



August 9, 2024

Medicon Hellas, S.A.  
Sotia Mitropoulou  
Regulatory Affairs Manager  
Melitona 5-7, 153 44 Gerakas  
Greece

Re: K232404

Trade/Device Name: CHOLESTEROL; HDL-Cholesterol; LDL-Cholesterol; TRIGLYCERIDES  
Regulation Number: 21 CFR 862.1175  
Regulation Name: Cholesterol (Total) Test System  
Regulatory Class: Class I, meets the limitations of exemptions 21 CFR 862.9(c)(4)  
Product Code: CHH, LBS, MRR, CDT  
Dated: July 9, 2024  
Received: July 10, 2024

Dear Sotia Mitropoulou:

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 (the 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 available 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](#).

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Paula V. Caposino -S

Paula Caposino, Ph.D.  
Deputy Division Director  
Division of Chemistry and Toxicology Devices  
OHT7: Office of In Vitro Diagnostics  
Office of Product Evaluation and Quality  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)  
K232404

Device Name

CHOLESTEROL, HDL-Cholesterol, LDL-Cholesterol, TRIGLYCERIDES

Indications for Use (Describe)

**CHOLESTEROL:** Reagent kit intended for the quantitative determination of Cholesterol in human serum. Cholesterol measurements are used in the diagnosis and treatment of disorders involving excess cholesterol in the blood, of lipid and lipoprotein metabolism disorders.

**HDL-Cholesterol:** Reagent kit intended for the quantitative determination of high-density lipoprotein in human serum. Measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

**LDL-Cholesterol:** Reagent kit intended for the quantitative determination of low-density lipoprotein in human serum. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

**TRIGLYCERIDES:** Reagent kit intended for the quantitative determination of triglycerides (neutral fat) in human serum. Measurements are used in the diagnosis and treatment of patients with diabetes mellitus, nephrosis, liver obstruction, other diseases involving lipid metabolism, or various endocrine disorders.

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

510(k) Number: K232404

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

**807.92 (a)(1): Name:** MEDICON HELLAS S.A.

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**US Agent:** Diatron US, Inc.

1.833.228.7931

Mr. Frank Matuszak

[frank.matuszak@diatron.com](mailto:frank.matuszak@diatron.com)

[All Supplemental testing was performed at the company premises, mentioned above.](#)

**807.92 (a)(2): Device name- trade name and common name, and classification**

**Trade Name:** CHOLESTEROL, HDL-Cholesterol, LDL-Cholesterol, and TRIGLYCERIDES.

**Common Name:** test systems for Cholesterol, HDL, LDL, and Triglycerides for testing human serum.

**Classification Name(s):**

21 CFR § 862.1175 - Cholesterol Test system - Product Code CHH

21 CFR § 862.1475 - HDL-Cholesterol Test system - Product Code LBS

21 CFR § 862.1475 - LDL-Cholesterol Test system - Product Code MRR

21 CFR § 862.1705 - Triglycerides Test system - Product Code CDT

**807.92 (a)(3): Identification of the legally marketed predicate devices**

Cholesterol - OLYMPUS CHOLESTEROL REAGENT (k925603)

HDL-Cholesterol - DIRECT HDL (k981224)

LDL-Cholesterol - DIRECT LDL (k981303)

Triglycerides - OLYMPUS TRIGLYCERIDE TEST SYSTEM (k063804)

**Intended Use/Indications for Use:**

**A) Intended Use(s):**

See Indications for Use below.

**B) Indications for Use:**

CHOLESTEROL: Reagent kit intended for the quantitative determination of Cholesterol in human serum. Cholesterol measurements are used in the diagnosis and treatment of disorders involving excess cholesterol in the blood, of lipid and lipoprotein metabolism disorders.

HDL-Cholesterol: Reagent kit intended for the quantitative determination of high-density lipoprotein in human serum. Measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

LDL-Cholesterol: Reagent kit intended for the quantitative determination of low-density lipoprotein in human serum. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

TRIGLYCERIDES: Reagent kit intended for the quantitative determination of triglycerides (neutral fat) in human serum. Measurements are used in the diagnosis and treatment of patients with diabetes mellitus, nephrosis, liver obstruction, other diseases involving lipid metabolism, or various endocrine disorders.

**C) Special Conditions for Use Statement(s):**

Rx – For Prescription Use Only

**D) Special Instrument Requirements:**

Diatron Pictus®500 Analyzers

**807.92 (a)(4): Device Description**

**CHOLESTEROL:**

**REF** 1419-0042 **Packaging:** 6 x 60 mL

**Reagent Composition:**

|                            |            |
|----------------------------|------------|
| 4-Chlorophenol             | 4.7 mM     |
| 4-Aminoantipyrine          | 1 mM       |
| Cholesterol esterase (CHE) | ≥ 500 U/L  |
| Cholesterol oxidase (CHOD) | ≥ 500 U/L  |
| Peroxidase (POD)           | ≥ 1000 U/L |

The Cholesterol Oxidase peroxidase (CHOD-PAP) enzymatic colorimetric method is used. The cholesterol esterase enzyme catalyzes the hydrolysis of cholesterol esters to cholesterol and free fatty acids. Free cholesterol, including that originally present in the sample, is then oxidized by the enzyme cholesterol oxidase (CHOD) to cholest-4-en-3-one, by using molecular oxygen as the electron acceptor and concurrently producing hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). The H<sub>2</sub>O<sub>2</sub> produced is then used in a subsequent chromogenic oxidative coupling reaction, catalyzed by the enzyme peroxidase, in the presence of a redox indicator system, which leads to the formation of a colored compound, absorbing light at 550 nm. The increase in absorbance is directly proportional to the cholesterol concentration in the sample.

**HDL-Cholesterol:**

**REF** 1419-0240 **Packaging:** 6 x 13.5 mL (R1) + 6 x 4.5 mL (R2)

**REF** 1419-0242 **Packaging:** 6 x 35.1 mL (R1) + 6 x 11.7 mL (R2)

**Reagent Composition**

| Reagent 1 (R1)                         |           | Reagent 2 (R2)                         |           |
|--|-----------|--|-----------|
| Cholesterol oxidase:                   | <1000 U/L | Cholesterol esterase:                  | <1500 U/L |
| Peroxidase:                            | <1300 U/L | 4-aminoantipyrine:                     | <1mM      |
| Ascorbate oxidase:                     | <3000U/L  | Non-reactive ingredients, preservative |           |
| Accelerator:                           | <1mM      |  |           |
| DSBmT:                                 | <1mM      |  |           |
| Non-reactive ingredients, preservative |           |  |           |

The Accelerator Selective Detergent method is applied. The determination of HDL-Cholesterol is based on the following reactions: LDL, VLDL, and chylomicrons are neutralized by the combined action of the enzymes Cholesterol Oxidase, Peroxidase, accelerators and N,N-bis-(4-sulfobutyl)-m-toluidine-disodium (DSBmT). HDL remaining in the sample is disrupted by the action of a selective detergent and cholesterol is converted to Δ4 Cholestenone by the enzymatic action of Cholesterol Esterase and Cholesterol Oxidase, with the subsequent production of H<sub>2</sub>O<sub>2</sub>, which reacts with DSBmT and 4-aminoantipyrine in the presence of Peroxidase to a colored complex that absorbs light at 590 nm. The absorbance measured is proportional to the concentration of HDL-Cholesterol in the sample.

**LDL-Cholesterol**

**REF** 1419-0220     **Packaging:** 6 x 13.5 mL (R1) + 6 x 4.5 mL (R2)

**REF** 1419-0222     **Packaging:** 6 x 35.1 mL (R1) + 6 x 11.7 mL (R2)

**Reagent Composition:**

| Reagent 1 (R1)                         |           | Reagent 2 (R2)                         |       |
|--|-----------|--|-------|
| Detergent 1                            | <1%       | Detergent 2                            | <1%   |
| 4-Aminoantipyrine                      | <0.1%     | DSBmT                                  | <1 mM |
| Cholesterol Oxidase (CHO)              | <1500 U/L | Non-reactive ingredients, preservative |       |
| Cholesterol Esterase (CHE)             | <2500 U/L |  |       |
| Peroxidase (POD)                       | <1300 U/L |  |       |
| Ascorbic oxidase                       | <3000 U/L |  |       |
| Non-reactive ingredients, preservative |           |  |       |

The Selective Detergent method is applied. The method is in a two-reagent format and depends on the properties of a unique detergent. The first detergent solubilizes only the non-LDL lipoprotein particles. The cholesterol released is consumed by cholesterol esterase and cholesterol oxidase in a non-color forming reaction. The second detergent solubilizes the remaining LDL particles, and a chromogenic coupler allows for color formation. The enzyme reaction with LDL-Cholesterol in the presence of the coupler at 590 nm produces color that is proportional to the amount of LDL cholesterol present in the sample.

**TRIGLYCERIDES:**

**REF** 1419-0068     **Packaging:** 6 x 30 mL (R1) + 6 x 4 mL (R2)

**Reagent Composition:**

| Reagent 1 (R1)                         |             | Reagent 2 (R2)                         |             |
|--|-------------|--|-------------|
| Pipes buffer (pH: 6.8):                | 240 mM      | 4-Aminoantipyrine:                     | < 15 mM     |
| Peroxidase:                            | > 5000 U/L  | GPO:                                   | > 55000 U/L |
| Glycerokinase:                         | > 1000 U/L  | Non-reactive ingredients, preservative |             |
| Lipoprotein Lipase:                    | > 15000 U/L |  |             |
| ATP:                                   | 4.5 mM      |  |             |
| TOOS:                                  | 4.8 mM      |  |             |
| Non-reactive ingredients, preservative |             |  |             |

The enzymatic glycerol-3-phosphate-peroxidase (GPO-POD) method is used. The method enzymatically hydrolyzes by lipase to free fatty acids and glycerol. Glycerol is phosphorylated by adenosine triphosphate (ATP) with glycerokinase (GK) to produce glycerol-3-phosphate and adenosine diphosphate (ADP). Glycerol-3-phosphate-oxidase oxidizes glycerol-3-phosphate to dihydroxyacetone phosphate and H<sub>2</sub>O<sub>2</sub>. The catalytic action of peroxidase (POD) forms quinoneimine from H<sub>2</sub>O<sub>2</sub>, aminoantipyrine, and Dihydrate (N-Ethyl-N-(2-hydroxy-3-sulfopropyl)-m-toluidine (TOOS). The absorption change at 550 nm is proportional to the triglycerides concentration in the sample.

**807.92 (a)(5): Intended Use -**

**CHOLESTEROL:** Reagent kit intended for the quantitative determination of Cholesterol in human serum. Cholesterol measurements are used in the diagnosis and treatment of disorders involving excess cholesterol in the blood, of lipid and lipoprotein metabolism disorders.

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**LDL-Cholesterol:** Reagent kit intended for the quantitative determination of low-density lipoprotein in human serum. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

**TRIGLYCERIDES:** Reagent kit intended for the quantitative determination of triglycerides (neutral fat) in human serum. Measurements are used in the diagnosis and treatment of patients with diabetes mellitus, nephrosis, liver obstruction, other diseases involving lipid metabolism, or various endocrine disorders.

**807.92 (a)(6): Technological Similarities and Differences to the Predicates**

See Comparison with Predicate(s), pg. 6.

**807.92 (b)(1,2): Brief Description of Nonclinical Data – Clinical Studies data does not apply**

Medicon Hellas (Medicon) has performed a series of studies to confirm the substantial equivalence of their test systems against the legally marketed predicate devices mentioned above, by demonstrating the candidate devices performance against the following current laboratory methods.

Several candidate-reagent lots were used for the studies. These covered early life, mid-life, end of life reagents when available (but always included three lots) as well as “end of on-board life”. Studies confirmed equivalent performance of the candidate systems during their noted life cycle stages in order to support total shelf-life assignment.

Studies included accuracy (method comparison), reportable range (linearity), precision (reproducibility, between run and within lab [total]) and interfering substances. The following tables provide summary results.

**Accuracy (Method Comparisons)** - A minimum of 75 left-over specimens, spanning the dynamic ranges, were assayed in singleton and in a blinded fashion on the candidate and predicate systems. Results were tabulated and evaluated using Analyse-it statistics calculator software to generate Passing-Bablok regression statistics. Accuracy statistics are reported as Passing-Bablok regression statistics.

**Substantial Equivalence Information:**

**A. Predicate Device Name(s):**

OLYMPUS CHOLESTEROL REAGENT (k925603)  
 DIRECT HDL (k981224)  
 DIRECT LDL (k981303)  
 OLYMPUS TRIGLYCERIDE TEST SYSTEM (k063804)

**B. Predicate 510(k) Numbers:**

k925603, k981224, k981303, and k063804

**C. Comparison with Predicate(s):**

**Device Comparison Table: CHOLESTEROL**

| Reagent  | CHOLESTEROL                               | OLYMPUS CHOLESTEROL REAGENT (k925603)   |
|--|---|---|
| <b>Classification</b>  | 21 CFR § 862.1175, CHH                    | Same                                    |
| <b>Method comparison (correlation to comparator)</b>                       | 0.9980                                    | 1.000                                   |
| <b>Reportable range</b>  | 20 to 700 mg/dL                           | 20 to 700 mg/dL                         |
| <b>Sensitivity LoD / LoQ</b>   | LoD 4.4 / LoQ 4.6 (mg/dL)                 | LoD 1mg/dL / Not defined                |
| <b>Precision (within run &amp; total for all LVs)</b>                      | <= 4%                                     | <= 3%                                   |
| <b>Endogenous Interferences - insignificant up to noted concentrations</b> |   |   |
| <b>Ascorbate</b>   | up to 5.25 mg/dL                          | up to 3 mg/dL                           |
| <b>Conjugated Bilirubin</b>  | up to 40 mg/dL                            | Not listed / Not defined                |
| <b>Unconj. Bilirubin</b>   | up to 40 mg/dL                            | up to 8 mg/dL                           |
| <b>Hemoglobin</b>  | up to 500 mg/dL                           | up to 500 mg/dL                         |
| <b>Triglycerides</b>   | up to 1,500 mg/dL                         | up to 1,000 mg/dL                       |
| <b>Exogenous Interferences</b>   | See pg. 12                                | Not listed / Not defined                |
| <b>Calibration frequency / On-board stability</b>                          | 14 days / 28 days                         | 30 days / Not defined days              |
| <b>Intended Use</b>  | Quantitative determination of Cholesterol | Quantitative measurement of cholesterol |
| <b>Testing Environment</b>   | Clinical labs                             | Same                                    |
| <b>Method Principle</b>  | Photometry                                | Same                                    |
| <b>Specimen Type</b>   | Human serum                               | Human serum, plasma and urine           |

Device Comparison Table: HDL-Cholesterol

| Reagent  | HDL-Cholesterol                               | DIRECT HDL (k981224)                        |
|--|---|---|
| Classification   | 21 CFR § 862.1475, LBS                        | Same  |
| Method comparison (correlation to comparator)                              | 0.997   | 1.999                                       |
| Reportable range   | 6.0 to 200 mg/dL                              | 5.0 to 221 mg/dL                            |
| Sensitivity LoD / LoQ  | LoD 3.0 / LoQ 5.8 (mg/dL)                     | LoD 2.5 / LoQ 5.0 (mg/dL)                   |
| Precision (within run & total for all LVs)                                 | <=4.0%  | <=4.0%                                      |
| <b>Endogenous Interferences - insignificant up to noted concentrations</b> |   |   |
| Ascorbate  | up to 5.25 mg/dL                              | up to 3.9 mg/dL                             |
| Conjugated Bilirubin   | up to 40 mg/dL                                | MDL1 32.4mg/dL & MDL2 67.1mg/dL             |
| Unconj. Bilirubin  | up to 40 mg/dL                                | up to 8 mg/dL                               |
| Hemoglobin   | up to 1,000mg/dL                              | up to 2,000mg/dL                            |
| Triglycerides  | up to 1,500 mg/dL                             | MDL1 1,000mg/dL & MDL2 2,000mg/dL           |
| Exogenous Interferences  | See pg. 13                                    | Not listed / Not defined                    |
| Calibration frequency / On-board stability                                 | 14 days / 28 days                             | 28 days / Not defined days                  |
| Intended Use   | Quantitative determination of HDL-Cholesterol | Quantitative measurement of HDL-Cholesterol |
| Testing Environment  | Clinical labs                                 | Same  |
| Method Principle   | Photometry                                    | Same  |
| Specimen Type  | Human serum                                   | Human serum & plasma                        |

Device Comparison Table: LDL-Cholesterol

| Reagent  | LDL-Cholesterol                               | DIRECT LDL (k981303)                        |
|--|---|---|
| Classification   | 21 CFR § 862.1475, MRR                        | Same  |
| Method comparison (correlation to comparator)                              | 0.999   | 0.960                                       |
| Reportable range   | 3 to 800mg/dL                                 | 1 to 800mg/dL                               |
| Sensitivity LoD / LoQ  | LoD 2 / LoQ 3 mg/dL                           | < 10mg/dL                                   |
| Precision (within run & total for all LVs)                                 | < 4.0%  | < 4.0%                                      |
| <b>Endogenous Interferences - insignificant up to noted concentrations</b> |   |   |
| Conjugated Bilirubin   | up to 40 mg/dL                                | up to 20mg/dL                               |
| Unconj. Bilirubin  | up to 40 mg/dL                                | up to 20mg/dL                               |
| Hemoglobin   | up to 1,000mg/dL                              | up to 500mg/dL                              |
| Triglycerides  | up to 1,500 mg/dL                             | up to 1,293 mg/dL                           |
| Exogenous Interferences  | See pg. 14                                    | Not listed / Not defined                    |
| Acetaminophen  | Tested up to 15.6mg/dL                        | 20.0mg/dL                                   |
| Dipyron  | Tested up to 3.3mg/dL                         | 10mg/dL                                     |
| N-Acetyl-L-Cysteine  | Tested up to 15mg/dL                          | 160mg/dL                                    |
| Calibration frequency / On-board stability                                 | new lot / 28 days                             | 28 days / not defined                       |
| Intended Use   | Quantitative determination of LDL-Cholesterol | Quantitative measurement of LDL-Cholesterol |
| Testing Environment  | Clinical labs                                 | Same  |
| Method Principle   | Photometry                                    | Same  |
| Specimen Type  | Human serum                                   | Human serum & plasma                        |

Device Comparison Table: TRIGLYCERIDES

| Reagent  | TRIGLYCERIDES                               | OLYMPUS TRIGLYCERIDE TEST SYSTEM (k063804) |
|--|---|--|
| Classification   | 21 CFR § 862.1705, CDT                      | Same                                       |
| Method comparison (correlation to comparator)                              | 0.999                                       | 0.999                                      |
| Reportable range   | 10 to 1,000mg/dL                            | 10 to 1,000mg/dL                           |
| Sensitivity LoD / LoQ  | LoD 5.5 / LoQ 9.7 mg/dL                     | < 0.31 / 5.0 mg/dL                         |
| Precision (within run & total for all LVs                                  | < 4.0%                                      | < 5.0%                                     |
| <b>Endogenous Interferences - insignificant up to noted concentrations</b> |   |  |
| Conjugated Bilirubin   | up to 40 mg/dL                              | Not listed / Not defined                   |
| Unconj. Bilirubin  | up to 40 mg/dL                              | up to 40mg/dL                              |
| Hemoglobin   | up to 400mg/dL                              | up to 500mg/dL                             |
| Exogenous Interferences  | See pg. 15                                  | Not listed / Not defined                   |
| Calibration frequency / On-board stability                                 | 28 days / 28 days                           | 30 days / 30 days                          |
| Intended Use   | Quantitative determination of triglycerides | Quantitative measurement of triglycerides  |
| Testing Environment  | Clinical labs                               | Same                                       |
| Method Principle   | Photometry                                  | Same                                       |
| Specimen Type  | Human serum                                 | Human serum, plasma & urine                |

**Standards/Guidance Documents Referenced:**

CLSI EP05-A3 – Evaluation of Precision Performance of Quantitative Measurement Procedures, 3rd ed. 2014

CLSI EP06-Ed02 – Evaluation of Linearity of Quantitative Measurement Procedures, 2nd ed., Nov.2020.

CLSI EP07 – Interference Testing in Clinical Chemistry, 3rd ed. 2018.

CLSI EP09c – Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 3rd ed. 2018.

CLSI EP15-A3 – User Verification of Precision and Estimation of Bias. 3rd ed. 2014.

CLSI EP17-A2 – Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, Approved guideline, 2nd ed. 2012.

CLSI EP37 – Supplemental Tables for Interference Testing in Clinical Chemistry, 1st ed., 2018

## 1. Analytical Performance:

### a) Precision/Reproducibility:

Precision studies were conducted according to the CLSI EP05-A3 guideline.

A precision evaluation study procedure was applied for one site and one analyzer in a standard 20x2x2 experiment. Three human serum pools were tested for CHOLESTEROL and TRIGLYCERIDES, two pools for HDL-Cholesterol and four pools for LDL-Cholesterol, near the Medical Decision Limits, for every analyte. The protocol uses measurements of each sample for 20 testing days, two different runs, and two replicate measurements per run (morning and afternoon run) for a total of 80 results per level concentration. When results were collected, analysis of the data was done using the 2-way factor nested ANOVA model. From the above analysis were calculated the mean, the standard deviation, the coefficient of variation (%CV) for repeatability (within-run), between run precision and total precision for each reagent Lot of Cholesterol reagent.

The Within-run precision, Between Day and Total precision results for a representative reagent lot for each analyte are presented in the tables below.

| CHOLESTEROL   |    | Mean<br>(mg/dL) | Repeatability<br>%CV | Between Run<br>%CV | Between Day<br>%CV | Total precision<br>%CV |
|---------------|----|-----------------|----------------------|--------------------|--------------------|------------------------|
| Sample        | N  |                 |                      |                    |                    |                        |
| Serum<br>Pool | 80 | 92              | 1.6                  | 0.0                | 1.6                | 2.2                    |
|               | 80 | 241             | 1.4                  | 2.0                | 1.5                | 2.8                    |
|               | 80 | 345             | 1.4                  | 0.8                | 2.5                | 3.0                    |

| HDL-Cholesterol |    | Mean<br>(mg/dL) | Repeatability<br>%CV | Between Run<br>%CV | Between Day<br>%CV | Total precision<br>%CV |
|-----------------|----|-----------------|----------------------|--------------------|--------------------|------------------------|
| Sample          | N  |                 |                      |                    |                    |                        |
| Serum<br>Pool   | 80 | 31              | 2.3                  | 2.0                | 2.3                | 3.8                    |
|                 | 80 | 57              | 1.2                  | 0.8                | 2.2                | 2.6                    |

| LDL-Cholesterol |    | Mean<br>(mg/dL) | Repeatability<br>%CV | Between Run<br>%CV | Between Day<br>%CV | Total precision<br>%CV |
|-----------------|----|-----------------|----------------------|--------------------|--------------------|------------------------|
| Sample          | N  |                 |                      |                    |                    |                        |
| Serum<br>Pool   | 80 | 98              | 1.0                  | 1.2                | 3.6                | 3.9                    |
|                 | 80 | 126             | 1.8                  | 2.3                | 1.9                | 3.5                    |
|                 | 80 | 156             | 1.1                  | 1.5                | 3.1                | 3.6                    |
|                 | 80 | 193             | 1.1                  | 1.6                | 2.5                | 3.2                    |

| TRIGLYCERIDES |    | Mean<br>(mg/dL) | Repeatability<br>%CV | Between Run<br>%CV | Between Day<br>%CV | Total precision<br>%CV |
|---------------|----|-----------------|----------------------|--------------------|--------------------|------------------------|
| Sample        | N  |                 |                      |                    |                    |                        |
| Serum<br>Pool | 80 | 41              | 1.0                  | 1.6                | 0.9                | 2.1                    |
|               | 80 | 148             | 1.3                  | 2.1                | 1.8                | 3.0                    |
|               | 80 | 399             | 0.7                  | 1.3                | 1.0                | 1.8                    |

b) Linearity:

Linearity studies were conducted according to the CLSI EP06-EdA2 guideline.

For each analyte 11 to 13 levels were prepared by dilution of a human serum pool with a concentration of analyte higher than the claimed upper limit of linearity. The human serum high pool was prepared from a human base pool after spiking with a purified concentrated analyte. The diluent it was a delipidized commercial preparation free of each analyte. The samples were assigned their reference values arithmetically from serial dilutions of the high-level sample. Each level was tested in 4 replicates using 1 instrument, and 3 Lots of reagents. Sample included target MDLs within the range tested. To validate the linearity a Least Square Linear Regression analysis was performed with intercept in the model. Statistics were calculated using Analyse-it standard algorithms. Levels below and above the defined reportable range limits were included. Results for a representative reagent lot for each analyte are presented in the tables below.

| Device          | Sample Matrix | Claimed Measurement Range | Slope | Intercept | R <sup>2</sup> |
|-----------------|---------------|---------------------------|-------|-----------|----------------|
| CHOLESTEROL     | Serum         | 20 – 700 mg/dL            | 1.001 | 0.409     | 0.9997         |
| HDL-Cholesterol | Serum         | 6 – 200 mg/dL             | 1.033 | -0.668    | 0.9984         |
| LDL-Cholesterol | Serum         | 3 – 800 mg/dL             | 1.099 | -0.40     | 0.9996         |
| TRIGLYCERIDES   | Serum         | 10 – 1000 mg/dL           | 0.978 | -0.236    | 0.9994         |

c) Analytical Specificity / Interference:

Interference studies were conducted according to the CLSI EP07-A3 guideline.

The study measured the effect of endogenous substances to act as interferents at recommended test level (CLSI EP37, Table 2) on two concentration levels of analyte (CLSI EP07, Table A1). The study measured also the effect of a number of exogenous substances (CLSI EP37, Table 1) which when present might interfere the final test reported by Medicon candidate reagents. Again, as previously noted the effect on 2 concentration levels was tested as per indicated in CLSI EP07 (Table A1). Serum pools at low and high levels of each analyte were prepared, then spiked with the interference compounds. The results define the level at which interferences of the noted compounds will affect results by more than +/- 10%.

**Endogenous interference procedure**

Low and high levels of each analyte were spiked with a recommended concentration of endogenous substance. The recommended concentration for endogenous substance which was tested was withdrawn from CLSI EP37 procedure.

| Interferent            | Highest recommended conc. |
|------------------------|---------------------------|
| Hemoglobin             | 1000 mg/dL                |
| Conjugated Bilirubin   | 40 mg/dL                  |
| Unconjugated Bilirubin | 40 mg/dL                  |
| Triglycerides          | 1500 mg/dL                |

In each case, the mean value of each spiked sample was compared to its neat (zero interferent) mean and % recovered values were calculated. Each measurement of the blank and the relative sample containing the interferent was repeated at least 5 times and means are compared. When interference was found for any tested compound(s), dose response studies were conducted to define the highest concentration which showed a deviation from control value lower than 10%.

**Exogenous interference procedure**

To assess the effect observed by the exogenous substance on two levels concentrations of the analyte in question (low and high), two different drug concentrations were studied. These are the highest drug concentration under the therapeutic treatment and the recommended test concentration in the sample as proposed by CLSI EP-37 protocol or from relative bibliographic data. Each measurement of the blank and the relative sample containing the interferent was repeated at least 5 times and means are compared. No interference was confirmed when the observed mean in the presence of interferent was within 10% of the blank mean. When interference was found for any tested compound(s), dose response studies were conducted to define interference limits for the drugs.

The following provides endogenous and exogenous study results for each reagent. In the following tables were summarized the highest concentrations for each interferent that that did not cause significant interference.

**CHOLESTEROL:**

| Sample Matrix | Interferent            | Highest concentration tested that did not cause significant interference |
|---------------|------------------------|--|
| Serum         | Hemoglobin             | 500 mg/dL  |
|               | Conjugated Bilirubin   | 40 mg/dL   |
|               | Unconjugated Bilirubin | 40 mg/dL   |
|               | Triglycerides          | 1500 mg/dL   |
|               | Acetaminophen          | 15.6 mg/dL   |
|               | Acetylsalicylic Acid   | 3 mg/dL  |
|               | Ampicillin             | 7.5 mg/dL  |
|               | Ascorbic Acid          | 5.25 mg/dL   |
|               | Atorvastatin           | 0.075 mg/dL  |
|               | Cefotaxime             | 52.8 mg/dL   |
|               | Cefoxitin              | 660 mg/dL  |
|               | Cyclosporine           | 0.18 mg/dL   |
|               | Dipyrene               | 3.3 mg/dL  |
|               | Dobesilate Calcium     | 6 mg/dL  |
|               | Dobutamine             | 0.121 mg/dL  |
|               | Doxycycline            | 1.8 mg/dL  |
|               | Fenofibrate            | 4.5 mg/dL  |
|               | Heparin                | 330 U/dL   |
|               | Ibuprofen              | 21.9 mg/dL   |
|               | Intralipid             | 2000 mg/dL   |
|               | Levodopa               | 0.75 mg/dL   |
|               | Methotrexate           | 136 mg/dL  |
|               | Methyldopa             | 2.25 mg/dL   |
|               | Metronidazole          | 12.3 mg/dL   |
|               | N-Acetyl-Cysteine      | 15 mg/dL   |
|               | Phenylbutazone         | 32.1 mg/dL   |
|               | Pravastatin            | 0.0207 mg/dL   |
|               | Rifampicin             | 4.8 mg/dL  |
| Rosuvastatin  | 0.0111 mg/dL           |  |
| Simvastatin   | 0.168 mg/dL            |  |
| Theophylline  | 6 mg/dL                |  |

**HDL-Cholesterol:**

| <b>Sample Matrix</b> | <b>Interferent</b>     | <b>Highest concentration tested that did not cause significant interference</b> |
|----------------------|------------------------|---|
| Serum                | Hemoglobin             | 1000 mg/dL  |
|                      | Conjugated Bilirubin   | 40 mg/dL  |
|                      | Unconjugated Bilirubin | 40 mg/dL  |
|                      | Triglycerides          | 1500 mg/dL  |
|                      | Acetaminophen          | 15.6 mg/dL  |
|                      | Acetylsalicylic Acid   | 3 mg/dL   |
|                      | Ampicillin             | 7.5 mg/dL   |
|                      | Ascorbic Acid          | 5.25 mg/dL  |
|                      | Atorvastatin           | 0.075 mg/dL   |
|                      | Cefotaxime             | 52.8 mg/dL  |
|                      | Cefoxitin              | 660 mg/dL   |
|                      | Cyclosporine           | 0.18 mg/dL  |
|                      | Dipyrene               | 3.3 mg/dL   |
|                      | Dobesilate Calcium     | 6 mg/dL   |
|                      | Dobutamine             | 0.121 mg/dL   |
|                      | Doxycycline            | 1.8 mg/dL   |
|                      | Fenofibrate            | 4.5 mg/dL   |
|                      | Heparin                | 330 U/dL  |
|                      | Ibuprofen              | 21.9 mg/dL  |
|                      | Intralipid             | 2000 mg/dL  |
|                      | Levodopa               | 0.75 mg/dL  |
|                      | Methotrexate           | 136 mg/dL   |
|                      | Methyldopa             | 1.35 mg/dL  |
|                      | Metronidazole          | 12.3 mg/dL  |
|                      | N-Acetyl-Cysteine      | 15 mg/dL  |
|                      | Phenylbutazone         | 32.1 mg/dL  |
|                      | Pravastatin            | 0.0207 mg/dL  |
|                      | Rifampicin             | 4.8 mg/dL   |
|                      | Rosuvastatin           | 0.0111 mg/dL  |
|                      | Simvastatin            | 0.168 mg/dL   |
| Theophylline         | 6 mg/dL                |   |

**LDL-Cholesterol:**

| Sample Matrix | Interferent            | Highest concentration tested that did not cause significant interference |
|---------------|------------------------|--|
| Serum         | Hemoglobin             | 1000 mg/dL   |
|               | Conjugated Bilirubin   | 40 mg/dL   |
|               | Unconjugated Bilirubin | 40 mg/dL   |
|               | Triglycerides          | 1500 mg/dL   |
|               | Acetaminophen          | 15.6 mg/dL   |
|               | Acetylsalicylic Acid   | 3 mg/dL  |
|               | Ampicillin             | 7.5 mg/dL  |
|               | Ascorbic Acid          | 5.25 mg/dL   |
|               | Atorvastatin           | 0.075 mg/dL  |
|               | Cefotaxime             | 52.8 mg/dL   |
|               | Cefoxitin              | 660 mg/dL  |
|               | Cyclosporine           | 0.18 mg/dL   |
|               | Dipyrene               | 3.3 mg/dL  |
|               | Dobesilate Calcium     | 6 mg/dL  |
|               | Dobutamine             | 0.121 mg/dL  |
|               | Doxycycline            | 1.8 mg/dL  |
|               | Fenofibrate            | 4.5 mg/dL  |
|               | Heparin                | 330 U/dL   |
|               | Ibuprofen              | 21.9 mg/dL   |
|               | Intralipid             | 2000 mg/dL   |
|               | Levodopa               | 0.75 mg/dL   |
|               | Methotrexate           | 136 mg/dL  |
|               | Methyldopa             | 2.25 mg/dL   |
|               | Metronidazole          | 12.3 mg/dL   |
|               | N-Acetyl-Cysteine      | 15 mg/dL   |
|               | Phenylbutazone         | 32.1 mg/dL   |
|               | Pravastatin            | 0.0207 mg/dL   |
|               | Rifampicin             | 4.8 mg/dL  |
|               | Rosuvastatin           | 0.0111 mg/dL   |
|               | Simvastatin            | 0.168 mg/dL  |
| Theophylline  | 6 mg/dL                |  |

**TRIGLYCERIDES:**

| Sample Matrix | Interferent            | Highest concentration tested that did not cause significant interference |
|---------------|------------------------|--|
| Serum         | Hemoglobin             | 400 mg/dL  |
|               | Conjugated Bilirubin   | 40 mg/dL   |
|               | Unconjugated Bilirubin | 40 mg/dL   |
|               | Acetaminophen          | 15.6 mg/dL   |
|               | Acetylsalicylic Acid   | 3 mg/dL  |
|               | Ampicillin             | 7.5 mg/dL  |
|               | Ascorbic Acid          | 5.25 mg/dL   |
|               | Atorvastatin           | 0.075 mg/dL  |
|               | Cefotaxime             | 52.8 mg/dL   |
|               | Cefoxitin              | 660 mg/dL  |
|               | Cyclosporine           | 0.18 mg/dL   |
|               | Dipyron                | 3.3 mg/dL  |
|               | Dobesilate Calcium     | 6 mg/dL  |
|               | Dobutamine             | 0.121 mg/dL  |
|               | Doxycycline            | 1.8 mg/dL  |
|               | Fenofibrate            | 4.5 mg/dL  |
|               | Heparin                | 330 U/dL   |
|               | Ibuprofen              | 21.9 mg/dL   |
|               | Intralipid             | 2000 mg/dL   |
|               | Levodopa               | 0.75 mg/dL   |
|               | Methotrexate           | 136 mg/dL  |
|               | Methyldopa             | 2.25 mg/dL   |
|               | Metronidazole          | 12.3 mg/dL   |
|               | N-Acetyl-Cysteine      | 15 mg/dL   |
|               | Phenylbutazone         | 32.1 mg/dL   |
|               | Pravastatin            | 0.0207 mg/dL   |
| Rifampicin    | 4.8 mg/dL              |  |
| Rosuvastatin  | 0.0111 mg/dL           |  |
| Simvastatin   | 0.168 mg/dL            |  |
| Theophylline  | 6 mg/dL                |  |

d) Assay Reportable Range:

| Device            | Sample Matrix | Claimed Measurement Range |
|-------------------|---------------|---------------------------|
| CHOLESTEROL       | Serum         | 20 – 700 mg/dL            |
| HDL -Cholesterol  | Serum         | 6 – 200 mg/dL             |
| LDL - Cholesterol | Serum         | 3 – 800 mg/dL             |
| TRIGLYCERIDES     | Serum         | 10 – 1000 mg/dL           |

e) Traceability, Stability, Expected Values (Controls, Calibrators or Methods):

The Medicon reagents are traceable to the following reference materials:

| Device          | Reference Method/Reference Materials   |
|-----------------|--|
| CHOLESTEROL     | Gas-chromatography-isotope dilution mass spectrometry (GC-IDMS) reference method |
| HDL-Cholesterol | Abell-Kendall (AK) reference method  |
| LDL-Cholesterol | Abell-Kendall (AK) reference method  |
| TRIGLYCERIDES   | Gas-chromatography-isotope dilution mass spectrometry (GC-IDMS) reference method |

f) Detection Limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation studies were performed according to CLSI EP17-A2 guideline.

LoB: For the Limit of Blank study 5 blank serum were measured in 4 replicates for 3 days for a total of 60 measurements. Each set of measurements was performed with 3 reagent Lots. LoB was estimated using non-parametric analysis of the data.

LoD: For the Limit of Detection study, 5 low level samples were measured in 4 replicates for 3 days for a total of 60 measurements. Each set of measurements was performed with 3 reagent Lots. LoD was calculated from the formula  $LoD = LoB + 1.654 * SD$ .

LoQ: The LoQ was calculated using a precision profile approach according to CLSI EP17-A2 procedure. For the determination of LoQ, 10 samples that span the low end of linearity were measured 5 times each day for a total of 150 measurements in 3 days with 3 Reagent Lots. The LoQ level was determined from the concentration that generated  $\leq 20\%$  CV.

The results are summarized in the table below:

| Device          | Sample Matrix | LoB (mg/dL) | LoD (mg/dL) | LoQ (mg/dL) |
|-----------------|---------------|-------------|-------------|-------------|
| CHOLESTEROL     | Serum         | 2.5         | 4.4         | 4.6         |
| HDL-Cholesterol | Serum         | 1.0         | 3.0         | 5.8         |
| LDL-Cholesterol | Serum         | 1.0         | 2.0         | 3.0         |
| TRIGLYCERIDES   | Serum         | 4.0         | 5.5         | 9.7         |

g) Assay Cut-Off:

Not applicable.

h) Stability and Calibration frequency and shelf-life confirmation;

**Calibration frequency / on-board stability –**

For the On-Board Stability and Calibration Frequency study, two (2) fresh serum pools with known analyte concentrations, and two (2) serum based commercial controls were analyzed on the Pictus 500 analyzer.

Reagents were loaded on to the Pictus P500 analyzer’s cooled reagent tray. Each reagent was calibrated at the start of each study. During the above stability studies, reagents were calibrated and 2 serum pools and 2 controls were measured in triplicate. Then the reagents were remained on the analyzer. The measurements were repeated in triplicate at regular time points to cover the claimed shelf life of the reagent (plus a 10% of this).

Reagent is calibrated at fixed time points according to calibration frequency mentioned in the relevant IFU the measured values at a time point should not exceed the 10% of initial value of the calculated mean for any concentration.

On Board stability /Calibration frequency: The un-capped on-board reagent stability claim is defined as the number of days between the start testing date and the last test day that results were within the acceptance limits. Calibration frequency is defined as the required time interval between calibrations to ensure reagent recovers values within the acceptance criteria. Limits are defined in each device’s IFU and were followed during all studies.

**Results were as follows:**

| Device          | On-Board Stability (days) | Calibration Frequency (days) |
|-----------------|---------------------------|------------------------------|
| CHOLESTEROL     | 28                        | 14                           |
| HDL-Cholesterol | 28                        | 28                           |
| LDL-Cholesterol | 28                        | At new lot                   |
| TRIGLYCERIDES   | 28                        | 28                           |

**2. Comparison Studies:**

**a. Method Comparison with Predicate Device:**

Performance of the CHOLESTEROL and TRIGLYCERIDES reagents for serum assayed on the Pictus P500 analyzer was compared with the comparator methods, Beckman Coulter reagents assayed on the Beckman Coulter AU400 analyzer. Performance of the HDL-Cholesterol and LDL-Cholesterol reagents assayed on the Pictus P500 analyzer was compared with the comparator methods, Abbott Diagnostics reagents on the ABBOTT Architect c8000 analyzer.

A minimum of 75 left over specimens, spanning the dynamic ranges, were assayed in singleton and in a blinded fashion on the candidate and predicate systems. Between 93-162 human serum samples were tested in a single measurement on the candidate and predicate systems using at least three lots of Medicon Hellas reagents. Less than 10% of samples were spiked or diluted to cover the analytical measurement ranges. Results were tabulated and evaluated using Analyse-it statistics calculator software to generate Passing-Bablok regression statistics for Cholesterol, HDL-Cholesterol, LDL-Cholesterol and Triglycerides.

The summary of the results for a representative lot are provided in the table below:

| Device          | Sample Matrix | N   | Sample concentration range tested | Slope  | Intercept | R <sup>2</sup> |
|-----------------|---------------|-----|-----------------------------------|--------|-----------|----------------|
| CHOLESTEROL     | Serum         | 93  | 44 – 666 mg/dL                    | 0.9769 | 5.098     | 0.999          |
| HDL-Cholesterol | Serum         | 141 | 6 – 177 mg/dL                     | 1.0180 | -0.028    | 0.997          |
| LDL-Cholesterol | Serum         | 107 | 5 – 721 mg/dL                     | 0.9821 | 1.750     | 0.999          |
| TRIGLYCERIDES   | Serum         | 163 | 26 – 975 mg/dL                    | 0.9774 | 2.041     | 0.999          |

**b. Matrix Comparison:**

Not applicable.

### 3. Expected Values / Reference Range:

The following reference ranges, cited from the scientific literature<sup>1</sup>, were included in the labeling.

| Analyte         | Sample Matrix | Reference Range   |
|-----------------|---------------|---|
| Cholesterol     | Serum         | Desirable < 200 mg/dL<br>Borderline 200-239 mg/dL<br>Abnormal ≥ 240 mg/dL   |
| HDL-Cholesterol | Serum         | Low Risk: HDL-C ≥ 60 mg/dL<br>High Risk: HDL-C ≤ 40 mg/dL   |
| LDL-Cholesterol | Serum         | Optimal: < 100 mg/dL<br>Near optimal/above optimal: 100 – 129 mg/dL<br>Borderline high risk: 131 – 159 mg/dL<br>High risk: 160 – 189 mg/dL<br>Very high risk: ≥ 190 mg/dL |
| Triglycerides   | Serum         | Normal: < 150mg/dL<br>Borderline high: 150 – 199 mg/dL<br>High: 200 – 499 mg/dL<br>Very high: ≥ 500 mg/dL   |

### CONCLUSION

The summary includes the conclusions drawn from the nonclinical and clinical tests (discussed above) that demonstrate that the device is as safe, as effective, and performs as well as or better than the predicate device.

<sup>1</sup> National Cholesterol Education Program. Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). National Institutes of Health, National Heart, Lung, and Blood Institute, NIH Publication No. 01-3670 May 2001