July 13, 2018

Phadia AB
% Martin Mann
Senior Regulatory Affairs Manager
Phadia US Inc.
4169 Commercial Avenue
Portage, Michigan 49002

Re: K181556
Trade/Device Name: EliA M2 Immunoassay
Regulation Number: 21 CFR 866.5090
Regulation Name: Antimitochondrial antibody immunological test system
Regulatory Class: Class II
Product Code: DBM
Dated: June 12, 2018
Received: June 13, 2018

Dear Martin Mann:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); 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,

Douglas A. Jeffery -S

For
Lea Carrington
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*

Device Name
EliA(TM) M2 Immunoassay

Indications for Use *(Describe)*
EliA M2 is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to M2 in human serum and plasma (Li-heparin, EDTA) to aid in the clinical diagnosis of primary biliary cirrhosis in conjunction with other laboratory and clinical findings. EliA M2 uses the EliA IgG method on the instrument Phadia 2500/5000.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

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A.6 510(k) Summary of Safety and Effectiveness per 21CFR 807.92(c).

This summary of safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR Part 807.92.

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

A. 510(k) Number:

B. Purpose for Submission:
Adding a previously cleared assay on a new instrument platform (Phadia® 2500/5000)

C. Measurand:
IgG antibodies specific for M2 protein

D. Type of Test:
Semi-quantitative measurement immunoassays

E. Applicant:
Phadia AB
Rapsgatan 7P
P.O. Box 6460
SE-751 37 Uppsala, Sweden
Tel: +46-18-16 50 60

510(k) Contact Person:
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Date of Summary Preparation: June 12, 2018

F. Proprietary and Established Names:
EliA™ M2 Immunoassay

G. Regulatory Information:

1. Regulation section:
   21 CFR §866.5090, Antimitochondrial antibody immunological test system

2. Classification:
   Class II

3. Product code:
   DBM, Antimitochondrial Antibody, Indirect Immunofluorescent, Antigen, Control

4. Panel: Immunology (82)

H. Intended use(s):

1. Intended use(s):

EliA M2 is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to M2 in human serum and plasma (Li-heparin, EDTA) to aid in the clinical diagnosis of primary biliary cirrhosis in conjunction with other laboratory and clinical findings. EliA M2 uses the EliA IgG method on the instrument Phadia 2500/5000.

2. Indication(s) for use:
Same as intended use

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

4. Special instrument requirements:
Performance studies were obtained from the Phadia® 2500/5000 instrument.
This device is not for point-of-care use.

I. Device Description:

The method-specific reagents are identical with K141375 (EliA M2 on Phadia 250), but are filled in containers specific for the Phadia 2500/5000 instrument. Each device consists of:

- Test Wells:
  EliA M2 Wells are coated with native pyruvate dehydrogenase complex from mitochondria and recombinant M2-antigen – 4 carriers (12 wells each), ready to use;
- EliA Sample Diluent: PBS containing BSA, detergent and 0.095% (w/v) sodium azide – 6 bottles, 48 mL each, ready to use; or 6 bottles, 400 mL each, ready to use;
- EliA IgG Conjugate 50 or 200: β-Galactosidase labeled anti-IgG (mouse monoclonal antibodies) in PBS containing BSA and 0.06% (w/v) sodium azide – 6 wedge shaped bottles, 5 mL each, ready to use; or 6 wedge shaped bottles, 19 mL each, ready to use
- EliA IgG Calibrator Strips: Human IgG (0, 4, 10, 20, 100, 600 µg/L) in PBS containing BSA, detergent and 0.095% (w/v) sodium azide – 5 strips, 6 single-use vials per strip, 0.3 mL each, ready to use;
- EliA IgG Curve Control Strips: Human IgG (20 µg/L) in PBS containing BSA, detergent and 0.095% (w/v) sodium azide – 5 strips, 6 single-use vials per strip, 0.3 mL each, ready to use;
- EliA IgG Calibrator Well: Coated with mouse monoclonal antibodies – 4 carriers (12 wells each), ready to use.

The Phadia EliA Immunodiagnostic System is an automated system for immunodiagnostic testing. The EliA reagents are available as modular packages, each purchased separately. All packages are required to carry out EliA M2 tests.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) number(s):

EliA M2 on Phadia 250 instrument, K141375

2. Comparison with predicate device:

EliA M2 Immunoassays on Phadia 250 and Phadia 2500/5000 instruments – Similarities to predicate devices

Feature	Predicate Device Phadia 250	New Device Phadia 2500/5000
Intended Use EliA M2	EliA M2 is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to M2 in human serum and plasma (heparin, EDTA) to aid in the clinical diagnosis of primary biliary cirrhosis in conjunction with other laboratory and clinical findings. EliA M2 uses the EliA IgG method on the instrument Phadia 250.	EliA M2 is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to M2 in human serum and plasma (Li-heparin, EDTA) to aid in the clinical diagnosis of primary biliary cirrhosis in conjunction with other laboratory and clinical findings. EliA M2 uses the EliA IgG method on the instrument Phadia 2500/5000.
Sample matrix; Serum or plasma type as indicated in the DFU dependent on assay	human serum and plasma (heparin, EDTA)	human serum and plasma (Li-heparin, EDTA)
Analytical technology: Immuno-fluorescence measurement	Same	Same
Assay process	Same	Same
Common, dedicated Phadia reagents	Same	Same Introduction of new article numbers for Development Solution, Stop Solution and Washing Solution is only due to larger filling volumes which are required for the bigger instruments Phadia 2500/5000
Result calculation software; Phadia Information Data Manager (IDM)	Same	Same
Sample volume	90 µL (20 µL of non-diluted sample)	90 µL (20 µL of non-diluted sample)
Incubation temperature	37°C	37°C
Conjugate volume	90 µL	90 µL
Development	90 µL	90 µL

Solution Volume		
Stop Solution Volume	200 µL	200 µL
Assay set-up	Random access	Random access
Reagent packaging size	Various/Common	Various/Common Introduction of new article number for EliA Sample Diluent (83-1071-01) is only due to larger filling volume.
Onboard storage of reagents	Yes	Yes
Time to 1st result	~2 h	~2 h

EliA M2 Immunoassays on Phadia 250 and Phadia 2500/5000 instruments – Differences to predicate device

Feature	Predicate Device Phadia 250	New Device Phadia 2500/5000
Daily throughput	~250 tests	~2500/5000 tests
Sample Dilution	Phadia 250 uses a steel pipette to dilute the samples in Dilution Plates (Art.No. 12-3907-08)	Phadia 2500/5000 uses disposable Pipette Tips in Racks (Art No. 12-3805-04) for pipetting samples in Dilution Well (Art.No. 12-4005-69)
Risk for carry-over	The warning “DO NOT REUSE” in the Phadia 250 DFU for EliA Conjugates is due to the fact that a low risk of conjugate contamination by carry-over from samples was identified. In order to reduce the risk, the single use statement for the conjugate was included in the Phadia 250 DFU.	When running EliA tests on the Phadia 2500/5000 instruments, there is no need for this warning statement because these instruments use disposable tips for pipetting samples and a separate pipette for the conjugate, and carry-over from samples to conjugate is impossible.
Loading of EliA Carriers	EliA carriers are loaded manually on the Loading Tray from where they can be processed directly or transferred to the cooled storage compartment.	The Phadia 2500/5000 instruments do not have such a Loading Tray. The EliA carriers are loaded into racks which are directly transferred to the cooled storage compartment
Barcode reader	The Phadia 250 instrument has a built-in barcode reader at the front of the instrument, but the operator needs to scan the barcodes manually by showing the reagents to the barcode reader. Alternatively, the operator can also enter the characters below the barcode manually.	The Phadia 2500/5000 instruments dispose of a built-in barcode reader, and the reagents are on a moving belt which conveys them past the barcode reader. The lot-specific information will be read automatically by the instrument during loading.
Process time / Time to patient result	Phadia 250 needs 1 minute to process one Well. Phadia 250 provides the results at a one minute interval.	Phadia 2500/5000 instruments process two Wells in parallel in 48 seconds. Phadia 2500/5000 provides the results at a 24 seconds interval.

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

CLSI EP05-A3; Evaluation of Precision Performance of Quantitative Measurement Methods; September 2014
CLSI EP06-A Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; April 2003
CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantification; October 2004.
CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

The EliA wells are molded cups comparable to excised wells from a microtiter plate. They are made of polystyrene and are coated with the respective antigen. The wells are at the same time a holder of the coupled antigen for convenient automation and a reaction chamber with reaction/washing solution handling based on pipetting to add and aspiration to remove liquids.

The EliA wells are coated with native pyruvate dehydrogenase complex from mitochondria and recombinant M2-antigen. If present in the patient's specimen, antibodies to M2 bind to the specific antigen. After washing away non-bound antibodies, enzyme-labeled antibodies against human IgG antibodies (EliA IgG Conjugate) are added to form an antibody-conjugate complex. After incubation, non-bound conjugate is washed away and the bound complex is incubated with a Development Solution. After stopping the reaction, the fluorescence in the reaction mixture is measured. The higher the response value, the more specific IgG is present in the specimen. To evaluate test results, the response for patient samples is compared directly to the response for calibrators.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

To determine the precision of the assay, the variability was assessed in a study with a total of 21 runs (3 instruments × 7 runs).
The study was performed with 1 run/day over a period of 7 days. Each sample was tested in four replicates/run giving in total 84 replicates per sample. The data was calculated against the calibration curve from Day 1.

We included only one lot of EliA M2 Well on the Phadia 2500/5000 instrument, as data for inter-lot-variation has already been shown in K141375.
The results are summarized in the table below:

EliA M2 on Phadia 2500/5000

Mean (U/mL)	Within-Run		Between-Run		Between-Instrument		Total Imprecision	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1.7	0.1	7.3	0.1	4.8	0.2	13.1	0.3	15.8
4.0	0.2	4.3	0.1	2.9	0.3	6.6	0.3	8.4
5.9	0.2	3.7	0.1	2.5	0.3	4.2	0.4	6.2
74.8	2.3	3.1	1.7	2.2	4.0	5.3	4.9	6.5
175.9	8.0	4.5	6.8	3.9	12.1	6.9	16.0	9.1

b. Linearity/assay reportable range:

Four patient serum samples were diluted in EliA Sample Diluent and tested with one batch of EliA M2 Immunoassay and one set of system reagents on Phadia 2500/5000. The ratios of observed/expected values were calculated. The results are summarized below:

EliA M2 on Phadia 2500/5000

Dilution range (U/mL)	Slope	Intercept	R^2
0.7 - 48.3	0.99	-0.32	1.00
2.1 - 211.3	1.02	1.90	1.00
5.7 - 253.2	1.03	2.36	1.00
0.5 - 16.6	1.02	0.13	1.00

The linear range and the measuring range are set to 0.8 U/mL (LoQ) to 220 U/mL (upper limit of measuring range).
The reportable range (Limit of Detection, upper limit of measuring range) for EliA M2 is from 0.5 to 220 U/mL. Concentration values between LoD and LoQ may show a higher uncertainty.

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

The EliA IgG method was previously reviewed in K061165.

d. Detection limit:

The limit of blank (LoB) and limit of detection (LoD) studies were performed on the Phadia 2500/5000 instrument. One blank sample and five low level samples were measured in twelve replicates in each of six runs spread over six different days.

The LoD for EliA M2 is 0.5 U/mL, determined consistent with the guidelines in CLSI document EP17-A and with proportions of false positives (α) less than 5% and false negatives (β) less than 5%; based on 432 determinations with 72 blank and 360 low level replicates; and LoB of 0.3 U/mL.

The LoQ for EliA M2 is 0.8 U/mL, determined consistent with the guidelines in CLSI document EP17-A, based on 360 determinations; and a target uncertainty goal of 20%.

The results are summarized in the table below:

EliA M2 (U/mL)	LoB	LoD	LoQ
Phadia 2500/5000	0.3	0.5	0.8

e. Analytical specificity:

Interference: Previously reviewed in K141375

Carry-over: Phadia 2500/5000 instruments use disposable tips for pipetting samples and a separate pipette for the conjugate, therefore carry-over from samples to conjugate is impossible.

f. Assay cut-off:

The ranges (negative, equivocal, positive) recommended for the evaluation of the test results were derived from the clinical studies (s. K141375).

EliA M2 Well

< 4 U/mL	Negative
4 – 6 U/mL	Equivocal
> 6 U/mL	Positive

2. Comparison studies:

a. Method comparison with predicate device (Instrument comparison):
See 2c Instrument Comparison below

b. Matrix comparison:

Previously reviewed under K141375.

c. Instrument comparison

In the Method Comparison studies for EliA M2, more than 100 samples (≥10% of the samples within ±25% of the medical decision point) were run in single replicates on one Phadia 250 and one Phadia 2500/5000 instrument. The acceptance criteria for the method comparison (the slope for the regression lines should be 0.9 – 1.1 for single replicate to single replicate and intercept close to 0) were met for EliA M2.

EliA M2:

Instrument	Intercept	95% CI	Slope	95% CI
PH2500/5000	-0.14	-0.46 to 0.03	1.04	1.02 to 1.06

equivocal results considered positive

criteria	PH2500/5000
PPA	100.0%
95% CI	96.0% – 100%
NPA	93.3%
95% CI	68.1% – 99.8%
TPA	99.1%
95% CI	94.9% – 100%

equivocal results considered negative

criteria	PH2500/5000
PPA	100.0%
95% CI	95.7% – 100%
NPA	95.5%
95% CI	77.2% – 99.9%
TPA	99.1%
95% CI	94.9% – 100%

3. Clinical studies:

a. Clinical sensitivity:
Not applicable.

b. *Clinical specificity:*
Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):
Clinical performance values were reviewed in K141375.

4. Clinical cut-off:
Same as assay cut-off.

5. Expected values/Reference range:
The frequency distribution for anti-M2 antibodies was investigated in a group of apparently healthy subjects equally distributed by age and gender, using sera from a Caucasian population obtained from a blood bank.

The results are given in the table below:

Test	n =	Median (U/mL)	95th percentile	99th percentile
EliA M2 on Phadia 2500/5000	400	0.9	1.9	5.2

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

All available data support that both instrument platforms, Phadia 250 and Phadia 2500/5000 perform substantially equivalent when using the EliA M2 immunoassays.

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.