September 4, 2018

Wallac Oy, Subsidiary of PerkinElmer, Inc.
Anne Marie Whalen
Director, Regulatory Affairs
940 Winter Street
Waltham, MA 02451

Re: K173568
Trade/Device Name: NeoBase 2 Non-derivatized MSMS Kit
Regulation Number: 21 CFR 862.1055
Regulation Name: Newborn screening test system for amino acids, free carnitine, and acylcarnitines using tandem mass spectrometry
Regulatory Class: Class II
Product Code: NQL
Dated: August 24, 2018
Received: August 27, 2018

Dear Anne Marie Whalen:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm -S

for Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K173568

Device Name
NeoBase™ 2 Non-derivatized MSMS kit

Indications for Use *(Describe)*
The NeoBase™ 2 Non-derivatized MSMS kit is intended for the measurement and evaluation of amino acid, succinylacetone, free carnitine, acylcarnitine, nucleoside and lysophospholipid concentrations (Table 1) with a tandem mass spectrometer from newborn heel prick blood specimens 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.

Table 1. Analytes measured by the NeoBase 2 Non-derivatized MSMS kit.

ANALYTE NAME	ABBREVIATION
Amino acids	
Alanine	Ala
Arginine	Arg
Argininosuccinic acid	Asa
Citrulline	Cit
Glutamine\Lysine (*)	Gln\Lys
Glutamic acid	Glu
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\ Heptadecanoylcarnitine (*)	C16:1OH\C17
Octadecanoylcarnitine (Stearoylcarnitine)	C18
Octadecenoylcarnitine (Oleylcarnitine)	C18:1
Octadecadienoylcarnitine (Linoleylcarnitine)	C18:2
3-Hydroxy-octadecanoylcarnitine	C18OH
3-Hydroxy-octadecenoylcarnitine	C18:1OH
3-Hydroxy-octadecadienoylcarnitine	C18:2OH
Ketones	
Succinylacetone	SA
Nucleotides	
Adenosine	ADO
2'-deoxyadenosine	D-ADO
Lysophospholipids	
C24:0 lysophosphatidylcholine	C24:0-LPC
C26:0 lysophosphatidylcholine	C26:0-LPC

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

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This 510(k) Summary information is supplied in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510 (k) number is K173568

Date: August 24, 2018

Submitted by: Wallac Oy, a subsidiary of PerkinElmer Inc.
940 Winter Street
Waltham, MA 02451

Wallac Oy
Mustionkatu 6
Turku Finland 20750

Submission Contact Person:
Primary: Anne Marie Whalen, PhD
Director, Regulatory Affairs
Tel:781-663-5651
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Trade Name: NeoBase 2 Non-derivatized MSMS kit

Common Name: Newborn screening test system for amino acids, succinylacetone, free carnitine, acylcarnitines, nucleosides, and lysophospholipids using tandem mass spectrometry

Regulation: 21 CFR 862.1055

Classification: II

Panel: Clinical Chemistry (75)

Product Code: NQL

Predicate device: PerkinElmer NeoBase Non-derivatized MSMS reagent kit (K093916)

Intended Use:

The NeoBase™ 2 Non-derivatized MSMS kit is intended for the measurement and evaluation of amino acid, succinylacetone, free carnitine, acylcarnitine, nucleoside and lysophospholipid concentrations (Table 1) with a tandem mass spectrometer from newborn heel prick blood specimens 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.

Table 1. Analytes measured by the NeoBase 2 Non-derivatized MSMS kit:

ANALYTE NAME	ABBREVIATION
Amino acids	
Alanine	Ala
Arginine	Arg
Argininosuccinic acid	Asa
Citrulline	Cit
Glutamine\Lysine[1]	Gln\Lys
Glutamic acid	Glu
Glycine	Gly
Leucine\Isoleucine\Hydroxyproline[1]	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[1]	C3DC\C4OH
Butyrylcarnitine	C4
Methylmalonyl\3-Hydroxy-isovalerylcarnitine[1]	C4DC\C5OH
Isovalerylcarnitine	C5
Tiglylcarnitine	C5:1
Glutarylcarnitine\3-Hydroxy-hexanoylcarnitine[1]	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\ Heptadecanoylcarnitine[1]	C16:1OH\C17
Octadecanoylcarnitine (Stearoylcarnitine)	C18
Octadecenoylcarnitine (Oleylcarnitine)	C18:1
Octadecadienoylcarnitine (Linoleylcarnitine)	C18:2
3-Hydroxy-octadecanoylcarnitine	C18OH
3-Hydroxy-octadecenoylcarnitine	C18:1OH
3-Hydroxy-octadecadienoylcarnitine	C18:2OH
Ketones	
Succinylacetone	SA
Nucleosides	
Adenosine	ADO
2'-deoxyadenosine	D-ADO
Lysophospholipids	
C24:0 lysophosphatidylcholine	C24:0-LPC
C26:0 lysophosphatidylcholine	C26:0-LPC

[1] Analytes in these rows are either isomers or isobars and cannot be distinguished in the tandem mass spectrometry experiment.

Summary of Non-Clinical Studies:

A summary of the verification studies is presented below:

Study	CLSI Guidance	Number of kit lots
Precision	EP5-A3	Precision study 1: 1 Instrument, 1 kit lot Precision study 2: 1 Instrument, 3 kit lots Precision study 3: 2 Instruments, 1 kit lot
Analytical Sensitivity	N/A	2 Instruments, 3 kit lots
Linearity	EP06-A	1 Instrument, 3 kit lots
Interference	EP7-A2	Mass transition overlap study: 1 Instrument Paired-difference study: 2 Instruments, 3 kit lot Dose-response study: 2 Instruments, 3 kit lot
Drift	N/A	1 Instrument, 1 kit lot
Recovery	N/A	1 Instrument, 3 kit lots
Method Comparison	EP9-A3	2 Instruments, 3 kit lots
Carry-over	N/A	2 Instruments, 1 kit lot
Incubation times and temperatures	N/A	1 Instrument, 1 kit lot
Real Time/Transport Stability	EP25-A	2 Instruments, 3 kit lots
Accelerated Stability	EP25-A	2 Instruments, 2 kit lots

Study	CLSI Guidance	Number of kit lots
In-use, On-board Stability	EP25-A	1 Instrument, 1 kit lot
Sample Stability	EP25-A	1 Instrument, 1 kit lot

All verification studies were successfully concluded and met the respective study's predetermined acceptance criteria.

Summary of Clinical Studies:

The 3044-0010U NeoBase 2 Non-derivatized MSMS kit was compared to 3040-001U NeoBase Non-derivatized MSMS kit by measuring analyte concentrations with a tandem quadrupole detector (TQD) in two CLIA-certified state laboratories responsible for routine newborn screening. Using data from routine newborn screening, the cut-offs for both methods were determined by calculating the 99.5th and 99th percentile for all analytes except C2. For C2, C3, C16, C18, C18:1 and Cit the low cut-off applied is based on 1st percentile. For C0, the low cut-off applied is based on 10th percentile. Please note that the cut-off values used in evaluating screening performance only apply to these studies.

The disorders and amount of confirmed positive specimens included in the studies 1 and 2 are listed in Tables A and B (study 1), and Tables C and D (study 2). In total, there were 37 specimens included in the group of amino acid disorders, 26 in the group of fatty acid oxidation disorders and 28 in the group of organic acid conditions. In addition, the group of other disorder contains adenosine deaminase severe combined immunodeficiency (ADA-SCID) and X-linked adrenoleukodystrophy (X-ALD) of which 8 specimens, 4 of each disorder, were included.

The results for the screening performance data including confirmed positive specimens tested with TQD in the study 1 are presented in Table A.

The screening performance for adenosine deaminase severe combined immunodeficiency (ADA-SCID) and X-linked adrenoleukodystrophy (X-ALD) was done by comparing the result of NeoBase 2 Non-derivatized MSMS kit to the clinical condition. Results of the study 1 are presented in Table B.

Table A. Agreement between NeoBase 2 Non-derivatized MSMS kit and NeoBase Non-derivatized MSMS kit in the study 1.

Amino acid disorders (AA)		NeoBase					
		99th percentile			99.5th percentile		
		Screening positive	Screening negative	Total	Screening positive	Screening negative	Total
NeoBase 2	Screening positive	62 [1]	70	132	45 [2]	41	86
	Screening negative	28	1591	1619	20	1645	1665
	Total	90	1661	1751	65	1686	1751

[1] Includes all 15 specimens confirmed positive for AA detected with both methods using 99th percentile cut-offs.
[2] Includes all 15 specimens confirmed positive for AA detected with both methods using 99.5th percentile cut-offs.

Amino acid disorders (AA)		NeoBase		
		1st percentile		
		Screening positive	Screening negative	Total
NeoBase 2	Screening positive	16 [1]	18	34
	Screening negative	16	1687	1703
	Total	32	1705	1737

[1] Includes 1 specimen confirmed positive for OTCD with both methods using 1st percentile cut-offs.

Fatty acid oxidation (FAO)		NeoBase					
		99th percentile			99.5th percentile		
		Screening positive	Screening negative	Total	Screening positive	Screening negative	Total
NeoBase 2	Screening positive	80 [1]	40	120	45 [1]	17	62
	Screening negative	45	1581	1626	23	1661	1684
	Total	125	1621	1746	68	1678	1746

[1] Includes all 10 specimens confirmed positive for FAO detected with both methods using 99th and 99.5th percentile cut-offs.

Fatty acid oxidation (FAO)		NeoBase		
		Low percentile		
		Screening positive	Screening negative	Total
NeoBase 2	Screening positive	173 [2]	29	202
	Screening negative	150	1386	1536
	Total	322	1415	1738

[1] "Low Percentile" reflects the positive C0 specimens detected with a 10% cut-off with other carnitine-positive samples at the 1% cut-off
[2] Includes 2 specimens confirmed positive for CUD detected with both methods using low percentile cut-offs.

Organic acid condition (OA)		NeoBase					
		99th percentile			99.5th percentile		
		Screening positive	Screening negative	Total	Screening positive	Screening negative	Total
NeoBase 2	Screening positive	57 [1]	23	80	36 [1]	13	49
	Screening negative	11	1660	1671	5	1697	1702
	Total	68	1683	1751	41	1710	1751

[1] Includes all 15 specimens confirmed positive for OA detected with both methods using 99th and 99.5th percentile cut-offs.

Table B. Screening performance for ADA-SCID and X-ALD using 99th and 99.5th percentile in study 1.

ADA-SCID		99th percentile			99.5th percentile		
		Positive	Normal	Total	Positive	Normal	Total
NeoBase 2	Screening positive	2 [1]	75	77	2 [1]	36	38
	Screening negative	0	1661	1661	0	1700	1700
	Total	2	1736	1738	2	1736	1738

[1] Includes both specimens confirmed positive for ADA-SCID.

X-ALD		99th percentile			99.5th percentile		
		Positive	Normal	Total	Positive	Normal	Total
NeoBase 2	Screening positive	2 [1]	12	14	2 [1]	5	7
	Screening negative	0	1724	1724	0	1731	1731
	Total	2	1736	1738	2	1736	1738

[1] Includes both specimens confirmed positive for X-ALD.

The results for the screening performance data including retrospective confirmed positive specimens tested with TQD in the study 2 are presented in Table C.

The screening performance for Adenosine deaminase severe combined immunodeficiency (ADA-SCID) and X-linked adrenoleukodystrophy (X-ALD) was done by comparing the result of NeoBase_2 Non-derivatized MSMS kit to the clinical condition. Results of the study 2 are presented in Table D.

Table C. Agreement between NeoBase_2 Non-derivatized MSMS kit and NeoBase Non-derivatized MSMS kit in the study 2.

Amino acid disorders (AA)		**NeoBase**					
		99th percentile			**99.5th percentile**		
		Screening positive	Screening negative	Total	Screening positive	Screening negative	Total
NeoBase 2	Screening positive	116 [1]	138	254	78 [2]	67	145
	Screening negative	41	2353	2394	29	2474 [3]	2503
	Total	157	2491	2648	107	2541	2648

[1] Includes all 19 specimens confirmed positive for AA detected with both methods using 99th percentile cut-offs.
[2] Includes 18 specimens confirmed positive for AA detected with both methods using 99.5th percentile cut-offs.
[3] Includes 1 specimen confirmed positive for AA not detected with either method using 99.5th percentile cut-offs.

Amino acid disorders (AA)		NeoBase		
		1st percentile		
		Screening positive	Screening negative	Total
NeoBase 2	Screening positive	14 [1]	40	54
	Screening negative	6	2571	2577
	Total	20	2611	2631

[1] Includes 2 specimens confirmed positive for OTCD detected with both methods using 1st percentile cut-offs.

Fatty acid oxidation (FAO)		NeoBase					
		99th percentile			99.5th percentile		
		Screening positive	Screening negative	Total	Screening positive	Screening negative	Total
NeoBase 2	Screening positive	160 [1]	83	243	108 [1]	37	145
	Screening negative	72	2326	2398	54	2442	2496
	Total	232	2409	2641	162	2479	2641

[1] Includes all 12 specimens confirmed positive for FAO detected with both methods using 99th and 99.5th percentile cut-offs.

Fatty acid oxidation (FAO)		NeoBase		
		Low percentile		
		Screening positive	Screening negative	Total
NeoBase 2	Screening positive	158[1]	45	203
	Screening negative	66	2363	2429
	Total	224	2408	2632

[1] "Low Percentile" reflects positive C0 specimens detected with a 10% cut-off with other carnitine-positive samples at the 1% cut-off
[2] Includes 3 specimens confirmed positive for FAO detected with both methods using low percentile cut-offs. CPT II was confirmed positive with both methods with each of the 99th, 99.5th and 1st percentile cut-offs.

Organic acid condition (OA)		NeoBase					
		99th percentile			99.5th percentile		
		Screening positive	Screening negative	Total	Screening positive	Screening negative	Total
NeoBase 2	Screening positive	86 [1]	52	138	42 [2]	27	69
	Screening negative	25	2479	2504	12	2561 [3]	2573
	Total	111	2531	2642	54	2588	2642

[1] Includes all 13 specimens confirmed positive for OA detected with both methods using 99th and 99.5th percentile cut-offs.
[2] Includes 12 specimens confirmed positive for OA detected with both methods using 99.5th percentile cut-offs.
[3] Includes 1 specimen confirmed positive for OA not detected with either method using 99.5th percentile cut-offs.

Table D. Screening performance for ADA-SCID and X-ALD using 99th and 99.5th percentile in the study 2.

ADA-SCID		99th percentile			99.5th percentile		
		Positive	Normal	Total	Positive	Normal	Total
NeoBase 2	Screening positive	2 [1]	66	68	2 [1]	51	53
	Screening negative	0	2563	2563	0	2578	2578
	Total	2	2629	2631	2	2629	2631

[1] Includes both specimens confirmed positive for ADA-SCID.

X-ALD		99th percentile			99.5th percentile		
		Positive	Normal	Total	Positive	Normal	Total
NeoBase 2	Screening positive	2 [1]	3	5	2 [1]	1	3
	Screening negative	0	2626	2626	0	2628	2628
	Total	2	2629	2631	2	2629	2631

[1] Includes both specimens confirmed positive for X-ALD.

Substantial Equivalency:

The proposed device and predicate device utilize similar design shown to produce equivalent screening performance in a clinical setting. Both devices are intended for the measurement and evaluation of multiple metabolite 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.

Conclusion:

The NeoBase 2 Non-derivatized MSMS kit demonstrates analytical and screening performance that supports its substantial equivalency with the predicate device, NeoBase 2 Non-derivatized MSMS kit (K093916).