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

A. 510(k) Number:

k093916

B. Purpose for Submission:

Addition of a new tandem mass spectrometry system to a previously cleared kit

C. Measurand:

Amino acids, free carnitine, acylcarnitines, and succinylacetone

D. Type of Test:

Quantitative measurement by mass spectrometry

E. Applicant:

PerkinElmer Inc.

F. Proprietary and Established Names:

NeoBase Non-derivatized MSMS Kit (for use on the PerkinElmer TQD MSMS Screening System)

G. Regulatory Information:

1. Regulation section: 21 CFR §862.1055 Newborn screening test system for amino acids, free carnitine, and acylcarnitines using tandem mass spectrometry

2 . Classification: Class II

3. Product code: NQL

4. Panel: Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See indications for use, below.

2. Indication(s) for use:

The NeoBase Non-derivatized MSMS reagent kit (for use on the PerkinElmer TQD MSMS Screening System) is intended for the measurement and evaluation of amino acids, succinylacetone, free carnitine, and acylcarnitine concentrations from newborn heel prick blood samples dried on filter paper. Quantitative analysis of these analytes and their relationship with each other is intended to provide analyte concentration profiles that may aid in screening newborns for metabolic disorders.

ANALYTE NAME	**ABBREVIATION**
Amino Acids	
Alanine	Ala
Arginine	Arg
Citrulline	Cit
Glycine	Gly
Leucine/Isoleucine/Hydroxyproline*	Leu/Ile/Pro-OH
Methionine	Met
Ornithine	Orn
Phenylalanine	Phe
Proline	Pro
Tyrosine	Tyr
Valine	Val
Carnitines	
Free carnitine	C0
Acetylcarnitine	C2
Propionylcarnitine	C3
Malonylcarnitine / 3-Hydroxy-butyrylcarnitine*	C3DC/C4OH
Butyrylcarnitine	C4
Methylmalonyl / 3-Hydroxy-isovalerylcarnitine*	C4DC/C5OH
Isovalerylcarnitine	C5
Tiglylcarnitine	C5:1
Glutarylcarnitine / 3-Hydroxy-hexanoylcarnitine*	C5DC/C6OH
Hexanoylcarnitine	C6
Adipylcarnitine	C6DC
Octanoylcarnitine	C8
Octenoylcarnitine	C8:1
Decanoylcarnitine	C10
Decenoylcarnitine	C10:1

Decadienoylcarnitine	C10:2
Dodecanoylcarnitine	C12
Dodecenoylcarnitine	C12:1
Tetradecanoylcarnitine (Myristoylcarnitine)	C14
Tetradecenoylcarnitine	C14:1
Tetradecadienoylcarnitine	C14:2
3-Hydroxy-tetradecanoylcarnitine	C14OH
Hexadecanoylcarnitine (palmitoylcarnitine)	C16
Hexadecenoylcarnitine	C16:1
3-Hydroxy-hexadecanoylcarnitine	C16OH
3-Hydroxy-hexadecenoylcarnitine	C16:1OH
Octadecanoylcarnitine (Stearoylcarnitine)	C18
Octadecenoylcarnitine (Oleylcarnitine)	C18:1
Octadecadienoylcarnitine (Linoleylcarnitine)	C18:2
3-Hydroxy-octadecanoylcarnitine	C18OH
3-Hydroxy-octadecenoylcarnitine	C18:1OH
Ketones	
Succinylacetone	SA

*Analytes in these rows are either isomers or isobars and cannot be distinguished in the tandem mass spectrometry assay.

3. Special conditions for use statement(s):

   For prescription use

   The NeoBase Non-derivatized MSMS Kit is a screening assay, not intended for confirmatory or prenatal testing. As with any other in vitro screening test, the data obtained using this kit should be used as an aid to other medically established procedures and results interpreted in conjunction with other clinical data available to the clinician. A diagnostic procedure should be used for confirmation of presumptive abnormal amino acid, succinylacetone, free carnitine and acylcarnitine profiles. Users should follow local guidelines for follow-up and confirmatory testing.
   Also see clinical cutoff section, below.

4. Special instrument requirements:

The assay is for use with the Perkin Elmer TQD MSMS Screening System (as well as with the PerkinElmer MS^2 Tandem Mass Spectrometer System, or PerkinElmer MSMS Quattro Micro (QMicro) Newborn Screening System, which were cleared under k083130).

I. Device Description:

Device components (in addition to the instrument systems listed in Section H-4, above) consist of the following:

- Amino acid internal standards vial
- Acylcarnitine internal standard vial
- Dried blood spot controls (3 filter paper cassettes [Whatman, no.903 paper] containing 3 spots of each low and high level per cassette)
- V-bottom heat-resistant micro plates (10 pcs)
- Truncated V-bottom clear micro plates (10 pcs)
- Aluminum foil microplate covers (20 pcs)
- Adhesive microplate covers (20 pcs)
- NeoBase Non-derivatized Assay Solutions (Flow Solvent and Extraction Solution)
- NeoBase Succinylacetone Assay Solution.

Also, see below in Sections O and P for the instrument features of this system.

This kit contains components manufactured from human blood. The source materials have been tested by FDA-approved methods for hepatitis B surface antigen, anti-hepatitis C and anti-HIV 1 and 2 antibodies and found to be negative.

J. Substantial Equivalence Information:

1. Predicate device name(s): NeoBase Non-derivatized MSMS Kit

2. Predicate 510(k) number(s): k083130

3. Comparison with predicate:

   The devices have the same indication and intended use. More specifics are in the table below:

Parameter	Modified Device	Predicate Device
Intended Use	The NeoBase Non-derivatized MSMS reagent kit is intended for the measurement and evaluation of amino acids, succinylacetone, free carnitine, and acylcarnitine concentrations from newborn heel prick blood samples dried on filter paper. Quantitative analysis of	Same

	these analytes (Table 1) and their relationship with each other is intended to provide analyte concentration profiles that may aid in screening newborns for metabolic disorders.	
Disorders Screened	Amino-, organic-, and fatty acid metabolic disorders	Same
Analytes Measured	Amino acids, free carnitine, acylcarnitines, and succinylacetone	Same
Methodology	Microplate based tandem mass spectrometric assay	Same
Test Principle	Amino acids and carnitines in sample are measured by tandem mass spectrometry through analyte-specific mass transitions appropriate for each type of analyte. The extracted analytes are measured for set time periods and compared to the signal intensities produced by the corresponding isotope-labeled internal standards. The concentrations are determined by comparing the signal intensities of the known standards to the measured analytes.	Same
Sample Requirements	Newborn blood collected on Whatman 903 filter paper per CLSI standards	Same
Throughput	Ninety-six tests per microtiter plate. Multiple plates can be analyzed	Same
Analysis Time	2 to 2.5 hours per plate.	Same
Controls	Controls are blood spots from processed human blood enriched with several amino acids, carnitines and succinylacetone.	Same
Calibrators	Internal calibration using several isotopically labeled standards, included as dried material in vials. Internal standards must be reconstituted with extraction solution prior to their use.	Same
Assay format	Non-derivatized (analytes measured in their native forms)	Same

DEVICE DIFFERENCES		
Parameter	**Modified Device**	**Predicate Device**
Instrumentation	PerkinElmer MS^2 Tandem Mass Spectrometer System PerkinElmer MS/MS Quattro Micro Screening System Perkin Elmer TQD MS/MS Screening System	PerkinElmer MS^2 Tandem Mass Spectrometer System - PerkinElmer MS/MS Quattro Micro Screening System

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

CLSI EP07-A2, Interference Testing in Clinical Chemistry; CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures

L. Test Principle:

The measurement of amino acids, succinylacetone, free carnitine, and acylcarnitines with the NeoBase assay involves extraction of dried blood spots from newborns with a solution containing stable-isotope labeled internal standards and analysis using a tandem mass spectrometry (MSMS) system. The response of each analyte relative to their corresponding stable-isotope labeled internal standard is proportional to analyte concentration.

In the NeoBase Non-derivatized MSMS Kit, data is acquired in the Multiple Reaction Monitoring (MRM) mode. During this acquisition, a collisionally induced of each analyte is measured for a set time period. Data acquisition and processing is performed by the software package included with the system.

The triple-quadrupole mass spectrometer that is used for these measurements is a computer-controlled device that separates and quantitates ions based on their mass to charge (m/z) ratio. The extracted sample is delivered to the ion source of the mass spectrometer by the liquid chromatography (LC) system consisting of the autosampler, micro pump(s) and solvent vacuum degasser. What is reported in the MSMS MRM spectrum is the m/z value of the precursor ions that generated a desired product.

Analyte extraction with the NeoBase assay is accomplished for the amino acids and carnitines by contacting the sample with the extraction solution containing the corresponding internal standards during the incubation step. However,

succinylacetone requires a specific derivatization reaction during the incubation step for its extraction and measurement. The derivatization and extraction of succinylacetone takes place simultaneously with the extraction of other analytes by addition of an aliquot of the Succinylacetone Assay Solution to the extraction mixture containing internal standards.

M. Performance Characteristics (if/when applicable):

Data shown are acquired using the Perkin Elmer TQD MS/MS Screening System in the MRM mode.

1. Analytical performance:

a. Precision/Reproducibility:

Study Design:
A reproducibility study using the NeoBase Assay and the PerkinElmer TQD MS/MS Screening System was performed across multiple instruments, operators, kit lots and sites. The plan consisted of the analysis of dried blood spots samples at three different analyte concentration levels. The study included three TQD instruments (one at each of the participating sites) six different operators, three different NeoBase kit lots (Lot # 493696, 504089, and 511546) and three different external sites.

Each run consisted of the analysis of 6 replicates of each sample level (6 distinct dried blood punches and sample preparations) by one operator using one kit lot on one instrument at each site. Each day, there were two runs (two different operators) per instrument and kit lot. The analysis was carried out for five days for each instrument and kit lot. Overall, there were a total of 30 runs per instrument (5 runs per operator and kit lot on each instrument). Each operator performed a run on each of 5 distinct days (not necessarily consecutively) for an instrument and kit lot.

The Total %CV was determined as the square root of the sum of squares of the variation components mentioned above and according the equation below, where Wr is the Within-Run variation, Br is the Between- Run component of variation, Bl is the Between-Lot variation and Bi/o is the Between-Instrument and Operator contribution to variability.

$$\text{Total imprecision} = [(Wr)^2 + (Br)^2 + (Bi/o)^2 + (Bl)^2\ ]^{1/2}$$

Results:
The overall results for the reproducibility study on the TQD platform are summarized in the tables below. For comparison purposes, these tables also present the original reproducibility results. Mean concentrations are in μM/L

Analyte	ALA									ARG								
Platform	QMicro			MS^2			TQD			QMicro			MS^2			TQD		
DBS Levels	1	2	4	1	2	4	1	2	4	1	2	4	1	2	4	1	2	4
Grand mean	662.2	849.3	1893.2	713.6	880.1	1898.3	650.0	830.6	1870.0	77.7	152.0	591.4	81.3	155.8	599.2	73.2	143.1	559.4
WR %CV Avg	5.1	5.4	5.4	5.1	4.6	4.7	5.0	5.3	4.8	4.5	4.3	4.6	4.7	4.2	4.3	4.9	4.9	4.8
Br %CV Avg	5.5	4.8	5.3	5.2	4.9	4.0	5.6	5.4	5.8	4.0	3.9	4.3	4.2	3.9	3.5	5.1	5.4	5.7
Bi/o %CV	3.3	3.1	3.4	7.3	7.5	6.2	5.2	6.0	5.9	3.2	1.9	2.6	4.8	6.8	7.3	5.3	6.5	6.5
Bl %CV	3.5	2.2	2.4	3.3	2.0	2.3	2.5	3.1	2.6	3.2	1.5	2.0	2.7	2.3	2.9	2.0	3.1	2.6
TOTAL %CV	9.0	8.2	8.6	10.9	10.3	9.1	9.5	10.1	9.9	7.5	6.3	7.1	8.4	9.2	9.6	9.0	10.2	10.2
Analyte	CIT									GLY								
Grand mean	86.7	147.6	486.6	86.3	145.6	487.0	81.6	139.0	463.0	551.5	730.7	1740.2	613.7	763.9	1781.6	532.2	707.0	1715.9
WR %CV Avg	6.6	6.3	5.5	5.2	5.2	4.7	7.0	6.6	5.8	7.6	6.7	6.6	10.7	10.2	8.0	5.9	5.8	5.1
Br %CV Avg	4.1	4.1	4.3	4.0	3.8	3.4	5.4	5.2	5.6	5.0	4.1	4.4	5.4	4.8	4.2	6.5	7.1	7.2
Bi/o %CV	3.2	2.3	2.9	6.3	6.4	5.5	5.0	5.8	6.0	4.0	3.6	3.7	8.2	8.1	5.8	4.8	6.2	6.3
Bl %CV	3.3	1.8	2.4	3.2	2.8	3.3	2.7	2.8	2.7	3.6	3.0	2.1	7.4	3.6	2.9	2.9	3.3	2.6
TOTAL %CV	9.0	8.1	8.0	9.7	9.5	8.7	10.5	10.6	10.4	10.6	9.1	9.0	16.3	14.3	11.1	10.4	11.6	11.1
Analyte	LEU									MET								
Grand mean	301.8	369.6	750.3	309.1	371.4	742.2	285.3	347.7	706.0	45.4	76.2	257.6	47.4	76.9	259.0	43.7	73.7	252.7
WR %CV Avg	68.1	67.2	67.5	4.5	4.4	4.4	5.0	5.0	4.7	6.0	5.7	4.9	6.0	4.7	4.6	6.3	5.9	5.2
Br %CV Avg	4.2	3.9	4.2	3.8	3.6	3.4	5.1	5.4	5.2	5.0	3.9	4.3	4.2	4.0	4.0	6.0	5.8	5.7
Bi/o %CV	3.3	1.9	2.6	6.8	7.2	6.7	6.5	6.8	6.5	3.5	3.0	3.4	12.2	11.4	10.2	7.2	7.5	7.3
Bl %CV	3.3	2.3	2.4	3.8	3.2	3.5	2.5	3.2	2.9	3.5	2.5	2.3	9.0	6.0	6.5	3.3	3.2	2.8
TOTAL %CV	7.8	6.7	7.2	9.8	9.7	9.4	10.0	10.5	10.0	9.2	7.9	7.7	16.8	14.3	13.5	11.8	11.6	11.0
Analyte	ORN									PHE								
Grand mean	204.6	292.3	785.5	198.8	283.1	767.7	185.9	267.4	734.1	125.5	187.4	549.6	131.8	191.3	548.9	117.1	175.0	515.8
WR %CV Avg	4.9	4.6	4.9	4.8	4.4	4.5	4.9	4.9	4.9	4.7	4.6	4.6	4.7	4.3	4.3	5.2	5.0	4.7
Br %CV Avg	5.7	5.0	5.7	4.0	3.9	3.4	6.1	6.2	5.9	4.5	4.0	4.4	3.7	3.3	3.2	5.1	5.3	5.4
Bi/o %CV	10.1	10.0	10.6	7.3	7.6	6.8	6.5	6.7	7.3	3.3	2.0	2.5	6.9	6.8	5.9	6.7	7.2	6.9
Bl %CV	3.4	2.1	2.3	3.3	3.5	3.8	2.4	2.9	2.7	2.8	1.6	1.8	3.7	2.7	3.0	2.6	3.3	2.9
TOTAL %CV	13.0	12.3	13.2	10.2	10.2	9.6	10.4	10.8	10.9	7.8	6.6	7.1	9.8	9.1	8.5	10.2	10.8	10.3
Analyte	PRO									SA								
Grand mean	279.6	383.5	959.6	286.4	375.4	914.9	264.5	360.3	907.5	2.72	4.89	17.9	2.85	4.95	17.9	2.80	5.25	20.3
WR %CV Avg	79.3	76.9	74.7	5.0	4.4	4.3	5.0	4.9	4.6	7.9	6.6	5.0	8.3	6.4	4.7	12.2	10.5	7.7
Br %CV Avg	4.5	4.4	4.9	3.9	3.8	3.5	4.9	5.5	5.7	5.3	5.8	4.9	6.8	6.5	7.5	10.3	8.6	9.5
Bi/o %CV	7.1	7.9	8.8	9.0	8.5	6.6	6.0	6.3	6.7	4.5	4.0	4.6	5.7	7.1	9.7	10.5	8.9	11.1
Bl %CV	3.2	1.8	1.9	5.6	3.5	3.4	2.4	2.9	2.7	4.2	3.2	3.4	2.5	3.3	2.6	6.0	5.4	4.8
TOTAL %CV	10.3	10.5	11.4	12.4	10.9	9.3	9.5	10.1	10.3	11.3	10.2	9.0	12.4	12.0	13.4	20.0	17.1	17.2
Analyte	TYR									VAL								
Grand mean	164.2	261.8	833.3	166.3	260.1	823.8	155.9	247.3	792.9	266.1	324.7	655.0	280.0	335.0	666.0	255.9	312.5	637.4
WR %CV Avg	5.0	4.7	4.6	4.8	4.5	4.5	6.2	5.9	5.2	4.6	4.7	4.6	4.4	4.4	4.4	4.9	4.9	4.5
Br %CV Avg	3.9	3.6	4.4	3.6	3.5	3.3	4.7	5.2	5.2	5.0	4.4	4.8	3.7	3.5	3.3	5.4	5.8	5.7
Bi/o %CV	2.9	2.2	2.8	5.3	5.5	4.4	5.4	6.4	6.7	3.8	3.4	3.7	5.3	5.8	5.3	8.9	9.3	9.7
Bl %CV	2.5	2.0	2.4	3.1	2.8	3.4	4.5	4.6	4.8	3.2	2.0	2.5	4.4	3.8	4.1	2.9	3.5	3.2
TOTAL %CV	7.4	6.7	7.4	8.6	8.4	7.9	10.5	11.2	11.0	8.4	7.6	8.0	8.9	8.9	8.7	11.8	12.5	12.5

Analyte	C0									C2								
Platform	QMicro			MS^2			TQD			QMicro			MS^2			TQD		
Levels	1	2	4	1	2	4	1	2	4	1	2	4	1	2	4	1	2	4
Grand mean	107.3	189.8	663.4	106.8	187.7	653.4	107.5	190.5	671.6	31.4	53.7	181.4	32.3	54.8	183.0	28.6	49.1	166.6
WR %CV Avg	5.2	5.0	5.2	5.2	4.8	4.7	5.9	5.7	5.5	5.4	5.3	5.4	5.5	5.1	5.1	6.1	6.0	5.7
Br %CV Avg	5.2	4.6	5.4	3.6	3.4	3.5	5.2	5.6	5.0	4.3	4.0	4.4	3.5	3.4	3.2	3.9	4.3	4.1
Bi/o %CV	2.8	2.9	3.0	5.4	5.2	5.1	4.0	4.3	3.7	2.7	2.7	2.3	4.5	4.6	4.2	8.5	9.4	10.1
Bl %CV	4.6	3.7	3.5	3.3	3.0	3.1	4.2	3.8	2.9	6.7	6.1	5.4	5.3	5.4	5.4	6.1	5.3	4.9
TOTAL %CV	9.2	8.3	8.8	9.0	8.4	8.4	9.8	9.8	8.8	9.9	9.4	9.1	9.6	9.4	9.1	12.7	13.1	13.2
Analyte	C3									C4								
Grand mean	3.89	6.49	21.3	3.90	6.45	21.3	3.90	6.52	21.6	1.61	2.99	10.8	1.59	2.94	10.8	1.59	2.97	11.0
WR %CV Avg	6.0	5.4	5.5	5.3	5.1	5.1	6.3	6.4	5.7	6.0	5.7	5.6	5.6	5.2	5.2	6.2	5.8	5.9
Br %CV Avg	4.1	4.4	4.7	3.7	3.6	3.2	4.1	4.7	4.5	4.4	3.9	4.4	4.9	4.4	4.0	4.2	4.6	4.1
Bi/o %CV	3.4	2.3	2.7	3.9	4.1	3.5	6.4	6.9	6.6	3.9	2.4	2.7	3.8	3.8	3.6	5.6	6.0	5.6
Bl %CV	5.3	5.0	5.0	5.1	4.3	4.6	5.7	5.2	4.5	5.7	5.1	5.0	4.5	4.7	4.3	5.5	5.1	4.0
TOTAL %CV	9.6	8.8	9.2	9.1	8.6	8.4	11.4	11.8	10.7	10.1	8.9	9.1	9.5	9.1	8.7	10.8	10.8	9.9
Analyte	C5									C5DC								
Grand mean	0.98	1.86	6.82	1.02	1.91	7.07	1.00	1.89	7.02	3.23	6.26	23.4	3.04	5.93	22.7	3.05	5.98	22.9
WR %CV Avg	6.1	5.7	5.8	5.7	5.1	5.2	6.1	5.6	5.5	6.1	5.8	5.7	7.9	6.9	7.3	5.8	6.3	5.7
Br %CV Avg	4.4	4.4	4.9	3.9	3.5	3.2	4.3	4.8	4.5	6.6	6.6	7.1	3.9	3.8	4.4	4.0	4.0	3.8
Bi/o %CV	3.5	3.4	3.4	5.1	5.5	4.6	6.2	6.7	7.7	7.0	5.0	3.8	4.9	4.5	3.9	6.3	7.3	7.7
Bl %CV	6.9	6.2	5.8	5.2	5.2	5.0	6.4	5.6	5.6	5.3	3.8	3.9	3.7	4.8	4.0	5.3	3.9	4.0
TOTAL %CV	10.8	10.2	10.1	10.0	9.8	9.1	11.6	11.4	11.8	12.6	10.8	10.6	10.7	10.2	10.1	10.8	11.1	11.0
Analyte	C6									C8								
Grand mean	1.52	2.96	11.3	1.43	2.83	10.8	1.50	2.97	11.5	1.28	2.51	9.60	1.28	2.50	9.61	1.18	2.34	9.04
WR %CV Avg	5.9	5.7	5.6	6.1	5.5	5.6	6.0	5.9	5.5	6.0	5.7	5.3	5.4	5.0	5.0	5.7	5.4	5.5
Br %CV Avg	4.2	4.0	4.5	8.8	8.4	9.4	4.8	5.5	5.0	4.8	4.3	4.5	3.9	3.8	3.3	5.6	6.7	6.4
Bi/o %CV	4.2	2.1	2.2	10.0	9.4	10.4	4.8	5.2	5.4	3.8	2.4	3.1	4.5	5.3	4.8	8.2	8.8	8.2
Bl %CV	6.8	5.1	5.2	4.5	5.1	4.1	5.6	5.4	4.6	6.3	5.3	5.5	4.8	4.7	5.2	6.1	5.6	5.0
TOTAL %CV	10.8	8.9	9.1	15.4	14.6	15.6	10.6	11.0	10.3	10.6	9.3	9.4	9.4	9.4	9.2	13.0	13.5	12.8
Analyte	C10									C12								
Grand mean	1.29	2.54	9.76	1.26	2.46	9.45	1.27	2.50	9.66	1.44	2.85	11.0	1.44	2.84	10.9	1.43	2.85	11.1
WR %CV Avg	6.1	5.3	5.5	5.5	5.2	5.1	5.7	5.9	5.5	5.6	5.2	5.2	5.5	5.3	5.2	6.0	5.6	5.3
Br %CV Avg	4.5	4.0	4.9	3.9	3.8	3.5	3.9	4.6	4.4	4.3	3.9	4.8	3.9	3.6	3.2	4.4	5.0	4.7
Bi/o %CV	3.1	1.9	2.1	4.9	4.4	4.1	5.2	5.5	5.4	3.1	2.2	2.6	5.1	4.9	4.5	4.9	5.6	5.7
Bl %CV	6.6	5.6	5.6	5.1	4.7	5.0	6.3	5.5	4.7	6.2	5.7	5.2	4.9	4.7	4.7	6.1	5.9	4.8
TOTAL %CV	10.5	8.9	9.5	9.8	9.1	8.9	10.7	10.8	10.0	9.9	8.9	9.2	9.8	9.3	8.9	10.8	11.1	10.3
Analyte	C14									C16								
Grand mean	1.25	2.42	9.14	1.26	2.41	9.16	1.23	2.37	9.06	4.41	7.94	28.1	4.49	7.95	28.1	4.32	7.80	27.7
WR %CV Avg	5.3	5.0	5.2	5.5	5.1	5.3	5.9	6.0	5.5	5.2	5.0	5.0	5.4	5.2	5.1	6.0	5.8	5.5
Br %CV Avg	4.5	4.1	4.9	3.8	3.9	3.3	4.3	4.9	4.9	4.6	4.0	4.8	3.8	3.3	3.3	4.3	5.0	4.7
Bi/o %CV	3.1	2.4	2.8	5.6	5.6	5.2	4.9	5.6	5.6	2.8	1.8	2.4	5.8	5.6	5.1	4.7	5.5	5.0
Bl %CV	6.4	5.7	5.7	4.8	4.8	5.1	5.8	5.8	5.0	6.9	6.1	6.3	5.2	5.3	5.7	6.8	6.4	5.4
TOTAL %CV	10.0	9.0	9.5	9.9	9.7	9.6	10.5	11.2	10.5	10.2	9.0	9.6	10.3	9.8	9.7	11.1	11.3	10.3
Analyte	C18																	
Grand mean	2.82	4.96	17.2	2.82	4.90	17.0	2.77	4.86	16.9									
WR %CV Avg	5.4	5.2	5.2	5.5	5.1	5.3	6.0	5.9	5.2									
Br %CV Avg	4.5	4.0	4.8	3.7	3.3	3.1	4.3	4.9	4.7									
Bi/o %CV	2.7	1.6	2.0	4.7	4.7	4.2	4.3	5.3	4.8									
Bl %CV	7.2	6.3	6.2	5.2	5.2	5.4	6.7	6.5	5.6									
TOTAL %CV	10.4	9.2	9.6	9.7	9.3	9.2	10.9	11.3	10.2									

Imprecision was also evaluated in-house for the analyte levels shown in the recovery study, and results are shown in that section below.

b Linearity/assay reportable range:

Linearity:
Linearity was determined by testing dried blood spots enriched with 12 analyte levels (μM/L), spanning the ranges shown in the table below.

Analyte	Lower	Upper
Ala	452	4841
Arg	27	4140
Cit	28	1716
Gly	309	4350
Leu	266	2992
Met	31	1252
Orn	110	3914
Phe	79	2607
Pro	248	3735
SA	0.6	164.9
Tyr	75	2980
Val	197	2300
C0	51	2930
C2	35	743
C3	3.3	96
C4	0.2	70.8
C5	0.2	62.9
C5DC	0.18	32.6
C6	0.03	67.6
C8	0.05	39.8
C10	0.07	29.8
C12	0.05	50.8
C14	0.1	42.7
C16	2.3	90.5
C18	2.2	34

A total of 5 linearity runs were performed with 4-6 replicates of each level per run. Three low and high blood spot controls were included for each run and used as plate qualifiers for this study. Results in terms of the ranges correlation coefficients observed for the multiple runs and slopes are shown below.

	ALA	ARG	CIT	GLY
R^2 Range	0.9985–0.9995	0.9990-0.9995	0.9990–0.9997	0.9979-0.9994
Slope Range	0.83–0.94	0.81–0.89	0.88–0.90	0.73–0.91
	LEU	**MET**	**ORN**	**PHE**
R^2 Range	0.9990–0.9997	0.9988–0.9995	0.9988-0.9994	0.9992-0.9997
Slope Range	0.92–1.09	0.93-0.97	0.91-0.94	0.91-1.06
	PRO	**SA**	**TYR**	**VAL**
R^2 Range	0.9993-0.9995	0.9972-0.9997	0.9965-0.9996	0.9987-0.9998
Slope Range	0.88-0.94	0.70-0.80	0.84-1.00	0.78-0.92

	C0	C2	C3	C4
R^2 Range	0.9984-0.9996	0.9967-0.9998	0.9980-0.9998	0.9985-0.9995
Slope range	1.00-1.08	0.77-0.95	0.86-0.91	0.85-0.92
	C5	**C5DC**	**C6**	**C8**
R^2 Range	0.9984-0.9999	0.9992-0.9996	0.9984-0.9993	0.9975-10.9995
Slope range	0.84-0.90	0.97-1.08	0.91-0.98	0.78-0.83
	C10	**C12**	**C14**	**C16**
R^2 Range	0.9987-0.9995	0.9989-0.9997	0.9989-0.9996	0.9985-0.9997
Slope range	0.93-1.04	0.91-1.05	0.89-0.96	0.91-0.98
	C18			
R^2 Range	0.9970-0.9997			
Slope range	0.91-0.97			

Recovery:
Analyte recovery for the NeoBase Non-derivatized MSMS kit was evaluated using the Perkin Elmer TQD tandem mass spectrometry system over a total of 21 runs, consisting of samples with 5 different levels analyzed in 6 replicates per run.

$$\% \text{ Recovery} = \frac{\text{Mean Measured concentration} - \text{Mean Endogenous concentration}}{\text{Mean spiked concentration}}$$

The analyte levels tested in this evaluation are listed in the table below (μM/L):

Analyte	ALA	ARG	CIT	GLY	LEU	MET	ORN	PHE	PRO	SA	TYR	VAL
L1	180	89	65	152	69	34	94	69.	99	4	107	69
L2	360	178	130	303	139	68	189	138	199	8	214	137
L3	721	356	261	606	278	136	378	276	397	16	427	274
L4	1442	712	521	1212	555	272	755	553	794	32	854	549
L5	2883	1424	1042	2423	1110	544	1511	1105	1588	64	1709	1097

Analyte	C0	C2	C3	C4	C5	C5D C	C6	C8	C10	C12	C14	C16	C18
L1	79	22	3	2	1	3	2	1	1	1	1	4	3
L2	158	44	6	3	2	6	3	2	3	3	3	8	5
L3	317	89	11	6	5	12	6	5	5	6	5	16	11
L4	633	178	22	12	9	24	13	10	11	12	11	32	22
L5	1266	355	45	23	18	48	26	19	21	23	22	63	43

Mean percent recoveries with standard deviations (over the 21 runs) are shown below. Recoveries were also presented separately for each level. Percent recoveries were similar across the assay range; no significant concentration-dependent trends in recovery were observed.

Analyte	Mean percent recovery	1 SD of mean % recoveries
ALA	100	7
ARG	86	7
CIT	93	6
GLY	90	19
LEU	101	14
MET	97	6
ORN	98	10
PHE	94	8
PRO	97	6
SA	57	6
TYR	84	6
VAL	90	9

Analyte	Mean percent recovery	1 SD of mean % recoveries
C0	104	5
C2	95	7
C3	93	4
C4	93	4
C5	86	5
C5DC	99	4
C6	91	6
C8	100	8

C10	92	3
C12	102	5
C14	92	6
C16	92	5
C18	89	10

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

The calibrator and control materials were previously cleared under the predicate 510(k), k083130. Mean values for controls are obtained by running replicate measurements using the Neobase Non-derivatized MSMS kit. The package insert states that laboratories should ensure compliance with appropriate local and national requirements.

d. Detection limit:

The evaluation consisted of excising discs from a set of blood spots that were placed in microtiter plate wells and extracted with the NeoBase extraction solution. Upon completion of the extraction, the extracts from each disc were pooled by transferring 80uL from each extraction well and into a common vial and mixed thoroughly. These solutions are referred to as "DBS extract diluents". Next, an aliquot of each of the pooled extracts was taken and spiked with amino acid and acylcarnitine internal standards resulting in a high internal standard concentration sample Level 1 which was mixed with the DBS extract diluent in a 1:1 v/v ratio to obtain a Level 2 sample whose internal standard concentration is expected to be one half of that present in the Level 1 sample This procedure was followed serially until a total of 17 dilutions were accomplished from which 18 sample levels with decreasing concentration of internal standards (Level 1 to 18) were obtained.

Three different approaches were employed for data analysis: 1) a stepwise linear regression analysis, 2) a relative concentration response of adjacent dilutions and 3) the precision of the replicate samples. Thresholds were determined for each of the above parameters and the functional sensitivities were established as the lowest concentration that met all three criteria. At these concentrations the sponsor's criteria for CV is less than or equal to 20%. In addition, the ratio of measured responses between two adjacent levels in a 1:1 serial dilution was near 0.5.

Analyte	TQD detection limit	Endogenous Concentration Range*
ALA	1.2	108 to 252
ARG	0.1	6 to 14
CIT	4.7	10 to 24

GLY	25.1	120 to 280
LEU	0.6	72 to 168
MET	0.7	9 to 21
ORN	1.1	30 to 70
PHE	0.3	36 to 84
PRO	0.6	60 to 140
SA	0.2	0.1 to 0.7
TYR	2.5	36 to 84
VAL	0.3	72 to 168

Analyte	**TQD**	**Endogenous Concentration Range***
C0	0.2	18 to 42
C2	0.09	12 to 28
C3	0.06	1.5 to 3.5
C4	0.08	0.12 to 0.28
C5	0.04	0.06 to 0.14
C5DC	0.08	0.12 to 0.28
C6	0.08	0.06 to 0.14
C8	0.04	0.06 to 0.14
C10	0.01	0.06 to 0.14
C12	0.01	0.06 to 0.14
C14	0.01	0.06 to 0.14
C16	0.08	0.6 to 1.4
C18	0.01	0.3 to 0.7

e. Analytical specificity:

Interfering substances tested:

The manufacturer considered potential interferents based on whether a substance could be found in the clinical sample and whether substances would have molecular mass overlap with any analytes or internal standards detected with the NeoBase assay. If the chemical structure of a substance indicated the potential to have the same mass-to-charge ratio (m/z) as an analyte or internal standard of interest, its structure was further examined to predict whether or not this substance would fragment in the tandem mass spectrometry experiment in such a way to produce the same mass transition as any of the analytes or internal standards in the assay. Overall, 16 compounds were identified as potential interfering candidates. These 16 substances and the respective target analyte/internal standard with which they would interfere (listed in the parenthesis) are Aminocaproic acid (Leu), Asparagine (Orn), Creatine (Ala), Creatine (Leu), Dihydroxybenzoic acid (SA), Folic acid (C18:1OH), Formiminoglutamic acid or FIGLU (Arg), Hydroxyproline ??

(Leu), Lidocaine (C4 IS), Malic acid (Leu IS), Methionine sulfone (Tyr), Ornithine (Pro), Salicylic acid (Orn), Sarcosine (Ala), Penicillamine (Met), Propranolol (C6), and Pseudoephedrine (Phe). Compounds that caused significant affects on results included:
Asparagine interference on ornithine; creatine interference on alanine and leucine; hydroxyproline interference on leucine; methionine sulfone interference on tyrosine; sarcosine interference on alanine; chlorhexidine gluconate interference on C5, C10 and other analytes. Results of these studies are described more fully in the assay package insert together with other reported potential interferents.

Carryover:
To evaluate carryover, six sets of borderline (i.e., within 2SD of the cutoff, or medical decision point) samples were measured immediately after high samples. When values remained below the established cutoff it was determined that there is not clinically significant carry over for that analyte. Some carryover was observed with Succinylacetone (SA). The results for the study demonstrate that SA carryover may occur in cases where a Tyrosinemia Type I patient with drastically elevated SA is followed by a borderline patient. This is noted in the package insert. Carryover was not detected for other analytes.

Drift:
This evaluation was set to run continuously for a total elapsed assay time of approximately 24 hours to determine within-day drifting. Dried blood spots were prepared using three enriched concentrations (Low, Mid, and High) of amino acids, succinylacetone, free carnitine and acylcarnitines spiked into whole blood.
Three low and three high blood spot controls were included for each run and used as run qualifiers for this study. The time elapsed during the acquisition of each run was 1.5 hours. The study analyzed a total of 16 runs (time points) collected throughout one 24 hour-period. Analysis of the data indicates that the assay variability over the 24-hour test period is well within the expected precision of the assay as demonstrated by Between Run % CV and no trends were detected in the mean measured concentrations for any of the analytes studied.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Correlation Study:

The clinical correlation study to evaluate addition of the TQD instrument to the previously cleared system was performed by evaluating paired samples from the same specimens TQD and MS2 (predicate) platforms. The sample set consisted of 2499 presumptive negative random neonatal samples, 19 samples with true positive diagnoses. Eighty artificially enriched dried blood spots were also evaluated. Clinical correlation was established by assessing whether or not the methods were concordant in determining the paired samples to have analyte concentration values above or below their pre-determined corresponding cutoffs. (The predetermined cutoffs were determined based on the 99.99th percentile of a negative sample set with removal of outliers based on Dixon's test (CLSI 28-A)). Percents agreement between the two methods is shown in the able below.

Percent agreement between both systems

Analyte	Total # of observations	% Agreement
ALA	2598	99.60%
ARG	2598	99.90%
CIT	2598	99.80%
GLY	2598	99.50%
LEU	2598	99.60%
MET	2598	100.00%
ORN	2598	99.60%
PHE	2598	99.90%
PRO	2598	99.80%
SA	2598	99.50%
TYR	2598	99.20%
VAL	2598	99.70%
C0	2598	100.00%
C2	2598	99.90%
C3	2598	100.00%
C4	2598	99.90%
C5	2598	99.90%
C5DC	2598	99.70%
C6	2598	99.70%
C8	2598	99.80%
C10	2598	99.90%
C12	2598	99.80%
C14	2598	99.90%
C16	2598	99.60%
C18	2598	99.90%
C4OH/C3DC	2518	99.90%
C5OH/C4DC	2518	99.90%
C5:1	2518	99.40%
C6DC	2518	99.80%

C8:1	2518	99.90%
C10:1	2518	100.00%
C10:2	2518	99.70%
C12:1	2518	100.00%
C14-OH	2518	99.70%
C14:1	2518	99.80%
C14:2	2518	99.80%
C16-OH	2518	99.80%
C16:1	2518	99.90%
C16:1-OH	2518	99.80%
C18-OH	2518	99.60%
C18:1	2518	99.90%
C18:1-OH	2518	99.20%
C18:2	2518	100.00%

Contingency tables for the same samples are shown below:

C5:1	MS2:		C6DC	MS2:	
	Above cutoff	Below cutoff		Above cutoff	Below cutoff
TQD:			TQD:		
Above cutoff	2	12	Above cutoff	2	3
Below cutoff	2	2502	Below cutoff	2	2511
C10:2			C14-OH		
TQD:			TQD:		
Above cutoff	0	3	Above cutoff	1	5
Below cutoff	4	2511	Below cutoff	2	2510
C16-OH			C16:1-OH		
TQD:			TQD:		
Above cutoff	1	2	Above cutoff	2	3
Below cutoff	3	2512	Below cutoff	1	2512
C18-OH			C18:1		
TQD:			TQD:		
Above cutoff	1	8	Above cutoff	1	1
Below cutoff	2	2507	Below cutoff	1	2515
C18:1- OH					
TQD:					

Above cutoff	5	12
Below cutoff	7	2494

C8:1	MS2:		C12:1	MS2:	
	Above cutoff	Below cutoff		Above cutoff	Below cutoff
TQD:			TQD:		
Above cutoff	1	1	Above cutoff	2	1
Below cutoff	2	2514	Below cutoff	0	2515
C14:1			C14:2		
TQD:			TQD:		
Above cutoff	3	4	Above cutoff	4	6
Below cutoff	1	2510	Below cutoff	0	2508
C16:1			C18:2		
TQD:			TQD:		
Above cutoff	2	0	Above cutoff	2	1
Below cutoff	2	2514	Below cutoff	0	2515

Ala	MS2:		Arg	MS2:	
	Above cutoff	Below cutoff		Above cutoff	Below cutoff
TQD:			TQD:		
Above cutoff	50	4	Above cutoff	82	1
Below cutoff	6	2538	Below cutoff	2	2513
Cit			Gly		
TQD:			TQD:		
Above cutoff	84	2	Above cutoff	40	6
Below cutoff	2	2510	Below cutoff	6	2546
Leu			Met		
TQD:			TQD:		
Above cutoff	35	1	Above cutoff	65	0
Below cutoff	10	2552	Below cutoff	1	2532
Orn			Phe		
TQD:			TQD:		
Above cutoff	44	7	Above cutoff	83	1
Below cutoff	4	2543	Below cutoff	1	2513
Pro			SA		
TQD:			TQD:		
Above cutoff	48	2	Above cutoff	71	10
Below cutoff	2	2546	Below cutoff	2	2515
Tyr			Val		
TQD:			TQD:		
Above cutoff	60	0	Above cutoff	48	7
Below cutoff	20	2518	Below cutoff	2	2541
C0			C2		
TQD:			TQD:		
Above cutoff	83	0	Above cutoff	64	1
Below cutoff	0	2515	Below cutoff	2	2531
C3			C4		
TQD:			TQD:		
Above cutoff	51	1	Above cutoff	81	1
Below cutoff	0	2546	Below cutoff	1	2515
C5			C5DC		
TQD:			TQD:		
Above cutoff	83	1	Above cutoff	81	1
Below cutoff	2	2512	Below cutoff	6	2510

C6	MS2		C8	MS2	
	above cutoff	below cutoff		above cutoff	below cutoff
TQD:			TQD:		
Above cutoff	85	1	Above cutoff	82	3
Below cutoff	6	2506	Below cutoff	1	2512
C10			C10:1		
TQD:			TQD:		
Above cutoff	81	1	Above cutoff	3	0
Below cutoff	1	2515	Below cutoff	0	2593
C12			C14		
TQD:			TQD:		
Above cutoff	80	5	Above cutoff	82	1
Below cutoff	1	2512	Below cutoff	1	2514
C16			C18		
TQD:			TQD:		
Above cutoff	56	7	Above cutoff	81	1
Below cutoff	3	2532	Below cutoff	1	2515

lts for confirmed true positive samples that were then analyzed on both the MS2 and TQD platforms. The results for all true positive samples are summarized in the Table below:

Disorder	TQD detected?	Predicate detected?	Elevated Analytes Detected by each Platform	
			TQD	Predicate
Tyrosinemia Type 1 (TYR1)	yes	yes	SA, TYR	SA, TYR
Carnitine Palmitoyltransferase II Deficiency (CPT II)	yes	yes	C12, C14, C16, C16:1, C16:1 OH, C16-OH, C18, C18:1, C18:1-OH	C14, C14:OH, C16, C16:1, C16:1 OH, C16-OH, C18, C18:1, C18:1-OH, C18-OH

Methylmalonic Aciduria (MMA)	yes	yes	C3, C6, C5OH/C4DC,	C3
HMG	yes	yes	C6DC	C5OH/C4DC
Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	yes	yes	C14:1	C14:1
Isovaleric acidemia (IVA)	yes	yes	C5	C5
MCC 3-Methylcrotonyl-CoA carboxylase deficiency -	yes	yes	C5OH/C4DC	C5OH/C4DC
BKT (beta-ketothiolase)	yes	yes	C0, C4, C5:1, C6, C8	C0, C4, C5:1
Maple Syrup Urine Disease	yes	yes	LEU	LEU
Medium-Chain Acyl-CoA Dehydrogenase Deficiency	yes	yes	C6, C8, C10:1	C8, C10:1
Propionic Acidemia	yes	yes	C3, C16:1 OH	C3, C16:1 OH
Phenylketonuria	yes	yes	PHE	PHE
CIT (Citrullinemia)	yes	yes	CIT	CIT
Phenylketonuria	yes	yes	PHE	PHE
Medium-Chain Acyl-CoA Dehydrogenase Deficiency	yes	yes	C6, C6DC, C8, C10, C10:1, C12:1	C6, C6DC, C8, C10, C10:1
GA1 (glutaric acidemia)	yes	yes	C5DC	C5DC
Phenylketonuria (PKU)	yes	yes	PHE	PHE
H-ALA (hyperalaninemia)	yes	yes	ALA	ALA
NKH (Nonketotic hyperglycinemia	yes	yes	GLY	GLY

b. Matrix comparison:

Not applicable. The test is only for use with newborn dried blood spots only.

3. Clinical studies:

a. Clinical Sensitivity:

Not reviewed for this device type.

b. Clinical specificity:

Not reviewed for this device type.

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

See drift and carryover studies in 1. e. above.

4. Clinical cut-off:

The package insert states the following:

Each laboratory should run a pilot study to determine the distribution of the concentrations for each analyte for their own population. From these distributions, means and cut-off values should be determined. Cut-off values for reporting abnormal result levels for each analyte should be established by using statistical measurements (e.g. percentiles, means, and standard deviations) in consultation with metabolic disease specialists who can provide additional guidance based on incidence rates, disease severity, and typical profiles of known positive patients. The determination of presumptive abnormal amino acid, succinylacetone, free carnitine and acylcarnitine concentration profiles should be based on predetermined cut-offs obtained from pilot studies performed with the NeoBase Non-derivatized MSMS kit. If available, samples from patients with known disorders (true positives) should be run to provide additional guidance in setting conservative abnormal and borderline cut-off levels. As larger numbers of samples and confirmation of presumptive positive results are obtained by each laboratory, it is recommended that this information be used for reviewing the cut-offs on a regular basis. The actions to be taken when specimens fall under either of three categories – presumptive positive, borderline, and presumptive negative – are described below.

Presumptive positives:

Results that are above (or below if it is a low cut-off) the abnormal cut-offs should be considered presumptive positive. Retesting of the original specimen with the original method is recommended for all specimens designated as presumptive positive for one or more disorders or analytes. Follow local regulations and guidelines for the handling and reporting of presumptive positive results.

Borderline specimens:

Results that fall between the abnormal cut-off and the borderline cut-off should be considered borderline results. Retesting of the original specimen with the origina method is recommended for specimens whose initial results are borderline.

Follow local regulations and guidelines for the handling and reporting of borderline results.

Repeat testing:

Regardless of whether retesting was initiated because of initial borderline or presumptive positive status, if the repeat testing result is above the abnormal cut-off (or below if it is a low cut-off) then the result should be considered presumptive positive. Follow local regulations and guidelines for the handling and reporting of presumptive positive results.

Regardless of whether retesting was initiated because of initial borderline or abnormal status, if the repeat testing result falls between the abnormal and borderline cut-offs, then all available data (initial and retesting) should be taken into consideration to report the values according to local regulations and guidelines.

Regardless of whether retesting was initiated because of initial borderline or abnormal status, follow local regulations and guidelines in cases where retesting results are below (or above if a low cut-off) the borderline cut-offs.

Presumptive negatives:

If all the initial results of any specimen, are below (or above if a low cut-off) all the borderline and abnormal cut-offs, the result can be treated as presumptive negative (or low risk) and reported appropriately.

5. Expected values/Reference range:

Published normal analyte ranges and typical results observed with the NeoBase Non-derivatized MSMS assay for neonatal populations for MS2, QMicro and TQD platforms.

Analyte	Published Normal Range[1]		NeoBase Observed Values[2]					
			TQD (N=2499)		QMicro (N=6864)		MS2 (N=2499)	
	Lower	Upper	Mean	SD	Mean	SD	Mean	SD
ALA	239	345	284	94	337	93	308	76
ARG	53	71	13	9	12	10	15	11
CIT	10	43	16	6	16	5	17	6
GLY	178	513	294	98	389	117	557	154
LEU/ILE	70	145	147	56	129	42	136	41
MET	15	37	17	6	25	9	25	9
ORN	39	61	88	47	121	45	122	41
PHE	45	93	53	12	66	16	61	27
PRO	110	417	171	43	161	42	189	46
SA	0.6	2.5	0.6	0.2	0.8	0.2	0.6	0.2
TYR	33	146	85	33	109	45	98	40

VAL	80	199	108	40	112	31	124	33
C0	9	52	34	11	24	9	26	12
C2	3	42	9	5	21	8	24	10
C3	0.21	4.70	1.13	0.67	1.87	0.78	1.62	0.72

C3DC/C4-OH	0.02	0.9	0.07	0.04	0.12	0.05	0.19	0.08
C4	0.05	1	0.23	0.09	0.26	0.12	0.36	0.12
C4DC/C5-OH	0.05	0.67	0.21	0.06	0.22	0.16	0.28	0.07
C5	0.04	0.61	0.12	0.06	0.12	0.07	0.16	0.08
C5:1	0.03	0.23	0.02	0.01	0.01	0.01	0.03	0.01
C5DC/C6-OH	0	0.21	0.23	0.09	0.16	0.07	0.24	0.09
C6	0.11	0.35	0.04	0.02	0.05	0.02	0.07	0.03
C6DC	0	0.13	0.12	0.04	0.12	0.04	0.33	0.13
C8	0.01	0.36	0.06	0.02	0.06	0.03	0.07	0.03
C8:1	0.01	0.33	0.13	0.06	0.16	0.05	0.13	0.05
C10	0.02	0.24	0.08	0.03	0.09	0.04	0.08	0.04
C10:1	0.03	1.1	0.05	0.02	0.07	0.02	0.06	0.03
C10:2	0.01	0.05	0.02	0.01	0.01	0.01	0.02	0.01
C12	0	0.36	0.10	0.05	0.11	0.05	0.12	0.06
C12:1	0.02	0.4	0.06	0.04	0.11	0.05	0.09	0.09
C14	0.08	0.52	0.17	0.08	0.21	0.07	0.23	0.09
C14:1	0.01	0.25	0.09	0.05	0.12	0.05	0.14	0.26
C14:2	0	0.11	0.03	0.01	0.02	0.01	0.03	0.03
C14OH	0.03	0.23	0.02	0.01	0.02	0.01	0.02	0.02
C16	0.25	9.7	2.09	1.20	2.96	1.00	3.07	1.26
C16:1	0.07	0.51	0.17	0.11	0.22	0.09	0.20	0.10
C16:1OH	0	0.32	0.04	0.02	0.05	0.01	0.04	0.02
C16OH	0.02	0.26	0.03	0.01	0.03	0.01	0.03	0.01
C18	0.3	2.3	0.67	0.31	0.86	0.28	0.86	0.31
C18:1	0.7	3.1	1.35	0.55	1.44	0.44	1.41	0.48
C18:1OH	0	0.16	0.03	0.01	0.03	0.01	0.02	0.01
C18:2	0.06	1.52	0.27	0.13	0.23	0.12	0.26	0.23
C18OH	0	0.09	0.02	0.01	0.01	0.01	0.01	0.01

N. Instrument Name:

PerkinElmer TQD MSMS Screening System

O. System Descriptions:

1. Modes of Operation:

   The TQ Detector used in the Perkin Elmer TQD MSMS Screening System is a tandem quadrupole atmospheric pressure ionization (API) mass spectrometer.

2. Software:

   Software (including firmware) documentation for all instrument components was included in the 510(k).

3. Specimen Identification:

   Barcodes are supplied for each plate as a whole, and each plate is scanned by the system's barcode reader. Scanning the plate creates a virtual 96 well map that can be assigned samples. Operators may input the patient sample identification (used by the laboratory) for each well in the plate either manually (by typing the information in the plate map) or by using the barcode reader. The results are generated according to the plate map and are thereby linked back to the sample.

4. Specimen Sampling and Handling:

   The Intellistart fluidics system built into the TQ detector delivers the sample. The extracted sample is delivered to the ion source of the mass spectrometer by the liquid chromatography (LC) system consisting of the autosampler, micro pump(s) and solvent vacuum degasser.

5. Calibration:

   Tuning and calibration is performed from the software. Calibration files are saved on the instrument setup parameters

6. Quality Control:

   Control materials are provided by the manufacturer, and instructions for running controls are provided in the labeling.

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

All recommended software elements were included in the submission.
Comparison of Quattro Micro instrument (k083130) and the TQD instrument features are in the table below. The PerkinElmer systems for both instruments use the same pump and sample manager. Information regarding these components was included in the 510(k):

Feature	Quattro Micro (predicate)	TQD
Sample Delivery		
Autosampler-MS System interface	Direct infusion from autosampler's Rheodyne valve to ion source inlet via standard PEEK tubing	Same
Ion Formation Methodology		
Ionization Mode	Electrospray Ionization	Same
Ion Source	Atmospheric Pressure Ionization (API) source featuring Z SPRAY dual orthogonal ion source	Same
Ion Source Desolvation Gas	Nitrogen	Same
Ion Source Transfer Optics	High efficiency hexapole ion guide	Same
Mass Analyzer		
Tandem analyzer	Two high resolution quadrupole analyzers (MS1 and MS2) plus pre-filters to enhance ion transmission	Same
Acquisition Modes	Full Scan MS (MS1 or MS2), Product Ion Scan, Precursor Ion Scan, Neutral loss Scan, Multiple Reaction Monitoring (MRM)	Same
Mass Range	2 to 2000 m/z	Same
Scan Speed	Up to 5000 Da/second	Up to 10,000 Da/second
Mass Stability	0.2 Da in 24Hrs	<0.1 Da in 8 Hrs
Tandem Mass Spectrometry (MS/MS)		
Collision Cell	High efficiency hexapole collision cell with beam focusing at cell entry and exit	Travelling Wave (T-Wave) collision cell technology for fast ion containment and transfer (allows fast MS/MS)
Collision Gas	Argon	Same

MS/MS scans	Product Ion Scan, Precursor Ion Scan, Neutral loss Scan, Multiple Reaction Monitoring (MRM)	Same
Detection System		
Detector	Off axis photomultiplier positioned after second quadrupole mass analyzer (MS2)	Same
Polarities Supported	Positive and Negative Ion Modes	Same
Vacuum System		
Rough Vacuum Pump	One Rotary pump backing the turbo-molecular pump	Same
Fine Vacuum Pump	Air-Cooled Turbo-molecular pump	Same
Software		
User interface and instrument Control	MassLynx 4.1	Same

The only difference between the instruments used in the predicate device (Quattro Micro) and the TQD instruments is the architecture of the collision cell. In the Quattro Micro the collision cell is a high efficiency hexapole, while in the TQD the collision cell employs proprietary Travelling Wave Technology where instead of using a hexapole as ion guide, a series of plates are stacked with concentric openings. Voltage is applied to the plates on and off consecutively to execute the same function of a hexapole but at faster speeds. This feature allows for the described enhanced scan speed and sensitivity to the TQD platform. Despite this difference, the two platforms are identical as far as the end user is concerned when employing the NeoBase application on either platform.

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.