g Hb
Standard Deviation (σ)	0.0573	0.0278
Limit of Blank (LoB) {LoB = μ+ 1.645σ}	0.08 U/g Hb	0.08 U/g Hb

GALT, Low-level Activity		
Method	SPOTCHECK Pro (Automated)	SPOTCHECK (Manual)
Number of Observations (N)	238	240
Number of Samples (K)	3	3
Standard Deviation (SD), pooled	0.063	0.034
Degrees of Freedom (f) {f = N – K}	235	237
cβ{cβ = 1.645 / (1 - 1 / (4 x f))}	1.647	1.647
Limit of Detection (LoD) {LoD = LoB + cβ SD}	0.186 U/g Hb	0.135 U/g Hb
Coefficient of variation (CV), pooled	9.1%	12.2%
Total Error, 2xSD (TE, 95.45% confidence limit)	0.127	0.068
Total Error, 3xSD (TE, 99.73% confidence limit)	0.190	0.102
LoQ (Limit of Quantitation)	0.2 U/g Hb	0.2 U/g Hb

The limit of detection (LoD) for GALT is calculated to be less than 0.2 U/g Hb (0.186 automated and 0.135 manually) using the guidelines in CLSI EP17-A protocol and with proportions of false positives (α) less than 0.3% and false negatives (β) less than 0.3%, based on 300 measurements, consisting of 60 blank and 240 low-level samples; limit of blank (LoB) = 0.08 U/g Hb. The total error (TE, 3xSD) is less than the goal of 0.2 U/g Hb, assuming that there is no bias due to the unavailability of standard reference materials. Therefore, the LoD = LoQ, according to the guidelines in CLSI EP17-A.

In order to establish the LoQ, CLSI EP17-A guidelines recommend using a functional sensitivity determination when reference data are not attainable. Precision data was obtained that reveal performance around the LoD. All samples around 0.2 U/g Hb had %CV less than 20%. However, the LoQ has been conservatively set to be 0.3 U/g Hb for the automated and manual method of the kit.

Samples with values below 0.3 U/g Hb should be reported as < 0.3 U/g Hb.

e. Analytical specificity:

Two samples were evaluated: one sample deficient of GALT (galactose-1-phosphate uridyl transferase) activity and the other with normal GALT activity. Three pools of blood spots from each sample were created; one with no added compounds and one with low level of potential interferent and one with a high level of potential interferent. Eight replicates from each pool were analyzed. The study was conducted according to CLSI EP7-A2: *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition.*

The overall acceptance criterion was that no potential interferents affected the results such that a true deficient newborn could possibly be misclassified

(false negative). An increase of 1 U/g Hb from the control would have been an indication that additional design controls should be considered to ensure safety and effectiveness. For compounds that did not cause interference, in no instance was an increase of > 0.3 U/g Hb over the control observed. Lipemia up to 3270 mg/dL can lower GALT activity results near the cutoff resulting in a false positive. Protein (albumin and gamma-globulin) up to 6000 mg/dL may cause minor (<10%) increases in response near the cutoff, but would not result in a galactosemic patient being classified as normal. Conjugated bilirubin up to 28.8 mg/dL and unconjugated bilirubin up to 20 mg/dL do not interfere significantly. Additional hemoglobin at levels below 200 mg/dL does not interfere significantly.

The drugs sulfamethoxazole (up to 400 µg/mL) and trimethoprim (up to 40 µg/mL) do not cause any significant interference.

Varying hematocrit predictably causes changes in response as GALT resides in the red blood cells. Mean changes in GALT activity response can be expected to be +20% for a hematocrit of 65% and -20% for a hematocrit of 45% when compared to a typical neonate hematocrit of 55%.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Internal method comparison of manual method of the Neonatal GALT kit and the predicate device: Newborn patient dried blood spot samples, dried blood spot controls manufactured to mimic newborn specimens, as well as dried specimens consisting of mixed adult blood were analyzed using both the Astoria-Pacific, Inc. SPOTCHECK Neonatal GALT Microplate Reagent Kit and the predicate device.

A total of 265 samples were analyzed using singlicate measurements for both devices. The range of the data was: 1.1 – 14.3 U/g Hb as measured on the proposed device.

A linear regression analysis of the data yields the following equation:
$y = 0.935\ x + 0.798$
$R^2 = 0.835$

Method comparison of manual method vs. automated SPOTCHECK Pro: Newborn patient dried blood spot samples, dried blood spot controls manufactured to mimic newborn specimens, as well as dried specimens consisting of mixed adult blood were analyzed using both manual processing and the SPOTCHECK Pro. A total of 204 samples were analyzed using singlicate measurements for both devices. To reduce sources of error not attributed to the different approaches, the same reagent preparations were used, and individual samples were punched and analyzed using each process

on the same day. The study was performed over three days.

Range of the samples:

Manual	Automated
1.3 – 14.6 U/g Hb	1.5 – 14.0 U/g Hb

A linear regression analysis of the data yields the following equation:
$y = 0.963x + 0.393$
$R^2 = 0.896$

b. Matrix comparison:

Not applicable. This assay only uses neonatal dried blood spots on filter paper.

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):

Screening study at state public health laboratory: To determine the correlation of results for neonatal Galactose-1-phosphate uridyl transferase (GALT) deficiency screening between the predicate device and the Astoria-Pacific, Inc. SPOTCHECK® Neonatal GALT Microplate Reagent Kit (proposed device) was assayed on the SPOTCHECK Pro (automated method). 1805 dried blood spot samples were analyzed by two operators, one using the proposed device and the other using the predicate device. The data was collected over the course of three winter days in a state newborn screening laboratory.

Both the predicate and proposed devices were employed to collect data for 1752 neonatal patient samples unclassified for GALT, 6 manufactured blood spot controls deficient in GALT, 9 retrospective samples from newborns affected with galactosemia, and 38 samples from non-neonate patients confirmed galactosemic. GALT-deficient controls were prepared to simulate neonatal blood and spotted on Whatman 903A® absorbent filter paper; prior to spotting, human serum and human red blood cells were combined to approximate a representative neonate hematocrit of 55%. Controls and known deficient samples were included in the study randomly.

1751 neonatal patient samples tested negative for galactosemia during routine GALT analysis using the newborn screening laboratory's implemented methodology, while one was classified as having partial activity. Cutoff values (clinical decision levels) for the proposed and predicate devices were established at both the lower 0.5th and 0.25th percentiles of the GALT results for each device, respectively. For the purposes of clinical classification, samples that fall into the category of deficient are presumed positive for galactosemia and referred for follow-up testing. Samples that are classified as normal are presumed negative for galactosemia and no follow-up testing is prescribed.

The data collected for this study is summarized and presented in the following tables. Numerical results are expressed as units of GALT enzyme activity per gram of hemoglobin or U/g Hb. A unit is defined as the quantity of GALT enzyme that catalyzes the formation of one micromole of UDP-galactose per minute at 37 ºC.

Results for the neonatal patient samples unclassified for GALT undergoing routing screening in the laboratory:

GALT (Routine)	Predicate device	Proposed device
Number of observations	1752	1752
Mean Value Observed	9.4 U/g Hb	7.9 U/g Hb
Standard Deviation	2.2	2.1
Range of the data	1.4 to 18.5 U/g Hb	2.5 to >15.0 U/g Hb
0.5^{th} percentile	3.5	3.2
0.25^{th} percentile	3.2	2.9

Results for the known deficient GALT specimens:

GALT (Deficient samples)	Predicate device	Proposed device
Number of observations	53	53
Mean Value Observed	0.095 U/g Hb	0.47 U/g Hb
Standard Deviation	0.31	0.29
Range of the data	-0.34 to 1.2 U/g Hb	<0.30 to 1.7 U/g Hb

Screening/classification results:

Summary of accuracy – 0.5^{th} percentile (All specimens)				
		Predicate device		
		Positive	Negative	Total
Proposed device	Positive	61*	2	63
	Negative	4	1738	1742
	total	65	1740	1805

* All known positive samples (53) were classified as positive by both methods. All but one of the remaining specimens (8) were classified by routine neonatal screening by the state public health laboratory to be

presumptive negative for galactosemia. The laboratory classified one specimen as having partial GALT activity using the predicate device.

Percent positive agreements (61/65) = 93.8%
Percent negative agreement (1738/1740) = 99.9%

Summary of accuracy – 0.25th percentile (All specimens)				
		Predicate device		
		Positive	Negative	Total
Proposed device	Positive	57*	1	58
	Negative	1	1746	1747
	Total	58	1747	1805

* All known positive samples (53) were classified as positive by both methods. All but one of the remaining specimens (4) were classified by routine neonatal screening by the state public health laboratory to be presumptive negative for galactosemia. The laboratory classified one specimen as having partial GALT activity using the predicate device.

Percent positive agreements (57/58) = 95.2%
Percent negative agreement (1746/1747) = 99.9%

4. Clinical cut-off**:**

In the labeling the manufacturer recommends that each laboratory must determine its range of normal, partial, and deficient levels of GALT activity, based on its population and analytical variables.

The activity of normal samples varies widely, and the activity of all samples decreases with time under any conditions of storage. Samples showing sufficient activity can be classified as negative (normal or non-galactosemic). However, the SPOTCHECK Neonatal GALT Microplate Reagent Kit assay cannot be used to classify a particular genotype.

Specimens producing deficient (presumed positive for galactosemia) or unexpected responses require confirmation or follow-up testing according to local, state and federal requirements.

5. Expected values/Reference range:

GALT values obtained from testing 1752 samples with the Neonatal GALT Microplate Reagent kit at a U.S. state laboratory:

GALT (Routine)	SPOTCHECK
Number of Observations	1752
Mean Value Observed	7.9 U/g Hb
Standard Deviation	2.1
Range of the Data	2.5 to 16.0 U/g Hb
0.5 Percentile	3.2
0.25 Percentile	2.9

In the labeling the manufacturer recommends that each laboratory must determine its range of normal and deficient levels of GALT activity, based on its patient population and analytical variables.

N. Instrument Name:

SPOTCHECK Pro

O. System Descriptions:

1. Modes of Operation:

   The instrument performs automatic liquid handling (pipetting) and robotic sample plate manipulation for incubation/shaking, filtering, reagent addition, absorbance measurements and data processing.

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:

   Samples are identified by microplate barcode and position on the microplate. The system software has built-in sample tracking. The system software includes export functions to allow integration with existing laboratory information systems.

4. Specimen Sampling and Handling:

   Dried blood spot samples are manually punched into microplates and placed onto the instrument for processing.

5. Calibration:

   The Astoria-Pacific SPOTCHECK® Neonatal GALT Microplate Reagent Kit includes calibrators to quantitate GALT results. GALT normal and GALT deficient dried blood spot controls are recommended and typically used to validate results.

6. Quality Control:

   The user should perform quality control testing to confirm that the SPOTCHECK Pro is working properly and providing reliable results. Assayed control material for the GALT assay can be obtained separately from Astoria-Pacific, Inc. (cleared under k090940). The manufacturer states in the labeling that all quality control testing should be performed in conformance with local, state, and/or federal regulations or accreditation requirements.

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.