January 28, 2022

Ortho Clinical Diagnostics
Declan Hynes
Regulatory Affairs Manager
Felindre Meadows
Pencoed, Bridgend CF35 5PZ
United Kingdom

Re: K212648
Trade/Device Name: VITROS Immunodiagnostic Products CK-MB Reagent Pack
Regulation Number: 21 CFR 862.1215
Regulation Name: Creatine Phosphokinase/Creatine Kinase Or Isoenzymes Test System
Regulatory Class: Class II
Product Code: JHX
Dated: September 23, 2021
Received: September 28, 2021

Dear Declan Hynes:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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)*
K212648

Device Name
VITROS Immunodiagnostic Products CK-MB Reagent Pack

Indications for Use *(Describe)*
Rx ONLY

For in vitro diagnostic use only.

For the quantitative measurement of CK-MB in human serum and plasma (EDTA or heparin) using the VITROS 3600 Immunodiagnostic System.

Measurements of creatine phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

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.

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510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: ___K212648_____

1. Submitter name, address, contact

Ortho Clinical Diagnostics
Felindre Meadows, Pencoed, Bridgend CF35 5PZ GBR
+44 (656) 778-032
Contact Person: Declan Hynes, Regulatory Affairs Manager

2. Preparation Date

January 27th, 2022

3. Device name

Trade or Proprietary Names:

VITROS Immunodiagnostic Products CK-MB Reagent Pack
Common Name: VITROS CK-MB
Assay Classification: 862.1215 Creatine phosphokinase/creatine kinase or isoenzymes test system.
Product Code: JHX

4. Predicate Device

VITROS Immunodiagnostic Products CK-MB Reagent Pack, K993068

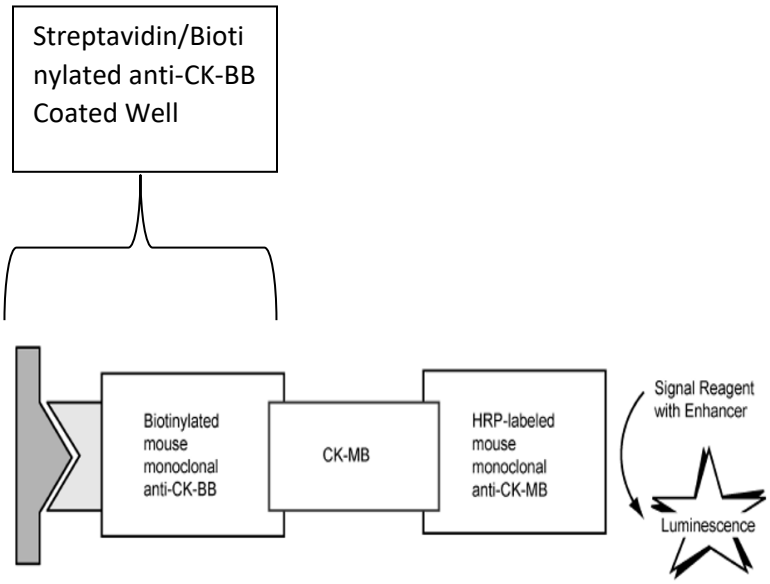
5. Device description

The VITROS Immunodiagnostic Products CK-MB assay is performed using the VITROS CK-MB Reagent Pack and the VITROS CK-MB Calibrators on the VITROS Systems.

The current VITROS Immunodiagnostic Products CK-MB assay is susceptible to interference from biotin. Ortho has made a modification to the manufacturing process to allow the biotinylated antibody capture conjugate to be pre-bound to the well, thus mitigating the risk of biotin interference.

The modified product utilizes all the same antibodies and raw materials with the exception of the addition of 0.7% Tween 20 and an increase in EDTA concentration from 0.001M to 0.030M, both of these modifications are to improve serum/plasma agreement which required a conversion factor in the previously cleared product.

Modified Assay Architecture



An immunometric immunoassay technique is used, which involves the reaction of CK-MB present in the sample with a microwell coated with biotinylated Antibody (Mouse monoclonal anti-CK-BB bound to Streptavidin), and a Horseradish Peroxidase (HRP)-labeled antibody conjugate (Mouse monoclonal anti-CK-MB). Unbound (HRP)-labeled anti-CK-MB antibody conjugate is removed by washing.

The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent, is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of CK-MB conjugate bound is directly proportional to the concentration of CK-MB present in the sample.

6. Device intended use

Rx ONLY

For *in vitro* diagnostic use only.

For the quantitative measurement of CK-MB in human serum and plasma (EDTA or heparin) using the VITROS 3600 Immunodiagnostic System.

Measurements of creatine phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

7. Comparison to predicate device:

The following tables provide a summary of the key features of the new device assessed against the predicate.

Device Characteristic	Predicate Device VITROS Immunodiagnostic Products CK-MB Reagent Pack , K993068, cleared 4 October 1999	Modified Device VITROS Immunodiagnostic Products CK-MB Reagent Pack
Intended Use	Rx ONLY For in vitro diagnostic use only. For the quantitative measurement of CK-MB in human serum and plasma (EDTA or heparin)	Same
Basic Principle	Sandwich immunoassay	Same
Antibody	Monoclonal anti-CK-MB and anti-CK-BB	Same
Sample Type	Serum and plasma	Same
Traceability	Calibrated against a commercially available CK-MB assay	Same
Measuring Range	0.22–400 ng/mL (µg/L)	0.22–400 ng/mL (µg/L)
Detection Limit	LOB: 0.07 ng/mL LOD: 0.22 ng/mL	LOB: 0.07 ng/mL LOD: 0.22 ng/mL LOQ: 0.22 ng/mL
Reagent Stability	Unopened: Up to expiration date stored at 2-8ºC Opened: 8 weeks on VITROS System	Unopened: Up to expiration date stored at 2-8ºC Opened: 8 weeks on VITROS System

Nonclinical performance

Several nonclinical tests were performed. See Instruction for Use claims below:

Precision

Precision was evaluated with patient pool on the systems in the table below following the CLSI document EP05.

System	Conventional & SI Units (ng/mL)					No. of Obs.	No. of Days
	Mean Activity	Repeatability		Within Lab			
		SD	CV%	SD	CV%		
3600	1.8	0.049	2.7%	0.129	7.1%	80	20
	16.90	0.397	2.4%	0.843	5.0%	80	20
	46.3	0.793	1.7%	2.529	5.5%	80	20
	256	4.238	1.7%	12.694	5.0%	80	20

*Repeatability (formerly called within-run precision) was determined using two replicates per run.

**Within Lab precision was determined using a single reagent lot and a single calibration.

Limit of Detection

The Limit of Detection (LoD) for the VITROS Immunodiagnostic CK-MB Reagent Pack is 0.07 mIU/mL (IU/L), determined consistent with CLSI document EP17. The Limit of Quantitation (LoQ) was determined consistent with CLSI document EP17.

LoB ng/mL (µg/L)	**LoD ng/mL (µg/L)**	**LoQ ng/mL (µg/L)**
0.07	**0.22**	**0.22**

Linearity/Measuring Range

VITROS System	Measuring (Reportable) Range
3600	0.22–400 ng/mL (µg/L)

Matrix Comparison

Specimens Recommended

• Serum

• Plasma (Lithium Heparin)

• Plasma (K2 EDTA)

Specimens Not Recommended

Do not use turbid specimens. Turbidity in specimens may affect test results.

Analytical Specificity

Known Interferences

The VITROS Immunodiagnostic CK-MB Reagent Pack was screened for interfering substances at CK-MB concentrations of approximately 3.00 ng/mL (µg/L) and 50.0 ng/mL (µg/L) following CLSI EP07 and EP37. The substances listed in the table demonstrated observed bias of > 10% when tested at the concentrations shown.

Interferent	Conventional Units		Alternate Units		% Bias
	CK-MB Conc. (ng/mL)	Interferent Concentration	CK-MB Conc. (µg/L)	Interferent Concentration	
Cefoxitin	3.00	521 mg/dL	3.00	11.6 mmol/L	-27.7
Cefoxitin	3.00	348 ng/dL	3.00	7.75 mmol/L	-8.1
Dextran 40	3.00	2400 mg/dL	3.00	600 µmol/L	-15.0
Dextran 40	3.00	1800 mg/dL	3.00	450 µmol/L	-8.9
Dextran 40	50.0	2400 mg/dL	50.0	600 µmol/L	-44.9
Dextran 40	50.0	1800 mg/dL	50.0	450 µmol/L	9.0

Other Limitations

The results from this or any other diagnostic test should be used and interpreted only in the context of the overall clinical picture.

The VITROS Immunodiagnostic CK-MB Reagent Pack has no high dose hook effect up to 44,200 ng/mL (µg/L).

Elevated CK-MB concentrations have been observed in patients experiencing skeletal muscle trauma, renal failure and certain chronic heart pathologies, as well as after strenuous exercise. Factors that may aid in the diagnosis of myocardial infarction include the pattern of rise and fall in CK-MB concentrations as well as the ratio of CK-MB concentration to total CK activity. These and other appropriate clinical factors should be considered when interpreting test results.
Heterophilic antibodies in the serum or plasma samples may cause interference in immunoassays. These antibodies may be present in blood samples from individuals regularly exposed to animals or who have been treated with animal serum products. Results that are inconsistent with clinical observations indicate the need for additional testing.
Certain drugs and clinical conditions are known to alter CK-MB concentrations in vivo. For additional information, refer to one of the published summaries referenced in the product Instruction for Use.

Specificity

Substances that Do Not Interfere

The substances listed in the table below were tested with the VITROS Immunodiagnostic CK-MB Reagent Pack following CLSI EP07 and EP37 and found not to cause bias > 10% at CK-MB concentrations of approximately 3.00 ng/mL (µg/L) and 50.0 ng/mL (µg/L) at the test concentrations shown.

Substance	Concentration	
Acetaminophen	15.6 mg/dL	1032 µmol/L
N-Acetylcysteine	15 mg/dL	920 µmol/L
Amoxicillin	5.40 mg/dL	148 µmol/L
Ascorbic acid	5.25 mg/dL	298 µmol/L
Bilirubin, conjugated	40 mg/dL	475 µmol/L
Bilirubin, unconjugated	40 mg/dL	475 µmol/L
Biotin	3510 ng/mL	14.3 µmol/L
Carbamazepine	4.50 mg/dL	191 µmol/L
Carvedilol	5 mg/dL	123 µmol/L
Captopril	0.264 mg/dL	12.2 µmol/L
Cholesterol	400 mg/dL	10.3 mmol/L
Clopidogrel	30 mg/dL	932 µmol/L
Codeine	0.141 mg/dL	5 µmol/L
Cotinine	0.24 mg/dL	13.6 µmol/L
Dextromethorphan	0.00156 mg/dL	0.042 µmol/L
Digoxin	0.0039 mg/dL	0.050 µmol/L

Substance	Concentration	
Enoxaparin (Low Molecular Weight Heparin)	360 U/dL	N/A
Ethanol	600 mg/dL	130 mmol/L
Furosemide	1.59 mg/dL	48 µmol/L
Hemoglobin	1000 mg/dL	155 µmol/L
Heparin (sodium)	330 U/dL	N/A
Hydralazine hydrochloride	1.44 mg/dL	73.2 µmol/L
Hydrocodone	0.0072 mg/dL	0.2 µmol/L
Ibuprofen	71 mg/dL	3.45 mmol/L
Levothyroxine	0.0429 mg/dL	0.552 µmol/L
Loratadine	0.0087 mg/dL	0.227 µmol/L
Naproxen	36 mg/dL	1.43 mmol/L
Nifedipine	0.0588 mg/dL	1.7 µmol/L
Oleic acid	40 mg/dL	0.142 µmol/L
Omeprazole	0.840 mg/dL	24.3 µmol/L
Phenytoin	6.00 mg/dL	238 µmol/L
Prednisone	0.010 mg/dL	0.280 µmol/L
Propranolol HCl	0.115 mg/dL	3.89 µmol/L
Rheumatoid factor	900 IU/mL	N/A
Rivaroxaban	0.270 mg/dL	6.19 µmol/L
Salicylic acid	2.86 mg/dL	207 mmol/L
Streptokinase	150,000 U/dL	N/A
Theophylline	6.0 mg/dL	333 µmol/L
Total protein	15 g/dL	17.1 nmol/L
Tissue Plasminogen Activator (TPA)	1.2 mg/dL	N/A
Triglycerides	1500 mg/dL	16.9 mmol/L
Triolein	3000 mg/dL	3.31 µmol/L
Vancomycin hydrochloride	12.3 mg/dL	8.28 mmol/L
Verapamil	0.160 mg/dL	3.52 µmol/L
Warfarin sodium	8.0 mg/dL	242 µmol/L

Cross-Reactivity

The cross-reactivity of the VITROS Immunodiagnostic CK-MB Reagent Pack was evaluated by adding the following substances to a sample containing no CK-MB.

Test Substance	Concentration	% Cross-reactivity
CK-BB	50 µg/dL	ND*
CK-MM	4 mg/dL	ND*

*Not Detectable. Concentration was below the measuring interval of the test, 0.22 to 400 ng/mL (µg/L).

Dilution

CK-MB samples with concentrations greater than the measuring range may be automatically diluted on the system 5- fold (1 part sample with 4 parts diluent) by the VITROS Immunodiagnostic System with the VITROS High Sample Diluent B Reagent Pack prior to test. Refer to the VITROS High Sample Diluent B Reagent Pack instructions for use.

High Dose Hook

The VITROS Immunodiagnostic CK-MB Reagent Pack has no high dose hook effect up to 44,200 ng/mL (µg/L).

Sample Stability

Same as K993068

Expected Values

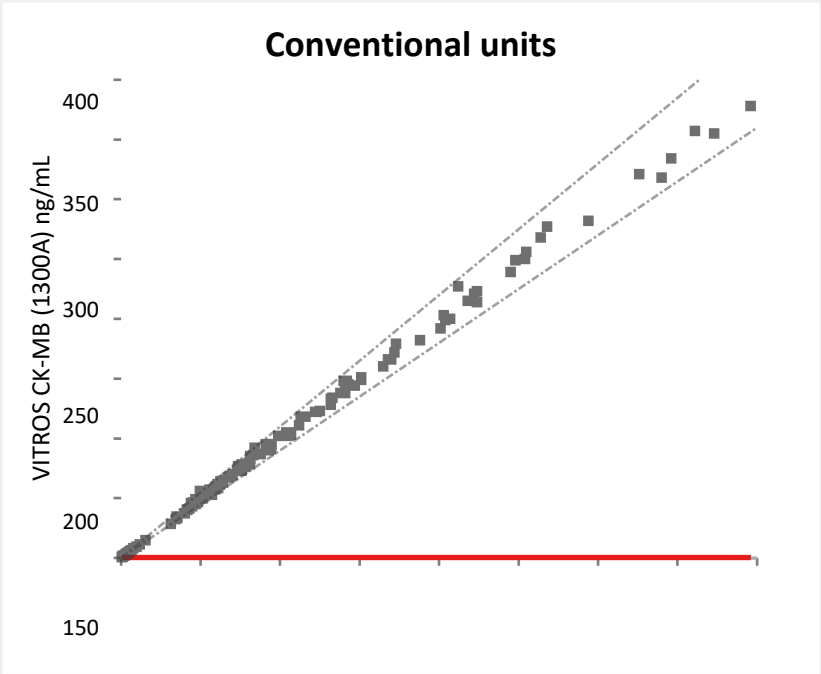
Same as K993068

Traceability of Calibration

Same as K993068

Method Comparison to Predicate Device

Accuracy was evaluated consistent with CLSI document EP09. The plot and table show the results of a method comparison study using patient (serum) samples analyzed on the VITROS 3600 Immunodiagnostic System using the candidate VITROS CK-MB Reagent Pack compared with those analyzed using the cleared predicate VITROS Immunodiagnostic CK-MB Reagent Pack. The relationship between the 2 methods was determined by Weighted Deming regression.



System	n	Slope	Correlation Coefficient	Conventional Units (ng/mL)		Alternate Units (µg/L)	
				Range of Sample Activity	Intercept	Range of Sample Activity	Intercept
3600 vs. Comparative Method	149	0.99	0.999	0.61-378	0.112	0.61-378	0.112

Parameter	95% CI
Intercept	0.05080 to 0.1723
Slope	0.9812 to 0.9950

9. Clinical performance

N/A

10. Conclusions

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