DiaSorin Inc.
Emily Peterson
Principal Regulatory Affairs Specialist
1951 Northwestern Avenue
Stillwater, Minnesota 55082

July 14, 2022

Re: K213936
Trade/Device Name: LIAISON MeMed BV, LIAISON MeMed BV Control Set
Regulation Number: 21 CFR 866.3215
Regulation Name: Device To Detect And Measure Non-Microbial Analyte(s) In Human Clinical Specimens To Aid In Assessment Of Patients With Suspected Sepsis
Regulatory Class: Class II
Product Code: QPS
Dated: December 15, 2021
Received: December 16, 2021

Dear Emily Peterson:

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,

Noel J. Gerald, Ph.D.
Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K213936

Device Name
LIAISON MeMed BV
LIAISON MeMed BV Control Set

Indications for Use *(Describe)*
The DiaSorin LIAISON® MeMed BV® is an automated in vitro diagnostic semi-quantitative assay that uses chemiluminescent immunoassay (CLIA) technology to measure three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection. The LIAISON® MeMed BV® assay is indicated for use in patients presenting to the emergency department or urgent care center and with samples collected at hospital admission from patients with suspected acute bacterial or viral infection, who have had symptoms for seven days or less. The LIAISON® MeMed BV® assay generates a numeric score that falls within discrete interpretation ranges based on the increasing likelihood of bacterial infection. The assay has to be performed on the automated LIAISON® XL Analyzer.

The DiaSorin LIAISON® MeMed BV® Control Set is intended for use as assayed quality control to monitor the performance of the DiaSorin LIAISON® MeMed BV® assay. The performance characteristics of the LIAISON® controls have not been established for any other assays or instrument platforms different from the automated LIAISON® XL Analyzer. The control set is intended for in vitro diagnostic use in a professional laboratory only.

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

SUBMITTED BY: Emily Peterson

DiaSorin Inc.
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Stillwater, MN 55082-0285
Phone (651) 351-5628
Fax (651) 351-5669
Email emily.peterson@diasorin.com

NAME OF DEVICE:

Trade Name:	LIAISON® MeMed BV® LIAISON® MeMed BV® Control Set
Common Names/Descriptions:	LIAISON® MeMed BV® LIAISON® MeMed BV® Control Set
Classification Names:	Immunoasssay for Host Biomarkers of Infection
Product Code:	QPS QCH
Predicate Device:	MeMed BV®

INTENDED USE:

The DiaSorin LIAISON® MeMed BV® is an automated *in vitro* diagnostic semi-quantitative assay that uses chemiluminescent immunoassay (CLIA) technology to measure three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection. The LIAISON® MeMed BV® assay is indicated for use in patients presenting to the emergency department or urgent care center and with samples collected at hospital admission from patients with suspected acute bacterial or viral infection, who have had symptoms for seven days or less. The LIAISON® MeMed BV® assay generates a numeric score that falls within discrete interpretation ranges based on the increasing likelihood of bacterial infection. The assay has to be performed on the LIAISON® XL Analyzer.

The DiaSorin LIAISON® MeMed BV® Control Set is intended for use as assayed quality control to monitor the performance of the DiaSorin LIAISON® MeMed BV® assay. The performance characteristics of the LIAISON® controls have not been established for any other assays or instrument platforms different from the automated LIAISON® XL Analyzer. The control set is intended for *in vitro* diagnostic use in a professional laboratory only.

KIT DESCRIPTION:

The LIAISON® MeMed BV® assay consists of three individual chemiluminescence immunoassay (CLIA) for quantitative determination of TRAIL, IP-10, and CRP. The LIAISON® MeMed BV® test result is a score between 0 and 100 derived from computational integration of the measurements of the three proteins TRAIL, IP-10, and CRP, where low scores are indicative of viral infection and high score of bacterial infection. All three reagent packs must be the same lot and present at the same time on the same instrument used for sample testing. All three reagent packs are individually calibrated and quality controlled. Specimens are to be assigned to the MMBV assay protocol where all three reagent packs will be utilized to provide combined results and a final score.

The TRAIL reagent pack uses a monoclonal antibody for capture of TRAIL and a polyclonal antibody for the detection of TRAIL. The assay incubates sample, calibrator or control with assay buffer and paramagnetic particles coated with a monoclonal antibody that specifically recognizes the TRAIL. Following the incubation, an isoluminol conjugated polyconal antibody that recognizes TRAIL is then added to the reaction and incubated. The unbound conjugate is removed with a wash step. Starter reagents are then added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of TRAIL present in the calibrators, controls or samples. The result of the TRAIL reagent pack is only used to calculate a final LIAISON® MeMed BV® Score and should not be used individually for diagnosis.

The IP-10 reagent pack uses a monoclonal antibody for the capture of IP-10 and a polyclonal antibody for the detection of IP-10. The assay incubates sample, calibrator or control with assay buffer and paramagnetic particles coated with a monoclonal antibody that specifically recognizes the IP-10. Following the incubation, an isoluminol conjugated polyclonal antibody that recognizes IP-10 is then added to the reaction and incubated. The unbound conjugate is removed with a wash step. Starter reagents are then added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of IP-10 present in the calibrators, controls or samples. The result of the IP-10 reagent pack is only used to calculate a final LIAISON® MeMed BV® Score and should not be used individually for diagnosis.

The CRP reagent pack uses monoclonal antibodies for capture and detection of CRP. First the patient serum sample is pre-diluted 1:196 with assay buffer. The assay incubates the pre-diluted sample, calibrator or control with assay buffer and paramagnetic particles coated with a monoclonal antibody that specifically recognizes the CRP. Following the incubation, an isoluminol conjugated monoclonal antibody that recognizes CRP is then added to the reaction and incubated. The unbound conjugate is removed with a wash step. Starter reagents are then added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of CRP present in the calibrators, controls or samples. The result of the CRP reagent pack is only used to calculate a final LIAISON® MeMed BV® Score and should not be used individually for diagnosis.

SUBSTANTIAL EQUIVALENCE:

The DiaSorin LIAISON® MeMed BV® is substantially equivalent in principle and performance to the MeMed Diagnostics Ltd. MeMed BV® assay which was FDA cleared on September 01, 2021-510k K210254.

The following comparison of the use, technology, and performance presented in Table 1 supports the Statement of Equivalence between the LIAISON® MeMed BV® assay to the MeMed Diagnostics Ltd. MeMed BV® test system. The differences (presented in Table 2) in technology do not raise additional concerns regarding safety and effectiveness. Safety and effectiveness are demonstrated to be substantially equivalent.

Table 1:

Table of Similarities		
Feature	**Candidate Device** **LIAISON® MeMed BV®**	**Predicate Device** **MeMed BV® System – K210254**
Intended Use	The DiaSorin LIAISON® MeMed BV® is an automated *in vitro* diagnostic semi-quantitative assay that uses chemiluminescent immunoassay (CLIA) technology to measure three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection. The LIAISON® MeMed BV® assay is indicated for use in patients presenting to the emergency department or urgent care center and with samples collected at hospital admission from patients with suspected acute bacterial or viral infection, who have had symptoms for seven days or less. The LIAISON® MeMed BV® assay generates a numeric score that falls within discrete interpretation ranges based on the increasing likelihood of bacterial infection.	The MeMed BV® test is an automated semi-quantitative immunoassay that measures three non-microbial (host) proteins (TRAIL, IP-10, and CRP) in adult and pediatric serum samples and is intended for use in conjunction with clinical assessments and other laboratory findings as an aid to differentiate bacterial from viral infection. The MeMed BV® is indicated for use in patients presenting to the emergency department or urgent care center and with samples collected at hospital admission from patients with suspected acute bacterial or viral infection, who have had symptoms for less than seven days. The MeMed BV® test generates a numeric score that falls within discrete interpretation bins based on the increasing likelihood of bacterial infection
Results	Semi-Quantitative	Same
Measurand	three non-microbial (host) proteins (TRAIL, IP-10, and CRP)	Same
Conjugate antibody specificities	Anti-TRAIL – polyclonal antibody IP-10 – polyclonal antibody CRP – monoclonal antibody	Same
Sample type	Human serum	Same
Antigen	Recombinant TRAIL, IP-10 and CRP	Same
Measurement System	Photomultiplier (flash chemiluminescence reader)	Photomultiplier (flash chemiluminescence reader)
Output	SCORE result	Same

Table 2:

Table of Differences		
Feature	**Candidate Device LIAISON®** MeMed BV®	**Predicate Device** MeMed BV® **System – K210254**
Conjugate antibody specificities	Conjugated to an Isoluminol derivative	Conjugated to Alkaline phosphatase
Sample size	200 µL	100 µL
Assay Procedure	Automated – LIAISON® XL Analyzer	Automated – MeMed Key Analyzer
Calibration	Two levels (low and high) of calibrators for each Analyte	3 calibrators containing high, medium and low concentration of each analyte
Calibration Interval	3 weeks	2 weeks

PERFORMANCE DATA:

CLINICAL AGREEMENT

A total of 285 serum samples from patients presenting with signs and symptoms suggestive of acute bacterial or viral infection were included in the study. Study populations included samples taken at hospital admission, Emergency Department and Urgent Care Centers. Patients ranged in age from 5 months to 92 years of age with 54.7% females (156) and 45.3% males (129).
The most common clinical syndrome was respiratory tract infections (67%) which included both upper and lower respiratory tract infections.

A primary and secondary endpoint analysis were performed to establish the diagnostic performance of the LIAISON® MeMed BV® test for differentiating bacterial from viral infection in patients with suspected acute bacterial or viral infection.
Primary Endpoint Analysis: The results of the LIAISON® MeMed BV® assay were compared to physician expert adjudication. Expert adjudication was used as the comparator method. Expert adjudication was determined through the process in which physicians were forced to make a bacterial, viral, or noninfectious diagnosis with categorization of patients. Panelists for each subject adjudication were drawn from a pool of 21 international experts, who were clinicians with at least 7 years of relevant clinical experience. Each panel comprised at least three experts who independently adjudicated the etiologic label for each patient. The etiologic label of the adjudicator was based on anonymized patient data. Importantly, the adjudicators were blinded to the MeMed BV result. The adjudicators were blinded to CRT and PCT results for the primary endpoint.

The performance of the LIAISON® MeMed BV® assay in differentiating between bacterial and viral infection /non-infection was assessed using two (2) statistical tests.

- A Cochran-Armitage test (Agresti 2010) of the slope of a weighted linear regression of the proportion of bacterial samples in each bin and SCORE range, respectively.
- The likelihood ratio of the bin number/SCORE range is the ratio of the proportion of all bacterial patients who fall in that bin to the proportion of nonbacterial patients who fall in that bin.

The analysis comprised 285 Apollo specimens characterized by expert adjudicated diagnosis, by either having a bacterial infection, or not having a bacterial infection, by having either no infection or a viral one. Each patient was also scored using the LIAISON® MeMed BV® assay and the predicate assay MeMed BV®. The subjects were distributed in five (5) bins corresponding to the degree of suspicion for bacterial infection. The predicate device SCORE value for each was also analyzed.

A significant trend is demonstrated between the LIAISON® MeMed BV® SCORE and the increasing likelihood of bacterial infections across the SCORE bins. In addition, a high percentage of patients are found in the outer bins (bin 1 and 5) representing a very high likelihood of viral or bacterial infection, respectively.

Primary Endpoint Analysis

Expert Adjudication Label							
LIAISON® MeMed BV® SCORE BIN	N	Reference Bacterial (N)	Reference Viral or Non-Infectious (N)	% Patients each Bin	% Reference Bacterial Patients	% Reference Viral or Non-Infectious Patients	Likelihood Ratio of Bacterial Basis Each Bin (95% CI)
BIN 5 90 ≤ score ≤ 100 (Bacterial)	33	22	11	11.6	66.7	33.3	13.00 (7.09-25.83)
BIN 4 65 < score < 90 (Mod Bacterial)	26	8	18	9.1	30.8	69.2	2.89 (1.27-5.95)
BIN 3 35 ≤ score ≤ 65 (Equivocal)	25	6	19	8.8	24.0	76.0	2.05 (0.79-4.51)
BIN 2 10 < score < 35 (Mod Viral)	48	1	47	16.8	2.1	97.9	0.14 (0.01-0.60)
BIN 1 0 ≤ score ≤ 10 (Viral)	153	1	152	53.7	0.70	99.3	0.043 (0.002-0.180)
TOTAL	285	38	247	100			

LIAISON® MeMed BV® results were also analyzed according to a secondary endpoint format in which the adjudicators were un-blinded to PCT and CRP results. For the secondary objective cohort, each patient that did not receive a final adjudication outcome was assigned an indeterminate comparator method outcome.
Twenty eight (28) of the 285 samples were excluded. The remaining 257 were characterized by either having a bacterial or a viral infection.

The performance of the secondary endpoint for the LIAISON® MeMed BV® assay in differentiating between bacterial and viral infection /non-infection was assessed using the same two (2) statistical tests.

A significant trend is demonstrated between the LIAISON® MeMed BV® SCORE and the increasing likelihood of bacterial infections across the SCORE bins. In addition, a high percentage of patients are found in the outer bins (bin 1 and 5) representing a very high likelihood of viral or bacterial infection, respectively

Secondary Endpoint Analysis

Expert Adjudication Label							
Score Bin LIAISON® MeMed BV®	N	N Reference Bacterial	N Reference Viral / Non-Infectious	% Patients Each Bin	% Reference Bacterial Patients	% Reference Viral / Non-Infectious Patients	Bacterial Likelihood Ratio (95% CI)
BIN 5 90 ≤ score ≤ 100 (High Bacterial)	24	21	3	9.3	87.5	12.5	52.97 (19.90-214.87)
BIN 4 65 < score <90 (Mod Bacterial)	20	5	15	7.8	25.0	75.0	2.52 (0.87-5.99)
BIN 3 35 ≤ score ≤ 65 (Eqv)	23	3	20	9.0	13.0	87.0	1.14 (0.28-3.07)
BIN 2 10 < score <35 (Mod Viral)	42	0	42	16.3	0.0	100.0	0.000 (0.000-0.341)
BIN 1 0 ≤ score ≤10 (High Viral)	148	1	147	57.6	0 .70	99.3	0.051 (0.003-0.214)
TOTAL	257	30	227	100			

METHOD CORRELATION:

The LIAISON® MeMed BV® and another commercially available method were directly compared to each other using the clinical samples linked to the primary and secondary endpoint formats. Overall Agreement with 95% Confidence Intervals (Wilson Approach) and individual Bin Agreements were calculated for the Primary and Secondary Endpoints and are provided below.

Primary Endpoint Analysis

LIAISON® MeMed BV® Bin Results	Predicate Bin Results (Primary Endpoint)				
	HighVIR Bin 1	ModVIR Bin 2	Equivocal Bin 3	ModBACT Bin 4	HighBACT Bin 5
HighVIR Bin 1	146	7	0	0	0
ModVIR Bin 2	13	28	7	0	0
Equivocal Bin 3	0	12	8	5	0
ModBACT Bin 4	0	1	9	15	1
HighBACT Bin 5	0	0	0	4	29
TOTAL	159	48	24	24	30
% Bin Agreement	146/159 (91.8%)	28/48 (58.3%)	8/24 (33.3%)	15/24 (62.5%)	29/30 (96.7%)
% Overall Agreement	226/285 (79.3%) 95% CI (Wilson Approach) 74.2% - 83.6%				

Secondary Endpoint Analysis

LIAISON® MeMed BV® Bin Results	Predicate Bin Results (Secondary Endpoint)				
	HighVIR Bin 1	ModVIR Bin 2	Equivocal Bin 3	ModBACT Bin 4	HighBACT Bin 5
HighVIR Bin 1	141	7	0	0	0
ModVIR Bin 2	12	24	6	0	0
Equivocal Bin 3	0	12	6	5	0
ModBACT Bin 4	0	1	7	12	0
HighBACT Bin 5	0	0	0	3	21
TOTAL	153	44	19	18	21
% Bin Agreement	141/153 (92.2%)	24/44 (54.5%)	6/19 (31.6%)	12/20 (60.0%)	21/21 (100%)
% Overall Agreement	203/257 (79.0%) 95% CI (Wilson Approach) 73.6% - 83.5%				

EXPECTED VALUES:

To assess the expected Reference range a study was performed with 150 serum samples collected from apparently healthy asymptomatic adults who met the following inclusion criteria of no flu-like symptoms i.e. fever, chills, headache, fatigue, muscle and joint aches or swollen lymph nodes. The subjects were 65% female (98) and 35% male (52) and ranged in age from 21 – 71. Samples were collected in the Southwestern U.S.

Based on the 95% Central interval, the following values were established following CLSI guideline C28-A3.

N	Mean SCORE	Median SCORE	Observed 95% SCORE range
150	6.9	4.0	1 to 33

REPRODUCIBILITY STUDY

A 5-day reproducibility study was conducted at DiaSorin Inc. and 2 external laboratories. This study included one (1) lot of LIAISON® MeMed BV® assay which includes 3 Reagent Integral kits for TRAIL, IP-10 and CRP and two (2) LIAISON® MeMed BV® Control Sets one (1) lot for daily quality control measurement and one (1) lot as precision samples on the LIAISON® XL Analyzer at 3 sites.

The study was performed for 5 days, 1 run/day and 6 reps/run for a total of 30 replicates per site. The coded panel consisted of the kit controls and 4 serum samples representing 1 normal, 1 viral, 1 bacterial, and 1 equivocal sample.

Sample ID	Mean	Repeatability		Between Days		Within Laboratory		Between Sites		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
TRAIL	**(pg/mL)**										
KC 1	134	2.547	1.9%	8.086	6.0%	8.478	6.3%	1.961	1.5%	8.702	6.5%
KC 2	27.8	0.581	2.1%	1.654	6.0%	1.753	6.3%	0.000	0.0%	1.620	5.8%
MMBV-PREC 1	189	4.996	2.6%	3.139	1.7%	5.900	3.1%	1.246	0.7%	6.030	3.2%
MMBV-PREC-2	27.9	0.596	2.1%	0.659	2.4%	0.889	3.2%	0.691	2.5%	1.125	4.0%
MMBV-PREC-3	60.4	1.080	1.8%	0.906	1.5%	1.410	2.3%	0.000	0.0%	1.355	2.2%
MMBV-PREC-4	70.1	1.583	2.3%	0.833	1.2%	1.789	2.6%	1.076	1.5%	2.088	3.0%
IP-10	**(pg/mL)**										
KC 1	1368	26.981	2.0%	57.916	4.2%	63.893	4.7%	191.797	14.0%	202.16	14.8%
KC 2	186	4.469	2.4%	8.944	4.8%	9.999	5.4%	26.118	14.0%	27.966	15.0%
MMBV-PREC 1	815	24.295	3.0%	11.595	1.4%	26.920	3.3%	81.234	10.0%	85.578	10.5%
MMBV-PREC-2	1348	33.589	2.5%	31.736	2.4%	46.210	3.4%	151.484	11.2%	158.38	11.7%
MMBV-PREC-3	567	13.573	2.4%	11.630	2.1%	17.874	3.2%	52.525	9.3%	55.483	9.8%
MMBV-PREC-4	9698*	255.236	2.6%	117.725	1.2%	281.078	2.9%	429.209	4.4%	513.06	5.3%
CRP	**(mg/L)**										
KC 1	13.7	0.398	2.9%	0.597	4.4%	0.718	5.2%	0.625	4.6%	0.952	7.0%
KC 2	129	4.312	3.3%	4.843	3.8%	6.484	5.0%	3.884	3.0%	7.558	5.9%
MMBV-PREC 1	14.7	0.283	1.9%	0.382	2.6%	0.476	3.2%	0.792	5.4%	0.924	6.3%
MMBV-PREC-2	201	4.200	2.1%	5.064	2.5%	6.579	3.3%	6.229	3.1%	9.061	4.5%
MMBV-PREC-3	50.0	2.416	4.8%	1.622	3.2%	2.910	5.8%	2.690	5.4%	3.963	7.9%
MMBV-PREC-4	2.60	0.095	3.6%	0.128	4.9%	0.159	6.1%	0.242	9.3%	0.290	11.1%
SCORE											
KC 1	2.24	0.231	N/A	0.666	N/A	0.705	N/A	0.000	N/A	0.688	N/A
KC 2	98.3	0.245	N/A	0.279	N/A	0.371	N/A	0.321	N/A	0.491	N/A
MMBV-PREC 1	1.00	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A
MMBV-PREC-2	99.0	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A	0.000	N/A
MMBV-PREC-3	55.0	1.914	N/A	1.307	N/A	2.317	N/A	1.508	N/A	2.765	N/A
MMBV-PREC-4	7.84	0.521	N/A	0.358	N/A	0.632	N/A	0.865	N/A	1.072	N/A

*IP-10 MMBV-PREC4 Dose result below assay measuring range. Results are presented for RLU's.

CROSS-REACTIVITY STUDY:

Testing was performed to determine potential cross-reactivity in the LIAISON® MeMed BV® assay. The CLSI Guidance "Interfering Substances" (EP07-Third Edition) was consulted in the preparation of the testing protocol. Cross-reactivity was evaluated using two (2) serum samples that included one (1) low, approximate SCORE 5 and one (1) high, approximate SCORE 95 on one (1) lot.

TRAIL Cross-reactants concentration evaluated at 50 ng/mL	
4-1BB Ligand	LT α2/β1
CD40 Ligand	TNF-α
LT α1/β2	TNF-β
Adiponectin	
IP-10 Cross-reactants concentration evaluated at 50 ng/mL	
BLC/BCA-1	IL-8
ENA-78	I-TAC
GCP-2	NAP-2
GROα	MIG
GROγ	SDF-1α
IFNγ	SDF-1β
CRP Cross-reactants concentration evaluated at 500 ng/mL	
Pentraxin 2/SAP	Pentraxin 3/TSG-14

INTERFERING SUBSTANCES:

Testing was performed to determine whether the presence of commonly encountered endogenous and exogenous substances interfere with the LIAISON® MeMed BV® assay results. Potentially interfering substances were evaluated on one (1) lot of the LIAISON® MeMed BV® assay using two (2) serum samples that included one (1) low, approximate SCORE 5 and one (1) high, approximate SCORE 95

The CLSI Guidelines EP07-A3, Interference Testing in Clinical Chemistry, 3rd Edition was consulted in the study design the MeMed BV® SCORE result was evaluated in the presence of interfering substances. The impact of selected interferents on the SCORE result was studied using serum samples that represented high (bacterial) and low (viral) SCORE. No interference was observed for substances.

Substance	**Concentration Tested**	**Substance**	**Concentration Tested**
Bilirubin (conjugated)	0.4 mg/mL	Azithromycin	11.1 µg/L
Bilirubin (unconjugated)	0.4 mg/mL	Caffeine	108 µg/mL
Hemoglobin	10 mg/mL	Cetirizine HCl	4.35 µg/mL
Triglycerides	15 mg/mL	Dextramethorphan	15.6 ng/mL
Cholesterol	4 mg/mL	Doxycycline	18 µg/mL
HAMA	600 ng/mL	Ethanol	0.5% v/v
Rheumatoid Factor	500 IU/mL	Heparin	3300 U/L
Human Serum Albumin	60 mg/mL	Ibuprofen	219 µg/mL
Biotin	3600 ng/mL	Levofloxacin	36 µg/mL
Acetaminophen	0.156 mg/mL	Loratidine	87 ng/mL
Acetyl Salicylic Acid	0.03 mg/mL	Oxymetazoline HCl	0.0006 ug/mL
Amoxicillin	54 µg/mL	Phenylephrine	30 ng/mL
Ampicillin	75 µg/mL	Prednisolone	1200 ng/L

MATRIX EQUIVALENCE STUDY:
Fresh vs Frozen Serum
Forty-three (43) fresh serum samples were collected from forty-three (43) individual patients. Twenty (20) samples were spiked with recombinant TRAIL, IP-10, and/or CRP in order to meet the requirement of samples across the range of the score, 0-100. The forty-three (43) sample values included twenty-four (24) viral score of 0-34, seven (7) equivocal score of 35-65, and twelve (12) bacterial with score of 66-100. Samples were tested fresh with validation lot 1 reagents in replicates of three (3). The samples were then frozen, thawed and tested with validation lot 1 reagents in replicates of three (3).

Mean Values for each sample were calculated for fresh and frozen samples and a Passing-Bablok regression line fitted to the data for each assay and SCORE Value. The regression shows Fresh and Frozen samples may be used interchangeably in the assay.

	Analysis	Slope	Intercept	R-squared	R
Fresh v. Frozen	SCORE	1.00	0.00	0.9843	0.992
	CRP	1.02	0.01	0.9968	0.998
	IP-10	1.04	-5.18	0.999	0.999
	TRAIL	0.93	4.63	0.9487	0.974

LIMIT of BLANK, LIMIT of DETECTION AND LIMIT of QUANTITATION
The Limit of Blank, Limit of Detection and Limit of Quantitation were determined according to CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline June 2012- Second Edition.

METHOD:
Limit of Blank (LoB):
Five (5) calibrator matrix samples without analyte were tested over three (3) days with two (2) runs per day and two (2) replicates per run for a total of sixty (60) results per lot. The equation used for determination of the Limit of Blank is as follows:
LoB = mean (Blank Dose) + 1.653 * SD (Blank Dose)
The higher LoB result was used in the IFU.

Limit of Detection (LoD):
Four (4) serum and/or spiked matrix samples were tested over three (3) days with two (2) runs per day and two (2) replicates per run for a total of twelve (12) results per sample. Samples were in the approximate ranges: CRP (0.09 to 4.1 mg/L), IP-10 (0.37 to 151 pg/mL) TRAIL (3.8 to 29.8 pg/mL). The equation used for determination of the Limit of Detection is as follows:
LoD = LoB + 1.654 * pooled SD (sample dose)
The higher LoD result was used in the IFU.

Limit of Quantitation (LoQ):
Seven (7) or eight (8) serum and/or spiked matrix samples (4 of which were used in the LoD determination) were tested over three (3) days with two (2) runs per day and two (2) replicates per run for a total of twelve (12) results per sample. Samples were in the approximate ranges: CRP (0.09 to 4.1 mg/L), IP-10 (0.37 to 151 pg/mL) TRAIL (3.8 to 29.8 pg/mL). The % CV for each individual sample was

plotted against the mean dose result and the best curve fit applied. LoQ is calculated as the lowest concentration at which the regression line crosses 20% CV.

The following limits were determined for the LIAISON® MeMed BV® assay.

	Limit of Blank (LoB)	Limit of Detection (LoD)	Limit of Quantitation (LoQ)
CRP (mg/L)	0.024	0.067	1.0
IP-10 (pg/mL)	0.578	4.31	100
TRAIL (pg/mL)	5.33	7.03	15.0

CONCLUSION:

The material submitted in this premarket notification supports a substantial equivalence decision. The labeling satisfies the requirements of 21CFR 809.10.