

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K042475

B. Purpose for Submission:

New device with instrument

C. Measurand:

Immunoglobulin G (IgG), Immunoglobulin A (IgA), and Immunoglobulin M (IgM),
Calibrator, and Protein Performance Verifiers I, II, and III

D. Type of Test:

Quantitative Immunospectrophotometric assay

E. Applicant:

Ortho-Clinical Diagnostics Inc.

F. Proprietary and Established Names:

Chemistry Products IgG, IgA, IgM, Chemistry Products Calibrator kit 20, Chemistry
Products Protein Performance Verifiers I, II, and III
Common Names: Immunoglobulin G assay, Immunoglobulin A assay, and
Immunoglobulin M assay; calibrator; Quality control material

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5510 (Immunoglobulins A, G, M, D, and E immunological test system),
CFR 862.1150 (Calibrator), and 862.1660 (Quality Control Material (assayed and
unassayed))

2. Classification:

II (Immunoglobulins A, G and M and Calibrator) and I (Quality Control Material)

3. Product code:

CFN, Immunoglobulins (G, A, M) nephelometric method
JIX calibrator multi-analyte mixture
JJY quality control material, multi-analyte, all kinds (assayed and unassayed)

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

Chemistry Products IgG Reagent: For in vitro diagnostic use only. Chemistry Products

IgG Reagent is used to quantitatively measure immunoglobulin G (IgG) concentration in human serum and plasma.

Chemistry Products IgA Reagent: For in vitro diagnostic use only. Chemistry Products IgA Reagent is used to quantitatively measure immunoglobulin A (IgA) concentration in human serum and plasma.

Chemistry Products IgM Reagent: For in vitro diagnostic use only. Chemistry Products IgM Reagent is used to quantitatively measure immunoglobulin M (IgM) concentration in human serum and plasma.

Chemistry Products Calibrator kit 20: For in vitro diagnostic use only. Chemistry Products Calibrator kit 20 is used to calibrate 5,1 FS Chemistry Systems for the quantitative measurement of transferrin, C3, C4, IgG, IgA, and IgM.

Chemistry Products Protein Performance Verifiers I, II, and III: For in vitro diagnostic use only. Chemistry Products Protein Performance Verifiers I, II, and III are assayed controls used to monitor the performance of transferrin, C3, C4, IgG, IgA, and IgM Reagents on 5,1 Chemistry Systems.

2. Indication(s) for use:

None specified. By regulation, an immunoglobulins A, G, M, D, and E immunological test system is a device that consists of the reagents used to measure by immunochemical techniques the immunoglobulins A, G, M, D, and E (serum antibodies) in serum.

Measurement of these immunoglobulins aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

A calibrator is a device intended for medical purposes for use in a test system to establish points of reference that are used in the determination of values in the measurement of substances in human specimens.

A quality control material (assayed and unassayed) for clinical chemistry is a device intended for medical purposes for use in a test system to estimate test precision and to detect systematic analytical deviations that may arise from reagent or analytical instrument variation. A quality control material (assayed and unassayed) may be used for proficiency testing in interlaboratory surveys. This generic type of device includes controls (assayed and unassayed) for blood gases, electrolytes, enzymes, multianalytes (all kinds), single (specified) analytes, or urinalysis controls.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

VITROS 5,1 FS Chemistry Systems instrument

I. Device Description:

The device is an in vitro diagnostic immunoturbidimetric assay system containing a set of individual reagents for detection of either serum immunoglobulin G (IgG), serum immunoglobulin A (IgA) or serum immunoglobulin M (IgM). The immunoglobulin specific reagents are utilized with a calibrator and quality control material on a specific clinical chemistry analyzer. Quantitative measurement of immunoglobulins in human serum is performed using the test system. The 5,1 FS chemistry system is a fully

automated clinical chemistry analyzer for use in the determination of various analytes in human specimens (serum, plasma, and cerebrospinal fluid). The analyzer has been previously cleared (K031924). Common reagents utilized on multiple assays with the analyzer include the assay diluent (BSA saline mixture). The three immunoglobulin assays utilize an additional common reagent containing a polymer and preservatives in a buffer of inorganic salts. The reagent for the IgG assay contains goat antisera to human IgG. The corresponding assay reagents for the other two assays include goat antisera to human IgA or IgM. The protein performance verifiers are quality control materials of 3 concentration levels (designated I, II, and III) containing processed human serum of assayed concentrations in a buffer containing preservatives and inorganic salts. The calibrator contains processed human serum in buffer containing preservatives and inorganic salts.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dade Behring N antisera to human immunoglobulins (IgG, IgA, and IgM) is the predicate for the immunoglobulin reagents. Dade Behring N Protein Standards SL is the predicate device for the calibrator kit 20. Dade Behring N/T Protein controls SL is the predicate for the Protein Performance Verifiers I, II, and III.

2. Predicate 510(k) number(s):

K860894, K012470, and K002804

3. Comparison with predicate:

Similarities of reagents and calibrators		
Item	Device	Predicate
Intended Use	Chemistry Products IgG, IgA, and IgM reagents quantitatively measure Immunoglobulin G (IgG), Immunoglobulin A (IgA), and Immunoglobulin M (IgM) concentration in human serum and plasma	In Vitro diagnostic reagents for the quantitative determination of immunoglobulins (IgG, IgA, and IgM) in human serum and of IgG in human CSF
Method	Immunoturbidimetric	Immunoturbidimetric
Reportable range	IgG: 270-2700 mg/dL IgA: 40-800 mg/dL IgM: 25-400 mg/dL	IgG: 140-4600 mg/dL IgA: 25-800 mg/dL IgM: 20-640 mg/dL
Calibrators	5 different nominal concentration levels linked to CRM 470	Multiple nominal concentration levels (number not specified) linked to CRM 470

Differences of reagents and calibrators		
Item	Device	Predicate
Reactive ingredient	Goat antisera to human IgG, IgA, or IgM	Rabbit antisera to human IgG, IgA, or IgM

Similarities of Quality control material		
Item	Device	Predicate
Matrix	Processed human serum	Processed human serum
Concentration levels	3 different levels (low, medium, and high)	3 different levels (low, medium, and high)

Differences of Quality control material		
Item	Device	Predicate
Intended Use	Assayed controls used to monitor the performance of transferring, C3, C4, IgA, IgG, IgM reagents on the 5,1 FS chemistry system	Assayed accuracy controls and precision controls in the determination of the following human serum proteins by immunonephelometry with the BN systems, by immunoturbidimetry with the TurbiTime Systems, and by radial immunodiffusion with Partigen plates. (List not reproduced here but contains 26 analytes including IgG, IgA, and IgM)

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

NCCLS EP9-A2 (Method Comparison and Bias Estimation using Patient samples: Approved Guideline – Second Edition)

NCCLS EP5-A (Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline)

NCCLS EP6-A (Evaluation of the Linearity of Quantitative Measurement Procedures: A statistical Approach; Approved Guideline)

NCCLS EP7-a (Interference Testing in Clinical Chemistry; Proposed guideline)

NCCLS C28-A2 (How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved guideline – second edition)

Consensus of a Group of Professional Societies and Diagnostic Companies on Guidelines for Interim Reference Ranges for 14 Proteins in Serum Based on the Standardization against the IFCC/BCR/CAP Reference Material (CRM 470)

L. Test Principle:

Quantitative measurement of immunoglobulins in human serum is performed using an immunoturbidimetric assay. Samples, calibrators, or controls are automatically diluted in saline and mixed with reagent 1 containing a polymer. Addition of antisera specific for human immunoglobulin (either IgG, IgA, or IgM) produces an immunochemical reaction yielding antigen/antibody complexes. The light scattering properties of complexes increase solution turbidity proportional to the immunoglobulin concentration in the sample. The turbidity is measured spectrophotometrically at 340 nm by the analyzer. The immunoglobulin concentration in an unknown sample is determined using an instrument stored calibration

curve relating the measured absorbance with concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

NCCLS testing protocol EP5-A was utilized to test within-day and total precision in 2 runs per day using three different analyzers on each of 22 days for 3 lots of reagent. Each run utilized a 3 concentration control (Protein Performance Verifiers level I, II, and III) and a human serum pool as a test sample. All samples were tested in duplicate. Calibrator material was run in duplicate on 4 days over the testing period. An outlier test in EP5-A was utilized to tested data for exclusion. In the IgG and IgM analysis, 2 replicate outliers were removed from the data. Analysis of variance as described in EP5 was used to estimate within-day, day-to-day, week-to-week and total imprecision. The results represent total imprecision using a single lot of reagents. The precision data for a single reagent lot and instrument combination was slightly higher than other lots and was chosen for inclusion in the labeling. The following tables summarize the data obtained:

IgG Imprecision

Mean IgG concentration	N	Within-day SD	Within-day %CV	Total SD	Total %CV
527.02	88	10.40	2.0%	12.97	2.5%
1079.20	86	19.92	1.8%	34.86	3.2%
1986.60	88	43.38	2.2%	74.89	3.8%

IgA Imprecision

Mean concentration	N	Within-day SD	Within-day %CV	Total SD	Total %CV
100.08	88	2.52	2.5%	3.37	3.4
225.81	88	5.64	2.5%	6.0	2.7%
413.27	88	5.99	1.4%	10.35	2.5%

IgM Imprecision

Mean concentration	N	Within-day SD	Within-day %CV	Total SD	Total %CV
46.04	88	1.47	3.2%	2.86	6.2%
78.27	86	1.56	2.0%	3.24	4.1%
193.69	88	2.43	1.2%	4.59	2.4%

The results are suggested as guidelines. Variables such as instrument maintenance, environment, reagent storage/handling, control material reconstitution, and sample handling can affect the reproducibility of test results.

b. *Linearity/assay reportable range:*

Two samples, one at each end of the calibration range, were utilized in the analysis. A high sample was created from a pool of patient samples. A low sample was created from saline. Mixtures of the high and low sample were admixed together to give 28-30 intermediate concentrations. Four replicates of each of samples were assayed along with 2 replicates of the protein performance verifiers for each of 3 lots of reagent using a single instrument. The data was screened for outliers using the outlier test in EP5-A. No data were excluded as outliers. Data was analyzed by linear regression of the expected concentration (x-axis) vs. the observed concentration (mean of 4 replicates at each concentration). Results from a particular lot will be used to determine the claim since the results with this lot defined the most conservative claim.

For the IgG assay, the high sample was created from a pool of patient samples to give a value of 3000 mg/dL. Mixtures of the high and low sample were admixed together to give 27 intermediate concentrations. The assay was linear from 270 to 2700 mg/dL for all three lots tested. The correlation coefficient was 0.9992. The graph shows the x-axis as % of the high pool. The y-axis shows the IgG concentration. The slope of the best fit line was 30.7. The intercept was 18.9 mg/dL. A plot of the difference between observed and expected IgG concentration vs. the measured result is also shown. The plot is centered about a difference of zero from 500 to 2200 mg/dL with slightly more bias near the extremes of concentration. The maximum difference in observed and expected concentration appears to be -50 mg/dL.

For IgA, the high sample had a concentration of 1000 mg/dL. Mixtures of the high pool and low pool were created giving 30 additional intermediate concentration samples. The linear range was defined for levels 1 through 28. The linear regression analysis resulted in a correlation coefficient of 0.9993. The slope of the best fit line was 10.1. The intercept was -3.2 mg/dL. A plot of the difference between observed and expected IgA concentration vs. the measured result indicates scattering of data centered about a difference of zero from 10 to 400 mg IgA/dL. Slightly more bias appears at the extremes of concentration. The maximum difference in observed and expected concentration was approximately 20 mg/dL. The reportable range for IgA was 40-800 mg/dL of IgA.

For IgM, the high sample had a concentration of 500 mg/dL. Mixtures of the high pool and low pool were created giving 27 additional intermediate concentration samples. The linear range was defined for levels 2 through 25. The linear regression analysis resulted in a correlation coefficient of 0.9995. The slope of the best fit line was 5.2. The intercept was -2.3 mg/dL. A plot of the difference between observed and expected IgM concentration vs. the measured result indicates scattering of data centered about a difference of zero from 10 to 400 mg IgM/dL. Slightly more bias

appears at the extremes of concentration. The maximum difference in observed and expected concentration was approximately 10 mg/dL. The reportable range for IgM was 25-400 mg/dL.

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

The calibrator contains processed human serum in buffer containing preservatives and inorganic salts. The values assigned to calibrators are traceable to a certified reference material (CRM470 Reference preparation for proteins in human serum) available from the Institute for Reference Methods and Materials of the International Federation of Clinical Chemistry and Laboratory Medicine. A Master Lot of calibrator having 5 concentrations was prepared utilizing dilutions of the Certified reference material on the analyzer using a standard measurement procedure. These standards are used with the analyzer to establish working calibrators from which each product lot of calibrators is assigned values.

d. *Detection limit:*

Using each of 3 reagent lots, assays were performed over the course of 1 day with 6 replicates of calibrators and controls as well as 24 replicates of a low concentration sample. The low concentration sample was diluted 5-fold prior to assay. It was assumed for analysis that the response is normally distributed about the predicted mean of the blank or low concentration sample. It was also assumed that the variability of a zero sample is approximately equal to the variability of a sample at the lower limit of detection. The lower limit is defined as 3.3 times the square root of the sum of squares of the calibration error standard deviation plus the pooled replicate standard deviation. Calibration error at the mean of the low concentration sample was estimated by Monte Carlo simulation using 6 replicates per calibrator level.

For each of 3 reagent lots of IgG reagent, a table shows the mean concentration of 24 replicates of the low IgG concentration (an in-house prepared solution whose undiluted nominal concentration was 360 mg/dL), the standard deviation of the 24 replicates, the calibration error standard deviation and the calculated lower limit of detection. A particular reagent lot with the highest limit as the lower limit of detection for the IgG assay was chosen as representative of the lower limit of detection. The calculated concentration was 54.2 mg/dL.

The calculation method is not described. The nominal concentration of the low IgG sample allowing for no dilution error was expected to be 72 mg/dL. The mean concentration across 3 lots of IgG reagent was 114.7 mg/dL. The lower 95% confidence limit of the pooled mean value for the 3 lots tested was 39.5 mg/dL. The sponsor's claim is 12% different from this lower 95% confidence limit. The percentage coefficient of variation of the 3 lot means is 15%. Therefore, since the sponsor's claim is within this coefficient of variation the value chosen by the sponsor is acceptable.

For IgA, assays were performed using each of 3 reagent lots over the course of 1 day with 6 replicates of calibrators and controls as well as 24 replicates of a low

concentration sample (an in-house prepared solution whose undiluted nominal concentration was 70 mg/dL). The low IgA concentration sample was diluted 5-fold prior to assay (final nominal concentration $70/5 = 14$ mg/dL). The method of analysis is the same method utilized for the IgG assessment. For each of 3 reagent lots of IgA reagent, the calculated concentration was 4.2 mg/dL. The mean concentration across 3 lots of IgA reagent was 9.9 mg/dL. The lower 95% confidence limit of the pooled mean value for the 3 lots tested was 0 mg/dL. The percentage coefficient of variation of the 3 lot means was 60%. Therefore, since the sponsor's claim is within this coefficient of variation, the value chosen by the sponsor is acceptable.

For IgM, assays were performed using each of 3 reagent lots over the course of 1 day with 6 replicates of calibrators and controls as well as 24 replicates of a low concentration sample (an in-house prepared solution whose undiluted nominal concentration was 28 mg/dL). The low IgM concentration sample was diluted 5-fold prior to assay (final nominal concentration $28/5 = 5.6$ mg/dL). The method of analysis is the same method utilized for the IgG assessment. The calculated concentration was 4.6 mg/dL. The percentage coefficient of variation of the 3 lot means is 37% with a mean lot value of 5.9 mg/dL. Therefore, since the sponsor's claim is within this coefficient of variation, the value chosen by the sponsor is acceptable.

e. Analytical specificity:

Various endogenous and exogenous substances were tested for interference in the assay using 2 types of samples. For hemoglobin, bilirubin, and lipid interference, 2 serum pools of different concentration specific for each immunoglobulin reagent were prepared. For interference studies with exogenous substances, a control material (protein performance verifier) with a defined concentration was used. Testing for interference from bilirubin, hemoglobin, and lipid utilized a paired difference method as described in NCCLS protocol EP7-A, "Interference Testing in Clinical Chemistry". Exogenous compounds were prepared at 20-fold concentration to be added to the sample of control material. Sample without interferent was apparently also tested, though a description of the control sample is not made. It is not clear if saline diluent or no diluent was added to create the sample without interferent. Bias was calculated as the difference between mean values with the interferent and mean values without interferent. The number of replicates of each sample with and without interferent is not mentioned. The mean value, standard deviation, and %CV was calculated for each control pool and test substance pool. A literature search was performed for interferences from therapeutic drugs and metabolites in immunoturbidimetric assays for IgG, IgA, and IgM. No drug or metabolite was identified from the search.

Bilirubin, hemoglobin, and intralipid were found not to interfere at IgG concentrations of 345 mg/dL and 1250 mg/dL. Bias from the 3 substances was < 45 mg/dL at 345 mg IgG/dL ($< 13\%$ bias) and < 112.5 at 1250 mg IgG/dL ($< 9\%$ bias). Of 18 exogenous substances tested for interference of an IgG solution at 725 mg/dL, no interference was found. The bias was < 65.3 mg/dL ($< 9\%$ bias) for all tested exogeneous substances. The following table lists the tested substances and the

Concentrations of the Interferent:

Compound	Concentration
Acetaminophen	20 mg/dL
Acetyl-L-cystein	100 mg/dL
Amoxicillin	20 ug/ml
Ascorbic acid	3 mg/dL
Bilirubin	60 mg/dL
Carbamazepine	120 ug/ml
Dipyron	30 mg/dL
Ethamsylate	3 mg/dL
Gentamicin sulfate	120 ug/ml
Hemoglobin	1000 mg/dL
Ibuprofen	400 ug/ml
Intralipid	800 mg/dL
Lidocaine	60 ug/ml
Methotrexate	90.9 mg/dL
Procainamide	100 ug/ml
Propanolol	5 ug/ml
Rantidine	200 ug/ml
Salicylic acid	50 mg/dL
Simvastin	16 ug/ml
Theophylline	25 mg/dL
Valproic acid	500 ug/ml

Bilirubin, hemoglobin, and intralipid were found not to interfere at IgA concentrations of 65 mg/dL and 275 mg/dL. Bias from the 3 substances was < 10.7 mg/dL at 65 mg IgA/dL (< 16% bias) and < 45.4 at 275 mg IgA/dL (<17% bias). Of 18 exogenous substances tested for interference of an IgA solution at 155 mg/dL, no interference was found. The bias was <25.6 mg/dL (< 17% bias) for all tested exogenous substances. The above table lists the tested substances and the concentrations of the interferent.

Bilirubin and hemoglobin were found not to interfere at IgM concentrations of 25 mg/dL and 190 mg/dL. Bias from hemoglobin and bilirubin was < 4.5 mg/dL at 25 mg IgM/dL (< 18% bias) and < 22.5 at 190 mg IgM/dL (<12% bias). Of 18 exogenous substances tested for interference of an IgM solution at 80 mg/dL, no

interference was found. The bias was <12 mg/dL (<% 15 bias) for all tested exogenous substances. The above table lists the tested substances and the concentrations of the interferent (with the exception that the listed concentration for hemoglobin is 500 mg/dL and the absence of a listed value for Intralipid).

- f. *Assay cut-off:*
No specific information provided.

2. Comparison studies:

a. *Method comparison with predicate device:*

To compare assays of the proposed and predicate device, human samples were tested using the respective test systems. The 5,1 FS chemistry system was utilized with 2 lots of the reagent, a single lot of calibrators and 3 lots of controls (Protein Performance Verifiers). The predicate test system utilized the Dade Behring BN ProSpec nephelometer with a single lot of reagent and calibrator and 3 lots of controls. The testing procedure was based on NCCLS guidelines from EP9-A2. Samples were assayed in both test systems (3 replicates using the proposed assay and 2 replicates using the predicate system) on the same test days. Two different analyzers were used, each using 2 reagent lots. No samples were excluded from analysis after screening for outliers using NCCLS EP5-A testing protocol. Though not stated by the applicant not all samples were tested on a single day but on an unspecified number of days. It is assumed that the same number of samples was tested in each assay system on a particular day. A Passing-Bablok linear regression analysis of the test results was performed with results from the proposed assay as the y-variable. The standard error of the regression was estimated with least squares regression analysis. Results for the best fit regression line are shown for each of 2 analyzers using 2 reagent lots. Results from a particular lot were used to describe in the labeling as the product claim.

For IgG, 139 samples were tested. The slope of the best fit line for 4 comparisons ranges from 0.93 to 0.99, though no standard error of the slope is shown. The intercept of the best fit line ranges from 48.9 mg/dL to 91.2 mg/dL, though no standard error of the intercept is shown. The correlation coefficients for each of the 4 comparisons were above 0.99. The relationship of the analysis described in the labeling is: $y = 0.98x + 91.2$.

To compare the IgA assays of the proposed and predicate device, 132 samples were assayed. Four samples were excluded for technical reasons, not due to failing an outlier test. The slope of the best fit line for 4 comparisons ranged from 1.04 to 1.07, though the standard error of the slopes is not given. The intercept of the best fit line ranges from -5.3 mg/dL to 7.2 mg/dL, though no standard error of the intercept is shown. The correlation coefficients for each of the 4 comparisons were above 0.999. The relationship of the analysis described in the labeling is: $y = 1.07x - 3.03$.

To compare the IgM assays of the proposed and predicate device, 129 samples were assayed. Five samples were excluded for technical reasons, not due to failing an

outlier test. The slope of the best fit line for 4 comparisons ranged from 1.00 to 1.10, though the standard error of the slopes is not given. The intercept of the best fit line ranges from -1.4 mg/dL to 3.6 mg/dL, though no standard error of the intercept is shown. The correlation coefficients for each of the 4 comparisons were above 0.99. The relationship of the analysis as described in the labeling is: $y = 1.02x + 1.1$.

b. Matrix comparison:

Serum concentrations were compared with concentrations using different anticoagulants or separator tubes from the same donor. Lithium-heparin plasma, EDTA-plasma, Lithium-heparin plasma separator tubes, and serum separator tubes were used in addition to standard serum collection tubes from the same donor to compare concentrations. Fifty (50) donors were utilized. The mean value for each specimen was calculated from the determinations, though the number of replicates of each specimen type is not given. Concentrations from serum were the control sample. Bias was calculated for each specimen where the bias was the “test condition prediction” minus the “serum sample prediction”. It is not noted how the sample predictions were made. Anti-coagulants were deemed acceptable if the mean bias was within predetermined specifications. The specifications are not noted.

For IgG, heparin-plasma and EDTA-plasma samples were within acceptance criteria compared with serum specimens. Both serum separator and heparin plasma separator tubes were also within acceptance criteria compared with serum specimens. The mean bias in each comparison is not given.

Serum IgA concentrations were compared with IgA concentrations from the same donor using different anticoagulants or separator tubes in the same manner as for IgG. Heparin-plasma and EDTA-plasma samples were within acceptance criteria compared with serum specimens. Both serum separator and heparin plasma separator tubes were also within acceptance criteria compared with serum specimens. The mean bias in each comparison is not given.

Serum IgM concentrations were compared with IgM concentrations from the same donor using different anticoagulants or separator tubes in the same manner as for IgG. Heparin-plasma and EDTA-plasma samples were within acceptance criteria compared with serum specimens. Both serum separator and heparin plasma separator tubes were also within acceptance criteria compared with serum specimens. The mean bias in each comparison is not given.

3. Clinical studies:

a. Clinical Sensitivity:

No information provided.

b. Clinical specificity:

No information provided.

c. Other clinical supportive data (when a. and b. are not applicable):

No information provided.

4. Clinical cut-off:

No information provided.

5. Expected values/Reference range:

Fresh serum samples were obtained from 126 individuals. Participants answered questions on age, sex, health status, and prescription drug received. Subjects were excluded if they had chronic liver disease, chronic infections, inflammatory bowel disease, multiple myeloma, systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, lymphomas, or immune deficiency. Subjects receiving the following prescription drugs were also excluded: CellCept, Genfrac, Imuran, Neoral, Prograf, Rapamune, Sandimmune, Simulect, thymoglobulin, or zenapax. Each of 2 reagent lots was utilized on 2 analyzers. The mean, median, 2.5, and 97.5 percentile values were calculated. Ninety percent confidence intervals for each central value were also calculated. For all subjects, the lower reference limit corresponded to the 2.5th percentile. The upper reference limit corresponded to the 97.5th percentile.

In determining the range for IgG, 6 subjects with the excluding criteria were found. Four additional specimens from 4 subjects were identified as statistical outliers. A total of 116 healthy subjects were tested using 2 analyzers. Subjects ranged in age from 19 to 59, 53% female (62 of 116), 47% male (54 of 116). The lower and upper reference limits were 758.3 mg/dL and 1571.7 mg/dL respectively. The 90% confidence intervals for the upper and lower reference limit were 638.4 – 818.1 mg/dl and 1504.5 – 1623.2 mg/dL respectively. The sponsor also cites additional information on the reference range from a published scientific reference. The range was 700 – 1600 mg/dL. The sponsor states that the data supports the consensus reference range.

For the expected value range of IgA, 126 individuals were tested in the same manner as for IgG. Six subjects with excluding diseases were found and excluded. % subjects were identified as statistical outliers and one specimen had values below the reportable range. Subjects ranged in age from 19 to 59, 54% female (62 of 114), 46% male (52 of 114). The lower and upper reference limits were 68.7 mg/dL and 398.9 mg/dL respectively. The 90% confidence intervals for the upper and lower reference limit were 55.4 – 98.9 mg/dl and 364.2 – 413.2 mg/dL respectively. The range was 70 – 400 mg/dL. The sponsor states that the data supports the consensus reference range.

For the expected value range of IgM, 126 individuals were tested in the same manner as above. Six subjects with excluding diseases were found and excluded. % subjects were identified as statistical outliers and 5 specimens were excluded. Subjects ranged in age from 19 to 59, 54% female (62 of 115), 46% male (53 of 115). The lower and upper reference limits were 39.6 mg/dL and 249.4 mg/dL respectively. The 90% confidence intervals for the upper and lower reference limit were 26.4 – 46.7 mg/dL and 221.3 – 252.7 mg/dL respectively. The range was 40 – 230 mg/dL. The sponsor states that the data supports the consensus reference range.

N. Instrument Name:

VITROS 5,1 FS chemistry system

O. System Descriptions:

1. Modes of Operation:

The system is a fully automated clinical chemistry analyzer for use in the determination of various analytes in human specimens (serum, plasma, and cerebrospinal fluid) using “MicroTip” and “Thin Film” assays. The analyzer has been previously cleared (K031924). The analyzer operates in conjunction with reagents, calibrators and controls designed for use with the system. Major components include a command center/operator interface, a sampling center, a disposable tip processing center, the Chemistry Slide General Chemistry Center, and the MicroTip Special Chemistry processing center.

2. Software:

As noted in K031924, the VITROS 5,1 FS Chemistry System utilizes the QNX Neutrino v 6 .1 or later operating system. It relies upon a touch screen or keyboard for user interface. Communications with external systems are run via Ethernet connection. Sample programming may be made from a Laboratory Information System to the analyzer via this connection.

FDA has reviewed applicant’s Hazard Analysis and software development processes for this line of product types:

Yes _____ or No _____

3. Specimen Identification:

No information provided. See K031924.

4. Specimen Sampling and Handling:

No information provided. See K031924.

5. Calibration:

No information provided. See K031924.

6. Quality Control:

No information provided. See K031924.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:

No information provided. See K031924.

Q. Proposed Labeling:

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

R. Conclusion:

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