CLIA Waiver by Application

Approval Determination Decision Summary

A. Document Number

CW170010

B. Parent Document Number

k163406

C. Purpose of the Submission

CLIA waiver application for the Mission Cholesterol Pro Monitoring System

D. Sample Type

Fingertip capillary whole blood and lithium heparin venous whole blood

E. Type of Test or Tests Performed

Quantitative, enzymatic assays by reflectance measurement for total cholesterol, high density lipoprotein (HDL) cholesterol, and triglycerides. Low density lipoprotein (LDL) cholesterol is calculated.

F. Applicant

ACON Laboratories Inc.

G. Proprietary and Established Names

Mission Cholesterol Pro Monitoring System

H. Test System Description

The Mission Cholesterol Pro Monitoring System is a portable system consisting of the Mission Cholesterol Pro Meter, Mission Cholesterol Pro Test Cartridge, Mission Cholesterol Optical Verifier, Mission Cholesterol Control solution, code chip, optional printer, safety lancet, carrying case, and capillary transfer tube.

The product labeling includes a User's Manual, Quick Reference Guide, test cartridge package insert, controls package insert, printer package insert, meter kit box, test cartridge box, meter serial number label, test cartridge pouch label, optical verifier package insert, optical verifier box label, and optical verifier canister label.

I. Demonstrating "Simple"

- The Mission Cholesterol Pro Monitoring System consists of a Mission Cholesterol Pro Meter and a self-contained, single use test cartridge.
- The Mission Cholesterol Pro Monitoring System uses direct, unprocessed whole blood specimens; i.e. venous and capillary.
- The Mission Cholesterol Pro Monitoring System requires no specimen manipulation.
- The Mission Cholesterol Pro Monitoring System requires no reagent manipulation.
- The Mission Cholesterol Pro Monitoring System requires no operator intervention during the analysis steps.
- The Mission Cholesterol Pro Monitoring System requires no technical or specialized training with respect to troubleshooting. Error messages displayed on the meter are unambiguously identifiable as errors, and the User's Manual includes solutions to each error.
- The Mission Cholesterol Pro Monitoring System requires no electronic or mechanical maintenance. Maintenance of the meter consists of general external cleaning, disinfection, and replacing the batteries.
- The Mission Cholesterol Pro Monitoring System provides direct readout of quantitative results, i.e., requires no calculation or conversion by the operator.
- The Mission Cholesterol Pro Monitoring System includes a Quick Reference Guide and User's Manual that are written at a reading level no higher than 7th grade.

J. Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-safe Mechanisms

1. Risk Assessment

   Following the two-tiered approach recommended in the FDA's *Guidance for Industry and FDA staff: Recommendations for Clinical Laboratory Improvement Amendments (CLIA) of 1988 Waiver Application for Manufacturers of In Vitro Diagnostics Devices*, a comprehensive risk analysis was conducted for the Mission Cholesterol Pro Monitoring system as a part of risk management process to demonstrate that the device is robust and has appropriate and effective risk control measures. The risk analysis was conducted per *ISO 14971:2012 - Medical Devices - Application of Risk Management to Medical Devices*. All risks of harm to the patient or operator were mitigated to an acceptable level, and were supported by flex studies and/or operator instructions.

2. Fail-Safe and Failure Alert Mechanisms

   a. Design of Fail-Safe and Failure Alert Mechanisms

      <u>Power on diagnostic test:</u> Mission Cholesterol Pro Monitoring system performs a power on diagnostic check. During this self-test, the meter performs various checks

including those for program errors or mechanical damage (E-0 error), temperature limits, battery check (E-4 error), and LED check (E-1 error). If any of the system checks fail, then the meter will prompt an error and a lock-out function is triggered.

E-1 error message: The Mission Cholesterol Pro monitoring system detects if the sensor area is damaged, dirty, blocked at power-on, or if a used test cartridge is inserted into the meter. Under any of these conditions, the meter displays an E-1 error message and a lock-out function is triggered.

Battery check: Mission Cholesterol Pro monitoring system is designed to detect low battery power. A battery icon on the display indicates that the meter batteries are low but have enough power to run 20 more tests. When batteries are discharged, the meter displays an E-4 error message.

E-6 error message: Mission Cholesterol Pro Monitoring system includes a function that prevents the output of incorrect test results when an expired test cartridge is used and displays an E-6 error message.

Code chip error message: The Mission Cholesterol Pro monitoring system detects if the code chip is missing, damaged, or inserted incorrectly, and displays a signal of three dashes.

Monitor of environmental conditions: When the ambient room temperature is below 15°C or higher than 40°C, the meter will display “LO.t” or “HI.t”, and a lock-out function is triggered.

Internal procedural controls: The Mission Cholesterol Pro Monitoring System includes various controls during the testing procedure:

- Detects insufficient specimen volume and displays an E-5 error message.
- Detects if the specimen was applied too soon and displays an E-3 error message.
- Detects if the test cartridge is removed during the test and displays an E-2 error message.
- Detects if the code chip is removed during the test and displays an E-7 error message.

Summary of error codes:

Error Condition	Display
Power On self-check error. The meter is damaged; data saved in memory is corrupted.	E-0
The sensor area is damaged, dirty, blocked at power-on, or a used test cartridge is inserted into the meter.	E-1
Test strip was removed during the test.	E-2
Blood was applied to cartridge before prompt.	E-3
Battery voltage low, 3.7V	Battery Symbol 
Battery discharged, ≤ 3.6V	E-4 and Battery Symbol
Insufficient sample volume.	E-5
Expired test cartridge.	E-6
Removed the code chip before testing finished.	E-7
Temperature is too high.	HI.t
Temperature is too low.	LO.t
No code chip in the meter, code chip is damaged, code chip is inserted incorrectly, or wrong code chip type is inserted.	- - -

b. Control Material.

External control material: User's Manual and Quick Reference Guide recommend using only the Mission Cholesterol Pro control solution with the meter.

i. Frequency recommendation - User's manual and Quick Reference Guide include the following recommendations: Conduct Control Solution Testing using quality controls under the following circumstances:

- Each new day of testing
- When a new box of test cartridges is opened
- When a new operator uses the meter
- When test results seem inaccurate
- After performing the meter maintenance (replacing batteries, general cleaning, and disinfection).
- After any service was performed on the meter

ii. Directions for use - Quick Reference Guide provide basic instructions for use of the external control material, and refers to the User's Manual for instruction for use of the external control material.

iii. Storage and stability - From the User's Manual and Quick Reference Guide:

- Store the control solution either refrigerated or at room temperature (36 - 86°F, 2 - 30°C).
- Use before the expiration date shown on the bottle.
- Control solution will expire 4 months after opening the bottle. Record the date that each bottle was opened on the bottle label.

iv. Number of levels - Two concentrations for total cholesterol, HDL cholesterol, and triglycerides.

v. Manufacturer - ACON Laboratories

Electronic controls: The Mission Cholesterol Pro Monitoring System includes an optical verifier as a check of the optical detection system. The optical verifier is a cartridge with a grey pad. When inserted into the meter, the reflectance intensity of the grey pad is measured and compared to the expected/correct range of the reflectance intensity.

i. Frequency recommendation - User's Manual and Quick Reference Guide include the following information: the optical verifier test be run under the following circumstances:

- When the meter is being used for the first time
- Each new day of testing
- If the meter is dropped, damaged or becomes wet
- When the results seem inconsistent or inaccurate
- After the cleaning or disinfection process

ii. Directions for use - the User's Manual and Quick Reference Guide provide basic instructions for testing the meter with the optical verifier. If the test fails, the meter is not functioning properly and a 'no' is displayed. The instructions provide actions for the untrained operator when the test fails – conduct routine cleaning of the test cartridge holder, repeat the test with a new optical verifier, or call customer support.

iii. Storage and stability - from the User's Manual and Quick Reference Guide:

- Store verifier in closed canister at temperatures between 36 - 86 ºF (2 - 30 ºC) with less than 90% humidity.
- Keep the verifier out of direct sunlight.
- Place the verifier back in the canister after each use.
- The verifiers will expire 12 months after opening. Record the date that the canister was first opened on the label.

iv. Number of levels - one.

v. Manufacturer - ACON Laboratories

c. Flex Studies and Studies for Fail-Safe and Failure Alert Mechanisms

Flex study - temperature of the specimen

A flex study was conducted to assess the effect of testing a specimen outside of the temperature operating conditions; e.g., testing a specimen taken immediately from refrigeration, 2-8°C. The product labeling instructs the operator to allow the specimen to come to operating temperature (59-104 °F or 15-40 °C) for approximately 15 minutes prior to testing. For the study, whole blood specimens were stored at refrigeration (2-8°C) for 1 hour and then tested immediately after taking out of the refrigerator. Lithium heparin venous whole blood samples with total cholesterol at 225 mg/dL, HDL at 55 mg/dL, and triglycerides at 230 mg/dL were tested in 5 replicates at each condition. The study found that the test results relative to the comparator method were not affected when the blood specimen was tested immediately after refrigerated storage.

Flex study - temperature of the test cartridge

A flex study was conducted to investigate the effect of using a test cartridge outside of the temperature operating conditions; i.e., use of a test cartridge taken immediately from refrigeration, 2-8°C. The product labeling instructs the operator to allow the test cartridge to reach operating temperature (59-104ºF, 15-40ºC) prior to use. The testing was performed using one meter and one lot of test cartridges across two conditions – (1) stored in the refrigerator, 2-8°C for 1 hour and (2) store at room temperature, 23°C-25°C. The test cartridges were run immediately after taking out of the refrigerator. Lithium heparin venous whole blood samples with total cholesterol at 225 mg/dL, HDL at 55 mg/dL, and triglycerides at 230 mg/dL were tested in 5 replicates at each condition. The results of the flex study found significant bias if the cartridge was used immediately after removing from the refrigerator. To mitigate the risk of erroneous result due to use of a cold refrigerated test cartridge, the product labeling instructs the operator to store test cartridges at room temperature (59-86ºF, 15-30°C).

Flex study - humidity operating range

A flex study was conducted to assess the impact on the test results when the system was operated outside of the humidity operating range; i.e. 15% and 95% RH. The claimed humidity operating range for the system is 20 to 90% RH. Two lithium heparin venous whole blood samples with total cholesterol at 150 and 350 mg/dL, HDL at 30 and 80 mg/dL, and triglycerides at 120 and 450 mg/dL were tested in 5 replicates at each concentration on each of three cartridge lots (n=15) at room temperature (23°C-25°C) and humidity's of 15%, 50%, and 95% RH. The study found that test results relative to the comparator method were not affected when the system was operated at 15% RH or 95% RH.

Flex study - specimen mixing by inversion

A flex study was conducted to evaluate specimen mixing by inversion as an alternative to mixing using the tube roller/rocker machine due to situations when a CLIA waived laboratory does not have a roller/rocker machine. The product labeling instructs the operator to mix venous specimens using a tube roller/rocker machine. The instructions also provide an alternative mixing method - a manual inversion method may be used by inverting the tube at least 10 times. For the study, lithium heparin blood collection tubes (total cholesterol at 225 mg/dL, HDL at 55 mg/dL, and triglycerides at 230 mg/dL) were manually inverted for 5, 10, 20, 30 times, and then immediately tested in replicates of four at each condition using the Mission Cholesterol Pro Monitoring System. The study found that test results relative to the comparator method were not affected when mixing the venous specimen by manual inversion of the blood collection tube between 5 and 30 times.

Flex study - specimen mixing time and testing time

A flex study was conducted to evaluate the effect of specimen mixing time and time after mixing on the performance of Mission Cholesterol Pro Monitoring System. The product labeling instructs the operator to mix venous specimens for 15 minutes before testing using a tube roller/rocker machine, and then test the specimen within 5 minutes. Fresh venous whole blood (total cholesterol at 225 mg/dL, HDL at 55 mg/dL, and triglycerides at 230 mg/dL) that was collected into a lithium heparin blood collection tube was mixed for different times using a roller/rocker machine followed by testing at different time points after mixing. The specimen was mixed for 5 minutes, 10 minutes, 15 minute, 20 minutes and 30 minutes, and then tested using the Mission Cholesterol Monitoring System at 5, 10, 13, 15, and 30 minutes in replicates of four for each condition. The study found that the test results relative to the comparator method were not affected by mixing of venous whole blood for 5 to 30 minutes when using roller/rocker machine or when performing testing within 5 to13 minutes.

Flex study - test cartridge drop study

A flex study was conducted to validate the integrity and performance of the Mission Cholesterol Pro Test Cartridges after being dropped onto a floor. The product labeling instructs the operator to discard damaged test cartridges. The testing comprised a 6.5 foot (2 meters) drop test of 5 test cartridges onto the floor (test height is higher than the normal expected height when an operator drops a test cartridge.) Following the drop test, each cartridge was tested with whole blood samples (total cholesterol at 117 mg/dL, HDL at 47 mg/dL, and triglycerides at 116 mg/dL) with a Mission Cholesterol Pro meter. The study found that after a drop of 6.5 feet to the floor, there was no physical damage or disassembly of the test cartridge and the test results relative to the comparator method were not affected.

Meter drop test

A meter drop test was conducted to demonstrate that the Mission Cholesterol Pro meter meets the requirements of *EN15197 section 6.10.2 Mechanical Resistance to*

Shock, Vibration and Impact: Drop Test. Data that supported robustness to drop were reviewed in k163406.

Flex study - test cartridge open pouch

A flex study was conducted to investigate the impact on the assay performance if the test cartridge was not used immediately after opening the foil pouch. The product labeling instructs the operator to open the pouch only for immediate use. Testing was performed using a lithium heparin whole blood sample at one concentration of total cholesterol (117 mg/dL), HDL cholesterol (47 mg/dL), and triglycerides (116 mg/dL) in replicates of five. The test cartridge was opened and placed in the ambient environment for the durations of <1 min, 5 min, 30 min, 60 min, 4 hour, 8 hour, and 24 hour. The study found that the test results relative to the comparator method were not affected when leaving the test cartridge pouch open from less than 1 minute to 24 hours.

Flex study - sample volume / operator applies blood directly to test cartridge

A flex study was conducted to investigate the effect on the performance of the Mission Cholesterol Pro Monitoring System when operator directly applies blood to the test cartridge instead of using a capillary transfer tube. The product labeling instructs the operator to apply blood to the cartridge using the capillary transfer tube, and instructs to never apply fingertip blood specimen directly onto the test cartridge. When operator applies blood to the test cartridge without using capillary tubes, the consequence is that the volume may be significantly greater or smaller than the target volume of 35 µL. Therefore, two flex studies (testing volumes below 35 µL and volumes above 35 µL) were conducted to assess the robustness of the system to variability in sample volume. For low sample volumes (i.e. < 35 µL), a previous sample volume flex study with test volumes from 15 to 35 µL, found that either an E5 error was reported or there was no effect on the final reading (see study for E-5 error message). The study was reviewed to support clearance of the device in k163406.

An additional flex study was conducted to assess the robustness of the system for samples volumes > 35 µL; simulating the application of excess blood to the test cartridge without a capillary transfer tube. In the study, whole blood specimens were spiked to concentrations of 117 mg/dL total cholesterol, 47 mg/dL HDL cholesterol and 116 mg/dL triglycerides. Whole blood volumes of 35, 50, 60, 75 and 100 µL were applied to separate test cartridges. Five cartridges were tested for each sample volume with the Mission Cholesterol Pro Monitoring System. The study found that the test results relative to the comparator method were not affected by sample volumes from 35 to 50 µL.

Error messages

The error messages displayed by the meter were previously reviewed in k163406 to verify that the error messages were generated and display as designed.

Test cartridge storage stability
The storage stability of the Mission Cholesterol Pro Test Cartridges in foil pouches was assessed in a real-time stability study. The product labeling instructs the operator to store the test cartridge at room temperature (temperature range of 36-86ºF). Data that supported this claim were reviewed in k163406.

Sample storage time
A study was conducted to assess the effect of venous blood storage time on the test results. The product labeling instructs the operator to use fresh capillary blood or venous whole blood collected in lithium heparin tubes, and that for venous blood specimens must be tested within 8 hours of collection. Data that supported this claim were reviewed in k163406.

Contamination of meter by specimens from multiple patients
Meter virucidal efficacy and disinfection robustness studies were conducted to establish that the recommended cleaning and disinfection procedures in the user manual are sufficient. Data that supported this claim were reviewed in k163406.

Temperature study
A study was conducted to demonstrate that when the ambient room temperature is below 15°C or higher than 40°C, the meter displayed "LO.t" or "HI.t", and was disabled so to not conduct a measurement. The product labeling instructs the user to not use the unit or the cartridges outside of the operating temperature range of 15 - 40 °F (59 - 104 °C). Data that supported this claim were reviewed in k163406.

Readings outside of reportable range
Bench studies and software verification studies were conducted to demonstrate that if the total cholesterol, HDL cholesterol, or triglycerides measurement was less than the lower end of the analytical measurement range, a '<' indicator was displayed preceding the lower limit; e.g. <100 mg/dL for total cholesterol. If a measurement exceeded the upper end of the analytical measurement range a '>' indicator was displayed preceding the upper limit; e.g. >400 mg/dL for total cholesterol. Data that supported this claim were reviewed in k163406.

LDL cholesterol
A software verification study was conducted to demonstrate that the reported LDL concentration is calculated according to the Friedewald equation when the triglycerides concentration is ≤ 400 mg/dL. A software verification study was also conducted to demonstrate that if the triglycerides concentration is > 400 mg/dL, the LDL cholesterol result will not be calculated, and the meter will display "--". Data that supported this claim were reviewed in k163406.

Ambient room light effects testing
A study was conducted to demonstrate that the Mission Cholesterol Pro Monitoring System performance is not susceptible to ambient room light variations. The product

insert instructs the operator to keep the system out of direct sunlight. Data that supported this claim were reviewed in k163406.

Code chip detection test
A test was conducted to verify that the meter can read the correct code on the code chip. Data that supported this claim were reviewed in k163406.

Drop volume study of lipid control dropper bottle
A study was conducted to assess the variability of the drop volume of the control dropper bottle. The nominal volume of a drop of control solution is 35 µL. Data demonstrating acceptable sample volume variability were reviewed in k163406.

Sample volume effects on control solution
A study was conducted to evaluate the effect of sample volume variability on the cholesterol control solution test results. Data demonstrating acceptable control solution volume variability were reviewed in k163406.

Cholesterol meter sample contamination testing
A study was conducted to verify that the meter test area is not contaminated when excess volume of blood sample (80 µL) is applied into the strip. Data that supported this claim were reviewed in k163406.

K. Demonstrating "Insignificant Risk of an Erroneous Result" (Accuracy)

To demonstrate that the Mission Cholesterol Pro Monitoring System poses an insignificant risk of erroneous results, the sponsor submitted a clinical study which was also used to support FDA clearance under k163406.

1. Clinical Study Design

The purpose of the clinical study was to evaluate the accuracy of the Mission Cholesterol Pro Monitoring System when operated by intended operators in sites representative of CLIA waived laboratories compared to a type B comparator (traceable calibration method) operated by a laboratory professional.

Clinical study sites: The clinical study was conducted at three physician offices which perform waived testing.

Operators: Eleven operators participated in the clinical study of the Mission Cholesterol Pro Monitoring System. The operators selected for the study were representative of operators in a CLIA waived setting and were untrained in the use of the Mission Cholesterol Pro Monitoring System.

Instructions for use: The operators were given the meter, test cartridges, Quick Reference Guide, and User's Manual. No other materials or instructions were provided, and the operators received no training on the use of the system.

Subject/patients: A total of 369 patients were recruited for the study. Study subjects were representative of the intended use population. Patient inclusion/exclusion criteria were as follows:

- Any subject 18 years and older is eligible for inclusion in this study.
- Subjects with conditions involving excessive water loss/severe dehydration will not be eligible for inclusion in this study.

No contrived or altered samples were tested in the clinical study.

2. Comparative Method (CM)

The comparator methods were quantitative traceable calibration methods for total cholesterol, HDL cholesterol and triglycerides performed in laboratories by professional laboratorians.

3. Allowable Total Error (ATE) and Limit of Erroneous Results (LER)

The allowable total error (ATE) and Limit of Erroneous Results (LER) for the waived method (WM) each analyte are given in the table below.

Analyte	ATE	LER
Total cholesterol	± 8.9%	• CM values <200 mg/dL, and WM values ≥240 mg/dL • CM values between 200 and 239 mg/dL, WM values are outside CM ±14.9% • CM values ≥240 mg/dL, and WM values <200 mg/dL
HDL cholesterol	± 13%	• CM values <40 mg/dL, and WM values ≥60 mg/dL • CM values between 40 and 59 mg/dL, WM values are outside CM ±25% • CM values ≥60 mg/dL, and WM values <40 mg/dL
Triglycerides	± 15%	• CM values <150 mg/dL, and WM values ≥200 mg/dL • CM values between 150 and 199 mg/dL, WM values are outside CM ±25% • CM values ≥200 mg/dL, and WM values <150 mg/dL

4. Data Analysis of the Clinical Study

For each analyte, the following data analyses were performed:

- Descriptive statistics - for both the WM and CM, including concentration mean, standard deviation, minimum, median, and maximum.

- Total Analytical Error as a percent relative difference from the CM was derived using the central 95% region of the distribution of relative differences between WM and CM; with low and high limits set at the 2.5th and 97.5th percentiles as per *Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures. 2nd ed. CLSI guideline EP21. Wayne, PA: Clinical and Laboratory Standards Institute; 2016.*

- Deming regression analysis is given along with 95% confidence intervals.

- Predicted bias at medical decision points - calculated as the percent difference between the Deming regression line and the unity line at each medical decision point.

- Allowable Total Error

- Limits of Erroneous Result

Total cholesterol

Descriptive statistics:

All sites combined

	N	**Mean**	**SD**	**Minimum**	**Median**	**Maximum**
CM	367	206	54.9	105	197	389
WM, capillary	367	206	55.4	101	197	379
WM, venous	367	204	54.7	102	196	392

Total Analytical Error (TAE):

Capillary

Group	**Range (mg/dL)**	**N**	**low TAE limit**	**high TAE limit**
Desirable	< 200	194	-6.2%	5.8%
Borderline high	200 - 239	90	-5.6%	6.3%
High	≥ 240	83	-5.8%	6.3%
Entire range	100 - 389	367	-6.0%	6.0%

Venous

Group	Range (mg/dL)	N	low TAE limit	high TAE limit
Desirable	< 200	194	-6.5%	6.0%
Borderline high	200 - 239	90	-5.2%	6.0%
High	≥ 240	83	-8.6%	4.0%
Entire range	100 - 389	367	-6.5%	5.4%

Regression analysis:

All sites combined

Specimen	Slope (95% CI)	Intercept (95% CI)	R^2	Range
Capillary	1.008 (0.996 to 1.019)	-1.7 (-4.1 to 0.7)	0.988	101 - 379 mg/dL
Venous	0.996 (0.984 to 1.008)	-0.6 (-3.2 to 2.0)	0.986	102 - 392 mg/dL

Regression analysis for each clinical study site data was performed and the results found to be similar across all sites.

Predicted bias at medical decision points:

	Predicated bias at medical decision points, (95% CI)	
Specimen	**200 mg/dL**	**240 mg/dL**
Capillary	-0.1% (-0.5% to 0.2%)	0.0% (-0.3% to 0.3%)
Venous	-0.7% (-1.1% to -0.4%)	-0.7% (-1.0% to -0.3%)

Allowable Total Error:

The clinical study found that greater than 95% of all results for total cholesterol were within the ATE zone (±8.9%). The results are presented in the tables below:

Capillary

Group	Range (mg/dL)	Within ATE zone
Desirable	< 200	99.5% (196/197)
Borderline high	200 - 239	100% (90/90)
High	≥ 240	100% (83/83)
Entire range	101 - 379	99.7% (366/367) 95% CI: 98.5% to 99.95%

Venous

Group	Range (mg/dL)	Within ATE zone
Desirable	< 200	100% (197/197)
Borderline high	200 - 239	100% (90/90)
High	≥ 240	100% (83/83)
Entire range	102 - 392	100% (367/367) 95% CI: 99.0% to 100.0%

Limits of Erroneous Results (LER):

The clinical study found no total cholesterol values within the LER zones across the low, medium, and high ranges of the CM (capillary specimens: 0% (0/367) with 95% CI: 0% to 1.04% and for venous specimens: 0% (0/367) with 95% CI: 0% to 1.04%).

HDL cholesterol

Descriptive statistics:

All sites combined

	N	Mean	SD	Minimum	Median	Maximum
CM	369	50	17.5	16	48	118
WM, capillary	362	49	16.2	15	47	99
WM, venous	364	50	16.4	15	48	100

Total Analytical Error (TAE):

Capillary

Group	Range (mg/dL)	N	low TAE limit	high TAE limit
Low	< 40	118	-13.6%	11.1%
Mid	40 - 59	161	-9.4%	9.1%
High	≥ 60	83	-7.5%	8.3%
Entire range	15 - 100	362	-10.9%	9.1%

Venous

Group	Range (mg/dL)	N	low TAE limit	high TAE limit
Low	< 40	118	-6.5%	14.8%
Mid	40 - 59	161	-7.3%	12.2%
High	≥ 60	85	-8.7%	9.4%
Entire range	15 - 100	364	-7.1%	12.2%

Regression analysis:

All sites combined

Specimen	Slope	Intercept	R^2	Range
Capillary	1.013 (0.997 to 1.029)	-0.7 (-1.5 to 0.1)	0.978	15 - 99 mg/dL
Venous	1.004 (0.988 to 1.019)	0.5 (-0.3 to 1.3)	0.979	15 - 100 mg/dL

Regression analysis for each clinical study site data was performed and the results found to be similar across all sites.

Predicted bias at medical decision points:

	Predicated bias at medical decision points, (95% CI)	
Specimen	**40 mg/dL**	**60 mg/dL**
Capillary	-0.5% (-1.3% to 0.3%)	0.0% (-0.5% to 0.7%)
Venous	3.0% (1.8% to 4.5%)	2.2% (1.3% to 3.0%)

Allowable Total Error:

The clinical study found that greater than 95% of all results for HDL cholesterol were within the ATE zone (±13%). The results are presented in the tables below:

HDL cholesterol - Capillary

Group	Range (mg/dL)	Within ATE zone
Low	< 40	96.6% (114/118)
Mid	40 - 59	98.7% (159/161)
High	≥ 60	100% (83/83)
Entire range	15 - 99	98.3% (356/362) 95% CI: 96.4% to 99.2%

Venous

Group	Range (mg/dL)	Within ATE zone
Low	< 40	96.6% (114/118)
Mid	40 - 59	97.5% (157/161)
High	≥ 60	100% (85/85)
Entire range	15 - 100	97.8% (356/364) 95% CI: 95.7% to 98.9%

Limits of Erroneous Results (LER):

The clinical study found no HDL cholesterol values within the LER zones across the low, medium, and high ranges of the CM (capillary specimens: 0% (0/362) with 95% CI: 0% to 1.05% and for venous specimens: 0% (0/364) with 95% CI: 0% to 1.04%).

Triglycerides

Descriptive statistics:

All sites combined

	N	Mean	SD	Minimum	Median	Maximum
CM	369	144	108.4	38	110	709
WM, capillary	357	144	101.3	45	113	616
WM, venous	355	142	100.8	45	109	596

Total Analytical Error:

Capillary

Group	Range (mg/dL)	N	low TAE limit	high TAE limit
Normal	< 150	243	-10.3%	13.6%
Borderline high	150 - 199	43	-7.5%	9.3%
High	200 - 499	64	-10.0%	14.0%
Very high	≥ 500	7	-7.5%*	6.3%*
Entire range	45 - 637	357	-10.1%	12.9%

Venous

Group	Range (mg/dL)	N	low TAE limit	high TAE limit
Normal	< 150	241	-12.5%	8.9%
Borderline high	150 - 199	43	-9.1%	7.7%
High	200 - 499	64	-9.4%	11.8%
Very high	≥ 500	7	-9.6%*	4.5%*
Entire range	45 - 637	355	-12.1%	8.9%

*Due to only 7 samples in this range, the TAE is calculated as average ±1.96SD.

Regression analysis:

All sites combined

Specimen	Slope	Intercept	R^2	Range
Capillary	0.999 (0.992 to 1.007)	0.6 (-0.8 to 1.9)	0.995	45 - 616 mg/dL
Venous	0.993 (0.985 to 1.002)	-1.7 (-3.1 to -0.2)	0.994	45 - 596 mg/dL

Regression analysis for each clinical study site data was performed and the results found to be similar across all sites.

Predicted bias at medical decision points:

	Predicated bias at medical decision points, (95% CI)		
Specimen	**150 mg/dL**	**200 mg/dL**	**500 mg/dL**
Capillary	0.3% (-0.2% to 0.8%)	0.2% (-0.3% to 0.7%)	0.0% (-0.5% to 0.6%)
Venous	-1.8% (-2.3% to -1.2%)	-1.5% (-2.0% to -1.0%)	-1.0% (-1.6% to -0.4%)

Allowable Total Error:

The clinical study found that greater than 95% of all results for triglycerides were within the ATE zone (±15%). The results are presented in the tables below:

Capillary

Group	Range (mg/dL)	Within ATE zone
Normal	< 150	97.5% (237/243)
Borderline high	150 - 199	100% (43/43)
High	200 - 499	98.4% (63/64)
Very high	≥ 500	100% (7/7)
Entire range	45 - 616	98% (350/357) 95% CI: 96.0% to 99.0%

Venous

Group	Range (mg/dL)	Within ATE zone
Normal	< 150	98.7% (238/241)
Borderline high	150 - 199	100% (43/43)
High	200 - 499	100% (64/64)
Very high	≥ 500	100% (7/7)
Entire range	45 - 596	99.1% (352/355) 95% CI: 97.5% to 99.7%

Limits of Erroneous Results (LER):

The clinical study found no triglycerides values within the LER zones across the low, medium, and high ranges of the CM (capillary specimens: 0% (0/357) with 95% CI: 0% to 1.06% and for venous specimens: 0% (0/355) with 95% CI: 0% to 1.07%).

Calculated LDL cholesterol

The clinical study results for calculated LDL cholesterol were assessed using a comparator method also based on calculated LDL. The total analytical error was within the ±12% total error goal recommended by NCEP (National Cholesterol Education Program - Working Group on Lipoprotein Measurement).

5. Questionnaire Results

Upon completion of the clinical study, each operator completed a questionnaire to rate the ease of use of the test procedure. The participants found Mission Cholesterol Pro Monitoring System clear and easy to follow.

L. Labeling for Waived Devices

- The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.
- The Quick Reference Guide and User's Manual are written at no higher than a 7th grade reading level.

- The User’s Manual and Quick Reference Guide identify the test as CLIA waived.

- The User’s Manual and test cartridge package insert contain a statement that a Certificate of Waiver is required to perform the test in a waived setting.

- The test cartridge package insert contains information on how operators may obtain a Certificate of Waiver.

- The User’s Manual and Quick Reference Guide contain a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test. 42 CFR 493.15(e)(1).

- The User’s Manual and Quick Reference Guide provide instructions for conducting quality control procedures.

M. Conclusion

The submitted information in this CLIA waiver application is complete and supports a CLIA waiver approval decision.