



Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

January 9, 2015

BIO-RAD LABORATORIES
JUANG WANG
REGULATORY AFFAIRS REPRESENTATIVE
5500 E. 2ND STREET
BENICIA CA 94510

Re: K141114

Trade/Device Name: BioPlex® 2200 25-OH Vitamin D Kit
BioPlex® 2200 25-OH Vitamin D Calibrator Set,
BioPlex® 2200 25-OH Vitamin D Control Set

Regulation Number: 21 CFR 862.1825

Regulation Name: Vitamin D test system

Regulatory Class: II

Product Code: MRG, JJX, JIT

Dated: November 25, 2014

Received: November 25, 2014

Dear Juang Wang:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. 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

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Stayce Beck -S

For : Courtney H. Lias, Ph.D.

Director

Division of Chemistry and Toxicology Devices

Office of In Vitro Diagnostics

and Radiological Health

Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
K141114

Device Name

BioPlex® 2200 25-OH Vitamin D Kit
BioPlex® 2200 25-OH Vitamin D Calibrator Set
BioPlex® 2200 25-OH Vitamin D Control Set

Indications for Use (Describe)

The BioPlex® 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex® 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

The BioPlex® 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex® 2200 25-OH Vitamin D Reagent Pack.

The BioPlex® 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex® 2200 System and the corresponding BioPlex® 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex® 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

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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BioPlex[®] 2200 25-OH Vitamin D 510(k) Summary

Bio-Rad Laboratories hereby submits this 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides detail as a basis for a determination of substantial equivalence for the BioPlex[®] 2200 25-OH Vitamin D kit.

510(k) Number:
k141114

Summary Preparation Date:
December 30, 2014

Applicant:
Bio-Rad Laboratories

Contact:
Juang Wang
Regulatory Affairs Representative
5500 E. Second Street
Benicia, CA 94510
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Purpose for Submission:
New Device

Measurand:
25-hydroxyvitamin D

Type of Test:
Quantitative multiplexed flow immunoassay

Proprietary and Established Names:
BioPlex[®] 2200 25-OH Vitamin D kit
BioPlex[®] 2200 25-OH Vitamin D Calibrator Set
BioPlex[®] 2200 25-OH Vitamin D Control Set

Regulatory Information:

1. Regulation section:
 - 21 CFR §862.1825 – Vitamin D test system
 - 21 CFR §862.1150 – Calibrator
 - 21 CFR §862.1660 – Quality Control Material (assayed and unassayed)

2. Classification:

Class II (Assays, Calibrator)
Class I (Controls)

3. Product code:

MRG, System, Test, Vitamin D
JIT, Calibrator, Secondary
JJX, Single (specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Clinical Chemistry (75)

Intended Use:

1. Intended use(s):

The BioPlex[®] 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex[®] 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

The BioPlex[®] 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex[®] 2200 25-OH Vitamin D Reagent Pack.

The BioPlex[®] 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex[®] 2200 System and the corresponding BioPlex[®] 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex[®] 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Bio-Rad BioPlex[®] 2200 System

Device Description:

BioPlex[®] 2200 25-OH Vitamin D kit includes the following components:

- One (1) 10 mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead

(SVB) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives.

- One (1) 10 mL vial of Release Buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (<1.0%) as preservative.
- One (1) 5 mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives and chemical blockers.
- One (1) 5 mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA -PE) in a buffer comprising protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives, chemical blockers and detergent (Tween 20).

BioPlex[®] 2200 25-OH Vitamin D Calibrator set contains six (6) 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

BioPlex[®] 2200 25-OH Control set contains two (2) 1.5 mL Level 1 and two (2) 1.5 mL Level 2 Control vials, each containing 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

Additional materials required but not supplied include BioPlex[®] 2200 Sheath Fluid containing Phosphate Buffered Saline (PBS), ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives; and BioPlex[®] 2200 Wash Solution containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives.

Substantial Equivalence Information:

1. Predicate device name(s):
EUROIMMUN 25-OH Vitamin D ELISA, k123660
2. Comparison with predicate:

Device Similarities		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Intended Use/Indication for Use	Intended for the quantitative determination of 25-hydroxyvitamin D in serum. To be used as an aid in the assessment of vitamin D sufficiency	Same
Measured Analyte	25-hydroxyvitamin D	Same
Assay Type	Quantitative	Same
Test Principle	Competitive immunoassay	Same
Antibody	Monoclonal Sheep antibody against 25-OH Vitamin D	Same
Signal Detection	Fluorescence	Same
Unit of Measure	ng/mL	Same
Calibrator(s) and Calibration	6 calibrator levels (sold separately); 4-PL (parameter logistic) curve fit algorithm	Same

Device Differences		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Assay Technology	Automated flow competitive immunoassay	Manual competitive immunoassay
Conjugate	Biotinylated 25-hydroxyvitamin D and phycoerythrin conjugated streptavidin	Biotin-labeled 25-OH vitamin D, Peroxidase-labeled streptavidin and substrate TMB
Solid Phase	Antibody-coated paramagnetic microbeads	Antibody coated 96 microwell ELISA plate
Measuring range	6.5 – 125.0 ng/mL	4 – 120 ng/mL
Sample Matrix	Serum	Serum or EDTA or Lithium heparin plasma
Sample Size	10 µL	20µL
Calibrator Matrix	25% horse serum and depleted human serum	Liquid in horse serum with preservatives

Device Differences		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
	with ProClin 950, sodium benzoate and BND	
Open Pack Stability	60 days	Not applicable
Reagent Integral Storage	On-board or in refrigerator at 2-8°C	Not applicable
Sample Handling/Process	Automated	Manual
Calibrator Open storage at 2-8°C	30 days	3 months
Calibration Frequency	Every 30 days	Every 96 well plate
Instrumentation	Bio-Rad BioPlex 2200 System	ELISA plate reader
Measuring wavelength	550 – 610 nm	450/620 nm

Control Set Similarities and Differences		
Characteristics	BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Intended Use	Use as an assayed quality control to monitor the overall performance of 25-OH Vitamin D reagent.	Same
Storage	Store at 2 -8°C until ready to use	Same
Matrix	Human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Control Open Stability at 2 – 8°C	60 days	No Applicable

Standard/Guidance Document Referenced (if applicable):

EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition (Vol. 24 No.25)

EP06-A, Evaluation of Linearity of Quantitative Measurement: A Statistical Approach, Approved Guideline (Vol. 23 No.16)

EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition (Vol. 25 No.27)
EP09-A2IR, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (Interim Revision) (Vol. 30 No. 17)
EP15-A2, User Verification of Performance for Precision and Trueness, Approved Guideline, Second Edition (Vol. 25 No.17)
EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline, Second Edition (Vol. 32 No.8)
EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (Vol. 29, No. 20)
C28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, Third Edition (Vol. 28 No.30)

Test Principle:

The BioPlex® 2200 25-OH Vitamin D assay is a multiplexed flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidin-phycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) are present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amount of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision testing of the BioPlex® 2200 25-OH Vitamin D kit on the BioPlex® 2200 instrument was performed in accordance with CLSI EP5-A2 guideline. A human serum panel consisting of 6 frozen samples spanning the measuring range was assayed in duplicate per run on two runs daily over 20 days (N=80) on one

reagent lot. Two levels of the BioPlex 25-OH Vitamin D controls were also included. The data were analyzed for within-run, between-run, between-day, and total precision and the mean (ng/mL), standard deviation (ng/mL) and percent coefficient of variation (%CV) are summarized below:

BioPlex® 2200 25-OH Vitamin D – CLSI EP5-A2 Precision

Serum Panel	N	Mean ng/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
Sample 2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
Sample 3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
Sample 4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
Sample 5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
Sample 6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Control 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Control 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

CLSI EP15-A2 Reproducibility

Precision and reproducibility was also evaluated in accordance with CLSI EP15-A2 guideline “User Verification of Performance for Precision and Trueness, Vol 25, No 17”.

A different serum panel consisting of 8 samples spanning the measuring range were assayed in 2 replicates per run, two runs per day over 5 days (n=20) using one lot of BioPlex 25-OH Vitamin D kit. Two levels of controls were also included. The data were analyzed for within-run, between run, between day, and total precision and the mean ng/mL, standard deviation and percent coefficient of variation (%CV) are summarized below:

BioPlex® 2200 25-OH Vitamin D - CLSI EP15-A2 Reproducibility

Serum Panel	N	Mean ng/mL	Within Run		Between Run		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Sample 1	20	11.5	0.69	6.0%	0.47	4.1%	1.71	14.8%
Sample 2	20	13.6	0.80	5.9%	0.26	1.9%	1.18	8.7%
Sample 3	20	26.1	0.88	3.4%	1.15	4.4%	1.59	6.1%
Sample 4	20	30.2	1.99	6.6%	0.00	0.0%	2.71	9.0%
Sample 5	20	50.2	2.23	4.4%	0.77	1.5%	2.96	5.9%
Sample 6	20	56.4	2.09	3.7%	2.79	4.9%	5.26	9.3%
Sample 7	20	100.5	4.52	4.5%	2.81	2.8%	5.32	5.3%
Sample 8	20	104.9	3.97	3.8%	1.54	1.5%	5.24	5.0%
Control 1	20	21.6	0.98	4.5%	1.00	4.6%	1.84	8.5%
Control 2	20	58.8	2.44	4.2%	1.29	2.2%	2.99	5.1%

b. *Linearity/assay reportable range:*

Five high patient serum samples extending 20% higher than upper limit of the assay range were tested to demonstrate linearity. These samples were serially diluted with low levels of human sample near LoQ in accordance with CLSI EP06-A guideline. Each sample and dilution was evaluated in replicates of four using one BioPlex 25-OH Vitamin D reagent lot on one instrument. Linear and polynomial regression analysis of 25-OH Vitamin D recovery vs. sample dilution was performed to determine if the dilution curves exhibit statistically significant non-linear regression based on the CLSI guideline EP06-A.

See one example below for the regression parameters (slope, intercept and r^2) of the observed values vs. predicted values.

Conc (ng/mL)	Slope	Intercept	r^2	Dilution range
168.9	1.0001	0.0045	0.9988	5.5 – 168.9

The BioPlex 2200 25-OH Vitamin D assay has demonstrated that the assay range is 6.5 to 125.0 ng/mL.

Over-Range (OR) results may be generated for values greater than the reportable measuring range and results are reported as > 125.0 ng/mL.

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

Traceability:

The BioPlex 25-OH Vitamin D Calibrators are traceable to internal standards which are determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength.

The six levels of Master calibrators are manufactured volumetrically from the internal standards into the depleted human serum except level 1 (25-hydroxyvitamin D free) in 25% horse serum. The Master calibrators are immediately frozen at <-70°C.

Value Assignment:

The BioPlex 25-OH Vitamin D kit calibrators are manufactured for each lot kit with the same matrix as the Master calibrators and are stabilized with $\leq 0.3\%$ ProClin 950, $\leq 0.1\%$ sodium benzoate, and $< 0.1\%$ 5-bromo-1,3-nitro-dioxane.

Calibrator assignment is established for the matched lot of BioPlex[®] 2200 25-OH Vitamin D kit using the Master calibrators as reference. Calibrator assignment is established for the matched lot of BioPlex[®] 2200 25-OH Vitamin D kit using the Master calibrators as reference. For each calibrator level except level 1, three vials are tested in replicates of five on three BioPlex 2200 analyzers for a total of 45 data points. The mean values obtained for each kit calibrator level are verified and must fall within specified acceptable range.

Two levels of the BioPlex 2200 25-OH Vitamin D control set are prepared from a pool of native human serum specimens. For each control level, three vials are tested in replicates of five using each of the kit lots on three BioPlex 2200 analyzers for a total of 45 replicates per reagent lot. The total number of replicates for each control level is 90 when two reagent lots are used and 135 when three reagent lots are used. For each control level, the mean values were derived from replicate analyses and should fall within the corresponding deviation.

The manufacturing target values of the Calibrator and Control Sets are listed below.

Calibrator Set	Target (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

Control Set	Target (ng/mL)	Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Stability:

Stability studies have been performed to support the following claims:

Calibrator and Control:

BioPlex® 2200 25-OH Control and Calibrator Sets: Calibrator Open Vial Stability (2 to 8°C), 30 days from first opening; Control Open Vial Stability (2 to 8°C), 60 days from first opening; Onboard Calibration Curve Stability, 30 days; Calibrators and Controls Real Time Stability (2 to 8°C), 24 months; labeled as until expiration date; Calibrators and Controls Accelerated Stability (2 to 8°C), 2 years predicted. Calibrators freeze-thaw (-20°C or -70°C), 5-freeze thaw cycles; Control freeze-thaw (-20°C or -70°C), 1-freezethaw cycle at -20°C and 5-freeze-thaw cycles at -70°C.

Kit Stability:

BioPlex® 2200 25-OH Vitamin D Kit: Real Time (unopened) Kit Stability, 9 months or until the date of expiration when stored unopened on the instrument or at 2 to 8°C; the open kit claim is 60 days.

Sample Stability:

Sample stability studies were also performed: Sample stability fresh (2 to 8°C), 7 days; Sample stability frozen (-20 or -70°C), 24 months; Sample Freeze-thaw (-20 or -70°C), up to 3-freeze thaw cycles at -20°C and 2-freeze thaw cycles at -

70°C acceptable.

d. *Detection limit:*

The study was conducted in accordance with CLSI EP17-A2 guideline for determining the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ).

Limit of Blank (LoB)

Five blank samples were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 4 replicates per day for 5 days yielding 100 data points per reagent lot.

A non-parametric statistical analysis at 95th percentile is used to calculate LoB.

Limit of Detection (LoD)

Six human samples with low level of 25-OH vitamin D in the range of 4 to 35 ng/mL were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 12 replicates per day for five days yielding 60 data points per sample per reagent lot. LoD is then calculated by the equation:

$LoD = LoB + c_p SD_{LoD}$ Where C_p is a multiplier to give the 95th percentile of a normal distribution and SD is from the linear regression of standard deviation versus 25-OH Vitamin D mean value.

Limit of Quantitation (LoQ)

The LoQ was evaluated based on the accuracy goal which was defined as precision \leq 20% CV. The %CV was calculated using the same measurement results of the 6 low level samples used for determining the LoD.

The results of LoB, LoD, and LoQ in ng/mL are summarized in the table below.

LoB	LoD	LoQ
0.8	2.5	6.5

e. *Analytical specificity:*

Interfering Substances:

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex® 2200 25-OH Vitamin D kit according to CLSI EP7-A2 guideline.

The effects of the test levels of potential interfering substances on the assay have been evaluated with samples containing 10 to 90 ng/mL Vitamin D. The percent difference between the mean value of each test substance and a corresponding control was calculated. No interference was observed with any of the substances

tested if the percent difference is $\leq 10\%$. The substances and the maximum levels of interfering substances tested are shown in the table below:

Substance	Concentration
Hemoglobin*	≤ 150 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 30 mg/dL
Triglycerides	≤ 400 mg/dL
Total Protein	≤ 12 g/dL
Cholesterol	≤ 500 mg/dL
Uric Acid	≤ 20 mg/dL
HAMA	≤ 100 ng/mL
Rheumatoid Factor	≤ 350 IU/mL
Ascorbic Acid	≤ 3 mg/dL

*Hemoglobin > 150 mg/dL may interfere. Do not use visibly hemolyzed samples.

Cross-Reactivity:

The study was conducted in accordance with CLSI EP17-A2 using 2 human serum pools at 25-hydroxyvitamin D concentrations of 20 and 35 ng/mL. Nine cross reactants at levels listed below were then spiked into the human serum pools. The spiked and non-spiked samples were then evaluated in replicates of five to calculate the cross reactivity as shown below.

$$\% \text{ Cross Reactivity} = (\text{spiked vitamin D} - \text{non-spiked vitamin D}) \div \text{Cross reactant concentration} \times 100\%$$

The results of each potential cross reactant are listed below.

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D2	30	103%
25-hydroxyvitamin D3	30	97%
Vitamin D2	1000	0.2%
Vitamin D3	1000	0.0%
1,25-dihydroxyvitamin D2	30	$>100\%$
1,25-dihydroxyvitamin D3	30	79%
3-epi 25-hydroxyvitamin D3	30	59%
24,25-dihydroxyvitamin D3	20	9%
Paricalcitol (Zemplar)*	24	$>100\%$

* Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex 2200 25-OH Vitamin D assay

High dose hook effect:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed following CLSI EP09-A2-IR guideline.

A total of 204 human samples spanning the entire measuring assay range were tested in singlicate on both the BioPlex 2200 25-OH Vitamin D kit and the predicate assay. Of the 204 samples, there were 185 unaltered samples and 19 samples spiked with 25-hydroxyvitamin D₃ to supplement the assay range. There are eight (8) samples with values lower or higher than the measuring range of the comparator method not including in the analysis. A total of 196 BioPlex 25-OH Vitamin D results were plotted using weighted Deming regression analysis for all samples spanning the measuring range of both assays. Results of the regression slope, intercept, and coefficient of correlation (r) are summarized in the table below:

Number of Results Analyzed	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r) (95%CI)	Test Range (ng/mL)
196	1.0039 (0.9365 to 1.0712)	-0.2256 (-2.4121 to 1.9608)	0.9553 (0.9412 to 0.9661)	BioPlex: 6.6 to 124.9 Comparator: 4.3 to 118.1

b. Matrix comparison:

Serum only

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical Specificity:

Not Applicable

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

Not Applicable

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:

The Expected Values study was conducted following CLSI C28-A3c guideline.

Two hundred and eighty-seven (287) samples from apparently healthy donors including 160 males ranging in age from 21 to 79 and 127 females ranging in age from 21 to 66 were collected from three regions (North, Central, and South) in the US in spring, summer and winter, including African Americans, Hispanics and Caucasians.

The 287 samples from apparently healthy donors met the following inclusion/exclusion criteria as follows and tested with the BioPlex 25-OH Vitamin D kit in singlicate.

- Age from 21 to 90
- Roughly 50% female and 50% male
- 20% from Northern. 20% from Central and 60% from Southern region
- 40% collected in Spring, 30% in Summer and 30% in Winter
- At least 30% African Americans and 30% Caucasians
- 90% not taking Vitamin D supplements and <30% of those taking Vitamin D supplements at or more than 1000 IU, but less than 2000 IU
- Normal TSH, PTH, and Total Calcium
- No family history of parathyroid or calcium regulatory disease. In addition, no personal history of kidney disease, GI disease, liver disease, and no bariatric surgery

The observed median, mean, and range between 2.5th to 97.5th percentile are summarized below

N	Mean	Median	2.5 th to 97.5 th Percentile
286*	29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

* One sample <6.5 ng/mL was excluded from the data analysis

Each laboratory should establish its own reference range pertinent to their specific patient populations.

Instrument Name:

The BioPlex 2200 System, software version 4.1 cleared in k130053

Conclusion:

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

TRIAGE-QUICK REVIEW ACCEPTANCE FORM

Reviewer: CONNORS, SHEILA

510(k) #: K141114

510(k) Holder: BIO-RAD LABORATORIES

Device Name: BIOPLEX 2200 25-OH VITAMIN D KIT, BIOPLEX 2200 25-OH VITAMIN D CALIBRATOR SET, BIOPLEX 2200 25-OH VITAMIN D CONTROL SET

Regulation Number (if multiple, choose the one likely to be in SE letter): 862.1825

Regulation Name: VITAMIN D TEST SYSTEM

Regulatory Class: 2

Primary Product Code: MRG

Quick Review Criteria	Yes	No
1. The submission passed the refuse-to-accept (RTA) checklist	<input checked="" type="checkbox"/>	<input type="checkbox"/>
2. The submission appears to be a quality submission	<input checked="" type="checkbox"/>	<input type="checkbox"/>
3. The division has review experience and knowledge of expected device performance	<input checked="" type="checkbox"/>	<input type="checkbox"/>
4. An extensive consult is not required*	<input checked="" type="checkbox"/>	<input type="checkbox"/>
5. TPLC review does not raise new postmarket issues**	<input checked="" type="checkbox"/>	<input type="checkbox"/>
6. Branch Concurrence	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Final Quick Review Decision		
<input checked="" type="checkbox"/> Accepted	<input type="checkbox"/> Not Accepted	<input type="checkbox"/> Converted***
Please summarize why the submission was "Not Accepted" or "Converted" (e.g., issues with labeling, consults, testing, major deficiencies, slow response from sponsor, etc.).		

*Assignment of consults is permissible if the consult is limited in scope and can be completed within the quick review timeframe.

If an answer to **1, 2, 3 or 4 is "No", you do not need to perform a TPLC review.

***If the submission is converted, please (1) complete a new evaluation form (by checking the "Converted" box and adding an explanation for the conversion), and (2) e-mail the sponsor (using the Triage-Conversion email template in the OIR Letter Generator).

Form submitted on Wednesday, May 14, 2014 at 7:44:07 AM.

Generated with tqrform.dot v1.08.



Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

BIO-RAD LABORATORIES
JUANG WANG
REGULATORY AFFAIRS REPRESENTATIVE
5500 E. 2ND STREET
BENICIA CA 94510

Re: K141114

Trade/Device Name: BioPlex® 2200 25-OH Vitamin D Kit
BioPlex® 2200 25-OH Vitamin D Calibrator Set,
BioPlex® 2200 25-OH Vitamin D Control Set

Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D test system
Regulatory Class: II
Product Code: MRG, JJX, JIT
Dated: November 25, 2014
Received: November 25, 2014

Dear Juang Wang:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. 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 <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

BioPlex® 2200 25-OH Vitamin D Control Set

REF 663-3730 **IVD** **CE**

INTENDED USE:

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 System and the corresponding BioPlex 2200 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex 2200 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

SUMMARY AND PRINCIPLE:

The use of quality control materials is indicated as an objective assessment of the precision of methods and techniques in use and is an integral part of good laboratory practices.

MATERIALS PROVIDED:

Reagents: All reagents contain preservatives including < 0.1% 5-Bromo-5-nitro-1,3-dioxane, ≤ 0.3% ProClin 950, ≤ 0.1% sodium benzoate.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Two (2) 1.5 mL vials. The Level 1 controls are provided in a human serum matrix.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Two (2) 1.5 mL vials. The Level 2 controls are provided in a human serum matrix.

Components: One (1) package insert providing instructions for use and one (1) assignment of values sheet.

MATERIALS REQUIRED BUT NOT PROVIDED

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

WARNINGS AND PRECAUTIONS FOR USERS:



Caution, consult accompanying documents. Biological source material. Treat as potentially infectious.

Refer to Safety Data Sheets (SDS) for more safety information and warnings about chemical and biological hazards. The Safety Data Sheets are available at www.bio-rad.com and on request. Each human donor unit used to manufacture this product was tested by FDA accepted methods and found non-reactive for Hepatitis B Surface Antigen (HBsAg), antibody to hepatitis C (HCV) and antibody to HIV-1/HIV-2. This product may also contain other human agents capable of transmitting infectious disease. In accordance with good laboratory practice, all human source material should be considered potentially infectious and handled with the same precautions used with patient specimens. Prepared in accordance with requirements for CE Label.

STORAGE AND STABILITY:

This product is stable until the expiration date when stored unopened at 2 to 8°C. Once opened, product is stable for 60 days when stored tightly capped at 2 to 8°C.

PROCEDURE:

This product should be treated the same as patient specimens and run in accordance with the instructions accompanying the BioPlex 2200 Instrument and the BioPlex 2200 25-OH Vitamin D Reagent Pack.

Before sampling, allow the controls to reach room temperature (18 to 25°C) and gently mix to ensure homogeneity. After each use, promptly cap the controls and return to 2 to 8°C storage.

Dispose of any discarded materials in accordance with the requirements of your local waste management authorities. In the event of damage to packaging, contact the local Bio-Rad Laboratories Sales Office or Bio-Rad Laboratories Technical Services.

PROCEDURAL PRECAUTIONS:

1. Do not use this product past the expiration date.
2. If there is evidence of microbial contamination or excessive turbidity in the product, discard the vial.
3. Do not interchange vial caps. This may lead to cross contamination of controls.
4. For professional use only.

LIMITATIONS:

1. This product is intended for use with BioPlex 2200 Instrument. Any other use has not been characterized.

ASSIGNMENT OF VALUES:

The BioPlex 2200 25-OH Vitamin D Control Set includes 2 vials each of Level 1 and Level 2 controls. The mean values were derived from replicate analyses and should fall within the corresponding deviation. It is recommended that an individual laboratory establish its own limits for each parameter and use those provided only as guides.

BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROMs are available to load the necessary value assignment data into the Instrument. Refer to the BioPlex 2200 System Operation Manual for more information regarding this activity.

DE VERWENDUNGSZWECK:

Das BioPlex 2200 25-OH Vitamin D Control Set dient als geprüfte Qualitätskontrolle zur Überwachung der Gesamtleistungsmerkmale des BioPlex 2200 Systems und der entsprechenden BioPlex 2200 25-OH Vitamin D Reagent Packs im klinischen Labor. Die Leistungsmerkmale des BioPlex 2200 25-OH Vitamin D Control Sets bei anderen 25-Hydroxy-Vitamin-D-Assays wurden nicht ermittelt.

EINLEITUNG UND ZUSAMMENFASSUNG:

Die Verwendung entsprechender Qualitätskontrollmaterialien dient der objektiven Beurteilung der Präzision der angewandten Methoden und Techniken und ist ein unerlässlicher Bestandteil der guten Laborpraxis.

GELIEFTE MATERIALIEN:

Reagenzien: Alle Reagenzien enthalten Konservierungsmittel einschließlich < 0,1 % 5-Brom-5-nitro-1,3-dioxan, ≤ 0,3 % ProClin 950 und ≤ 0,1 % Natriumbenzoat.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Zwei (2) 1,5-mL-Fläschchen. Die Level-1-Kontrollen werden in einer Humanserummatrix geliefert.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Zwei (2) 1,5-mL-Fläschchen. Die Level-2-Kontrollen werden in einer Humanserummatrix geliefert.

Beilagen: Eine (1) Packungsbeilage mit Gebrauchsanleitung und ein (1) Datenblatt mit Wertzuordnungen.

ERFORDERLICHE, IM LIEFERUMFANG NICHT ENTHALTENE MATERIALIEN

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

WARNHINWEISE UND VORSICHTSMASSNAHMEN FÜR BENUTZER:



Achtung, Begleitdokumente beachten. Material biologischer Herkunft. Als potenziell infektiös behandeln.

Die Sicherheitsdatenblätter (SDS) enthalten weitere Sicherheitsinformationen und Warnhinweise zu chemischen und biologischen Gefahren. Die Sicherheitsdatenblätter sind unter www.bio-rad.com und auf Anfrage erhältlich. Jede zur Herstellung dieses Produkts verwendete humane Spenderreinheit wurde nach FDA-anerkannten Methoden geprüft und erwies sich als nicht reaktiv für Hepatitis-B-Oberflächenantigen (HBsAg), Antikörper gegen das Hepatitis-C-Virus (HCV) und Antikörper gegen HIV-1 und HIV-2. Dieses Produkt kann auch andere humane Substanzen enthalten, die infektiöse Krankheiten übertragen können. In Übereinstimmung mit den Richtlinien der guten Laborpraxis sollten alle Materialien humanen Ursprungs als potenziell infektiös betrachtet und mit der gleichen Sorgfalt wie Patientenproben behandelt werden. Hergestellt gemäß den Anforderungen für die CE-Kennzeichnung.

LAGERUNG UND STABILITÄT:

Dieses Produkt ist bis zum Verfallsdatum stabil, sofern es ungeöffnet bei 2-8 °C gelagert wird. Nach dem Öffnen sind die Kontrollen 60 Tage stabil, sofern sie fest verschlossen bei 2-8 °C gelagert werden.

VERFAHREN:

Dieses Produkt ist genauso wie Patientenproben zu behandeln und gemäß dem dem BioPlex 2200-Gerät und dem BioPlex 2200 25-OH Vitamin D Reagent Pack beiliegenden Anleitungen zu analysieren. Die Kontrollen vor der Probenentnahme Raumtemperatur (18-25 °C) erreichen lassen und vorsichtig durchmischen, um die Homogenität sicherzustellen. Die Kontrollen nach jedem Gebrauch sofort wieder verschließen und bei 2-8 °C aufbewahren. Die Entsorgung aller Abfälle ist nach den geltenden örtlichen Bestimmungen vorzunehmen. Falls die Verpackung beschädigt ist, nehmen Sie bitte Kontakt zur Bio-Rad Laboratories Niederlassung oder dem Bio-Rad Laboratories Kundendienst auf.

VORSICHTSHINWEISE ZUR TESTDURCHFÜHRUNG:

1. Dieses Produkt nicht nach dem Verfallsdatum verwenden.
2. Bei Anzeichen einer mikrobiellen Kontamination oder einer starken Trübung des Produkts ist das Fläschchen zu verwerfen.
3. Die Fläschchendeckel dürfen nicht miteinander vertauscht werden. Dies kann zur Kreuzkontamination der Kontrollen führen.
4. Nur zum professionellen Gebrauch.

EINSCHRÄNKUNGEN:

1. Dieses Produkt ist zur Verwendung mit dem BioPlex 2200 Instrument bestimmt. Andere Verwendungszwecke sind nicht vorgesehen.

WERTEZUORDNUNG:

Das BioPlex 2200 25-OH Vitamin D Control Set enthält je 2 Fläschchen Level-1- und Level-2-Kontrolle. Die Mittelwerte stammen aus Mehrfachbestimmungen und sollten innerhalb der entsprechenden Standardabweichung liegen. Das Labor sollte für jeden Parameter seine eigenen Grenzwerte festlegen und die vorgegebenen Werte lediglich als Richtwerte ansehen. Die erforderlichen Wertzuordnungsdaten können von den BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROMs in das Gerät geladen werden. Nähere Informationen zu diesem Vorgang sind der Bedienungsanleitung für das BioPlex 2200 System zu entnehmen.

FR UTILISATION:

Le BioPlex 2200 25-OH Vitamin D Control Set est prévu pour être utilisé comme contrôle de qualité dosé destiné à contrôler la performance globale du BioPlex 2200 System et des BioPlex 2200 25-OH Vitamin D Reagent Packs correspondants dans le laboratoire clinique. La performance du BioPlex 2200 25-OH Vitamin D Control Set n'a pas été déterminée avec d'autres tests de la 25-hydroxyvitamine D.

INTRODUCTION ET PRINCIPE:

L'utilisation de produits de contrôle de qualité est indiquée à titre d'évaluation objective de la précision des méthodes et des techniques utilisées et fait partie intégrante des bonnes pratiques de laboratoire.

MATÉRIEL FOURNI:

Réactifs: Tous les réactifs contiennent des conservateurs, incluant < 0,1 % 5-bromo-5-nitro-1,3-dioxane, ≤ 0,3 % ProClin 950, ≤ 0,1 % benzoate de sodium.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Deux (2) flacons de 1,5 mL. Les contrôles de niveau 1 sont fournis dans une matrice de sérum humain.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Deux (2) flacons de 1,5 mL. Les contrôles de niveau 2 sont fournis dans une matrice de sérum humain.

Composants: Une (1) notice d'utilisation fournissant le mode d'emploi et une (1) feuille des valeurs assignées.

MATÉRIEL NÉCESSAIRE MAIS NON FOURNI

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

AVERTISSEMENTS ET PRÉCAUTIONS À L'ATTENTION DES UTILISATEURS:



Attention, consulter la documentation jointe. Produit d'origine biologique. Traiter comme s'il était potentiellement infectieux.

Consulter les fiches de données de sécurité (FDS) pour plus d'informations sur la sécurité et les avertissements se rapportant aux dangers chimiques et biologiques. Les fiches de données de sécurité sont disponibles sur www.bio-rad.com et sur demande. Chaque don de sérum humain contribuant à la fabrication de ce produit a été testé par des méthodes acceptées par la FDA et trouvé négatif pour l'antigène de surface de l'hépatite B (AgHBs), l'anticorps anti-virus de l'hépatite C (anti-VHC) et l'anticorps anti-VIH 1 et 2. Ce produit peut également contenir d'autres agents humains capables de transmettre des maladies infectieuses. Conformément aux bonnes pratiques de laboratoire, tous les produits d'origine humaine doivent être considérés comme étant potentiellement infectieux et manipulés avec les mêmes précautions que celles utilisées pour les échantillons patients. Préparer conformément aux exigences pour le marquage CE.

CONSERVATION ET STABILITÉ:

Ce produit reste stable jusqu'à sa date de péremption lorsqu'il est conservé dans son flacon fermé entre 2 °C et 8 °C. Une fois ouvert, le produit reste stable pendant 60 jours s'il est conservé entre 2 °C et 8 °C avec son bouchon bien vissé.

PROCÉDURE:

Ce produit doit être traité de la même manière que les échantillons patients et utilisé conformément aux instructions fournies avec l'instrument BioPlex 2200 et le BioPlex 2200 25-OH Vitamin D Reagent Pack.

Avant de tester un échantillon, laissez les contrôles revenir à température ambiante (entre 18 °C et 25 °C) et les mélangez doucement pour assurer leur homogénéité. Reboucher les contrôles rapidement après chaque utilisation et les remettre au réfrigérateur entre 2 °C et 8 °C.

Éliminer tout produit restant conformément aux exigences des organismes locaux de gestion des déchets. Si l'emballage est endommagé, contacter le bureau de ventes local ou le service technique de Bio-Rad Laboratories.

PRÉCAUTIONS RELATIVES À LA PROCÉDURE:

1. Ne pas utiliser ce produit au-delà de la date de péremption.
2. Si une contamination microbienne ou une turbidité excessive du produit est constatée, jeter le flacon.
3. Ne pas échanger les bouchons des flacons. Ceci risque de provoquer une contamination croisée des contrôles.
4. Réserver à un usage professionnel.

LIMITES:

1. Ce produit est destiné à être utilisé avec l'instrument BioPlex 2200. Aucune autre utilisation n'a été caractérisée.

ASSIGNATION DES VALEURS:

Le BioPlex 2200 25-OH Vitamin D Control Set inclut 2 flacons de contrôle de niveau 1 et 2 flacons de contrôle de niveau 2. Les valeurs moyennes ont été dérivées d'analyses de répliques et doivent se situer dans l'écart-type correspondant. Il est recommandé que chaque laboratoire établisse ses propres limites pour chaque paramètre et n'utilise celles fournies qu'à titre indicatif.

Le BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM sont disponibles afin de charger les données nécessaires à l'assignation des valeurs sur l'instrument. Consulter le manuel d'utilisation du BioPlex 2200 System pour plus d'informations sur cette activité.

IT USO PREVISTO:

Il BioPlex 2200 25-OH Vitamin D Control Set è destinato all'uso come controllo di qualità analizzato per il monitoraggio delle prestazioni complessive del BioPlex 2200 System e dei relativi BioPlex 2200 25-OH Vitamin D Reagent Pack nel laboratorio di analisi cliniche. Le prestazioni del BioPlex 2200 25-OH Vitamin D Control Set non sono state stabilite con nessun altro dosaggio per 25-idrossi-vitamina D.

SOMMARIO E SPIEGAZIONE DEL METODO

L'uso di materiali di controllo di qualità è indicato come valutazione obiettiva della precisione dei metodi e delle tecniche in uso, e fa parte integrante delle buone pratiche di laboratorio.

MATERIALI FORNITI

Reagenti: Tutti i reagenti contengono conservanti, tra cui 5-bromo-5-nitro-1,3-dioxano < 0,1%, ProClin 950 ≤ 0,3%, sodio benzoato ≤ 0,1%.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Due (2) flaconi da 1,5 mL. I controlli di livello 1 sono forniti in una matrice di siero umano.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Due (2) flaconi da 1,5 mL. I controlli di livello 2 sono forniti in una matrice di siero umano.

Componenti: un (1) foglietto illustrativo contenente le istruzioni per l'uso e una (1) scheda contenente i valori assegnati.

MATERIALI NECESSARI MA NON FORNITI

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

AVVERTENZE E PRECAUZIONI PER GLI UTENTI



Attenzione, consultare la documentazione allegata. Materiale di origine biologica. Trattare come un prodotto potenzialmente infettivo.

Per ulteriori informazioni sulla sicurezza e le avvertenze relative ai pericoli chimici e biologici, consultare le schede dati di sicurezza (SDS). Le schede dati di sicurezza sono disponibili nel sito www.bio-rad.com e su richiesta.

Ciascuna unità di donatore umano utilizzata per preparare questo prodotto è stata analizzata con metodi approvati dall'ente di controllo statunitense FDA ed è risultata non reattiva per l'antigene di superficie dell'epatite B (HBsAg), per l'anticorpo diretto contro l'epatite C (HCV) e per l'anticorpo anti-HIV-1/HIV-2. Questo prodotto può anche contenere altri agenti di origine umana in grado di trasmettere malattie infettive. In base alle buone pratiche di laboratorio, tutto il materiale di origine umana deve essere considerato potenzialmente infettivo e trattato con le stesse precauzioni osservate con i campioni dai pazienti. Preparato in conformità ai requisiti per l'apposizione dell'etichetta CE.

CONSERVAZIONE E STABILITÀ

Questo prodotto è stabile fino alla data di scadenza se conservato sigillato a 2-8 °C. Una volta aperto, il prodotto rimane stabile per 60 giorni, se conservato a 2-8 °C e perfettamente sigillato.

PROCEDURA

Il presente prodotto deve essere trattato analogamente ai campioni dei pazienti e analizzato in base alle istruzioni allegate allo strumento BioPlex 2200 e al BioPlex 2200 25-OH Vitamin D Reagent Pack.

Prima di prelevare le aliquote, consentire la stabilizzazione dei controlli a temperatura ambiente (18-25 °C) e agitarli con delicatezza per garantirne l'omogeneità. Dopo ciascun uso, chiudere immediatamente i controlli e rimetterli in frigorifero (2-8 °C).

Smaltire i rifiuti in base alle norme in vigore stabilite dalle autorità competenti. Se la confezione presenta danni, rivolgersi all'ufficio commerciale o al servizio di assistenza tecnica della Bio-Rad Laboratories di zona.

PRECAUZIONI PROCEDURALI

1. Non utilizzare il prodotto dopo la data di scadenza.
2. Eliminare il flacone se eccessivamente torbido o se presenta segni di contaminazione batterica.
3. Non scambiare tra loro i tappi dei flaconi. Ciò può comportare la contaminazione crociata dei controlli.
4. Esclusivamente per uso professionale.

LIMITAZIONI

1. Il presente prodotto è previsto per l'uso con lo strumento BioPlex 2200. Non è stato caratterizzato alcun altro uso.

ASSEGNAZIONE DEI VALORI

Il BioPlex 2200 25-OH Vitamin D Control Set è composto da 2 flaconi di controllo di livello 1 e 2 flaconi di controllo di livello 2. I valori medi sono stati derivati dalle analisi dei replicati e devono rientrare nella deviazione standard corrispondente. Si consiglia a ciascun laboratorio di stabilire i propri limiti per ciascun parametro e di usare quelli forniti unicamente a scopo indicativo. Per caricare nello strumento i dati necessari relativi all'assegnazione dei valori, sono disponibili i BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM. Per ottenere ulteriori informazioni su questa operazione, consultare il manuale d'uso del BioPlex 2200 System.

ES INDICACIONES:

El BioPlex 2200 25-OH Vitamin D Control Set está previsto para su uso como control de calidad del análisis, para supervisar el rendimiento global del BioPlex 2200 System y los BioPlex 2200 25-OH Vitamin D Reagent Packs correspondientes en el laboratorio clínico. No se ha determinado el rendimiento del BioPlex 2200 25-OH Vitamin D Control Set con otros análisis para la 25-hidroxivitamina D.

RESUMEN Y PRINCIPIO:

La utilización de materiales de control de calidad es necesaria para valorar de modo objetivo la precisión de los métodos y técnicas utilizados, y es parte integral de las Buenas Prácticas de Laboratorio.

MATERIAL SUMINISTRADO:

Reactivos: Todos los reactivos contienen conservantes, incluidos < 0,1 % de 5-bromo-5-nitro-1,3-dioxano, ≤ 0,3 % de ProClin 950 y ≤ 0,1 % de benzoato de sodio.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Dos (2) frascos de 1,5 mL. Los controles de nivel 1 se suministran en una matriz de suero humano.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Dos (2) frascos de 1,5 mL. Los controles de nivel 2 se suministran en una matriz de suero humano.

Componentes: Un (1) prospecto con instrucciones de uso y una (1) hoja de asignación de valores.

MATERIAL NECESARIO NO SUMINISTRADO

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

ADVERTENCIAS Y PRECAUCIONES PARA LOS USUARIOS:



Precaución, consulte los documentos adjuntos. Material de origen biológico. Manipúlelo como si fuese potencialmente infeccioso.

Consulte las hojas de datos de seguridad (SDS) para obtener más información de seguridad y advertencias acerca de los riesgos químicos y biológicos. Las hojas de datos de seguridad se encuentran disponibles en www.bio-rad.com y a petición del interesado.

Todas las unidades procedentes de donantes humanos utilizadas para la fabricación de este producto se analizaron con métodos aceptados por la FDA y se comprobó que no son reactivas a los antígenos de superficie de la hepatitis B (HBsAg), a los anticuerpos contra el virus de la hepatitis C (VHC) ni a los anticuerpos contra el VIH-1/VIH-2. Este producto puede contener también otros agentes de origen humano capaces de transmitir enfermedades infecciosas. En conformidad con las Buenas Prácticas de Laboratorio, todo el material de origen humano debe considerarse potencialmente infeccioso y debe manipularse con las mismas precauciones empleadas con las muestras de pacientes. Preparado en conformidad con los requisitos de etiquetado de la CE.

CONSERVACIÓN Y ESTABILIDAD:

Este producto es estable hasta la fecha de caducidad, siempre y cuando se almacene sin abrir a una temperatura entre 2 °C y 8 °C. Una vez abierto, el producto es estable durante 60 días si se almacena herméticamente tapado entre 2 °C y 8 °C.

PROCEDIMIENTO:

Este producto debe manipularse igual que las muestras de pacientes y procesarse de acuerdo con las instrucciones suministradas con el instrumento BioPlex 2200 y con el BioPlex 2200 25-OH Vitamin D Reagent Pack.

Antes del muestreo, deje que los controles alcancen la temperatura ambiente (entre 18 °C y 25 °C) y mézclelos suavemente para garantizar su homogeneidad. Después de cada uso, tape los controles lo antes posible y guárdelos a una temperatura de 2 °C a 8 °C.

Elimine todos los materiales de desecho de acuerdo con los requisitos establecidos por las autoridades locales en materia de gestión de residuos. Si el envase está dañado, póngase en contacto con su oficina de ventas de Bio-Rad Laboratories o con el servicio técnico de Bio-Rad Laboratories más cercano.

PRECAUCIONES PROCEDIMENTALES:

1. No utilice este producto después de la fecha de caducidad.
2. Deseche el frasco si existen indicios de contaminación microbiana o el producto presenta excesiva turbidez.
3. No intercambie las tapas de los frascos. Esto podría ocasionar la contaminación cruzada de los controles.
4. Solo para uso profesional.

LIMITACIONES:

1. Este producto está indicado para utilizarse con el instrumento BioPlex 2200. No se ha caracterizado ningún otro uso.

ASIGNACIÓN DE VALORES:

El BioPlex 2200 25-OH Vitamin D Control Set incluye 2 frascos de controles de nivel 1 y otros 2 de nivel 2. Los valores medios se obtuvieron de análisis de repeticiones y deben estar dentro de la desviación estándar correspondiente. Se recomienda que cada laboratorio establezca sus propios límites para cada parámetro, y que utilice los suministrados solamente como guía.

Hay disponibles BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM, a fin de cargar en el instrumento los datos necesarios para la asignación de valores en el instrumento. Consulte el manual de uso del BioPlex 2200 System para obtener más información sobre esta actividad.

UTILIZACIÓN PREVISTA:

El BioPlex 2200 25-OH Vitamin D Control Set destina-se a ser utilizado como un control de qualidade testado para monitorizar o desempenho global do BioPlex 2200 System e os correspondentes BioPlex 2200 25-OH Vitamin D Reagent Packs no laboratório clínico. O desempenho do BioPlex 2200 25-OH Vitamin D Control Set não foi estabelecido com quaisquer outros ensaios da 25-hidroxitivitamina D.

RESUMO E PRINCÍPIOS:

A utilização de materiais de controlo da qualidade está indicada como uma forma de avaliação objectiva da precisão dos métodos e técnicas utilizados, sendo parte integrante das boas práticas laboratoriais.

MATERIAIS FORNECIDOS:

Reagentes: Todos os reagentes contêm conservantes, incluindo 5-bromo-5-nitro-1,3-dioxano a < 0,1%, ProClin 950 a ≤ 0,3% e benzoato de sódio a ≤ 0,1%.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Dois (2) frascos de 1,5 mL. Os controles de Nível 1 são fornecidos numa matriz de soro humano.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Dois (2) frascos de 1,5 mL. Os controles de Nível 2 são fornecidos numa matriz de soro humano.

Componentes: Um (1) folheto informativo com instruções de utilização e uma (1) folha de registo de valores.

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

ADVERTÊNCIAS E PRECAUÇÕES PARA UTILIZADORES:



Atenção, consultar os documentos incluídos. Material de origem biológica. Trate como potencialmente infeccioso.

Consulte as Fichas de Dados de Segurança (FDS) para obter mais informações e advertências de segurança acerca dos riscos químicos e biológicos. As fichas de dados de segurança estão disponíveis em www.bio-rad.com e mediante pedido. Cada unidade de dador humano utilizada no fabrico deste produto foi testada segundo métodos aceites pela FDA, tendo sido considerada não reactiva para o antígeno de superfície da hepatite B (AgHBs), anticorpos contra a hepatite C (VHC) e anticorpos contra VIH-1/VIH-2. Este produto também pode conter outros agentes humanos passíveis de transmitir doenças infecciosas. De acordo com as boas práticas laboratoriais, todos os materiais de origem humana devem ser considerados como sendo potencialmente infecciosos e manuseados com as mesmas precauções empregues no manuseamento das amostras de doentes. Preparado em conformidade com os requisitos do rótulo CE.

CONSERVAÇÃO E ESTABILIDADE:

Este produto mantém-se estável até ao fim do prazo de validade, desde que armazenado não aberto entre 2 °C e 8 °C. Depois de aberto, o produto mantém-se estável durante 60 dias quando conservado, em frasco bem fechado, entre 2 °C e 8 °C.

PROCEDIMENTO:

Este produto deve ser tratado da mesma forma que amostras de doentes e utilizado de acordo com as instruções que acompanham o instrumento BioPlex 2200 e o BioPlex 2200 25-OH Vitamin D Reagent Pack.

Antes das amostragens, permita que os controlos atinjam a temperatura ambiente (18 °C a 25 °C) e misture suavemente para assegurar a homogeneidade. Após cada utilização, coloque imediatamente a tampa nos controlos e volte a armazenar a uma temperatura de 2 °C a 8 °C.

Elimine os materiais rejeitados de acordo com os requisitos das autoridades locais de tratamento de resíduos. Caso a embalagem se encontre danificada, contacte o Departamento de Ventas local ou a Assistência Técnica da Bio-Rad Laboratories.

PRECAUÇÕES RELATIVAS AO PROCEDIMENTO:

1. Não utilize este produto depois do seu prazo de validade.
2. Se existirem sinais de contaminação microbiana ou turvação excessiva do produto, rejeite o frasco.
3. Não troque as tampas dos frascos. Isto poderá conduzir à contaminação cruzada dos controlos.
4. Apenas para utilização por profissionais.

LIMITAÇÕES:

1. Este produto destina-se a ser utilizado com o instrumento BioPlex 2200. Não foram caracterizados outros tipos de utilização.

ATRIBUIÇÃO DE VALORES:

O BioPlex 2200 25-OH Vitamin D Control Set inclui 2 frascos de cada um controles, de Nível 1 e de Nível 2. Os valores médios foram obtidos a partir de análises de replicados e devem situar-se dentro do desvio correspondente. Recomenda-se que cada laboratório estabeleça os seus próprios limites para cada parâmetro e utilize os limites fornecidos apenas como orientação. Estão disponíveis BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM para carregar no instrumento os dados de registo de valores necessários. Consulte o Manual de funcionamento do BioPlex 2200 System para obter mais informações relacionadas com esta actividade.

SV AVSEDD ANVÄNDNING:

BioPlex 2200 25-OH Vitamin D Control Set är avsett för användning som en analyserad kvalitetskontroll för att övervaka allmän prestanda för BioPlex 2200 System och motsvarande BioPlex 2200 25-OH Vitamin D Reagent Packs i det kliniska laboratoriet. Prestandan för BioPlex 2200 25-OH Vitamin D Control Set har inte fastställts med några andra analyser för 25-hydroxy-D-vitamin.

SAMMANFATTNING OCH PRINCIP:

Användningen av kvalitetskontrollmaterial är indicerat för objektiv bedömning av precisionen i använda metoder och tekniker och ingår i god laboratoripraxis.

MEDFÖLJANDE MATERIAL:

Reagenter: Alla reagenter innehåller konserveringsmedel, inklusive < 0,1 % 5-bromo-5-nitro-1,3-dioxan, ≤ 0,3 % ProClin 950, ≤ 0,1 % natriumbenzoat.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Två (2) 1,5 mL flaskor. Kontroller av nivå 1 tillhandahålls i en humanserummatris.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Två (2) 1,5 mL flaskor. Kontroller av nivå 2 tillhandahålls i en humanserummatris.

Componenter: En (1) bipacksedel med bruksanvisning samt ett (1) blad med tilldelade värden.

MATERIAL SOM KRÄVS MEN INTE MEDFÖLJER

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

VARNINGAR OCH FÖRSIKTIGHETSÅTGÄRDER FÖR ANVÄNDARE:



Försiktighet, se medföljande dokument. Biologiskt källmaterial. Behandlas som potentiellt smittsamt.

Se säkerhetsdatabladet (SDS) för mer säkerhetsinformation och varningar angående kemiska och biologiska risker. Säkerhetsdatablad finns tillgängliga på www.bio-rad.com och på begäran. Varje enhet från humana donatorer som använts för att tillverka denna produkt har testats med FDA-godkända metoder och har visat sig icke-reaktiv för hepatit B-yntigen (HBsAg), antikroppar mot hepatit C (HCV) och antikroppar mot HIV-1/HIV-2. Denna produkt innehåller kanske även andra humana agenser som kan överföra smittsamma sjukdomar. Enligt god laboratoripraxis bör allt material av human ursprung betraktas som potentiellt smittsamt och bör hanteras med samma försiktighetsåtgärder som patientprover. Beredd enligt kraven för CE-märkning.

FÖRVARING OCH STABILITET:

Produkten är stabil fram till förfallodatum om den förvaras öppnad i 2 till 8 °C. När den har öppnats är produkten stabil i 60 dagar om den förvaras med tättslutande lock i 2 till 8 °C.

PROCEDUR:

Denna produkt bör behandlas på samma sätt som patientprover och köras i enlighet med instruktionerna som medföljer BioPlex 2200-instrumentet och BioPlex 2200 25-OH Vitamin D Reagent Pack.

Före provtagning ska kontrollerna få nå rumstemperatur (18 till 25 °C) och blandas försiktigt för att säkerställa homogenitet. Efter varje användning ska locket sättas tillbaka på kontrollflaskorna. Förvara flaskorna återigen i 2 till 8 °C temperatur.

Kasserat material ska hanteras enligt de lokala föreskrifterna för avfallshantering. Om förpackningen är skadad ska du kontakta Bio-Rad Laboratories lokala försäljningskontor eller Bio-Rad Laboratories tekniska service.

PROCEDURMÄSSIGA FÖRSIKTIGHETSÅTGÄRDER:

1. Använd inte den här produkten efter förfallodatumet.
2. Om det finns tecken på mikrobiell kontaminering eller produkten är starkt grumlig, ska flaskan kastas.
3. Byt inte ut flaskornas lock mot varandra. Det kan leda till kontaminering mellan kontrollerna.
4. Endast för professionell användning.

BEGRENSNINGAR:

1. Denna produkt är avsedd för användning med BioPlex 2200-instrument. Ingen annan användning har föreskrivits.

TILDELNING AV VÄRDEN:

BioPlex 2200 25-OH Vitamin D Control Set omfattar 2 flaskor var av nivå 1 och nivå 2 kontroller. Medelvärdena har erhållits från analyser av replikat och borde falla inom motsvarande avvikelse. Vi rekommenderar att varje individuellt laboratorium fastställer sina egna gränser för varje parameter och använder de tillhandahållna gränsvärdena endast som vägledning. BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROMs finns tillgängliga för att ladda in nödvändiga värdetilldelningsdata i instrumentet. Se användarhandboken för BioPlex 2200 System för mer information om denna aktivitet.

DA ANVENDELSE:

BioPlex 2200 25-OH Vitamin D Control Set är beregnet til anvendelse som en analyseret kvalitetskontrol for at overvåge den samlede ydeevne for BioPlex 2200 System og de tilsvarende BioPlex 2200 25-OH Vitamin D Reagent Packs i det kliniske laboratorum. Ydeevnen for BioPlex 2200 25-OH Vitamin D Control Set er ikke blevet fastlagt med andre 25-hydroxy-vitamin D-analyser.

RESUMÉ OG PRINCIP:

Brug af kvalitetskontrolmaterialer er indiceret som en objektiv vurdering af de anvendte metoders og teknikkers præcision og er en integreret del af god laboratoripraksis.

MATERIALER, DER MEDFØLGER:

Reagenser: Alle reagenser indeholder konserveringsmidler, inklusive < 0,1 % 5-brom-5-nitro-1,3-dioxan, ≤ 0,3 % ProClin 950, ≤ 0,1 % natriumbenzoat.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- To (2) 1,5 mL ampuller Niveau 1-kontroller medfølger i en human serummatris.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- To (2) 1,5 mL ampuller Niveau 2-kontroller medfølger i en human serummatris.

Componenter: En (1) indlægsedel med bruksanvisning og å (1) ark med tildeling af værdier.

PÅKRÆVEDE, MEN IKKE MEDFØLGENDE MATERIALER

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

ADVARSLER OG FÖRSIKTIGHETSREGLER FÖR BRUGERE:



Försiktig, der henvises til de medföljande dokumenter. Materiale af biologisk oprindelse. Behandles som potentielt smittomt.

Se sikkerhedsdatabladene (SDS) for at få mere sikkerhedsinformation og advarsler om kemiske og biologiske farer. Sikkerhedsdatabladene kan rekvireres fra www.bio-rad.com og efter anmodning.

Hver human donorenhed anvendt til at fremstille dette produkt er testet med metoder godkendt af FDA (USAs regeringskontor for fødevarer- og medicinkontrol), og fandtes at være non-reaktiv over for hepatitis B overfladeantigen (HBsAg), antistof mod hepatitis C (HCV) og antistof mod HIV-1/2. Dette produkt kan desuden indeholde andre stoffer af human oprindelse, som er potentielt smittefarlige. I overensstemmelse med god laboratoripraksis skal alt materiale af human oprindelse anses som potentielt smittefarligt og håndteres med de samme forholdsregler som ved patientprøvet. Præpareret i overensstemmelse med kravene til CE-mærket.

OPBEVARING OG STABILITET:

Produktet er stabilt indtil udløbsdatoen, når det opbevares uåbnet ved 2 til 8 °C. Når produktet er åbnet, er det stabilt i 60 dage, når det opbevares tæt lukket ved 2 til 8 °C.

PROCEDURE:

Produktet bør håndteres på samme måde som patientprøver og køres i overensstemmelse med anvisningerne, der er vedlagt BioPlex 2200 Instrument og BioPlex 2200 25-OH Vitamin D Reagent Pack.

Før prøvetagning skal kontrollerne nå op på stuetemperatur (18 til 25 °C), og skal blandes forsigtigt for at sikre homogenitet. Efter hver anvendelse skal hættens straks sættes på kontrollerne, og de lægges til opbevaring ved 2 til 8 °C.

Bortskaf alle kasserede materialer i overensstemmelse med kravene fra de lokale renovationsmyndigheder. I tilfælde af beskadigelse af emballagen kontaktes det lokale salgskontor for Bio-Rad Laboratories eller Bio-Rad Laboratories teknisk service.

PROCEDUREMÆSSIGE FÖRHÖLDSREGLER:

1. Brug ikke produktet efter udløbsdatoen.
2. Hvis der er tegn på mikrobiel kontaminering eller for megen uklarhed i produktet, kasseres ampullen.
3. Ampulhættene må ikke ombyttes frit mellem hinanden. Dette kan føre til krydskontaminering af kontroller.
4. Kun til erhvervsmæssig anvendelse.

BEGRENSNINGER:

1. Dette produkt er beregnet til anvendelse med BioPlex 2200 Instrument. Enhver anden anvendelse er ikke blevet karakteriseret.

TILDELING AF VÆRDIER:

BioPlex 2200 25-OH Vitamin D Control Set inkluderer 2 ampuller med niveau 1-kontroller og 2 ampuller med niveau 2-kontroller. Middelværdierne blev deriveteret fra replikate analyser og skal falde indenfor den tilsvarende afvigelse. Det anbefales, at det enkelte laboratorium fastsætter sine egne grænser for hvert enkelt parameter, samt at det kun anvender de fremsatte grænser som vejledning.

BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM'et er tilgængeligt til indlæsning af nødvendige værditildelingsdata til instrumentet. Se brugervejledningen til BioPlex 2200 System, hvis du ønsker flere oplysninger om denne aktivitet.

CS URČENÉ POUŽITÍ:

BioPlex 2200 25-OH Vitamin D Control Set je určena k použití jako kontrola s ověřenou kvalitou ke sledování celkové účinnosti systému BioPlex 2200 System a příslušných reagenčních sad BioPlex 2200 25-OH Vitamin D Reagent Pack v klinické laboratorii. Účinnost BioPlex 2200 25-OH Vitamin D Control Set nebyla stanovena pro žádné další testy 25-hydroxyvitaminu D.

SOUHRN A PRINCIP:

Materiály pro kontrolu kvality jsou používány za účelem objektivního zhodnocení přesnosti laboratorních metod a technik a jsou nedílnou součástí správné laboratorní praxe.

DODÁVANÝ MATERIÁL:

Reagencie: Všechny reagencie obsahují konzervanty, mezi něž patří < 0,1 % 5-brom-5-nitro-1,3-dioxan, ≤ 0,3 % ProClin 950, ≤ 0,1 % benzoát sodný.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- Dvě (2) lahvičky o objemu 1,5 mL. Kontroly úrovně 1 se dodávají v matrici lidského séra.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- Dvě (2) lahvičky o objemu 1,5 mL. Kontroly úrovně 2 se dodávají v matrici lidského séra.

Složky: Jedna (1) příbalová informace s návodem k použití a jedna (1) tabulka s přiřazenými hodnotami.

POTŘEBNÝ MATERIÁL, KTERÝ NENÍ SOUČÁSTÍ DODÁVKY

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

VÝSTRAHY A BEZPEČNOSTNÍ OPATŘENÍ PRO UŽIVATELE:



Pozor, prostudujte příloženou dokumentaci. Materiál biologického původu. Zacházejte s prostředkem jako s potenciálně infekční látkou.

Další bezpečnostní informace a výstrahy týkající se chemických a biologických rizik najdete v bezpečnostních listech. Bezpečnostní listy jsou dostupné na www.bio-rad.com a na požádání. Každá jednotka od lidského dárce, který poskytl materiál pro výrobu tohoto produktu, byla testována metodami schválenými FDA a byla shledána neresaktivní na povrchový antigen hepatitidy B (HBsAg), na přítomnost protilátek proti hepatitidě C (HCV) a protilátek proti viru HIV-1/HIV-2. Tento produkt může také obsahovat jiná agens lidského původu, která mohou přenášet infekční onemocnění. Dle správné laboratorní praxe musí být se všemi materiály z lidských zdrojů nakládáno jako s potenciálně infekčními a se stejnými bezpečnostními opatřeními jako se vzorky pacientů. Přípraveno ve shodě s požadavky pro značení CE.

USKLADNĚNÍ A STABILITA:

Neotevřený výrobek je při skladování za teploty 2 °C až 8 °C stabilní až do data expirace. Po otevření je produkt stabilní 60 dnů při skladování od 2 °C do 8 °C v těsně uzavřené nádobě.

POSTUP:

S tímto výrobkem se musí zacházet stejně jako s patientskými vzorky a musí se používat podle návodu přiloženého k přístroji BioPlex 2200 a k BioPlex 2200 25-OH Vitamin D Reagent Pack. Před testováním ponechte kontroly vytemperovat na pokojovou teplotu (18 °C až 25 °C) a mírně promíchejte je pro zajištění homogenity. Po každém použití kontroly ihned uzavřete uzávěrem a vraťte do skladovací teploty 2 °C až 8 °C.

Likvidace nespotebtevaného materiálu musí probíhat v souladu s požadavky místních úřadů pro likvidaci odpadu. V případě poškození obalu kontaktujte místní prodejní zastoupení nebo technický servis společnosti Bio-Rad Laboratories.

PRACOVNÍ BEZPEČNOSTNÍ OPATŘENÍ:

1. Nepoužívejte výrobek po datu expirace.
2. Při známkách mikrobiální kontaminace nebo při pozorovaném zvýšeném zákalu v produktu je nutno lahvičku zlikvidovat.
3. Nezaměňujte navzájem uzávěry lahviček. To může způsobit zkříženou kontaminaci kontrol.
4. Pouze pro profesionální použití.

OMEZENÍ:

1. Tento výrobek je určen pro použití s přístrojem BioPlex 2200. Žádné jiné použití nebylo popsáno.

PŘÍŘAZENÍ HODNOT:

BioPlex 2200 25-OH Vitamin D Control Set obsahuje 2 lahvičky kontroly stupně 1 a 2 lahvičky kontroly stupně 2. Střední hodnoty byly získány několikanásobnou analýzou a měly by se pohybovat v rámci odpovídající odchylky. Doporučujeme, aby si každá laboratoř vytvořila svoje vlastní limity pro každý parametr a poskytnuté hodnoty používala pouze jako vodítko.

Pro načtení potřebných údajů přiřazených hodnot do přístroje jsou k dispozici CD-ROM šarží kontrol BioPlex 2200 25-OH Vitamin D Control Lot. Další informace týkající se této činnosti najdete v příručce pro obsluhu systému BioPlex 2200 System.

NO TILTENKT BRUK:

BioPlex 2200 25-OH Vitamin D Control Set er ment til bruk som en analysert kvalitetskontroll for å overvåke totalytelsen til BioPlex 2200 System og tilsvarende BioPlex 2200 25-OH Vitamin D Reagent Packs i det kliniske laboratoriet. Ytelsen til BioPlex 2200 25-OH Vitamin D Control Set er ikke blitt etablert med andre 25-hydroksyvitamin D-analyser.

OPPSUMMERING OG PRINSIPP:

Bruken av kvalitetskontrollmateriale er indisert som en objektiv beregning av presisjonen til metodene og teknikkene som brukes og er en integrert del av god laboratoriepraksis.

MEDFØLGENDE MATERIALER:

Reagenser: Alle reagenser inneholder konserveringsmidler, inkludert < 0,1 % 5-bromo-5-nitro-1,3-dioxan, ≤ 0,3 % ProClin 950, ≤ 0,1 % natriumbensoat.

BioPlex 2200 25-OH Vitamin D Level 1 Controls

- To (2) 1,5 mL rør. Nivå 1-kontrollene leveres i en human serummatrix.

BioPlex 2200 25-OH Vitamin D Level 2 Controls

- To (2) 1,5 mL rør. Nivå 2-kontrollene leveres i en human serummatrix.

Komponenter: Ett (1) pakningsvedlegg med bruksanvisning og ett (1) ark for tilordning av verdier.

NØDVENDIGE MATERIALER SOM IKKE LEVERES

REF 663-3740: BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM

ADVARSLER OG FORHOLDSREGLER FOR BRUKERE:



Forsiktig, se medfølgende dokumentasjon. Biologisk kildemateriale. Behandles som potensielt smittefarlig.

Se sikkerhetsdatablad (SDS) for ytterligere sikkerhetsinformasjon og advarsler om kjemiske og biologiske farer. Sikkerhetsdatabladene er tilgjengelige på www.bio-rad.com og på forespørsel. Alle humane donorenheter som er brukt til å framstille dette produktet er testet i henhold til FDA-godkjente metoder og funnet ikke-reaktive for Hepatitt B-overflateantistoff (HBsAg), antistoff mot hepatitt C (HCV) og antistoff mot HIV-1/HIV-2. Dette produktet kan også inneholde andre humane agenser som kan overføre smittsom sykdom. I henhold til god laboratoriepraksis, skal alt humant kildemateriale anses som potensielt smittefarlig og håndteres med samme forholdsregler som pasientprøver. Framstilt i henhold til kravene til CE-merking.

LAGRING OG STABILITET:

Dette produktet er stabilt til utløpsdatoen når det lagres uåpnet ved 2 til 8 °C. Etter åpning er produktet stabilt i 60 dager når det lagres tett korket ved 2 til 8 °C.

PROSEDYRE:

Dette produktet skal behandles på samme måte som pasientprøver og kjøres i henhold til anvisningene som følger med BioPlex 2200-instrumentet og BioPlex 2200 25-OH Vitamin D Reagent Pack.

Før prøvetaking skal kontrollene nå romtemperatur (18 til 25 °C) og blandes forsiktig for å sikre homogenitet. Etter hver bruk settes lokket på kontrollene umiddelbart og returneres til lagring ved 2 til 8 °C.

Kasser eventuelle ubrukte materialer i henhold til lokale avfallsforskrifter. I tilfelle av skadet emballasje, kontakt ditt lokale salgskontor for Bio-Rad Laboratories, eller Bio-Rad Laboratories teknisk service.

FORHOLDSREGLER VED PROSEDYREN:

1. Dette produktet må ikke brukes etter utløpsdato.
2. Dersom det er tegn til mikrobiell forurensning eller stor turbiditet i produktet, skal røret kastes.
3. Løkkene på rørene må ikke byttes. Dette kan føre til kryssforurensning av kontrollene.
4. Kun til profesjonelt bruk.

BEGRENSNINGER:

1. Dette produktet er ment til bruk med BioPlex 2200-instrumentet. Annen bruk er ikke evaluert.

TILORDNING AV VERDIER:

BioPlex 2200 25-OH Vitamin D Control Set inneholder 2 rør hver av nivå 1- og nivå 2-kontroller. Gjennomsnittsverdiene er derivert fra replikatanalyser og bør falle innenfor tilsvarende standardavvik. Det anbefales at hvert laboratorium etablerer egne grenser for hver parameter og bruker de angitte kun som retningslinjer. BioPlex 2200 25-OH Vitamin D Control Lot Data CD-ROM-er er tilgjengelige for å kunne laste inn nødvendige verditilordningsdata i instrumentet. Se BioPlex 2200 System-bruksanvisningen for ytterligere informasjon om disse tiltakene.



For In Vitro Diagnostic Use
In-vitro-Diagnostikum
Utilisation comme test de diagnostic in vitro
Per uso diagnostico in vitro
Para uso en diagnóstico in vitro
Para utilização em diagnóstico in vitro
För in vitro-diagnostik
Til in vitro-diagnostisk brug
Pro diagnostické použití in vitro
Til in vitro-diagnostisk bruk



European Conformity
CE-Kennzeichnung
Conformité européenne
Conformità Europea
Conforme a la normativa europea
Conformidade Europeia
Europeisk överensstämmelse
CE-mærkning
Evropská shoda
Europeisk Standard (CE)



Temperature Limit
Temperaturgrenze
Limite de température
Limiti di temperatura
Límite de temperatura
Limite da temperatura
Temperaturgränser
Temperaturområde
Teplotní limit
Temperaturgrense



Consult Instructions for Use
Gebrauchsanleitung beachten
Consulter le mode d'emploi
Consultare le istruzioni per l'uso
Consulte las instrucciones de uso
Consulte as instruções de utilização
Se bruksanvisningen
Se bruksanvisningen
Viz návod k použití
Se bruksanvisning



Lot Number
Chargennummer
Numéro de lot
Numero de lotto
Número de lote
Número de lote
Batchnummer
Lotnummer
Číslo šarže
Lotnummer



Use by (YYYY-MM-DD)
Verwendbar bis (JJJJ-MM-TT)
Utiliser avant (AAAA-MM-JJ)
Data di scadenza (AAAA-MM-GG)
Fecha de caducidad (AAAA-MM-DD)
Prazo de validade (AAAA-MM-DD)
Använd före (ÅÅÅÅ-MM-DD)
Användes inden (ÅÅÅÅ-MM-DD)
Použitje do (RRRR-MM-DD)
Brukes før (ÅÅÅÅ-MM-DD)



Manufactured by
Hersteller
Fabriqué par
Fabbricato da
Fabricado por
Fabricado por
Tilberkald av
Fremstillet af
Výrobce
Produsert av



Authorized Representative
Bevollmächtigter
Mandataire agréé
Rappresentante autorizzato
Representante autorizado
Representante autorizado
Auktoriserad representant
Autoriseret repræsentant
Autorizovaný zástupce
Autoriseret representant



Catalog Number
Katalognummer
Numéro de référence
Numero di catalogo
Número de catálogo
Número de catálogo
Katalognummer
Katalognummer
Katalogové číslo
Katalognummer



Control 1, Control 2
Kontrolle 1, Kontrolle 2
Contrôle 1, Contrôle 2
Controllo 1, Controllo 2
Control 1, Control 2
Controllo 1, Controllo 2
Kontrol 1, kontrol 2
Kontrol 1, kontrol 2
Kontrola 1, kontrola 2
Kontrol 1, Kontroll 2

Technical Information Contacts / Technische Unterstützung / Pour tous renseignements techniques / Servizio di assistenza tecnica /
Contactos para obtener información técnica / Contactos para informações técnicas / Kontakter for teknisk information /
Teknisk information / Kontakty pro technické informace / Kontakter for teknisk informasjon /
USA & Puerto Rico: 1-800-2-BIORAD (224-6723).

Outside the U.S.A., please contact your regional Bio-Rad office for assistance.

Außerhalb der USA wenden Sie sich bitte an Ihre örtliche Bio-Rad-Vertretung.

En dehors des États-Unis, contacter le bureau Bio-Rad local pour toute assistance.

Fuori dagli Stati Uniti, per ottenere assistenza, rivolgersi all'ufficio Bio-Rad di zona.

Fuera de EE.UU., póngase en contacto con la oficina regional de Bio-Rad si necesita ayuda.

Fora dos EUA, por favor contacte os seus escritórios regionais da Bio-Rad para assistência.

Utanför USA, var god kontakta ett regionalt Bio-Rad-kontor för assistans.

Uden for USA bedes man kontakte det lokale Bio-Rad kontor for assistance.

Pro podporu mimo území USA požádejte o pomoc svoji oblastní pobočku společnosti Bio-Rad.

Utanför USA, kontakt ditt regionale Bio-Rad-salgskontor for assistanse.

BioPlex is a registered trademark of Bio-Rad Laboratories, Inc.



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FRANCE: Bio-Rad, 3 boulevard Raymond Poincaré, 92430 Marnes-la-Coquette

BIO-RAD

**Bio-Rad
Laboratories**

Clinical
Diagnostics Group

Website www.bio-rad.com/diagnostics **Gladesville, Australia**, Ph. 61-2-9914-2800, Fx. 61-2-9914-2888 **Vienna, Austria**, Ph. 43-1-877-8901, Fx. 43-1-876-5629
Nazareth, Belgium, Ph. 32-9-385-5511, Fx. 32-9-385-6554 **Lagoa Santa, Brazil**, Ph. +55 (31)3689-6600, Fx. +55 (31)3689-6611
Montréal, Canada, Ph. 1-514-334-4372, Fx. 1-514-334-4415 **Shanghai, China**, Ph. 86-21-61698500, Fx. 86-21-61698599
Prague, Czech Republic, Ph. 420-241-430-532, Fx. 420-241-431-642 **Symbion Science Park, Denmark**, Ph. +45-4452-1000, Fx. +45-4452-1001
Espoo, Finland, Ph. 358-9-904-22-00, Fx. 358-9-7597-5010 **Marnes-la-Coquette, France**, Ph. 33-1-47-95-60-00, Fx. 33-1-47-41-91-33
Munich, Germany, Ph. +49 (0)89-318-840, Fx. +49 (0)89-318-84100 **Athens, Greece**, Ph. 30-210-7774396, Fx. 30-210-7774376
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Seoul, Korea, Ph. 82-2-3473-4480, Fx. 82-2-3472-7003 **Mexico D.F., Mexico**, Ph. +52 (55)5488-7670, Fx. +52 (55)1107-7246
Veenendaal, The Netherlands, Ph. +31-318-540666, Fx. +31-318-542216 **Auckland, New Zealand**, Ph. 64-9-415-2280, Fx. 64-9-415-2284
Oslo, Norway, Ph. +47-23-38-41-30, Fx. +46(0)8-5551-2780 **Warsaw, Poland**, Ph. 48-22-3319999, Fx. 48-22-3319998
Amadora, Portugal, Ph. 351-21-472-7700, Fx. 351-21-472-7777 **Moscow, Russia**, Ph. 7-495-721-14-04, Fx. 7-495-721-14-12
Singapore, Ph. 65-6415-3170, Fx. 65-6415-3189 **Johannesburg, South Africa**, Ph. 27-11-442-85-08, Fx. 27-11-442-85-25
Madrid, Spain, Ph. 34-91-590-5200, Fx. 34-91-590-5211 **Sofia, Sweden**, Ph. +46-8-555-127-00, Fx. +46-8-555-127-80
Cressler, Switzerland, Ph. +41 (0)26-674-55-05/08, Fx. +41 (0)26-674-52-19 **Taipei, Taiwan**, Ph. 886-2-2578-7188, Fx. 886-2-2578-6890
Bangkok, Thailand, Ph. 662-651-8311, Fx. 662-651-8312 **Hemel Hempstead, United Kingdom**, Ph. +44 (0)20-8328-2000, Fx. +44 (0)20-8328-2550

BioPlex® 2200 25-OH Vitamin D Calibrator Set



EN INTENDED USE

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D Reagent Pack.

SUMMARY AND PRINCIPLE

The BioPlex 2200 25-OH Vitamin D Reagent Pack is calibrated using a set of six (6) distinct calibrators. Calibrators are used in a test system to establish points of reference that are used in the quantitative measurement of the presence of substances in human specimens.

MATERIALS PROVIDED

- **Reagents** - Six (6) 0.5 mL 25-OH Vitamin D calibrator vials. Calibrator level 1 contains 25% horse serum without vitamin D. The calibrator levels 2 to 6 are provided in a vitamin D depleted human serum matrix supplemented with known concentration of 25-OH Vitamin D₃. All Calibrators contain preservatives including $\leq 0.3\%$ ProClin 950, $\leq 0.1\%$ sodium benzoate and $< 0.1\%$ 5-bromo-5-nitro-1,3-dioxane (BND).
- **Analytes** - 25-hydroxyvitamin D
- **Component** - One (1) instructions for use

MATERIALS REQUIRED BUT NOT PROVIDED

REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Important! The file selected and loaded (ng/mL or nmol/L) must be compatible with the Assay Protocol file (APF).

Note: See the ASSIGNED VALUES section below.

WARNINGS AND PRECAUTIONS FOR USERS

- For In Vitro Diagnostic use
- This product should not be used past the expiration date.
- If there is evidence of microbial contamination or excessive turbidity in the product, discard the vial.
- Do not interchange vial caps. This may lead to cross contamination of calibrators.
- For professional use only.



Caution, consult accompanying documents. Biological source material. Treat as potentially infectious.

Refer to Safety Data Sheets (SDS) for more safety information and warnings about chemical and biological hazards. The Safety Data Sheets are available at www.bio-rad.com and on request. Each human donor unit used to manufacture this product was tested by FDA accepted methods and found non-reactive for Hepatitis B Surface Antigen (HBsAg), antibody to hepatitis C (HCV) and antibody to HIV-1/HIV-2. This product may also contain other human agents capable of transmitting infectious disease. In accordance with good laboratory practice, all human source material should be considered potentially infectious and handled with the same precautions used with patient specimens. Prepared in accordance with requirements for CE Label.

STORAGE AND STABILITY

This product is stable until the expiration date when stored unopened at 2 to 8°C. Once opened, the calibrators are stable for 30 days when stored tightly capped at 2 to 8°C.

PROCEDURE

This product should be run in accordance with the instructions accompanying the BioPlex 2200 Instrument and BioPlex 2200 25-OH Vitamin D Reagent Pack.

Before sampling, allow the calibrators to reach room temperature (18 to 25°C) and gently mix to ensure homogeneity. After each use, promptly cap the reagents and return to 2 to 8°C storage. Dispose of any discarded materials in accordance with the requirements of your local waste management authorities. In the event of damage to packaging, contact the local Bio-Rad Laboratories Sales Office or Bio-Rad Laboratories Technical Services.

LIMITATIONS

This product is intended for use with the BioPlex 2200 Instrument. Any other use has not been characterized.

ASSIGNED VALUES

Reagent-assigned, lot-specific values are included as printable PDF files on each Calibrator Lot Data CD-ROM. There is a separate file, one in ng/mL and one in nmol/L, on the Calibrator Lot Data CD-ROM for each associated Reagent Pack lot. Values can be automatically loaded from the BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Refer to the Operation Manual for more information regarding this activity.

Results are expressed as ng/mL or nmol/L. Calibrator assignment is established using a Master Set of calibrators and a specific lot of BioPlex 2200 25-OH Vitamin D Reagent Packs on multiple BioPlex 2200 instruments. A 4-PL (4-Parameter Logistic) curve fit using six calibrator levels is used to calculate quantitative results.

TRACEABILITY

The BioPlex 2200 25-OH Vitamin D assay is calibrated to reference materials using UV absorbance spectrometry.

DE VERWENDUNGSZWECK

Das BioPlex 2200 25-OH Vitamin D Calibrator Set dient zur Kalibrierung des BioPlex 2200 25-OH Vitamin D Reagent Pack.

EINLEITUNG UND ZUSAMMENFASSUNG

Der BioPlex 2200 25-OH Vitamin D Reagent Pack wird mit Hilfe eines Sets mit sechs (6) verschiedenen Kalibratoren kalibriert. Die Kalibratoren dienen in einem Testsystem zur Bestimmung von Bezugspunkten für die quantitative Messung des Vorliegens von Substanzen in Humanproben.

GELIEFERTE MATERIALIEN

- **Reagenzien** - Sechs (6) 0,5-mL-Fläschchen 25(OH)-Vitamin-D-Kalibrator. Der Level-1-Kalibrator enthält 25 % Pferdeserum ohne Vitamin D. Die Level-2- bis Level-6-Kalibratoren werden in einer Vitamin-D-verarmten Humanserummatrix mit einer bekannten Konzentration 25(OH)-Vitamin D₃ bereitgestellt. Alle Kalibratoren enthalten Konservierungsmittel einschließlich $\leq 0,3\%$ ProClin 950, $\leq 0,1\%$ Natriumbenzoat und $< 0,1\%$ 5-Brom-5-nitro-1,3-dioxan (BND).
- **Analyten** - 25-Hydroxy-Vitamin D
- **Beilagen** - Eine (1) Gebrauchsanleitung

ERFORDERLICHE, IM LIEFERUMFANG NICHT ENTHALTENE MATERIALIEN

REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Wichtig! Die ausgewählte und geladene Datei (ng/mL oder nmol/L) muss mit der Assay-Protokolldatei (APF) kompatibel sein.

Hinweis: Siehe den Abschnitt ZUGEORNETE WERTE weiter unten.

WARNHINWEISE UND VORSICHTSMASSNAHMEN FÜR BENUTZER

- In-vitro-Diagnostikum.
- Dieses Produkt nach Ablauf des Verfallsdatums nicht mehr verwenden.
- Bei Anzeichen einer mikrobiellen Kontamination oder einer starken Trübung des Produkts ist das Fläschchen zu verwerfen.
- Die Fläschchendeckel dürfen nicht miteinander vertauscht werden. Dies kann zu einer Kreuzkontamination der Kalibratoren führen.
- Nur zum professionellen Gebrauch.



Achtung, Begleitdokumente beachten. Material biologischer Herkunft. Als potenziell infektiös behandeln.

Die Sicherheitsdatenblätter (SDS) enthalten weitere Sicherheitsinformationen und Warnhinweise zu chemischen und biologischen Gefahren. Die Sicherheitsdatenblätter sind unter www.bio-rad.com und auf Anfrage erhältlich.

Jede zur Herstellung dieses Produkts verwendete humane Spendereinheit wurde nach FDA-anerkannten Methoden geprüft und erwies sich als nicht reaktiv für Hepatitis-B-Oberflächenantigen (HBsAg), Antikörper gegen das Hepatitis-C-Virus (HCV) und Antikörper gegen HIV-1 und HIV-2. Dieses Produkt kann auch andere humane Substanzen enthalten, die infektiöse Krankheiten übertragen können. In Übereinstimmung mit den Richtlinien der guten Laborpraxis sollten alle Materialien humanen Ursprungs als potenziell infektiös betrachtet und mit der gleichen Sorgfalt wie Patientenproben behandelt werden. Hergestellt gemäß den Anforderungen für die CE-Kennzeichnung.

LAGERUNG UND STABILITÄT

Dieses Produkt ist bis zum Verfallsdatum stabil, sofern es ungeöffnet bei 2 °C bis 8 °C gelagert wird. Nach dem Öffnen sind die Kalibratoren 30 Tage stabil, sofern sie fest verschlossen bei 2 °C bis 8 °C gelagert werden.

TESTDURCHFÜHRUNG

Dieses Produkt ist gemäß den dem BioPlex 2200 Instrument und dem BioPlex 2200 25-OH Vitamin D Reagent Pack beiliegenden Anleitungen zu analysieren.

Die Kalibratoren vor der Probenentnahme Raumtemperatur (18-25 °C) erreichen lassen und vorsichtig durchmischen, um die Homogenität sicherzustellen. Die Reagenzien nach jedem Gebrauch sofort wieder verschließen und bei 2-8 °C aufbewahren. Die Entsorgung aller Abfälle ist nach den geltenden örtlichen Bestimmungen vorzunehmen. Falls die Verpackung beschädigt ist, nehmen Sie bitte Kontakt zur Bio-Rad Laboratories Niederlassung oder dem Bio-Rad Laboratories Kundendienst auf.

EINSCHRÄNKUNGEN

Dieses Produkt ist zur Verwendung mit dem BioPlex 2200-Gerät bestimmt. Andere Verwendungszwecke sind nicht vorgesehen.

ZU GEORNETE WERTE

Jede CD-ROM mit Kalibratorchargendaten enthält ausdrückbare PDF-Dateien mit den Reagenzien zugeordneten, chargenspezifischen Werten. Die CD-ROM mit Kalibratorchargendaten enthält für jede zugehörige Reagenzienpackcharge jeweils eine separate Datei in ng/mL und eine in nmol/L.

Die Werte können automatisch von der BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM geladen werden.

Weitere Informationen zu diesem Vorgang finden Sie in der Bedienungsanleitung.

Die Ergebnisse werden in ng/mL oder nmol/L angegeben. Die Zuordnung der Kalibratorwerte erfolgt unter Verwendung eines Kalibratoren-Mastersets und einer bestimmten Charge von

BioPlex 2200 25-OH Vitamin D Reagent Packs auf mehreren BioPlex 2200-Geräten. Zur Berechnung der quantitativen Ergebnisse wird eine 4-PL-Kurvenanpassung (4-Parameter-Logistik) mit sechs Kalibratorschritten verwendet.

RÜCKVERFOLGBARKEIT

Der BioPlex 2200 25-OH Vitamin D Assay wurde mittels UV-Absorptionsspektrometrie gegen Referenzmaterialien kalibriert.

FR UTILISATION

Le BioPlex 2200 25-OH Vitamin D Calibrator Set est destiné à la calibration du BioPlex 2200 25-OH Vitamin D Reagent Pack.

INTRODUCTION ET PRINCIPE

Le BioPlex 2200 25-OH Vitamin D Reagent Pack est calibré au moyen d'un jeu de six (6) calibrateurs différents. Les calibrateurs sont utilisés dans le cadre d'un système de test pour établir des points de référence qui sont utilisés pour le dosage quantitatif de la présence de certaines substances dans des échantillons humains.

MATÉRIEL FOURNI

- **Réactifs** - Six (6) flacons de 0,5 mL de calibrateurs de 25-OH vitamine D. Le calibrateur de niveau 1 contient 25 % de sérum équin sans vitamine D. Les calibrateurs de niveaux 2 à 6 sont fournis dans une matrice de sérum humain dépourvue de vitamine D et additionnée d'une concentration connue de 25-OH vitamine D₃. Tous les calibrateurs contiennent des conservateurs, incluant $\leq 0,3\%$ ProClin 950, $\leq 0,1\%$ benzoate de sodium et $< 0,1\%$ 5-bromo-5-nitro-1,3-dioxanne (BND).
- **Analytes** - 25-hydroxyvitamine D
- **Composants** - Un (1) mode d'emploi

MATÉRIEL NÉCESSAIRE MAIS NON FOURNI

REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Important ! Le fichier sélectionné et chargé (ng/mL ou nmol/L) doit être compatible avec le Fichier de protocole du test (APF).

Remarque : Voir la section VALEURS ASSIGNÉES ci-dessous.

AVERTISSEMENTS ET PRÉCAUTIONS À L'ATTENTION DES UTILISATEURS

- Utilisation comme test de diagnostic in vitro.
- Ne pas utiliser ce produit au-delà de sa date de péremption.
- Si une contamination microbienne ou une turbidité excessive du produit est constatée, jeter le flacon.
- Ne pas échanger les bouchons des flacons. Ceci risque d'entraîner une contamination croisée des calibrateurs.
- Réservé à un usage professionnel.



Attention, consulter la documentation jointe. Produit d'origine biologique. Traiter comme s'il était potentiellement infectieux.

Consulter les fiches de données de sécurité (FDS) pour plus d'informations sur la sécurité et les avertissements se rapportant aux dangers chimiques et biologiques. Les fiches de données de sécurité sont disponibles sur www.bio-rad.com et sur demande. Chaque don de sérum humain contribuant à la fabrication de ce produit a été testé par des méthodes acceptées par la FDA et trouvé négatif pour l'antigène de surface de l'hépatite B (AgHBs), l'anticorps anti-virus de l'hépatite C (anti-HVC) et l'anticorps anti-VIH 1 et 2. Ce produit peut également contenir d'autres agents humains capables de transmettre des maladies infectieuses. Conformément aux bonnes pratiques de laboratoire, tous les produits d'origine humaine doivent être considérés comme étant potentiellement infectieux et manipulés avec les mêmes précautions que celles utilisées pour les échantillons patients. Préparé conformément aux exigences pour le marquage CE.

CONSERVATION ET STABILITÉ

Ce produit reste stable jusqu'à sa date de péremption lorsqu'il est conservé dans son flacon fermé entre 2 °C et 8 °C. Une fois ouverts, les calibrateurs restent stables pendant 30 jours s'ils sont conservés entre 2 °C et 8 °C avec leurs bouchons bien vissés.

PROCÉDURE

Ce produit doit être utilisé conformément au mode d'emploi de l'instrument BioPlex 2200 et du BioPlex 2200 25-OH Vitamin D Reagent Pack.

Avant de tester un échantillon, laisser les calibrateurs revenir à température ambiante (entre 18 °C et 25 °C) et les mélanger doucement pour assurer leur homogénéité. Raboucher les réactifs rapidement après chaque utilisation et les remettre au réfrigérateur entre 2 °C et 8 °C.

Éliminer tout produit restant conformément aux exigences des organismes locaux de gestion des déchets. Si l'emballage est endommagé, contacter le bureau de ventes local ou le service technique de Bio-Rad Laboratories.

LIMITES

Ce produit est destiné à être utilisé avec l'instrument BioPlex 2200. Aucune autre utilisation n'a été caractérisée.

VALEURS ASSIGNÉES

Les valeurs assignées, spécifiques aux lots de réactifs, sont incluses sous la forme de fichiers PDF imprimables sur chaque CD-ROM des données relatives au lot de calibrateurs. Il existe un fichier distinct (un fichier en ng/mL et un fichier en nmol/L) sur le CD-ROM des données relatives au lot de calibrateurs pour chaque lot de cartouches de réactifs associé.

Les valeurs peuvent être automatiquement chargées à partir du BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM.

Se reporter au manuel d'utilisation pour des informations complémentaires concernant cette activité.

Les résultats sont exprimés en ng/mL ou nmol/L. On établit l'assignation du calibrateur au moyen d'un jeu de calibrateurs de référence et d'un lot spécifique de BioPlex 2200 25-OH Vitamin D Reagent Packs sur plusieurs instruments BioPlex 2200. Un ajustement de courbe 4-PL (logistique à 4 paramètres) utilisant six niveaux de calibrateurs est utilisé pour calculer les résultats quantitatifs.

TRAÇABILITÉ

Le test BioPlex 2200 25-OH Vitamin D est calibré par référence des matériaux utilisant une spectrométrie d'absorbance des UV.

IT USO PREVISTO

Il BioPlex 2200 25-OH Vitamin D Calibrator Set è destinato alla calibrazione del BioPlex 2200 25-OH Vitamin D Reagent Pack.

SOMMARIO E SPIEGAZIONE DEL METODO

Il BioPlex 2200 25-OH Vitamin D Reagent Pack viene calibrato con una serie di sei (6) diversi calibratori. I calibratori vengono usati in un sistema di analisi per stabilire punti di riferimento da utilizzare per la determinazione quantitativa di sostanze nei campioni umani.

MATERIALI FORNITI

- **Reagenti** - Sei (6) flaconi di calibratori da 0,5 mL per 25-idrossi-vitamina D. Il calibratore di livello 1 contiene siero equino al 25% senza vitamina D. I calibratori dal livello 2 al livello 6 sono forniti in una matrice di siero umano priva di vitamina D e con l'aggiunta di 25-idrossi-vitamina D₃ a concentrazioni note. Tutti i calibratori contengono conservanti, tra cui ProClin 950 ($\leq 0,3\%$), sodio benzoato ($\leq 0,1\%$) e 5-bromo-5-nitro-1,3-diossano (BND) ($< 0,1\%$).
- **Analiiti** - 25-idrossi-vitamina D
- **Componenti** - Un (1) manuale di istruzioni per l'uso

MATERIALI NECESSARI MA NON FORNITI

REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Importante. Il file selezionato e caricato (ng/mL o nmol/L) deve essere compatibile con il file del protocollo di analisi (APF).

Nota - Vedere più avanti la sezione VALORI ASSEGNATI.

AVVERTENZE E PRECAUZIONI PER GLI UTENTI

- Per uso diagnostico in vitro.
- Non usare il prodotto dopo la data di scadenza.
- Eliminare il flacone se eccessivamente torbido o se presenta segni di contaminazione batterica.
- Non scambiare tra loro i tappi dei flaconi. Ciò può comportare la contaminazione crociata dei calibratori.
- Esclusivamente per uso professionale.



Attenzione, consultare la documentazione allegata. Materiale di origine biologica. Tratarlo come un prodotto potenzialmente infettivo.

Per ulteriori informazioni sulla sicurezza e le avvertenze relative ai pericoli chimici e biologici, consultare le schede dati di sicurezza (SDS). Le schede dati di sicurezza sono disponibili sul sito www.bio-rad.com e su richiesta.

Ciascuna unità di donatore umano utilizzata per preparare questo prodotto è stata analizzata con metodi approvati dall'ente di controllo statunitense FDA ed è risultata non reattiva per l'antigene di superficie dell'epatite B (HBsAg), per l'anticorpo diretto contro l'epatite C (HCV) e per l'anticorpo anti-HIV-1/HIV-2. Questo prodotto può anche contenere altri agenti di origine umana in grado di trasmettere malattie infettive. In base alle buone pratiche di laboratorio, tutto il materiale di origine umana deve essere considerato potenzialmente infettivo e trattato con le stesse precauzioni osservate con i campioni dei pazienti. Preparato in conformità ai requisiti per l'apposizione dell'etichetta CE.

CONSERVAZIONE E STABILITÀ

Questo prodotto è stabile fino alla data di scadenza se conservato sigillato a 2-8 °C. Una volta aperti, i calibratori rimangono stabili per 30 giorni, se conservati a 2-8 °C e perfettamente sigillati.

PROCEDURA

Il presente prodotto deve essere analizzato in base alle istruzioni allegate allo strumento BioPlex 2200 e al BioPlex 2200 25-OH Vitamin D Reagent Pack.

Prima di prelevare le aliquote, consentire la stabilizzazione dei calibratori a temperatura ambiente (18-25 °C) e agitarli con delicatezza per garantirne l'omogeneità. Dopo ciascun uso, chiudere immediatamente i reagenti e rimetterli in frigorifero (2-8 °C).

Smaltire i rifiuti in base alle norme in vigore stabilite dalle autorità competenti. Se la confezione presenta danni, rivolgersi all'ufficio commerciale o al servizio di assistenza tecnica della Bio-Rad Laboratories di zona.

LIMITAZIONI

Il presente prodotto è previsto per l'uso con lo strumento BioPlex 2200. Non è stato caratterizzato alcun altro uso.

VALORI ASSEGNATI

I valori assegnati ai reagenti e specifici per lotto sono inclusi sotto forma di file PDF stampabili, contenuti su ciascun CD-ROM con i dati dei lotti dei calibratori. Per ogni lotto di cartucce reagenti è disponibile un file separato, uno in ng/mL e uno in nmol/L, sul CD-ROM con i dati dei lotti dei calibratori.

I valori possono essere caricati automaticamente dal BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Per ulteriori informazioni al riguardo, consultare il manuale d'uso.

I risultati sono espressi in ng/mL o nmol/L. L'assegnazione dei calibratori viene stabilita mediante un set principale di calibratori e un lotto specifico di BioPlex 2200 25-OH Vitamin D Reagent Pack su tutti strumenti BioPlex 2200. Per calcolare i risultati quantitativi utilizzando calibratori di sei livelli, viene utilizzato un adattamento della curva logistica a 4 parametri (4-PL).

BIO-RAD BioPlex® 2200 25-OH Vitamin D Calibrator Set

RICONDUIBILITÀ
Il dosaggio BioPlex 2200 25-OH Vitamin D viene calibrato secondo i materiali di riferimento tramite spettrometria di assorbimento UV.

ES INDICACIONES
El BioPlex 2200 25-OH Vitamin D Calibrator Set está indicado para la calibración del BioPlex 2200 25-OH Vitamin D Reagent Pack.

RESUMEN Y PRINCIPIOS
El BioPlex 2200 25-OH Vitamin D Reagent Pack se calibra usando un conjunto de seis (6) calibradores diferentes. Los calibradores se utilizan en un sistema de prueba para establecer puntos de referencia que se utilizan para la determinación cuantitativa de la presencia de sustancias en muestras humanas.

MATERIAL SUMINISTRADO

- **Reactivos** - Seis (6) frascos de 0,5 mL de calibrador 25-OH Vitamin D. El calibrador de nivel 1 contiene suero de caballo al 25 % sin vitamina D. Los calibradores de niveles 2 a 6 se suministran en matriz de suero humano con reducción de la vitamina D, suplementados con una concentración conocida de 25-hidroxitamina D₃. Todos los calibradores contienen conservantes, incluidos ProClin 950 (≤0,3 %), benzoato de sodio (≤0,1 %) y 5-bromo-5-nitro-1,3-dioxano (<0,1 %).
- **Análisis** - 25-hidroxitamina D
- **Componentes** - Unas (1) instrucciones de uso

MATERIAL NECESARIO NO SUMINISTRADO
REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

¡Importante! El archivo seleccionado y cargado (ng/mL o nmol/L) debe ser compatible con el archivo de protocolos de análisis (APF).
Nota: Consulte el apartado VALORES ASIGNADOS a continuación.

ADVERTENCIAS Y PRECAUCIONES PARA LOS USUARIOS
Para uso en diagnóstico in vitro.

- Este producto no debe emplearse una vez transcurrida la fecha de caducidad.
- Deseche el frasco si existen indicios de contaminación microbiana o el producto presenta excesiva turbidez.
- No intercambie las tapas de los frascos. Eso podría ocasionar la contaminación cruzada de los calibradores.
- Solo para uso profesional.

Precaución, consulte los documentos adjuntos. Material de origen biológico. Manipúlelo como si fuese potencialmente infeccioso.

Consulte las hojas de datos de seguridad (SDS) para obtener más información de seguridad y advertencias acerca de los riesgos químicos y biológicos. Las hojas de datos de seguridad se encuentran disponibles en www.bio-rad.com y a petición del interesado.

Todas las unidades procedentes de donantes humanos utilizadas para la fabricación de este producto se analizaron con métodos aceptados por la FDA y se comprobó que no son reactivas a los antígenos de superficie de la hepatitis B (HBsAg), a los anticuerpos contra el virus de la hepatitis C (VHC) ni a los anticuerpos contra el VIH-1/VIH-2. Este producto puede contener también otros agentes de origen humano capaces de transmitir enfermedades infecciosas. En conformidad con las Buenas Prácticas de Laboratorio, todo el material de origen humano debe considerarse potencialmente infeccioso y debe manipularse con las mismas precauciones empleadas con las muestras de pacientes. Preparado en conformidad con los requisitos de etiquetado de la CE.

ALMACENAMIENTO Y ESTABILIDAD
Este producto es estable hasta la fecha de caducidad, siempre y cuando se almacene sin abrir a una temperatura entre 2 y 8 °C. Una vez abiertos, los calibradores son estables durante 30 días, si se almacenan herméticamente tapados entre 2 y 8 °C.

PROCEDIMIENTO
Este producto debe procesarse de acuerdo con las instrucciones suministradas con el instrumento BioPlex 2200 y con el BioPlex 25-OH Vitamin D Reagent Pack.

Antes del muestreo, deje que los calibradores alcancen la temperatura ambiente (entre 18 y 25 °C) y mézclelos suavemente para garantizar su homogeneidad. Después de cada uso, tape los reactivos lo antes posible y guárdelos a una temperatura de 2 a 8 °C.

Elimine todos los materiales de desecho de acuerdo con los requisitos establecidos por las autoridades locales en materia de gestión de residuos. Si el envase está dañado, póngase en contacto con su oficina de ventas de Bio-Rad Laboratories o con el servicio técnico de Bio-Rad Laboratories más cercano.

LIMITACIONES
Este producto está indicado para utilizarse con el instrumento BioPlex 2200. No se ha caracterizado ningún otro uso.

VALORES ASIGNADOS
Los valores asignados, específicos para cada lote de reactivos, están incluidos como archivos PDF imprimibles en el CD-ROM de datos de cada lote de calibradores. Hay un archivo separado, uno en ng/mL y uno en nmol/L, en el CD-ROM de datos del lote de calibradores para cada lote de paquetes de reactivos asociado. Los valores se pueden cargar automáticamente desde el BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Consulte el manual de uso para obtener más información sobre esta actividad.

Los resultados se expresan en ng/mL o nmol/L. Los valores de los calibradores se determinan con un conjunto maestro de calibradores y un lote específico de BioPlex 2200 25-OH Vitamin D Reagent Packs en varios instrumentos BioPlex 2200. Se usa un

ajuste de curva logístico de 4 parámetros (4-PL) con seis niveles de calibradores para calcular los resultados cuantitativos.

TRAZABILIDAD
El análisis BioPlex 2200 25-OH Vitamin D se calibra según los materiales de referencia mediante espectrometría de absorción UV.

PT UTILIZAÇÃO PREVISTA
O BioPlex 2200 25-OH Vitamin D Calibrator Set é concebido para a calibração do BioPlex 2200 25-OH Vitamin D Reagent Pack.

RESUMO E PRINCÍPIOS
O BioPlex 2200 25-OH Vitamin D Reagent Pack é calibrado utilizando um conjunto de seis (6) calibradores diferentes. Os calibradores são utilizados num sistema de teste para estabelecimento de pontos de referência que são usados na medição quantitativa da presença de substâncias em amostras humanas.

MATERIAIS FORNECIDOS

- **Reagentes** - Seis (6) frascos de calibradores de 0,5 mL de 25-OH Vitamina D. O calibrador de nível 1 contém soro equino a 25% sem vitamina D. Os níveis 2 a 6 do calibrador são fornecidos numa matriz de soro humano sem vitamina D suplementada com uma concentração conhecida de 25-OH Vitamina D₃. Todos os calibradores contêm conservantes, incluindo ProClin 950 a ≤ 0,3%, benzoato de sódio a ≤ 0,1% e 5-bromo-5-nitro-1,3-dioxano (BND) a < 0,1%.
- **Substâncias a analisar** - 25-hidroxitamina D
- **Componentes** - Um (1) conjunto de instruções de utilização

MATERIAIS NECESSÁRIOS MAS NÃO FORNECIDOS
REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Importante! O ficheiro seleccionado e carregado (ng/mL ou nmol/L) tem de ser compatível com o ficheiro do protocolo do ensaio (FPE).
Observação: Consulte a secção VALORES ATRIBUÍDOS abaixo.

ADVERTÊNCIAS E PRECAUÇÕES PARA UTILIZADORES
Para utilização em diagnóstico in vitro.

- Este produto não deve ser utilizado após o fim do prazo de validade.
- Se existirem sinais de contaminação microbiana ou turvação excessiva do produto, rejeite o frasco.
- Não troque as tampas dos frascos. Isto poderá conduzir à contaminação cruzada dos calibradores.
- Apenas para utilização por profissionais.

Atenção, consultar os documentos incluídos. Material de origem biológica. Trate como potencialmente infeccioso.

Consulte as Fichas de Dados de Segurança (FDS) para obter mais informações e advertências de segurança acerca dos riscos químicos e biológicos. As fichas de dados de segurança estão disponíveis em www.bio-rad.com e mediante pedido. Cada unidade de dador humano utilizada no fabrico deste produto foi testada segundo métodos aceites pela FDA, tendo sido considerada não reactiva para o antígeno de superfície da hepatite B (AgHBs), anticorpos contra a hepatite C (VHC) e anticorpos contra VIH-1/VIH-2. Este produto também pode conter outros agentes humanos passíveis de transmitir doenças infecciosas. De acordo com as boas práticas laboratoriais, todos os materiais de origem humana devem ser considerados como sendo potencialmente infecciosos e manuseados com as mesmas precauções empregues no manuseamento das amostras de doentes. Preparado em conformidade com os requisitos do rótulo CE.

ARMAZENAMENTO E ESTABILIDADE
Este produto mantém-se estável até ao fim do prazo de validade, desde que armazenado não aberto entre 2 °C e 8 °C. Depois de abertos, os calibradores mantêm-se estáveis durante 30 dias quando conservado, em frascos bem fechados, entre 2 °C e 8 °C.

PROCEDIMENTO
Este produto deve ser utilizado de acordo com as instruções que acompanham o Instrumento BioPlex 2200 e o BioPlex 2200 25-OH Vitamin D Reagent Pack.

Antes da amostragem, permita que os calibradores atinjam a temperatura ambiente (18 °C a 25 °C) e misture suavemente para assegurar a homogeneidade. Após cada utilização, coloque imediatamente a tampa nos reagentes e volte a conservá-los a uma temperatura de 2 °C a 8 °C.

Elimine os materiais rejeitados de acordo com os requisitos das autoridades locais de tratamento de resíduos. Caso a embalagem se encontre danificada, contacte o Departamento de Vendas local ou a Assistência Técnica da Bio-Rad Laboratories.

LIMITAÇÕES
Este produto destina-se a ser utilizado com o instrumento BioPlex 2200. Não foram caracterizados outros tipos de utilização.

VALORES ATRIBUÍDOS
Os valores específicos para o lote, atribuídos por reagente, são incluídos sob a forma de ficheiros em formato PDF, que podem ser impressos, em cada CD-ROM de dados do lote dos calibradores. Existe um ficheiro separado, um em ng/mL e um em nmol/L, no CD-ROM de dados do lote dos calibradores para cada lote do kit de reagentes associado. Os valores podem ser automaticamente carregados a partir do BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Consulte o Manual de funcionamento para obter mais informações relacionadas com esta actividade.

Os resultados são expressos em ng/mL ou nmol/L. Os valores atribuídos aos calibradores são estabelecidos utilizando

um conjunto principal de calibradores e um lote específico de BioPlex 2200 25-OH Vitamin D em vários instrumentos BioPlex 2200. Utiliza-se um ajuste de curva 4-PL (logística de 4 parâmetros) com seis níveis do calibrador para calcular os resultados quantitativos.

RASTREABILIDADE
O ensaio BioPlex 2200 25-OH Vitamin D é calibrado segundo os materiais de referência utilizando a espectrometria por absorvência UV.

SV AVSEDD ANVÄNDNING
BioPlex 2200 25-OH Vitamin D Calibrator Set är avsedd för kalibrering av BioPlex 2200 25-OH Vitamin D Reagent Pack.

SAMMANFATTNING OCH PRINCIP
BioPlex 2200 25-OH Vitamin D Reagent Pack är kalibrerad med hjälp av en uppsättning med sex (6) olika kalibratorer. Kalibratorerna används i ett testsystem för att fastställa referenspunkter som används vid kvantitativ mätning avseende förekomst av ämnen i humana prover.

Medföljande material

- **Reagenser** - Sex (6) kalibratorflaskor på 0,5 mL för 25-OH D-vitamin. Kalibratornivå 1 innehåller 25 % hästerserum utan D-vitamin. Kalibratornivåerna 2 till 6 tillhandahålls i en humanserummatris som är tömd på D-vitamin, kompletterad med känd koncentration av 25-OH vitamin D₃. Alla kontroller innehåller konserveringsmedel inklusive ≤ 0,3 % ProClin 950, ≤ 0,1 % natriumazoch och < 0,1 % 5-bromo-5-nitro-1,3-dioxan (BND).
- **Analytör** - 25-hydroxy-D-vitamin
- **Komponenter** - En (1) bruksanvisning

MATERIAL SOM KRÄVS MEN INTE MEDFÖLJER
REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Viktigt! Filer som väljs och laddas (ng/mL eller nmol/L) måste vara kompatibla med analysprotokollen (APF).
OBS! Se avsnittet TILLDELADE VÄRDEN nedan.

VARNINGAR OCH FÖRSIKTIGHETSÅTGÄRDER FÖR ANVÄNDARE
För in vitro-diagnostik.

- Denna produkt får inte användas efter förfallodatumet.
- Om det finns tecken på mikrobiell kontaminering eller produkten är starkt grumlig, ska flaskan kastas.
- Byt inte ut flaskornas lock mot varandra. Det kan leda till kontaminering mellan kalibratorerna.
- Endast för professionell användning.

Försiktighet, se medföljande dokument. Biologiskt källmaterial. Behandlas som potentiellt smittsamt.

Se säkerhetsdatabladet (SDS) för mer säkerhetsinformation och varningar angående kemiska och biologiska risker. Säkerhetsdatablad finns tillgängliga på www.bio-rad.com och på begäran.

V varje enhet från humana donatorer som används för att tillverka denna produkt har testats med FDA-godkända metoder och har visat sig icke-reaktiv för hepatit B-antigen (HBsAg), antikroppar mot hepatit C (HCV) och antikroppar mot HIV-1/2. Denna produkt innehåller kanske även andra humana agenser som kan överföra smittsamma sjukdomar. Enligt god laboratoriepraxis bör allt material av human ursprung betraktas som potentiellt smittsamt och bör hanteras med samma försiktighetsåtgärder som patientprover. Beredd enligt kraven för CE-märkning.

FÖRVARING OCH HÅLLBARHET
Produkten är stabil fram till förfallodatum om den förvaras oöppnad i 2 till 8 °C. När kalibratorerna har öppnats är de stabila i 30 dagar om de förvaras med tätslutande lock i 2 till 8 °C.

PROCEDUR
Denna produkt bör köras i enlighet med instruktionerna som medföljer BioPlex 2200-instrumentet och BioPlex 2200 25-OH Vitamin D Reagent Pack.

Före provtagningen ska kalibratorerna få nå rumstemperatur (18 till 25 °C) och blandas försiktigt för att säkerställa enhetlighet. Sätt genast på locket på reagenterna efter varje användning och ställ dem tillräckligt för förvaring i 2 till 8 °C.

Kasserat material ska hanteras enligt de lokala föreskrifterna för avfallshantering. Om förpackningen är skadad ska du kontakta Bio-Rad Laboratories lokala försäljningskontor eller Bio-Rad Laboratories tekniska service.

BEGRÄNSNINGAR
Denna produkt är avsedd för användning med BioPlex 2200-instrumentet. Ingen annan användning har föreskrivits.

TILLDELADE VÄRDEN
Reagensstuldelade, batchspecifika värden ingår som utskrivbara PDF-filer på varje CD-ROM-skiva med kalibratorbatchdata. Det finns en separat fil, en med ng/mL och en med nmol/L, på CD-ROM-skivan med kalibratorbatchdata för varje tilldelad reagensförpackningsbatch.

Värden kan laddas automatiskt från BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Se användarhandboken för ytterligare information om denna åtgärd.

Värden uttrycks i ng/mL eller nmol/L. Kalibratortilldelning fastställs med hjälp av en huvuduppsättning av kalibratorer och en specifik batch för BioPlex 2200 25-OH Vitamin D Reagent Packs på flera BioPlex 2200-instrument. En 4-PL (4-parameterslogistisk) kurvpassning med sex kalibratornivåer används för att beräkna kvantitativa resultat.

SPÅRBARHET
BioPlex 2200 25-OH Vitamin D-analysen är kalibrerad till referensmaterial med hjälp av UV-absorptionsspektrometri.

DA ANVENDELSE
BioPlex 2200 25-OH Vitamin D Calibrator Set er beregnet til kalibrering af BioPlex 2200 25-OH Vitamin D Reagent Pack.

OVERSIGT OG PRINCIP
BioPlex 2200 25-OH Vitamin D Reagent Pack kalibreres vha. et sæt af seks (6) forskellige kalibratorer. Kalibratorerne bruges i et testsystem til at fastlægge referencenpunkter, der bruges til kvantitativ måling af tilstedeværelsen af stoffer i humane prøver.

MATERIALER, DER MEDFØLGER

- **Reagenser** - Seks (6) 0,5 mL 25-OH vitamin D-kalibratorampuller. Kalibratorniveau 1 indeholder 25 % hesteserum uden vitamin D. Kalibratorniveauerne fra 2 til 6 er leveret i en human serummatris depletet for vitamin D og suppleret med en kendt koncentration af 25-OH vitamin D₃. Alle kalibratore indeholder konserveringsmidler, inklusive ≤ 0,3 % ProClin 950, ≤ 0,1 % natriumbenzoat og < 0,1 % 5-brom-5-nitro-1,3-dioxan (BND).
- **Analytør** - 25-hydroxy-vitamin D
- **Komponenter** - En (1) brugsanvisning

PÅKRÆVEDE, MEN IKKE MEDFØLGENDE MATERIALER
REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Vigtigt! Den valgte og indlæste fil (ng/mL eller nmol/L) skal være kompatibel med analyseprotokollen (APF).
Bemærk: Der henvises til afsnittet om TILDELTE VÆRDIER nedenfor.

ADVARSLER OG FÖRSIGTIGHEDSREGLER FOR BRUGERE
Kun til in vitro diagnostik.

- Produktet må ikke anvendes efter udløbsdatoen.
- Hvis der er tegn på mikrobiel kontaminering eller for megen uklarhed i produktet, kasseres ampullen.
- Ampulhætterne må ikke ombyttes frit mellem hinanden. Dette kan føre til krydskontaminering af kalibratorer.
- Kun til erhvervsråmsig anvendelse.

Forsigtig, der henvises til de medfølgende dokumenter. Materiale af biologisk oprindelse. Behandles som potentielt smittsamt.

Se sikkerhedsdatabladet (SDS) for at få mere sikkerhedsinformation og advarsler om kemiske og biologiske farer. Sikkerhedsdatablad kan rekvireres fra www.bio-rad.com og efter anmodning.

Hver human donorhenne anvendt til at fremstille dette produkt er testet med metoder godkendt af FDA i USA's regeringskontor for fødevarer- og medicinkontrol, og fandtes at være non-reaktiv over for hepatitis B overfladensantigen (HBsAg), antistof mod hepatitis C (HCV) og antistof mod HIV-1/2. Dette produkt kan desuden indeholde andre stoffer af human oprindelse, som er potentielt smittefarlige. I overensstemmelse med god laboratoriepraksis skal alt materiale af human oprindelse anses som potentielt smittefarligt og håndteres med de samme forholdsregler som ved patientpræparater. Præpareret i overensstemmelse med kravene til CE-mærket.

OPBEVARING OGS STABILITET
Produktet er stabilt indtil udløbsdatoen, når det opbevares uåbnet ved 2 til 8 °C. Når kalibratorerne er åbnet, er de stabile i 30 dage, når de opbevares tæt lukket ved 2 til 8 °C.

PROCEDURE
Dette produkt skal behandles i overensstemmelse med anvisningerne, der er vedlagt BioPlex 2200 Instrument og BioPlex 2200 25-OH Vitamin D Reagent Pack. Før provtagning skal kalibratorerne nå op på stuetemperatur (18 til 25 °C), og prøverne skal blandes godt for at sikre homogenitet. Efter hver anvendelse skal hættens straks sættes på reagenterne, som skal lægges til opbevaring ved 2 til 8 °C. Bortskaf alle kasserede materialer i overensstemmelse med kravene fra de lokale renovationsmyndigheder. I tilfælde af beskadigelse af emballagen kontaktes det lokale salgskontor for Bio-Rad Laboratories eller Bio-Rad Laboratories teknisk service.

BEGRENSNINGER
Produktet er beregnet til anvendelse med BioPlex 2200 Instrument. Enhver anden anvendelse er ikke blevet karakteriseret.

TILDELTE VÆRDIER
Reagensstuldelte, lot-specifikke værdier er inkluderet i form af printbare PDF-filer på hver CD-ROM med kalibratorlotdata. For hvert tilknyttet reagenspakkelet findes der en separat fil, en i ng/mL og en i nmol/L, på CD-ROM'en med kalibratorlotdata. Værdier kan automatisk indlæses fra BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Se brugervejledningen for at få yderligere information om denne aktivitet.

Resultater udtrykkes som ng/mL eller nmol/L. Kalibratortildelingen fastlægges ved hjælp af et hovedkalibratorsæt og et specifikt lot af BioPlex 2200 25-OH Vitamin D Reagent Packs på flere BioPlex 2200-instrumenter. Der anvendes en 4-PL (4-parameter logistisk) kurvetilpasning til at beregne kvantitative resultater ved brug af seks kalibratorniveauer.

SPORBARHED
BioPlex 2200 25-OH Vitamin D-analysen kalibreres til referencematerialer ved brug af UV-absorptionsspektrometri.

CS URČENÉ POUŽITÍ
BioPlex 2200 25-OH Vitamin D Calibrator Set je určena ke kalibraci reagenční sady BioPlex 2200 25-OH Vitamin D Reagent Pack.

SOUHRN A PRINCIP
Reagenční sada BioPlex 2200 25-OH Vitamin D Reagent Pack se kalibruje pomocí soupravy šesti (6) různých kalibrátorů. Kalibrátory se používají v testovacím systému ke stanovení referenčních bodů, které slouží ke kvantitativnímu určení přítomnosti látek v lidských vzorcích.

DODÁVANÝ MATERIÁL

- **Reagenzie** - Šest (6) 0,5 mL lahviček s kalibrátorem 25-hydroxyvitaminu D. Kalibrátor úrovně 1 obsahuje 25 % koňského séra bez vitamínu D. Kalibrátory úrovně 2 až 6 jsou

dodávány v matrici lidského séra s odstraněným vitamínem D suplementované 25-hydroxyvitamínem D₃ o známé koncentraci. Všechny kalibrátory obsahují jako konzervanty přípravek ProClin 950 (≤ 0,3 %), benzoát sodný (≤ 0,1 %) a 5-brom-5-nitro-1,3-dioxan (BND) (< 0,1 %).

- Analyty** - 25-hydroxyvitamin D
- Slůžky** - Jeden (1) návod k použití

POTŘEBNÝ MATERIÁL, KTERÝ NENÍ SOUČÁSTÍ DODÁVKY

REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Důležité! Vybraný a načtený soubor (ng/mL nebo nmol/L) musí být kompatibilní se souborem protokolu analýzy (APF).
Poznámka: Viz oddíl PŘÍRAŽENÉ HODNOTY níže.

VÝSTRAHY A BEZPEČNOSTNÍ OPATŘENÍ PRO UŽIVATELE

Pro diagnostické použití in vitro.

- Tento produkt nesmí být používán po datu expirace.
- Při známkách mikrobiální kontaminace nebo při pozorovaném zvýšeném zákalu v produktu je nutno lahvičku zlikvidovat.
- Nezaměňujte navzájem uzávěry lahvíček. To může způsobit křížovou kontaminaci kalibrátorů.
- Pouze pro profesionální použití.



Pozor, prostudujte příloženou dokumentaci. Materiál biologického původu. Zacházejte s prosředkem jako s potenciálně infekční látkou.

Další bezpečnostní informace a výstrahy týkající se chemických a biologických rizik najdete v bezpečnostních listech. Bezpečnostní listy jsou dostupné na www.bio-rad.com a na požádání.

Každá jednotka od lidského dárce, který poskytl materiál pro výrobu tohoto produktu, byla testována metodami schválenými FDA a byla shledána nereaktivní na povrchový antigen hepatitidy B (HBsAg), na přítomnost protilátek proti hepatitidě C (HCV) a protilátek proti viru HIV-1/HIV-2. Tento produkt může také obsahovat jiná agens lidského původu, která mohou přenášet infekční onemocnění. Dle správné laboratorní praxe musí být se všemi materiály z lidských zdrojů nakládáno jako s potenciálně infekčními a se stejnými bezpečnostními opatřeními jako se vzorky pacientů. Připraveno ve shodě s požadavky pro značení CE.

USKLADNĚNÍ A STABILITA

Neotevřený výrobek je při skladování za teploty 2 °C až 8 °C stabilní až do data expirace. Po otevření jsou kalibrátory stabilní 30 dnů při skladování od 2 °C do 8 °C v těsně uzavřené nádobě.

POSTUP

Tento výrobek musí být používán podle návodu přiloženého k přístroji BioPlex 2200 a k reagenční sadě BioPlex 2200 25-OH Vitamin D Reagent Pack.

Před testováním ponechte kalibrátory vytemperovat na pokojovou teplotu (18 °C až 25 °C) a jemně je promíchejte pro zajištění homogenity. Po každém použití reagencie ihned uzavřete uzávěrem a vraťte do skladovací teploty 2 °C - 8 °C.

Likvidace nepotřebovaného materiálu musí probíhat v souladu s požadavky místních úřadů pro likvidaci odpadu. V případě poškození obalu kontaktujte místní prodejní zastoupení nebo technický servis společnosti Bio-Rad Laboratories.

OMEZENÍ

Tento výrobek je určen pro použití s přístrojem BioPlex 2200. Žádné jiné použití nebylo popsáno.

PŘÍRAŽENÉ HODNOTY

Přířazené hodnoty reagonci specifické šarže jsou přiřazeny jako tiskutelné soubory PDF na každém datovém disku CD-ROM šarže kalibrátorů. Na datovém disku CD-ROM šarže kalibrátorů je pro každou příslušnou šarži reagenční sady k dispozici samostatný soubor, jeden v ng/mL a druhý v nmol/L.

Hodnoty lze automaticky načíst z datového disku CD-ROM šarže kalibrátorů BioPlex 2200 25-OH Vitamin D Calibrator Lot. Pro podrobnější informace spojené s těmito postupy odkazujeme na příručku pro obsluhu.

Výsledky jsou vyjádřeny v ng/mL nebo v nmol/L. Přířazené hodnoty kalibrátorů jsou vytvořeny pomocí hlavní sady kalibrátorů a specifické šarže reagenčních sad BioPlex 2200 25-OH Vitamin D Reagent Pack na několika přístrojích BioPlex 2200. Pro výpočet kvantitativních výsledků se používá proložení 4-parametrové logistické křivky (4-PL) s použitím šesti úrovní kalibrátorů.

SLEDOVATELNOST

Analýza BioPlex 2200 25-OH Vitamin D je kalibrována podle referenčních materiálů pomocí UV absorpční spektrometrie.

NO TILTENKT BRUK

BioPlex 2200 25-OH Vitamin D Calibrator Set er ment for kalibrering av BioPlex 2200 25-OH Vitamin D Reagent Pack.

OPPSUMMERING OG PRINSIPP

BioPlex 2200 25-OH Vitamin D Reagent Pack kalibreres ved bruk av et sett med seks (6) forskjellige kalibratorer. Kalibratorer brukes i et testsystem for å etablere referansepunkter som brukes i bestemmelse av kvantitativ måling av stoffer i humane prøver.

LEVERTE MATERIALER

- Reagenser** - Seks (6) 0,5 mL 25-OH-vitamin D-kalibreringsrør. Kalibratornivå 1 inneholder 25 % hesteserum uten D-vitamin. Kalibratornivåene 2 til 6 leveres i en D-vitaminreduisert human serummatrix supplert med kjent konsentrasjon av 25-OH-vitamin D₃. Alle kalibratorene inneholder konserveringsmidler, herunder ≤ 0,3 % ProClin 950, ≤ 0,1 % natriumbensoat og < 0,1 % 5-bromo-5-nitro-1,3-dioxan (BND).
- Analytter** - 25-hydroksyvitamin D
- Komponenter** - En (1) bruksanvisning

NODVENDIGE MATERIALER SOM IKKE LEVERES

REF 663-3720: BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM

Viktig! Filen som selges og lastes inn (ng/mL eller nmol/L), må være kompatibel med analyseprotokollfilen (APF).

Merk: Se avsnittet TILORDNEDE VERDIER nedenfor.

ADVARSLER OG FORHOLDSREGLER FOR BRUKERE

Til in vitro-diagnostisk bruk.

- Dette produktet skal ikke brukes etter utløpsdatoen.
- Dersom det er tegn til mikrobiell forurensning eller stor turbiditet i produktet, skal røret kastes.
- Lokkene på rørene må ikke byttes. Dette kan føre til kryssforurensning av kalibratorene.
- Kun til profesjonelt bruk.



Forsiktig, se medfølgende dokumentasjon. Biologisk kildemateriale. Behandles som potensielt smittefarlig.

Se sikkerhetsdatablad (SDS) for ytterligere sikkerhetsinformasjon og advarsler om kjemiske og biologiske farer. Sikkerhetsdatabladene er tilgjengelige på www.bio-rad.com og på forespørsel.

Alle humane donorenheter som er brukt til å framstille dette produktet er testet i henhold til FDA-godkjente metoder og funnet ikke-reaktive for Hepatitt B-overflateantistoff (HBsAg), antistoff mot hepatitt C (HCV) og antistoff mot HIV-1/HIV-2. Dette produktet kan også inneholde andre humane agenser som kan overføre smittsom sykdom. I henhold til god laboratoriepraksis, skal all human kildemateriale anses som potensielt smittefarlig og håndteres med samme forholdsregler som pasientprøver. Framstilt i henhold til kravene til CE-merking.

LAGRING OG STABILITET

Dette produktet er stabilt til utløpsdatoen når det lagres uåpnet ved 2 til 8 °C. Etter åpning er kalibratorene stabile i 30 dager når de lagres tett korket ved 2 til 8 °C.

PROSEDYRE

Dette produktet skal kjøres i henhold til instruksjonene som følger med BioPlex 2200-instrumentet og BioPlex 2200 25-OH Vitamin D Reagent Pack.

Før testing, la kalibratorene nå romtemperatur (18 til 25 °C) og bland forsiktig for å sikre homogenitet. Etter hver bruk settes lokket på reagensene umiddelbart og returneres til lagring ved 2 til 8 °C.

Kasser eventuelle brukte materialer i henhold til lokale avfallstørskrifter. I tillegg av skadet emballasje, kontakt ditt lokale salgskontor for Bio-Rad Laboratories, eller Bio-Rad Laboratories teknisk service.

BEGRENSNINGER

Dette produktet er ment til bruk med BioPlex 2200-instrumentet. Annen bruk er ikke evaluert.

TILORDNEDE VERDIER

Reagenstilorndede, lotspesifikke verdier er inkludert som utskrivbare PDF-filer på hver CD-ROM med kalibratorlotdata. Det finnes separate filer, én i ng/mL og én i nmol/L, for hvert assosierte reagenspakkelot på CD-ROM-en med kalibratorlotdata. Verdier kan lastes automatisk fra BioPlex 2200 25-OH Vitamin D Calibrator Lot Data CD-ROM. Se bruksanvisningen for mer informasjon om denne aktiviteten.

Resultater uttrykkes som ng/mL eller nmol/L. Kalibratorordning etableres ved hjelp av et mastersett av kalibratorer og et spesifikt lot av BioPlex 2200 25-OH Vitamin D Reagent Packs på flere BioPlex 2200-instrumenter. En 4-PL (4-parameters logistikk)-kurvetilpassning som bruker seks kalibratornivåer brukes for å beregne kvantitative resultater.

SPORBARHET

BioPlex 2200 25-OH Vitamin D-analysen er kalibrert etter referansematerialer ved hjelp av UV-absorbansspektrometri.



For In Vitro Diagnostic Use
In-vitro-Diagnostikum
Utilisation comme test de diagnostic in vitro
Per uso diagnostico in vitro
Para uso en diagnóstico in vitro
Para utilização em diagnóstico in vitro
För in vitro-diagnostik
Til in vitro-diagnostisk brug
Pro diagnostické použití in vitro
Til in vitro-diagnostisk bruk



European Conformity
CE-Kennzeichnung
Conformité européenne
Conformità Europea
Conforme a la normativa europea
Conformidade Europeia
Europeisk överensstämmelse
CE-mærkning
Evropská shoda
Europeisk Standard (CE)



Temperature Limit
Temperaturgrenze
Limite de température
Limiti di temperatura
Limite da temperatura
Limite da temperatura
Temperaturgränser
Temperaturområde
Teplotní limit
Temperaturgrense



Consult Instructions for Use
Gebrauchsanleitung beachten
Consulter le mode d'emploi
Consultare le istruzioni per l'uso
Consulte las instrucciones de uso
Consulte as instruções de utilização
Se bruksanvisningen
Se bruksanvisningen
Viz návod k použití
Se bruksanvisning



Lot Number
Chargennummer
Número de lot
Numero di lotto
Número de lote
Número de lote
Batchnummer
Lotnummer
Číslo šarže
Lotnummer



Use by (YYYY-MM-DD)
Verwendbar bis (JJJJ-MM-TT)
Utiliser avant (AAAA-MM-JJ)
Data di scadenza (AAAA-MM-GG)
Fecha de caducidad (AAAA-MM-DD)
Prazo de validade (AAAA-MM-DD)
Använd före (ÅÅÅÅ-MM-DD)
Anvendes inden (ÅÅÅÅ-MM-DD)
Použijte do (RRRR-MM-DD)
Brukes før (ÅÅÅÅ-MM-DD)



Manufactured by
Hersteller
Fabriqué par
Fabricado da
Fabricado por
Fabricado por
Tilberkad av
Fremstillet af
Výrobce
Produser av



Authorized Representative
Bevollmächtigter
Mandataire agréé
Rappresentante autorizzato
Representante autorizado
Representante autorizado
Auktoriserad representant
Autoriseret repræsentant
Autorizovaný zástupce
Autoriseret representant



Catalog Number
Katalognummer
Número de référence
Numero di catalogo
Número de catálogo
Número de catálogo
Katalognummer
Katalognummer
Katalogové číslo
Katalognummer



Calibrator // Level
Kalibrator // Niveau
Calibrateur // Niveau
Calibratore // Livello
Calibrador // Nivel
Calibrador // Nivel
Kalibrator // Nivå
Kalibrator // Niveau
Kalibrátor // Úroveň
Kalibrator // Nivå

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Teknisk information / Kontakty pro technické informace / Kontakter for teknisk informasjon /
USA & Puerto Rico: 1-800-2-BIORAD (224-6723).

Outside the U.S.A., please contact your regional Bio-Rad office for assistance.
Außerhalb der USA wenden Sie sich bitte an Ihre örtliche Bio-Rad-Vertretung.
En dehors des États-Unis, contacter le bureau Bio-Rad local pour toute assistance.
Fuori dagli Stati Uniti, per ottenere assistenza, rivolgersi all'ufficio Bio-Rad di zona.
Fuera de EE.UU., póngase en contacto con la oficina regional de Bio-Rad si necesita ayuda.
Fora dos EUA, por favor contacte os seus escritórios regionais da Bio-Rad para assistência.
Utanför USA, var god kontakta ett regionalt Bio-Rad-kontor för assistans.
Uden for USA bedes man kontakte det lokale Bio-Rad kontor for assistance.
Pro podporu mimo území USA požádejte o pomoc svoji oblastní pobočku společnosti Bio-Rad.
Utenför USA, kontakt ditt regionale Bio-Rad-salgskontor for assistanse.

BioPlex is a registered trademark of Bio-Rad Laboratories, Inc.

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Laboratories**

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Diagnostics Group

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BioPlex® 2200 System

25-OH Vitamin D Instructions For Use

REF 665-3750

 200

IVD

CE

Federal law restricts this device to sale by or on the order of a physician, or to a clinical laboratory; and use is restricted to, by, or on the order of a physician.

This IFU is effective beginning with Lot # 300142 of the 25-OH Vitamin D Reagent Pack and above, and BioPlex 2200 Software Version 4.0 and above.

 **UNITED STATES:** Bio-Rad Laboratories, Inc., Clinical Diagnostics Group,
4000 Alfred Nobel Drive, Hercules, CA 94547

EC REP **FRANCE:** Bio-Rad, 3 boulevard Raymond Poincaré,
92430 Marnes-la-Coquette

SYMBOLS LEXICON



Catalog Number



WARNING



Lot Number



Manufactured by



Number of Tests

Temperature Limit



Use by (YYYY-MM-DD)



For In Vitro Diagnostic Use



Consult Instructions for Use

European Conformity



Authorized Representative in the European Community



25-OH Vitamin D Reagent Pack



Bead Set

Release Buffer



Conjugate



Conjugate



Contains



Version

Caution, consult accompanying documents

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INTENDED USE

The BioPlex[®] 2200 25-OH Vitamin D Kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

SUMMARY AND EXPLANATION

Vitamin D is a fat-soluble steroid prohormone produced mainly photochemically in the skin from 7-dehydrocholesterol.

Two forms of vitamin D are biologically relevant – vitamin D3 (Cholecalciferol) and vitamin D2 (Ergocalciferol). Both vitamins D2 and D3 can be absorbed from food. However only an estimated 10-20% of vitamin D is supplied through nutritional intake. Vitamins D2 and D3 can both be found in vitamin D supplements. Vitamin D is converted to the active hormone 1,25-(OH)₂-vitamin D (Calcitriol) through two hydroxylation reactions. The first hydroxylation occurs in the liver and converts vitamin D into 25-hydroxyvitamin D. The second hydroxylation occurs in the kidneys, and converts 25-OH Vitamin D into the biologically active 1,25-(OH)₂-vitamin D. Most cells express the vitamin D receptor and about 3% of the human genome is directly or indirectly regulated by the vitamin D endocrine system.

The major physiological function of vitamin D in vertebrates is to maintain extracellular fluid concentrations of calcium and phosphorus within a normal range. Vitamin D accomplishes this by increasing the efficiency of the small intestine to absorb dietary calcium and phosphorus, and by stimulating the mobilization of calcium and phosphorus stores from the bone.¹

The major storage form of Vitamin D is 25-OH Vitamin D which is present in the blood at up to 1,000 fold higher concentration compared to the active 1,25-(OH)₂-vitamin D. 25-OH Vitamin D has a half-life of 2-3 weeks versus 4 hours for 1,25-(OH)₂-vitamin D. Therefore, 25-OH Vitamin D is the analyte of choice for determination of the vitamin D status.

Vitamin D deficiency is a cause of secondary hyperparathyroidism and diseases related to impaired bone metabolism, like rickets, osteoporosis, and osteomalacia. Epidemiological studies have shown a high global prevalence of vitamin D insufficiency and deficiency.

PRINCIPLE OF THE PROCEDURE

The BioPlex 2200 25-OH Vitamin D assay is a flow competitive immunoassay for quantitative determination of 25-hydroxyvitamin D in human serum.

A population of dyed paramagnetic beads is coated with anti-25-OH Vitamin D antibody. The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-OH Vitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex 2200 system adds the 25-OH Vitamin D-Biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidin-phycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The detected fluorescence of the SA-PE in relative fluorescence intensity (RFI) is inversely proportional to the concentration of 25-OH Vitamin D in the sample.

Two additional dyed beads, an Internal Standard Bead (ISB) and a Serum Verification Bead (SVB), are present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel. Refer to the BioPlex 2200 System Operation Manual for more information.

The instrument is calibrated using a set of six (6) distinct calibrator vials, supplied separately by Bio-Rad Laboratories.

The six (6) vials representing six (6) different concentrations of 25-OH Vitamin D are used for quantitative calibration. The BioPlex 2200 25-OH Vitamin D results are each expressed in ng/mL or nmol/L.

KIT COMPONENTS

BioPlex 2200 25-OH Vitamin D Reagent Pack (**REF** 665-3750) contains supplies sufficient for 200 tests.

Vial	Description
Bead Set	One (1) 10 mL vial, containing dyed beads coated with anti-25-OH Vitamin D (sheep), an Internal Standard bead (ISB), a Serum Verification bead (SVB) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives.
Release Buffer	One (1) 10 mL vial, containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (< 1.0%) as preservative.
Conjugate 1	One (1) 5 mL vial, containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and 5-Bromo-5-nitro-1,3-dioxane (< 0.1%) as preservatives and chemical blockers.
Conjugate 2	One (1) 5 mL vial, containing phycoerythrin conjugated streptavidin (SA-PE) in a buffer comprising protein stabilizer (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives, chemical blockers and detergent (Tween 20).

ADDITIONAL REQUIRED ITEMS, AVAILABLE FROM BIO-RAD

REF	Description
663-3700	BioPlex 2200 25-OH Vitamin D Calibrator Set: Six (6) 0.5 mL 25-OH Vitamin D calibrator vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D3. All calibrators contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-Bromo-5-nitro-1,3-dioxane (< 0.1%) as preservatives.
663-3730	BioPlex 2200 25-OH Vitamin D Control Set: Two (2) 1.5 mL Level 1 and two (2) 1.5 mL Level 2 Control vials, each containing 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-Bromo-5-nitro-1,3-dioxane (< 0.1%) as preservatives.
660-0817	BioPlex 2200 Sheath Fluid: Two (2) 4 L bottles containing Phosphate Buffered Saline (PBS). ProClin 300 (0.03%) and sodium azide (< 0.1%) as preservatives.
660-0818	BioPlex 2200 Wash Solution: One (1) 10 L bottle containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin 300 (0.03%) and sodium azide (< 0.1%) as preservatives.
660-0000	BioPlex 2200 Instrument and Software System.

PRECAUTIONS/WARNINGS**1. For In Vitro Diagnostic (IVD) Use.**

2. For professional use only.
3. Each unit of human serum used in the manufacture of the BioPlex 2200 25-OH Vitamin D kits (including calibrator and control sets) was tested by FDA accepted methods and found non-reactive for Hepatitis B surface antigen (HBsAg), antibody to HIV-1, HIV-2 and Hepatitis C (HCV). No test method can offer complete assurance that products containing human source materials will be absent of these and other infectious agents. In accordance with good laboratory practice (GLP), all human source material should be considered potentially infectious for Hepatitis B (HBV), Hepatitis C (HCV), HIV-1, HIV-2, and all other infectious agents; therefore, handle the BioPlex 2200 25-OH Vitamin D (including reagent packs, calibrators and control sets) with the same precautions used with patient specimens. It is recommended that these reagents and human specimens be handled in accordance with the Biosafety in Microbiological and Biomedical Laboratories³, WHO Laboratory Biosafety Manual Biosafety Level 2⁴ or other appropriate biosafety practices⁵ for materials which contain or are suspected of containing infectious agents.
4. Consider any materials of human origin as infectious and handle them using typical biosafety procedures and Universal Precautions according to 29 CFR 1910.1030⁶ and in accordance with local, regional, and national regulations.
5. Do not smoke, eat, or drink in areas where patient samples and kit reagents are handled.
6. Do not pipette by mouth.
7. Wear personal protective equipment while handling all reagents and samples and while operating the BioPlex 2200 System.
8. Dispose of all wastes in accordance with applicable national, and/or local regulations.
9. Waste material containing patient samples or biological products should be considered biohazardous when disposing or treating.
10. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal of liquids, flush with a large volume of water to prevent azide build-up.⁷
11. Chemical reagents should be handled in accordance with Good Laboratory Practices.
12. Refer to the kit and additional required component Safety Data Sheets (SDS) for more safety information and warnings about chemical and biological hazards. The Safety Data Sheets are available at www.bio-rad.com and on request.
13. Clean up all spills immediately and thoroughly. Decontaminate the area for any spills involving biohazardous materials with an effective disinfectant. Dispose of all contaminated materials appropriately.
14. Do not use tests beyond their expiration date. The date is printed on all boxes.
15. Do not interchange vial or bottle caps and stoppers; this will lead to cross-contamination of reagents.
16. Adherence to the protocol specified herein is necessary to ensure proper performance of this product. If aberrant results are obtained, contact Bio-Rad Technical Service.
17. Never mix the contents from different bottles of the same reagent. Doing so may lead to reagent contamination and compromise the performance of the product.

SPECIMEN COLLECTION AND HANDLING

Specimen Collection Precaution

Consider any materials of human origin as infectious and handle them using typical biosafety procedures.

Specimen Type

Serum (including serum collected in serum separator tubes) is the recommended sample. Avoid visibly hemolyzed and lipemic samples.

Specimen Storage

Serum may be stored under refrigeration (2-8°C) for up to 7 days. For longer storage of samples, keep at -20°C or colder.

Specimen Preparation

Thoroughly mix thawed specimens; it is also recommended to centrifuge thawed specimens to remove gross particulate matter. Avoid multiple freeze/thaw cycles (up to 3 cycles at -20°C and up to 2 cycles at -70°C are acceptable).

Specimen Shipping

All specimens and other samples of human origin must be shipped in accordance with national and international transportation regulations. Do not exceed the storage time and temperature limitations listed above.

Preparation and Storage of Reagents

Reagents in the BioPlex 2200 25-OH Vitamin D kit are ready to use. After initial use, the reagents are stable for 60 days or until the date of expiration when stored unopened on the instrument or refrigerated at 2-8°C.

Do not use reagents beyond expiration dates.

INDICATIONS OF INSTABILITY OR DETERIORATION OF REAGENTS

Store all reagents at the labeled temperature and do not use past their expiration dates.

Do not use any reagents which have any indications of discoloration, cloudiness or excessive precipitation. Do not use any reagents that show any signs of leakage.

PROCEDURE

In order to obtain reliable and consistent results, strictly adhere to the instructions in this Instructions for Use. Do not modify the handling and storage conditions for kit reagents or patient samples.

Operating instructions, including calibration, quality control, and maintenance for the BioPlex 2200 System are further described in the BioPlex 2200 System Operation Manual. Prior to using the BioPlex 2200 25-OH Vitamin D kit, ensure that the BioPlex 2200 System is powered on, loaded with reagent packs and bulk solutions, and that all required maintenance has been performed. Please refer to the BioPlex 2200 System Operation Manual for more information regarding these activities.

Any lots of the BioPlex 2200 System Sheath Fluid and BioPlex 2200 System Wash Solution can be interchanged.

Calibration

The BioPlex 2200 25-OH Vitamin D Calibrator Set should be loaded and assayed at minimum in duplicate every 30 days or with each new Reagent Pack lot. A 4-parameter logistic (4PL) curve fit algorithm, using 6 calibrators is used to establish a calibration curve for the BioPlex 2200 25-OH Vitamin D assay. Refer to the BioPlex 2200 System Operation Manual for more information.

Quality Control

At the beginning of each day that the BioPlex 2200 25-OH Vitamin D kit is to be used, load and process the corresponding BioPlex 2200 25-OH Vitamin D Control Set as indicated in the BioPlex 2200 System Operation Manual.

The BioPlex 2200 25-OH Vitamin D Control Set includes two levels of controls for 25-OH Vitamin D in a human serum matrix.

Lot specific values for each control are loaded into the BioPlex 2200 System database via the provided media or by manual input. After identifying the control via the barcoded vial, the BioPlex 2200 System compares the control results to the expected lot specific control values stored in the BioPlex 2200 System database.

Failure to obtain the appropriate values for controls will invalidate the assay and indicates procedural error, improper sample handling or deterioration of reagents. Additional controls may be tested in accordance with local, state and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

If a control result is out of its specified range, any test results generated since the last acceptable control results must be evaluated to determine if test results may have been adversely affected. Adversely affected results are invalid, and these samples must be retested.

Load/Process Samples

Load samples into the racks provided with the BioPlex 2200 System as indicated in the BioPlex 2200 System Operation Manual. Sample processing on the BioPlex 2200 System is fully automated. Refer to the BioPlex 2200 System Operation Manual for appropriate software setup.

Traceability to Reference Material

The BioPlex 2200 25-OH Vitamin D assay is calibrated to reference materials using UV absorbance spectrometry.

GUIDELINES FOR INTERPRETATION OF RESULTS

Calculation

All calculations necessary to interpret the results are performed automatically by the BioPlex 2200 System Software. If desired, the assay parameter for nmol/L can be used, and it converts the results to SI units: ng/mL x 2.5 = nmol/L.

Data Analysis

Specimens cannot be diluted for the BioPlex 2200 25-OH Vitamin D assay. Specimens with a 25-OH Vitamin D concentration > 125 ng/mL (> 313 nmol/L) are reported as "> 125 ng/mL" ("> 313 nmol/L").

LIMITATIONS OF THE PROCEDURE

Hemoglobin > 150 mg/dL may interfere and cause increased Vitamin D results. Do not use visibly hemolyzed samples.

The BioPlex 2200 25-OH Vitamin D test results should be considered in conjunction with other laboratory test results and the clinical presentation of the patient. Only a physician should interpret results.

If the BioPlex 2200 25-OH Vitamin D results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.

Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex 2200 25-OH Vitamin D assay.

EXPECTED VALUES

Reference Range

It is recommended that each laboratory establish its own reference range^{8,9}, which may be unique to the population it serves depending on geographical, seasonal, patient, dietary or environmental factors.

A reference range study was conducted based on guidance from the Clinical and Laboratory Standards Institute (CLSI), Protocol C28-A3c. Serum specimens of apparently healthy individuals from the US (North, Central and South states), collected during summertime, wintertime and springtime were evaluated in singlicate using the BioPlex 2200 25-OH Vitamin D assay. The tested population was distributed over an age range of 21 – 79 years, and included African Americans, Hispanics and Caucasians. The observed values are summarized in Table A.

Table A: Reference Range, BioPlex 2200 25-OH Vitamin D

N = 286	Concentration (ng/mL)	Concentration (nmol/L)
Median	27.7	69.3
Mean	29.7	74.3
2.5 th – 97.5 th Percentile	12.7 – 65.7	31.8 – 164.3

PERFORMANCE CHARACTERISTICS

Precision

A human serum panel consisting of 6 frozen samples spanning the measuring range was assayed in duplicate per run on two runs daily over 20 days (N=80) on one reagent lot. Two levels of the BioPlex 25-OH Vitamin D controls were also included.

The data were analyzed for within-run, between-run, between-day, and total precision in accordance with CLSI EP05-A2 guideline and the mean (ng/mL), standard deviation (ng/mL) and percent coefficient of variation (%CV) are summarized below.

Table B: Precision; BioPlex 2200 25-OH Vitamin D, ng/mL

Serum Panel	N	Mean ng/mL	Within-Run		Between-Run		Between-Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
Sample 2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
Sample 3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
Sample 4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
Sample 5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
Sample 6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Level 1 Control	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Level 2 Control	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

Reproducibility

Each of the eight (8) panel members was tested in duplicate on two (2) runs per day for five (5) days using one (1) lot of 25-OH Vitamin D Reagent Pack and one (1) lot of 25-OH Vitamin D Calibrator Set at one (1) testing facility. (2 replicates x 2 runs x 5 days x 1 site = 20 replicates per panel member and controls). In addition, the Level 1 control and the Level 2 control were tested.

The data were analyzed for intra-assay and inter-assay reproducibility according to the principles described in the Clinical and Laboratory Standards Institute (CLSI) guidance EP15-A2. The standard deviation (SD) and percent coefficient of variation (%CV) were calculated. Results can be found in Table C (ng/mL).

Table C: Reproducibility; BioPlex 2200 25-OH Vitamin D, ng/mL

Sample	N	Mean Conc. (ng/mL)	Within-Run		Between-Run		Total	
			SD	%CV	SD	%CV	SD	%CV
Sample 1	20	11.5	0.69	6.0%	0.47	4.1%	1.71	14.8%
Sample 2	20	13.6	0.80	5.9%	0.26	1.9%	1.18	8.7%
Sample 3	20	26.1	0.88	3.4%	1.15	4.4%	1.59	6.1%
Sample 4	20	30.2	1.99	6.6%	0.00	0.0%	2.71	9.0%
Sample 5	20	50.2	2.23	4.4%	0.77	1.5%	2.96	5.9%
Sample 6	20	56.4	2.09	3.7%	2.79	4.9%	5.26	9.3%
Sample 7	20	100.5	4.52	4.5%	2.81	2.8%	5.32	5.3%
Sample 8	20	104.9	3.97	3.8%	1.54	1.5%	5.24	5.0%
Level 1 Control	20	21.6	0.98	4.5%	1.00	4.6%	1.84	8.5%
Level 2 Control	20	58.8	2.44	4.2%	1.29	2.2%	2.99	5.1%

LINEARITY

Based on the guidance from the CLSI Protocol EP6-A, a study was performed to establish the linear range of the BioPlex 2200 25-OH Vitamin D assay.

Five samples with high 25-OH Vitamin D levels were serially diluted in a sample with low levels of Vitamin D (near the limit of quantitation) and tested using the BioPlex 2200 25-OH Vitamin D assay. The results are shown in Table D. Using an absolute deviation from linearity of ≤ 10%, a linear range of 6.5 ng/mL (16.3 nmol/L) to 125 ng/mL (313 nmol/L) was established for the BioPlex 2200 25-OH Vitamin D assay.

Table D: Linearity

Conc (ng/mL)	Slope	Intercept	r ²
168.9	1.0001	0.0045	0.9988

Measuring Range

Measuring interval is defined as the range of concentration values which meets the limits of acceptable performance for imprecision, bias and linearity.

The measuring range is 6.5 ng/mL to 125.0 ng/mL (16.3 nmol/L to 313.0 nmol/L) and was established based on the limit of quantitation and linearity. The lowest reportable value is 6.5 ng/mL (16.3 nmol/L) as determined by the limit of quantitation. Values below 6.5 ng/mL (16.3 nmol/L) should be reported as < 6.5 ng/mL (< 16.3 nmol/L) and values above 125.0 ng/mL (313.0 nmol/L) should be reported as > 125.0 ng/mL (> 313.0 nmol/L).

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ)

Based on guidance from the CLSI Protocol EP17-A2, a study was performed with 5 blank samples and 6 low samples with 25-OH Vitamin D concentrations ranging from 3.0 ng/mL (7.5 nmol/L) to 35.0 ng/mL (87.5 nmol/L). These samples were tested in 4 replicates per run for LoB and 12 replicates for LoD over 5 days using two reagent lots and one instrument.

In the above-described study, the LoB was 0.8 ng/mL (2.0 nmol/L), the LoD was 2.5 ng/mL (6.3 nmol/L), and the LoQ was 6.5 ng/mL (16.3 nmol/L).

Specificity (Cross-Reactivity)

The specificity of the BioPlex 2200 25-OH Vitamin D assay was assessed by testing the Cross-Reactants listed in Table D. A study was performed with the BioPlex 2200 25-OH Vitamin D assay based on guidance from the CLSI Protocol EP7-A2. Aliquots of human samples were supplemented with potential Cross-Reactants at the concentrations listed and tested with the BioPlex 2200 25-OH Vitamin D assay. The percent cross reactivity is calculated as: % Cross Reactivity = (spiked vitamin D – non-spiked vitamin D) ÷ Cross reactant concentration × 100%. Data from this study are summarized in Table E.

Table E: Cross-Reactivity

Cross-Reactant	Concentration (ng/mL)	% Cross-Reactivity
25-OH Vitamin D3	30 ng/mL	97%
25-OH Vitamin D2	30 ng/mL	103%
Vitamin D2 (Ergocalciferol)	1000 ng/mL	0.2%
Vitamin D3	1000 ng/mL	0.0%
24,25-(OH)2-Vitamin D3	20 ng/mL	9%
1,25-(OH)2 Vitamin D3	30 ng/mL	79%
1,25-(OH)2 Vitamin D2	30 ng/mL	>100%
3-epi-25-OH Vitamin D3	30 ng/mL	59%
Paricalcitol (Zemplar)*	24 ng/mL	>100%

* *Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex 2200 25-OH Vitamin D assay.*

Interference

Testing for interfering substances was conducted according to CLSI Protocol EP7-A2. No significant interference ($\leq 10\%$ deviation from expected) was observed in any of the substances tested as listed below in Table F.

Table F: Interfering Substances

Substance	Concentration
Hemoglobin [*]	≤ 150 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 30 mg/dL
Triglycerides	≤ 400 mg/dL
Protein (total)	≤ 12 g/dL
Cholesterol	≤ 500 mg/dL
Ascorbic Acid	≤ 3 mg/dL
Rheumatoid Factor	≤ 350 IU/mL
Uric Acid	≤ 20 mg/dL

^{}Hemoglobin > 150 mg/dL may interfere and cause increased Vitamin D results. Do not use visibly hemolyzed samples.*

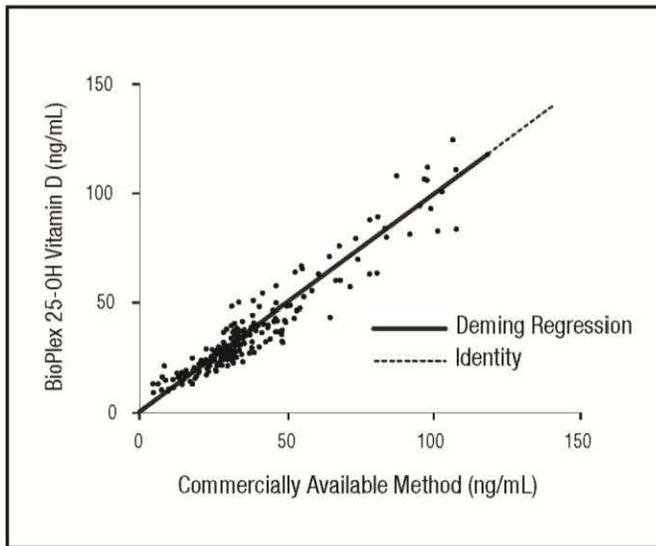
Method Comparison

A study was performed with the BioPlex 2200 25-OH Vitamin D assay, using regression analysis by the Weighted Deming method. The BioPlex 2200 25-OH Vitamin D assay was evaluated against a corresponding commercially available method using 196 samples. Results are shown in Table G and Graph 1.

Table G: BioPlex 2200 25-OH Vitamin D versus Commercially Available Assay

Regression Method	N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (95% CI)
Weighted Deming	196	1.0039 (0.9365-1.0712)	-0.2256 (-2.4121-1.9608)	0.9553 (0.9412-0.9661)

Graph 1. BioPlex 2200 25-OH Vitamin D vs. Commercially Available Method



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TRADEMARK INFORMATION

BioPlex is a registered trademark of Bio-Rad Laboratories, Inc.

TECHNICAL INFORMATION CONTACTS

Bio-Rad provides a toll free line for technical assistance, available 24 hours a day, 7 days a week. In the United States of America and Puerto Rico toll free 1-800-2BIORAD (224-6723).

Outside the U.S.A., please contact your regional Bio-Rad office for assistance.



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**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k141114

B. Purpose for Submission:

New Device

C. Measurand:

25-hydroxyvitamin D [25(OH) Vitamin D]

D. Type of Test:

Quantitative multiplexed flow immunoassay

E. Applicant:

Bio-Rad Laboratories

F. Proprietary and Established Names:

BioPlex® 2200 25-OH vitamin D kit

BioPlex® 2200 25-OH Vitamin D Calibrator Set

BioPlex® 2200 25-OH Vitamin D Control Set

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
MRG	II	862.1825 Vitamin D Test System	Chemistry (75)
JIT	II	862.1150 Calibrator	Chemistry (75)
JJX	I, Reserved	862.1660 Quality Control Material (Assayed and Unassayed)	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indication for use below.

2. Indication(s) for use:

The BioPlex 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH vitamin D assay is to be used to aid in the assessment of vitamin D sufficiency. The BioPlex 2200 25-OH Vitamin D kit is intended for use with the BioPlex 2200 System.

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D reagent Pack when performed on the Bio-Rad BioPlex 2200 System.

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 system and corresponding BioPlex® 25-OH Vitamin D reagent pack in the clinical laboratory. The performance of the BioPlex 2200 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

3. Special conditions for use statement(s):

For *in vitro* diagnostics

For prescription use only

4. Special instrument requirements:

BioPlex 2200 system

I. Device Description:

The BioPlex 2200 25-OH Vitamin D Kit consists of the following:

1. One 10mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead (SVB) in buffer with protein stabilizers (bovine). ProClin 950 (<1.0%) and sodium azide (<0.1%) as preservatives.
2. One 10mL vial of Release Buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (<1.0%) as preservative.
3. One 5mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizer (bovine). ProClin 950 (<1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives

(b) (4)

and chemical blockers.

4. One 5mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA-PE) in buffer comprising protein stabilizers (bovine). ProClin 950 (<1.0%) and sodium azide (<0.1%) as preservatives, chemical blockers and detergent (Tween 20).

BioPlex 2200 25-OH Vitamin D Calibrator set (sold separately) contains six 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (≤0.1%) as preservatives.

Calibrator Set	Target (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

BioPlex 2200 25-OH control set (sold separately) contains two 1.5 mL of Level 1 and two 1.5 mL of Level 2 control vials. Each vial contains 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (≤0.1%) as preservatives.

Control Set	Target (ng/mL)	Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Calibrator and Control contain human source material. Each donor unit of serum in the preparation of these materials were tested and found negative for the Human Immunodeficiency Virus Antibody (HIV I/II Ab), Hepatitis B Surface Antigen (HBsAg), and Hepatitis C Virus Antibody (HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):
EUROIMMUN 25-OH Vitamin D ELISA
2. Predicate 510(k) number(s):
k123660

3. Comparison with predicate:

Assay:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Kit Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Predicate Device (k123660)
Intended Use	For the quantitative determination of 25-hydroxyvitamin D in human serum.	Same
Assay Type	Quantitative	Same
Test Principle	Competitive immunoassay	Same
Antibody	Monoclonal Sheep antibody against 25 OH Vitamin D	Same
Signal Detection	Fluorescence	Same
Unit of Measure	ng/mL	Same
Assay Technology	Automated multiplex flow competitive immunoassay	Manually competitive immunoassay
Conjugate	Biotinylated 25-hydroxyvitamin D and phycoerythrin streptavidin	Biotinylated 25-hydroxyvitamin D and Peroxidase-labeled streptavidin and substrate TMB
Solid Phase	Antibody-coated paramagnetic microbeads	Antibody coated 96 microwell ELISA plate
Measuring Range	6.5 ng/mL – 125.0 ng/mL	4.0 ng/mL – 120 ng/mL
Sample Matrix	Serum	Serum or EDTA or Lithium heparin plasma
Sample Size	10µL	20µL
Open Pack Stability	60 days	Not Applicable
Reagent Storage	On-board or in refrigerator at 2-8°C	Not Applicable
Sample Handling	Automated	Manually
Instrumentation	Bio-Rad BioPlex® 2200 System	ELISA plate reader
Measuring Wavelength	550-610 nm	450/620 nm

Calibrator:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Calibrator Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Calibrator Predicate Device
Intended Use	For the calibration of the Vitamin D reagent pack.	Same
Calibrator(s) and Calibration	6 calibrator levels (sold separately); 4-PL (parameter logistic) curve fit algorithm	Same
Calibrator Matrix	25% horse serum and depleted human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Calibrator Open Storage at 2-8°C	30 days	3 months
Calibration Frequency	Every 30 days	Every 96 well plate

Controls:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Control Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Controls Predicate Device
Intended Use	Use as an assayed quality control to monitor the overall performance of the Vitamin D reagent.	Same
Storage	Store at 2-8°C until ready to use	Same
Matrix	Human serum with ProClin 950, Sodium benzoate and BND	Liquid in horse serum with preservatives

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

CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods
CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures
CLSI EP07-A2: Interference Testing in Clinical Chemistry
CLSI EP09-A2IR: Method comparison and Bias Estimation
CLSI EP15-A2: User Verification of Performance for Precision and Trueness
CLSI EP17-A2: Evaluation of Detection Capability for Clinical laboratory measurements Procedure
CLSI EP25-A: Evaluation of Stability of In-vitro diagnostic Reagents
C28-A3c: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory

L. Test Principle:

The BioPlex 2200 25-OH Vitamin D assay is a multiplex flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first Incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex® 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidinphycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) is present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex® 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amounts of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All performance testing were conducted on the Bio-Rad BioPlex 2200 System

a. *Precision/Reproducibility:*

The precision of Bio-Rad BioPlex 2200 25-OH Vitamin D assay was evaluated according to CLSI EP5-A2 guideline. Serum samples with low, medium, and high levels (6 total)

of 25-OH Vitamin D and two levels of serum controls were assayed in duplicate per run with two runs per day for twenty days (N=80) on one reagent lot.

Sample	N	Mean (ng/mL)	Within-Run		Between Run		Between Day		Total Precision	
			SD	%C V	SD	%CV	SD	%CV	SD	%CV
1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Control 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Control 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

b. Linearity/assay reportable range:

Linearity samples were prepared by diluting natural and spiked highly concentrated patient serum samples with a low-level human serum sample (<6.5 ng/mL). Each sample and dilution was evaluated in replicates of four on a single analyzer using one lot of reagent. Linearity was evaluated by calculating a linear regression comparing observed values versus expected values based on the CLSI EP6-A guideline. The regression parameters (slope, intercept, and r^2) of the observed values vs. expected values are shown below:

Slope	Intercept	r^2	Sample range tested
1.0001	0.0045	0.9988	5.5-168.9

Based on the results of the linearity study the sponsor claimed that the candidate assay is linear from 6.5 to 125 ng/mL

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

Traceability:

The BioPlex 25-OH Vitamin D Calibrators are traceable to internal standards, which are determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength.

The six levels of Master Calibrators are manufactured volumetrically from the internal standards into the depleted human serum except level 1 (25-OH hydroxyvitamin D free) in 25% horse serum. The Master Calibrators are immediately frozen at -70°C.

Value Assignment:

The BioPlex® 25-OH Vitamin D kit calibrators are manufactured for each lot kit with the same matrix as the Master Calibrators.

The BioPlex 2200 25-OH Vitamin D calibrator value assignments is established for the BioPlex 2200 25-OH Vitamin D kit using Master Calibrators as reference. For each calibrator level except level 1, three vials are tested in replicates of five on three BioPlex analyzers for a total of 45 points. Target values of the calibrators are listed in the table below.

Calibrator Set	Target value (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

Controls:

The two levels of BioPlex 2200 25-OH Vitamin D control set are prepared from a pool of native serum specimen. For each control level, three vials are tested in replicates of five using each of the kit lots on three BioPlex 2200 analyzers for a total of 45 replicates per reagent lot. Target values and QC ranges of the controls are listed in the table below.

Control Set	Target value (ng/mL)	QC Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Stability:

Shelf life stability studies: Real-time stability studies were performed for the BioPlex 2200 25-OH Vitamin D kit. The stability study protocol and the acceptance criteria have been reviewed and found acceptable. The real time ongoing kit stability study supports a stability of 9 months or until expiration date when stored unopened on the instrument or at 2-8°C.

Shelf-life stability for calibrators and controls: The stability study used elevated storage temperatures to model potential real time stability under normal conditions (2-8°C).

Accelerated stability studies protocol and acceptance criteria have been reviewed and found acceptable. The accelerated stability model estimates that the BioPlex® 2200 25-OH Vitamin D Calibrator and controls are stable for more than two years at 2-8°C. Real-time stability study is on-going. Real-time stability studies protocol and acceptance criteria have been reviewed and found acceptable.

Open vial stability: The open vial stability studies were performed to assess the stability over time with BioPlex® 2200 25-OH calibrator and control materials stored at 2-8°C. The stability study protocol and the acceptance criteria have been reviewed and found acceptable. The study supports an open vial stability of 30 days for the BioPlex 2200 25-OH calibrator and supports an open vial stability of 60 days for BioPlex 2200 25-OH controls.

d. Detection limit:

The limit of blank (LoB), limit of detection (LoD), and the limit of quantitation (LoQ) were determined following CLSI Document EP17-A2 guideline. The LoD is defined as the lowest concentration of 25-OH Vitamin D that can be detected with 95% probability. LoB was performed using two BioPlex 25-OH Vitamin reagent lots on one instrument in 4 replicates per day for 5 days yielding 100 data points per reagent lot. LoD was performed with six serum samples with mean measured concentration ranging from 3.89 to 34.29 ng/mL. The samples were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 12 replicates per day for five days yielding 60 data points per sample per reagent lot. LoQ: The precision was calculated with the same six low level samples used for the LoD. The mean, standard deviation, and coefficient of variation for each sample were calculated. LoQ was defined as precision \leq 20% CV.

The LoB, LoD, and LoQ are summarized below:

LoB	LoD	LoQ
0.8 ng/mL	2.5 ng/mL	6.5 ng/mL

The sponsor claimed that the candidate assay has a measuring range from 6.5 to 125 ng/mL

e. Analytical specificity:

Interference study:

To measure the effects of endogenous serum components and exogenous molecules on the 25-OH Vitamin D assay. Three sample pools were prepared to achieve a low (10-20 ng/mL), medium (30-50 ng/mL), and high (70-90 ng/mL). The samples were spiked with the interfering substances. The tests and controls were evaluated for a total of ten replicates per interferent using BioPlex 2200 25-OH Vitamin D reagent. Substances are considered interfering if their presence in a sample results in more than \pm 10% deviation

in quantitation relative to the value determined in the absence of the substance. The protocol and calculations were based on CLSI EP7-A2 guideline. The substances and the maximum levels tested are shown in the table below:

Substances	Highest Concentration of substance tested which demonstrated no significant interference.
Hemoglobin	150 mg/dL
Bilirubin (conjugated)	20 mg/dL
Bilirubin (unconjugated)	30 mg/dL
Triglycerides	400 mg/dL
Total Protein	12 g/dL
Cholesterol	500 mg/dL
Uric Acid	20 mg/dL
HAMA	100 ng/mL
Rheumatoid Factor	350 IU/mL
Ascorbic Acid	3 mg/dL

The sponsor has the following limitations in their labeling:

“Hemoglobin > 150 mg/dL may interfere and cause increased Vitamin D results. Do not use visibly hemolyzed samples.”

Cross-Reactivity:

The study was conducted using 2 serum pools at 25-hydroxyvitamin D concentrations of 20 ng/mL and 35 ng/mL. Nine cross reactants at levels listed below were spiked into the serum pools. The spiked and non-spiked samples were then evaluated in replicates of five to calculate the cross reactivity as shown below:

$\% \text{ cross reactivity} = \frac{[(\text{mean recovery of test samples in ng/mL}) - (\text{mean recovery of control sample in ng/mL})]}{(\text{concentration of cross reactant in ng/mL})} * 100$

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D2	30	103%
25-hydroxyvitamin D3	30	97%
Vitamin D2	1000	0.2%
Vitamin D3	1000	0.0%
1,25-dihydroxyvitamin D2	30	>100%
1,25-dihydroxyvitamin D3	30	79%
3-epi 25-hydroxyvitamin D3	30	59%
24,25-dihydroxyvitamin D3	20	9%
Paricalcitol (Zemplar)	24	>100%

(b) (4)

The sponsor has the following limitations in their labeling:

“Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex® 2200 25- OH Vitamin D assay.”

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study using 204 human serum samples was performed to compare the candidate device BioPlex 2200 25-OH Vitamin D to the predicate device EUROIMMUN 25-OH Vitamin D ELISA. 185 samples were unaltered and 19 samples were spiked with 25-hydroxyvitamin D₃. A total of 196 human serum samples with 25-OH Vitamin D values ranging from 6.6 ng/mL to 124.9 ng/mL were analyzed. There were eight samples with values lower or higher than the measuring range of the predicate method that were excluded in the data analysis. The samples were assayed in singlicate using one reagent lot of the candidate and predicate device. Deming regression was used for the regression analysis and the results are summarized below:

Number of Results Analyzed	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r) (95% CI)	Sample Range Tested (ng/mL)
196	1.0039 (0.9365 to 1.0712)	-0.2256 (-2.4121 to 1.9608)	0.9553 (0.9412 to 0.9661)	BioPlex: 6.6 – 124.9

b. Matrix comparison:

Not Applicable, only serum is recommended

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

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

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The study was performed in accordance with CLSI C28-A3c guideline. Two hundred and eighty-seven samples from apparently healthy donors including 160 males and 127 female were collected from three regions (North, Central, and South) in the US and in three seasons (spring, summer and winter), including Caucasians and African American subjects. The 287 samples from apparently healthy donors met the following inclusion / exclusion criteria as follows and tested with the BioPlex 25-OH Vitamin D kit in singlicate. *One sample <6.5 ng/ml was excluded from the data analysis.

- Age from 21 to 90
- 50% female and 50% male
- 20% from Northern, 20% from Central, and 60% from Southern region
- 40% collected in Summer and 60% in Winter
- At least 30% dark and 30% light skin
- 90% not taking Vitamin D supplements and <30% of those taking Vitamin D supplements at or more than 1000 IU, but less than 2000 IU
- Normal TSH, PTH, and Total Calcium
- No family history of parathyroid or calcium regulatory disease. In addition, no personal history of kidney disease, GI disease, and no bariatric surgery

The observed median, mean, and ranges between 2.5th to 97.5th percentile are summarized below:

N	Mean	Median	2.5 th to 97.5 th Percentile
286	29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

Each laboratory should establish its own reference range pertinent to their specific populations.

N. Proposed Labeling:

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

O. Conclusion:

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

(b) (4)

P. Other Supportive Device and Instrument Information:

TPLC for post market signals:

TPLC database search has been performed and no issues with this product were identified.

Q. Administrative Information:

1. Applicant contact information:

a. Name of applicant:

Bio-Rad Laboratories

b. Mailing address:

5500 E. Second Street

Benicia, CA 94510

c. Phone #:

510-741-4609

d. Fax #:

510-741-3941

e. E-mail address (optional):

Juang_wang@bio-rad.com

f. Contact:

Juang Wang

2. Review documentation:

2. May 1, 2014 assigned the submission in CTS

3. May 13, 2014 Meet with Tracey Bosworth (Product Specialist) and Chris King (Mentor) to discuss the submission.

4. May 14, 2014 RTAA Triage-Quick Review program
5. May 14, 2014 Notify the sponsor that they are included in the Triage-Quick Review program. Requested the sponsor to provide the new IFU form.
6. May 21, 2014 Meet with Tracey to discuss the submission issues, clarification, and additional information needed from the sponsor.
7. May 27, 2014 Emailed Tracey a draft TH letter and draft DS for review.
8. May 30, 2014 Meet with Yung Chan (Branch Manager) and Tracey to decide to remove the submission from the Triage program and to place the submission on hold.
9. June 2, 2014 Meet with Yung Chan (Branch Manager) and Tracey to discuss all the issues in the TH letter to the sponsor.

Method Comparison:

(b)(4)

Value assignment, Traceability and Stability:

(b)(4)

Interference / Cross Reactivity

(b)(4)

Update the proposed labeling and 510 (k) Summary, labeling and IFU

10. June 4, 2014 Finalized the TH letter with Yung and the submission was placed on

(b)(4)

- ~~10-10.10-~~ June 5, 2014 Received an email from the sponsor regarding the TH letter. The sponsor had questions and needed clarification on the issues with the Method

(b)(4)

11. July 17 & 18, 2014 The sponsor emailed the unofficial response to the TH letter. The sponsor response (b)(4)
(b)(4)
12. August 11, 2014 The sponsor requested guidance on what would be an acceptable (b)(4)
(b)(4) We indicated to the sponsor that the responses sent in via email required further internal discussion and ~~We-we~~ recommended the sponsor use the Submission Issue Meeting.
13. August 15, 2014 sponsor request a teleconference with management to better understand the need for a Submission Issue Meeting
14. August 18, 2014 Sponsor agreed during the teleconference to submit for a Submission Issue Meeting (b)(4)
(b)(4)
(b)(4)
15. August 21, 2014 Sponsor sent in the official request for a Submission Issue Meeting (b)(4)
(b)(4)
16. August 21, 2014 Q141077 RTAA
17. August 28, 2014 Internal Meeting scheduled to discuss the submission.
- ~~18.~~ September 4, 2014 Submission Issue Meeting Teleconference held. FDA attendees: Katie Serrano (Deputy Director), Yung Chan (Chemistry Branch Manager), Tracey Bosworth (Product Specialist), Meshawn Payne (Product Specialist) and Sheila Connors (Lead Reviewer). Bio-Rad attendees: Juang Wang (Regulatory Affairs), Patricia Klimley (Regulatory Affairs Manager) (b)(4)
(b)(4)
(b)(4)
- ~~19.~~18. September 12, 2014 Sponsor sent in the Submission Issue Meeting Teleconference ~~Call~~ minutes.
- ~~20.~~19. September 16, 2014 Sent the meeting minutes to the FDA attendees for edits and comments
20. October 10, 2014 Meet with the Yung to finalize the minutes and emailed the sponsor the final edits to the minutes. Please see the submission issue meeting minutes in docman.
- ~~21.~~
- ~~22.~~21. November 21, 2014 Received an email from the sponsor with a request for an extension beyond the 180 days (Dec. 1, 2014) because of the need to perform a new comparison study with new samples.
- ~~23.~~22. November 21, 2014 Discussed the request for an extension with Yung. We had a teleconference with the sponsor explaining the FDA no longer allow extensions and that the official response must be sent to the DCC by Dec. 1, 2014.
- ~~24.~~23. November 21, 2014 Sponsor emailed a follow up to the teleconference about

Comment [SEB5]: What did they want to discuss in this meeting?
SAC: Added

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receiving the official response and if the response is not acceptable or still missing information. We replied: As long as you send the complete response to the DCC by the 180th day, we will continue with our review. If we do not receive your complete response by the 180 days, the system will automatically delete your submission. You will **not** receive a NSE letter because we did not make any decision on your submission.

~~25~~-24. November 26, 2014 Sponsor sent in the supplement response.

~~26~~-25. December 10, 2014 Meet with Tracey to discuss the supplement response

~~27~~-26. December 12, 2014 Received Tracey's comments on the draft DM

~~28~~-27. December 12, 2014 request the sponsor to send an example of the value

(b)(4)

~~29~~-28. December 15, 2014 Received an example of (b)(4) from the sponsor. Also discussed the (b)(4) with Yung.

(b)(4)

(b)(4)

~~30~~-29. December 18, 2014 arranged a teleconference with the sponsor to discuss the

(b)(4)

3

~~31~~

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~~32~~-December 26, 2014 Received the (b)(4)

(b)(4)

Comment [SEB6]: How did they address your concerns? Were all of your concerns addressed? Why was it okay to do a new study, was their a root cause of the interferences? How were they addressed?

SAC: Added

~~33~~-31. December 29, 2014 Received the updated IFU, 510(k) Summary and labeling from the sponsor with all the new study information.

~~34~~-32. December 30, 2014 Received the final updated 510(k) Summary and labeling from the sponsor with all edits and corrections.

3. Substantial Equivalence Discussion:

	Yes	No	
<i>(Identify the new device and the predicate device)</i> 1. Is the predicate device legally marketed?	X		If YES = Go To 2 If NO = Stop NSE
<i>(Review all labeling and assure that it is consistent with IFU statements)</i> 2. Do the devices have the same intended use?	X		If YES = Go to 3, Respond to "A." below If NO = Stop NSE , Respond to "A." below
<i>(Review design, materials, energy source and other features of the devices)</i> 3. Do the devices have the same technological characteristics?		X	If YES = Stop SE If NO = Go to 4, Respond to "B." below
<i>(Determine what questions of safety and effectiveness the different technological characteristics raise)</i> 4. Do the different technological characteristics of the devices raise different questions of safety and effectiveness?		X	If YES = Stop NSE , Respond to "C." below If NO = Go to 5
<i>(Review the proposed scientific methods for evaluating new/ different characteristics' effects on safety and effectiveness)</i> 5a. Are the methods acceptable?	X		If YES = Go to 5b If NO = Stop NSE , Respond to "D." below
<i>(Evaluate performance data)</i> 5b. Do the data demonstrate substantial equivalence?	X		If YES = Stop SE , Respond to "E." below If NO = Stop NSE , Respond to "E." below

Final Decision:

Note: Please complete the following table and answer the corresponding questions.

A. Please explain how the intended use of the subject device is similar to or different from the predicate device.

The subject device has the same intended use as the predicate device.

B. Please describe the different technological characteristics.

The different technological characteristics are described in the device description section, the comparison with the predicate section, and the test principle section. See details in section I, J and L above for more information.

- C. Please explain how the technological characteristics raise different questions of safety and effectiveness
- D. Please explain why the proposed scientific method for evaluating new/ different characteristics' effects on safety and effectiveness are not acceptable.
- E. Please explain how the data do or do not demonstrate substantial equivalence.

The performance data submitted by the sponsor has demonstrated that the candidate device is substantial equivalent to the predicate device. See section M. above for more information.

R. Reviewer Name and Signature:

Digital Signature Concurrence Table	
Reviewer Sign-Off	
Branch Chief Sign-Off (optional)	
Division Sign-Off (optional)	

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k141114

B. Purpose for Submission:

New Device

C. Measurand:

25-hydroxyvitamin D [25(OH) Vitamin D]

D. Type of Test:

Quantitative multiplexed flow immunoassay

E. Applicant:

Bio-Rad Laboratories

F. Proprietary and Established Names:

BioPlex® 2200 25-OH vitamin D kit

BioPlex® 2200 25-OH Vitamin D Calibrator Set

BioPlex® 2200 25-OH Vitamin D Control Set

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
MRG	II	862.1825 Vitamin D Test System	Chemistry (75)
JIT	II	862.1150 Calibrator	Chemistry (75)
JJX	I, Reserved	862.1660 Quality Control Material (Assayed and Unassayed)	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indication for use below.

2. Indication(s) for use:

The BioPlex 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH vitamin D assay is to be used to aid in the assessment of vitamin D sufficiency. The BioPlex 2200 25-OH Vitamin D kit is intended for use with the BioPlex 2200 System.

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D reagent Pack.

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 system and corresponding BioPlex® 25-OH Vitamin D reagent pack in the clinical laboratory. The performance of the BioPlex 2200 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

3. Special conditions for use statement(s):

For *in vitro* diagnostics

For prescription use only

4. Special instrument requirements:

BioPlex 2200 system

I. Device Description:

The BioPlex 2200 25-OH Vitamin D Kit consists of the following:

1. One 10mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead (SVB) in buffer with protein stabilizers (bovine). ProClin 950 (<1.0%) and sodium azide (<0.1%) as preservatives.
2. One 10mL vial of Release Buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (<1.0%) as preservative.
3. One 5mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizer (bovine). ProClin 950 (<1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives

and chemical blockers.

4. One 5mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA-PE) in buffer comprising protein stabilizers (bovine). ProClin 950 (<1.0%) and sodium azide (<0.1%) as preservatives, chemical blockers and detergent (Tween 20).

BioPlex 2200 25-OH Vitamin D Calibrator set (sold separately) contains six 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (≤0.1%) as preservatives.

Calibrator Set	Target (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

BioPlex 2200 25-OH control set (sold separately) contains two 1.5 mL of Level 1 and two 1.5 mL of Level 2 control vials. Each vial contains 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (≤0.1%) as preservatives.

Control Set	Target (ng/mL)	Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Calibrator and Control contain human source material. Each donor unit of serum in the preparation of these materials were tested and found negative for the Human Immunodeficiency Virus Antibody (HIV I/II Ab), Hepatitis B Surface Antigen (HBsAg), and Hepatitis C Virus Antibody (HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):
EUROIMMUN 25-OH Vitamin D ELISA
2. Predicate 510(k) number(s):
k123660

3. Comparison with predicate:

Assay:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Kit Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Predicate Device (k123660)
Intended Use	For the quantitative determination of 25-hydroxyvitamin D in human serum.	Same
Assay Type	Quantitative	Same
Test Principle	Competitive immunoassay	Same
Antibody	Monoclonal Sheep antibody against 25 OH Vitamin D	Same
Signal Detection	Fluorescence	Same
Unit of Measure	ng/mL	Same
Assay Technology	Automated multiplex flow competitive immunoassay	Manually competitive immunoassay
Conjugate	Biotinylated 25-hydroxyvitamin D and phycoerythrin streptavidin	Biotinylated 25-hydroxyvitamin D and Peroxidase-labeled streptavidin and substrate TMB
Solid Phase	Antibody-coated paramagnetic microbeads	Antibody coated 96 microwell ELISA plate
Measuring Range	6.5 ng/mL – 125.0 ng/mL	4.0 ng/mL – 120 ng/mL
Sample Matrix	Serum	Serum or EDTA or Lithium heparin plasma
Sample Size	10µL	20µL
Open Pack Stability	60 days	Not Applicable
Reagent Storage	On-board or in refrigerator at 2-8°C	Not Applicable
Sample Handling	Automated	Manually
Instrumentation	Bio-Rad BioPlex® 2200 System	ELISA plate reader
Measuring Wavelength	550-610 nm	450/620 nm

Calibrator:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Calibrator Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Calibrator Predicate Device
Intended Use	For the calibration of the Vitamin D reagent pack.	Same
Calibrator(s) and Calibration	6 calibrator levels (sold separately); 4-PL (parameter logistic) curve fit algorithm	Same
Calibrator Matrix	25% horse serum and depleted human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Calibrator Open Storage at 2-8°C	30 days	3 months
Calibration Frequency	Every 30 days	Every 96 well plate

Controls:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Control Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Controls Predicate Device
Intended Use	Use as an assayed quality control to monitor the overall performance of the Vitamin D reagent.	Same
Storage	Store at 2-8°C until ready to use	Same
Matrix	Human serum with ProClin 950, Sodium benzoate and BND	Liquid in horse serum with preservatives

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

CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods

CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures

CLSI EP07-A2: Interference Testing in Clinical Chemistry

CLSI EP09-A2IR: Method comparison and Bias Estimation

CLSI EP15-A2: User Verification of Performance for Precision and Trueness

CLSI EP17-A2: Evaluation of Detection Capability for Clinical laboratory measurements

Procedure

CLSI EP25-A: Evaluation of Stability of In-vitro diagnostic Reagents

CLSI C28-A3c: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory

L. Test Principle:

The BioPlex 2200 25-OH Vitamin D assay is a multiplex flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex® 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidinphycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) is present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex® 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amounts of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All performance testing were conducted on the Bio-Rad BioPlex 2200 System

a. Precision/Reproducibility:

The precision of Bio-Rad BioPlex 2200 25-OH Vitamin D assay was evaluated according to CLSI EP5-A2 guideline. Serum samples with low, medium, and high levels (6 total) of 25-OH Vitamin D and two levels of serum controls were assayed in duplicate per run with two runs per day for twenty days (N=80) on one reagent lot.

Sample	N	Mean (ng/mL)	Within-Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Control 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Control 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

b. *Linearity/assay reportable range:*

Linearity samples were prepared by diluting natural and spiked highly concentrated patient serum samples with a low-level human serum sample (<6.5 ng/mL). Each sample and dilution was evaluated in replicates of four on a single analyzer using one lot of reagent. Linearity was evaluated by calculating a linear regression comparing observed values versus expected values based on the CLSI EP6-A guideline. The regression parameters (slope, intercept, and r^2) of the observed values vs. expected values are shown below:

Slope	Intercept	r^2	Sample range tested
1.0001	0.0045	0.9988	5.5-168.9

Based on the results of the linearity study the sponsor claimed that the candidate assay is linear from 6.5 to 125 ng/mL

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

Traceability:

The BioPlex 25-OH Vitamin D Calibrators are traceable to internal standards, which are determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength.

The six levels of Master Calibrators are manufactured volumetrically from the internal standards into the depleted human serum except level 1 (25-OH hydroxyvitamin D free) in 25% horse serum. The Master Calibrators are immediately frozen at -70°C.

Value Assignment:

The BioPlex® 25-OH Vitamin D kit calibrators are manufactured for each lot kit with the

same matrix as the Master Calibrators.

The BioPlex 2200 25-OH Vitamin D calibrator value assignments is established for the BioPlex 2200 25-OH Vitamin D kit using Master Calibrators as reference. For each calibrator level except level 1, three vials are tested in replicates of five on three BioPlex analyzers for a total of 45 points. Target values of the calibrators are listed in the table below.

Calibrator Set	Target value (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

Controls:

The two levels of BioPlex 2200 25-OH Vitamin D control set are prepared from a pool of native serum specimen. For each control level, three vials are tested in replicates of five using each of the kit lots on three BioPlex 2200 analyzers for a total of 45 replicates per reagent lot. Target values and QC ranges of the controls are listed in the table below.

Control Set	Target value (ng/mL)	QC Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Stability:

Shelf life stability studies: Real-time stability studies were performed for the BioPlex 2200 25-OH Vitamin D kit. The stability study protocol and the acceptance criteria have been reviewed and found acceptable. The real time ongoing kit stability study supports a stability of 9 months or until expiration date when stored unopened on the instrument or at 2-8C.

Shelf-life stability for calibrators and controls: The stability study used elevated storage temperatures to model potential real time stability under normal conditions (2-8°C). Accelerated stability studies protocol and acceptance criteria have been reviewed and found acceptable. The accelerated stability model estimates that the BioPlex® 2200 25-OH Vitamin D Calibrator and controls are stable for more than two years at 2-8°C. Real-time stability study is on-going. Real-time stability studies protocol and acceptance criteria have been reviewed and found acceptable.

Open vial stability: The open vial stability studies were performed to assess the stability over time with BioPlex® 2200 25-OH calibrator and control materials stored at 2-8°C. The stability study protocol and the acceptance criteria have been reviewed and found acceptable. The study supports an open vial stability of 30 days for the BioPlex 2200 25-OH calibrator and supports an open vial stability of 60 days for BioPlex 2200 25-OH controls.

d. Detection limit:

The limit of blank (LoB), limit of detection (LoD), and the limit of quantitation (LoQ) were determined following CLSI Document EP17-A2 guideline. The LoD is defined as the lowest concentration of 25-OH Vitamin D that can be detected with 95% probability. LoB was performed using two BioPlex 25-OH Vitamin reagent lots on one instrument in 4 replicates per day for 5 days yielding 100 data points per reagent lot. LoD was performed with six serum samples with mean measured concentration ranging from 3.89 to 34.29 ng/mL. The samples were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 12 replicates per day for five days yielding 60 data points per sample per reagent lot. LoQ: The precision was calculated with the same six low level samples used for the LoD. The mean, standard deviation, and coefficient of variation for each sample were calculated. LoQ was defined as precision \leq 20% CV.

The LoB, LoD, and LoQ are summarized below:

LoB	LoD	LoQ
0.8 ng/mL	2.5 ng/mL	6.5 ng/mL

The sponsor claimed that the candidate assay has a measuring range from 6.5 to 125 ng/mL.

e. Analytical specificity:

Interference study:

To measure the effects of endogenous serum components and exogenous molecules on the 25-OH Vitamin D assay. Three sample pools were prepared to achieve a low (10-20 ng/mL), medium (30-50 ng/mL), and high (70-90 ng/mL). The samples were spiked with the interfering substances. The tests and controls were evaluated for a total of ten replicates per interferent using BioPlex 2200 25-OH Vitamin D reagent. Substances are considered interfering if their presence in a sample results in more than \pm 10% deviation in quantitation relative to the value determined in the absence of the substance. The protocol and calculations were based on CLSI EP7-A2 guideline. The substances and the

maximum levels tested are shown in the table below:

Substances	Highest Concentration of substance tested which demonstrated no significant interference.
Hemoglobin	150 mg/dL
Bilirubin (conjugated)	20 mg/dL
Bilirubin (unconjugated)	30 mg/dL
Triglycerides	400 mg/dL
Total Protein	12 g/dL
Cholesterol	500 mg/dL
Uric Acid	20 mg/dL
HAMA	100 ng/mL
Rheumatoid Factor	350 IU/mL
Ascorbic Acid	3 mg/dL

The sponsor has the following limitations in their labeling:

“Hemoglobin > 150 mg/dL may interfere and cause increased Vitamin D results. Do not use visibly hemolyzed samples.”

Cross-Reactivity:

The study was conducted using 2 serum pools at 25-hydroxyvitamin D concentrations of 20 ng/mL and 35 ng/mL. Nine cross reactants at levels listed below were spiked into the serum pools. The spiked and non-spiked samples were then evaluated in replicates of five to calculate the cross reactivity as shown below:

% cross reactivity = [(mean recovery of test samples in ng/mL) – (mean recovery of control sample in ng/mL) / (concentration of cross reactant in ng/mL)] * 100

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D2	30	103%
25-hydroxyvitamin D3	30	97%
Vitamin D2	1000	0.2%
Vitamin D3	1000	0.0%
1,25-dihydroxyvitamin D2	30	>100%
1,25-dihydroxyvitamin D3	30	79%
3-epi 25-hydroxyvitamin D3	30	59%
24,25-dihydroxyvitamin D3	20	9%
Paricalcitol (Zemplar)	24	>100%

The sponsor has the following limitations in their labeling:

“Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex® 2200 25- OH Vitamin D assay.”

f. *Assay cut-off:*

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

A method comparison study using 204 human serum samples was performed to compare the candidate device BioPlex 2200 25-OH Vitamin D to the predicate device EUROIMMUN 25-OH Vitamin D ELISA. 185 samples were unaltered and 19 samples were spiked with 25-hydroxyvitamin D₃. A total of 196 human serum samples with 25-OH Vitamin D values ranging from 6.6 ng/mL to 124.9 ng/mL were analyzed. There were eight samples with values lower or higher than the measuring range of the predicate method that were excluded in the data analysis. The samples were assayed in singlicate using one reagent lot of the candidate and predicate device. Deming regression was used for the regression analysis and the results are summarized below:

N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r) (95% CI)	Sample Range Tested (ng/mL)
196	1.0039 (0.9365 to 1.0712)	-0.2256 (-2.4121 to 1.9608)	0.9553 (0.9412 to 0.9661)	BioPlex: 6.6 – 124.9

b. *Matrix comparison:*

Not Applicable, only serum is recommended

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable

b. *Clinical specificity:*

Not Applicable

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

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The study was performed in accordance with CLSI C28-A3c guideline. Two hundred and eighty-seven samples from apparently healthy donors including 160 males and 127 female were collected from three regions (North, Central, and South) in the US and in three seasons (spring, summer and winter), including Caucasians and African American subjects. The 287 samples from apparently healthy donors met the following inclusion / exclusion criteria as follows and tested with the BioPlex 25-OH Vitamin D kit in singlicate. *One sample <6.5 ng/ml was excluded from the data analysis.

- Age from 21 to 90
- 50% female and 50% male
- 20% from Northern, 20% from Central, and 60% from Southern region
- 40% collected in Summer and 60% in Winter
- At least 30% dark and 30% light skin
- 90% not taking Vitamin D supplements and <30% of those taking Vitamin D supplements at or more than 1000 IU, but less than 2000 IU
- Normal TSH, PTH, and Total Calcium
- No family history of parathyroid or calcium regulatory disease. In addition, no personal history of kidney disease, GI disease, and no bariatric surgery

The observed median, mean, and ranges between 2.5th to 97.5th percentile are summarized below:

N	Mean	Median	2.5 th to 97.5 th Percentile
286	29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

Each laboratory should establish its own reference range pertinent to their specific populations.

N. Proposed Labeling:

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

O. Conclusion:

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

BioPlex[®] 2200 25-OH Vitamin D 510(k) Summary

Bio-Rad Laboratories hereby submits this 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides detail as a basis for a determination of substantial equivalence for the BioPlex[®] 2200 25-OH Vitamin D kit.

510(k) Number:
k141114

Summary Preparation Date:
December 30, 2014

Applicant:
Bio-Rad Laboratories

Contact:
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Purpose for Submission:
New Device

Measurand:
25-hydroxyvitamin D

Type of Test:
Quantitative multiplexed flow immunoassay

Proprietary and Established Names:
BioPlex[®] 2200 25-OH Vitamin D kit
BioPlex[®] 2200 25-OH Vitamin D Calibrator Set
BioPlex[®] 2200 25-OH Vitamin D Control Set

Regulatory Information:

1. Regulation section:
 - 21 CFR §862.1825 – Vitamin D test system
 - 21 CFR §862.1150 – Calibrator
 - 21 CFR §862.1660 – Quality Control Material (assayed and unassayed)

2. Classification:

Class II (Assays, Calibrator)
Class I (Controls)

3. Product code:

MRG, System, Test, Vitamin D
JIT, Calibrator, Secondary
JJX, Single (specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Clinical Chemistry (75)

Intended Use:

1. Intended use(s):

The BioPlex[®] 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex[®] 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

The BioPlex[®] 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex[®] 2200 25-OH Vitamin D Reagent Pack.

The BioPlex[®] 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex[®] 2200 System and the corresponding BioPlex[®] 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex[®] 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Bio-Rad BioPlex[®] 2200 System

Device Description:

BioPlex[®] 2200 25-OH Vitamin D kit includes the following components:

- One (1) 10 mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead

(SVB) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives.

- One (1) 10 mL vial of Release Buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (<1.0%) as preservative.
- One (1) 5 mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives and chemical blockers.
- One (1) 5 mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA -PE) in a buffer comprising protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives, chemical blockers and detergent (Tween 20).

BioPlex[®] 2200 25-OH Vitamin D Calibrator set contains six (6) 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

BioPlex[®] 2200 25-OH Control set contains two (2) 1.5 mL Level 1 and two (2) 1.5 mL Level 2 Control vials, each containing 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

Additional materials required but not supplied include BioPlex[®] 2200 Sheath Fluid containing Phosphate Buffered Saline (PBS), ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives; and BioPlex[®] 2200 Wash Solution containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives.

Substantial Equivalence Information:

1. Predicate device name(s):
EUROIMMUN 25-OH Vitamin D ELISA, k123660
2. Comparison with predicate:

Device Similarities		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Intended Use/Indication for Use	Intended for the quantitative determination of 25-hydroxyvitamin D in serum. To be used as an aid in the assessment of vitamin D sufficiency	Same
Measured Analyte	25-hydroxyvitamin D	Same
Assay Type	Quantitative	Same
Test Principle	Competitive immunoassay	Same
Antibody	Monoclonal Sheep antibody against 25-OH Vitamin D	Same
Signal Detection	Fluorescence	Same
Unit of Measure	ng/mL	Same
Calibrator(s) and Calibration	6 calibrator levels (sold separately); 4-PL (parameter logistic) curve fit algorithm	Same

Device Differences		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Assay Technology	Automated flow competitive immunoassay	Manual competitive immunoassay
Conjugate	Biotinylated 25-hydroxyvitamin D and phycoerythrin conjugated streptavidin	Biotin-labeled 25-OH vitamin D, Peroxidase-labeled streptavidin and substrate TMB
Solid Phase	Antibody-coated paramagnetic microbeads	Antibody coated 96 microwell ELISA plate
Measuring range	6.5 – 125.0 ng/mL	4 – 120 ng/mL
Sample Matrix	Serum	Serum or EDTA or Lithium heparin plasma
Sample Size	10 µL	20µL
Calibrator Matrix	25% horse serum and depleted human serum	Liquid in horse serum with preservatives

Device Differences		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
	with ProClin 950, sodium benzoate and BND	
Open Pack Stability	60 days	Not applicable
Reagent Integral Storage	On-board or in refrigerator at 2-8°C	Not applicable
Sample Handling/Process	Automated	Manual
Calibrator Open storage at 2-8°C	30 days	3 months
Calibration Frequency	Every 30 days	Every 96 well plate
Instrumentation	Bio-Rad BioPlex 2200 System	ELISA plate reader
Measuring wavelength	550 – 610 nm	450/620 nm

Control Set Similarities and Differences		
Characteristics	BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Intended Use	Use as an assayed quality control to monitor the overall performance of 25-OH Vitamin D reagent.	Same
Storage	Store at 2 -8°C until ready to use	Same
Matrix	Human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Control Open Stability at 2 – 8°C	60 days	No Applicable

Standard/Guidance Document Referenced (if applicable):

EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition (Vol. 24 No.25)

EP06-A, Evaluation of Linearity of Quantitative Measurement: A Statistical Approach, Approved Guideline (Vol. 23 No.16)

EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition (Vol. 25 No.27)
EP09-A2IR, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (Interim Revision) (Vol. 30 No. 17)
EP15-A2, User Verification of Performance for Precision and Trueness, Approved Guideline, Second Edition (Vol. 25 No.17)
EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline, Second Edition (Vol. 32 No.8)
EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (Vol. 29, No. 20)
C28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, Third Edition (Vol. 28 No.30)

Test Principle:

The BioPlex® 2200 25-OH Vitamin D assay is a multiplexed flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidin-phycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) are present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amount of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision testing of the BioPlex® 2200 25-OH Vitamin D kit on the BioPlex® 2200 instrument was performed in accordance with CLSI EP5-A2 guideline. A human serum panel consisting of 6 frozen samples spanning the measuring range was assayed in duplicate per run on two runs daily over 20 days (N=80) on one

reagent lot. Two levels of the BioPlex 25-OH Vitamin D controls were also included. The data were analyzed for within-run, between-run, between-day, and total precision and the mean (ng/mL), standard deviation (ng/mL) and percent coefficient of variation (%CV) are summarized below:

BioPlex® 2200 25-OH Vitamin D – CLSI EP5-A2 Precision

Serum Panel	N	Mean ng/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
Sample 2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
Sample 3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
Sample 4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
Sample 5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
Sample 6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Control 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Control 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

CLSI EP15-A2 Reproducibility

Precision and reproducibility was also evaluated in accordance with CLSI EP15-A2 guideline “User Verification of Performance for Precision and Trueness, Vol 25, No 17”.

A different serum panel consisting of 8 samples spanning the measuring range were assayed in 2 replicates per run, two runs per day over 5 days (n=20) using one lot of BioPlex 25-OH Vitamin D kit. Two levels of controls were also included. The data were analyzed for within-run, between run, between day, and total precision and the mean ng/mL, standard deviation and percent coefficient of variation (%CV) are summarized below:

BioPlex® 2200 25-OH Vitamin D - CLSI EP15-A2 Reproducibility

Serum Panel	N	Mean ng/mL	Within Run		Between Run		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Sample 1	20	11.5	0.69	6.0%	0.47	4.1%	1.71	14.8%
Sample 2	20	13.6	0.80	5.9%	0.26	1.9%	1.18	8.7%
Sample 3	20	26.1	0.88	3.4%	1.15	4.4%	1.59	6.1%
Sample 4	20	30.2	1.99	6.6%	0.00	0.0%	2.71	9.0%
Sample 5	20	50.2	2.23	4.4%	0.77	1.5%	2.96	5.9%
Sample 6	20	56.4	2.09	3.7%	2.79	4.9%	5.26	9.3%
Sample 7	20	100.5	4.52	4.5%	2.81	2.8%	5.32	5.3%
Sample 8	20	104.9	3.97	3.8%	1.54	1.5%	5.24	5.0%
Control 1	20	21.6	0.98	4.5%	1.00	4.6%	1.84	8.5%
Control 2	20	58.8	2.44	4.2%	1.29	2.2%	2.99	5.1%

b. *Linearity/assay reportable range:*

Five high patient serum samples extending 20% higher than upper limit of the assay range were tested to demonstrate linearity. These samples were serially diluted with low levels of human sample near LoQ in accordance with CLSI EP06-A guideline. Each sample and dilution was evaluated in replicates of four using one BioPlex 25-OH Vitamin D reagent lot on one instrument. Linear and polynomial regression analysis of 25-OH Vitamin D recovery vs. sample dilution was performed to determine if the dilution curves exhibit statistically significant non-linear regression based on the CLSI guideline EP06-A.

See one example below for the regression parameters (slope, intercept and r^2) of the observed values vs. predicted values.

Conc (ng/mL)	Slope	Intercept	r^2	Dilution range
168.9	1.0001	0.0045	0.9988	5.5 – 168.9

The BioPlex 2200 25-OH Vitamin D assay has demonstrated that the assay range is 6.5 to 125.0 ng/mL.

Over-Range (OR) results may be generated for values greater than the reportable measuring range and results are reported as > 125.0 ng/mL.

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

Traceability:

The BioPlex 25-OH Vitamin D Calibrators are traceable to internal standards which are determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength.

The six levels of Master calibrators are manufactured volumetrically from the internal standards into the depleted human serum except level 1 (25-hydroxyvitamin D free) in 25% horse serum. The Master calibrators are immediately frozen at <-70°C.

Value Assignment:

The BioPlex 25-OH Vitamin D kit calibrators are manufactured for each lot kit with the same matrix as the Master calibrators and are stabilized with $\leq 0.3\%$ ProClin 950, $\leq 0.1\%$ sodium benzoate, and $< 0.1\%$ 5-bromo-1,3-nitro-dioxane.

Calibrator assignment is established for the matched lot of BioPlex[®] 2200 25-OH Vitamin D kit using the Master calibrators as reference. Calibrator assignment is established for the matched lot of BioPlex[®] 2200 25-OH Vitamin D kit using the Master calibrators as reference. For each calibrator level except level 1, three vials are tested in replicates of five on three BioPlex 2200 analyzers for a total of 45 data points. The mean values obtained for each kit calibrator level are verified and must fall within specified acceptable range.

Two levels of the BioPlex 2200 25-OH Vitamin D control set are prepared from a pool of native human serum specimens. For each control level, three vials are tested in replicates of five using each of the kit lots on three BioPlex 2200 analyzers for a total of 45 replicates per reagent lot. The total number of replicates for each control level is 90 when two reagent lots are used and 135 when three reagent lots are used. For each control level, the mean values were derived from replicate analyses and should fall within the corresponding deviation.

The manufacturing target values of the Calibrator and Control Sets are listed below.

Calibrator Set	Target (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

Control Set	Target (ng/mL)	Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Stability:

Stability studies have been performed to support the following claims:

Calibrator and Control:

BioPlex® 2200 25-OH Control and Calibrator Sets: Calibrator Open Vial Stability (2 to 8°C), 30 days from first opening; Control Open Vial Stability (2 to 8°C), 60 days from first opening; Onboard Calibration Curve Stability, 30 days; Calibrators and Controls Real Time Stability (2 to 8°C), 24 months; labeled as until expiration date; Calibrators and Controls Accelerated Stability (2 to 8°C), 2 years predicted. Calibrators freeze-thaw (-20°C or -70°C), 5-freeze thaw cycles; Control freeze-thaw (-20°C or -70°C), 1-freezethaw cycle at -20°C and 5-freeze-thaw cycles at -70°C.

Kit Stability:

BioPlex® 2200 25-OH Vitamin D Kit: Real Time (unopened) Kit Stability, 9 months or until the date of expiration when stored unopened on the instrument or at 2 to 8°C; the open kit claim is 60 days.

Sample Stability:

Sample stability studies were also performed: Sample stability fresh (2 to 8°C), 7 days; Sample stability frozen (-20 or -70°C), 24 months; Sample Freeze-thaw (-20 or -70°C), up to 3-freeze thaw cycles at -20°C and 2-freeze thaw cycles at -

70°C acceptable.

d. *Detection limit:*

The study was conducted in accordance with CLSI EP17-A2 guideline for determining the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ).

Limit of Blank (LoB)

Five blank samples were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 4 replicates per day for 5 days yielding 100 data points per reagent lot.

A non-parametric statistical analysis at 95th percentile is used to calculate LoB.

Limit of Detection (LoD)

Six human samples with low level of 25-OH vitamin D in the range of 4 to 35 ng/mL were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 12 replicates per day for five days yielding 60 data points per sample per reagent lot. LoD is then calculated by the equation:

$LoD = LoB + c_p SD_{LoD}$ Where C_p is a multiplier to give the 95th percentile of a normal distribution and SD is from the linear regression of standard deviation versus 25-OH Vitamin D mean value.

Limit of Quantitation (LoQ)

The LoQ was evaluated based on the accuracy goal which was defined as precision $\leq 20\%$ CV. The %CV was calculated using the same measurement results of the 6 low level samples used for determining the LoD.

The results of LoB, LoD, and LoQ in ng/mL are summarized in the table below.

LoB	LoD	LoQ
0.8	2.5	6.5

e. *Analytical specificity:*

Interfering Substances:

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex® 2200 25-OH Vitamin D kit according to CLSI EP7-A2 guideline.

The effects of the test levels of potential interfering substances on the assay have been evaluated with samples containing 10 to 90 ng/mL Vitamin D. The percent difference between the mean value of each test substance and a corresponding control was calculated. No interference was observed with any of the substances

tested if the percent difference is $\leq 10\%$. The substances and the maximum levels of interfering substances tested are shown in the table below:

Substance	Concentration
Hemoglobin*	≤ 150 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 30 mg/dL
Triglycerides	≤ 400 mg/dL
Total Protein	≤ 12 g/dL
Cholesterol	≤ 500 mg/dL
Uric Acid	≤ 20 mg/dL
HAMA	≤ 100 ng/mL
Rheumatoid Factor	≤ 350 IU/mL
Ascorbic Acid	≤ 3 mg/dL

*Hemoglobin > 150 mg/dL may interfere. Do not use visibly hemolyzed samples.

Cross-Reactivity:

The study was conducted in accordance with CLSI EP17-A2 using 2 human serum pools at 25-hydroxyvitamin D concentrations of 20 and 35 ng/mL. Nine cross reactants at levels listed below were then spiked into the human serum pools. The spiked and non-spiked samples were then evaluated in replicates of five to calculate the cross reactivity as shown below.

$$\% \text{ Cross Reactivity} = (\text{spiked vitamin D} - \text{non-spiked vitamin D}) \div \text{Cross reactant concentration} \times 100\%$$

The results of each potential cross reactant are listed below.

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D2	30	103%
25-hydroxyvitamin D3	30	97%
Vitamin D2	1000	0.2%
Vitamin D3	1000	0.0%
1,25-dihydroxyvitamin D2	30	$>100\%$
1,25-dihydroxyvitamin D3	30	79%
3-epi 25-hydroxyvitamin D3	30	59%
24,25-dihydroxyvitamin D3	20	9%
Paricalcitol (Zemplar)*	24	$>100\%$

* Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex 2200 25-OH Vitamin D assay

High dose hook effect:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed following CLSI EP09-A2-IR guideline.

A total of 204 human samples spanning the entire measuring assay range were tested in singlicate on both the BioPlex 2200 25-OH Vitamin D kit and the predicate assay. Of the 204 samples, there were 185 unaltered samples and 19 samples spiked with 25-hydroxyvitamin D₃ to supplement the assay range. There are eight (8) samples with values lower or higher than the measuring range of the comparator method not including in the analysis. A total of 196 BioPlex 25-OH Vitamin D results were plotted using weighted Deming regression analysis for all samples spanning the measuring range of both assays. Results of the regression slope, intercept, and coefficient of correlation (r) are summarized in the table below:

Number of Results Analyzed	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r) (95%CI)	Test Range (ng/mL)
196	1.0039 (0.9365 to 1.0712)	-0.2256 (-2.4121 to 1.9608)	0.9553 (0.9412 to 0.9661)	BioPlex: 6.6 to 124.9 Comparator: 4.3 to 118.1

b. Matrix comparison:

Serum only

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical Specificity:

Not Applicable

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

Not Applicable

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:

The Expected Values study was conducted following CLSI C28-A3c guideline.

Two hundred and eighty-seven (287) samples from apparently healthy donors including 160 males ranging in age from 21 to 79 and 127 females ranging in age from 21 to 66 were collected from three regions (North, Central, and South) in the US in spring, summer and winter, including African Americans, Hispanics and Caucasians.

The 287 samples from apparently healthy donors met the following inclusion/exclusion criteria as follows and tested with the BioPlex 25-OH Vitamin D kit in singlicate.

- Age from 21 to 90
- Roughly 50% female and 50% male
- 20% from Northern. 20% from Central and 60% from Southern region
- 40% collected in Spring, 30% in Summer and 30% in Winter
- At least 30% African Americans and 30% Caucasians
- 90% not taking Vitamin D supplements and <30% of those taking Vitamin D supplements at or more than 1000 IU, but less than 2000 IU
- Normal TSH, PTH, and Total Calcium
- No family history of parathyroid or calcium regulatory disease. In addition, no personal history of kidney disease, GI disease, liver disease, and no bariatric surgery

The observed median, mean, and range between 2.5th to 97.5th percentile are summarized below

N	Mean	Median	2.5 th to 97.5 th Percentile
286*	29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

* One sample <6.5 ng/mL was excluded from the data analysis

Each laboratory should establish its own reference range pertinent to their specific patient populations.

Instrument Name:

The BioPlex 2200 System, software version 4.1 cleared in k130053

Conclusion:

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

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014



Product Code	Class	Regulation Device Classification	Regulion Number	Device Name	Date Created
JIS	2	Calibrator.	862.1150	CALIBRATOR , PRIMARY	1/1/1990
JJX	1	Quality control material (assayed and unassayed).	862.1660	SINGLE (SPECIFIED) ANALYTE CONTROLS (ASSAYED AND UNASSAYED)	2/19/1998
MRG	2	Vitamin D test system.	862.1825	SYSTEM, TEST, VITAMIN D	9/16/1996

CDRH Gen Docs (2)

Document / Type / Title / Manufacturer	Decision	Reviewer	Description
GEN1100548 / Network Signal OIVD Diasorin erroneous Vit D DIASORIN	Store for Future Access	Yung Chan	Trend MW5019608. Interference due to a protein affecting results of test resulting in clinically significant errors. 2/28/11
GEN1300649 / OIR OC Complaints OIR/Trade/Critical Diagnostics/Presage ST2 ALL	Issue Resolved	Ana Maldonado	A trade complaint was received on November 1, 2013 providing information about Presage ST2 assay and Aspect-LF kits unlawful promotional and marketing claims being made by Critical Diagnostics. We were also provided with details about misguiding information that appears on the website of Critical Diagnostics. (www.criticaldiagnostics.com). We also received recent press releases and a special edition of the company's own Heart Failure Today magazine, used by the firm to support off-labels uses of the ST2 assay, outside the 510(k) cleared indications for use, and to assert superiority claims that lacks adequate substantiation. Two follow-up supplements were received on January 7 and April 08, 2014, containing additional information about Critical Diagnostics marketing practices.

Premarket Reviews (120)

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
AALTO SCIENTIFIC LTD.	JJX	510(k)	3	3			
AALTO SCIENTIFIC LTD.	JJX,OYG	510(k)	1	1			
ABBOTT DIAGNOSTICS INTERNATIONAL, LTD.	JJX,KHP	510(k)	1	1			
ABBOTT GMBH & CO. KG	JIS,LOL,MJX,MJY	510(k)	1	1			
ABBOTT IRELAND DIAGNOSTICS DIVISION	CDD,JIT,JJX	510(k)	1	1			
ABBOTT LABORATORIES	CDD,JIT,JJX	510(k)	1	1			
ABBOTT LABORATORIES	CDZ,JIT,JJX	510(k)	1	1			
ABBOTT LABORATORIES	CEC,JIT,JJX	510(k)	1	1			
ABBOTT LABORATORIES	JIT,JJX,MMI	510(k)	1				1
ABBOTT VASCULAR	JJX,KHP	510(k)	1	1			
ACON BIOTECH (HANGZHOU) CO., LTD.	CGA,JJX,NBW	510(k)	3	2			1
ACON BIOTECH (HANGZHOU) CO., LTD.	GKR,JJX	510(k)	1	1			
ACON BIOTECH (HANGZHOU) CO., LTD.	JJX,LFM,NBW	510(k)	1	1			
ACON LABORATORIES, INC.	CGA,FMK,JJX,NBW	510(k)	1				1

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
ACON LABORATORIES, INC.	CGA,JJX,NBW	510(k)	3	2		1	
ACTHERM, INC.	CGA,JJX,KNK,NBW,NFX	510(k)	1			1	
ACTHERM, INC.	CHH,JJX,KNK,LFR,NBW	510(k)	1			1	
ALERE SAN DIEGO INC. DBA BIOSITE,INNOVACON,HEMOSEN	DHA,JJX	510(k)	1			1	
ALPCO DIAGNOSTICS	JIS,JJX,MRG	510(k)	3			3	
AML MEDICAL DEVICES LIMITED	CGA,JJX,JQP,NBW	510(k)	1	1			
ANDON HEALTH CO., LTD	CGA,JJX,JQP,NBW	510(k)	1	1			
ANDON HEALTH CO.,LTD	CGA,JJX,NBW	510(k)	1	1			
ANDON MEDICAL CO., LTD.	CGA,JJX,JQP,NBW	510(k)	1	1			
ANDON MEDICAL CO., LTD.	CGA,JJX,NBW	510(k)	3	3			
APEX BIOTECHNOLOGY CORP.	CGA,JJX,JQP,NBW	510(k)	1	1			
APEX BIOTECHNOLOGY CORP.	CGA,JJX,NBW	510(k)	6	6			
APEX BIOTECHNOLOGY CORP.	JJX,LFR,NBW	510(k)	1			1	
AXIS-SHIELD DIAGNOSTICS, LTD.	CDD,JIT,JJX	510(k)	1	1			
AXIS-SHIELD POC AS	DCK,JFY,JIR,JJX,JJY,JQT,LCP	510(k)	1	1			
BECKMAN COULTER, INC.	JIT,MRG	510(k)	1			1	
BECKMAN COULTER, INC.	JJX	510(k)	1	1			
BECKMAN COULTER, INC.	MRG	510(k)	1			1	
BIOCARE CORPORATION	CGA,JJX,NBW	510(k)	1	1			
BIOCHECK, INC.	JJX,OYG	510(k)	1	1			
BIOKIT S.A.	JIT,JJX	510(k)	1	1			
BIOKIT S.A.	JIT,JJX,MRG	510(k)	2	2			
BIONIME CORPORATION	JJX	510(k)	1	1			
BIONIME CORPORATION	JJX,LFR,NBW	510(k)	2	2			
BIONOSTICS, INC.	CGA,JJX,NBW	510(k)	1				1
BIONOSTICS, INC.	JJX	510(k)	7	7			
BIONOSTICS, INC.	JJX,LFR,NBW	510(k)	3	2		1	
BIOPORTO DIAGNOSTICS A/S	JFY,JIT,JJX,ORN	510(k)	1			1	
BIO-RAD, DIAGNOSTICS GRP.	JJX	510(k)	1	1			
BIO-RAD LABORATORIES	JIX,JJX,MID,MSV	510(k)	2	2			
BIO-RAD LABORATORIES, INC.	JIX,JJX,MST,MVM	510(k)	1	1			
BIOTEST MEDICAL CORP.	CGA,JJX,NBW	510(k)	3	3			

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
BODITECH MED INC.	JJX,OOX	510(k)	1	1			
BROADMASTER BIOTECH CORPERATION	CGA,JJX,NBW	510(k)	1	1			
BROADMASTER BIOTECH CORPORATION	CGA,JJX,NBW	510(k)	2	1			1
CERAGEM MEDISYS INC.	CGA,JJX,NBW	510(k)	1	1			
CERAGEM MEDISYS INC.	JJX,JQP,LFR,NBW	510(k)	1	1			
CLINICAL INNOVATIONS, LLC	JJX,NQM	510(k)	1	1			
CLINIQA CORPORATION	JJX	510(k)	1	1			
CONE BIOPRODUCTS	JJX	510(k)	1	1			
DELBIO INCORPORATION	CGA,JJX,JQP,NBW	510(k)	1	1			
DELBIO INCORPORATION	CGA,JJX,NBW	510(k)	4	4			
DELBIO INCORPORATION	JJX,LFR,NBW	510(k)	1			1	
DENKA SEIKEN CO., LTD (KAGAMIDA FACILITY)	JFY,JIT,JJX,ORN	510(k)	1			1	
DIAGNOSTICA STAGO	GGN,JIS,KFF	510(k)	1	1			
DIASORIN INC.	CJM,JJX	510(k)	1	1			
DIASORIN INC.	JJX,MRG	510(k)	2	2			
DIASORIN INC.	MRG	510(k)	1	1			
DIASORIN, INC.	CDZ,JJX	510(k)	1	1			
DIASORIN, INC.	CEC,JJX	510(k)	1	1			
DIASORIN, INC.	CEW,JJX	510(k)	1	1			
DIASORIN, INC.	CIB,JJX	510(k)	1	1			
DIASORIN, INC.	JJX,LFX	510(k)	1	1			
DIASORIN S.P.A.	JJX,JLW	510(k)	1	1			
DIASOURCE IMMUNOASSAYS, S.A.	MRG	510(k)	1	1			
DIAZYME LABORATORIES	DCK,JIT,JJX	510(k)	1	1			
DIAZYME LABORATORIES	DCK,JJX	510(k)	1	1			
DIAZYME LABORATORIES	DDR,JIT,JJX	510(k)	1	1			
DIAZYME LABORATORIES	JIS,JJX,MRG	510(k)	3	3			
DIAZYME LABORATORIES	JIT,JJX	510(k)	1	1			
DIAZYME LABORATORIES	JIT,JJX,LCP	510(k)	1	1			
DIAZYME LABORATORIES	JJX,MRG	510(k)	4	4			
DIAZYME LABORATORIES	JJX,NDY	510(k)	1	1			
DREW SCIENTIFIC, INC.	JIT,JJE,JJX,LCP	510(k)	1			1	
ELITECHGROUP	JIT,JJX	510(k)	1	1			
EPS BIO TECHNOLOGY CORP.	JJX,LFR,NBW	510(k)	5	5			

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
EUROIMMUN US	MRG	510(k)	1	1			
FLEXTRONICS INDUSTRIAL (SHENZHEN) COMPANY LIMITD	JJX,LFR,NBW	510(k)	1	1			
FLEXTRONICS INDUSTRIAL (SHENZHEN) COMPANY LTD	CGA,JJX,NBW	510(k)	1				1
FUJIFILM TECHNO PRODUCTS CO., LTD.	JIT,JJX,NSF,OAU,OUE	510(k)	1	1			
FUJIREBIO DIAGNOSTICS, INC	JJX	510(k)	3	3			
FUJIREBIO DIAGNOSTICS, INC.	JJX	510(k)	2	2			
GENERAL LIFE BIOTECHNOLOGY CO., LTD.	CGA,JJX,NBW	510(k)	1	1			
GONOTEC	JFS,JJX	510(k)	1	1			
HEALTH & LIFE CO., LTD.	CGA,JJX,NBW	510(k)	1	1			
HEALTH & LIFE (SUZHOU) CO., LTD.	CGA,JJX,NBW	510(k)	1	1			
HMD BIOMEDICAL, INC.	CGA,JJX,NBW	510(k)	2			2	
HMD BIOMEDICAL, INC.	JJX,JQP,LFR,NBW	510(k)	1				1
HMD BIOMEDICAL, INC.	JJX,LFR	510(k)	1	1			
HMD BIOMEDICAL, INC.	JJX,LFR,NBW	510(k)	2	2			
IMMUNODIAGNOSTIC SYSTEMS LTD.	CEW,JIT,JJX	510(k)	1	1			
IMMUNODIAGNOSTIC SYSTEMS LTD.	JJX	510(k)	4	4			
IMMUNODIAGNOSTIC SYSTEMS LTD.	JJX,MRG	510(k)	4	2			2
INFOPIA CO., LTD	CGA,CHH,JGY,JJX,LB R,NBW	510(k)	1	1			
INFOPIA CO., LTD	CGA,JJX,NBW	510(k)	5	4		1	
INFOPIA CO., LTD	JJX,JQP,LFR,NBW	510(k)	1	1			
INFOPIA CO., LTD	JJX,LFR,NBW	510(k)	2	2			
INOVA DIAGNOSTICS, INC.	JIT,JJX,LKO,LKP	510(k)	1	1			
INOVA DIAGNOSTICS, INC.	JIX,JJX,LJM	510(k)	1	1			
INOVA DIAGNOSTICS, INC.	JIX,JJX,LLL	510(k)	1	1			
INOVA DIAGNOSTICS, INC.	JIX,JJX,LSW	510(k)	1				1
INOVA DIAGNOSTICS, INC.	JIX,JJX,MOB,MVJ	510(k)	1	1			
INOVA DIAGNOSTICS, INC.	JIX,JJX,MST	510(k)	2	2			
INOVA DIAGNOSTICS, INC.	JIX,JJX,MVM	510(k)	1	1			
INOVA DIAGNOSTICS, INC.	JJX,MID,MSV	510(k)	1	1			
INTEGRA BIOTECHNICAL LLC.	JJX,PFQ	510(k)	1	1			
I-SENS, INC.	CGA,JJX,JQP,NBW	510(k)	1	1			

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
I-SENS, INC.	CGA,JJX,NBW	510(k)	8	6		2	
LIFESCAN PRODUCTS LLC	CGA,JJX,NBW	510(k)	1				1
LIFESCAN SCOTLAND LTD	JJX,LFR,NBW	510(k)	1	1			
LIFESCAN SCOTLAND LTD.	CGA,JJX,NBW	510(k)	1				1
MAINE STANDARDS CO.	JJX	510(k)	2	2			
MAINE STANDARDS COMPANY LLC	JJX	510(k)	1	1			
MAJOR BIOSYSTEM CORPORATION	CGA,JJX,NBW	510(k)	2	2			
MAJOR BIOSYSTEM CORPORATION	JJX,LFR,NBW	510(k)	1				1
MEDICA CORP.	JIT,JJX,LCP	510(k)	1	1			
MEDICA CORPORATION	DCK,JHY,JIT,JJX	510(k)	1				1
MICROBIOMED CO, LTD	CGA,JJX,NBW	510(k)	2	2			
NIPRO DIAGNOSTICS, INC.	JJX,LFR,NBW	510(k)	2	1		1	
NIPRO DIAGNOSTICS TAIWAN, INC.	JJX,LFR,NBW	510(k)	2	1		1	
NOVA BIOMEDICAL CORP.	JJX,KHP	510(k)	1	1			
NOVA BIOMEDICAL CORPORATION	CGA,JIN,JJX,NBW	510(k)	1			1	
NOVA BIOMEDICAL CORPORATION	JJX,KHP	510(k)	1	1			
NOVA BIOMEDICAL CORPORATION	JJX,LFR,NBW	510(k)	3	3			
NOVA BIOMEDICAL CORPORATION DIABETES PRODUCTS	CGA,JIN,JJX,NBW	510(k)	1			1	
OK BIOTECH CO., LTD.	CGA,JJX,NBW	510(k)	1			1	
ORTHO-CLINICAL DIAGNOSTICS	JJX	510(k)	1			1	
ORTHO-CLINICAL DIAGNOSTICS, INC.	JIT,MRG	510(k)	1	1			
ORTHO-CLINICAL DIAGNOSTICS, INC.	JJX,LPS	510(k)	1	1			
PANASONIC HEALTH CARE CO. LTD	JJX,LFR,NBW	510(k)	1	1			
PANASONIC SHIKOKU ELECTRONICS CO., LTD.	JJX,LFR,NBW	510(k)	2	2			
PHADIA AB	DGC,JJX	510(k)	1	1			
PHILOSYS CO. LTD	CGA,JJX,NBW	510(k)	1	1			
QUALIGEN, INC.	JIT,JJX,MRG	510(k)	2	2			
QUANTIMETRIX CORP.	JJX	510(k)	2	2			
R3DSTAR BIOMEDICAL CORPORATION	CGA,JJX,NBW	510(k)	1			1	
RANDOX LABORATORIES LIMITED	JIS	510(k)	1	1			
RANDOX LABORATORIES, LTD.	JIT,JJX,LDJ	510(k)	1	1			
RANDOX LABORATORIES, LTD.	JJX	510(k)	4	4			
ROCHDIAG	JJX,LFR,NBW	510(k)	1	1			

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
ROCHE DIAGNOSTICS	CGN,JIT,JJX	510(k)	1	1			
ROCHE DIAGNOSTICS	JIT,JJX,JJY,MRG	510(k)	2	2			
ROCHE DIAGNOSTICS	JIT,JJX,OIU	510(k)	1	1			
ROCHE DIAGNOSTICS	JJX	510(k)	7	7			
ROCHE DIAGNOSTICS	JJX,LFR,NBW	510(k)	1	1			
ROCHE DIAGNOSTICS	JJX,LFZ	510(k)	1	1			
ROCHE DIAGNOSTICS CORPORATION	JJX	510(k)	1	1			
ROCHE DIAGNOSTICS GMBH	DFC,JIT,JJX	510(k)	1	1			
ROCHE DIAGNOSTICS GMBH	JIT,JJX,JJY,MRG	510(k)	2	2			
ROCHE DIAGNOSTICS GMBH	JIT,JJX,OIU	510(k)	1	1			
ROCHE DIAGNOSTICS GMBH	JJX	510(k)	4	4			
ROCHE DIAGNOSTICS GMBH	JJX,LFZ	510(k)	1	1			
ROCHE DIAGNOSTICS GMBH	JJX,MXJ	510(k)	1	1			
ROCHE DIAGNOSTICS GMBH	JJX,MYF	510(k)	1	1			
ROCHE DIAGNOSTICS OPERATIONS	JJX	510(k)	1	1			
ROCHE DIAGNOSTICS OPERATIONS	JJX,MXJ	510(k)	1	1			
ROCHE DIAGNOSTICS OPERATIONS	JJX,MYF	510(k)	1	1			
ROCHE DIAGNOSTICS OPERATIONS INC	DFC,JIT,JJX	510(k)	1	1			
ROCHE DIAGNOSTICS OPERATIONS INC	JJX	510(k)	2	2			
RR DONNELLEY-GLOBAL TURNKEY SOLUTIONS	JJX,LFR,NBW	510(k)	3	3			
SD BIOSENSOR	CGA,JJX,NBW	510(k)	1	1			
SEBIA	JIS,JJX,LCP	510(k)	4	4			
SEKISUI MEDICAL CO., LTD.	JIT,JJX,LCP,PDJ	510(k)	1	1			
SEPPIM S.A.S.	JIT,JJX,LCP	510(k)	1	1			
SIEMENS HEALTHCARE DIAGNOSTICS	DAP,JIT,JJX	510(k)	1			1	
SIEMENS HEALTHCARE DIAGNOSTICS	JIT,JJX	510(k)	1	1			
SIEMENS HEALTHCARE DIAGNOSTICS	JJX	510(k)	2	2			
SIEMENS HEALTHCARE DIAGNOSTICS	JJX,LCP	510(k)	1	1			
SIEMENS HEALTHCARE DIAGNOSTICS INC.	JIS,JJX,MRG	510(k)	6	3			3
SIEMENS HEALTHCARE DIAGNOSTICS INC.	JJX	510(k)	1	1			
SIEMENS HEALTHCARE DIAGNOSTICS, INC.	JJX	510(k)	1	1			
SIEMENS HEALTHCARE DIAGNOSTICS PRODUCTS, LTD	JJX	510(k)	7	6			1

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

Manufacturer	Product Code	Type	Total	Approved	Denied	Other	Pending
SIEMENS HEALTHCARE DIAGNOSTICS PRODUCTS, LTD.	JJX	510(k)	1	1			
SIEMENS HELATHCARE DIAGNOSTICS PRODUCTS, LTD	JJX	510(k)	1	1			
SIEMENS MEDICAL SOLUTIONS DIAGNOSTICS	JJX	510(k)	1	1			
SIEMENS MEDICAL SOLUTIONS DIAGNOSTICS LIMITED	JJX	510(k)	3	3			
SIMPLE DIAGNOSTICS, INC.	CGA,JJX,NBW	510(k)	1	1			
STAT MEDICAL DEVICES, INC.	CGA,JJX,JQP,NBW	510(k)	1	1			
STERIGENICS, US, INC.	JJX,KHP	510(k)	1	1			
STERIS ISOMEDIX SERVICES	JJX,PFQ	510(k)	1	1			
TAIDOC TECHNOLOGY CORPORATION	CGA,JJX,NBW	510(k)	1	1			
TAIDOC TECHNOLOGY CORPORATION	JJX,LFR,NBW	510(k)	2	2			
TELCARE, INC.	CGA,JJX,JQP,NBW	510(k)	1	1			
TIANJIN EMPECS MEDICAL DEVICE CO., LTD.	CGA,JJX,NBW	510(k)	2	1			1
TOSOH BIOSCIENCE, INC.	CKG,JIT,JJX	510(k)	1	1			
TOSOH BIOSCIENCE, INC.	JIT,JJX,LPS	510(k)	1	1			
TOSOH BIOSCIENCE, INC.	JIT,JJX,MRG	510(k)	2	2			
TYSON BIORESEARCH, INC.	CGA,JJX,NBW	510(k)	1	1			
TYSON BIORESEARCH, INC.	JJX,LFR,NBW	510(k)	2	1		1	
VISGENEER, INC.	CGA,JJX,NBW	510(k)	1	1			
WAKO CHEMICALS USA, INC.	JIT,JJX,NSF,OUA,OUE	510(k)	1	1			
WAKO PURE CHEMICAL INDUSTRIES, LTD.	JIT,JJX,NSF,OUA,OUE	510(k)	1	1			

Standards and Guidance (2)

Reference Number	Title	Contact	Relevant Guidance
C24-A3	Statistical Quality Control for Quantitative Measurements Procedures	Lili Duan	<p>Points to Consider for Collection of Data in Support of In Vitro Device Submission for 510(k) Clearance</p> <p>Guidance for Industry and FDA Staff - Assayed and Unassayed Quality Control Material</p> <p>Points to Consider for Review of Calibration and Quality Control Labeling for In Vitro Diagnostic Devices/Cover Letter dated 3/14/1996</p> <p>Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Quality Control Material for Cystic Fibrosis Nucleic Acid Assays</p>

Reference Number	Title	Contact	Relevant Guidance
C39-A	A Designated Comparison Method for the Measurement of Ionized Calcium in Serum; Approved Standard (2000) ISBN1-56238-398-1	Meshaun Payne	Points to consider for collection of data in support of in-vitro device submissions for 510(k), clearing guidance for industry - abbreviated 510(k) submissions for in vitro diagnostic calibrators

MDR Summary (235)

	2011	2012	2013	2014	Total
INJURY	1	4	5	2	12
MALFUNCTION	13	110	68	23	214
INVALID DATA		2			2
OTHER	1	5			6
			1	2	3
Total	15	119	74	27	235

MDR distribution by Product Code (235)

	Product Code	2011	2012	2013	2014	Total
INJURY	JJX	1	4	4	2	11
INJURY	MRG			1		1
MALFUNCTION	JIS	2	9	1		12
MALFUNCTION	JJX	11	87	40	21	159
MALFUNCTION	MRG	1	15	27	2	45
INVALID DATA	JJX		2			2
OTHER	JJX	1	5			6
	JJX			1	2	3
Total		15	119	74	27	235

MDR distribution by manufacturer - Death or Injury (5)

Manufacturer	Total
BAYER HEALTHCARE, LLC	7
ORTHO-CLINICAL DIAGNOSTICS, INC.	2
HAEMONETICS CORP.	1
ORTHOCLINICAL DIAGNOSTICS	1
TOSOH BIOSCIENCE, INC.	1

Patient Problems (13)

Patient Problems	Total
No known impact or consequence to patient	182
No Consequences Or Impact To Patient	31
No Information	10
Chemical Exposure	5
Test Result	3
Cross-patient exposure to body fluids	2
Blood loss	1
Injury	1
No Patient Involvement	1
Reaction	1
Venipuncture	1

Patient Problems	Total
Vision, Impaired	1
	1

Device Problems (62)

	INJURY	MALFUNCTION	INVALID DATA	OTHER	
Break		17			
Burn of device or device component		2			
Burst		1			
Calibration error		2			
Calibration issue		5		1	
Calibrator		2			
Cap		4			
Chemical spillage	1				
Component missing		1			
Contamination of device ingredient or reagent		2			
Cover		1			
Cut in material		4			
Data Issue		1			
Device alarm system Issue		1			
Device Contamination with biological material		2			
Device contamination with blood or blood product		1			
Device damaged prior to use		4			
Device displays error message		1		1	
Device Ingredient or Reagent		1			
Device operates differently than expected	2	20			
Device packaging compromised		2			
Electrical shorting		3			
False reading from device non-compliance		1			
Filter		1			
Fire		1			
Fluid leak	1	21			
High test results		64		1	1
Human-Device Interface Issue	1				
Image display error		1			
Improper or incorrect procedure or method	6	2		1	
Incorrect display		16			
Incorrect or inadequate result		6			
Incorrect or inadequate test results		37	2	3	1
Item contaminated during manufacturing or shipping		1			
Leak		13			

	Total
Break	17
Burn of device or device component	2
Burst	1
Calibration error	2
Calibration issue	6
Calibrator	2
Cap	4
Chemical spillage	1
Component missing	1
Contamination of device ingredient or reagent	2
Cover	1
Cut in material	4
Data Issue	1
Device alarm system issue	1
Device Contamination with biological material	2
Device contamination with blood or blood product	1
Device damaged prior to use	4
Device displays error message	2
Device Ingredient or Reagent	1
Device operates differently than expected	22
Device packaging compromised	2
Electrical shorting	3
False reading from device non-compliance	1
Filter	1
Fire	1
Fluid leak	22
High test results	66
Human-Device Interface Issue	1
Image display error	1
Improper or incorrect procedure or method	9
Incorrect display	16
Incorrect or inadequate result	6
Incorrect or inadequate test results	43
Item contaminated during manufacturing or shipping	1
Leak	13

TPLC Product Code Combined View

from 1/01/2011 to 5/13/2014

	INJURY	MALFUNCTION	INVALID DATA	OTHER	
Loose or intermittent connection		3			
Loss of power		1			
Low test results	1	14		1	
Material frayed		8			
Naturally worn		1			
No code available		1			
No display or display failure		3			
Noise, Audible		2			
No Known Device Problem		1			
Nonstandard device or device component		2			
Output above specifications		2			
Packaging issue		1			
Patient-device incompatibility	1				
Poor quality image		1			
Power cord		17			
Power module		2			
Power supply		2			
Reflux within device		1			
Sensor		1			
Shipping damage or problem		1			
Slippage of device or device component		1			
Smoking		6			
Spark		4			
Switches		1			
Unexpected therapeutic results					1
Use of Incorrect Control Settings		1			
		3			
Total	13	321	2	8	3

Recalls (12)

		Class II	Class III	Total
ABBOTT GMBH & CO. KG	Product Code	1		1
BECKMAN COULTER, INC.	Product Code	4		4
BIOKIT SA	Product Code	1		1
IDS (IMMUNODIAGNOSTIC SYSTEMS LTD)	Product Code	1		1
LIFESCAN INC	Product Code	2		2
MICROGENICS CORPORATION	Product Code	1		1
QUALIGEN INC	Product Code	1		1
SIEMENS HEALTHCARE DIAGNOSTICS	Product Code	1		1
SIEMENS HEALTHCARE DIAGNOSTICS,	Product Code	4	1	5
SIEMENS HEALTHCARE DIAGNOSTICS,	Product Code		1	1
Total	#MULTIVALUE	16	2	18

	Total
Loose or intermittent connection	3
Loss of power	1
Low test results	16
Material frayed	8
Naturally worn	1
No code available	1
No display or display failure	3
Noise, Audible	2
No Known Device Problem	1
Nonstandard device or device component	2
Output above specifications	2
Packaging issue	1
Patient-device incompatibility	1
Poor quality image	1
Power cord	17
Power module	2
Power supply	2
Reflux within device	1
Sensor	1
Shipping damage or problem	1
Slippage of device or device component	1
Smoking	6
Spark	4
Switches	1
Unexpected therapeutic results	1
Use of Incorrect Control Settings	1
	3
Total	347

Inspections and EIRs (6 manufacturers)

Manufacturer	Product Code	Inspections		EIRs			
BIOKIT, S.A.	JJX	1	0	1	0	1	0
CAMBRIDGE SENSORS LIMITED	JJX	1	0	1	0	1	0
EPS BIO TECHNOLOGY CORP.	JJX	1	0	1	0	1	0
IMMUNODIAGNOSTICS SYSTEMS LTD	MRG	0	0	1	0	1	0
IMMUNODIAGNOSTIC SYSTEMS SA	MRG	1	0	1	0	0	1
		4	0	5	0	4	1

Rad Health Reports (None)

Rad Health Correspondence (None)

Rad Health Adverse Events (None)

Rad Health EIRs (None)

TPLC disclaimers

We are continuing to improve and enhance the TPLC Universe and the TPLC sheets. When more data is available we will update this message.

Please realize that in this initial release:

- Recall data is only available since October, 2009.
- In the Premarket Under Review section and the Recall section, the premarket submission or recall is only included if the product code is specified in CTS.
- The MDR count is a count of reports and contains duplicate reports.
- MDR track action or additional information letters is not available yet.
- EIR data related to inspections is not yet displayed.
- The TPLC name which consolidates variations on manufacturer names is not yet implemented.
- Publications are not yet linked in.

We are working hard to address these issues and many can be addressed before the next release.

assay. You provided the results for all (b)(4)

(b)(4)

as

presented on page 7 of the 510(k) Summary.

5. 510 (k) Summary

(b)(4)

6. Please add to your (b)(4)

(b)(4)

7. Please provide any updated/revised documents as needed to address the above issues including a revised 510 (k) Summary and labeling

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device.

Please feel free to contact me if you have any questions or concerns.

Thank you,

Sheila A. Connors -S

Sheila Connors

Scientific Reviewer

FDA/CDRH/OIR/DCTD

sheila.connors@fda.hhs.gov

301-796-6181

Yung W. Chan -S

Yung Chan

Chemistry Branch Chief

FDA/CDRH/OIR/DCTD

statement (b)(4) in the 510 (k) summary and in the BioPlex 2200 System 25-OH Vitamin D Instruction for use (package insert).

- c. Your cross reactivity studies indicate the (b)(4) (b)(4) cross react and interfere with the Vitamin D assay.” in the 510 (k) Summary and the package insert.
- d. In the provided “Intended for Use” for the BioPlex 2200 25-OH Vitamin D kit, you state that the kit is for the quantitative determination of 25-hydroxyvitamin D in human serum. If you are not claiming the use of (b)(4) (b)(4) study chart in the 510 (k) Summary and the package insert. The appearance may (b)(4) (b)(4) be acceptable for use with the BioPlex 2200 25-OH vitamin D assay.

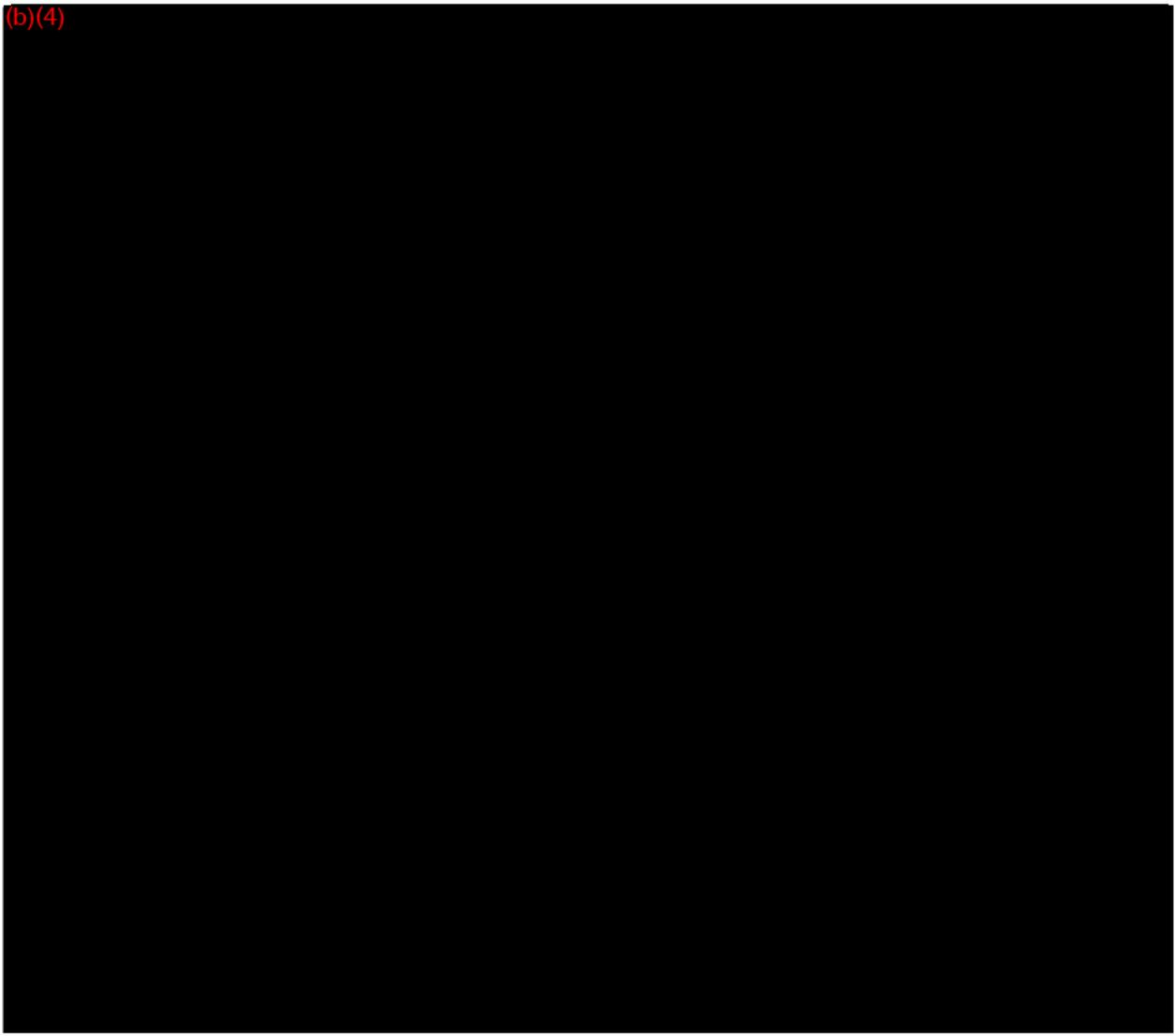
4. Proposed Labeling

You provided BioPlex 2200 System 25-OH Vitamin D Instruction For Use (package insert).

(b)(4)

2. Traceability, Stability, Expected Values

(b)(4)

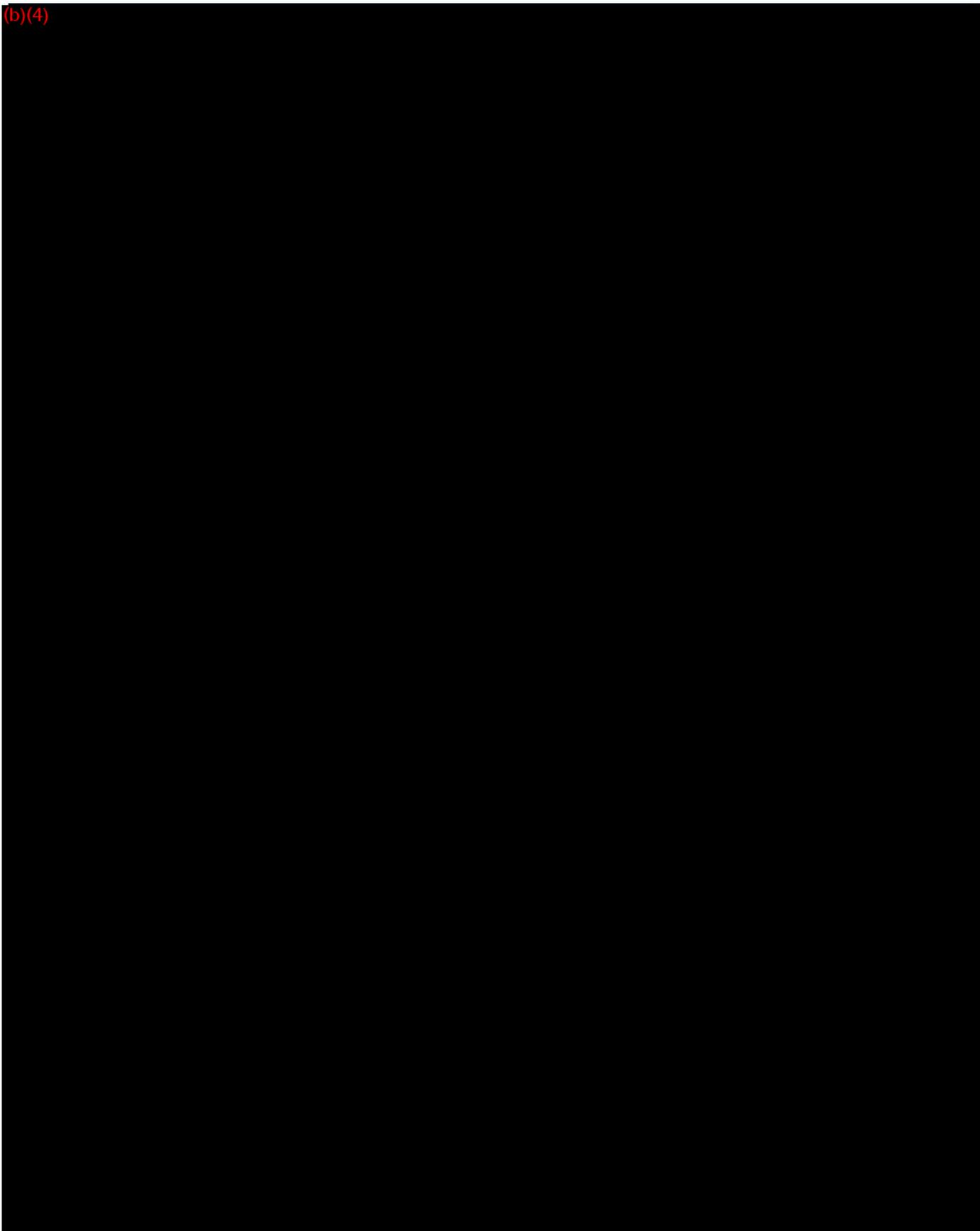


3. Interference / Cross Reactivity

(b)(4)



(b)(4)



Juang Wang
Regulatory Affairs Representative
Bio-Rad Laboratories
Clinical Immunology Division
5500 E. 2nd Street Benicia, CA, 94510, US

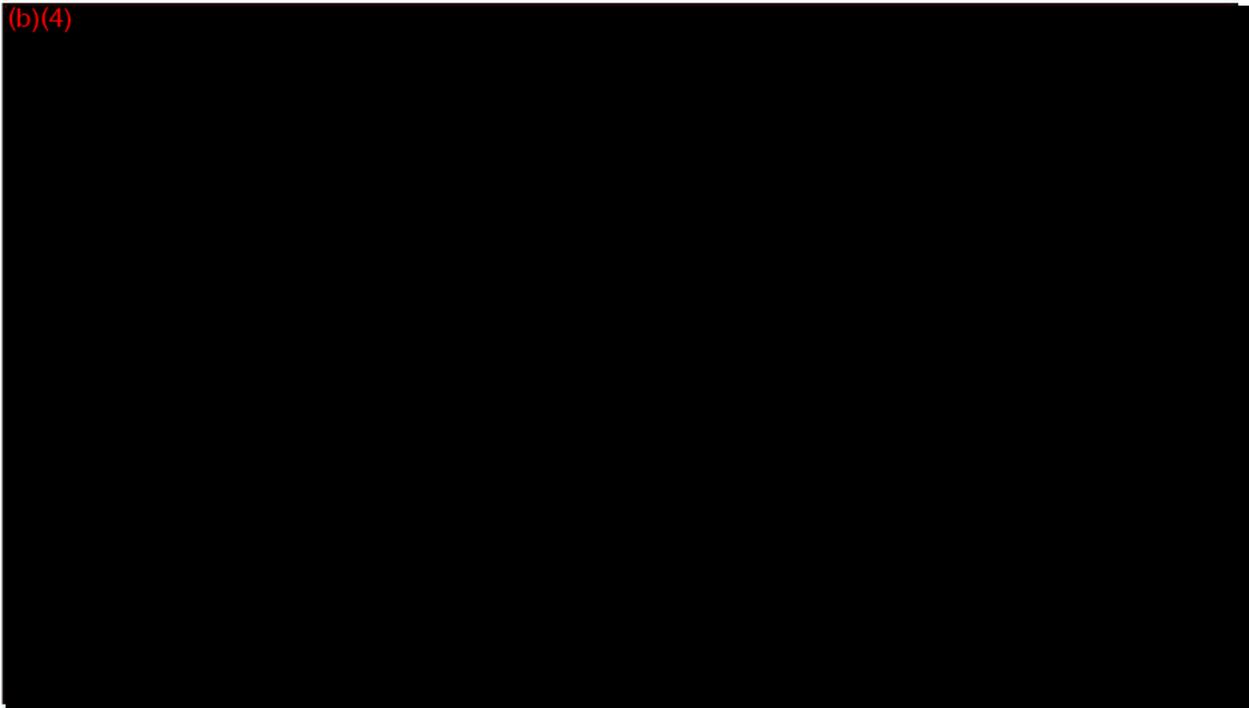
Re: k141114
Bio-Rad Laboratories
Device name: BioPlex 2200 25 OH Vitamin D assay
Dated: April 29, 2014
Received: April 30, 2014

Dear Dr. Wang:

We have reviewed your Section 510(k) notification of intent to market the device referenced above. We cannot determine if the device is equivalent to a legally marketed predicate device based solely on the information you provided. Therefore, we are placing you on telephone hold. To complete the review of your submission, please address the follow concerns.

1. Method comparison

(b)(4)



Decision: Accept Refuse to Accept

If Accept, notify applicant.

If Refuse to Accept, notify applicant in writing and include a copy of this checklist.

Digital Signature Concurrence Table

Reviewer Sign-Off	Sheila A. Connors -S 2014.05.13 12:55:39 -04'00'
Branch Chief Sign-Off (digital signature optional)*	Yung W. Chan -S 2014.05.13 16:20:51 -04'00'
Division Sign-Off (digital signature optional)*	

* Branch and Division review of checklist and concurrence with decision required.
Branch and Division digital signature optional.

Elements of a Complete Submission (RTA Items)

(21 CFR 807.87 unless otherwise indicated)

Submission should be designated RTA if not addressed.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.

- Any "No" answer will result in a "Refuse to Accept" decision. - Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.	Yes	No	N/A	Comment
b) Accuracy(includes as appropriate linearity; calibrator or assay traceability; calibrator and/or assay stability protocol and acceptance criteria; assay cut-off; method comparison or comparison to clinical outcome; matrix comparison; and clinical reference range or cutoff.	✗	<input type="checkbox"/>	<input type="checkbox"/>	
c) Sensitivity (detection limits, LoB, LoD, LoQ where relevant for the device type).	✗	<input type="checkbox"/>	<input type="checkbox"/>	
d) Analytical specificity	✗	<input type="checkbox"/>	<input type="checkbox"/>	
41)				<input type="checkbox"/>
a) If there are requirements regarding performance data, such as special controls, in a device-specific regulation that are applicable to the device, the submission includes performance data to establish that the submitter has followed the device-specific requirement.	<input type="checkbox"/>	<input type="checkbox"/>	✗	
b) If there is a device-specific guidance, other than a special controls guidance document, applicable to the device, the submission includes performance data to establish that the submitter has addressed the recommendations or otherwise has met the applicable statutory or regulatory criteria through an alternative approach.	<input type="checkbox"/>	<input type="checkbox"/>	✗	
c) If there is a special controls document applicable to the device, the submission includes performance data to establish that the submitter has complied with the particular mitigation measures set forth in the special controls document or uses alternative mitigation measures but provides a rationale to demonstrate that those alternative measures identified by the firm will provide at least an equivalent assurance of safety and effectiveness.	<input type="checkbox"/>	<input type="checkbox"/>	✗	

Elements of a Complete Submission (RTA Items)

(21 CFR 807.87 unless otherwise indicated)

Submission should be designated RTA if not addressed.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.

	Yes	No	N/A	Comment
- Any "No" answer will result in a "Refuse to Accept" decision. - Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.				

27) For sterile device, submission includes summary of methods used to establish that device will remain sterile through the proposed shelf life or a rationale for why testing to establish shelf life is not applicable.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
--	--------------------------	--------------------------	-------------------------------------	--------------------------

28) Submission includes summary of methods used to establish that device performance is not adversely affected by aging or includes a rationale for why the storage conditions are not expected to affect device safety or effectiveness.	<input checked="" type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>
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G. Biocompatibility

If IVD device, select "N/A" and the below criteria will be omitted from checklist.			<input checked="" type="checkbox"/>	<input type="checkbox"/>
--	--	--	-------------------------------------	--------------------------

H. Software

Submission states that the device: (one of the below must be checked)				<input type="checkbox"/>
---	--	--	--	--------------------------

does contain software/firmware.

does not contain software/firmware.

Information regarding whether the device contains software is not provided.

This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.

I. EMC and Electrical Safety

Submission states that the device: (one of the below must be checked)				<input type="checkbox"/>
---	--	--	--	--------------------------

does require EMC and Electrical Safety evaluation.

does not require EMC and Electrical Safety evaluation.

Information regarding whether the device requires EMC and Electrical Safety evaluation is not provided.

This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.

J. Performance Data - General

If IVD device, select "N/A" and the below criteria will be omitted from checklist. Performance data criteria relating to IVD devices will be addressed in Section K.			<input checked="" type="checkbox"/>	
--	--	--	-------------------------------------	--

K. Performance Characteristics - In Vitro Diagnostic Devices Only

(Also see [21 CFR 809.10\(b\)\(12\)](#))

Submission states that the device: (one of the below must be checked)				<input type="checkbox"/>
---	--	--	--	--------------------------

is an in vitro diagnostic device.

is not an in vitro diagnostic device.

40) Submission includes the following studies, as appropriate for the device type, including associated protocol descriptions, study results and line data:				<input type="checkbox"/>
---	--	--	--	--------------------------

a) Precision/reproducibility

Elements of a Complete Submission (RTA Items)

(21 CFR 807.87 unless otherwise indicated)

Submission should be designated RTA if not addressed.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.

- Any "No" answer will result in a "Refuse to Accept" decision.
 - Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.

	Yes	No	N/A	Comment
b) The identified predicate(s) is consistent throughout the submission (i.e., the predicate(s) identified in the Substantial Equivalence section is the same as that listed in the 510(k) Summary (if applicable) and that used in comparative performance testing.	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
15) Submission includes a comparison of the following for the predicate(s) and subject device				<input type="checkbox"/>
a) Indications for Use	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
b) Technology, including features, materials, and principles of operation	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
16) Submission includes an analysis of why any differences between the subject device and predicate(s) do not render the device NSE (e.g., does not constitute a new intended use; and any differences in technological characteristics are accompanied by information that demonstrates the device is as safe and effective as the predicate and do not raise different questions of safety and effectiveness than the predicate), affect safety or effectiveness, or raise different questions of safety and effectiveness (see section 513(i)(1)(A) of the FD&C Act and 21 CFR 807.87(f))	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

D. Proposed Labeling (see also 21 CFR part 801)

If *in vitro* diagnostic (IVD) device, criteria 17 & 19 may be omitted.

18) If indicated for prescription use, labeling includes the prescription use statement (see 21 CFR 801.109(b)(1)) or "Rx only" symbol [See also Alternative to Certain Prescription Device Labeling Requirements]	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
20)				<input type="checkbox"/>
a) If there are requirements regarding labeling, such as special controls, in a device-specific regulation that are applicable to the device, the submission includes labeling to establish that the submitter has followed the device-specific requirement.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
b) If there is a device-specific guidance, other than a special controls guidance document, applicable to the device, the submission includes labeling to establish that the submitter has addressed the recommendations or otherwise has met the applicable statutory or regulatory criteria through an alternative approach.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
c) If there is a special controls document applicable to the device, the submission includes labeling to establish that the submitter has complied with the particular mitigation measures set forth in the special controls document or uses alternative mitigation measures but provides a rationale to demonstrate that those alternative measures identified by the firm will provide at least an equivalent assurance of safety and effectiveness.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
21) If the device is an <i>in vitro</i> diagnostic device, provided labeling includes all applicable information required per 21 CFR 809.10 .	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

E. Sterilization

If IVD device and sterilization is not applicable, select "N/A" and criteria below will be omitted from checklist.

F. Shelf Life

26) Proposed shelf life/expiration date stated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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Elements of a Complete Submission (RTA Items)

(21 CFR 807.87 unless otherwise indicated)

Submission should be designated RTA if not addressed.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.

- Any "No" answer will result in a "Refuse to Accept" decision.
 - Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.

	Yes	No	N/A	Comment
a) If there were prior submissions, the submitter has identified where in the current submission any issues related to a determination of substantial equivalence outlined in prior communications are addressed. For additional information regarding the Pre-Submission process, please refer to the Draft Guidance " Medical Devices: The Pre-Submission Program and Meetings with FDA Staff. " Once finalized, this guidance will represent the Agency's current thinking on this topic.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

B. Device Description

10)				<input type="checkbox"/>
a) If there are requirements regarding the device description, such as special controls, in a device-specific regulation that are applicable to the device, the submission includes device description information to establish that the submitter has followed the device-specific requirement.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
b) If there is a device-specific guidance, other than a special controls guidance document, applicable to the device, the submission includes device description information to establish that the submitter has addressed the recommendations or otherwise has met the applicable statutory or regulatory criteria through an alternative approach.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
11) Descriptive information is present and consistent within the submission (e.g., the device description section is consistent with the device description in the labeling), including:				<input type="checkbox"/>
a) A description of the principle of operation and mechanism of action for achieving the intended effect.	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
b) A description of proposed conditions of use, such as surgical technique for implants; anatomical location of use; user interface; how the device interacts with other devices; and/or how the device interacts with the patient.	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
c) A list and description of each device for which clearance is requested.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12) Submission contains representative engineering drawing(s), schematics, illustrations and/or figures of the device that are clear, legible, labeled, and include dimensions.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
13) If device is intended to be marketed with multiple components, accessories, and/or as part of a system			<input type="checkbox"/>	<input type="checkbox"/>
a) Submission includes a list of all components and accessories to be marketed with the subject device.	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
b) Submission includes a description (as detailed in item 11(a) and (b) and 12 above) of each component or accessory.	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
c) A 510(k) number is provided for each component or accessory that received a prior 510(k) clearance.	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

C. Substantial Equivalence Discussion

14) Submitter has identified a predicate device.	<input checked="" type="checkbox"/>	<input type="checkbox"/>		<input type="checkbox"/>
a) Predicate's 510(k) number, trade name, and model number (if applicable) provided. For predicates that are preamendments devices, information is provided to document preamendments status. <i>Information regarding documenting preamendment status is available online.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

Elements of a Complete Submission (RTA Items)

(21 CFR 807.87 unless otherwise indicated)

Submission should be designated RTA if not addressed.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.

- Any "No" answer will result in a "Refuse to Accept" decision.
 - Each element on the checklist should be addressed within the submission. An applicant may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criteria is considered Present (Yes). An assessment of the rationale will be considered during the review of the submission.

Yes

No

N/A

Comment

A. Administrative

1) All content used to support the submission is written in English (including translations of test reports, literature articles, etc.)	✗	<input type="checkbox"/>		<input type="checkbox"/>
2) Submission identifies the following (such as in CDRH Premarket Review Submission Cover Sheet (Form 3514) or 510(k) cover letter):	✗	<input type="checkbox"/>		<input type="checkbox"/>
a) Device trade name or proprietary name	✗	<input type="checkbox"/>		
b) Device common name	✗	<input type="checkbox"/>		
c) Device class and panel or Classification regulation or Statement that device has not been classified with rationale for that conclusion	✗	<input type="checkbox"/>		
3) Submission contains Indications for Use Statement with Rx and/or OTC designation (see also 21 CFR 801.109).	✗	<input type="checkbox"/>		<input type="checkbox"/>
4) Submission contains 510(k) Summary or 510(k) Statement	✗	<input type="checkbox"/>		<input type="checkbox"/>
a) Summary contains all elements per 21 CFR 807.92 (See also 510(k) Summary Checklist)	✗	<input type="checkbox"/>	<input type="checkbox"/>	
b) Statement contains all elements per 21 CFR 807.93	✗	<input type="checkbox"/>	<input type="checkbox"/>	
5) Submission contains Truthful and Accuracy Statement per 21 CFR 807.87(k) See <i>recommended format</i> .	<input type="checkbox"/>	✗		✗
Comments? Will request a Truthful and Accuracy statement interactively from the sponsor.				
6) Submission contains Class III Summary and Certification. See <i>recommended content</i> .	<input type="checkbox"/>	<input type="checkbox"/>	✗	<input type="checkbox"/>
7) Submission contains clinical data	✗		<input type="checkbox"/>	<input type="checkbox"/>
a) Submission includes completed Financial Certification (Form 3454) or Disclosure (Form 3455) information for each covered clinical study included in the submission.	✗	<input type="checkbox"/>	<input type="checkbox"/>	
b) Submission includes completed Certification of Compliance with the requirements of ClinicalTrials.gov Data Bank (Form 3674) (42 U.S.C. 282(j)(5)(B)) for each applicable device clinical trial included in the submission.	✗	<input type="checkbox"/>	<input type="checkbox"/>	
8) If submission references use of a national or international standard as part of demonstration of substantial equivalence, submission contains Standards Data Report for 510(k)s (Form 3654) or includes detailed information about how and the extent to which the standard has been followed.	✗	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9) The submission identifies prior submissions for the same device for which FDA provided feedback related to the data or information needed to support substantial equivalence (e.g., submission numbers for Pre-Submission, IDE, prior not substantially equivalent (NSE) determination, prior 510(k) that was deleted or withdrawn) or states that there were no prior submissions for the subject device.	✗	<input type="checkbox"/>		<input type="checkbox"/>

Organizational Elements

Failure to include these items alone generally should not result in an RTA designation.

	Yes	No
1) Submission contains a Table of Contents	✕	<input type="checkbox"/>
2) Each section is labeled (e.g., headings or tabs designating Device Description section, Labeling section, etc.)	✕	<input type="checkbox"/>
3) All pages of the submission are numbered.	✕	<input type="checkbox"/>
4) Type of 510(k) is identified (i.e., traditional, abbreviated, or special)	✕	<input type="checkbox"/>
Comments?		

<p>5) Is there a pending PMA for the same device with the same indications for use?</p> <p>If yes, consult division management and the CDRH 510(k) Program Director or appropriate CBER staff to determine the appropriate action.</p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<p>Comments? <input style="width: 100%;" type="text"/></p>		
<p>6) If clinical studies have been submitted, is the submitter the subject of an Application Integrity Policy (AIP)?</p> <p>If yes, consult with the CDRH Office of Compliance/Division of Bioresearch Monitoring (OC/DBM - BIMO) or CBER Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Bioresearch Monitoring Branch (OCBQ/DIS/BMB) to determine the appropriate action. Check on web at http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm134453.htm</p>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<p>Comments? <input style="width: 100%;" type="text"/></p>		

If the answer to 1 or 2 appears to be "No," then stop review of the 510(k) and issue the "Original Jurisdictional Product" letter.

If the answer to 3a or 3b appears to be "No," then stop the review and contact the CDRH Jurisdictional Officer or CBER Office of Jurisdiction Liaison.

If the answer to 4 is "No," the lead reviewer should consult division management and other Center resources to determine the appropriate action.

If the answer to 5 is "Yes," then stop review of the 510(k), contact the CDRH 510(k) Staff and PMA Staff, or appropriate CBER staff.

If the answer to 6 is "Yes," then contact CDRH/OC/DBM-BIMO or CBER/OCBQ/DIS/BMB, provide a summary of the discussion with the BIMO Staff, and indicate BIMO's recommendation/action.



Contains Nonbinding Recommendations

Print Form

Acceptance Checklist for Traditional 510(k)s

(Should be completed within 15 days of DCC receipt)

The following information is not intended to serve as a comprehensive review.

510(k) #: K141114 Date Received by DCC: April 30, 2014

Lead Reviewer: Sheila Connors

Branch: CHTB Division: DCTD Center/Office: CDRH/OIR

Note: If an element is left blank on the checklist, it does not mean the checklist is incomplete. It means the reviewer did not assess the element during RTA and the element will be assessed during the substantive review.

Preliminary Questions		
Answers in the shaded blocks indicate consultations with Center advisor is needed	Yes	No
<p>1) Is the product a device (per section 201(h) of the FD&C Act) or a combination product (per 21 CFR 3.2(e)) with a device constituent part subject to review in a 510(k)?</p> <p>If it appears not to be a device (per section 201(h) of the FD&C Act) or such a combination product, or you are unsure, consult with the CDRH Jurisdictional Officer or the CBER Office Jurisdiction Liaison to determine the appropriate action, and inform division management. <i>Provide a summary of the Jurisdictional Officer's/Liaison's determination.</i> If the product does not appear to be a device or such a combination product, mark "No."</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Comments?		
<p>2. Is the application with the appropriate Center?</p> <p>If the product is a device or a combination product with a device constituent part, is it subject to review by the Center in which the submission was received? If you believe the application is not with the appropriate Center or you are unsure, consult with the CDRH Jurisdictional Officer or CBER Office Jurisdiction Liaison to determine the appropriate action and inform your division management. <i>Provide a summary of the Jurisdictional Officer's/Liaison's determination.</i> If application should not be reviewed by your Center mark "No."</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Comments?		
<p>3) If a Request for Designation was submitted for the device or combination product with a device constituent part and assigned to your center, identify the RFD # and confirm the following:</p> <p>a) Is the device or combination product the same (e.g., design, formulation) as that presented in the RFD submission?</p> <p>b) Are the indications for use for the device or combination product identified in the 510(k) the same as those identified in the RFD submission ?</p> <p>If you believe the product or the indications presented in the 510(k) have changed from the RFD, or you are unsure, consult with the CDRH Jurisdictional Officer or appropriate CBER Jurisdiction Liaison to determine the appropriate action and inform your division management. Provide summary of Jurisdictional Officer's/Liaison's determination. If the answer to either question is no, mark "No." If there was no RFD, skip this question.</p>	<input type="checkbox"/>	<input type="checkbox"/>
Comments?		
<p>4) Is this device type eligible for a 510(k) submission?</p> <p>If a 510(k) does not appear to be appropriate (e.g., Class III type and PMA required, or Class I or II type and 510(k)-exempt), you should consult with the CDRH 510(k) Program Director or appropriate CBER staff during the acceptance review. If 510(k) is not the appropriate regulatory submission, mark "No."</p>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Comments?		

Memo

To: k141114 Bio-Rad BioPlex 2200 25-OH Vitamin D System

From: Sheila Connors

Date: June 4, 2014

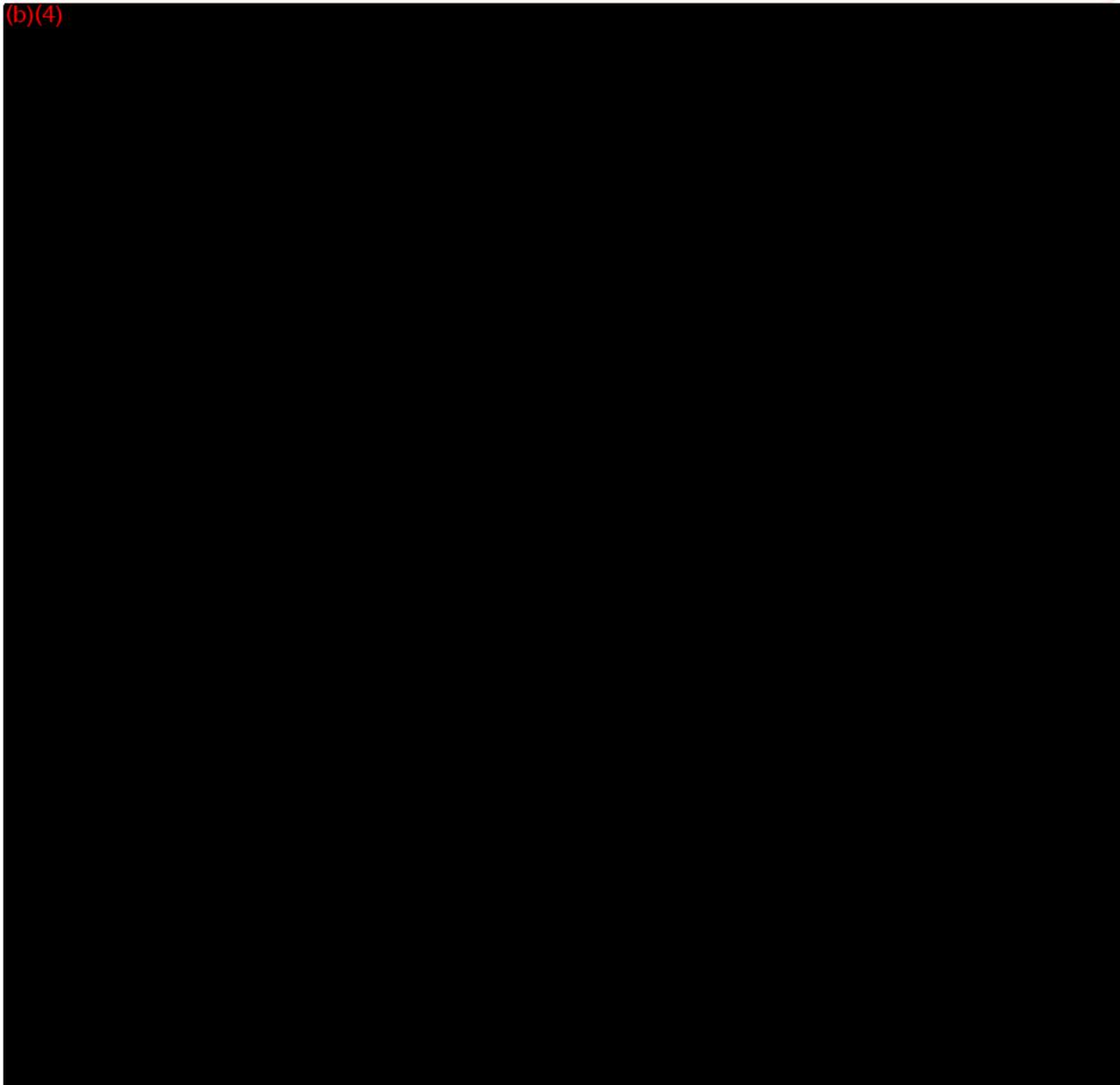
Re: (b)(4)

(b)(4)

1. Method comparison

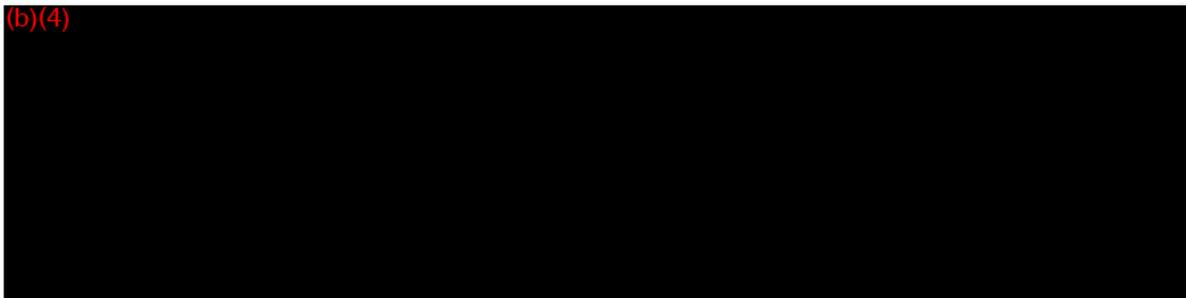
(b)(4)

(b)(4)

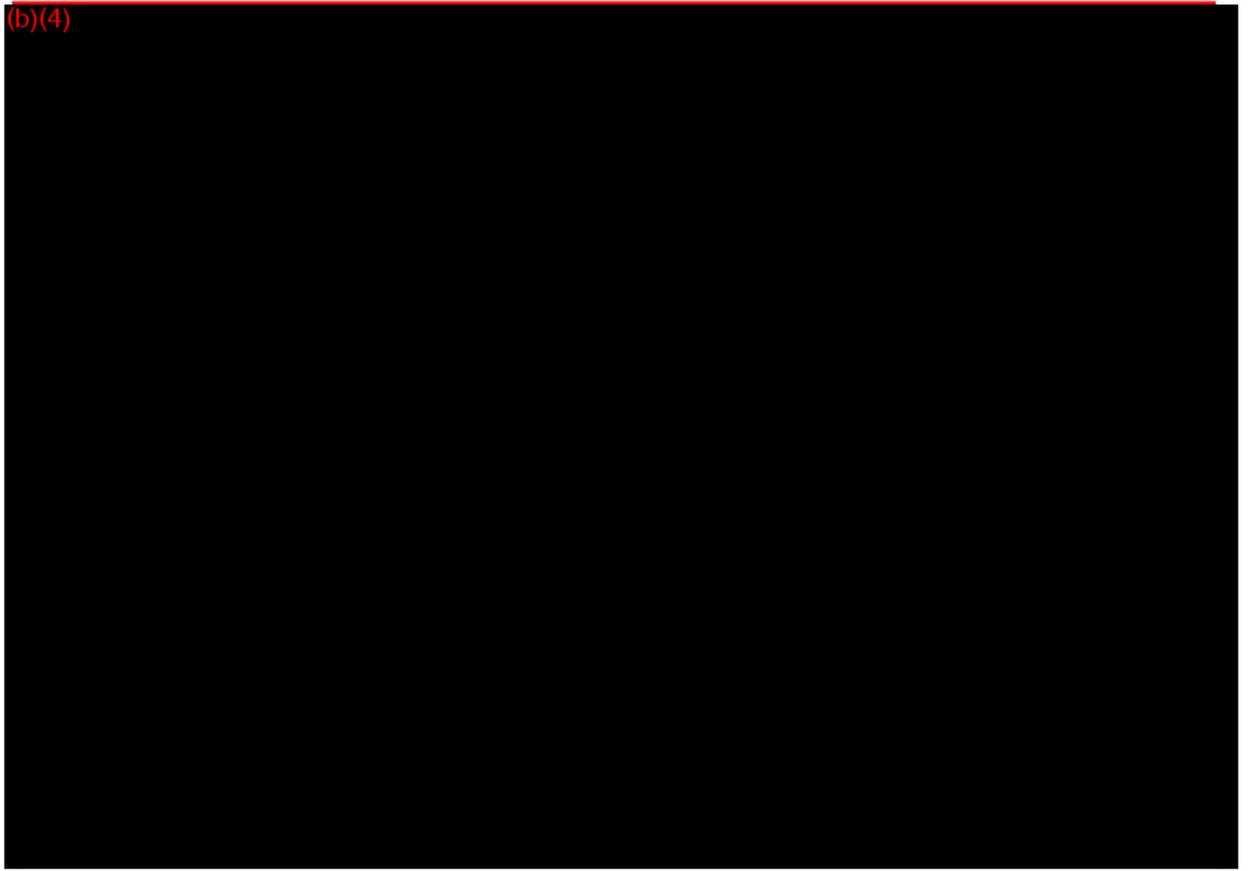


2. Traceability, Stability, Expected Values

(b)(4)

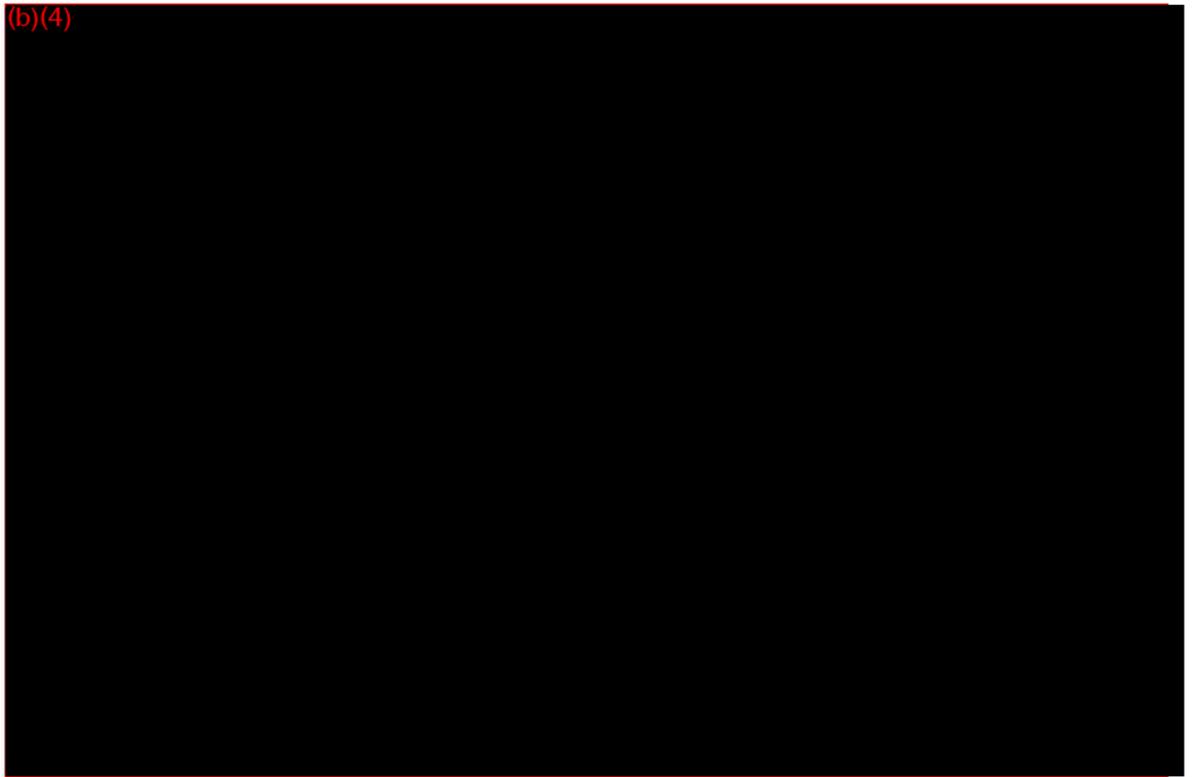


(b)(4)



3. Interference / Cross Reactivity

(b)(4)



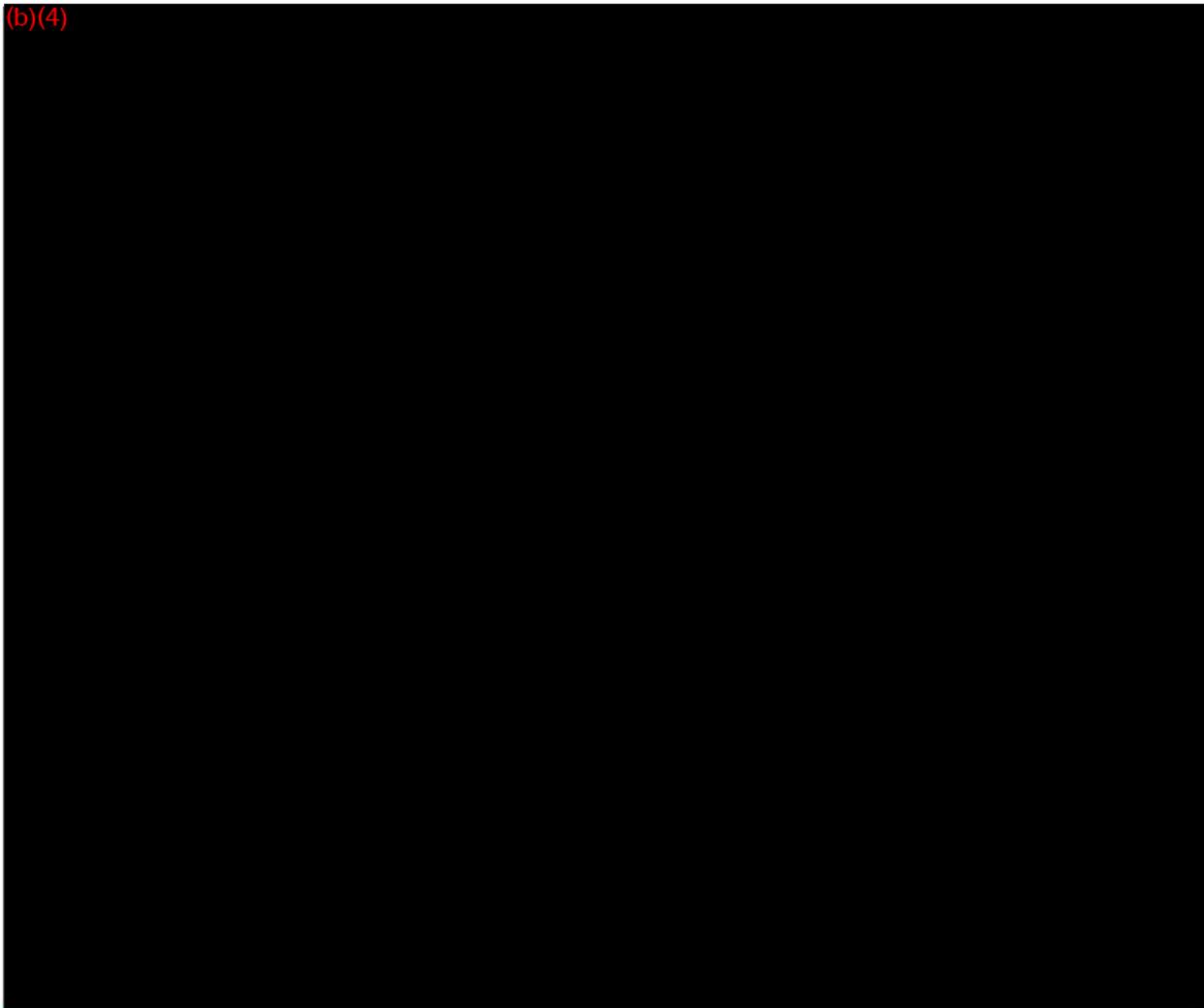
(b)(4)

A large black rectangular redaction box covers the majority of the page's content, starting below the first redaction code and ending above the second.

4. Proposed Labeling

You provided BioPlex 2200 System 25-OH Vitamin D Instruction For Use (package insert).

(b)(4)

A large black rectangular redaction box covers the majority of the page's content, starting below the second redaction code and ending above the third.

5. 510 (k) Summary

- a. Please also add your contact information (name, address, phone, fax, and email).

b. Please add a conclusion section at the end of your 510(k) summary. Please make sure your 510(k) summary follows the content and format according to our regulation in 807.92.

6. Please add to you (b)(4)
(b)(4)

7. Please provide any updated/revised documents as needed to address the above issues including a revised 510 (k) Summary and labeling

Indications for Use

510(k) Number (if known)

K141114

Device Name

BioPlex® 2200 25-OH Vitamin D Kit

BioPlex® 2200 25-OH Vitamin D Calibrator Set

BioPlex® 2200 25-OH Vitamin D Control Set

Indications for Use (Describe)

The BioPlex® 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex® 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

The BioPlex® 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex® 2200 25-OH Vitamin D Reagent Pack.

The BioPlex® 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex® 2200 System and the corresponding BioPlex® 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex® 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

25-OH calibrator and supports an open vial stability of 60 days for BioPlex 2200 25-OH controls.

d. Detection limit:

The limit of blank (LoB), limit of detection (LoD), and the limit of quantitation (LoQ) were determined following CLSI Document EP17-A2 guideline. The LoD is defined as the lowest concentration of 25-OH Vitamin D that can be detected with 95% probability. LoB was performed using two BioPlex 25-OH Vitamin reagent lots on one instrument in 4 replicates per day for 5 days yielding 100 data points per reagent lot. LoD was performed with six serum samples with mean measured concentration ranging from 3.89 to 34.29 ng/mL. The samples were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 12 replicates per day for five days yielding 60 data points per sample per reagent lot. LoQ: The precision was calculated with the same six low level samples used for the LoD. The mean, standard deviation, and coefficient of variation for each sample were calculated. LoQ was defined as precision \leq 20% CV.

The LoB, LoD, and LoQ are summarized below:

LoB	LoD	LoQ
0.8 ng/mL	2.5 ng/mL	6.5 ng/mL

The sponsor claimed that the candidate assay has a measuring range from 6.5 to 125 ng/mL.

e. Analytical specificity:

Interference study:

To measure the effects of endogenous serum components and exogenous molecules on the 25-OH Vitamin D assay. Three sample pools were prepared to achieve a low (10-20 ng/mL), medium (30-50 ng/mL), and high (70-90 ng/mL). The samples were spiked with the interfering substances. The tests and controls were evaluated for a total of ten replicates per interferent using BioPlex 2200 25-OH Vitamin D reagent. Substances are considered interfering if their presence in a sample results in more than \pm 10% deviation in quantitation relative to the value determined in the absence of the substance. The protocol and calculations were based on CLSI EP7-A2 guideline. The substances and the maximum levels tested are shown in the table below:

- C. Please explain how the technological characteristics raise different questions of safety and effectiveness
- D. Please explain why the proposed scientific method for evaluating new/ different characteristics' effects on safety and effectiveness are not acceptable.
- E. Please explain how the data do or do not demonstrate substantial equivalence.

The performance data submitted by the sponsor has demonstrated that the candidate device is substantial equivalent to the predicate device. See section M. above for more information.

R. Reviewer Name and Signature:

Digital Signature Concurrence Table	
Reviewer Sign-Off	Sheila A. Connors -A
Branch Chief Sign-Off (optional)	
Division Sign-Off (optional)	

	Yes	No	
<i>(Identify the new device and the predicate device)</i> 1. Is the predicate device legally marketed?	X		If YES = Go To 2 If NO = Stop NSE
<i>(Review all labeling and assure that it is consistent with IFU statements)</i> 2. Do the devices have the same intended use?	X		If YES = Go to 3, Respond to "A." below If NO = Stop NSE, Respond to "A." below
<i>(Review design, materials, energy source and other features of the devices)</i> 3. Do the devices have the same technological characteristics?		X	If YES = Stop SE If NO = Go to 4, Respond to "B." below
<i>(Determine what questions of safety and effectiveness the different technological characteristics raise)</i> 4. Do the different technological characteristics of the devices raise different questions of safety and effectiveness?		X	If YES = Stop NSE, Respond to "C." below If NO = Go to 5
<i>(Review the proposed scientific methods for evaluating new/ different characteristics' effects on safety and effectiveness)</i> 5a. Are the methods acceptable?	X		If YES = Go to 5b If NO = Stop NSE, Respond to "D." below
<i>(Evaluate performance data)</i> 5b. Do the data demonstrate substantial equivalence?	X		If YES = Stop SE, Respond to "E." below If NO = Stop NSE, Respond to "E." below

Final Decision:

Note: Please complete the following table and answer the corresponding questions.

A. Please explain how the intended use of the subject device is similar to or different from the predicate device.

The subject device has the same intended use as the predicate device.

B. Please describe the different technological characteristics.

The different technological characteristics are described in the device description section, the comparison with the predicate section, and the test principle section. See details in section I, J and L above for more information.

26. December 10, 2014 Meet with Tracey to discuss the supplement response
27. December 12, 2014 Received Tracey's comments on the draft DM
28. December 12, 2014 request the sponsor to send an example of the value assignments for calibrators and controls.
29. December 15, 2014 Received an example of the (b)(4) from the sponsor.
(b)(4)
30. December 18, 2014 arranged a teleconference with the sponsor to discuss the (b)(4)
31. December 19, 2014 During the teleconference the sponsor agreed to (b)(4)
(b)(4)
32. December 26, 2014 Received the (b)(4)
(b)(4)
33. December 29, 2014 Received the updated IFU, 510(k) Summary and labeling from the sponsor with all the new study information.
34. December 30, 2014 Received the final updated 510(k) Summary and labeling from the sponsor with all edits and corrections.

3. Substantial Equivalence Discussion:

(b)(4)

13. August 11, 2014 The sponsor requested guidance on what would be an acceptable amount of scatter. We indicated to the sponsor that the responses sent in via email required further internal discussion and we recommended the sponsor use the Submission Issue Meeting.
14. August 15, 2014 sponsor request a teleconference with management to better understand the need for a Submission Issue Meeting
15. August 18, 2014 Sponsor agreed during the teleconference to submit for a Submission Issue Meeting (b)(4)
- (b)(4)
16. August 21, 2014 Sponsor sent in the official request for a Submission Issue Meeting
Please refers to (b)(4)
- (b)(4)
17. August 21, 2014 Q141077 RTAA
18. August 28, 2014 Internal Meeting scheduled to discuss the submission.
19. September 4, 2014 Submission Issue Meeting Teleconference held. FDA attendees: Katie Serrano (Deputy Director), Yung Chan (Chemistry Branch Manager), Tracey Bosworth (Product Specialist), Meshawn Payne (Product Specialist) and Sheila Connors (Lead Reviewer). Bio-Rad attendees: Juang Wang (Regulatory Affairs), Patricia Klimlev (Regulatory Affairs Manager). (b)(4)
- (b)(4)
20. September 16, 2014 Sent the meeting minutes to the FDA attendees for edits and comments
21. October 10, 2014 Meet with the Yung to finalize the minutes and emailed the sponsor the final edits to the minutes. Please see the submission issue meeting minutes in docman.
22. November 21, 2014 Received an email from the sponsor with a request for an extension beyond the 180 days (Dec. 1, 2014) because of the need to perform a new comparison study with new samples.
23. November 21, 2014 Discussed the request for an extension with Yung. We had a teleconference with the sponsor explaining the FDA no longer allow extensions and that the official response must be sent to the DCC by Dec. 1, 2014.
24. November 21, 2014 Sponsor emailed a follow up to the teleconference about receiving the official response and if the response is not acceptable or still missing information. We replied: As long as you send the complete response to the DCC by the 180th day, we will continue with our review. If we do not receive your complete response by the 180 days, the system will automatically delete your submission. You will **not** receive a NSE letter because we did not make any decision on your submission.
25. November 26, 2014 Sponsor sent in the supplement response.

4. May 14, 2014 RTAA Triage-Quick Review program
5. May 14, 2014 Notify the sponsor that they are included in the Triage-Quick Review program. Requested the sponsor to provide the new IFU form.
6. May 21, 2014 Meet with Tracey to discuss the submission issues, clarification, and additional information needed from the sponsor.
7. May 27, 2014 Emailed Tracey a draft TH letter and draft DS for review.
8. May 30, 2014 Meet with Yung Chan (Branch Manager) and Tracey to decide to remove the submission from the Triage program and to place the submission on hold.
9. June 2, 2014 Meet with Yung Chan (Branch Manager) and Tracey to discuss all the issues in the TH letter to the sponsor.

Method Comparison:

(b)(4)



Value assignment, Traceability and Stability:

(b)(4)



Interference / Cross Reactivity

(b)(4)



Update the proposed labeling and 510 (k) Summary, labeling and IFU

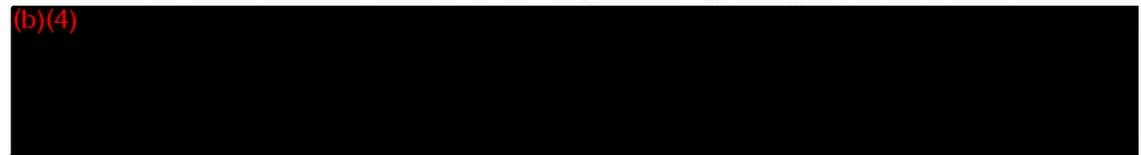
10. June 4, 2014 Finalized the TH letter with Yung and the submission (b)(4)

(b)(4)



11. June 5, 2014 Received an email from the sponsor regarding the TH letter. The

(b)(4)



12. July 17 & 18, 2014, the sponsor emailed the unofficial response to the TH letter. The

(b)(4)



P. Other Supportive Device and Instrument Information:

TPLC for post market signals:

TPLC database search has been performed and no issues with this product were identified.

Q. Administrative Information:

1. Applicant contact information:

a. *Name of applicant:*

Bio-Rad Laboratories

b. *Mailing address:*

5500 E. Second Street

Benicia, CA 94510

c. *Phone #:*

510-741-4609

d. *Fax #:*

510-741-3941

e. *E-mail address (optional):*

Juang_wang@bio-rad.com

f. *Contact:*

Juang Wang

2. Review documentation:

2. May 1, 2014 assigned the submission in CTS
3. May 13, 2014 Meet with Tracey Bosworth (Product Specialist) and Chris King (Mentor) to discuss the submission.

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The study was performed in accordance with CLSI C28-A3c guideline. Two hundred and eighty-seven samples from apparently healthy donors including 160 males and 127 female were collected from three regions (North, Central, and South) in the US and in three seasons (spring, summer and winter), including Caucasians and African American subjects.

The 287 samples from apparently healthy donors met the following inclusion / exclusion criteria as follows and tested with the BioPlex 25-OH Vitamin D kit in singlicate. *One sample <6.5 ng/ml was excluded from the data analysis.

- Age from 21 to 90
- 50% female and 50% male
- 20% from Northern, 20% from Central, and 60% from Southern region
- 40% collected in Summer and 60% in Winter
- At least 30% dark and 30% light skin
- 90% not taking Vitamin D supplements and <30% of those taking Vitamin D supplements at or more than 1000 IU, but less than 2000 IU
- Normal TSH, PTH, and Total Calcium
- No family history of parathyroid or calcium regulatory disease. In addition, no personal history of kidney disease, GI disease, and no bariatric surgery

The observed median, mean, and ranges between 2.5th to 97.5th percentile are summarized below:

N	Mean	Median	2.5 th to 97.5 th Percentile
286	29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

Each laboratory should establish its own reference range pertinent to their specific populations.

N. Proposed Labeling:

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

O. Conclusion:

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

A method comparison study using 204 human serum samples was performed to compare the candidate device BioPlex 2200 25-OH Vitamin D to the predicate device EUROIMMUN 25-OH Vitamin D ELISA. 185 samples were unaltered and 19 samples were spiked with 25-hydroxyvitamin D₃. A total of 196 human serum samples with 25-OH Vitamin D values ranging from 6.6 ng/mL to 124.9 ng/mL were analyzed. There were eight samples with values lower or higher than the measuring range of the predicate method that were excluded in the data analysis. The samples were assayed in singlicate using one reagent lot of the candidate and predicate device. Deming regression was used for the regression analysis and the results are summarized below:

Number of Results Analyzed	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r) (95% CI)	Sample Range Tested (ng/mL)
196	1.0039 (0.9365 to 1.0712)	-0.2256 (-2.4121 to 1.9608)	0.9553 (0.9412 to 0.9661)	BioPlex: 6.6 – 124.9

b. *Matrix comparison:*

Not Applicable, only serum is recommended

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable

b. *Clinical specificity:*

Not Applicable

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

Not Applicable

Substances	Highest Concentration of substance tested which demonstrated no significant interference.
Hemoglobin	150 mg/dL
Bilirubin (conjugated)	20 mg/dL
Bilirubin (unconjugated)	30 mg/dL
Triglycerides	400 mg/dL
Total Protein	12 g/dL
Cholesterol	500 mg/dL
Uric Acid	20 mg/dL
HAMA	100 ng/mL
Rheumatoid Factor	350 IU/mL
Ascorbic Acid	3 mg/dL

The sponsor has the following limitations in their labeling:

“Hemoglobin > 150 mg/dL may interfere and cause increased Vitamin D results. Do not use visibly hemolyzed samples.”

Cross-Reactivity:

The study was conducted using 2 serum pools at 25-hydroxyvitamin D concentrations of 20 ng/mL and 35 ng/mL. Nine cross reactants at levels listed below were spiked into the serum pools. The spiked and non-spiked samples were then evaluated in replicates of five to calculate the cross reactivity as shown below:

$\% \text{ cross reactivity} = \frac{[(\text{mean recovery of test samples in ng/mL}) - (\text{mean recovery of control sample in ng/mL})]}{(\text{concentration of cross reactant in ng/mL})} * 100$

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D2	30	103%
25-hydroxyvitamin D3	30	97%
Vitamin D2	1000	0.2%
Vitamin D3	1000	0.0%
1,25-dihydroxyvitamin D2	30	>100%
1,25-dihydroxyvitamin D3	30	79%
3-epi 25-hydroxyvitamin D3	30	59%
24,25-dihydroxyvitamin D3	20	9%
Paricalcitol (Zemplar)	24	>100%

The sponsor has the following limitations in their labeling:

“Paricalcitol (Zemplar) has been found to cross-react and interfere with the BioPlex® 2200 25- OH Vitamin D assay.”

calibrator level except level 1, three vials are tested in replicates of five on three BioPlex analyzers for a total of 45 points. Target values of the calibrators are listed in the table below.

Calibrator Set	Target value (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

Controls:

The two levels of BioPlex 2200 25-OH Vitamin D control set are prepared from a pool of native serum specimen. For each control level, three vials are tested in replicates of five using each of the kit lots on three BioPlex 2200 analyzers for a total of 45 replicates per reagent lot. Target values and QC ranges of the controls are listed in the table below.

Control Set	Target value (ng/mL)	QC Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Stability:

Shelf life stability studies: Real-time stability studies were performed for the BioPlex 2200 25-OH Vitamin D kit. The stability study protocol and the acceptance criteria have been reviewed and found acceptable. The real time ongoing kit stability study supports a stability of 9 months or until expiration date when stored unopened on the instrument or at 2-8C.

Shelf-life stability for calibrators and controls: The stability study used elevated storage temperatures to model potential real time stability under normal conditions (2-8°C). Accelerated stability studies protocol and acceptance criteria have been reviewed and found acceptable. The accelerated stability model estimates that the BioPlex® 2200 25-OH Vitamin D Calibrator and controls are stable for more than two years at 2-8°C. Real-time stability study is on-going. Real-time stability studies protocol and acceptance criteria have been reviewed and found acceptable.

Open vial stability: The open vial stability studies were performed to assess the stability over time with BioPlex® 2200 25-OH calibrator and control materials stored at 2-8°C. The stability study protocol and the acceptance criteria have been reviewed and found acceptable. The study supports an open vial stability of 30 days for the BioPlex 2200

2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Control 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Control 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

b. *Linearity/assay reportable range:*

Linearity samples were prepared by diluting natural and spiked highly concentrated patient serum samples with a low-level human serum sample (<6.5 ng/mL). Each sample and dilution was evaluated in replicates of four on a single analyzer using one lot of reagent. Linearity was evaluated by calculating a linear regression comparing observed values versus expected values based on the CLSI EP6-A guideline. The regression parameters (slope, intercept, and r^2) of the observed values vs. expected values are shown below:

Slope	Intercept	r^2	Sample range tested
1.0001	0.0045	0.9988	5.5-168.9

Based on the results of the linearity study the sponsor claimed that the candidate assay is linear from 6.5 to 125 ng/mL

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

Traceability:

The BioPlex 25-OH Vitamin D Calibrators are traceable to internal standards, which are determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength.

The six levels of Master Calibrators are manufactured volumetrically from the internal standards into the depleted human serum except level 1 (25-OH hydroxyvitamin D free) in 25% horse serum. The Master Calibrators are immediately frozen at -70°C.

Value Assignment:

The BioPlex® 25-OH Vitamin D kit calibrators are manufactured for each lot kit with the same matrix as the Master Calibrators.

The BioPlex 2200 25-OH Vitamin D calibrator value assignments is established for the BioPlex 2200 25-OH Vitamin D kit using Master Calibrators as reference. For each

L. Test Principle:

The BioPlex 2200 25-OH Vitamin D assay is a multiplex flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex® 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidinphycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) is present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex® 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amounts of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All performance testing were conducted on the Bio-Rad BioPlex 2200 System

a. *Precision/Reproducibility:*

The precision of Bio-Rad BioPlex 2200 25-OH Vitamin D assay was evaluated according to CLSI EP5-A2 guideline. Serum samples with low, medium, and high levels (6 total) of 25-OH Vitamin D and two levels of serum controls were assayed in duplicate per run with two runs per day for twenty days (N=80) on one reagent lot.

Sample	N	Mean (ng/mL)	Within-Run		Between Run		Between Day		Total Precision	
			SD	%C V	SD	%CV	SD	%CV	SD	%CV
1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5

Calibrator:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Calibrator Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Calibrator Predicate Device
Intended Use	For the calibration of the Vitamin D reagent pack.	Same
Calibrator(s) and Calibration	6 calibrator levels (sold separately); 4-PL (parameter logistic) curve fit algorithm	Same
Calibrator Matrix	25% horse serum and depleted human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Calibrator Open Storage at 2-8°C	30 days	3 months
Calibration Frequency	Every 30 days	Every 96 well plate

Controls:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Control Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Controls Predicate Device
Intended Use	Use as an assayed quality control to monitor the overall performance of the Vitamin D reagent.	Same
Storage	Store at 2-8°C until ready to use	Same
Matrix	Human serum with ProClin 950, Sodium benzoate and BND	Liquid in horse serum with preservatives

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

CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods

CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures

CLSI EP07-A2: Interference Testing in Clinical Chemistry

CLSI EP09-A2IR: Method comparison and Bias Estimation

CLSI EP15-A2: User Verification of Performance for Precision and Trueness

CLSI EP17-A2: Evaluation of Detection Capability for Clinical laboratory measurements

Procedure

3. Comparison with predicate:

Assay:

Similarities / Differences		
Item	BioPlex® 2200 25-OH Vitamin D Kit Candidate Device	EUROIMMUN 25-OH Vitamin D ELISA Predicate Device (k123660)
Intended Use	For the quantitative determination of 25-hydroxyvitamin D in human serum.	Same
Assay Type	Quantitative	Same
Test Principle	Competitive immunoassay	Same
Antibody	Monoclonal Sheep antibody against 25 OH Vitamin D	Same
Signal Detection	Fluorescence	Same
Unit of Measure	ng/mL	Same
Assay Technology	Automated multiplex flow competitive immunoassay	Manually competitive immunoassay
Conjugate	Biotinylated 25-hydroxyvitamin D and phycoerythrin streptavidin	Biotinylated 25-hydroxyvitamin D and Peroxidase-labeled streptavidin and substrate TMB
Solid Phase	Antibody-coated paramagnetic microbeads	Antibody coated 96 microwell ELISA plate
Measuring Range	6.5 ng/mL – 125.0 ng/mL	4.0 ng/mL – 120 ng/mL
Sample Matrix	Serum	Serum or EDTA or Lithium heparin plasma
Sample Size	10µL	20µL
Open Pack Stability	60 days	Not Applicable
Reagent Storage	On-board or in refrigerator at 2-8°C	Not Applicable
Sample Handling	Automated	Manually
Instrumentation	Bio-Rad BioPlex® 2200 System	ELISA plate reader
Measuring Wavelength	550-610 nm	450/620 nm

4. One 5mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA-PE) in buffer comprising protein stabilizers (bovine). ProClin 950 (<1.0%) and sodium azide (<0.1%) as preservatives, chemical blockers and detergent (Tween 20).

BioPlex 2200 25-OH Vitamin D Calibrator set (sold separately) contains six 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (≤0.1%) as preservatives.

Calibrator Set	Target (ng/mL)
Level 1	0.0
Level 2	10.0
Level 3	30.0
Level 4	75.0
Level 5	110.0
Level 6	165.0

BioPlex 2200 25-OH control set (sold separately) contains two 1.5 mL of Level 1 and two 1.5 mL of Level 2 control vials. Each vial contains 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (≤0.1%) as preservatives.

Control Set	Target (ng/mL)	Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Calibrator and Control contain human source material. Each donor unit of serum in the preparation of these materials were tested and found negative for the Human Immunodeficiency Virus Antibody (HIV I/II Ab), Hepatitis B Surface Antigen (HBsAg), and Hepatitis C Virus Antibody (HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):
EUROIMMUN 25-OH Vitamin D ELISA
2. Predicate 510(k) number(s):
k123660

H. Intended Use:

1. Intended use(s):

See indication for use below.

2. Indication(s) for use:

The BioPlex 2200 25-OH Vitamin D kit is a flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH vitamin D assay is to be used to aid in the assessment of vitamin D sufficiency. The BioPlex 2200 25-OH Vitamin D kit is intended for use with the BioPlex 2200 System.

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D reagent Pack.

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 system and corresponding BioPlex® 25-OH Vitamin D reagent pack in the clinical laboratory. The performance of the BioPlex 2200 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

3. Special conditions for use statement(s):

For *in vitro* diagnostics

For prescription use only

4. Special instrument requirements:

BioPlex 2200 system

I. Device Description:

The BioPlex 2200 25-OH Vitamin D Kit consists of the following:

1. One 10mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead (SVB) in buffer with protein stabilizers (bovine). ProClin 950 (<1.0%) and sodium azide (<0.1%) as preservatives.
2. One 10mL vial of Release Buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (<1.0%) as preservative.
3. One 5mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizer (bovine). ProClin 950 (<1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives and chemical blockers.

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k141114

B. Purpose for Submission:

New Device

C. Measurand:

25-hydroxyvitamin D [25(OH) Vitamin D]

D. Type of Test:

Quantitative multiplexed flow immunoassay

E. Applicant:

Bio-Rad Laboratories

F. Proprietary and Established Names:

BioPlex® 2200 25-OH vitamin D kit

BioPlex® 2200 25-OH Vitamin D Calibrator Set

BioPlex® 2200 25-OH Vitamin D Control Set

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
MRG	II	862.1825 Vitamin D Test System	Chemistry (75)
JIT	II	862.1150 Calibrator	Chemistry (75)
JJX	I, Reserved	862.1660 Quality Control Material (Assayed and Unassayed)	Chemistry (75)

Submitter:

Juang Wang
Regulatory Affairs Representative
Bio-Rad Laboratories
Clinical Immunology Division
5500 E. 2nd Street
Benicia, CA, 94510, US
Phone: (510) 741-4609
Fax: (510) 741-3941

Secondary Contact:

Patricia M. Klimley
CID RA Manager
Bio-Rad Laboratories
Clinical Immunology Division
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Benicia, CA, 94510, US
Phone: (510) 741-6263
Fax: (510) 741-3941

April 29, 2014

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Attn: eSubmitter Team
Document Mail Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Sir or Madam:

This submission dated April 29, 2014, is filed pursuant to the In Vitro Diagnostic Device Evaluation and Safety program's Electronic Review (eReview).

The submission is a(n) **510(k), Original Submission, Traditional** referring to the product, BioPlex® 2200 25-OH Vitamin D Kit also known as trade name(s): BioPlex® 2200 25-OH Vitamin D Kit, BioPlex® 2200 25-OH Vitamin D Calibrator Set, and BioPlex® 2200 25-OH Vitamin D Control Set with model(s): Not Applicable, Not Applicable, and Not Applicable. The classification panel for this submission is CLINICAL CHEMISTRY.

Indications for Use

Indications For Use Statement**BioPlex® 2200 25-OH Vitamin D Kit**

The BioPlex 2200 25-OH Vitamin D kit is a multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

BioPlex® 2200 25-OH Vitamin D Calibrator Set

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D Reagent Pack.

BioPlex® 2200 25-OH Vitamin D Control Set

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 System and the corresponding BioPlex 2200 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

The prior submissions that are related to this release are as follows: k130528 BioPlex APLS IgM, k130058 BioPlex Celiac IgA and IgG, K103834 BioPlex APLS IgG and IgA, k092587 BioPlex Rubella and CMV IgM, k093954 BioPlex Anti-CCP, k091616 BioPlex MMRV IgG, k090409 BioPlex HSV-1 and HSV-2 IgG, k080008 BioPlex ToRC IgG, k072358 BioPlex Vasculitis, k063866 BioPlex Syphilis IgG.

The devices to which substantial equivalence is claimed are as follows: K132492 Liaison 25 Total D, K132492 Liaison 25 Total D Control Set.

User Fee Payment ID: MD6071339956733

Truth and Accuracy Statement

To the best of my knowledge, the data and information submitted in this premarket notification are truthful and accurate, and no material fact has been omitted (as required by 21 CFR 807.87).

Sincerely,

Juang Wang
Regulatory Affairs Representative
Bio-Rad Laboratories

Submission Report

Admin

1.0 Type of Submission

Introduction

*Department of Health and Human Services
Food and Drug Administration*

CDRH PreMarket Review Submission Cover Sheet

*Form Approval
OMB No. 0910-0120*

Note:	Please be advised that: 1) under 21 CFR 807.7(1), we may request any additional information that is necessary to reach a determination regarding substantial equivalence and 2) supportive raw data may be provided as attachments to this submission.
Information:	Whenever possible, please enter descriptions in executive summary format because this information will be used to generate the FDA Decision summary. If additional information is needed, please attach the appropriate file.

Section A **Type of Submission**

Submission Type	*	510(k)
▪ Submission Sub-Type	*	Original Submission
- Submission Sub-Sub-Type	*	Traditional
Enter the original submission number.		
Is this a bundled submission?	*	No

User Fee Payment ID Number	*	MD6071339956733
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[MDUFMA Cover Sheet](#)

Please attach the completed MDUFMA Cover Sheet.		*
File Attachment	<u>MDUFMA Cover Sheet MD6071339-956733</u>	

2.0 Contact Information

Section B **Primary Contact (Submitter, Applicant, or Sponsor)**

Primary Contact Information *	
<i>Contact Information:</i>	
Contact Name	Dr. Juang Wang
Occupation Title	Regulatory Affairs Representative
Email Address	juang_wang@bio-rad.com
<i>Address</i>	
Establishment Name	Bio-Rad Laboratories
Division Name	Clinical Immunology Division
Address	5500 E. 2nd Street Benicia, CA, 94510, US
Telephone Number	(510) 741-4609
Fax Number	(510) 741-3941

Section C	Secondary Contact (Applicant Correspondent, US Agent, or Consultant)
------------------	---

Secondary Contact Information	
<i>Contact Information:</i>	
Contact Name	Ms. Patricia M. Klimley
Occupation Title	CID RA Manager
Email Address	patricia_klimley@bio-rad.com
<i>Address</i>	
Establishment Name	Bio-Rad Laboratories
Division Name	Clinical Immunology Division
Address	5500 E. Second Street Benicia, CA, 94510, US
Telephone Number	(510) 741-6263
Fax Number	(510) 741-3941

Who should be contacted for issues related to this submission?	* Primary Contact
--	-------------------

Section D	Manufacturing Location (Physical Location of the Manufacturing Plant)
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Manufacturing Location (Optional)	
<i>Establishment Information:</i>	
Establishment Name	Bio-Rad Laboratories, Inc
FDA Establishment Identifier (FEI)	1000135116
Central File Number (CFN)	
Registration Number	2950880
Owner/Operator Number	9929003
D&B D-U-N-S Number	
<i>Physical Location:</i>	
Address	4000 Alfred Nobel Dr. Hercules, CA, 94547, US
Telephone Number	(510) 724-7000

Fax Number	
------------	--

3.0 Reason for Submission

Section D3	Reason for Submission - 510(k)
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New Device	* Yes
Additional or Expanded Indications	
Change in technology	
If additional information is required, attach file.	

Section E	Additional Information on 510(k) submissions
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Information on Device to which substantial equivalence is claimed. 510(k) Number - Trade or Proprietary or Model Name		*
Item 1	(b)(4)	
Item 2	(b)(4)	

For this submission, are you including a 510(k) Statement or Summary?	* 510(k) Summary
---	------------------

Enter your 510(k) Summary or Statement.	*
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Device Description

The BioPlex® 2200 25-OH Vitamin D assay is a multiplex flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidin-phycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) are present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amount of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

Intended Use Statement

The BioPlex® 2200 25-OH Vitamin D kit is a multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

The BioPlex® 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex® 2200 25-OH Vitamin D Reagent Pack.

The BioPlex® 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex® 2200 System and the corresponding BioPlex® 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex® 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

Performance Characteristics

A series of studies were conducted to evaluate the performance of the BioPlex 2200 25-OH Vitamin D kit. These studies included precision, reproducibility,

linearity, limits of detection, interfering substances, cross reactivity, expected values, method comparison and stability. The results of all studies demonstrated that the BioPlex 2200 25-OH Vitamin D kit performed according to its specifications.

Please refer to the attached [Bio-Rad BioPlex 2200 25-OH Vitamin D 510\(k\) Summary Report](#)

File Attachment [510k summary - Bio-Rad BioPlex 2200 25-OH Vitamin D](#)

4.0 Product Information

Section F Product Information

Common or classification name *

BioPlex® 2200 25-OH Vitamin D Kit

FDA Document Numbers of all prior related submissions (regardless of outcome) *

Item 1	k130528 BioPlex APLS IgM
Item 2	k130058 BioPlex Celiac IgA and IgG
Item 3	K103834 BioPlex APLS IgG and IgA
Item 4	k092587 BioPlex Rubella and CMV IgM
Item 5	k093954 BioPlex Anti-CCP
Item 6	k091616 BioPlex MMRV IgG
Item 7	k090409 BioPlex HSV-1 and HSV-2 IgG
Item 8	k080008 BioPlex ToRC IgG
Item 9	k072358 BioPlex Vasculitis
Item 10	k063866 BioPlex Syphilis IgG

4.1 Trade, Proprietary, or Model Names

Item: 1

Trade, proprietary, or model name for this device * BioPlex® 2200 25-OH Vitamin D Kit

Model number * Not Applicable

Item: 2

Trade, proprietary, or model name for this device * BioPlex® 2200 25-OH Vitamin D Calibrator Set

Model number * Not Applicable

Item: 3

Trade, proprietary, or model name for this device * BioPlex® 2200 25-OH Vitamin D Control Set

Model number * Not Applicable

5.0 Product Classification

Section G1 **Product Classification**

Choose the product code for this submission.

Product Code	SYSTEM, TEST, VITAMIN D (MRG)
Device Class	CLASS II
Classification Panel	CLINICAL CHEMISTRY
C.F.R. Section	862.1825 - VITAMIN D TEST SYSTEM.

Add any other product codes that are applicable to this submission.

Item	Product Code	Device Class	Classification Panel	C.F.R. Section
Item 1	CALIBRATOR, PRIMARY (JIS)	CLASS II	CLINICAL CHEMISTRY	862.1150 - CALIBRATOR.
Item 2	SINGLE (SPECIFIED) ANALYTE CONTROLS (ASSAYED AND UNASSAYED) (JJX)	CLASS I	CLINICAL CHEMISTRY	862.1660 - QUALITY CONTROL MATERIAL (ASSAYED AND UNASSAYED).

If the product code(s) is/are unknown, please describe the classification of the product.

If necessary, identify the secondary Classification Panel

Item	
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Section G2 **Intended Use and Indications for Use**

Information: *Intended use refers to "the objective intent of the persons legally responsible for the labeling of devices. The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article..." (see 21 CFR 801.4).*

[Code of Federal Regulations](#)

Enter the intended use of the product. *

Intended Use Statement

BioPlex[®] 2200 25-OH Vitamin D Kit

The BioPlex 2200 25-OH Vitamin D kit is a multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

BioPlex[®] 2200 25-OH Vitamin D Calibrator Set

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D Reagent Pack.

BioPlex[®] 2200 25-OH Vitamin D Control Set

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 System and the corresponding BioPlex 2200 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

	Intended Use
--	--------------

Information: *For AST devices, the Indication For Use statement should indicate: whether the assay is quantitative (MIC) or qualitative (breakpoint devices); whether results may be read and reported manually; which organism groups the device is indicated for testing; and any instrumentation the device may be used with, if applicable. A typical example of an intended use statement is: "ABC's system is intended for the in vitro qualitative or quantitative determination of antimicrobial susceptibility of rapidly growing aerobic non-fastidious Gram positive and Gram negative organisms on the ABC Instrument."*

[Code of Federal Regulations](#)

Information: Please attach the Indication(s) for Use Form to the following question.

[Indication\(s\) for Use Form](#)

Enter the product's indications for use. *

Indications For Use Statement

BioPlex[®] 2200 25-OH Vitamin D Kit

The BioPlex 2200 25-OH Vitamin D kit is a multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

BioPlex[®] 2200 25-OH Vitamin D Calibrator Set

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D Reagent Pack.

BioPlex[®] 2200 25-OH Vitamin D Control Set

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 System and the corresponding BioPlex 2200 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

File Attachment 1	BioPlex 2200 25-OH Vitamin D Kit - IU
File Attachment 2	BioPlex 2200 25-OH Vitamin D Calibrator Set - IU
File Attachment 3	BioPlex 2200 25-OH Vitamin D Control Set - IU

Enter any special applications of the device or contraindications not addressed in the Intended Use Statement.

6.0 Manufacturing/Packaging/Sterilization Sites

Item: 1

Status Change * No

Site Operation

<input checked="" type="checkbox"/> Manufacturer	* Yes
<input type="checkbox"/> Contract Manufacturer	* No
<input type="checkbox"/> Contract Sterilizer	* No
<input type="checkbox"/> Repackager/Relabeler	* No

Contact Information

Contact Information:

Contact Name	Dr. Michael Jackson
Occupation Title	CSD General Manager
Email Address	michael_jackson@bio-rad.com

Establishment Information:

Establishment Name	Bio-Rad Laboratories, Inc
--------------------	---------------------------

Division Name	Clinical System Division
FDA Establishment Identifier (FEI)	
Central File Number (CFN)	
Registration Number	2915274
Owner/Operator Number	9929003
D&B D-U-N-S Number	
<i>Physical Location:</i>	
Address	4000 Alfred Nobel Dr. Hercules, CA, 94547, US
Telephone Number	(510) 724-7000
Fax Number	
<i>Mailing Location:</i>	
Address	4000 Alfred Nobel Dr. Hercules, CA, 94547, US

Item: 2

Status Change	* No
Site Operation	
▪ Manufacturer	* No
▪ Contract Manufacturer	* No
▪ Contract Sterilizer	* No
▪ Repackager/Relabeler	* No

Contact Information	
<i>Contact Information:</i>	
Contact Name	Ms. Patricia M. Kimley
Occupation Title	CID RA Manager
Email Address	patricia_kimley@bio-rad.com
<i>Establishment Information:</i>	
Establishment Name	Bio-Rad Laboratories
Division Name	Clinical Immunology Division
FDA Establishment Identifier (FEI)	
Central File Number (CFN)	
Registration Number	2950880
Owner/Operator Number	9929003
D&B D-U-N-S Number	
<i>Physical Location:</i>	
Address	5500 E. Second Street Benida, CA, 94510, US
Telephone Number	(510) 741-6263
Fax Number	(510) 741-3941
<i>Mailing Location:</i>	

Address	5500 E. Second Street Benida, CA, 94510, US
---------	--

Item: 3

Status Change	* No
---------------	------

Site Operation	
<input type="checkbox"/> Manufacturer	* Yes
<input type="checkbox"/> Contract Manufacturer	* Yes
<input type="checkbox"/> Contract Sterilizer	* No
<input type="checkbox"/> Repackager/Relabeler	* No

Contact Information	
<i>Contact Information:</i>	
Contact Name	(b)(4)
Occupation Title	
Email Address	
<i>Establishment Information:</i>	
Establishment Name	
Division Name	
FDA Establishment Identifier (FEI)	
Central File Number (CFN)	
Registration Number	
Owner/Operator Number	
D&B D-U-N-S Number	
<i>Physical Location:</i>	
Address	
Telephone Number	
Fax Number	
<i>Mailing Location:</i>	
Address	

Item: 4

Status Change	* No
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Site Operation	
<input type="checkbox"/> Manufacturer	* Yes
<input type="checkbox"/> Contract Manufacturer	* No

Contract Sterilizer	*	No
Repackager/Relabeler	*	No

Contact Information	
<i>Contact Information:</i>	
Contact Name	Mr. Scott Dennis
Occupation Title	Manager, Regulatory and Quality Assurance
Email Address	scott_dennis@bio-rad.com
<i>Establishment Information:</i>	
Establishment Name	Bio-Rad Laboratories - Redmond Operations
Division Name	
FDA Establishment Identifier (FEI)	
Central File Number (CFN)	
Registration Number	3032705
Owner/Operator Number	3022521
D&B D-U-N-S Number	
<i>Physical Location:</i>	
Address	14620 NE North Woodinville Way Suite 200 Woodinville, WA, 98072, US
Telephone Number	(425) 498-1709
Fax Number	(425) 498-1651
<i>Mailing Location:</i>	
Address	6565 185th Avenue NE Redmond, WA, 98052, US

7.0 Utilization of Standards

<i>Information:</i>	Select the CDRH Recognized Standard from the available list.
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Select all standards referenced.			
Item	Standard Title and Reference Number	Category	Organization
Item 1	Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (EP5-A)(EP5-A)	InVitro	NCCLS
Item 2	Interference Testing in Clinical Chemistry; Approved Guideline (EP 7-A)(EP 7-A)	InVitro	NCCLS
Item 3	Protocols for Determination of Limits of Detection and Limits of Quantitation (EP17-A)(EP17-A)	InVitro	CLSI
Item 4	User Verification of Performance for Precision and Trueness (EP15-A2)(EP15-A2)	InVitro	CLSI
Item 5	Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (EP25-A)(EP25-A)	InVitro	CLSI
Item 6	Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline (EP6-A)(EP6-A)	InVitro	CLSI
Item 7	Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Second Edition (Interim Revision) (EP09-A2-1R)(EP09-A2-1R)	InVitro	NCCLS
Item 8	Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory (C28-A3)(C28-A3)	InVitro	CLSI

[Standards Data Report for 510\(k\)s \(FDA Form #3654, Form Approved OMB #0910-0120\)](#)

For each standard selected above, please fill out the Standards Data Report for 510(k)s (FDA Form #3654) and attach it here.

File Attachment 1	Form 3654 - Precision EP5-A2
File Attachment 2	Form 3654 - Linearity EP6-A
File Attachment 3	Form 3654 - Interference EP7-A2
File Attachment 4	Form 3654 - Method Comparison EP09-A2IR
File Attachment 5	Form 3654 - User Precision and Trueness Evaluation EP15-A2
File Attachment 6	Form 3654 - Detection Capability EP17-A2
File Attachment 7	Form 3654 - Stability IVD Reagent EP25-A
File Attachment 8	Form 3654 - Reference Intervals C28-A3c
Details	

Did you reference any other standards? No

8.0 Utilization of Guidance Documents

Please enter all referenced Guidance Documents.

Item	Document Title	Office	Division	Web Page
Item 1	Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff			http://www.fda.gov/cdrh/civd/guidance/1588.html
Item 2	Guidance for Industry and FDA Staff - Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests			http://www.fda.gov/cdrh/ocb/guidance/1620.html
Item 3	Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff	ODE		http://www.fda.gov/cdrh/ode/guidance/337.html

9.0 Certification of Compliance with Clinical Trials

Information: *The Food and Drug Administration has issued draft guidance titled: "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007".*

The draft guidance can be found at: <http://www.fda.gov/RegulatoryInformation/Guidances/ucm125335.htm>
[Form FDA-3674, ClinicalTrials.gov Data Bank](#)

Information: *Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) included a provision that all MA applications are required to be accompanied with certification that all applicable clinical trial information has been submitted to the ClinicalTrials.gov data bank.*

Beginning December 26, 2007, submissions must include form FDA-3674. If your submission includes data from a clinical trial, you must determine if your study is applicable for entry into the clinical trial registry data bank at ClinicalTrials.gov.

[Form FDA-3674, ClinicalTrials.gov Data Bank](#)

For each clinical trial, complete form FDA-3674 and attach it here.

File Attachment	Form 3674 - Compliance Certificate
Details	

OVD Submission

OVD 510(k)

OIVD 510(k) Submission

In vitro diagnostic (IVD) products are those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

IVDs are medical devices as defined in section 210(h) of the Federal Food, Drug, and Cosmetic Act, and may also be biological products subject to section 351 of the Public Health Service Act. Like other medical devices, IVDs are subject to premarket and postmarket controls. IVDs are also subject to the Clinical Laboratory Improvement Amendments (CLIA '88) of 1988.

Is this an Antimicrobial Susceptibility Testing Device? * No

Is this a Collection Device? * No

Note: The 510(k) Short Form is intended for experienced submitters who are familiar with the Turbo 510(k) program and the level of detail that is required when completing the submission.

Would you like to complete the OIVD 510(k) Short Form? * No

1.0 Type of Product

Please select one: * Both Assay/Reagents Including Controls and Instrument

Select Device Type: * Quantitative and Semi-quantitative

Select device technology: * Other

Enter the device technology if you chose "Other." *

Multiplex Flow Immunoassay (multiple fluoromagnetic bead assay)

2.0 System Description

Information: Please enter descriptions in executive summary format because this information will be used to generate the FDA Decision summary.

Device Description

Enter a brief description of the characteristics of the device, i.e., physical design, components, etc. Include information on any specific accessories (e.g., specialized collection devices, materials for pre-analytical steps). *

BioFlex[™] 2200 25-OH Vitamin D kit includes the following components:

- One (1) 10 mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead (SVB) in buffer with protein stabilizers (bovine). ProClin 950 (1.0%) and sodium azide (< 0.1%) as preservatives.
- One (1) 10 mL vial of Release buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (1.0%) as preservative.

- One (1) 5 mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizers (bovine), ProClin 950 (1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives and chemical blockers.
- One (1) 5 mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA -PE) in a buffer comprising protein stabilizers (bovine), ProClin 950 (1.0%) and sodium azide (<0.1%) as preservatives, chemical blockers and detergent (T ween 20).

BioPlex[®] 2200 25-OH Vitamin D Calibrator Set contains six (6) 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

BioPlex[®] 2200 25-OH Control Set contains two (2) 1.5 mL Level 1 and two (2) 1.5 mL Level 2 Control vials, each containing 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤0.3%), sodium benzoate (≤0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

Additional materials required but not supplied include:

BioPlex[®] 2200 Sheath Fluid containing Phosphate Buffered Saline (PBS), ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives; and BioPlex[®] 2200 Wash Solution containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives.

Is there an instrument associated with this assay?		* Yes
Has this instrument previously been deared?		* Yes
Please enter the 510(k) number.		*
Item 1	k130528 BioPlex APLS IgM	
Item 2	k130053 BioPlex Celiac A and G	
Item 3	k103834 APLS IgG and IgA	
Item 4	K092587 Ribella and CMV IgM	
Item 5	k093954 BioPlex Anti-CCP	
Item 6	k091616 BioPlex MMRV IgG	
Item 7	k090409 BioPlex HSV-1/-2 IgG	
Item 8	k080008 BioPlex TORC IgG	
Item 9	k072358 BioPlex Vasculitis	
Item 10	k063866 BioPlex Syphilis IgG	
Item 11	k062211 BioPlex EBV IgG	
Item 12	k062213 BioPlex EBV IgM	
Item 13	k043341 BioPlex ANA w/MDSS	
Item 14	k041658 BioPlex ANA Screen	
Have there been any modifications to the deared instrument for this particular assay?		* No
Please describe the modification to the deared instrument.		

Information: The following questions relate to the instrument.

Modes of Operation

What are the modes of operation (i.e., random access, batch, stat, open tube, closed tube, automatic, manual, etc.)?

Software

What kind of software does the system use (i.e., operating system, user interface, data management, communications, laboratory information system, etc.)?

Has the FDA reviewed the applicant's Hazard Analysis and software documentation for this line of product types?

Sample Identification

Describe how samples are identified (i.e., barcode, rack/position, instrument auto numbering, etc.).

Specimen Sampling and Handling

Describe how specimens are mixed (for whole blood), sampled, (i.e., direct open tube or closed tube piercing) and handled (i.e., manual, etc.).

Assay Types

What kinds of assays are run on the system (i.e., chemistry, immunoassay, cytochemistry, image analysis, Immunohistochemistry, etc.)?

Reaction Types

Describe what types of reactions the system is capable of measuring (i.e., photometric, fluorometric, nephelometric, turbidometric, etc.).

Calibration

Describe the calibration procedures for the system (i.e., use of whole blood and commercial calibration materials).

Quality Control

Describe the quality control procedures and the use of commercial quality control materials for Point-of-Care or home-use devices (i.e., handheld meters, describe any electronic QC procedures or process controls).

Other Supportive Performance Characteristics

Enter other supportive performance characteristics that were not covered in the Performance Characteristics section above. This information could include performance characteristics data unique to an instrument class in your division (i.e., flow cytometer, glucose meter, automated cell locating device, etc.).

Principles of Operation

Provide a description of the technology utilized in the device. Discuss the principles of the device methodology and indicate whether it is well established or new and unproven.

3.0 Substantial Equivalence Information

Item: 1

Note: The predicate device drop-down is populated with the list created in Section 3.0 of the Admin Tab.

Predicate device *

(b)(4)

Describe the item being compared *

(b)(4)

Similarities *

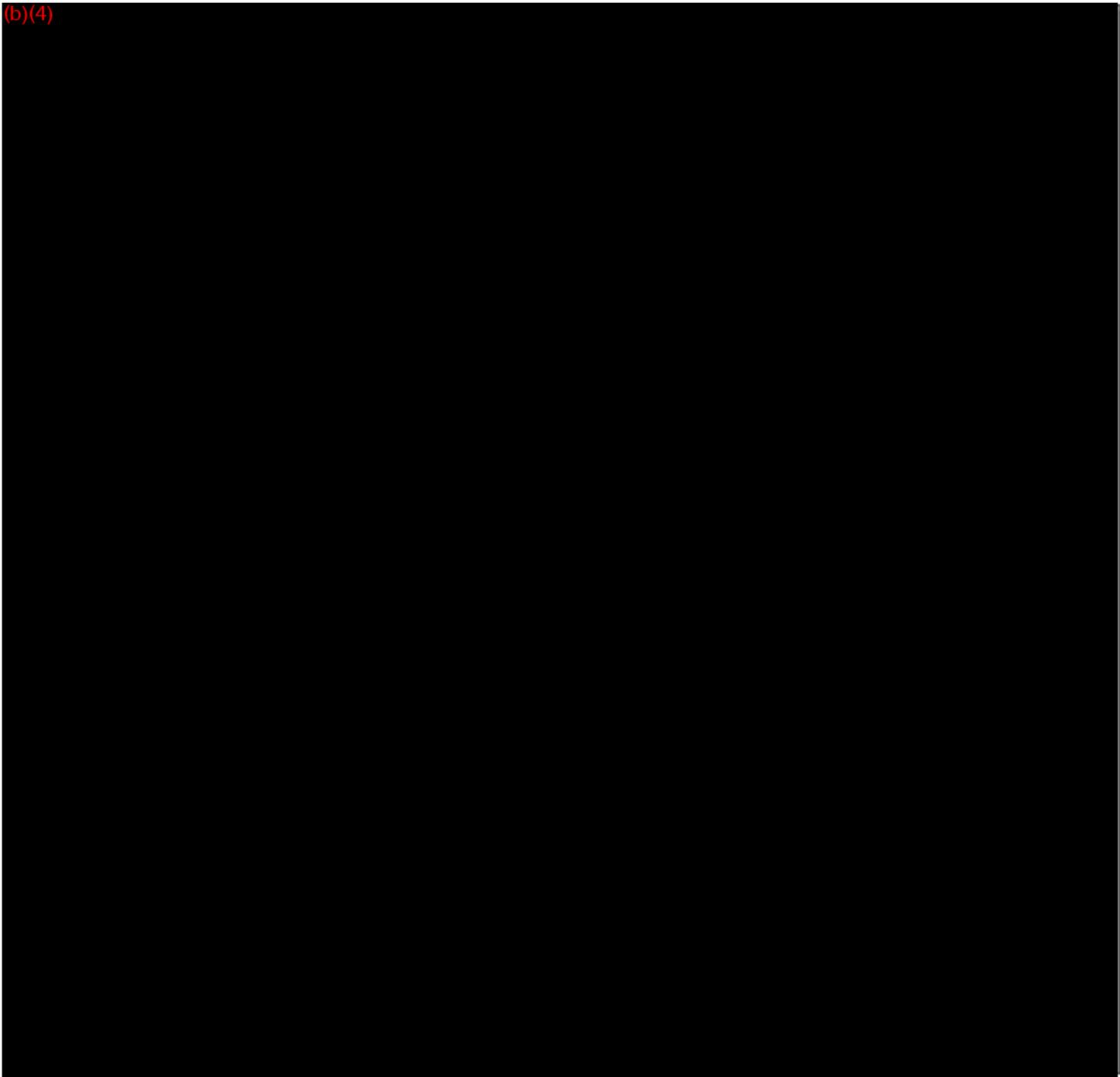
(b)(4)

Differences *

(b)(4)

(b)(4)

(b)(4)



Item: 2

Note: *The predicate device drop-down is populated with the list created in Section 3.0 of the Admin Tab.*

Predicate device *

(b)(4)

Describe the item being compared *

(b)(4)

(b)(4)

Similarities

(b)(4)

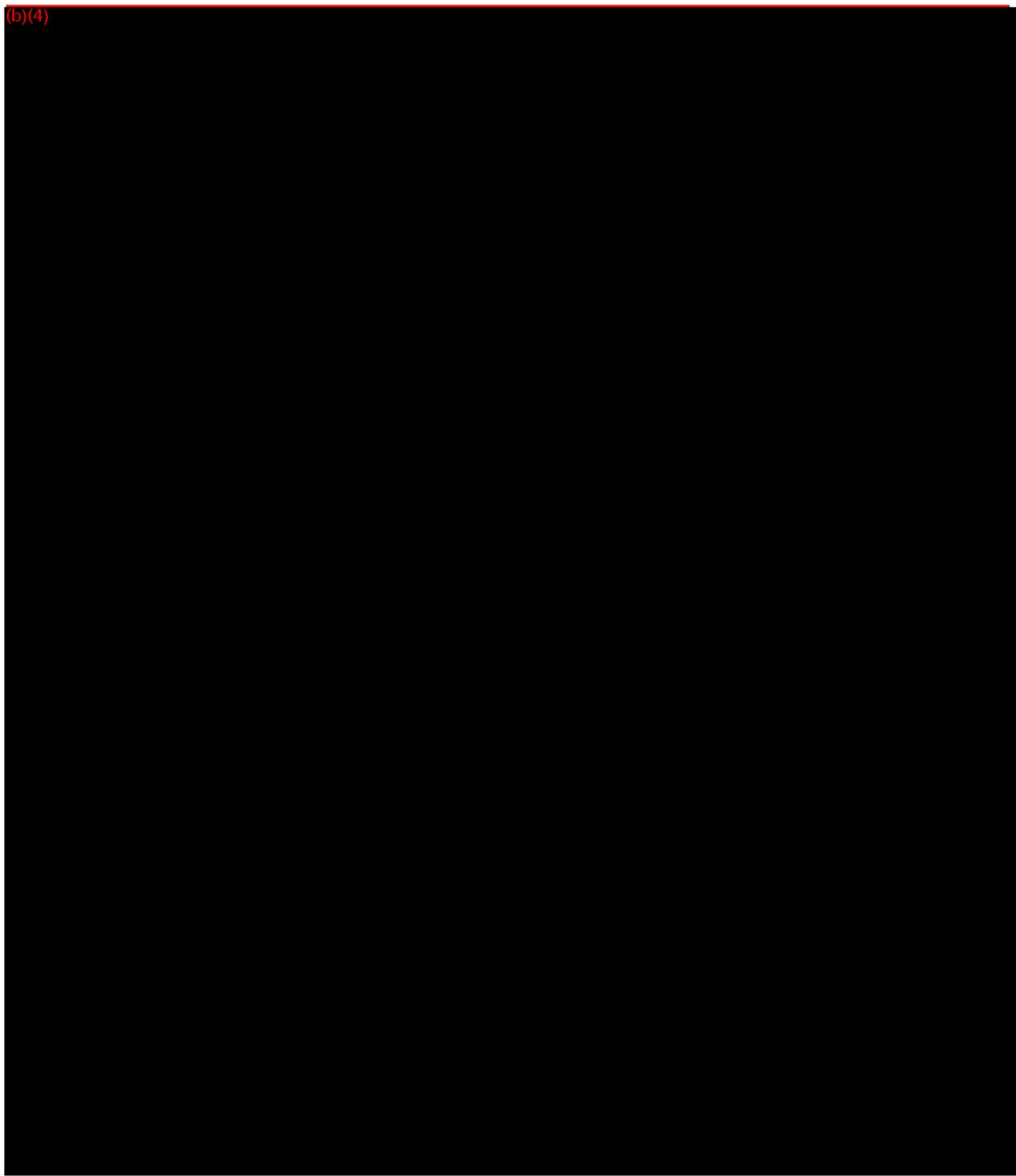
(b)(4)

4.0 Test Principle

Enter a brief description of the technology/methodology utilized in the device (i.e., describe how the device works). Describe the principles of the device methodology and whether it is well established or new for the intended use (provide references). Include relevant technical specifications of material and methods not included in the draft package insert (e.g., description of antibodies and epitopes). *

(b)(4)

(b)(4)



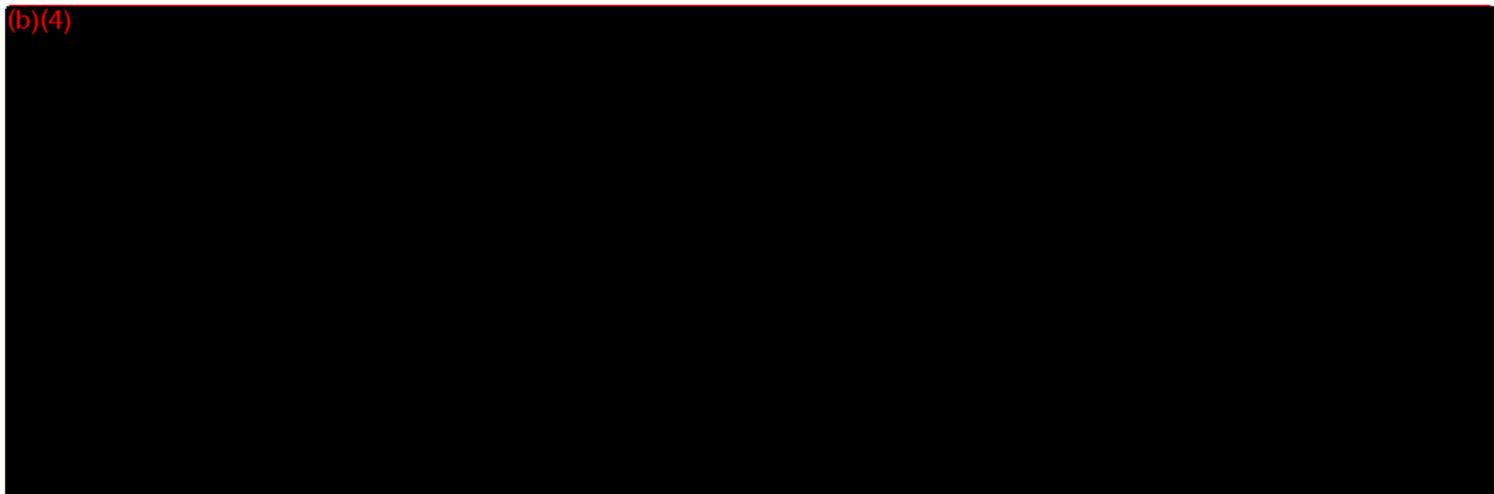
Biological specimens

The biological specimen types validated for use in the BioPlex 2200 25-OH Vitamin D assay is human serum only

File Attachment 1	13231_25-OH Vitamin D Assay - Assay Parameters and Test Principle
File Attachment 2	C of A - Antibody to 25-hydroxyvitamin D
File Attachment 3	C of A - Biotinylated 25-OH Vitamin D
File Attachment 4	C of A - SA-PE

5.0 Performance Characteristics

(b)(4)



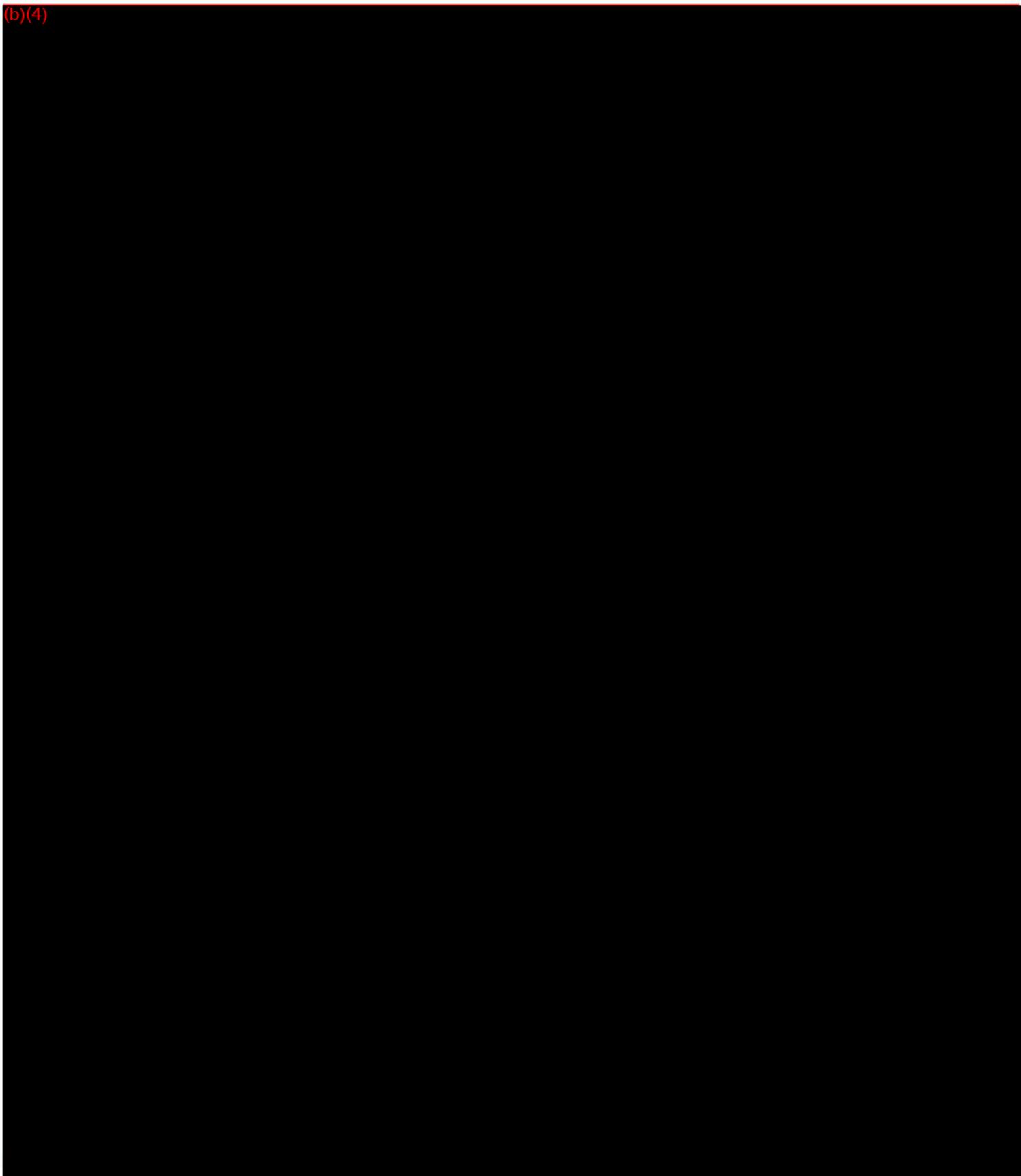
5.1 Analytical Performance

5.1.1 Analytical Limits at Low Levels

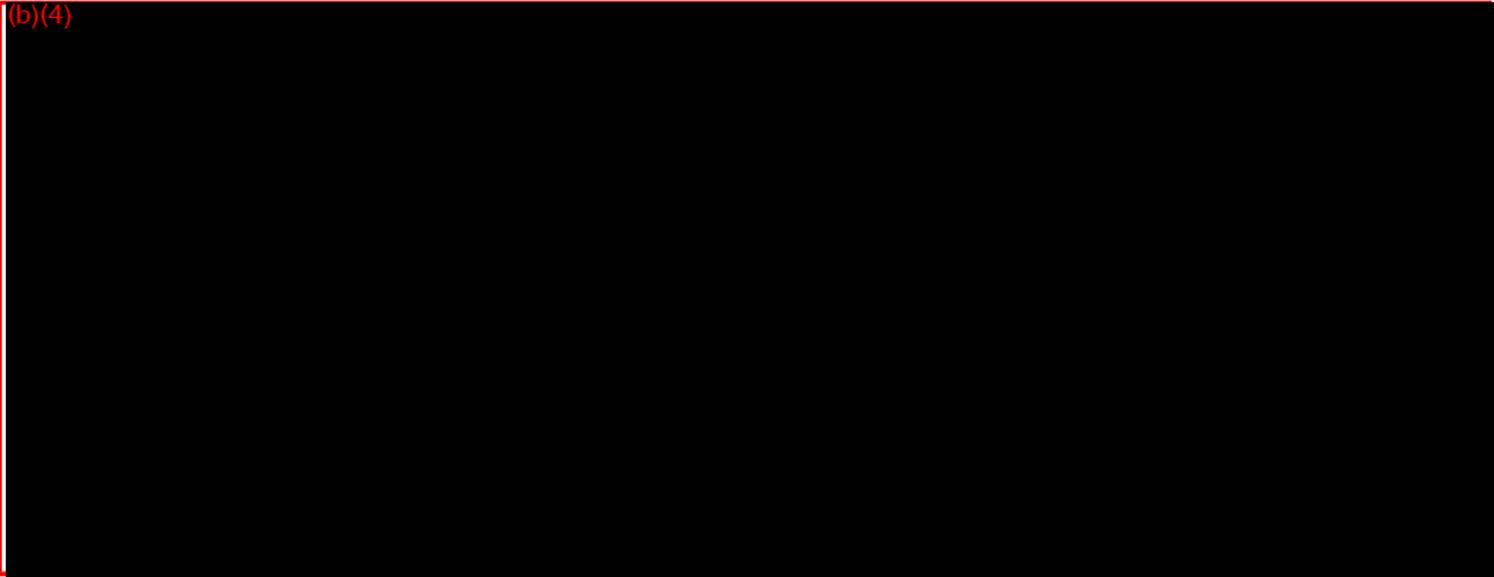
(b)(4)



(b)(4)



(b)(4)

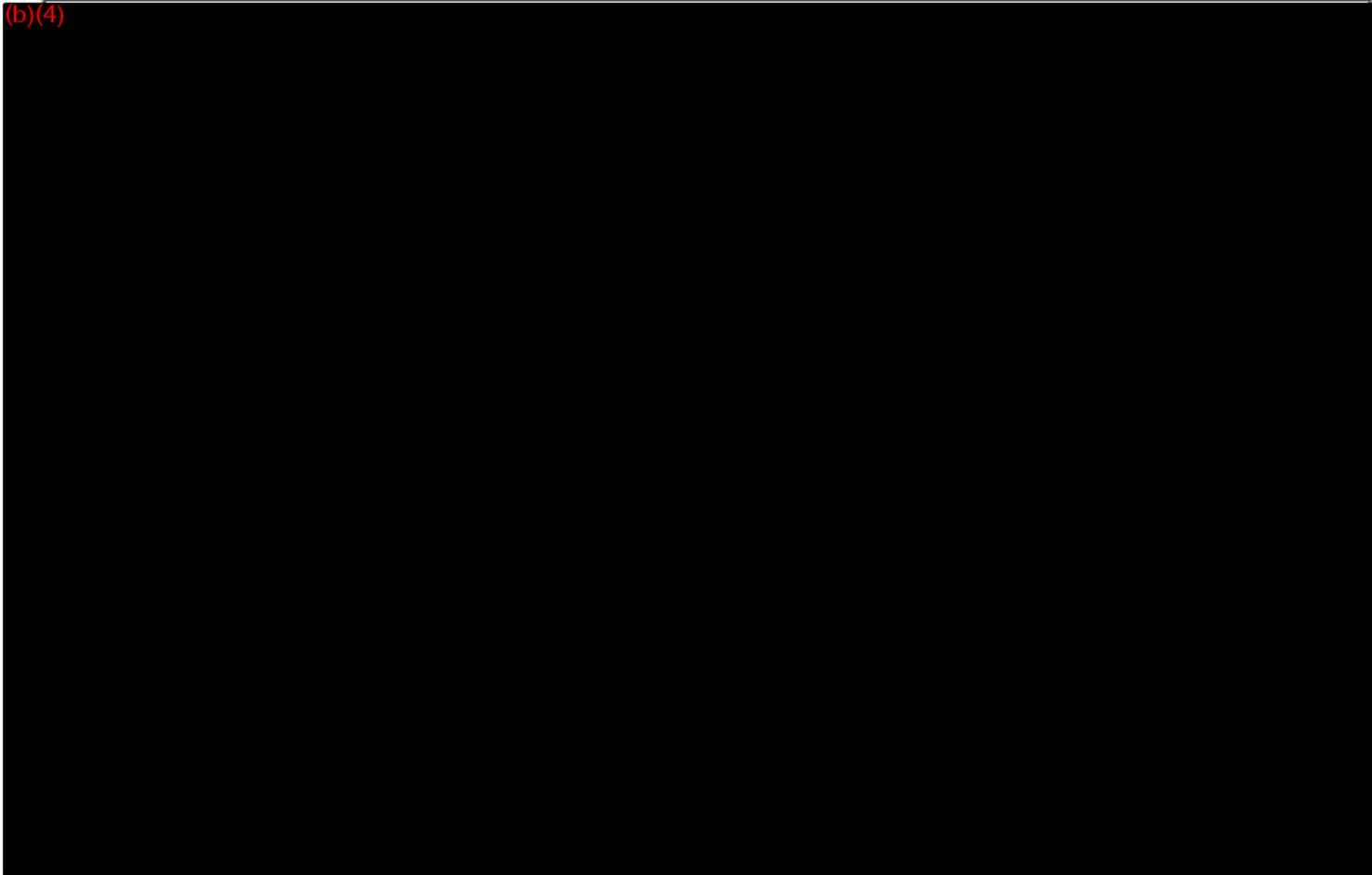


5.1.2 Precision (Repeatability/Reproducibility)

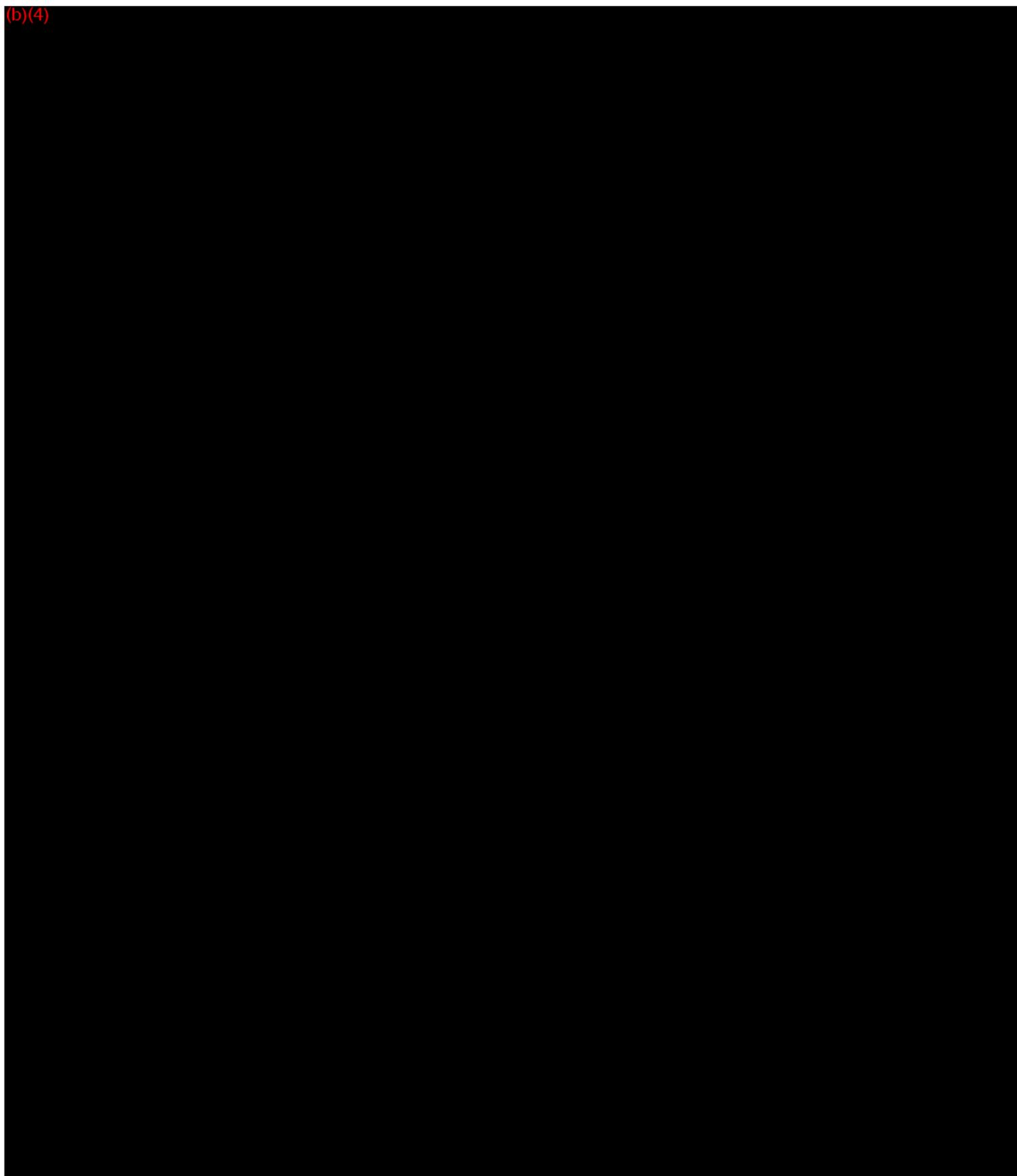
Enter a description of studies and results to evaluate estimates of total variability for each specimen type. Include, as appropriate, repeatability (within-run) and reproducibility such as between-day, between-run, within-day, between-sites, between-lots, between instrument, and between operator(s), etc.

*

(b)(4)



(b)(4)



Enter a description of specimens (samples) used to study variability including matrix, sample type (e.g., patient samples, spiked samples, control material), and preparation, including analyte levels and how they were established. Describe the relationship between the analyte levels to measuring (reportable) range and medical decision points.

*

CLSI EP5-A2 Reproducibility

Serum samples spanning the range of the assay (6.5 to 150 ng/mL) were procured from commercial vendors. Samples were drawn naturally from individual subjects and grouped into three analyte concentration categories (10 – 24.5, 25 – 50, and 51 – 150 ng/mL). The BioPlex 25-OH Vitamin D Control Set (two levels) was also included in the study.

CLSI EP15-A2 Reproducibility Study

The BioPlex 2200 25-OH Vitamin D reproducibility panel consists 8 members that were made in serum and two levels of QC controls. Serum samples spanned the assay range as shown below were collected from individual subject and provided to the clinical trial site.

- two (2) between 6.5 and 15 ng/mL
- two (2) between 20 and 30 ng/mL
- two (2) between 40 and 60 ng/mL
- two (2) between 80 and 150 ng/mL

Enter a description of sources of variability examined (e.g. runs, instruments, operators, days; sites at which variability studies were performed; reagent lots and instruments studies with identifying information).

*

EP5-A2 Reproducibility Study

One lot each of the BioPlex 25-OH Vitamin D Reagent pack, Calibrator set and Control set was evaluated internally at Bio-Rad. Each of panel sample members (Serum) plus two levels of controls were tested in duplicates on two runs per day over 20 days (2 replicates x 2 runs x 20 days = 80 replicates per panel member).

CLSI EP15-A2 Reproducibility Study

One validation lot each of the BioPlex 25-OH Vitamin D reagent pack, calibrator set and control set was evaluated internally at Bio-Rad. Each of the sample panel members (serum) plus two levels of QC controls were tested in duplicates on two runs per day over 5 days on each one BioPlex 2200 instruments (2 replicates x 2 run per day x 5 days = 20 replicates per panel member).

Enter a description of statistical methods used to analyze data; include any model assumptions.

*

CLSI EP5-A2 Reproducibility

Twenty days of precision data were collected using a single instrument and one lot each reagent pack, calibrator set, and control set. Two runs were performed each day separated by at least two hours. Assay calibration was conducted at the start of the study and all samples were randomized for each run. Controls were run before and after each run to qualify the run. Each sample was run in duplicate per run for a total of eighty data points per sample for the twenty day analysis. Precision was determined by calculating the within-run (intra-assay), between-run (inter-assay), between-day (inter-assay), and total precision based on CLSI EP5-A2 guideline, *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline*.

CLSI EP15-A2 Reproducibility Study

Each of the serum sample panel members plus controls were tested in duplicates on two runs per day over 5 days on one BioPlex 2200 instrument (4 replicates x 1 run per day x 5 days = 20 replicates per panel member). Precision was determined by calculating the within-run (intra-assay), between run (inter-assay), between day (inter-assay), and total precision based on CLSI EP15-A2 guideline, *User Verification of Performance for Precision and Trueness; Approved Guideline*.

For quantitative or qualitative assays with numerical values, report the number of measurements, mean, standard deviation, and %CV for each parameter tested and for each level tested.

*

CLSI EP5-A2 Reproducibility Study

All precision results passed the specifications (%CV) for the panel members above or at 25 ng/mL : Within run ≤ 8%, Between-run ≤ 10%, Between-day ≤ 10% and Total precision ≤ 12%.

The within run, between-run, between-day, and total precision for the serum panel are summarized below. Please refer to [13285 BioPlex 25-OH Vitamin D CLSI Precision Report and Data Line Listing](#).

BioPlex®2200 25-OH Vitamin D: Serum Samples

Precision Sample	N	Mean	Within Run	Between Run	Between Day	Total
------------------	---	------	------------	-------------	-------------	-------

		(ng/mL)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
Sample 2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
Sample 3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
Sample 4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
Sample 5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
Sample 6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
QC Control Level 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
QC Control Level 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

CLSI EP15-A2 Reproducibility Study

The results of within-run, between-day and total precision for the serum panel are presented below. Please refer to [13294 BioPlex 25-OH Vitamin D EP15-A2 Reproducibility Summary Report](#).

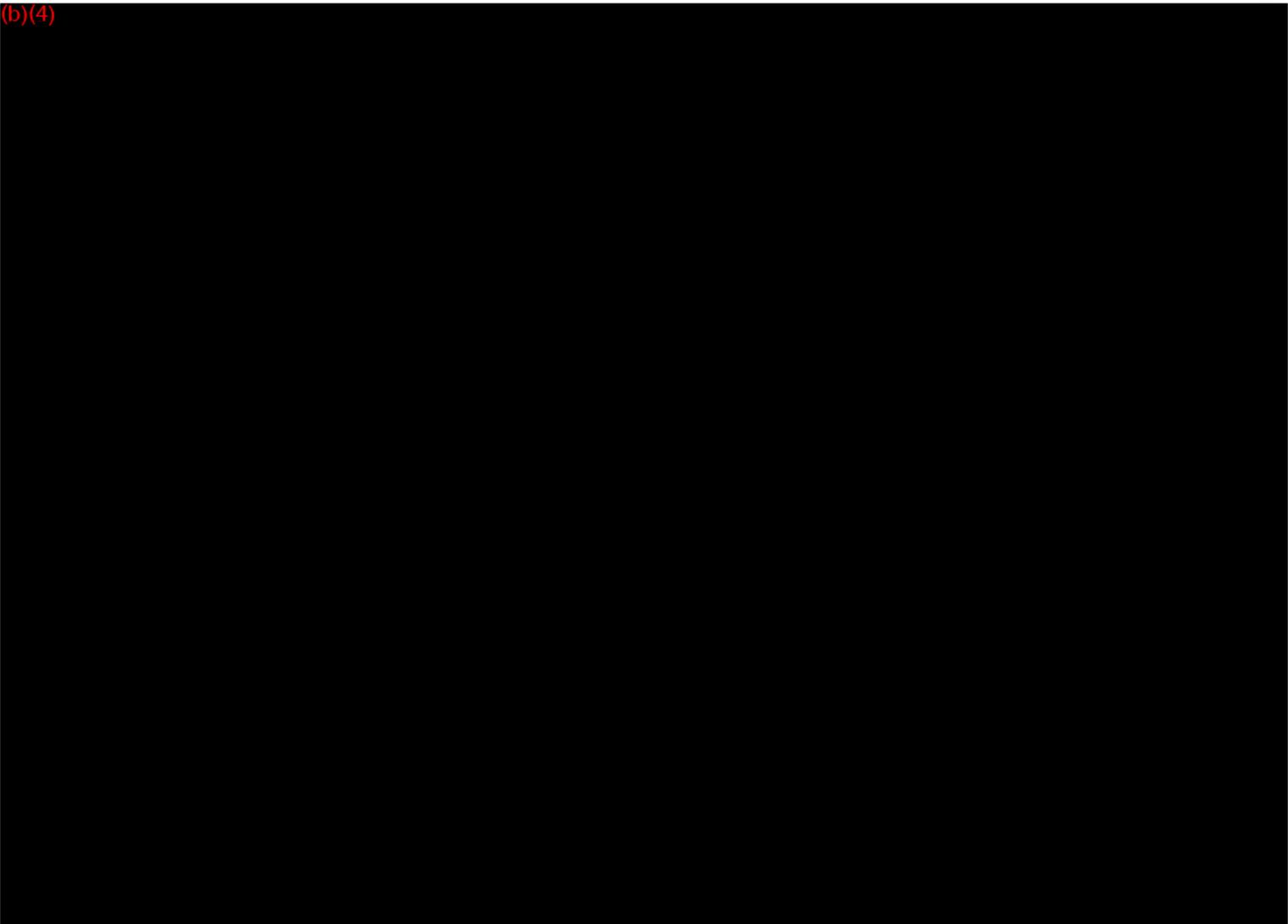
BioPlex®2200 25-OH Vitamin D – CLSI EP15-A2 Precision

Precision Sample	N	Mean (ng/mL)	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	20	11.5	0.69	6.0%	0.47	4.1%	1.49	12.9%	1.71	14.8%
Sample 2	20	13.6	0.80	5.9%	0.26	1.9%	0.84	6.2%	1.18	8.7%
Sample 3	20	26.1	0.88	3.4%	1.15	4.4%	0.65	2.5%	1.59	6.1%
Sample 4	20	30.2	1.99	6.6%	0.00	0.0%	1.84	6.1%	2.71	9.0%
Sample 5	20	50.2	2.23	4.4%	0.77	1.5%	1.79	3.6%	2.96	5.9%
Sample 6	20	56.4	2.09	3.7%	2.79	4.9%	3.94	7.0%	5.26	9.3%
Sample 7	20	100.5	4.52	4.5%	2.81	2.8%	0.00	0.0%	5.32	5.3%

Sample 8	20	104.9	3.97	3.8%	1.54	1.5%	3.06	2.9%	5.24	5.0%
QC Control Level 1	20	21.6	0.98	4.5%	1.00	4.6%	1.19	5.5%	1.84	8.5%
QC Control Level 2	20	58.8	2.44	4.2%	1.29	2.2%	1.16	2.0%	2.99	5.1%

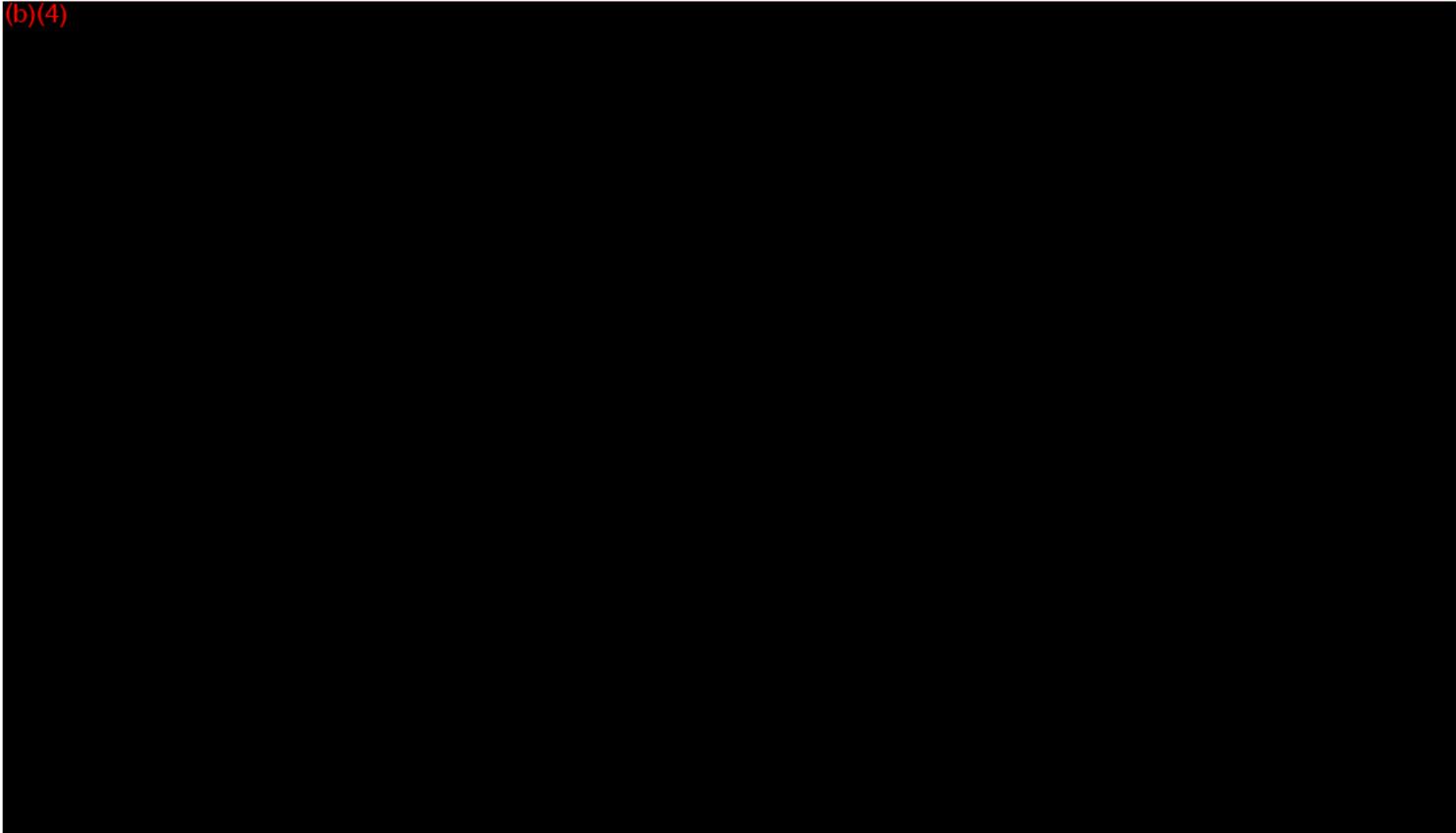
For qualitative assays, report the number of replicates, the concentration of the sample, the number of positive and negative results, and the number of invalid or equivocal results, if applicable. For reproducibility studies for qualitative tests, provide an estimate of the precision of the method at analyte concentrations near the cutoff.

5.1.3 Linearity/Assay's Measuring (Reportable) Range



(b)(4)

(b)(4)



Enter the linear range and measuring (reportable) range. Include the measure of deviation from linearity, if applicable. *

The assay linearity testing is to validate the reportable range of the BioPlex 2200 25-OH Vitamin D kit. The assay range was established by examining the clinical relevance of reporting high value results and the ability of the calibration curve to discriminate sample dilutions.

Five samples with high Vitamin D levels (10 to 20% higher than the expected upper limit) were serially diluted in a sample with low levels of vitamin D (near the limit of quantitation) according to CLSI EP06-A. Each one of the diluted samples was evaluated in replicates of four using 25-OH Vitamin D kit. High dose hook effect was not evaluated because it is not relevant for two-step indirect assays with a washing cycle implemented.

(b)(4)



Enter a description of how reportable range is determined including acceptance criteria or results for accuracy, precision, or other characteristics within this range. *



(b)(4)

Enter a description of specimen type and preparation including information on matrix, analyte levels, and the methods used to determine the target levels. *

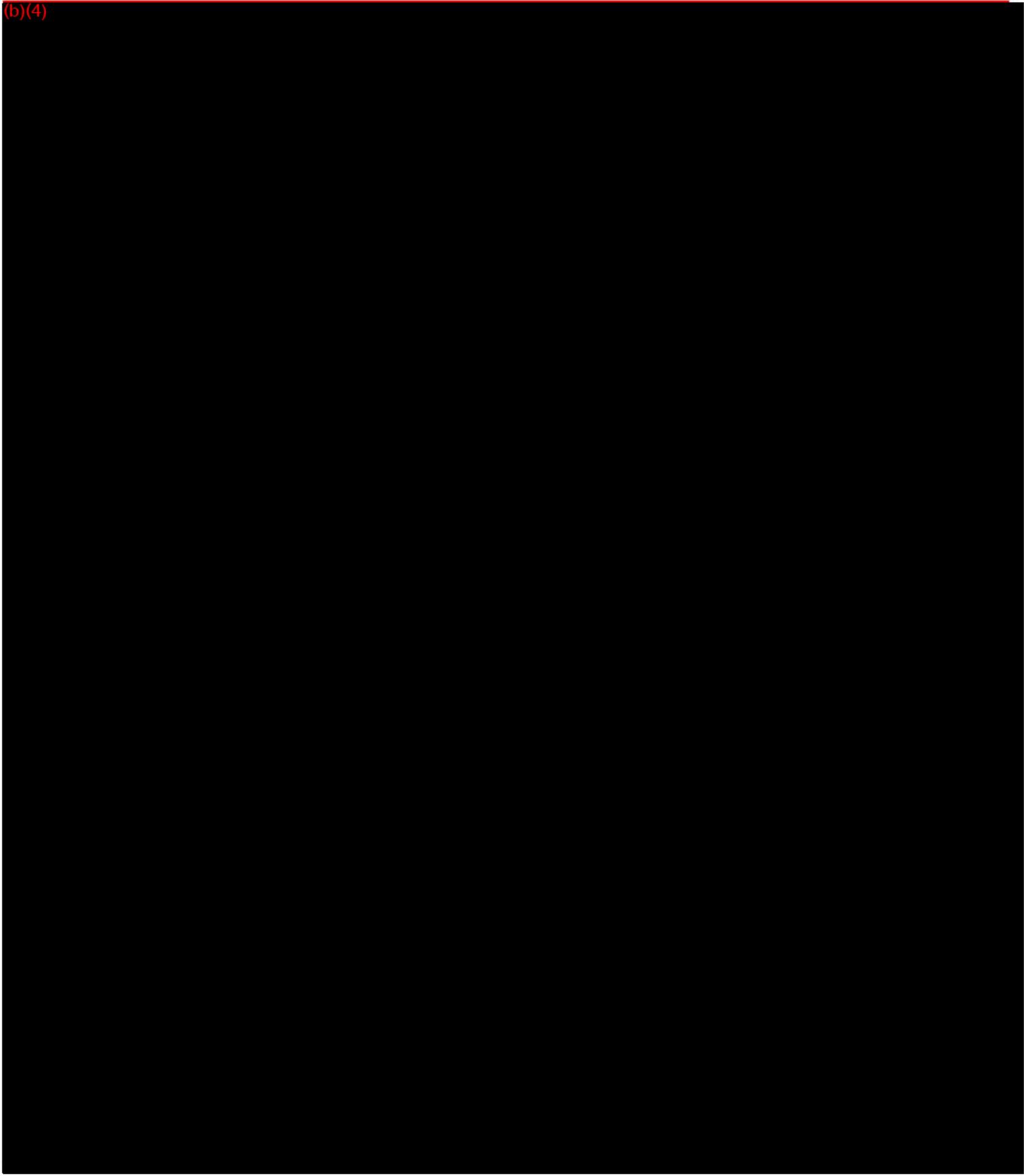
The assay linearity testing is to validate the reportable range of the BioPlex 2200 25-OH Vitamin D kit. The assay range was established by examining the clinical relevance of reporting high value results and the ability of the calibration curve to discriminate sample dilutions.

Five samples with high Vitamin D levels (10 to 20% higher than the expected upper limit) were serially diluted in a sample with low levels of vitamin D (near the limit of quantitation) according to CLSI EP06-A. Each one of the diluted samples was evaluated in replicates of four using 25-OH Vitamin D kit. High dose hook effect was not evaluated because it is not relevant for two-step indirect assays with a washing cycle implemented.

(b)(4)



(b)(4)



ng/mL.

The BioPlex 2200 System does not support an on-board dilution feature for testing over-range samples.

Describe validation of instructions for out-of-range specimens, if applicable.

*

the BioPlex 2200 System does not support an on-board dilution feature for testing over-rang samples.

Enter discussion of possible high-dose hook effect, if applicable.

*

high does hook effect was not evaluated because it is not relevant for a two-step indirect assay with a wash cycle.

5.1.4 Calibrators and Controls

Are calibrators or controls included in the submission?

* Yes

If you answered "no" to the above questions explain why.

Enter the 510(k) number.

Provide information on the commercial source and control preparation methods.

Enter information if external calibrators or controls are to be cleared with this device. Include analyte levels, matrix, preparation method, value assignment and validation, traceability of the calibrator to a reference material as appropriate, stability study summary, storage conditions, frequency of testing, control reference, acceptance limit, how the recommended calibration and control testing frequency were established, validation of the standard curve by replicate analysis of calibrators, and validation of quality control, as appropriate (e.g., novel, internalized quality control).

*

BioPlex 2200 25-OH Vitamin D Calibrator Set

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D Reagent Pack.

The BioPlex 2200 25-OH Vitamin D Reagent Kit is calibrated using a set of six distinct serum based calibrators, which are used to establish points of reference for determining the presence of 25-OH Vitamin D in human serum. Calibrator Levels 2-6 are made in human serum matrix derived from Vitamin D depleted human plasma. Known concentrations of 25-OH Vitamin D3 determined by UV spectrophotometric analysis are added to the depleted serum that is supplemented with ProClin 950 ($\leq 0.3\%$), sodium benzoate ($\leq 0.1\%$) and 5-bromo-5-nitro-1,3-dioxane ($< 0.1\%$). Calibrator level 1 was prepared by diluting inactivated horse serum in 50 mM phosphate buffer saline to a final concentration of 25% supplemented with ProClin® 950, sodium benzoate and 5-bromo-5-nitro-1,3-dioxane. Level 1 is manufactured independent of Levels 2-6.

The calibrators are loaded directly into the BioPlex 2200 instrument sample racks and assayed before control or patient samples are processed. The assay output signal is correlated to the analyte concentration of each calibrator level in order to generate the assay calibration curve, and the analyte concentrations of the controls and patient samples using 4-Parameter Logistic (4-PL) curve fit. Measurement of the ability of a stored calibration curve to quantify controls and samples over time without significant shift in quantitation demonstrated on-board calibration curve stability of at least 30 days. (b)(4)

(b)(4)

Calibrator assignment is established for matched lots of BioPlex 2200 25-OH Vitamin D kits by comparing the results with the Master set. The Master calibrator set is traceable to internal standard (stock), the value of which was determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength. The mean values listed in the Assigned Calibrator Values Sheet for the BioPlex 2200 25-OH Vitamin D Calibrator Set are derived from replicate measurements on multiple BioPlex 2200 instruments with specific reagent lot. (b)(4)

(b)(4)

(b)(4)

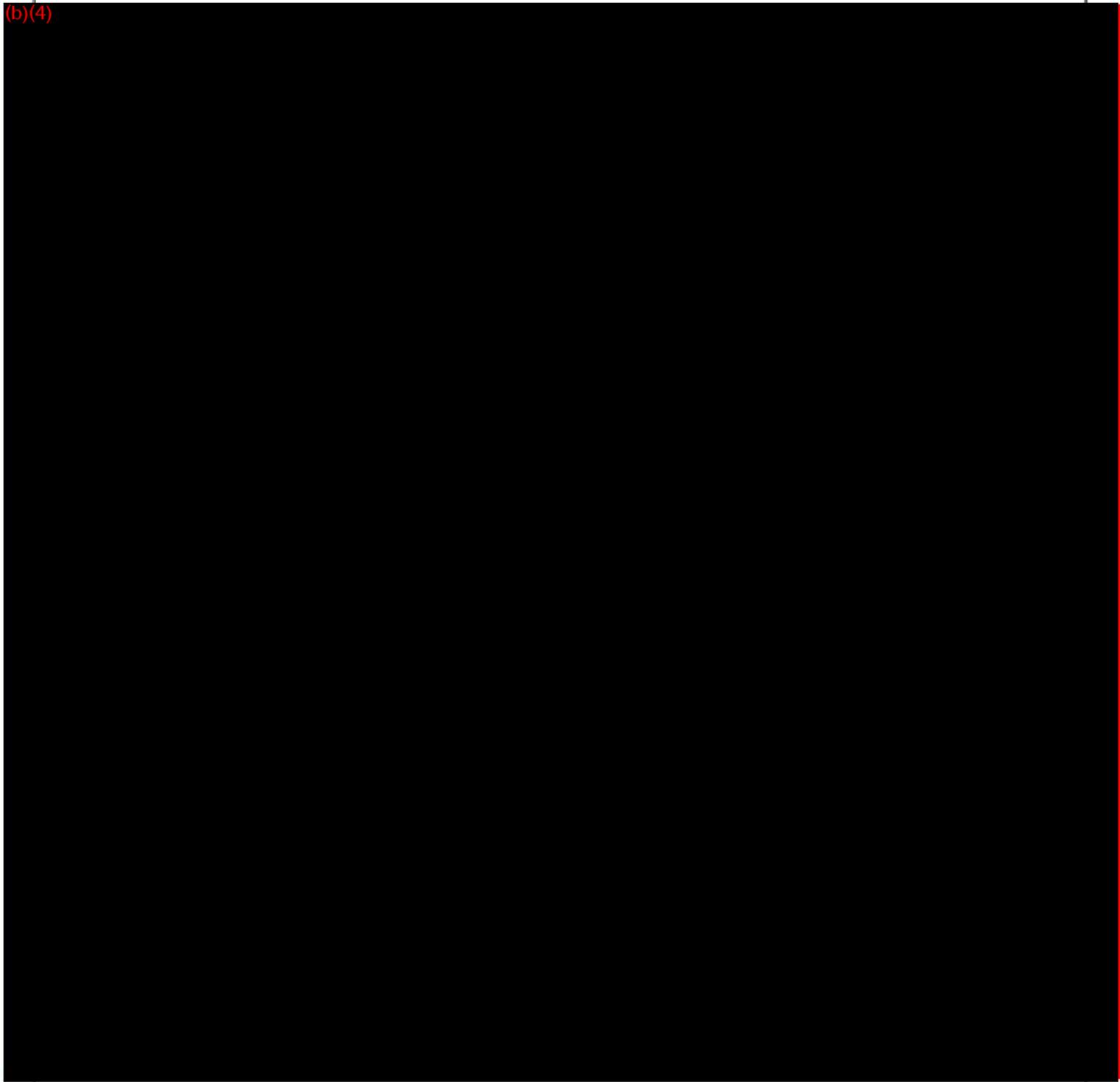
(b)(4)

is required for 25-OH Vitamin D calibration.

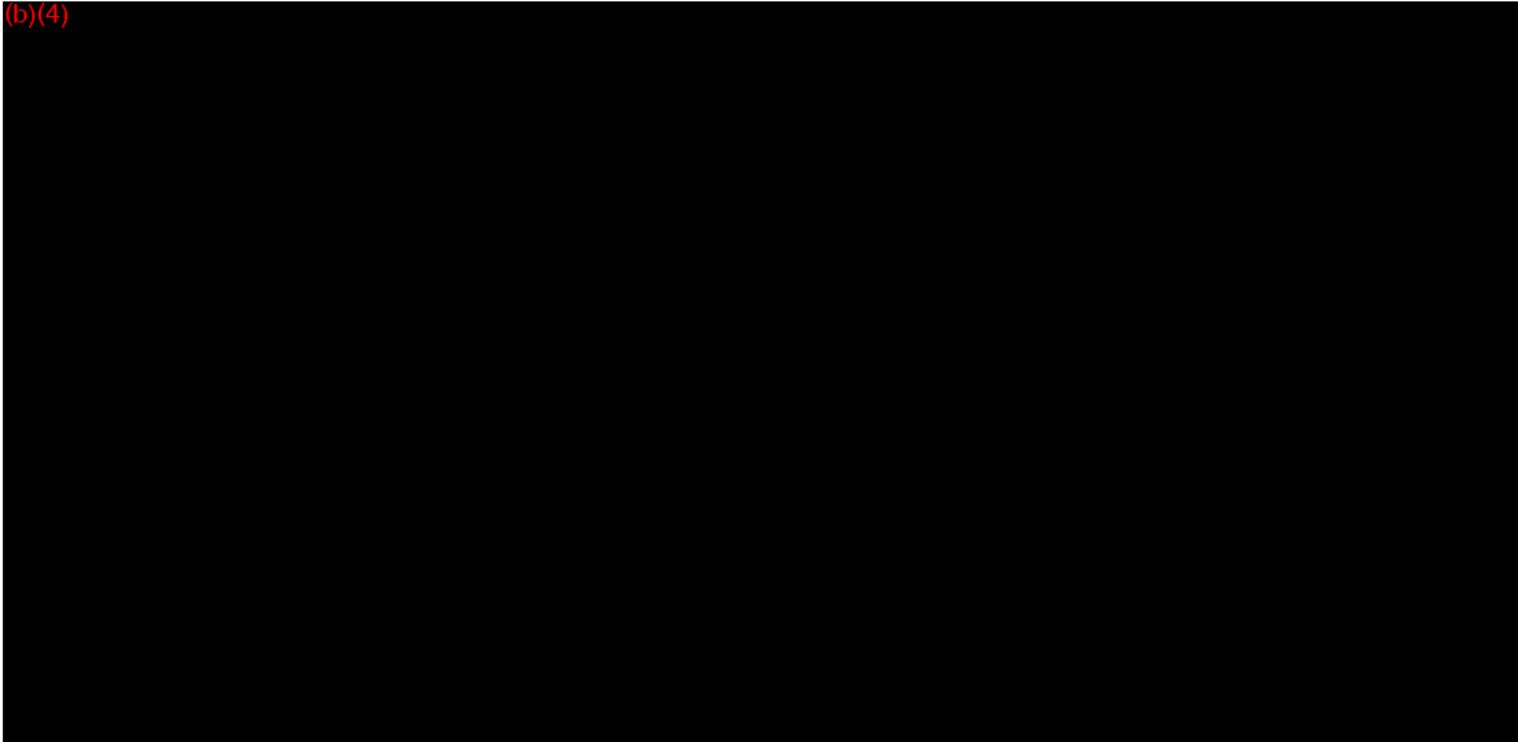
BioPlex 2200 25-OH Vitamin D Control Set

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 25-OH Vitamin D Kit in the clinical laboratory. The performance of the BioPlex 2200 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

(b)(4)



(b)(4)



Enter the description of internal controls, the reaction, functions monitored, and frequency of controls needed, if applicable. *

Not Applicable

Please refer to attached 13288 BioPlex 25-OH Vitamin D Calibrator and Control Stability Report and data line listing shown above.

5.1.5 Traceability, Stability, Expected Values (Controls, Calibrators, Methods)

Where applicable, briefly summarize the following information about calibrators and controls: method and acceptance criteria for opened and closed stability studies, traceability to reference material, and description of value assignment, validation, and acceptance criteria. *

BioPlex 2200 25-OH Vitamin D Calibrator Set

Calibrator assignment is established for matched lots of BioPlex 2200 25-OH Vitamin D kits by comparing the results with the Master set. The Master calibrator set is traceable to internal standard (stock), the value of which was determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength. The mean values listed in the Assigned Calibrator Values Sheet for the BioPlex 2200 25-OH Vitamin D Calibrator Set are derived from replicate measurements on multiple BioPlex 2200 instruments with specific reagent lot. (b)(4)

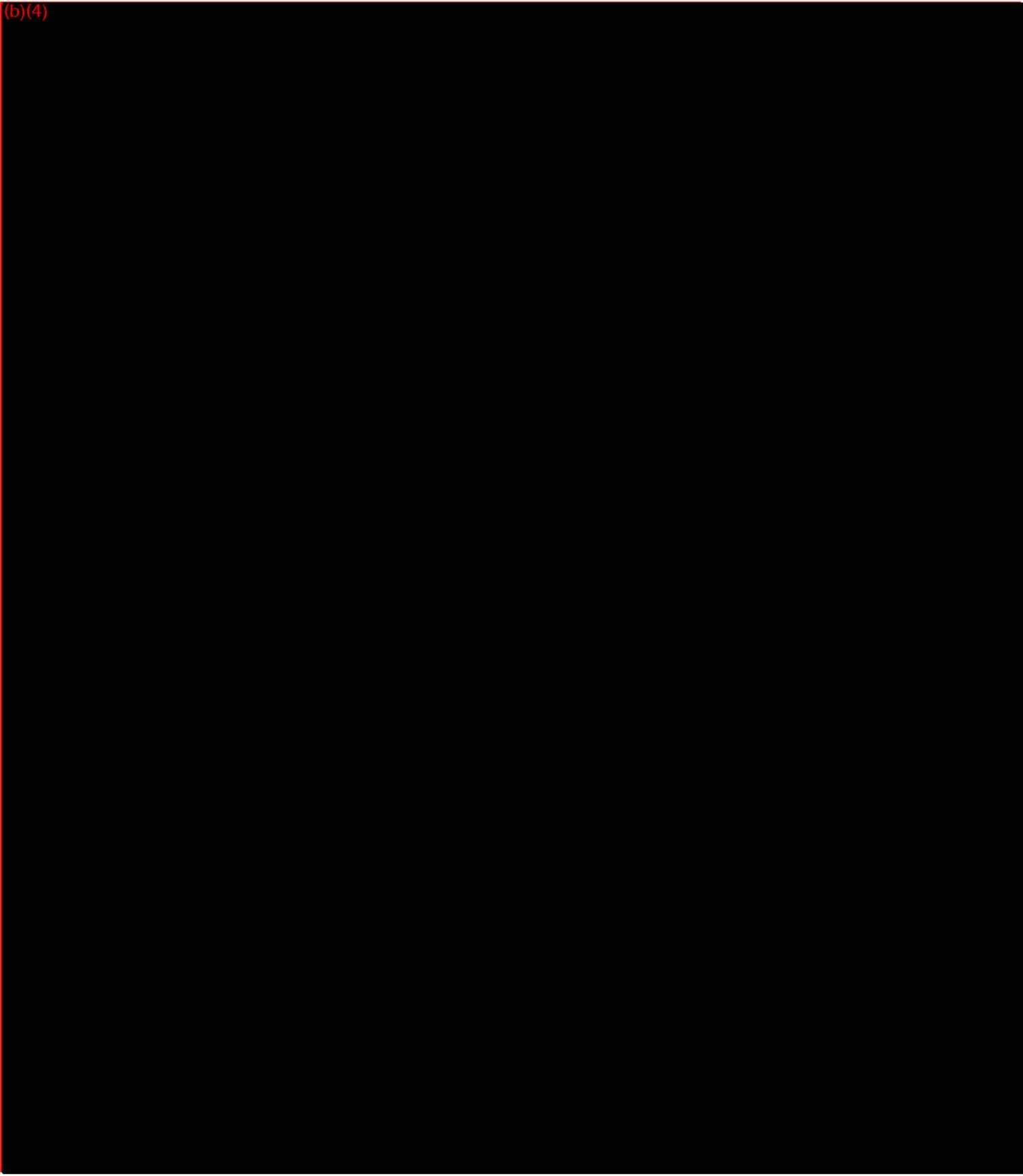
(b)(4)

(b)(4)

(b)(4)



(b)(4)



calibration curve stability claim. The study is repeated every three months for up to 27 months in order to verify the stability of the calibration curve as the kits age.

Please refer to the attached [13282 BioPlex 25-OH Vitamin D Onboard Calibration Curve Stability Report and data line listing](#).

Expected Values (Method)

The study was performed in accordance with CLSI C28-A3c guideline. Two hundred and eighty-seven (287) samples from apparently healthy light and dark skin donors including 160 males ranging in age from 21 to 79 and 127 females ranging in age from 21 to 66 were collected from three regions (North, Central, and South) in the US over three seasons (spring, summer and winter). The healthy donors met the selection criteria as described in the attached clinical summary report.

The observed expected values (Reference Values) including median, mean, and range between 2.5th to 97.5th percentile in ng/mL is shown below.

Please refer to the attached [14004 BioPlex 25-OH Vitamin D Clinical Study Summary Report and data line listing](#) in Section 5.2.1.

Mean	Median	2.5 th – 97.5 th percentile
29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

File Attachment 1	12984 Kit Real Time Stability Report
File Attachment 2	13282 Calibration Curve Stability Report
File Attachment 3	Data line listing - Calibration Curve Stability

5.1.6 Analytical Specificity

Enter a description of study design and statistical methods. *

Separate interfering substances and cross reactivity studies were conducted internally at Bio-Rad to evaluate the potential interference of specific endogenous and exogenous substances and to determine if cross reactivity occurs with the BioPlex 25-OH Vitamin D kit.

Interfering Substances

The purpose of interference testing is to measure the effects of structurally unrelated substances such as endogenous serum components (proteins and lipids) and exogenous molecules such as anticoagulants on assay performance. This study was conducted internally at Bio-Rad in accordance with CLSI guideline EP7-A2, *Interference Testing in Clinical Chemistry*, in which it defines interference as an effect that exceeds the normal assay variability and where incremental error caused by the substance is large enough to affect clinical decision making. Substances are considered interfering if their presence in a sample results in more than $\pm 10\%$ deviation in quantitation relative to the value determined in the absence of the substance.

(b)(4)

Please refer to the attached [13280 BioPlex 25-OH Vitamin D Analytical Specificity Interfering Substances Report and data line listing](#).

Cross Reactivity

The purpose of this study is to determine whether structurally similar vitamin D compounds and its analogs cross react with the BioPlex 2200 25-OH Vitamin D assay. Testing was performed on one of the BioPlex 2200 platforms using two reagent lots with spiked cross reactants and endogenous (non-spiked) serum samples.

(b)(4)

(b)(4)

(b)(4)

Please refer to the attached [13281 BioPlex 25-OH Vitamin D Cross Reactivity Report and data line listing](#).

File Attachment 1	13280 Analytical Specificity - Interfering Substance Report
File Attachment 2	Data line listing - Interfering Substances
File Attachment 3	13281 Cross Reactivity Report
File Attachment 4	Data line listing - Cross Reactivity

Enter the specimen description and preparation including matrix, analyte levels present in the sample, and how these levels were established. *

Interfering Substances

(b)(4)

Cross Reactivity

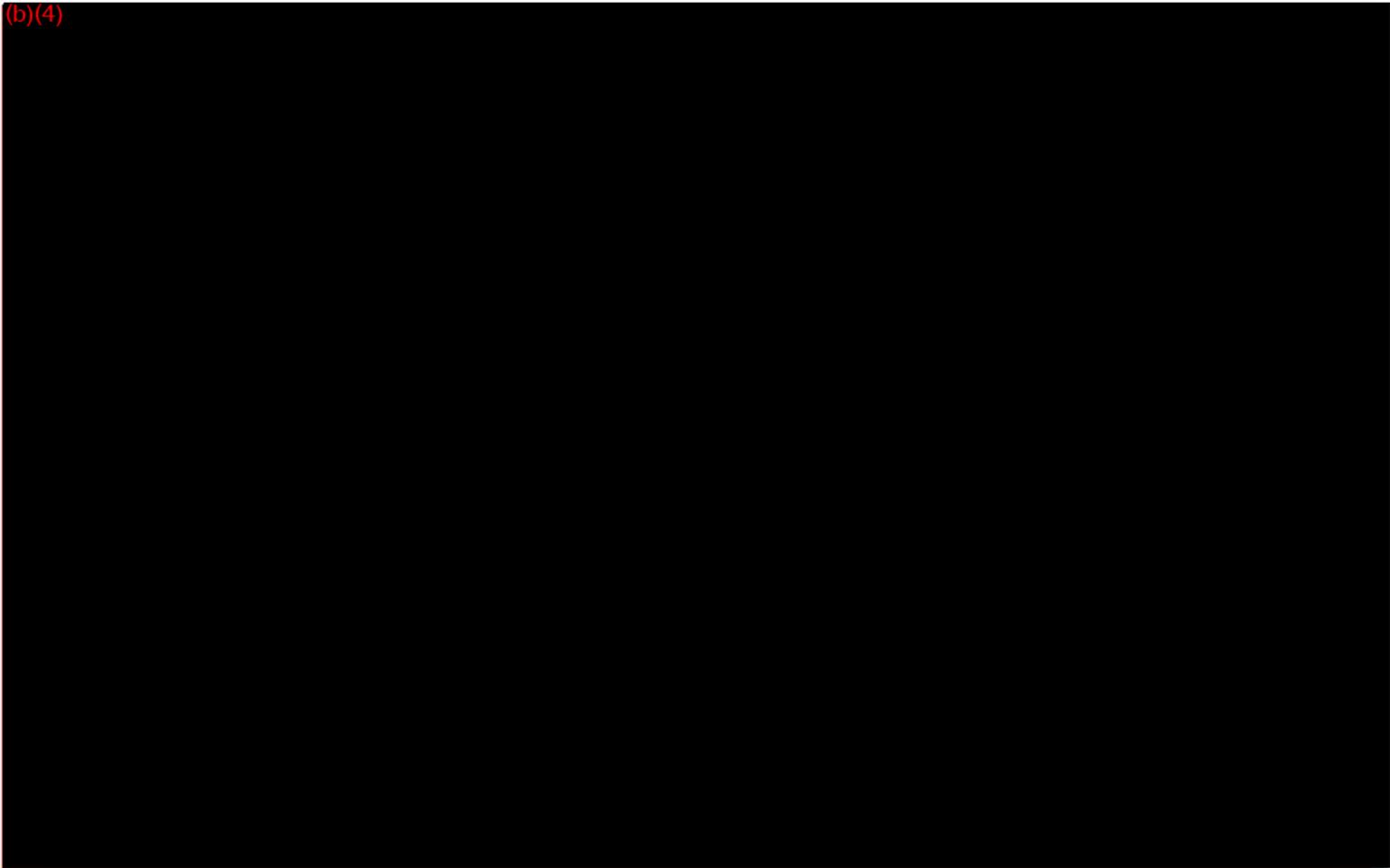
(b)(4)

Enter a list of the potentially cross-reactive and interfering substances tested including those where a similar syndrome can be associated with more than one analyte/agent/organism. Also include the concentrations at which these substances were present in the samples (indicate highest concentration tested and/or lowest concentration at which an effect was observed). Finally, include the number of replicates tested for each substance. *

Interfering Substances

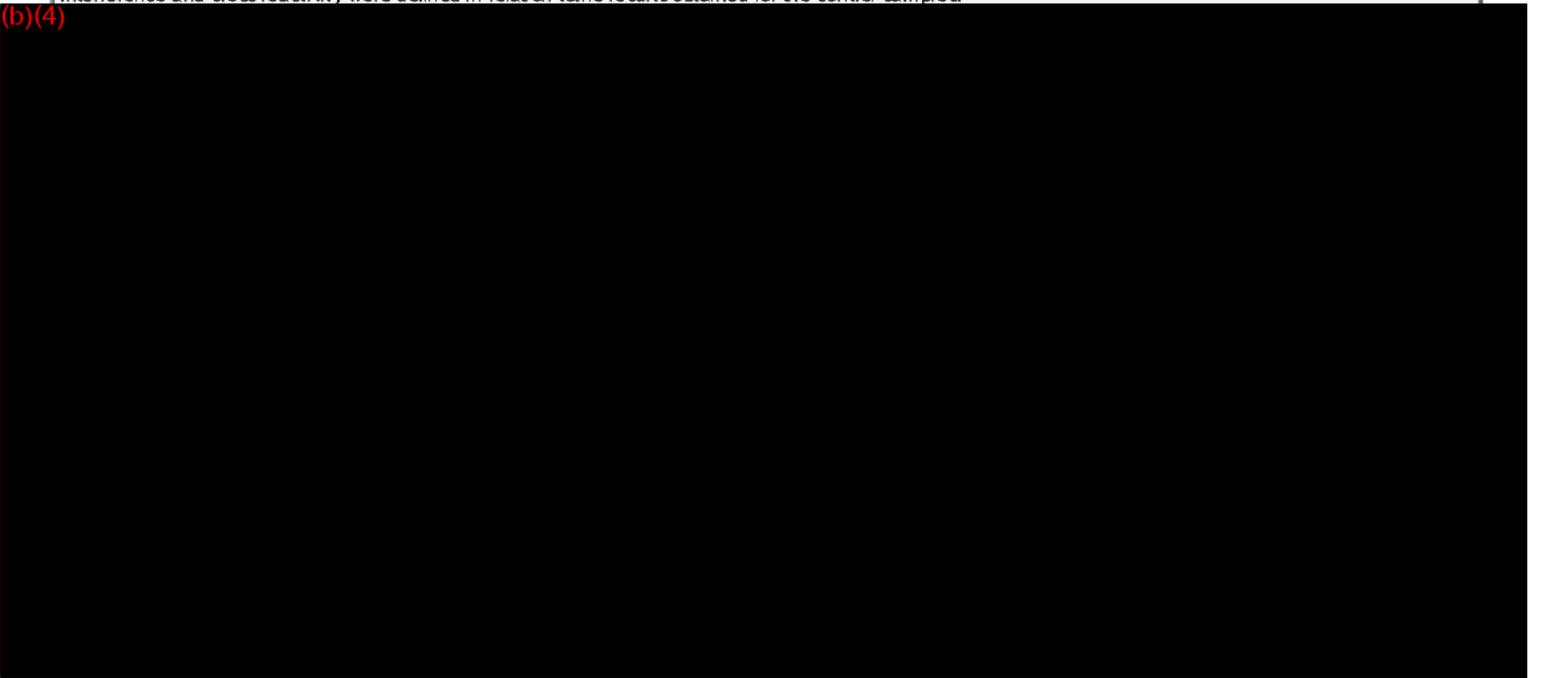
(b)(4)

(b)(4)



Enter a description of the positive and negative control samples that served as a reference to identify any interference or cross reactivity. Describe how interference and cross reactivity were defined in relation to the results obtained for the control samples. *

(b)(4)



Interfering Substances

(b)(4)
(b)(4)

Please refer to the attached [13280 BioPlex 25-OH Vitamin D Analytical Specificity Interfering Substances Report](#) in this section.

Cross Reactivity

Cross reactivity, expressed as percentage, is calculated by the ratio of the difference between test and control results divided by the spiked cross reactant concentration.

Please refer to the attached [13281 BioPlex 25-OH Vitamin D Cross Reactivity Report](#) in this section.

Bio-Rad proposes listing the following mean cross-reactivity results of the BioPlex 25-OH Vitamin D assay in the IFU.

Cross Reactant	Mean % Cross Reactivity
25-hydroxyvitamin D2	103%
25-hydroxyvitamin D3	97%
Vitamin D2	0.2%
Vitamin D3	0.0%
1,25-dihydroxyvitamin D2	>100%
1,25-dihydroxyvitamin D3	79%
3-epi 25-hydroxyvitamin D3	59%
24,25-dihydroxyvitamin D3	9%
Paricalcitol (Zemplar)	>100%

5.1.7 Analytical Characterization of Cut-off

Enter the rationale for the units, cut-off and/or categories of the results.

*

Not Applicable - BioPlex 2200 25-Oh Vitamin D is a quantitative assay.

Enter a description of specimen preparation including analyte levels, matrix, and how level was established.

*

Not Applicable - BioPlex 2200 25-Oh Vitamin D is a quantitative assay.

Enter a definition of "equivocal zone," if applicable.

*

Not Applicable - BioPlex 2200 25-OH Vitamin D is a quantitative assay.

Enter the statistical method used (e.g., Receiver Operator Characteristic Analysis). *

Not Applicable - BioPlex 2200 25-OH Vitamin D is a quantitative assay.

5.1.8 Instrument Only

Accuracy

Compare each test parameter to either a reference method or a predicate device with the same intended use. Use a testing pool that contains samples representative of the appropriate population. Include an equal number of males and females for which samples span the reportable range. Include specimens that are close to the clinically critical decision point(s). Present the data using linear regression, including 95% confidence intervals for the slope and y-intercept. Provide scatter plots.

Precision/Reproducibility

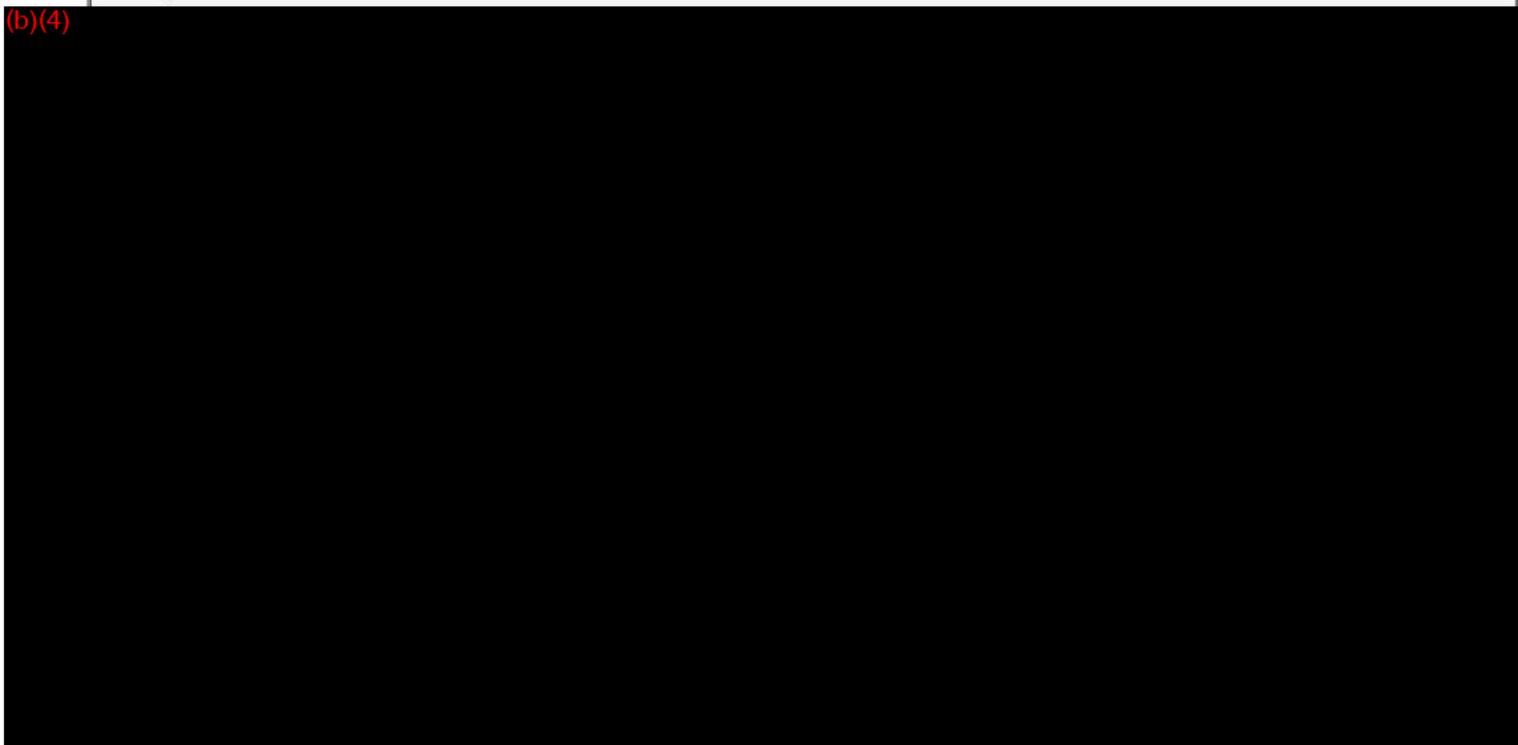
Provide estimates of intra, inter, lot-to-lot, operator-to-operator, and total imprecision for each measurand parameter of the device using samples that span the testing range.

Linearity

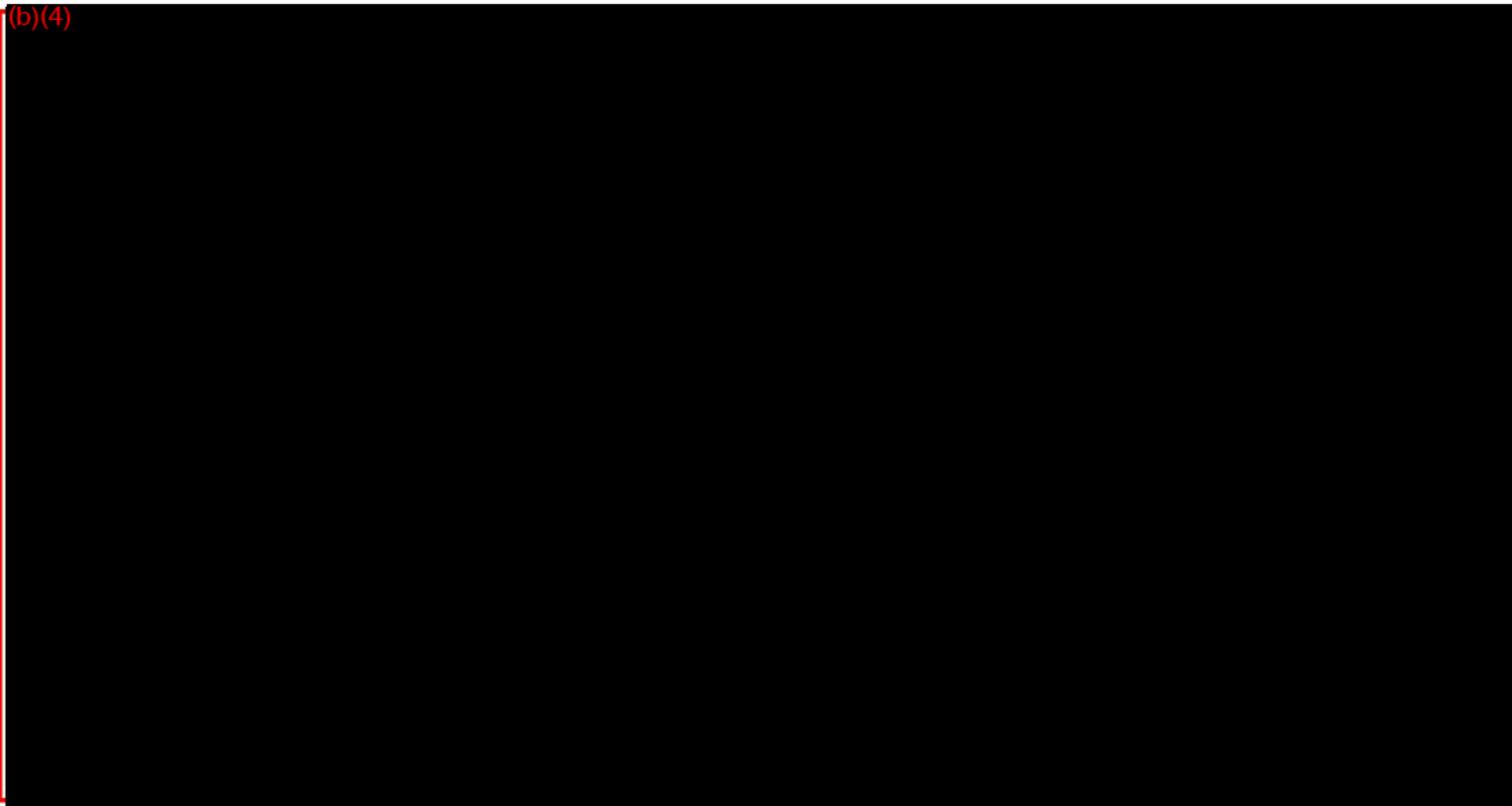
Provide information on how linearity was established and indicate whether this conformed to EP6-PS or any other appropriate methodology.

Carryover

Provide studies to demonstrate lack of overestimation of results due to the carryover effect. The testing pool should consist of samples at clinically meaningful levels. *



(b)(4)



File Attachment 1	13286 Sample Probe Carryover Report
File Attachment 2	Data line listing - Sample Probe Carryover
File Attachment 3	13298 Purposeful Pollution Reagent Report

Interfering Substances
Provide studies to show possible interference of substances such as lipids, hemoglobin, bilirubin, etc.

5.2 Comparison Studies Using Clinical Specimens

5.2.1 Method Comparison

Note:	<i>For method comparison describe bias/agreement between the new device and comparator (i.e., predicate, reference method, disease state or a combination thereof as appropriate for the desired claim). This also includes a description of study design and statistical methods. For examples of information to be included in study design description, see the article reporting the STARD initiative (Clin Chem 2003; 49(1): 7-18).</i>
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5.2.1.1 Study Design

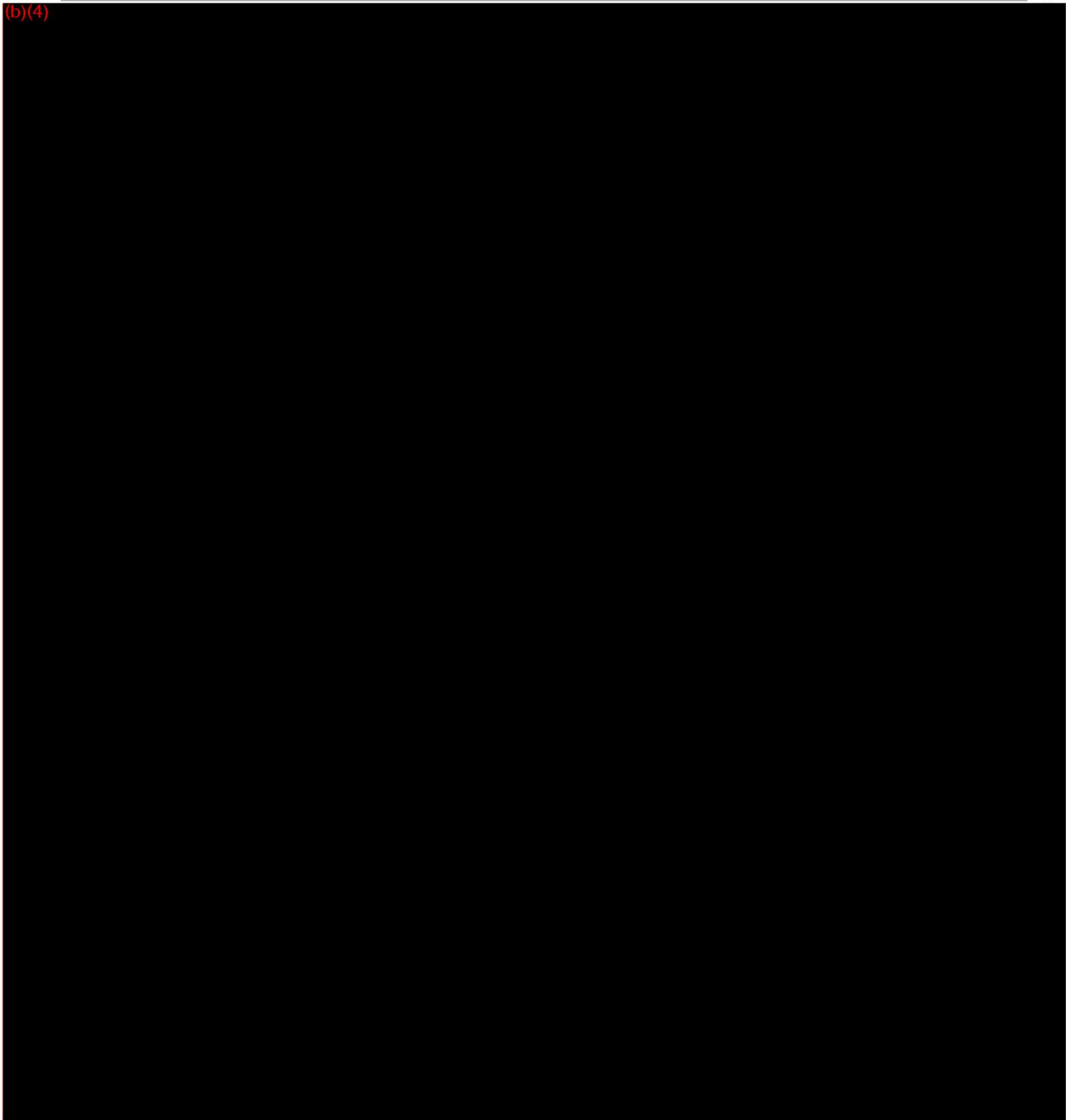


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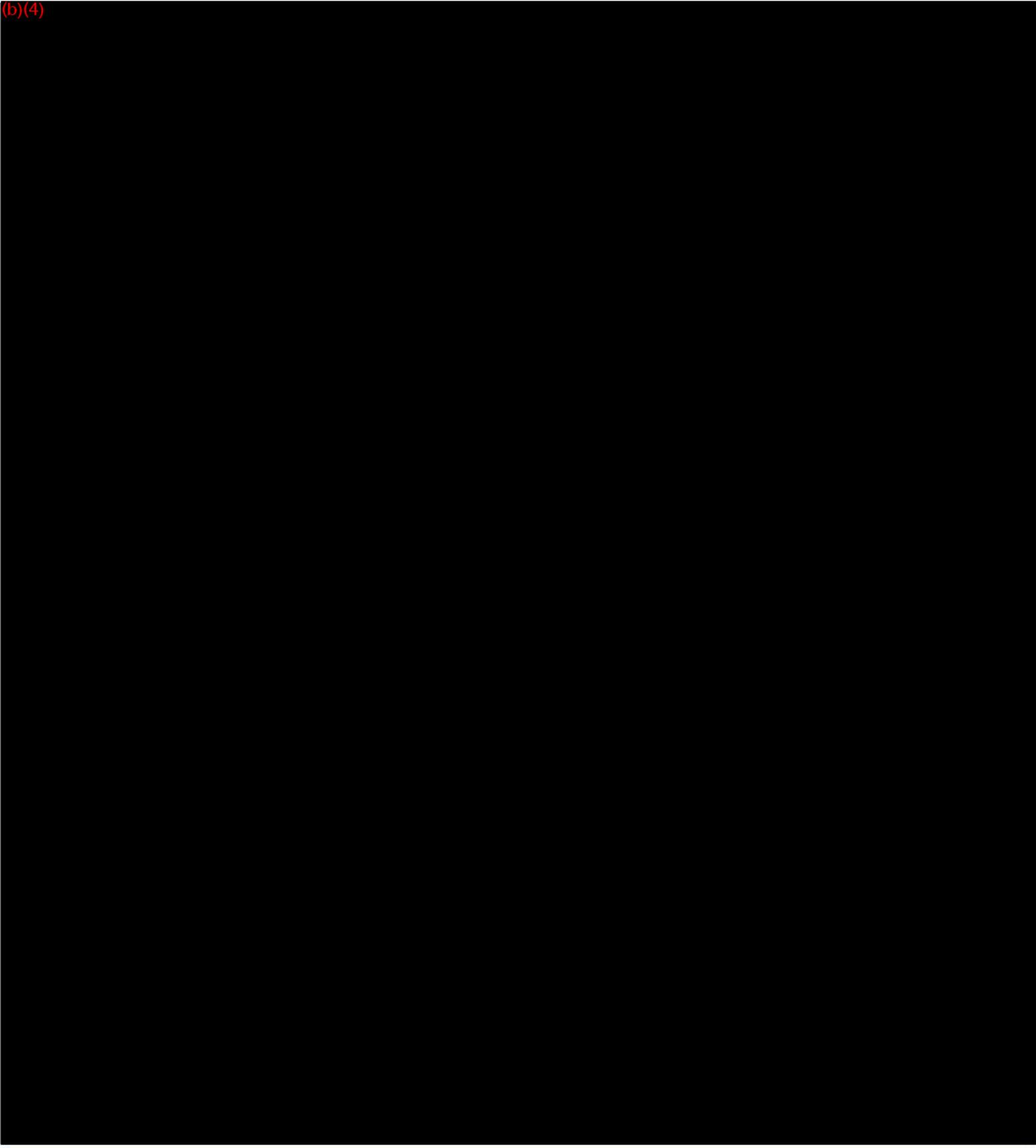
File Attachment

[12999 BioFlex 25-OH Vitamin D - Clinical Study Protocol](#)

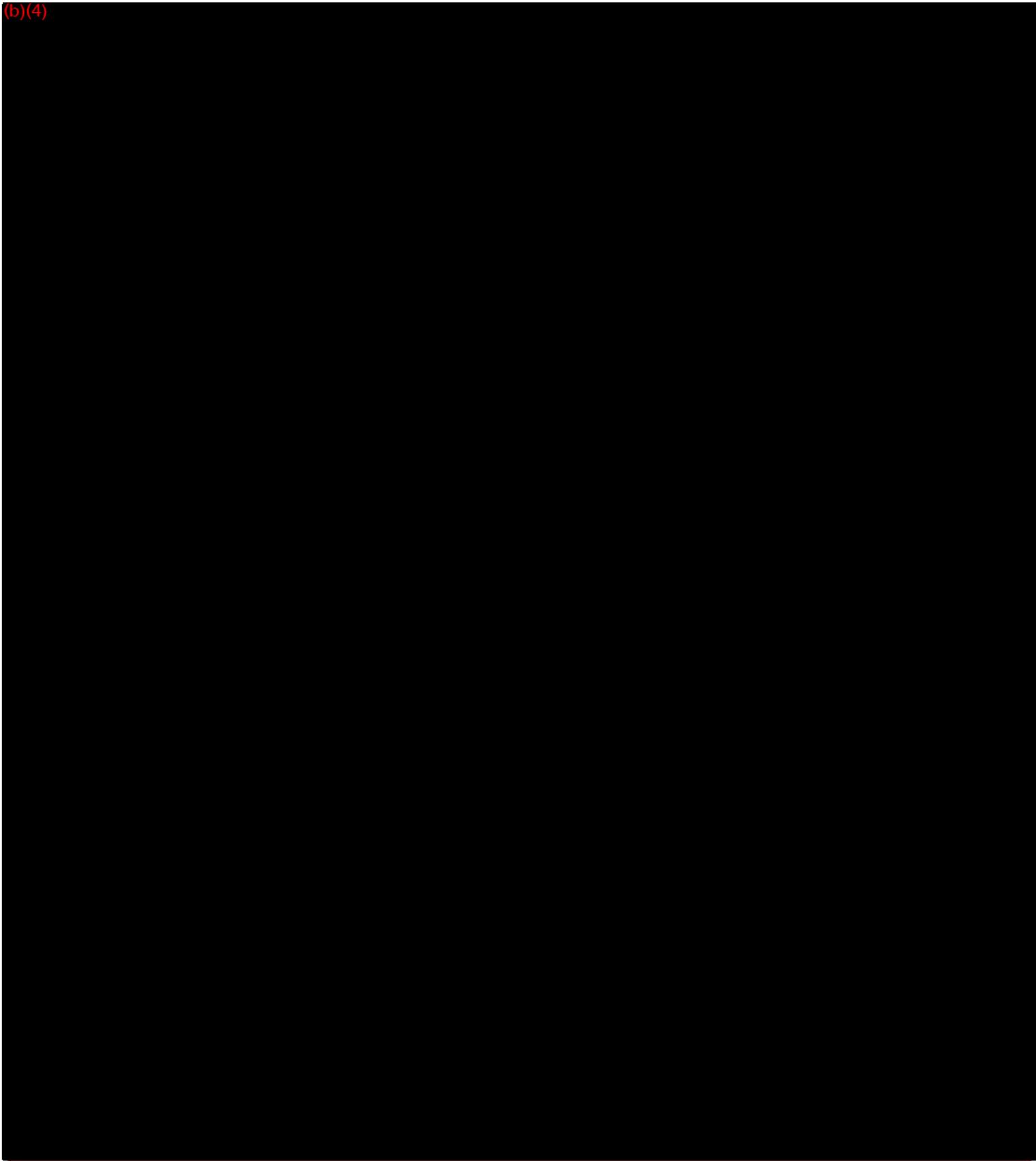
(b)(4)



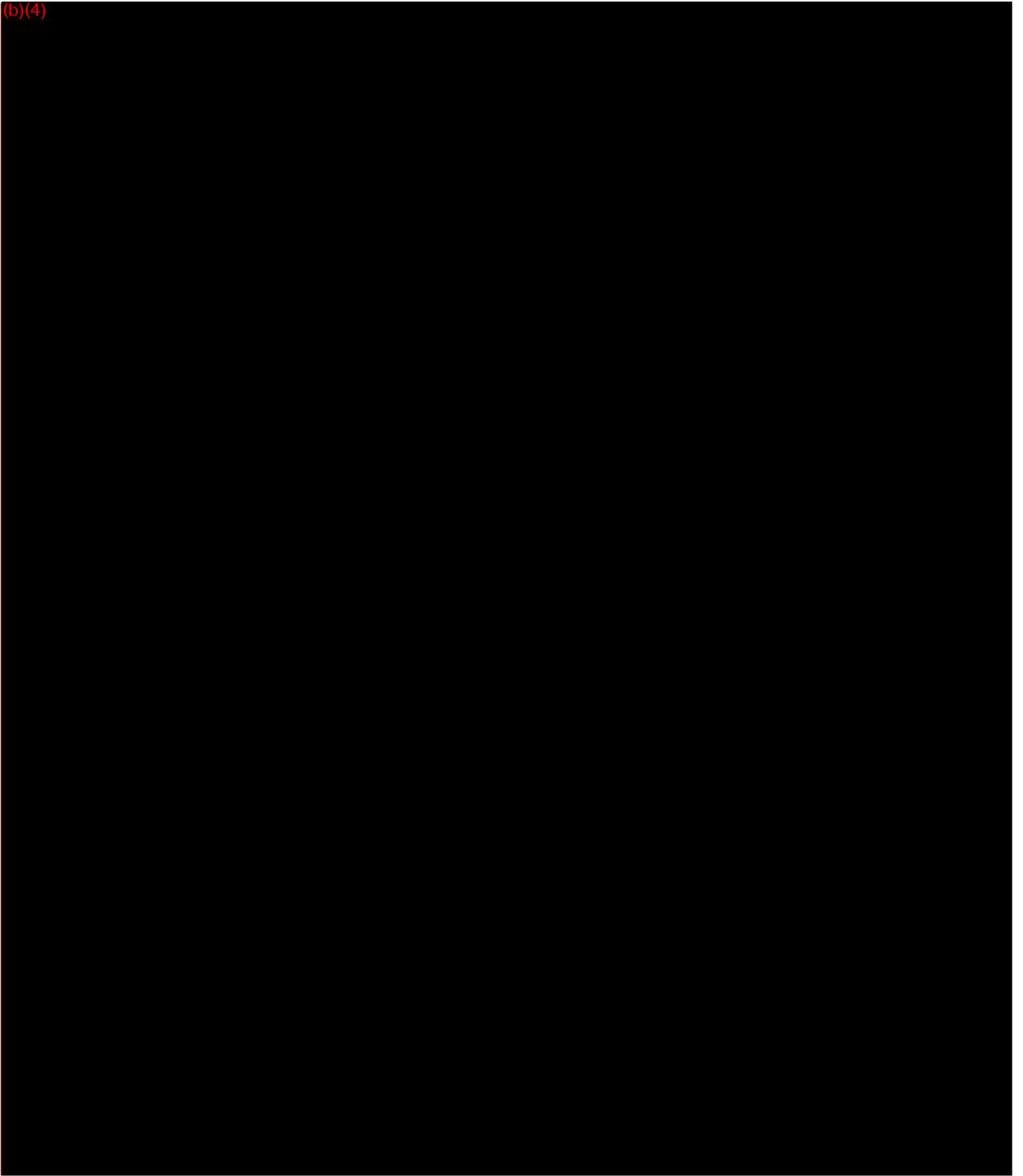
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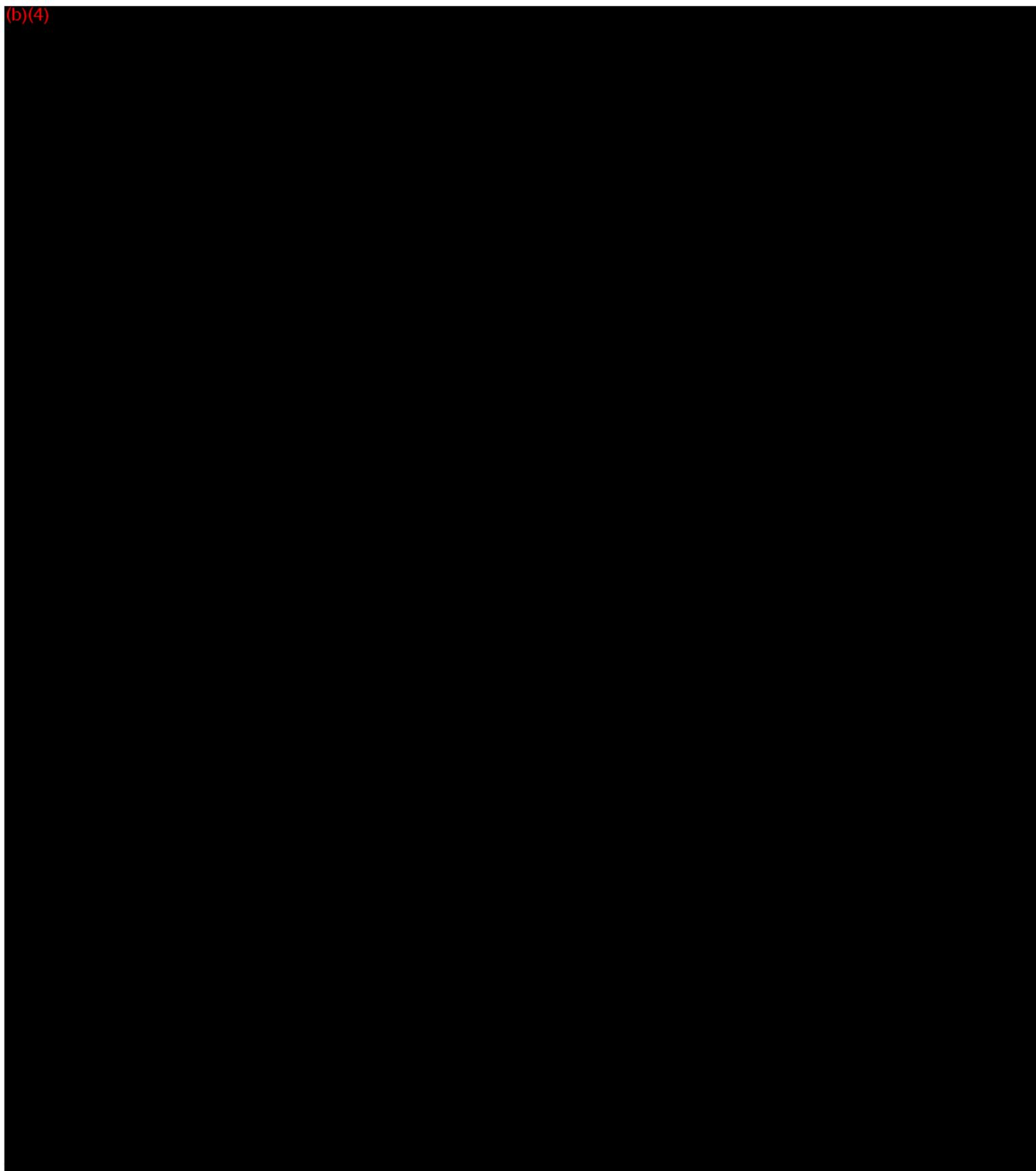
(b)(4)



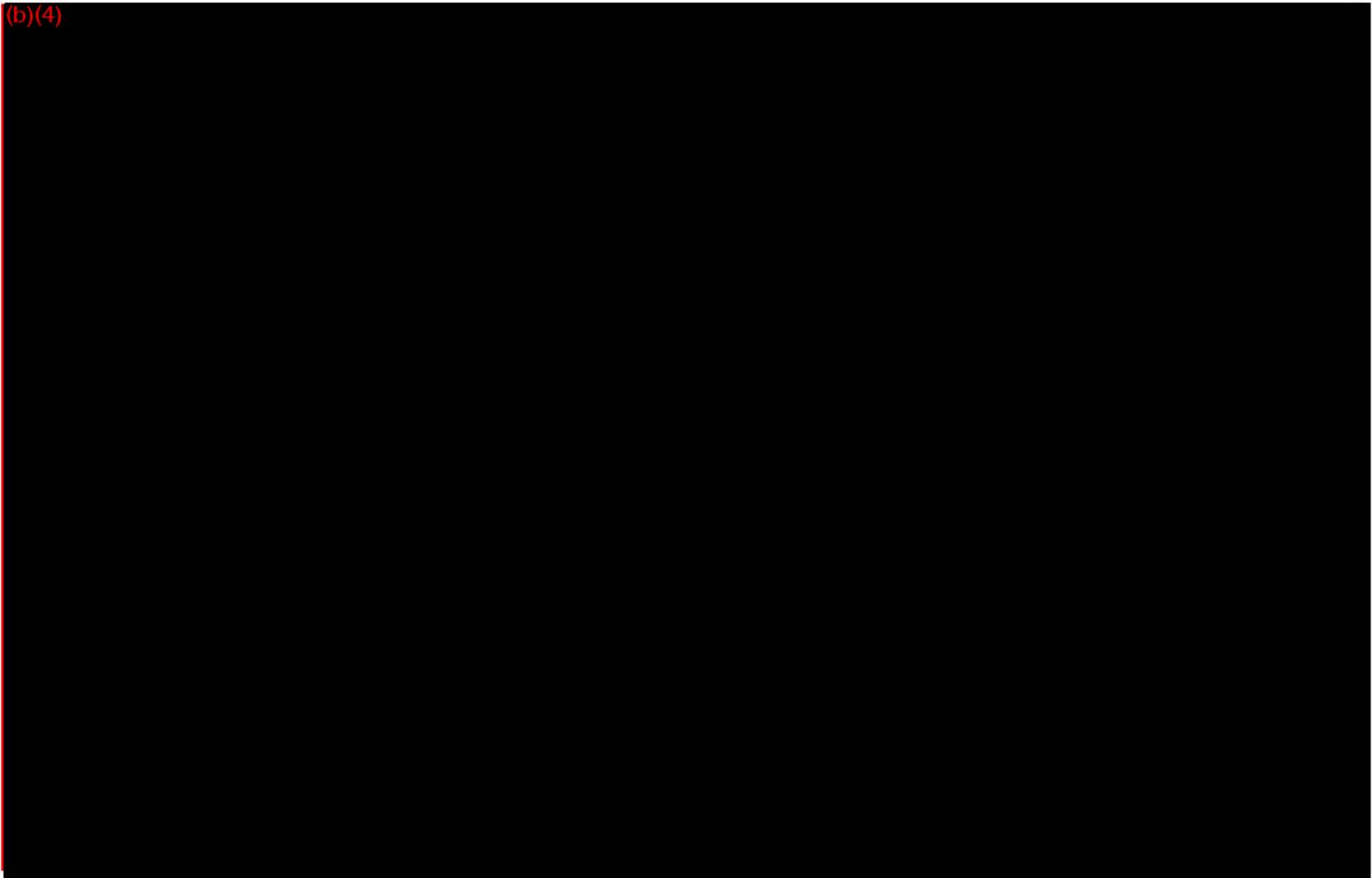
(b)(4)



(b)(4)



(b)(4)



5.2.2 Matrix Description and Comparison

Describe, where appropriate, the additional studies characterizing agreement and precision for each matrix. When appropriate, include an analytical study of specimen transport conditions and analyte stability. *

(b)(4)



(b)(4)

File Attachment 1	13287 Sample Stability Report
File Attachment 2	Data line listing - Sample Stability

5.3 Clinical Studies (where applicable)

Are there clinical studies included in this submission? * No

Note: Also see information in the "comparison studies using clinical specimens" section above as well as the CLSI GP10-A, Assessment of the Clinical Accuracy of Laboratory Tests Using Receiver Operating Characteristic (ROC) Plots. Definition and rationale for "Clinical Truth," statistical methods applied.

Enter the clinical sensitivity and clinical specificity: estimates of diagnostic accuracy with confidence intervals such as sensitivity, specificity, positive and negative predictive values, etc.

Include any other clinical supportive data, statistical analysis, and results if applicable: (e.g., other clinical supporting data such as clinical therapy monitoring data, etc.).

5.4 Clinical Cut-off

Describe the established cut-off and its validation for the new device. Define "equivocal zone" if applicable, and include a description of how results within this zone are reported to the user. *

Not Applicable - BioPlex 2200 25-OH Vitamin D is a quantitative assay.

5.5 Reference Interval (Expected Values)

(b)(4)

(b)(4)

File Attachment

[Data line listing - Expected Values](#)

Include a description of your methods for determining the reference intervals if they are not well established from the literature or if the range cannot be transferred to the new device. Also, describe the population studied (demographics, inclusion/exclusion criteria, number of individuals). Indicate if separate reference intervals for subclasses where clinically justified. Determine the method of clinical diagnosis of the reference population(s). Finally, include the statistical method used to calculate ranges. *

(b)(4)

6.0 Labeling

Provide proposed package labeling to demonstrate conformance to 21 CFR 809.10. Also, include package insert for the predicate device, if available. Labeling at a minimum should include: device components and specifications, reagent composition and important specifications, precautions/warnings, limitations, storage requirements, specimen handling and storage requirements, expiration/stability dating, instructions for reconstitution, mixing, and dilution, assay procedure, calibration, quality controls, results (calculations, formulas), results (interpretation), performance characteristics (summarize reproducibility, etc.), and study design (population studied, N, type of sample, matrix, dilution, target concentrations, etc.). *

Bio-Rad BioPlex 2200 25-OH Vitamin D kit proposed labeling, which demonstrates the requirements of 21 CFR 809.10, is provided and listed below.

Please refer to the attached labeling files.

Item #	BioPlex 2200 25-OH Vitamin D Proposed Labeling
1	665-0542b Instructions For Use (IFU), BioPlex 2200 25-OH Vitamin D Kit
2	665-3780Aa IFU CD Label, 25-OH Vitamin D Kit
3	663-3770a Assay Protocol File (APF) CD Label, 25-OH Vitamin D Kit
4	505749 Reagent Pack Label, 25-OH Vitamin D Reagent Pack
5	665-3750 Box Label, 25-OH Vitamin D Reagent Pack
6	505762b Product Insert, 25-OH Vitamin D Calibrator Set
7	505750a Vial Label, 25-OH Vitamin D Calibrator Level 1
8	505751a Vial Label, 25-OH Vitamin D Calibrator Level 2
9	505752a Vial Label, 25-OH Vitamin D Calibrator Level 3
10	505753a Vial Label, 25-OH Vitamin D Calibrator Level 4
11	505754a Vial Label, 25-OH Vitamin D Calibrator Level 5
12	505755a Vial Label, 25-OH Vitamin D Calibrator Level 6
13	603171a Box Label, 25-OH Vitamin D Calibrator Set
14	663-3720 CD Label, 25-OH Vitamin D Calibrator

	Lot Data
15	663-3700 Data Sheet, 25-OH Vitamin D Calibrator Lot Data
16	505763b Product Insert, 25-OH Vitamin D Control Set
17	505756a Vial Label, 25-OH Vitamin D Control Level 1
18	505757a Vial Label, 25-OH Vitamin D Control Level 2
19	603188a Box Label, 25-OH Vitamin D Control Set
20	663-3740 CD Label, 25-OH Vitamin D Control Lot Data
21	663-3730 Data Sheet, 25-OH Vitamin D Control Lot Data
22	(b)(4)

File Attachment 1	665-0542b Instruction For Use- BioPlex 2200 25-OH Vitamin D Kit
File Attachment 2	665-3780Aa IFU CD Label - 25-OH Vitamin D Kit
File Attachment 3	665-3770a Assay Protocol File CD Label - 25-OH Vitamin D Kit
File Attachment 4	505749 Reagent Pack Label - 25-OH Vitamin D Reagent Pack
File Attachment 5	665-3750 Box Label - 25-OH Vitamin D Reagent Pack
File Attachment 6	505762b Product Insert - 25-OH Vitamin D Calibrator Set
File Attachment 7	505750a Vial Label - 25-OH Vitamin D Calibrator Level 1
File Attachment 8	505751a Vial Label - 25-OH Vitamin D Calibrator Level 2
File Attachment 9	505752a Vial Label - 25-OH Vitamin D Calibrator Level 3
File Attachment 10	505753a Vial Label - 25-OH Vitamin D Calibrator Level 4
File Attachment 11	505754a Vial Label - 25-OH Vitamin D Calibrator Level 5
File Attachment 12	505755a Vial Label - 25-OH Vitamin D Calibrator Level 6
File Attachment 13	603171a Box Label - 25-OH Vitamin D Calibrator Set
File Attachment 14	663-3720 CD Label - 25-OH Vitamin D Calibrator Lot data
File Attachment 15	663-3700 Data Sheet - 25-OH Vitamin D Calibrator Lot Data
File Attachment 16	505763b Product Insert - 25-OH Vitamin D Control Set
File Attachment 17	505756a Vial Label - 25-OH Vitamin D Control Level 1
File Attachment 18	505757a Vial Label - 25-OH Vitamin D Control Level 2
File Attachment 19	603188a Box Label - 25-OH Vitamin D Control Set
File Attachment 20	663-3740 CD Label - 25-OH Vitamin D Control Lot Data
File Attachment 21	663-3730 Data Sheet - 25-OH Vitamin D Control Lot Data
File Attachment 22	(b)(4)

Note: *The minimum requirements above do not include requirements for instruments. Additional labeling recommendations may apply to Class II devices with special controls and Guidance.*

7.0 Other Supportive Information

Enter any additional supporting information for this submission such as: manufacturing information for critical reagents, copies of bibliography references, financial disclosures, and software validation or certification statements, if necessary to support equivalence. *

(b)(4)



Pre-Sub questioner for BioPlex 25-OH Vitamin D - Email communication with the FDA for reference only. 11/20/2020.

File Attachment 1	BioPlex 25-OH Vitamin D - Calibration Report
File Attachment 2	BioPlex 25-OH Vitamin D - Control Report Levels 1 and 2
File Attachment 3	BioPlex 25-OH Vitamin D - Patient Result Summary Report
File Attachment 4	Financial Disclosure Statement - Principal Investigator
File Attachment 5	BioPlex 2200 System Software Version - Level of Concern
File Attachment 6	Luminex Master File Access Authorization
File Attachment 7	Pre-IDE and Pre-Sub email communication file

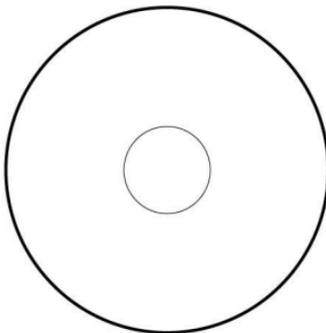
REF 663-3720

BioPlex® 2200

25-OH Vitamin D Calibrator Lot Data



For use with 25-OH Vitamin D Reagent Pack Lot # / Zum Gebrauch mit 25-OH Vitamin D Reagent Pack Charge Nr. / À utiliser avec les cartouches de réactifs 25-OH Vitamin D Lot no / Per l'uso con il lotto n. di 25-OH Vitamin D Reagent Pack / Para uso con el 25-OH Vitamin D Reagent Pack, n.º de lote / Para utilização com o lote de 25-OH Vitamin D Reagent Pack n.º / För användning med 25-OH Vitamin D Reagent Pack batch nr / Til brug sammen med 25-OH Vitamin D Reagent Pack lot nr. / K použítí s 25-OH Vitamin D Č. šarže reagenční sady / Til bruk med 25-OH Vitamin D-reagenspakke, lotnr.



LOT XXXXX-Z

CAL **LOT** XXXXX

VER X.X
Version

XXXXXX
YYYYYY
ZZZZZZ

990906-1

BIO-RAD

 **UNITED STATES:** Bio-Rad Laboratories, Inc. Clinical Diagnostics Group, 4000 Alfred Nobel Drive Hercules, CA 94547

EC REP **FRANCE:** Bio-Rad
3 boulevard Raymond Poincaré
92430 Marnes-la-Coquette

REF 663-3740

BioPlex® 2200

25-OH Vitamin D Control Lot Data



LOT XXXXX-Z

CTRL **LOT** XXXXX

VER X.X

Version

990905-1

BIO-RAD

 **UNITED STATES:** Bio-Rad Laboratories, Inc.
Clinical Diagnostics Group
4000 Alfred Nobel Drive
Hercules, CA 94547

EC REP **FRANCE:** Bio-Rad
3 boulevard Raymond Poincaré
92430 Marnes-la-Coquette

REF 665-3770A

BioPlex® 2200

25-OH Vitamin D
Assay Protocol File CD

BIO-RAD

**Bio-Rad
Laboratories**

 **UNITED STATES:**
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Clinical Diagnostics Group,
4000 Alfred Nobel Drive,
Hercules, CA 94547

EC REP **FRANCE:**
Bio-Rad
3 boulevard Raymond Poincaré
92430 Marnes-la-Coquette



VER SW4_v1
Version



LOT XXXXXXXXX

REF 665-3780A

BioPlex 2200

25-OH Vitamin D
Instructions for Use CD

Instructions For Use
Gebrauchsanleitung
Notice d'emploi
Istruzioni per l'uso
Folheto Informativo
Instrucciones de uso
Bruksanvisning
Brugervejledning
Návod k použití
Bruksanvisning

IVD



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4000 Alfred Nobel Drive, Hercules, CA 94547

EC REP

FRANCE:

Bio-Rad, 3 boulevard Raymond Poincaré
92430 Marnes-la-Coquette

Indications for Use

510(k) Number (if known)

Unknown

Device Name

BioPlex® 2200 25-OH Vitamin D Calibrator Set

Indications for Use (Describe)

The BioPlex 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex 2200 25-OH Vitamin D Reagent Pack.

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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) (Signature)

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

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Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

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Indications for Use

510(k) Number (if known)

Unknown

Device Name

BioPlex® 2200 25-OH Vitamin D Control Set

Indications for Use (Describe)

The BioPlex 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 System and the corresponding BioPlex 2200 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex 2200 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

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)

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Indications for Use

510(k) Number (if known)

Unknown

Device Name

BioPlex® 2200 25-OH Vitamin D Kit

Indications for Use (Describe)

The BioPlex 2200 25-OH Vitamin D kit is a multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPiex 2200 25-0H Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

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)

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DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS¹

BioPlex 2200 25-OH Vitamin D Clinical Study
CE.PR.BPX.VITD (and all mutually agreed upon revised versions thereof)

For the purposes of this statement, a clinical investigator includes any identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

Please check the following statements if applicable. If a statement cannot be checked, please attach a separate statement disclosing any financial arrangements/interests. This disclosure should include (1) any financial arrangement for conducting the study whereby the value of the compensation to you, the investigator, could be influenced by the outcome of the study; (2) any significant payments of other sorts, such as a grant to fund on-going research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria; (3) any proprietary interest such as property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement; (4) any significant equity interest in the sponsor; (5) any steps taken to minimize the potential for bias resulting from any of the disclosed arrangements, interests, or payments.

- I have **NOT** entered into any financial arrangement with Bio-Rad Laboratories, Inc. whereby the value of the compensation to me, the clinical investigator, for conducting the study could be influenced by the outcome of the study;
- I am **NOT** receiving any significant payments of other sorts made on or after February 2, 1999 from Bio-Rad Laboratories, Inc. such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- I do **NOT** have any proprietary interest (means property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement) in the product tested in this covered study;
- I do **NOT** have any significant ownership interest, stock options, other financial interest whose value cannot be readily determined through reference to public prices, or an equity interest in Bio-Rad Laboratories, Inc. that exceeds \$50,000 during the time I am participating in this clinical study or for one year following completion of the study.

NAME OF INVESTIGATOR (b) (6)		TITLE R&D Manager
ORGANIZATION Bio-Rad Laboratories 5500 E. Second St. Benicia, CA 94510		
SIGNATURE (b) (6)		DATE 2/13/2014

¹ Code of Federal Regulations 21, Part 54 Financial Disclosure by Clinical Investigators, pp251 –254.

Department of Health and Human Services
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STANDARDS DATA REPORT FOR 510(k)s
 (To be filled in by applicant)

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; (Vol. 32 No. 8)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # 7-233

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
 If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
 If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
 If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
 If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
 If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
 If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
 If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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DESCRIPTION

JUSTIFICATION

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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition (Vol. 25 No.27)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number³ # 7-127

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

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Were there any deviations or adaptations made in the use of the standard?
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Were deviations or adaptations made beyond what is specified in the FDA SIS?
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If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

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² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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SUMMARY REPORT TABLE**

STANDARD TITLE

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP06-A, Evaluation of Linearity of Quantitative Measurement: A Statistical Approach, Approved Guideline (Vol. 23 No.16)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number³ #7-193

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

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Were there any exclusions from the standard?
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Is there an FDA guidance ⁶ that is associated with this standard?
If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

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² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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0900262181991cb8.pdf

System attempted to attach the file. Please look at attachments to open this file manually.

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Vol. 24 No 25

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # 7-110

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

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TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

C28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; (Vol. 28 No. 30)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ # 7-224

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
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⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

[‡] Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
1350 Piccard Drive, Room 400
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Department of Health and Human Services
 Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
 (To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (Vol. 29, No. 20)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number³ #7-235

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
 If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
 If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
 If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?
 If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?
 If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
 If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?
 If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or

certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
----------------	---------------	---

TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

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[‡] Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

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 Food and Drug Administration
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 Rockville, MD 20850

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Department of Health and Human Services
Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP15-A2, User Verification of Performance for Precision and Trueness, Approved Guideline, Second Edition (Vol. 25 No.17)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number ³ #7-153

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?
If yes, report options selected in the summary report table.

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If yes, report these deviations or adaptations in the summary report table.

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If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

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⁶ The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

[‡] Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

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 Rockville, MD 20850

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Certification of Compliance

Under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. Name of Sponsor/Applicant/Submitter Bio-Rad Laboratories		2. Date of the Application/Submission Which This Certification Accompanies 04/29/2014	
3. Address		4. Telephone and Fax Numbers (Include country code if applicable and area code)	
Address 1 (Street address, P.O. box, company name c/o) 5500 E. Second Street		(Tel): 510-741-6263	
Address 2 (Apartment, suite, unit, building, floor, etc.)		(Fax): 510-741-3941	
City Benicia	State/Province/Region CA		
Country USA	ZIP or Postal Code 94510		

PRODUCT INFORMATION

5. For Drugs/Biologics: Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s).
For Devices: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)

BioPlex 2200 25-OH Vitamin D Kit
BioPlex 2200 25-OH Vitamin D Calibrator Set
BioPlex 2200 25-OH Vitamin D Control Set

Classification Names
MRG, System, Test, Vitamin D (Class II)
JIS, Calibrator, Primary (Class II) ; JJX, Single (specified) Analyte Controls (Assayed and Unassayed) (Class I)

Regulation Description
21 CFR §862.1825 – Vitamin D test system
21 CFR §862.1150 – Calibrator, 21 CFR §862.1660 – Quality Control Material (assayed and unassayed)

Continuation Page for #5

APPLICATION / SUBMISSION INFORMATION

6. Type of Application/Submission Which This Certification Accompanies

IND NDA ANDA BLA PMA HDE 510(k) PDP Other

7. Include IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/ Other Number (If number previously assigned) _____ If BLA was selected in item 6, provide Supplement Number _____

8. Serial Number Assigned to Application/Submission Which This Certification Accompanies _____

CERTIFICATION STATEMENT / INFORMATION

9. Check only one of the following boxes (See instructions for additional information and explanation)

A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

C. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that those requirements have been met.

Certification Statement / Information section continued on page 2

CERTIFICATION STATEMENT / INFORMATION (Continued)

10. If you checked box C, in number 9, provide the National Clinical Trial (NCT) Number(s) for any "applicable clinical trial(s)," under 42 U.S.C. § 282(J)(1)(a)(i), section 402(j)(1)(a)(i) of the Public Health Service Act, referenced in the application/ submission which this Certification accompanies. (Add continuation page as necessary.)

NCT Number(s): _____

Continuation Page for #10

The undersigned declares, to the best of her/his knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 331, section 301 of the Federal Food, Drug, and Cosmetic Act.

Warning: A willfully and knowingly false statement is a criminal offense, U.S. Code, title 18, section 1001.

11. Name and Title of the Person who Signs Number 15

Name Patricia M. Klimley	Title RA Manager
------------------------------------	----------------------------

12. Address

Address 1 (Street address, P.O. box, company name c/o) 5500 E. Second Street	
Address 2 (Apartment, suite, unit, building, floor, etc.)	
City Benicia	State/Province/Region CA
Country USA	ZIP or Postal Code 94510

13. Telephone and Fax Numbers

(Include country code if applicable and area code)
 (Tel): 510-741-6263
 (Fax): 510-741-3941

14. Date of Certification

04/29/2014

15. Signature of Sponsor/Applicant/Submitter or an Authorized Representative (Sign)

Patricia M Klimley

Sign

This section applies only to requirements of the Paperwork Reduction Act of 1995.

*****DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*****

The burden time for this collection of information is estimated to average 15 minutes and 45 minutes (depending on the type of application/ submission) per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to:

Department of Health and Human Services
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 Office of Chief Information Officer
 Paperwork Reduction Act (PRA) Staff
 PRAStaff@fda.hhs.gov

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Form Approved OMB No. 0910-0511 Expiration Date April 30, 2016. See Instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION MEDICAL DEVICE USER FEE COVER SHEET		PAYMENT IDENTIFICATION NUMBER: (b) (4) Write the Payment Identification number on your check.	
A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: http://www.fda.gov/oc/mdufma/coversheet.html			
1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code) BIO RAD LABORATORIES 5500 E. 2nd Street Benicia Contra Costa CA 94510 US		2. CONTACT NAME Juang Wang 2.1 E-MAIL ADDRESS juang_wang@bio-rad.com 2.2 TELEPHONE NUMBER (include Area code) 510-741-4609 2.3 FACSIMILE (FAX) NUMBER (Include Area code) 510-741-3941	
4.1 EMPLOYER IDENTIFICATION NUMBER (EIN) (b) (4)			
3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm345263.htm <u>Select an application type:</u>			
<input checked="" type="checkbox"/> Premarket notification (510(k)); except for third party <input type="checkbox"/> 513(g) Request for Information <input type="checkbox"/> Biologics License Application (BLA) <input type="checkbox"/> Premarket Approval Application (PMA) <input type="checkbox"/> Modular PMA <input type="checkbox"/> Product Development Protocol (PDP) <input type="checkbox"/> Premarket Report (PMR) <input type="checkbox"/> 30-Day Notice		3.1 Select a center <input checked="" type="checkbox"/> CDRH <input type="checkbox"/> CBER <u>3.2 Select one of the types below</u> <input checked="" type="checkbox"/> Original Application <u>Supplement Types:</u> <input type="checkbox"/> Efficacy (BLA) <input type="checkbox"/> Panel Track (PMA, PMR, PDP) <input type="checkbox"/> Real-Time (PMA, PMR, PDP) <input type="checkbox"/> 180-day (PMA, PMR, PDP)	
4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status) <input type="checkbox"/> YES, I meet the small business criteria and have submitted the required qualifying documents to FDA <input checked="" type="checkbox"/> NO, I am not a small business 4.1 If Yes, please enter your Small Business Decision Number:			
5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA? <input checked="" type="checkbox"/> YES (All of our establishments have registered and paid the fee, or this is our first device, and we will register and pay the fee within 30 days of FDA's approval/clearance of this device.) <input type="checkbox"/> NO (If "NO," FDA will not accept your submission until you have paid all fees due to FDA. This submission will not be processed; see http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/ucm053165.htm for additional information)			
6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION. <input type="checkbox"/> This application is the first PMA submitted by a qualified small business, including any affiliates <input type="checkbox"/> This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only <input type="checkbox"/> The sole purpose of the application is to support conditions of use for a pediatric population <input type="checkbox"/> The application is submitted by a state or federal government entity for a device that is not to be distributed commercially			
7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA). <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO			
PAPERWORK REDUCTION ACT STATEMENT Public reporting burden for this collection of information is estimated to average 18 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the address below. Department of Health and Human Services, Food and Drug Administration, Office of Chief Information Officer, 1350 Piccard Drive, 4th Floor Rockville, MD 20850 [Please do NOT return this form to the above address, except as it pertains to comments on the burden estimate.]			
8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION (b) (4)		17-Oct-2013	

Form FDA 3601 (01/2007)

["Close Window"](#) [Print Cover sheet](#)



RE: (b) (4)
Juang Wang to: Antonovic, Lepasava
Bcc: Patricia Klimley, Candice DiDominick, Sarah Paul, Ravi Kaul, Lori Finucane

01/24/2014 01:20 PM

Dear Dr. Antonovic,

We appreciate your quick reply and will collect additional samples accordingly.

Have a great weekend.

Regards,

Juang

"Antonovic, Lepasava" Greetings Dr. Wang, Thank you for your foll... 01/24/2014 12:32:52 PM

From: "Antonovic, Lepasava" <Lepasava.Antonovic@fda.hhs.gov>
To: 'Juang Wang' <Juang_Wang@bio-rad.com>
Date: 01/24/2014 12:32 PM
Subject: RE: (b) (4)

Greetings Dr. Wang,

Thank you for your follow-up e-mail. Yes, your stated approach for collecting additional samples in winter is acceptable to us.

Kind regards,

Lepasava Antonovic Ph.D.

Scientific Reviewer
CDRH/OIR
Food and Drug Administration
10903 New Hampshire Avenue
WO66, RM5624
Silver Spring, MD 20993-0002
Tel: 301-796-4998
Fax: 301-847-8513
leposava.antonovic@fda.hhs.gov

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From: Juang Wang [mailto:Juang_Wang@bio-rad.com]
Sent: Thursday, January 23, 2014 6:03 PM

To: Antonovic, Leosava

Subject: RE: (b) (4)

Dear Dr. Antonovic,

(b) (4)

Juang

From: "Antonovic, Leosava" <Leosava_Antonovic@fda.hhs.gov>

To: 'Juang Wang' <Juang_Wang@bio-rad.com>,

Date: 01/23/2014 12:52 PM

Subject: RE: (b)(4)

Greetings Dr. Wang.

(b)(4)

Kind regards,

Leosava Antonovic Ph.D.

Scientific Reviewer

CDRH/OIR

Food and Drug Administration

10903 New Hampshire Avenue

WO66, RM5624
Silver Spring, MD 20993-0002
Tel: 301-796-4998
Fax: 301-847-8513
leposava.antonovic@fda.hhs.gov

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From: Juang Wang [mailto:Juang_Wang@bio-rad.com]
Sent: Thursday, January 16, 2014 7:43 PM
To: Antonovic, Leposava
Subject: RE: (b)(4)

Dear Dr. Antonovic,

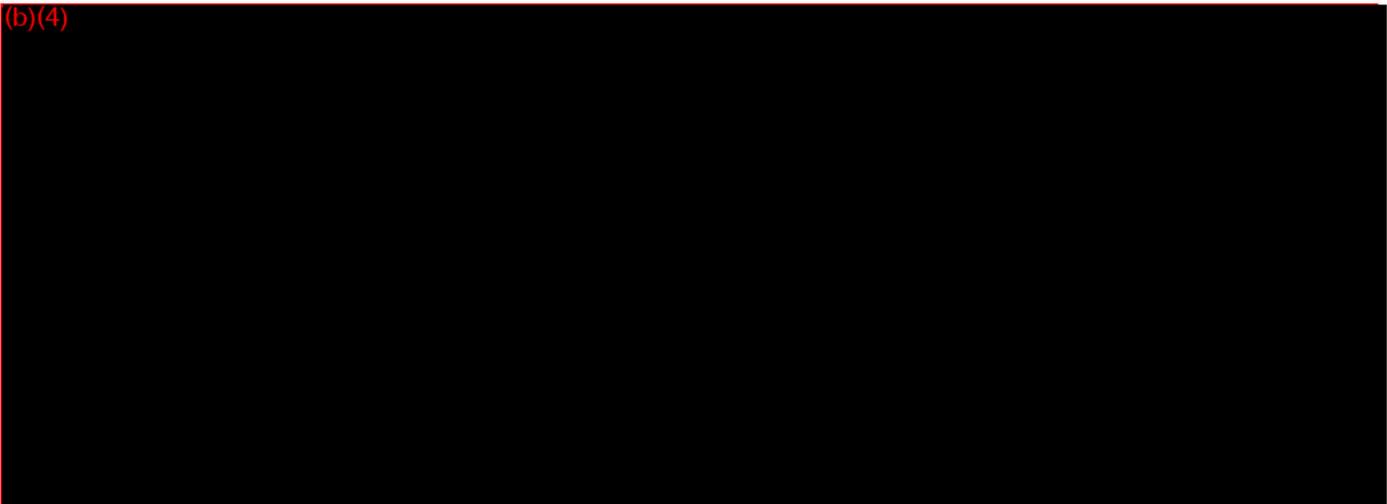
We have retrieved collection date information. Please see our response to each of your questions below and let me know if you need additional information.

Your feedback is very appreciated.

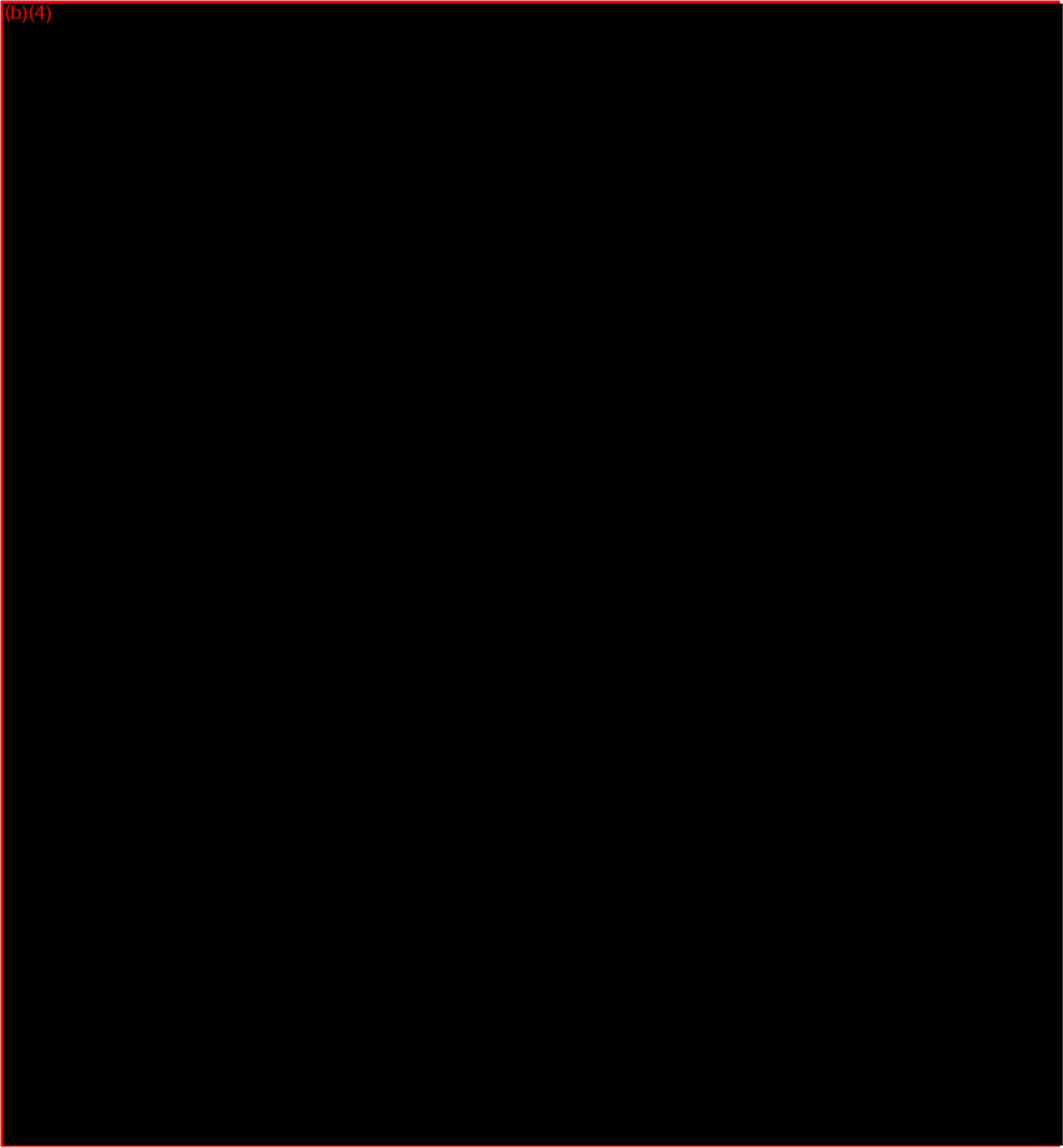
Regards,

Juang

(b)(4)



(b)(4)



From: "Antonovic, Leposava" <Leposava_Antonovic@fda.hhs.gov>
To: 'Juang Wang' <Juang_Wang@bio-rad.com>,
Date: 01/16/2014 11:19 AM
Subject: RE: (b)(4)

Greetings Dr. Wang,

(b)(4)



Thank you and kind regards,

Leposava Antonovic Ph.D.

Scientific Reviewer

CDRH/OIR

Food and Drug Administration

10903 New Hampshire Avenue

WO66, RM5624

Silver Spring, MD 20993-0002

Tel: 301-796-4998

Fax: 301-847-8513

leposava.antonovic@fda.hhs.gov

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From: Juang Wang [mailto:Juang_Wang@bio-rad.com]
Sent: Wednesday, January 15, 2014 11:19 AM
To: Antonovic, Leposava
Subject: RE: (b)(4)

Dear Dr. Antonovic,

Thanks for your email. I look forward to your comments.

Regards,

Juang

From: "Antonovic, Leposava" <Leposava.Antonovic@fda.hhs.gov>
To: 'Juang Wang' <Juang_Wang@bio-rad.com>,
Date: 01/14/2014 12:37 PM
Subject: RE: (b)(4)

Greetings Dr. Wang,

Happy New Year to you too! We will do our best to follow up with you regarding your request for additional feedback by the end of the week.

Thank you and kind regards.

Leposava Antonovic Ph.D.

Scientific Reviewer

CDRH/OIR

Food and Drug Administration

10903 New Hampshire Avenue

WO66, RM5624

Silver Spring, MD 20993-0002

Tel: 301-796-4998

Fax: 301-847-8513

leposava.antonovic@fda.hhs.gov

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From: Juang Wang [mailto:Juang_Wang@bio-rad.com]
Sent: Monday, January 13, 2014 6:45 PM
To: Antonovic, Leposava
Subject: RE: (b)(4)

Dear Dr, Antonovic,

(b)(4)

Regards,

Juang

From: Juang Wang/Hercules/US/BIO-RAD
To: "Antonovic, Leposava" <Leposava.Antonovic@fda.hhs.gov>,
Date: 12/23/2013 01:57 PM
Subject: RE: (b)(4)

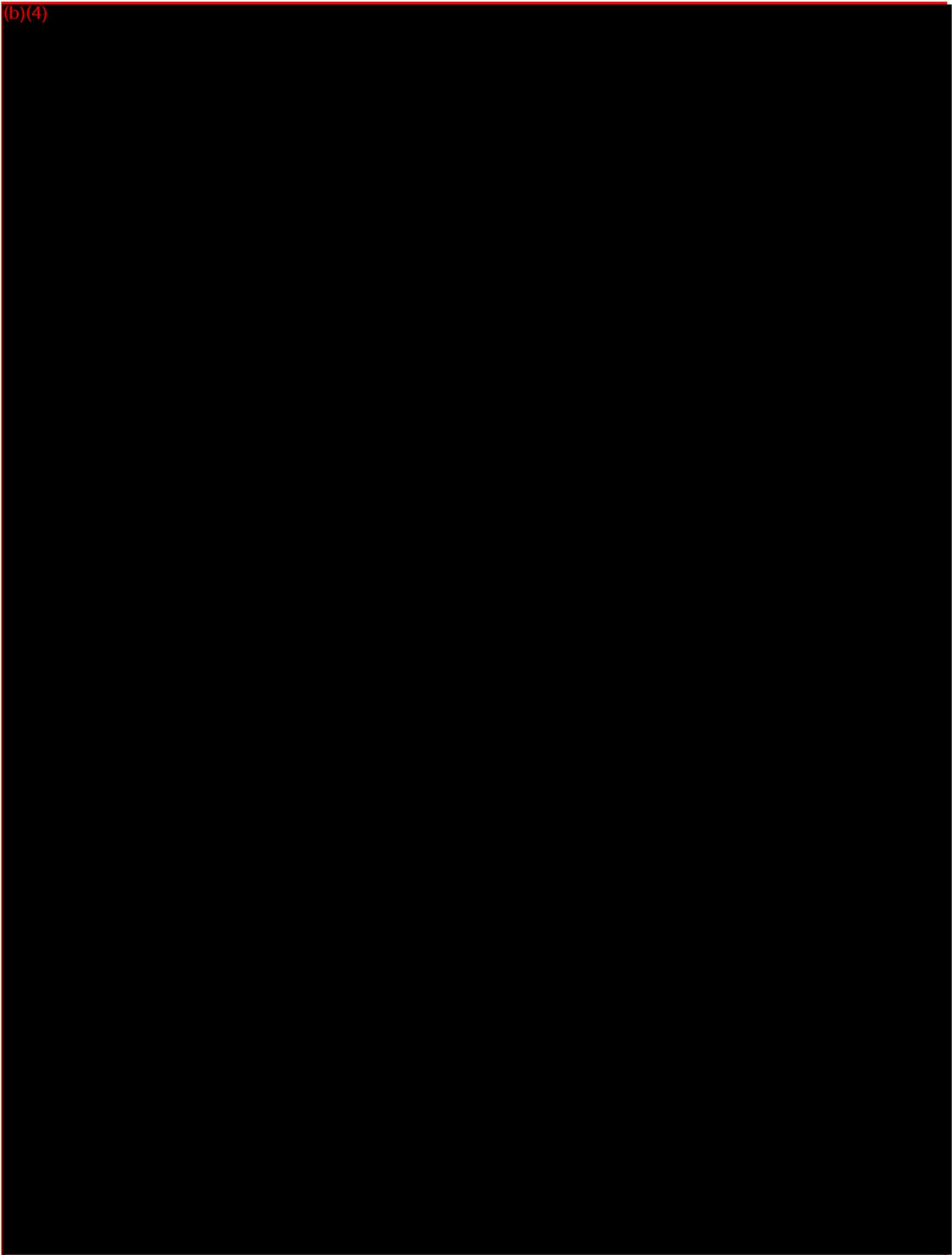
Dear Dr. Antonovic,

(b)(4)

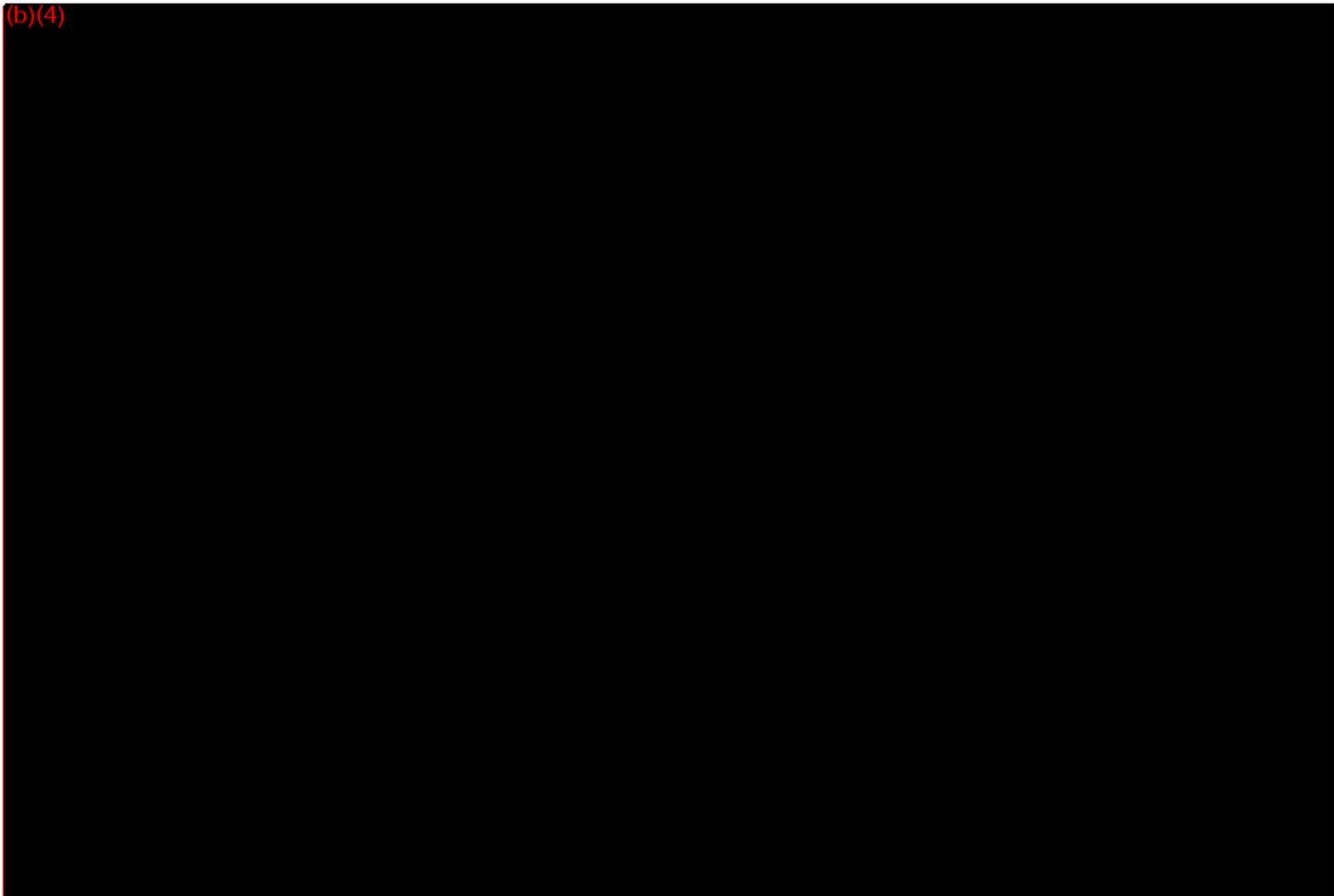
Thanks,

Juang

(b)(4)



(b)(4)



From: "Antonovic, Leposava" <Leposava.Antonovic@fda.hhs.gov>
To: 'Juang Wang' <Juang_Wang@bio-rad.com>,
Date: 12/23/2013 01:07 PM
Subject: RE: (b)(4)

Greetings Dr. Wang,

(b)(4)



Leposava Antonovic Ph.D.

Scientific Reviewer

CDRH/OIR

Food and Drug Administration

10903 New Hampshire Avenue

WO66, RM5624

Silver Spring, MD 20993-0002

Tel: 301-796-4998

Fax: 301-847-8513

leposava.antonovic@fda.hhs.gov

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From: Juang Wang [mailto:Juang_Wang@bio-rad.com]

Sent: Friday, December 20, 2013 11:36 AM

To: Antonovic, Leposava

Subject: (b)(4)

Greetings Dr. Antonovic,

(b)(4)

Juang

----- Forwarded by Juang Wang/Hercules/US/BIO-RAD on 12/20/2013 08:31 AM -----

From: Juang Wang/Hercules/US/BIO-RAD

To: "Antonovic, Leposava" <Leposava.Antonovic@fda.hhs.gov>

Date: 12/12/2013 11:57 AM

Subject: RE: (b)(4)

Dear Dr. Antonovic,

(b)(4)

(b)(4)

Juang

From: "Antonovic, Leposava" <Leposava.Antonovic@fda.hhs.gov>
To: "Juang Wang" <Juang_Wang@bio-rad.com>,
Cc: Patricia Klimley <Patricia_Klimley@bio-rad.com>
Date: 08/24/2012 10:24 AM
Subject: RE: (b)(4)

Greetings Dr. Wang,

(b)(4)

Kind regards,

Leposava Antonovic Ph.D.

Scientific Reviewer

CDRH/OIVD

Food and Drug Administration

10903 New Hampshire Avenue

WO66, G306

Silver Spring, MD 20993-0002

Tel: 301-796-4998

Fax: 301-847-8513

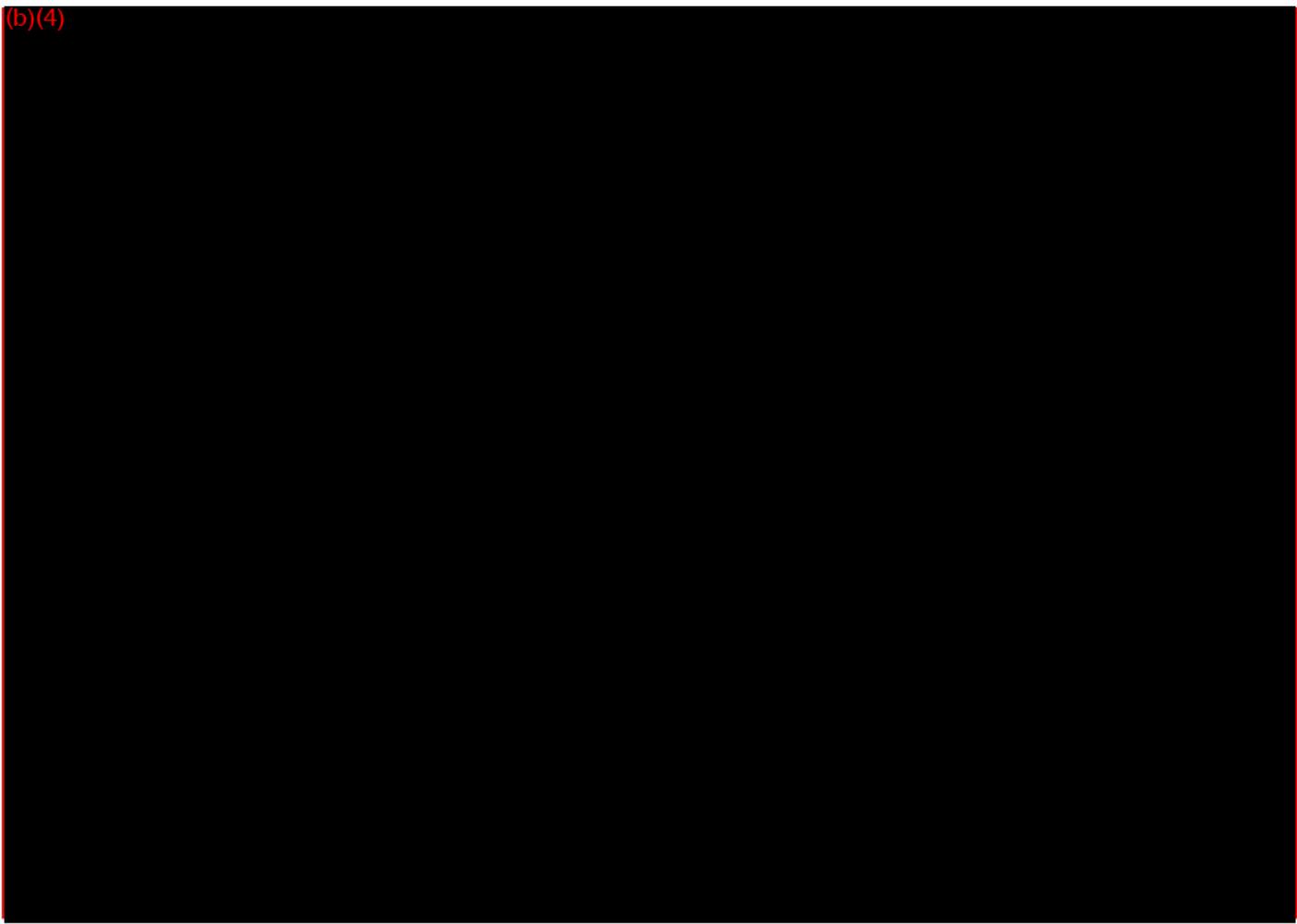
leposava.antonovic@fda.hhs.gov

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From: Juang Wang [mailto:Juang_Wang@bio-rad.com]
Sent: Thursday, August 02, 2012 8:00 PM
To: Antonovic, Laposava
Cc: Patricia Klimley
Subject: Re: (b)(4)

Dear Dr, Antonovic,

(b)(4)



Best regards,

Juang Wang, Ph.D., RAC(US)
Regulatory Affairs Representative

BioPlex Division
Bio-Rad Laboratories, Inc
5500 E 2nd Street
Benicia, CA 94510
(510)741-4609
(510)741-4650(fax)
juang_wang@bio-rad.com

From: "Antonovic, Leposava" <Leposava.Antonovic@fda.hhs.gov>
To: "juang_wang@bio-rad.com" <juang_wang@bio-rad.com>,
Date: 07/13/2012 01:59 PM
Subject: (b)(4)

RE: (b)(4)
DEVICE: BioPlex 2200 25-OH Vitamin D Kit
DATED: May 18, 2012
RECEIVED: May 21, 2012

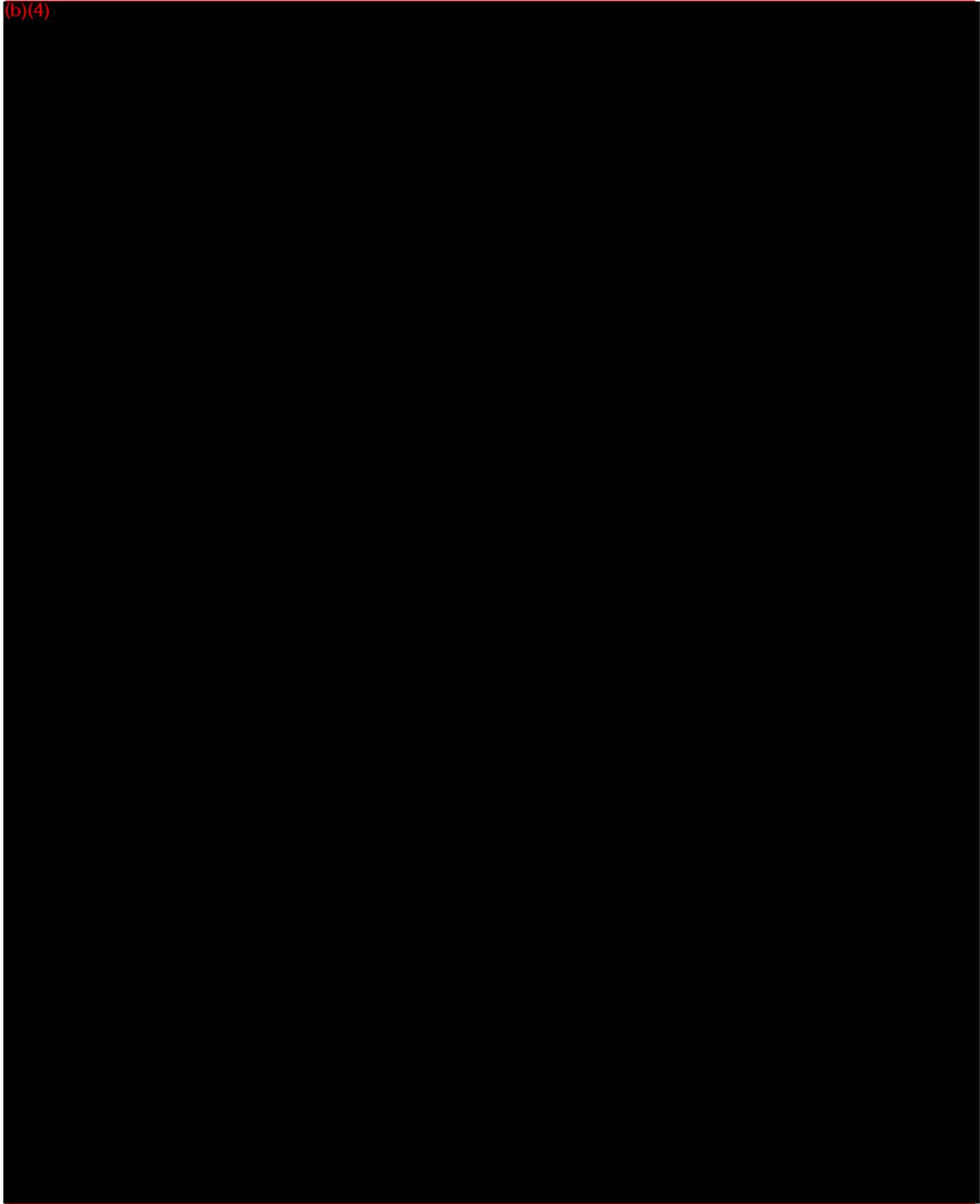
DATE: July 11, 2012

Dear Mr. Wang,

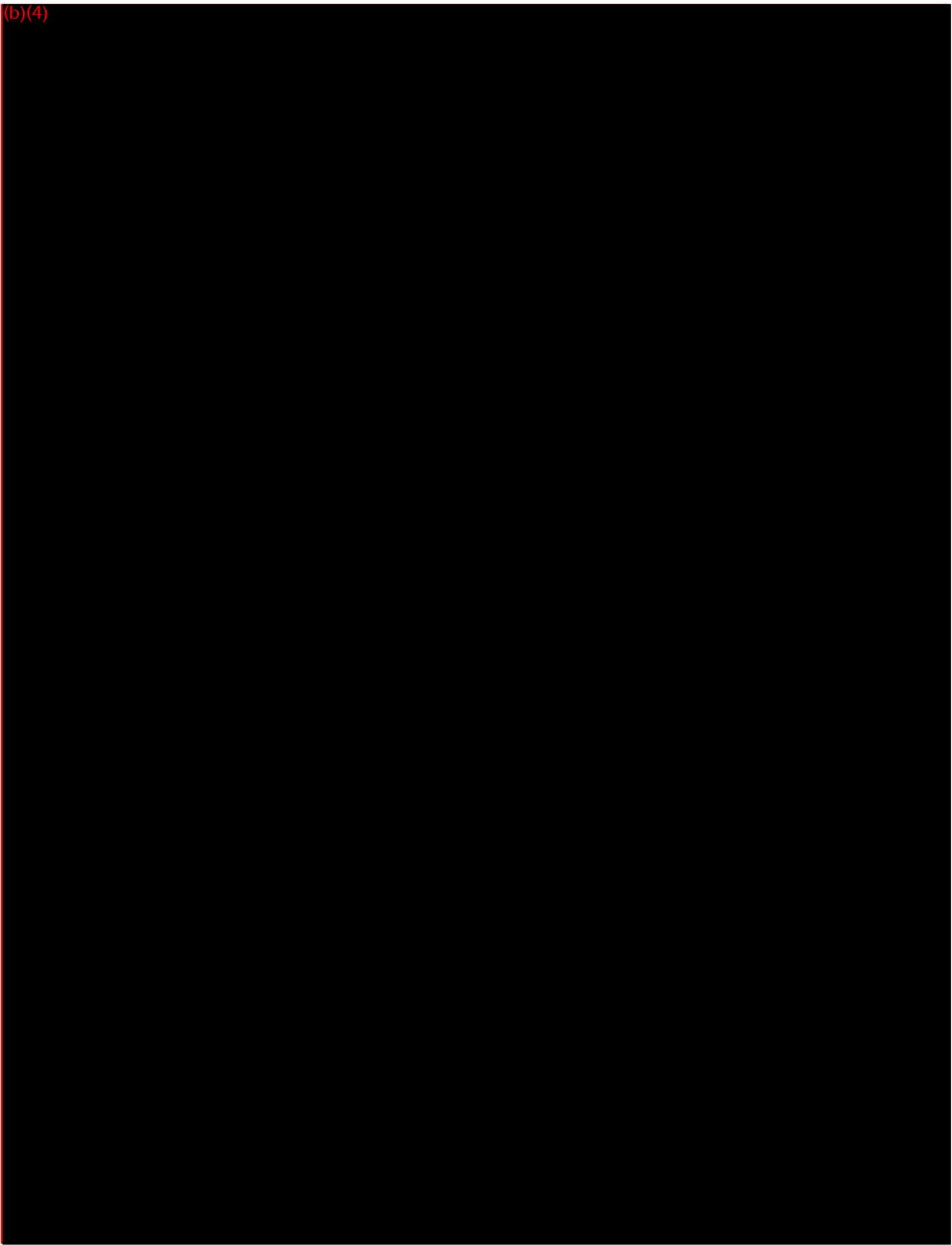
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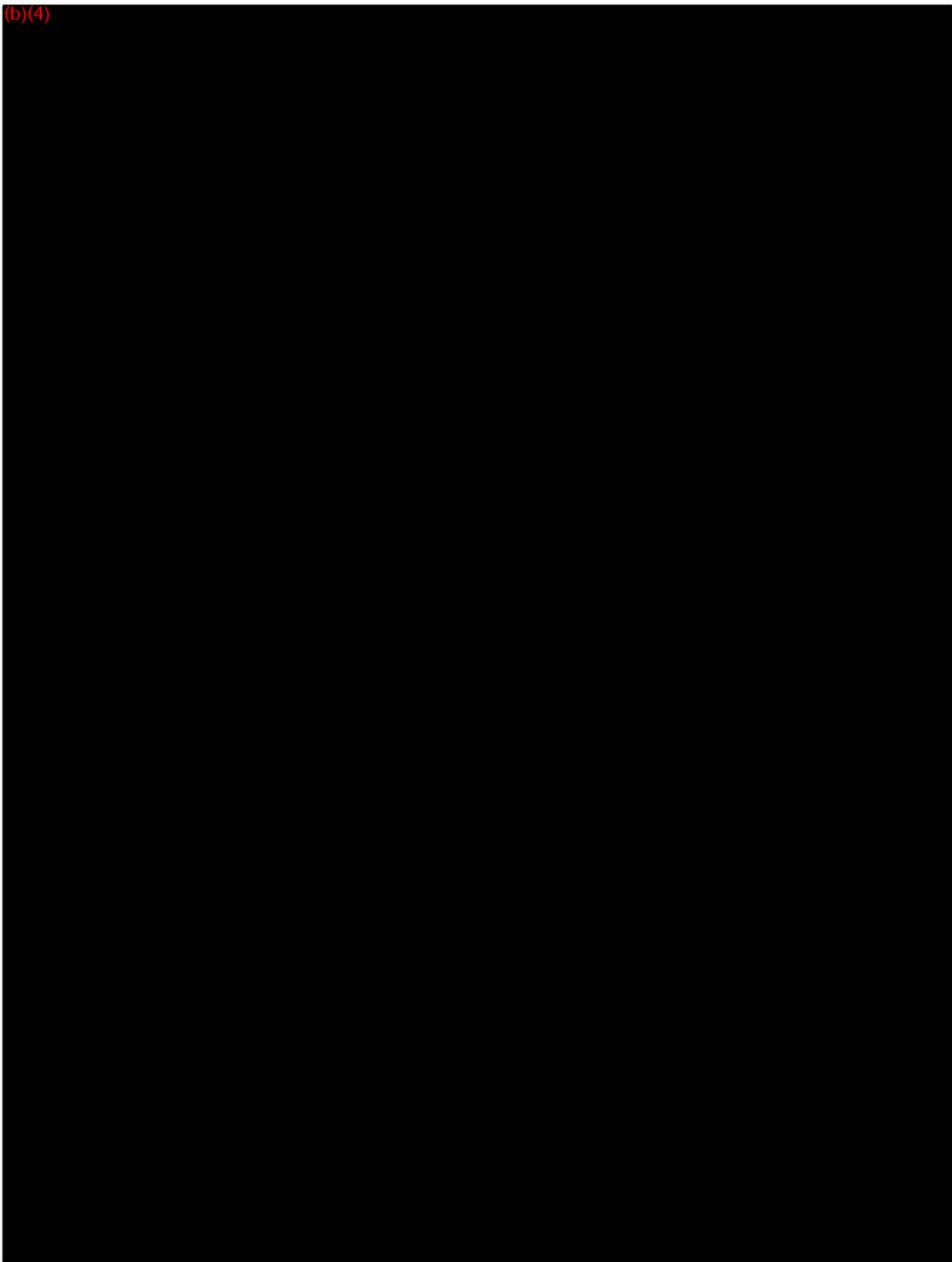
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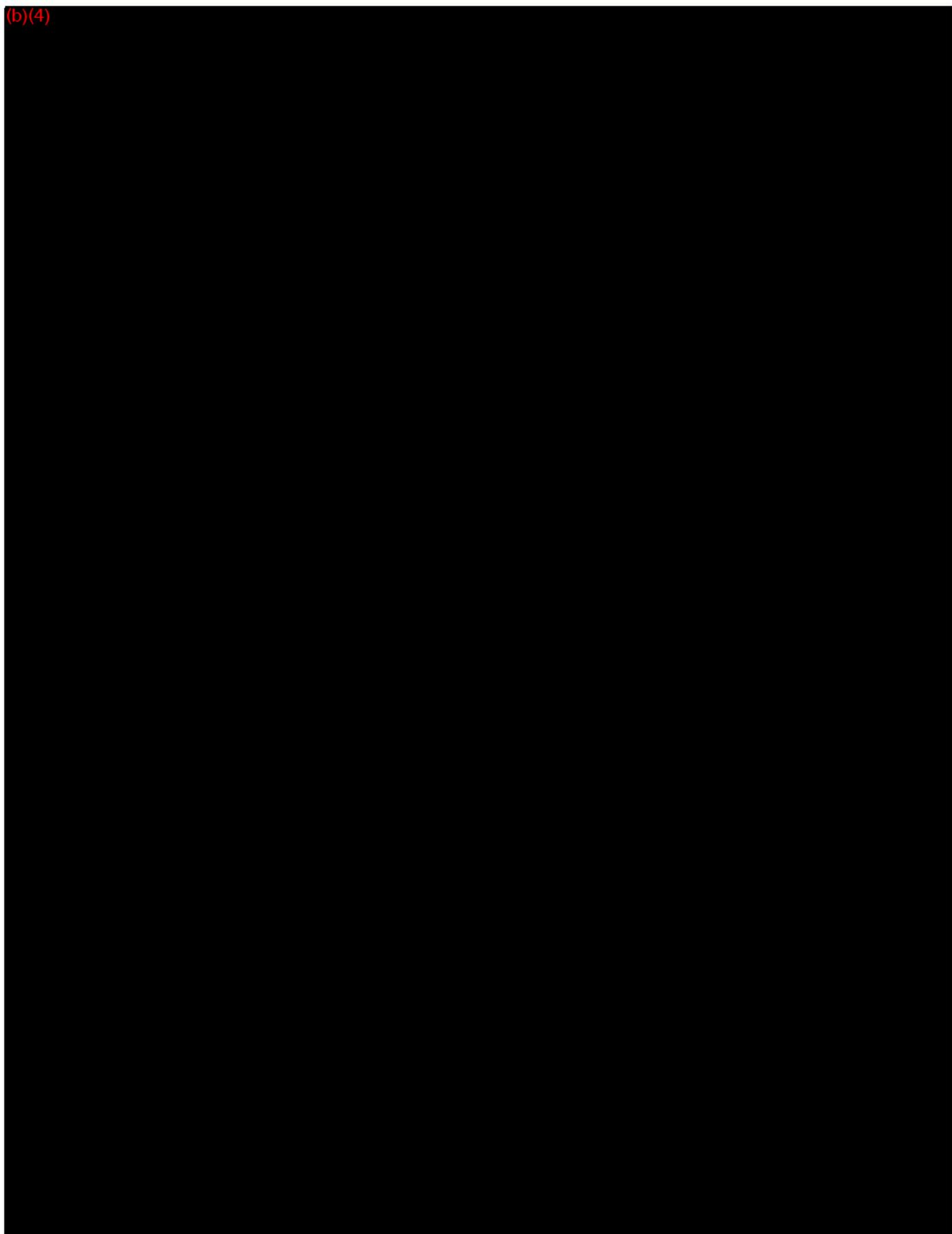
(b)(4)



(b)(4)



(b)(4)



(b)(4)



Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions or comments regarding this review, please contact Leposava Antonovic, at (301) 796-4998 or at leposava.antonovic@fda.hhs.gov.

Leposava Antonovic Ph.D.

Scientific Reviewer

CDRH/OIVD

Food and Drug Administration

10903 New Hampshire Avenue

WO66, G306

Silver Spring, MD 20993-0002

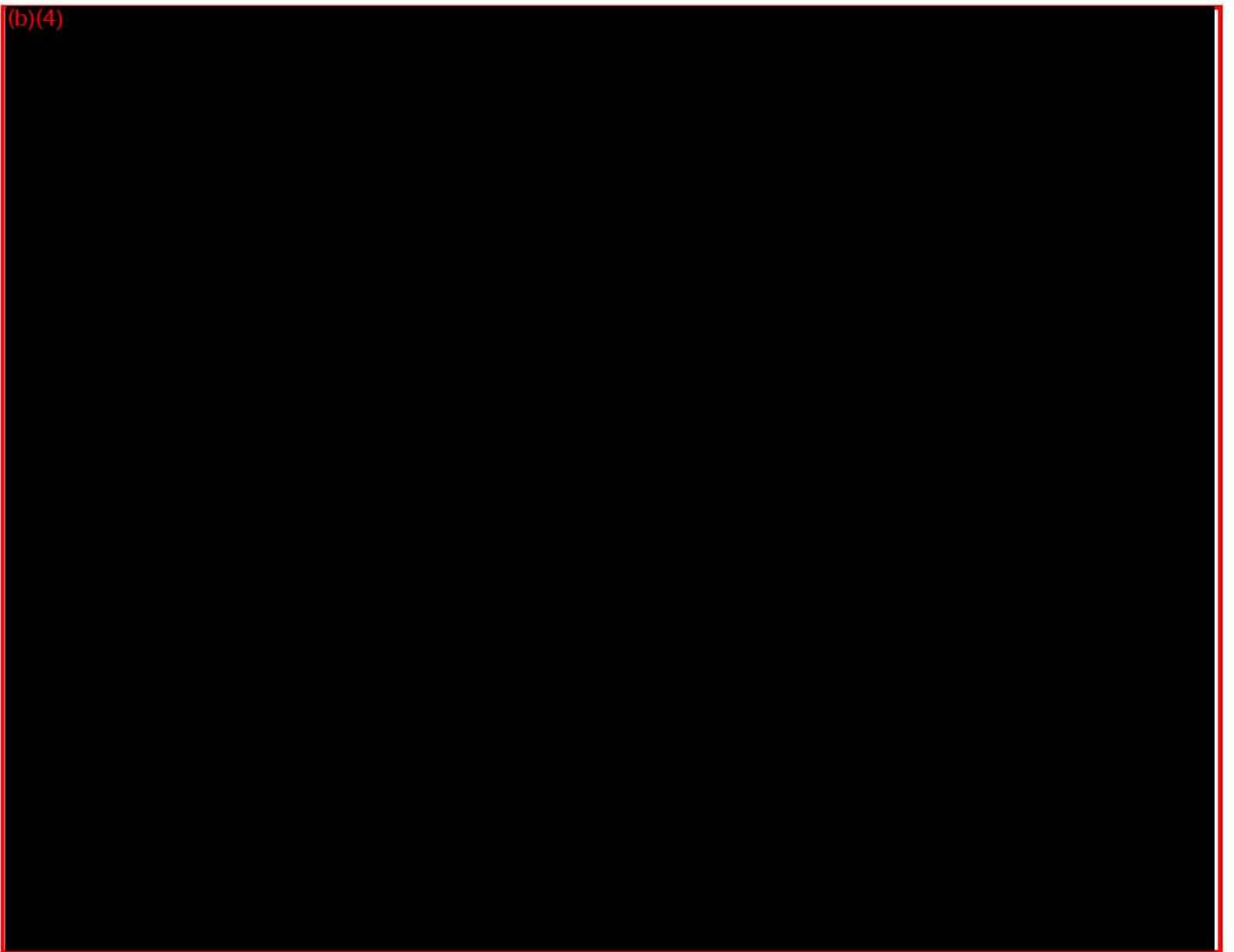
Tel: 301-796-4998

Fax: 301-847-8513

leposava.antonovic@fda.hhs.gov

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(b)(4)



Submitter:

Juang Wang
Regulatory Affairs Representative
Bio-Rad Laboratories
Clinical Immunology Division
5500 E. 2nd Street
Benicia, CA, 94510, US
Phone: (510) 741-4609
Fax: (510) 741-3941

Secondary Contact:

Patricia M. Kimley
CID RA Manager
Bio-Rad Laboratories
Clinical Immunology Division
5500 E. Second Street
Benicia, CA, 94510, US
Phone: (510) 741-6263
Fax: (510) 741-3941

November 25, 2014

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Attn: eSubmitter Team
Document Mail Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Sir or Madam:

This submission dated November 25, 2014, is filed pursuant to the In Vitro Diagnostic Device Evaluation and Safety program's Electronic Review (eReview).

The submission is a Supplement to K141114.

Truth and Accurate Statement

To the best of my knowledge, the data and information submitted in this premarket notification are truthful and accurate, and no material fact has been omitted (as required by 21 CFR 807.87).

Sincerely,

Juang Wang
Regulatory Affairs Representative
Bio-Rad Laboratories

Submission Report

Admin

1.0 Type of Submission

Introduction

*Department of Health and Human Services
Food and Drug Administration*

CDRH PreMarket Review Submission Cover Sheet

*Form Approval
OMB No. 0910-0120*

Note:	Please be advised that: 1) under 21 CFR 807.7(1), we may request any additional information that is necessary to reach a determination regarding substantial equivalence and 2) supportive raw data may be provided as attachments to this submission.
Information:	Whenever possible, please enter descriptions in executive summary format because this information will be used to generate the FDA Decision summary. If additional information is needed, please attach the appropriate file.

Section A **Type of Submission**

Submission Type	*	510(k)
▪ Submission Sub-Type	*	Supplement
- Submission Sub-Sub-Type		
Enter the original submission number.	*	K141114
Is this a bundled submission?		

User Fee Payment ID Number

[MDUFMA Cover Sheet](#)

Please attach the completed MDUFMA Cover Sheet.

2.0 Contact Information

Section B **Primary Contact (Submitter, Applicant, or Sponsor)**

Primary Contact Information *

<i>Contact Information:</i>	
Contact Name	Dr. Juang Wang
Occupation Title	Regulatory Affairs Representative
Email Address	juang_wang@bio-rad.com
<i>Address</i>	
Establishment Name	Bio-Rad Laboratories
Division Name	Clinical Immunology Division
Address	5500 E. 2nd Street Benicia, CA, 94510, US
Telephone Number	(510) 741-4609
Fax Number	(510) 741-3941

Section C	Secondary Contact (Applicant Correspondent, US Agent, or Consultant)
------------------	---

Secondary Contact Information	
<i>Contact Information:</i>	
Contact Name	Ms. Patricia M. Klimley
Occupation Title	CID RA Manager
Email Address	patricia_klimley@bio-rad.com
<i>Address</i>	
Establishment Name	Bio-Rad Laboratories
Division Name	Clinical Immunology Division
Address	5500 E. Second Street Benicia, CA, 94510, US
Telephone Number	(510) 741-6263
Fax Number	(510) 741-3941

Who should be contacted for issues related to this submission?	* Primary Contact
--	-------------------

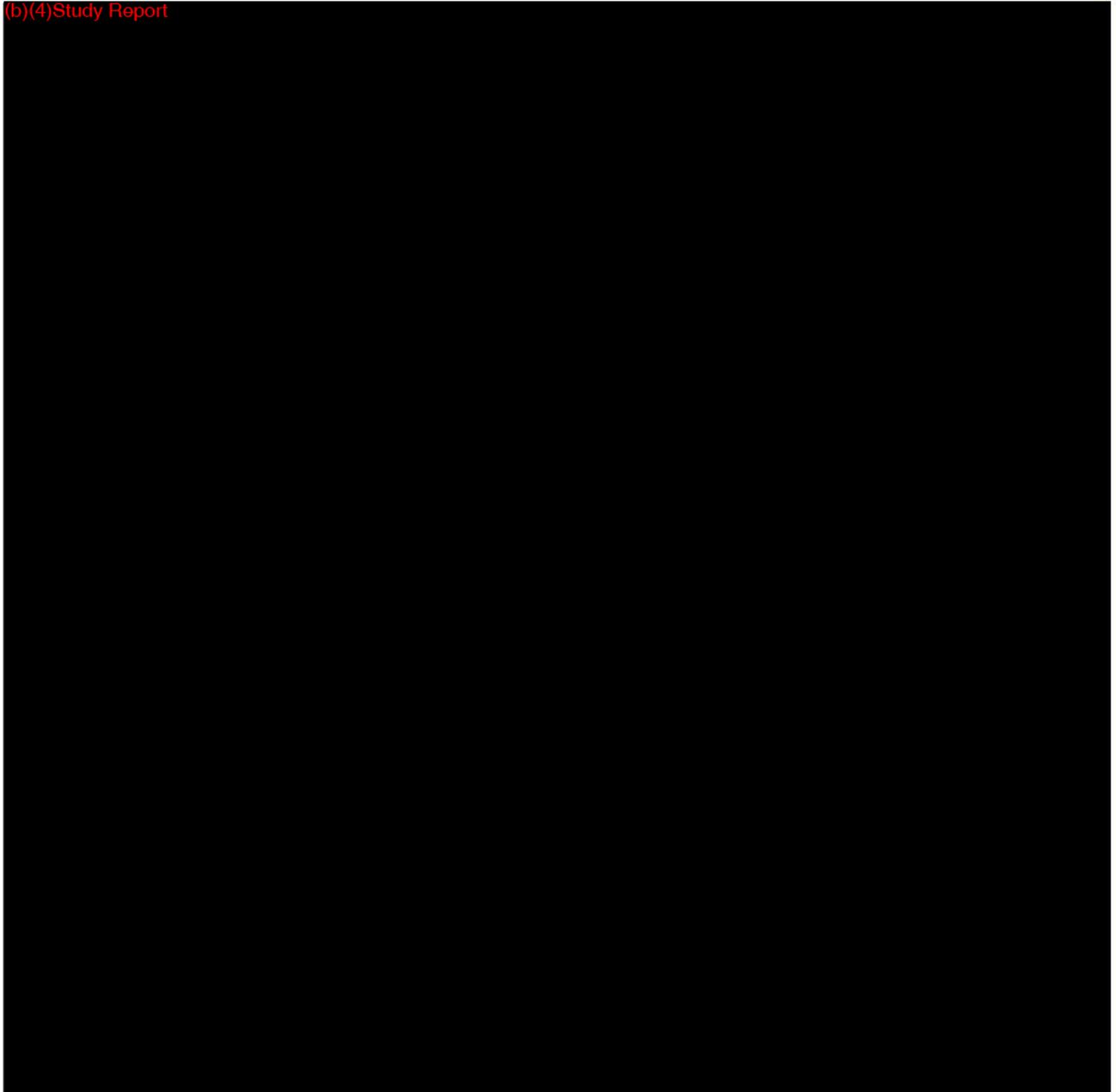
Section D	Manufacturing Location (Physical Location of the Manufacturing Plant)
------------------	--

Manufacturing Location (Optional)	
<i>Establishment Information:</i>	
Establishment Name	Bio-Rad Laboratories, Inc
FDA Establishment Identifier (FEI)	1000135116
Central File Number (CFN)	
Registration Number	2950880
Owner/Operator Number	9929003
D&B D-U-N-S Number	
<i>Physical Location:</i>	
Address	4000 Alfred Nobel Dr. Hercules, CA, 94547, US
Telephone Number	(510) 724-7000
Fax Number	

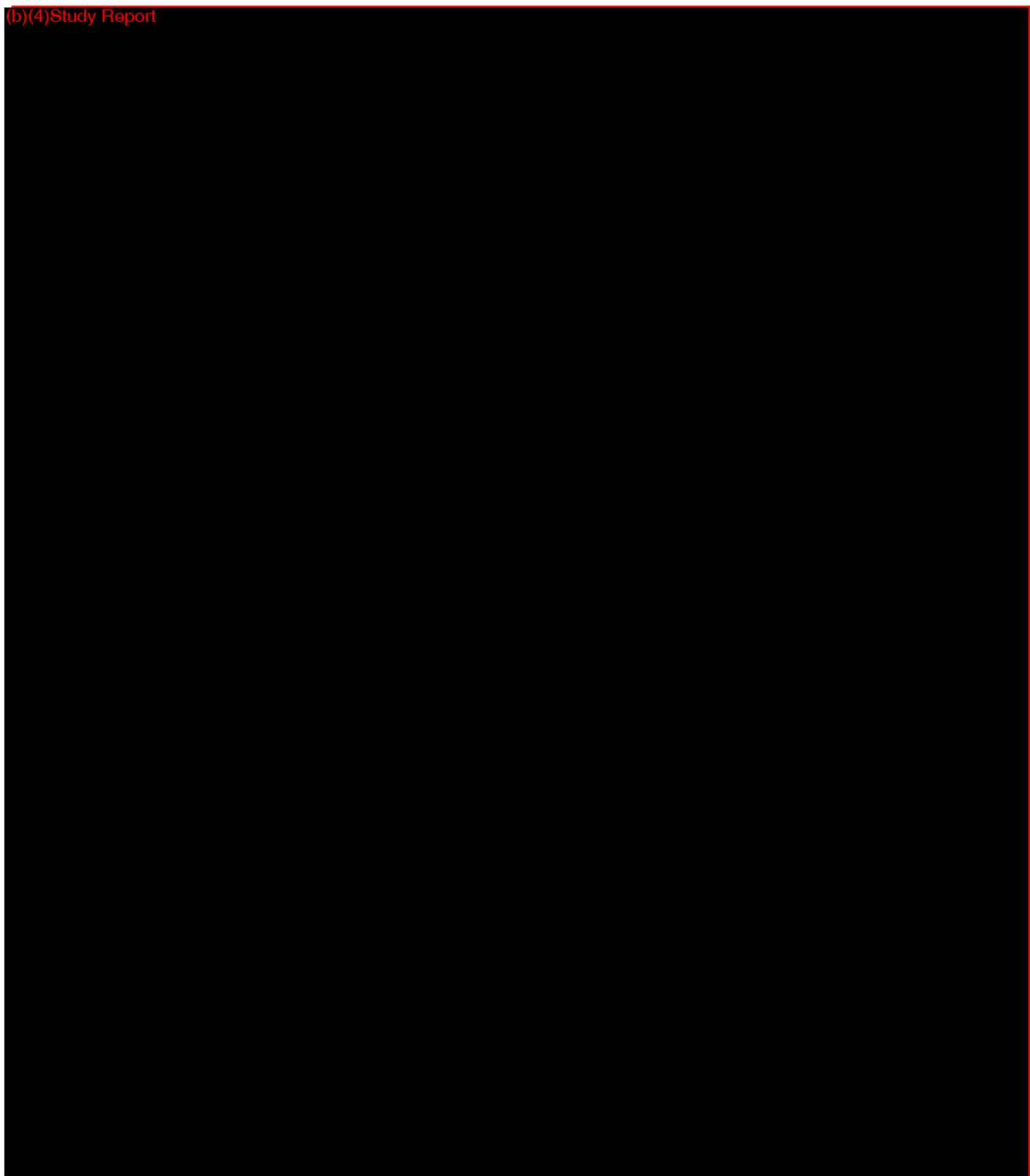
Supplement

1.0 Deficiencies and Responses

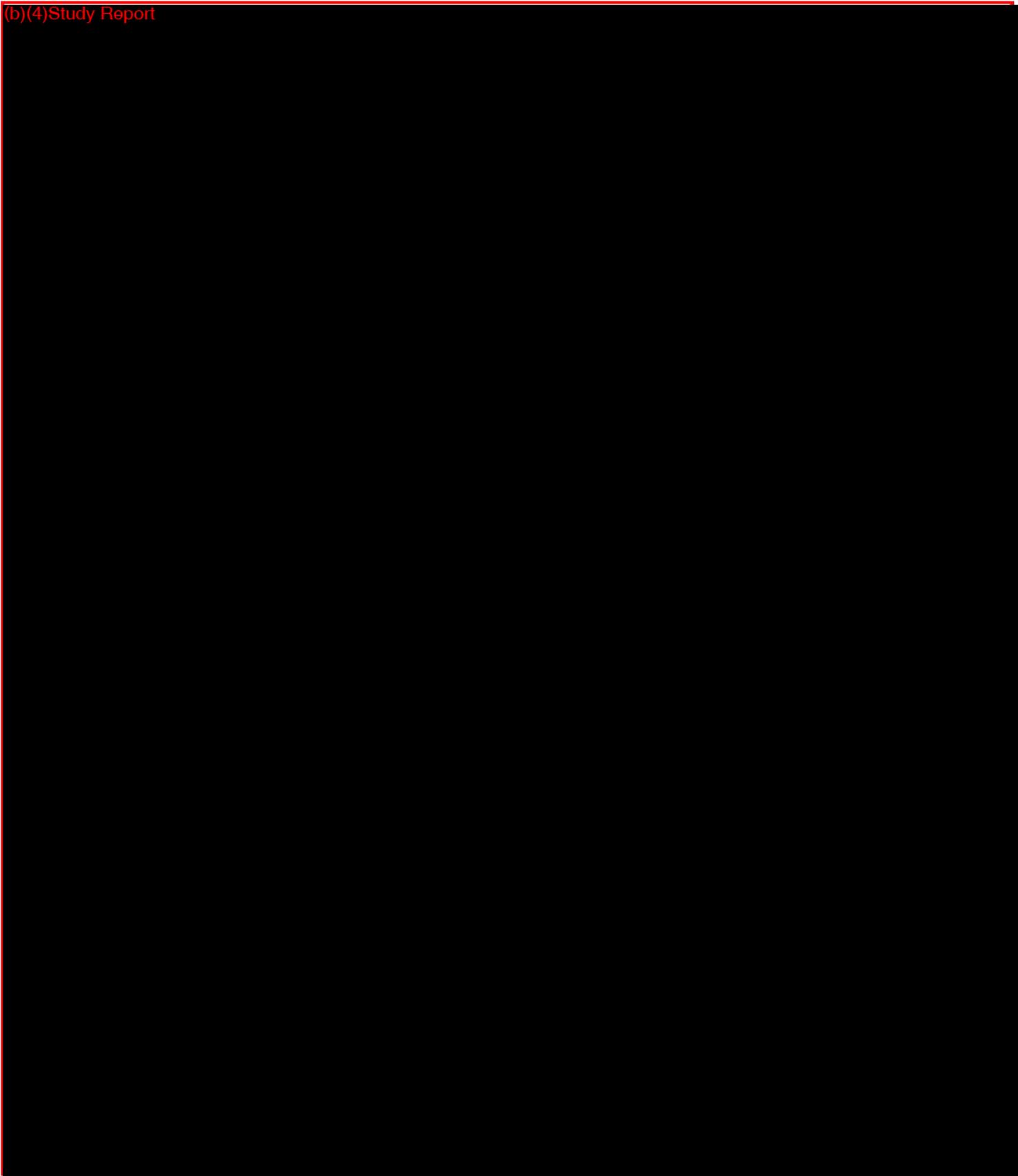
(b)(4) Study Report



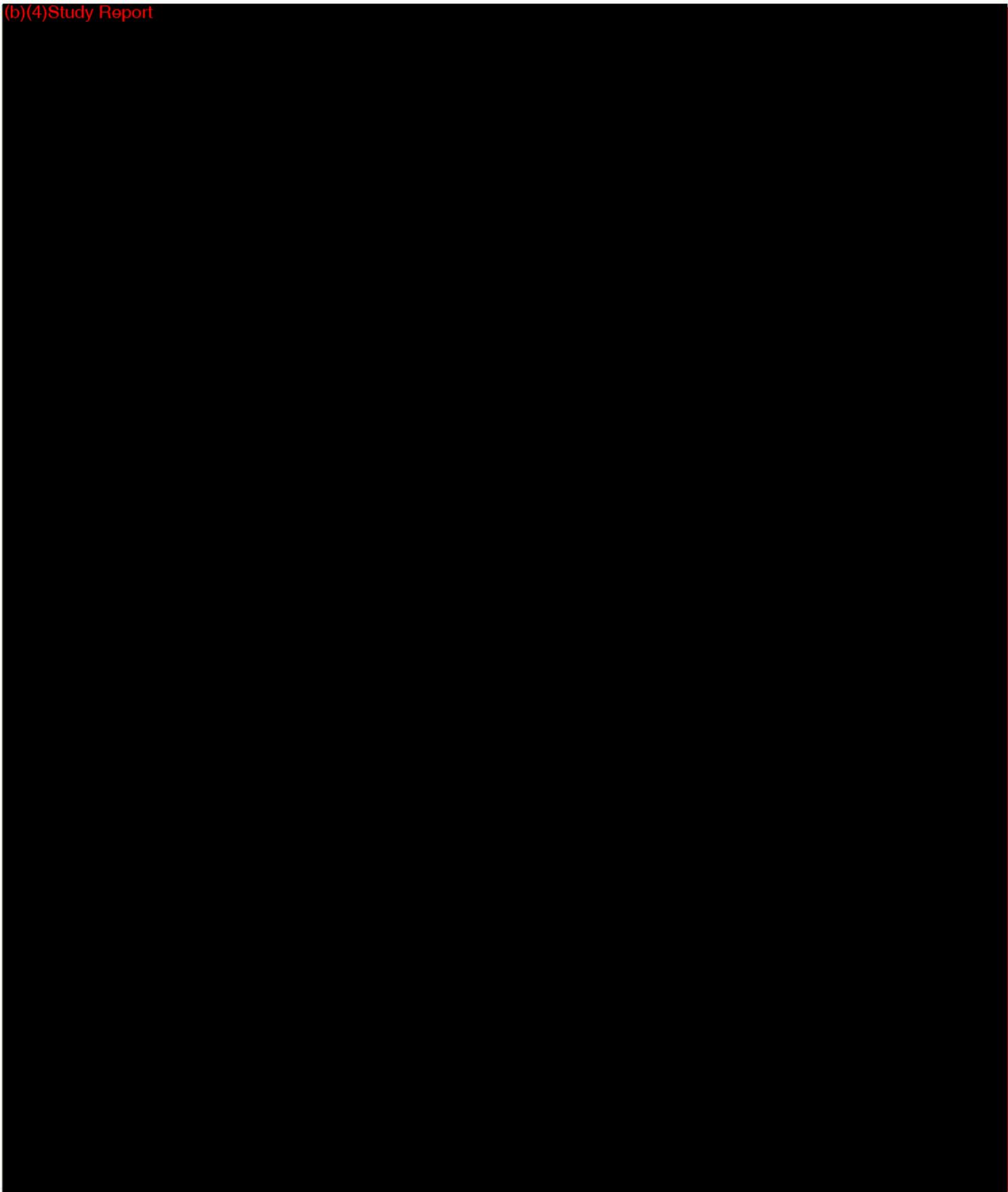
(b)(4) Study Report



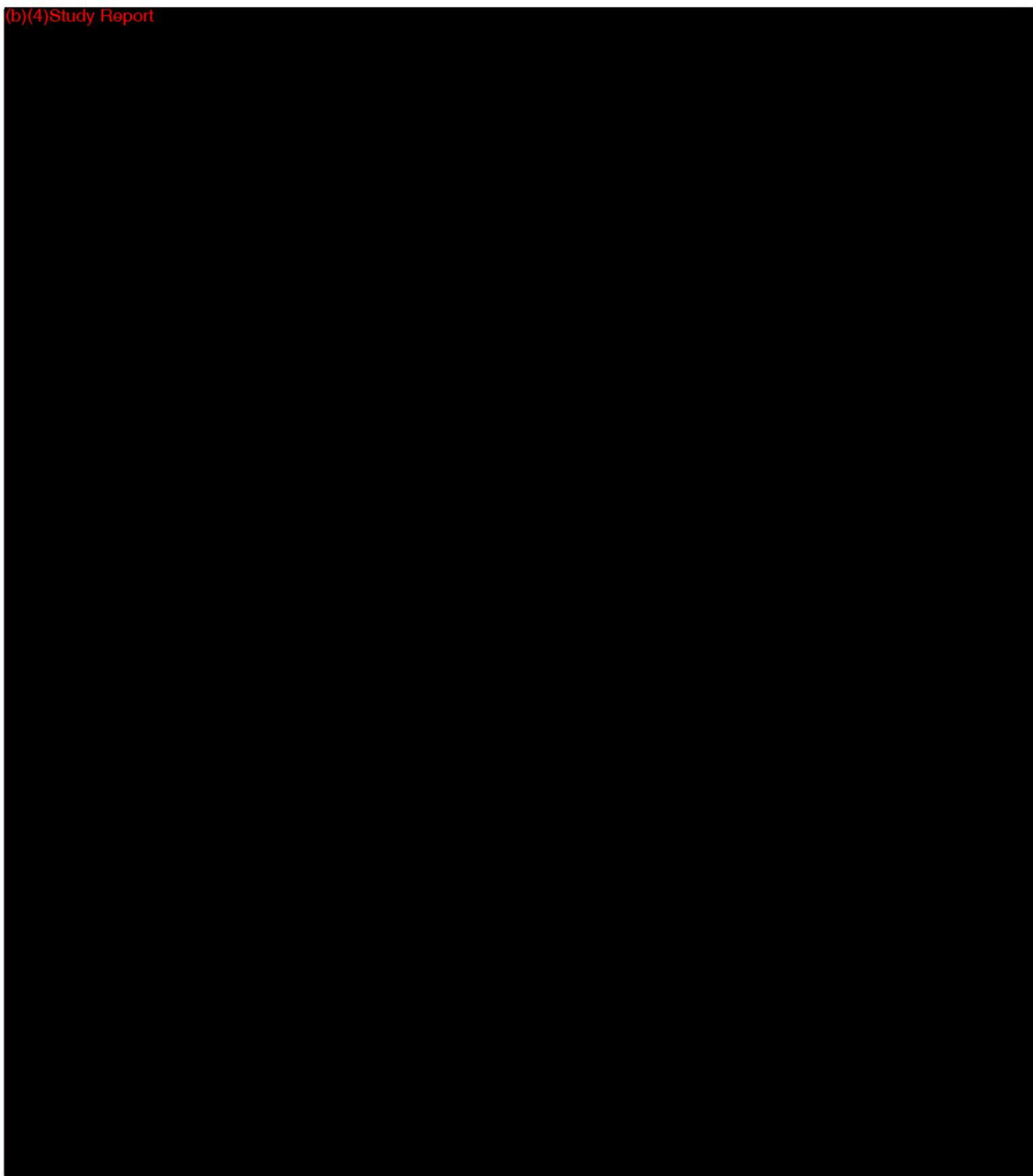
(b)(4) Study Report



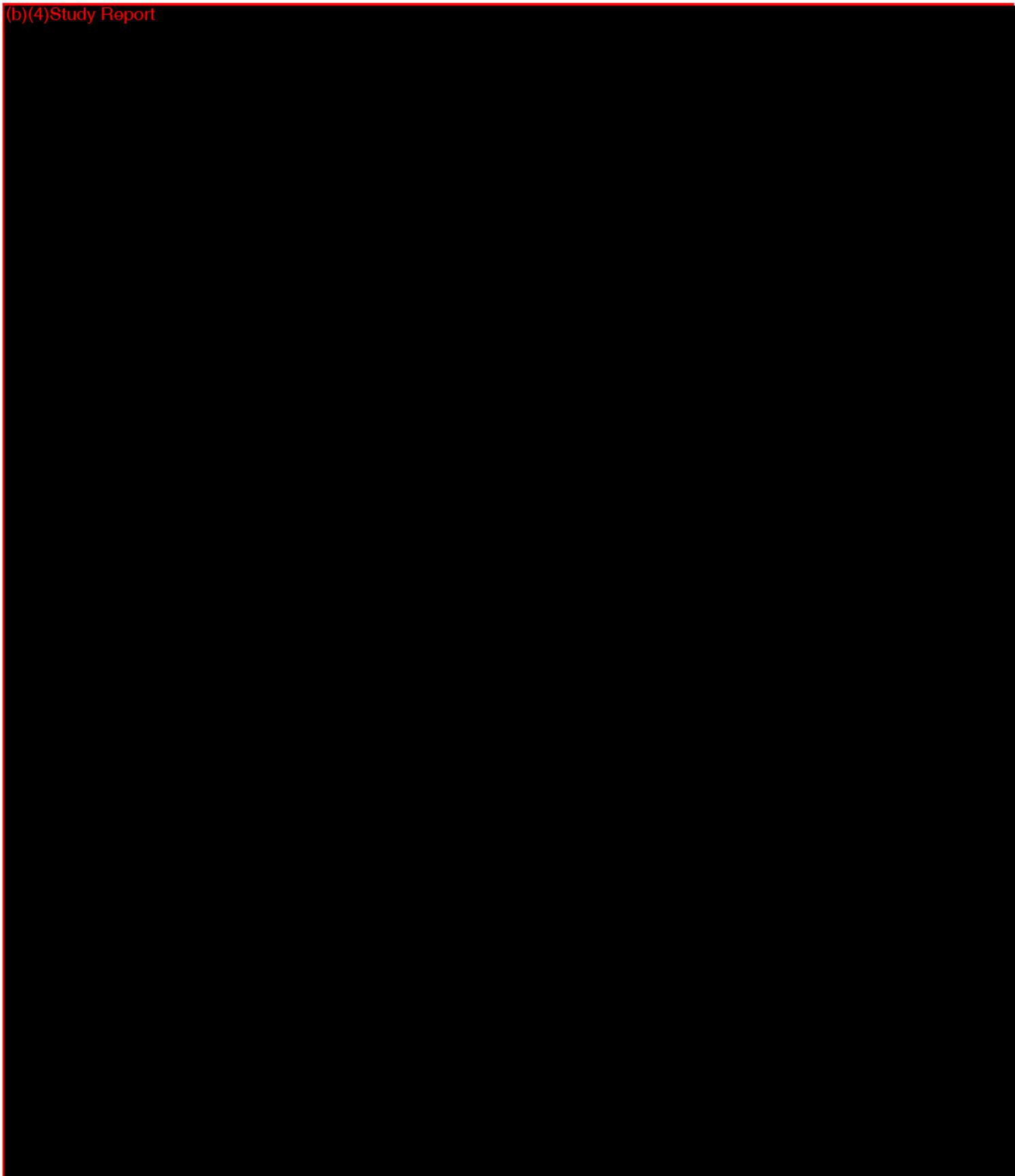
(b)(4) Study Report



(b)(4) Study Report



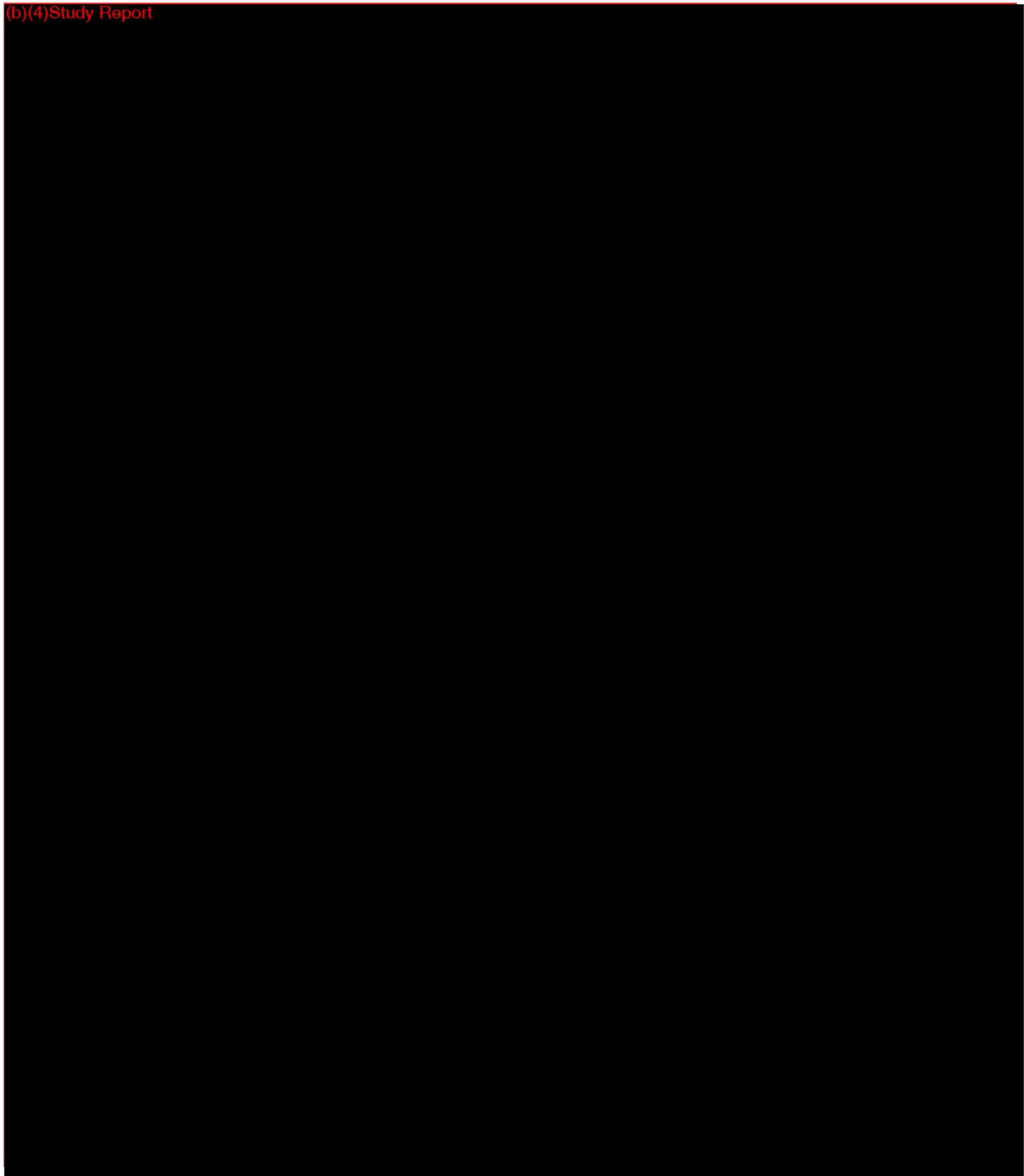
(b)(4) Study Report



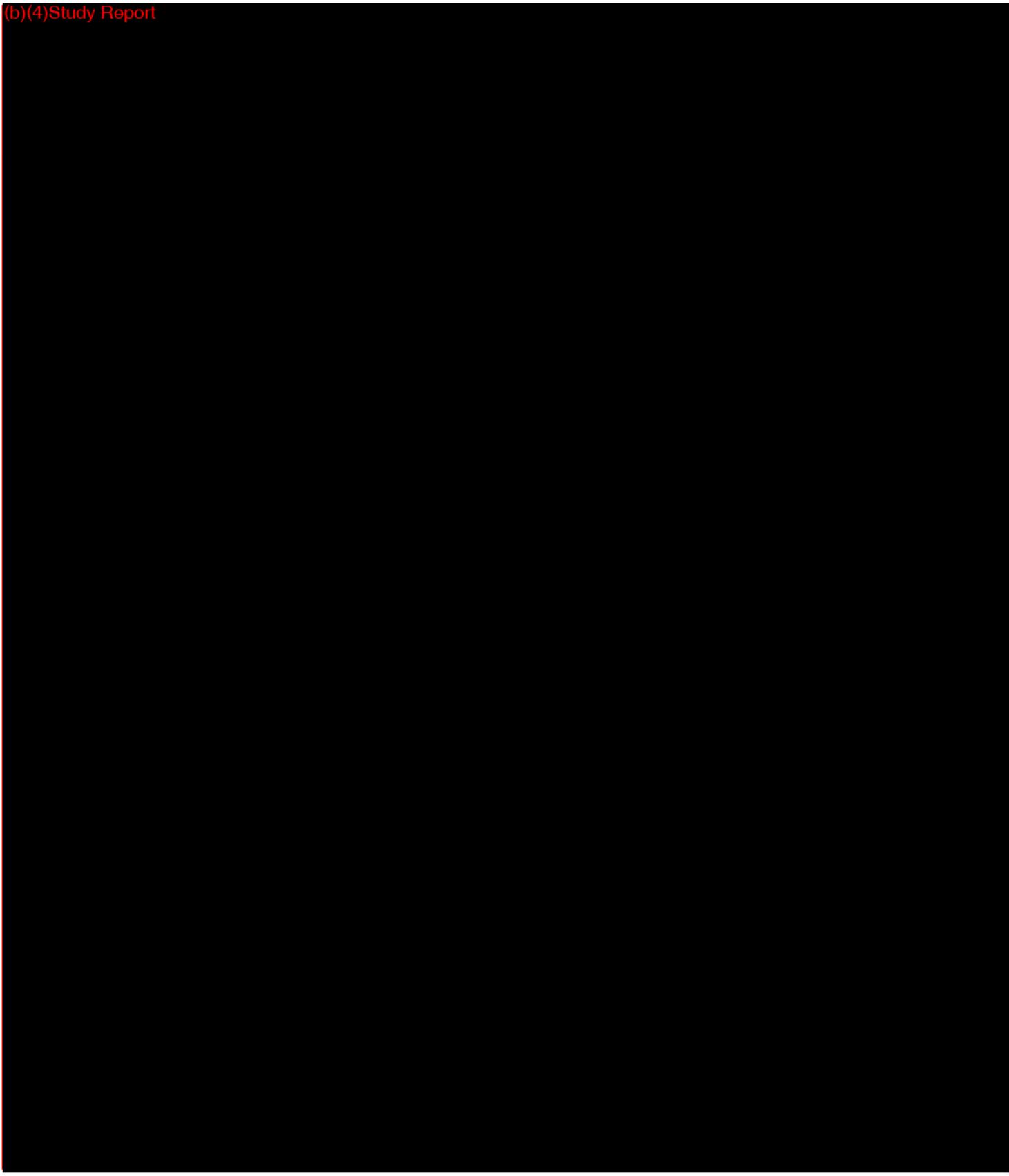
(b)(4) Study Report



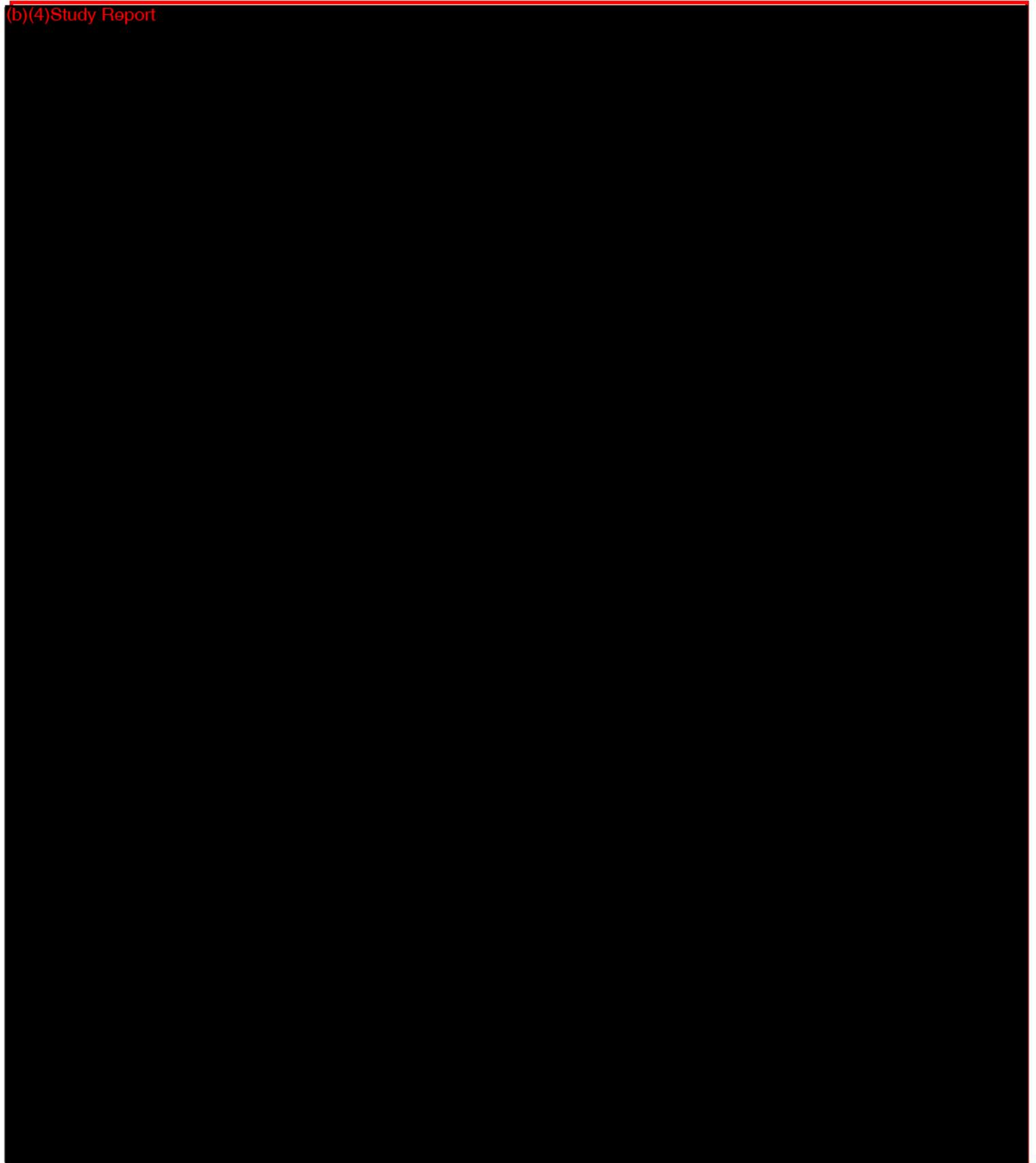
(b)(4) Study Report



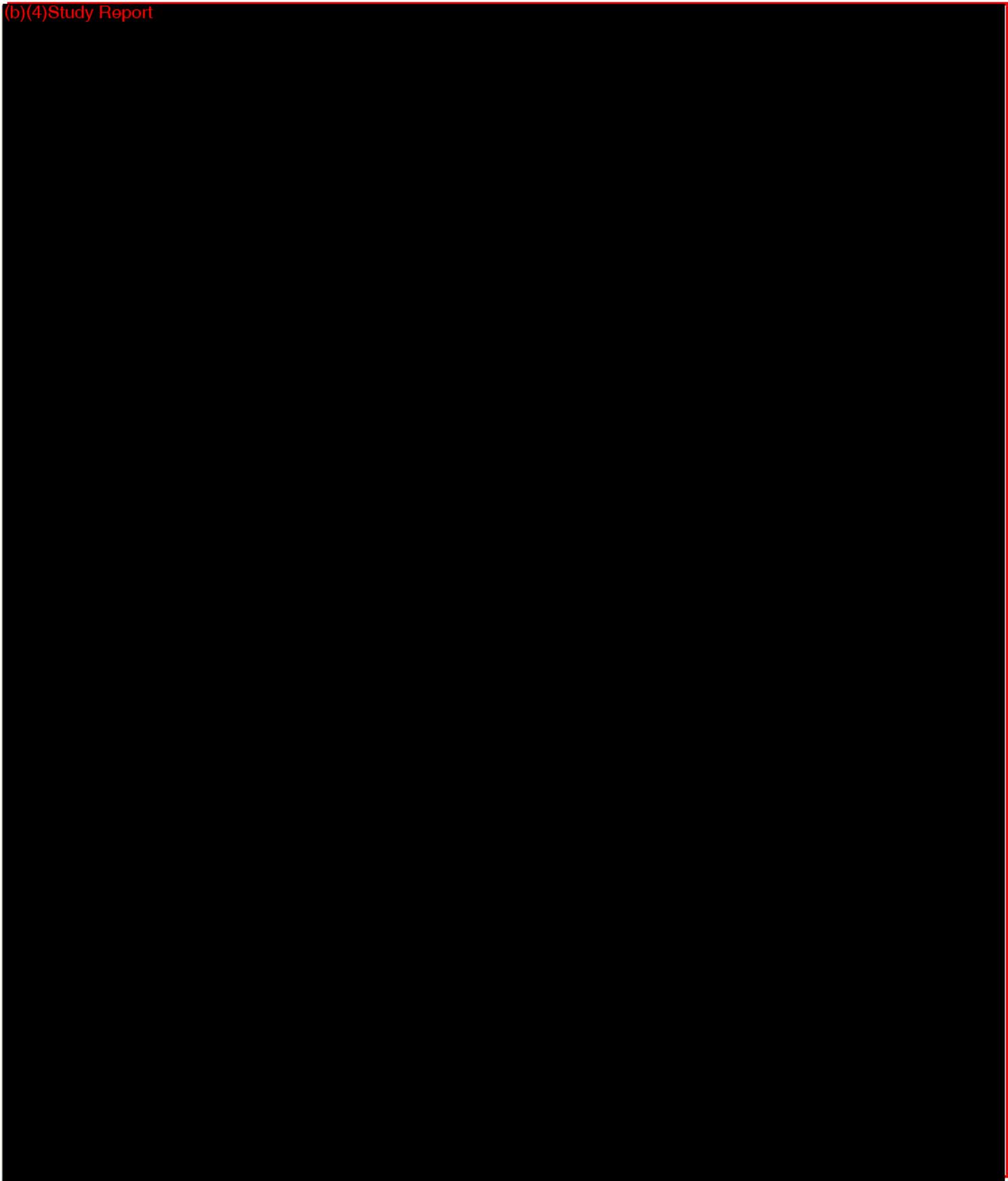
(b)(4) Study Report



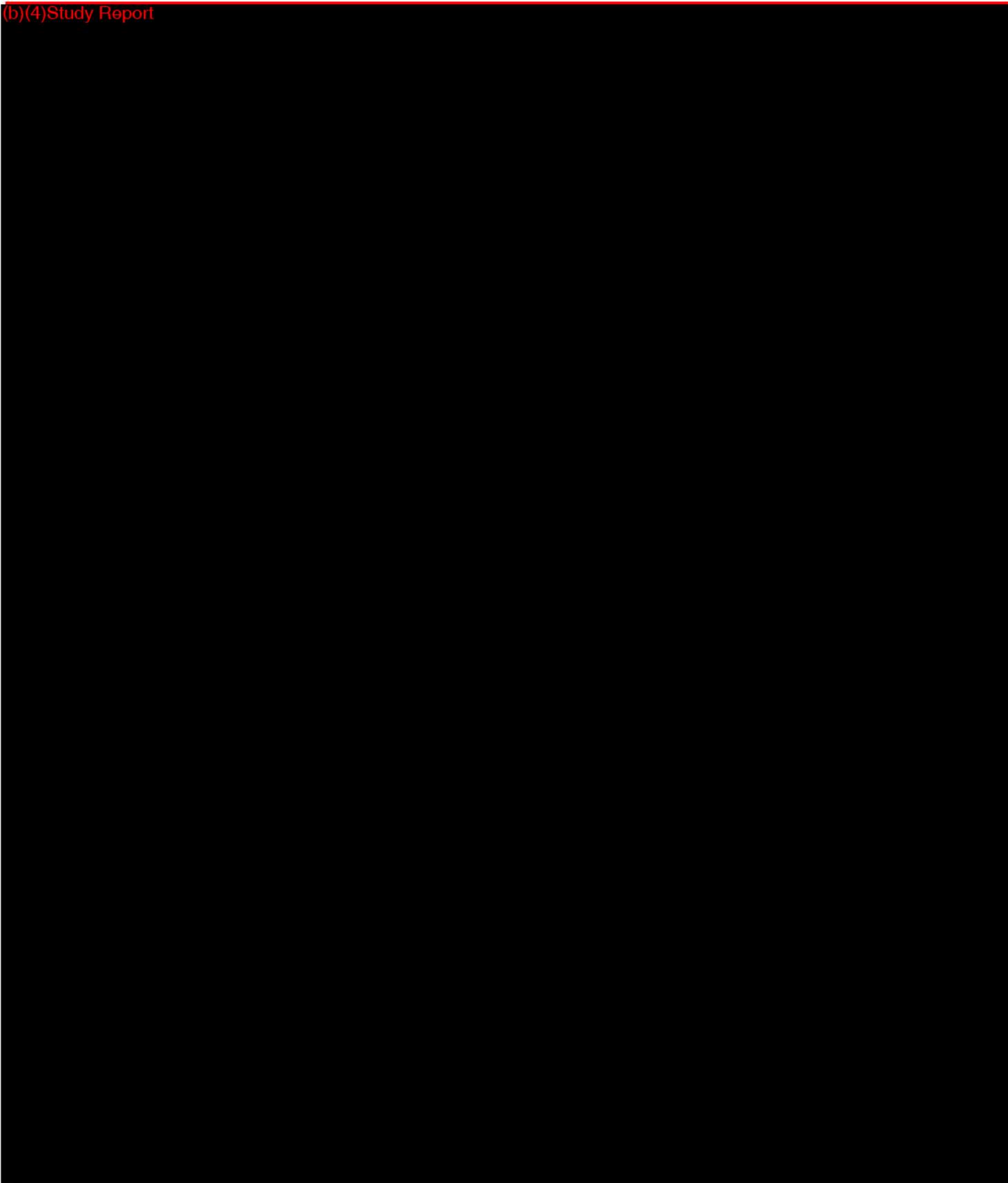
(b)(4) Study Report



(b)(4) Study Report



(b)(4) Study Report



(b)(4) Study Report



BioPlex[®] 2200 25-OH Vitamin D 510(k) Summary

Bio-Rad Laboratories hereby submits this 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides detail as a basis for a determination of substantial equivalence for the BioPlex[®] 2200 25-OH Vitamin D kit.

510(k) Number:

k141114

Summary Preparation Date:

November 24 , 2014

Applicant:

Bio-Rad Laboratories

Contact:

Juang Wang
Regulatory Affairs Representative
5500 E. Second Street
Benicia, CA 94510
[Tel:510-741-4609](tel:510-741-4609)
FAX: 510-741-3941
Juang_wang@bio-rad.com

Purpose for Submission:

New Device

Measurand:

25-hydroxyvitamin D

Type of Test:

Quantitative multiplexed flow immunoassay

Proprietary and Established Names:

BioPlex[®] 2200 25-OH Vitamin D kit
BioPlex[®] 2200 25-OH Vitamin D Calibrator Set
BioPlex[®] 2200 25-OH Vitamin D Control Set

Regulatory Information:

1. Regulation section:
 - 21 CFR §862.1825 – Vitamin D test system
 - 21 CFR §862.1150 – Calibrator

21 CFR §862.1660 – Quality Control Material (assayed and unassayed)

2. Classification:

Class II (Assays, Calibrator)
Class I (Controls)

3. Product code:

MRG, System, Test, Vitamin D
JIS, Calibrator, Primary
JJX, Single (specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Clinical Chemistry (75)

Intended Use:

1. Intended use(s):

The BioPlex[®] 2200 25-OH Vitamin D kit is a multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in human serum. The BioPlex 2200 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

The BioPlex 2200 25-OH Vitamin D kit is intended for use with the Bio-Rad BioPlex 2200 System.

The BioPlex[®] 2200 25-OH Vitamin D Calibrator Set is intended for the calibration of the BioPlex[®] 2200 25-OH Vitamin D Reagent Pack.

The BioPlex[®] 2200 25-OH Vitamin D Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex[®] 2200 System and the corresponding BioPlex[®] 25-OH Vitamin D Reagent Packs in the clinical laboratory. The performance of the BioPlex[®] 25-OH Vitamin D Control Set has not been established with any other 25-hydroxyvitamin D assays.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Bio-Rad BioPlex[®] 2200 System

Device Description:

BioPlex[®] 2200 25-OH Vitamin D kit includes the following components:

- One (1) 10 mL vial of Bead Set containing dyed beads coated with anti-25-OH D antibody (sheep), an Internal Standard bead (ISB), and a Serum Verification bead (SVB) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives.
- One (1) 10 mL vial of Release Buffer containing 25-OH Vitamin D releasing reagents in citrate and trisodium citrate acid buffer at pH 4.1 and ProClin 950 (<1.0%) as preservative.
- One (1) 5 mL vial of Conjugate 1 containing biotinylated 25-OH Vitamin D conjugate and biotinylated anti-human FXIII antibody conjugate (murine) in buffer with protein stabilizers (bovine). ProClin 950 (< 1.0%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives and chemical blockers.
- One (1) 5 mL vial of Conjugate 2 containing phycoerythrin conjugated streptavidin (SA -PE) in a buffer comprising protein stabilizers (bovine). ProClin 950 (< 1.0%) and sodium azide (< 0.1%) as preservatives, chemical blockers and detergent (Tween 20).

BioPlex[®] 2200 25-OH Vitamin D Calibrator set contains six (6) 0.5 mL 25-OH Vitamin D vials. Calibrator level 1 contains 25% horse serum without 25-OH Vitamin D. The calibrator levels 2 to 6 are provided in a Vitamin D depleted human serum matrix supplemented with known concentration of 25-hydroxyvitamin D₃. All calibrators contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

BioPlex[®] 2200 25-OH Control set contains two (2) 1.5 mL Level 1 and two (2) 1.5 mL Level 2 Control vials, each containing 25-OH Vitamin D in human serum matrix. All controls contain ProClin 950 (≤ 0.3%), sodium benzoate (≤ 0.1%) and 5-bromo-5-nitro-1, 3-dioxane (<0.1%) as preservatives.

Additional materials required but not supplied include BioPlex[®] 2200 Sheath Fluid containing Phosphate Buffered Saline (PBS), ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives; and BioPlex[®] 2200 Wash Solution containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin 300 (0.03%) and sodium azide (<0.1%) as preservatives.

Substantial Equivalence Information:

1. Predicate device name(s):
EUROIMMUN 25-OH Vitamin D ELISA, k123660
2. Comparison with predicate:

Device Similarities		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Intended Use	Multiplex flow competitive immunoassay intended for the quantitative determination of 25-hydroxyvitamin D in serum.	Quantitative determination of 25-OH Vitamin D and other hydroxylated vitamin D metabolites in human serum or plasma.
Indications for Use	To be used as an aid in the assessment of vitamin D sufficiency.	Results are to be used in conjunction with other clinical and laboratory data to assist the clinician in the assessment of vitamin D sufficiency in adult populations
Measured Analyte	25-hydroxyvitamin D	Same
Assay Type	Quantitative	Same
Test Principle	Competitive immunoassay	Same
Antibody	Monoclonal Sheep antibody against 25 OH Vitamin D	Same
Signal Detection	Fluorescence	Same
Unit of Measure	ng/mL	Same
Calibrator(s) and Calibration	6 calibrator levels (sold separately); 4-PL (parameter logistic) curve fit algorithm	Same

Device Differences		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Assay Technology	Automated multiplex flow competitive immunoassay	Manually competitive immunoassay
Conjugate	Biotinylated 25-hydroxyvitamin D and	Biotin-labeled 25-OH vitamin D, Peroxidase-

Device Differences		
Characteristics	New Device BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
	phycoerythrin conjugated streptavidin	labeled streptavidin and substrate TMB
Solid Phase	Antibody-coated paramagnetic microbeads	Antibody coated 96 microwell ELISA plate
Measuring range	6.5 – 150.0 ng/mL	4 – 120 ng/mL
Sample Matrix	Serum	Serum or EDTA or Lithium heparin plasma
Sample Size	10 µL	20µL
Calibrator Matrix	25% horse serum and depleted human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Open Pack Stability	60 days	Not applicable
Reagent Integral Storage	On-board or in refrigerator at 2-8°C	Not applicable
Sample Handling/Process	Automated	Manually
Calibrator Open storage at 2-8°C	30 days	3 months
Calibration Frequency	Every 30 days	Every 96 well plate
Instrumentation	Bio-Rad BioPlex 2200 System	ELISA plate reader
Measuring wavelength	550 – 610 nm	450/620nm

Control Set Similarities and Differences		
Characteristics	BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
Intended Use	Use as an assayed quality control to monitor the overall performance of the BioPlex 2200 System and the corresponding BioPlex 2200 25-OH Vitamin D reagent packs in the clinical laboratory	Intended for use as assayed quality control samples to monitor the accuracy and precision of the assay
Storage	Store at 2 -8°C until ready to	Same

Control Set Similarities and Differences		
Characteristics	BioPlex 2200 25-OH Vitamin D Kit	Predicate Device EUROIMMUN 25-OH Vitamin D ELISA K123660
	use	
Matrix	Human serum with ProClin 950, sodium benzoate and BND	Liquid in horse serum with preservatives
Control Open Stability at 2 – 8°C	60 days	No Applicable

Standard/Guidance Document Referenced (if applicable):

EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition (Vol. 24 No.25)
 EP06-A, Evaluation of Linearity of Quantitative Measurement: A Statistical Approach, Approved Guideline (Vol. 23 No.16)
 EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition (Vol. 25 No.27)
 EP09-A2IR, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition (Interim Revision) (Vol. 30 No. 17)
 EP15-A2, User Verification of Performance for Precision and Trueness, Approved Guideline, Second Edition (Vol. 25 No.17)
 EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline, Second Edition (Vol. 32 No.8)
 EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (Vol. 29, No. 20)
 C28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, Third Edition (Vol. 28 No.30)

Test Principle:

The BioPlex® 2200 25-OH Vitamin D assay is a multiplex flow competitive immunoassay for the quantitative determination of 25-hydroxyvitamin D in human serum.

The BioPlex 2200 System combines an aliquot of patient sample with the Vitamin D Release Buffer to dissociate the 25-hydroxyvitamin D from its binding protein. After the first incubation, the bead reagent is added to the reaction vessel and incubated at 37°C. After the second incubation, the BioPlex 2200 System adds the vitamin D-biotin conjugate 1. The excess conjugate 1 is removed during a wash cycle and the streptavidin-phycoerythrin (SA-PE) conjugate 2 is added. The excess conjugate 2 is removed during a wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of 25-hydroxyvitamin D captured is inversely proportional to the fluorescence of the attached SA-PE. Raw data is calculated in relative fluorescence intensity (RFI). Two additional dyed beads, Internal Standard Bead (ISB) and

Serum Verification Bead (SVB) are present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel, respectively.

The BioPlex 25-OH Vitamin D assay is calibrated using a set of 6 distinct calibrators supplied separately by Bio-Rad Laboratories. Results are calculated from a 4-PL (parameter logistic) calibration curve in which an inverse relationship exists between the amount of 25-hydroxyvitamin D in the patient sample and the amount of RFI detected by the system. The results are expressed in ng/mL.

Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision testing of the BioPlex® 2200 25-OH Vitamin D kit on the BioPlex® 2200 instrument was performed in accordance with CLSI EP5-A2 guideline. A human serum panel consisting of 6 frozen samples spanning the measuring range was assayed in duplicate per run on two runs daily over 20 days (N=80) on one reagent lot. Two levels of the BioPlex 25-OH Vitamin D controls were also included. The data were analyzed for within-run, between-run, between-day, and total precision and the mean (ng/mL), standard deviation (ng/mL) and percent coefficient of variation (%CV) are summarized below:

BioPlex® 2200 25-OH Vitamin D – CLSI EP5-A2 Precision

Serum Panel	N	Mean ng/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	80	15.0	1.19	7.9	0.69	4.60	0.77	5.2	1.58	10.5
Sample 2	80	17.2	1.02	5.9	0.86	5.00	1.19	6.9	1.78	10.4
Sample 3	80	36.1	1.61	4.5	1.30	3.60	1.56	4.3	2.59	7.2
Sample 4	80	47.2	2.20	4.7	1.24	2.60	1.85	3.9	3.13	6.6
Sample 5	80	77.9	1.99	2.6	1.42	1.80	1.98	2.5	3.15	4.0
Sample 6	80	110.8	3.60	3.2	3.00	2.7	2.62	2.4	5.37	4.8
Control 1	80	22.1	1.30	5.9	0.87	3.9	1.04	4.7	1.88	8.5
Control 2	80	50.0	2.38	4.8	1.18	2.4	1.52	3.0	3.07	6.1

CLSI EP15-A2 Reproducibility

Precision and reproducibility was also evaluated in accordance with CLSI EP15-A2 guideline “User Verification of Performance for Precision and Trueness, Vol 25, No 17”.

A different serum panel consisting of 8 samples spanning the measuring range were assayed in 2 replicates per run, two runs per day over 5 days (n=20) using one lot of BioPlex 25-OH Vitamin D kit. Two levels of controls were also included. The data were analyzed for within-run, between run, between day, and total precision and the mean ng/mL, standard deviation and percent coefficient of variation (%CV) are summarized below:

BioPlex® 2200 25-OH Vitamin D - CLSI EP15-A2 Reproducibility

Serum Panel	N	Mean ng/mL	Within Run		Between Run		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Sample 1	20	11.5	0.69	6.0%	0.47	4.1%	1.71	14.8%
Sample 2	20	13.6	0.80	5.9%	0.26	1.9%	1.18	8.7%
Sample 3	20	26.1	0.88	3.4%	1.15	4.4%	1.59	6.1%
Sample 4	20	30.2	1.99	6.6%	0.00	0.0%	2.71	9.0%
Sample 5	20	50.2	2.23	4.4%	0.77	1.5%	2.96	5.9%
Sample 6	20	56.4	2.09	3.7%	2.79	4.9%	5.26	9.3%
Sample 7	20	100.5	4.52	4.5%	2.81	2.8%	5.32	5.3%
Sample 8	20	104.9	3.97	3.8%	1.54	1.5%	5.24	5.0%
Control 1	20	21.6	0.98	4.5%	1.00	4.6%	1.84	8.5%
Control 2	20	58.8	2.44	4.2%	1.29	2.2%	2.99	5.1%

b. Linearity/assay reportable range:

Five high patient serum samples extending 20% higher than upper limit of the assay range were tested to demonstrate linearity. These samples were serially diluted with low levels of human sample near LoQ in accordance with CLSI EP06-A guideline. Each sample and dilution was evaluated in replicates of four using one BioPlex 25-OH Vitamin D reagent lot on one instrument. Linear and polynomial regression analysis of 25OH Vitamin D recovery vs. sample dilution was performed to determine if the dilution curves exhibit statistically significant non-linear regression based on the CLSI guideline EP06-A.

The regression parameters (slope, intercept and r^2) of the observed values vs. predicted values are show below.

Sample	Conc (ng/mL)	Slope	Intercept	r^2	Dilution range
1	168.9	0.9999	-0.0034	0.9974	4.4 – 168.9
2	188.7	0.9999	0.0194	0.9971	4.3 – 188.7
3	183.4	1.0001	0.0083	0.9971	4.9 – 183.4
4	168.9	1.0001	0.0045	0.9988	5.5 – 168.9
5	172.5	0.9999	0.0168	0.9970	5.8 – 172.5

The BioPlex 2200 25-OH Vitamin D assay has demonstrated that the assay range is up to 150.0 ng/mL.

Over-Range (OR) results may be generated for values greater than the reportable measuring range and results are reported as > 150.0 ng/mL.

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

Traceability:

The BioPlex 25-OH Vitamin D Calibrators are traceable to internal standards which are determined by UV spectrophotometric analysis using the extinction coefficient of 18,000 mL/mmol/cm at 264 nm wavelength.

The six levels of Master calibrators are manufactured volumetrically from the internal standards into the depleted human serum except level 1 (25-hydroxyvitamin D free) in 25% horse serum. The Master calibrators are immediately frozen at <-70°C.

Value Assignment:

The BioPlex 25-OH Vitamin D kit calibrators are manufactured for each lot kit with the same matrix as the Master calibrators and are stabilized with ≤0.3% ProClin 950, ≤0.1% sodium benzoate, and <0.1% 5-bromo-1,3-nitro-dioxane.

Calibrator assignment is established for the matched lot of BioPlex® 2200 25-OH Vitamin D kit using the Master calibrators as reference. Calibrator assignment is established for the matched lot of BioPlex® 2200 25-OH Vitamin D kit using the Master calibrators as reference. For each calibrator level except level 1, three vials are tested in replicates of five on three BioPlex 2200 analyzers for a total of 45 data points. The mean values obtained for each kit calibrator level are verified and must fall within specified acceptable range.

Two levels of the BioPlex 2200 25-OH Vitamin D control set are prepared from a pool of native human serum specimens. For each control level, three vials are tested in replicates of five using each of the kit lots on three BioPlex 2200 analyzers for a total of 45 replicates per reagent lot. The total number of replicates for each control level is 90 when two reagent lots are used and 135 when three reagent lots are used. For each control level, the mean values were derived from replicate analyses and should fall within the corresponding deviation.

The manufacturing target values and ranges of the Calibrator and Control Sets are listed below.

Calibrator Set	Target (ng/mL)	Range(ng/mL)
Level 1	0.0	N/A
Level 2	10.0	8.0 – 12.0
Level 3	30.0	20.0 – 40.0
Level 4	75.0	65.0 – 85.0
Level 5	110.0	100.0 – 120.0
Level 6	165.0	155.0 – 175.0

Control Set	Target (ng/mL)	Range (ng/mL)
Level 1	19.0	14.5 – 23.5
Level 2	55.0	45.0 – 65.0

Stability:

Stability studies have been performed to support the following claims:

Calibrator and Control:

BioPlex® 2200 25-OH Control and Calibrator Sets: Calibrator Open Vial Stability (2 to 8°C), 30 days from first opening; Control Open Vial Stability (2 to 8°C), 60 days from first opening; Onboard Calibration Curve Stability, 30 days; Calibrators and Controls Real Time Stability (2 to 8°C), 24 months; labeled as until expiration date; Calibrators and Controls Accelerated Stability (2 to 8°C), 2 years predicted. Calibrators freeze-thaw (-20°C or -70°C), 5-freeze thaw cycles; Control freeze-thaw (-20°C or -70°C), 1-freezethaw cycle at -20°C and 5-freeze-thaw cycles at -70°C.

Kit Stability:

BioPlex® 2200 25-OH Vitamin D Kit: Real Time (unopened) Kit Stability, 9 months or until the date of expiration when stored unopened on the instrument or at 2 to 8°C; the open kit claim is 60 days.

Sample Stability:

Sample stability studies were also performed: Sample stability fresh (2 to 8°C), 7 days; Sample stability frozen (-20 or -70°C), 24 months; Sample Freeze-thaw (-20 or -70°C), up to 3-freeze thaw cycles at -20°C and 2-freeze thaw cycles at -70°C acceptable.

d. *Detection limit:*

The study was conducted in accordance with CLSI EP17-A2 guideline for determining the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ).

Limit of Blank (LoB)

Five blank samples were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 4 replicates per day for 5 days yielding 100 data points per reagent lot.

A non-parametric statistical analysis at 95th percentile is used to calculate LoB.

Limit of Detection (LoD)

Six human samples with low level of 25-OH vitamin D in the range of 4 to 35 ng/mL were tested with two BioPlex 25-OH Vitamin D reagent lots on one instrument in 12 replicates per day for five days yielding 60 data points per sample per reagent lot. LoD is then calculated by the equation:

$LoD = LoB + c_p SD_{LoD}$ Where C_p is a multiplier to give the 95th percentile of a normal distribution and SD is from the linear regression of standard deviation versus 25-OH Vitamin D mean value.

Limit of Quantitation (LoQ)

The LoQ was evaluated based on the accuracy goal which was defined as precision $\leq 20\%$ CV. The %CV was calculated using the same measurement results of the 6 low level samples used for determining the LoD.

The results of LoB, LoD, and LoQ in ng/mL are summarized in the table below.

LoB	LoD	LoQ
0.8	2.5	6.5

e. Analytical specificity:

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex® 2200 25-OH Vitamin D kit according to CLSI EP7-A2 guideline. No interference was observed with any of the substances tested. The substances and the maximum levels tested are shown in the table below:

Substance	Concentration
Hemoglobin	≤ 150 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 30 mg/dL
Triglycerides	≤ 250 mg/dL
Total Protein	≤ 12 g/dL
Cholesterol	≤ 250 mg/dL
Uric Acid	≤ 20 mg/dL
HAMA	≤ 100 ng/mL
Rheumatoid Factor	≤ 350 IU/mL
Ascorbic Acid	≤ 3 mg/dL

Cross-Reactivity:

The study was conducted in accordance with CLSI EP17-A2 using 2 human serum pools at 25-hydroxyvitamin D concentrations of 20 and 35 ng/mL. Nine cross reactants at levels listed below were then spiked into the human serum pools. The spiked and non-spiked samples were then evaluated in replicates of five to calculate the cross reactivity as shown below.

$$\% \text{ Cross Reactivity} = (\text{spiked vitamin D} - \text{non-spiked vitamin D}) \div \text{Cross reactant concentration} \times 100\%$$

The results of each potential cross reactant are listed below.

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D2	30	103%

Cross Reactant	Spiked Concentration (ng/mL)	% Cross Reactivity
25-hydroxyvitamin D3	30	97%
Vitamin D2	1000	0.2%
Vitamin D3	1000	0.0%
1,25-dihydroxyvitamin D2	30	>100%
1,25-dihydroxyvitamin D3	30	79%
3-epi 25-hydroxyvitamin D3	30	59%
24,25-dihydroxyvitamin D3	20	9%
Paricalcitol (Zemplar)	24	>100%

High dose hook effect:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed following CLSI EP09-A2-IR guideline.

A total of 204 human samples spanning the entire measuring assay range were tested in singlicate on both the BioPlex 2200 25-OH Vitamin D kit and the predicate assay. Of the 204 samples, there were 185 unaltered samples and 19 samples spiked with 25-hydroxyvitamin D₃ to supplement the assay range. There are eight (8) samples with values lower or higher than the measuring range of the comparator method not including in the analysis. A total of 196 BioPlex 25-OH Vitamin D results were plotted using weighted Deming regression analysis for all samples spanning the measuring range of both assays. Results of the regression slope, intercept, and coefficient of correlation (r) are summarized in the table below:

Number of Results Analyzed	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r) (95%CI)	Assay Range (ng/mL)
196	1.0039	-0.2256	0.9553	BioPlex: 6.6 to 124.9

	(0.9365 to 1.0712)	(-2.4121 to 1.9608)	(0.9412 to 0.9661)	Comparator: 4.3 to 118.1
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b. *Matrix comparison:*
Serum only

3. Clinical studies:

a. *Clinical Sensitivity:*
Not Applicable

b. *Clinical Specificity:*
Not Applicable

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

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:

The Expected Values study was conducted following CLSI C28-A3c guideline.

Two hundred and eighty-seven (287) samples from apparently healthy donors including 160 males ranging in age from 21 to 79 and 127 females ranging in age from 21 to 66 were collected from three regions (North, Central, and South) in the US in spring, summer and winter, including African Americans, Hispanics and Caucasians.

The 287 samples from apparently healthy donors met the following inclusion/exclusion criteria as follows and tested with the BioPlex 25-OH Vitamin D kit in singlicate.

- Age from 21 to 90
- Roughly 50% female and 50% male
- 20% from Northern. 20% from Central and 60% from Southern region
- 40% collected in Spring, 30% in Summer and 30% in Winter
- At least 30% African Americans and 30% Caucasians
- 90% not taking Vitamin D supplements and <30% of those taking Vitamin D supplements at or more than 1000 IU, but less than 2000 IU
- Normal TSH, PTH, and Total Calcium
- No family history of parathyroid or calcium regulatory disease. In addition, no personal history of kidney disease, GI disease, liver disease, and no bariatric surgery

The observed median, mean, and range between 2.5th to 97.5th percentile are summarized below

N	Mean	Median	2.5 th to 97.5 th Percentile
286*	29.7 ng/mL	27.7 ng/mL	12.7 – 65.7 ng/mL

* One sample <6.5 ng/mL was excluded from the data analysis

Each laboratory should establish its own reference range pertinent to their specific patient populations.

Instrument Name:

The BioPlex 2200 System, software version 4.1 cleared in k130053

Conclusion:

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

MEMORANDUM

TO: Juang Wang, PhD, RAC
Regulatory Affairs Representative
Bio-Rad Laboratories, Inc.
5500 E. 2nd Street
Benicia, CA 94510

FROM: Sheila Connors
FDA/CDRH/OIR/DCTD

RE: Q141077
DEVICE: BioPlex 2200 25-OH Vitamin D Kit
DATED: August 20, 2014
RECEIVED: August 21, 2014

DATE: September 2, 2014

Thank you for submitting the application to request a Submission Issue meeting through the Pre-submission process. The purpose of the pre-submission meeting with FDA staff is to give clarification on the deficiencies identified during the review of the 510(k) premarket submission and answer questions and concerns regarding the proposed response to the deficiencies documented in the telephone hold letter.

This informal communication represents the best judgment of the Office of In Vitro Diagnostics and Radiological Health staff and consultants who reviewed the protocol. It does not constitute an advisory opinion and does not bind or otherwise obligate or commit the agency to the views expressed, as per 21 CFR 10.85(k).

Please note that the pre-submission review focuses on the specific questions that you provided in your cover letter. Therefore, the comments provided in this memorandum are not intended to comprehensively include all issues that may arise during a pre-market review.

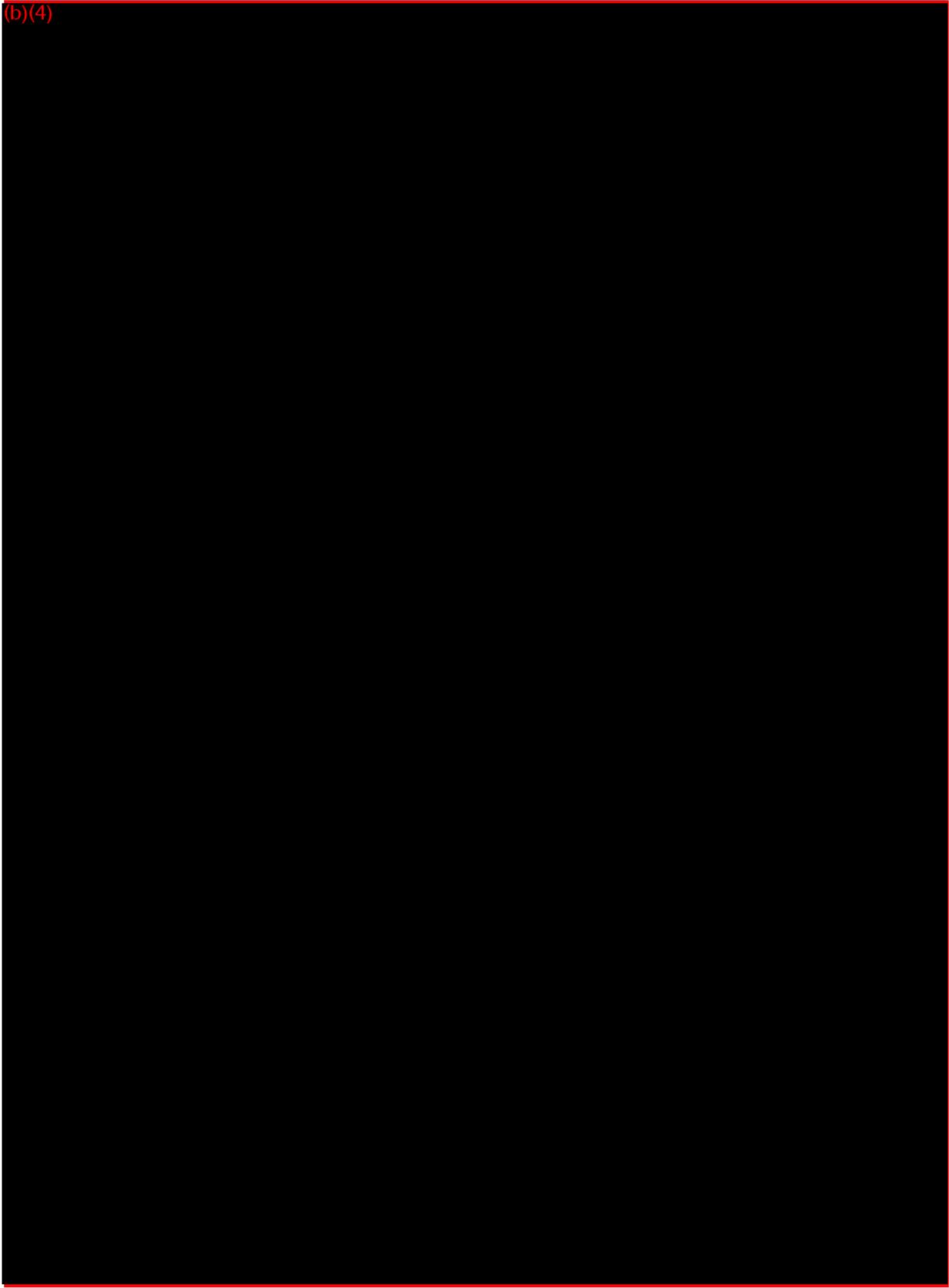
Background:

The purpose of this Pre-submission and teleconference-meeting request is to clarify the deficiencies identified during the review of submission k141114.

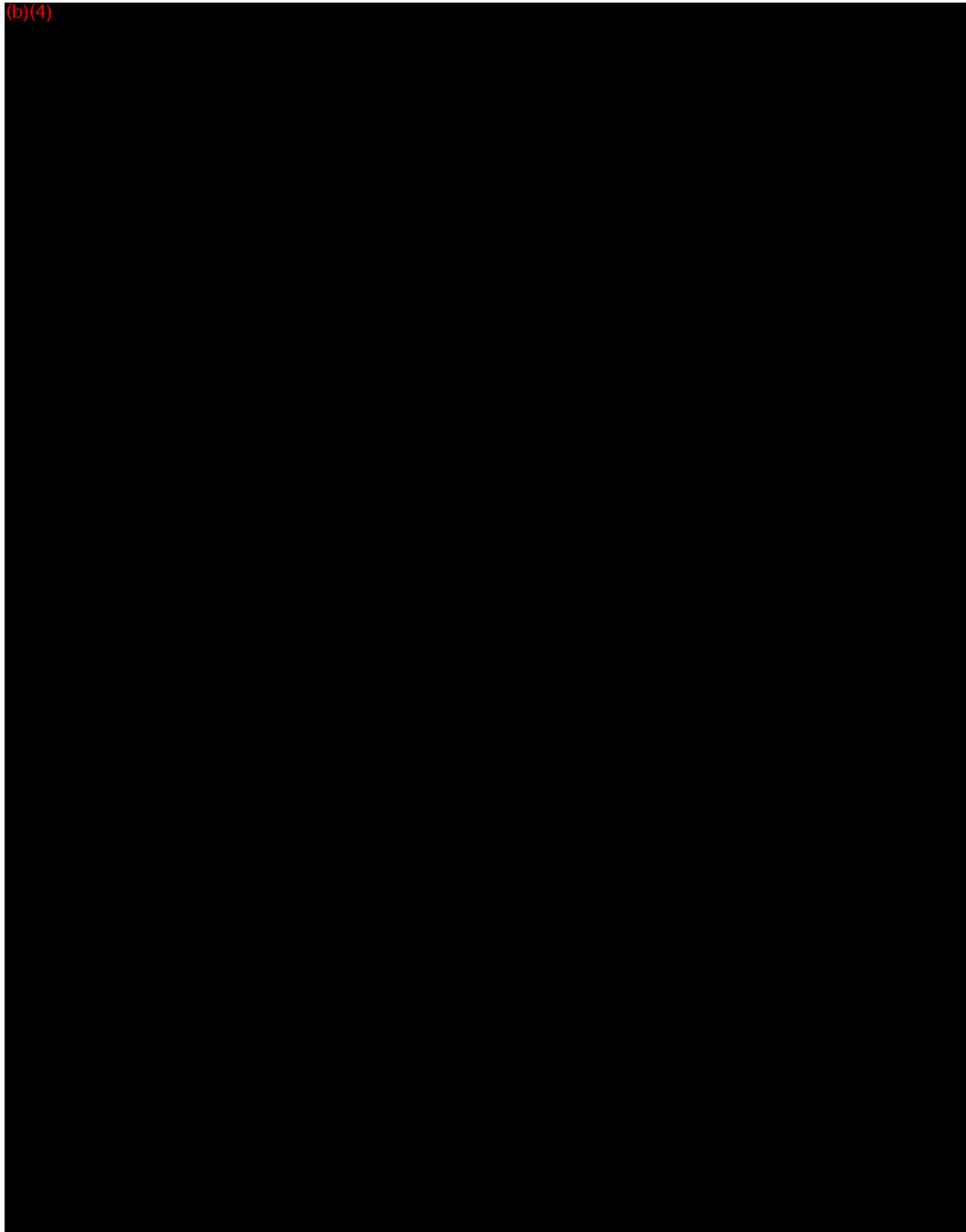
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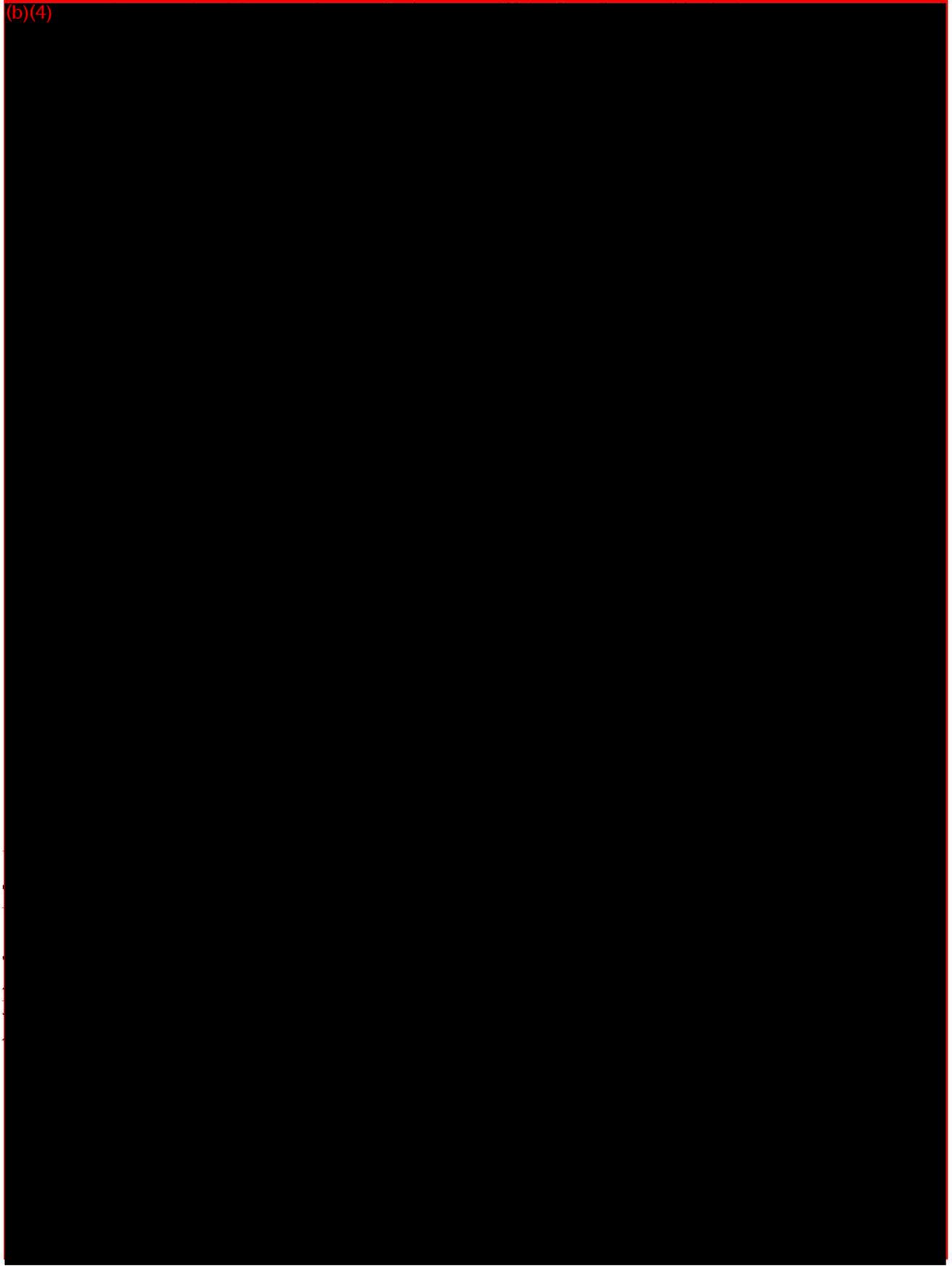
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(b)(4)



If you have any questions or comments regarding this review, please contact Sheila Connors, at (301) 796-6181, sheila.connors@fda.hhs.gov.

Sheila A. Connors -S
2014.09.03 11:01:26 -04'00'

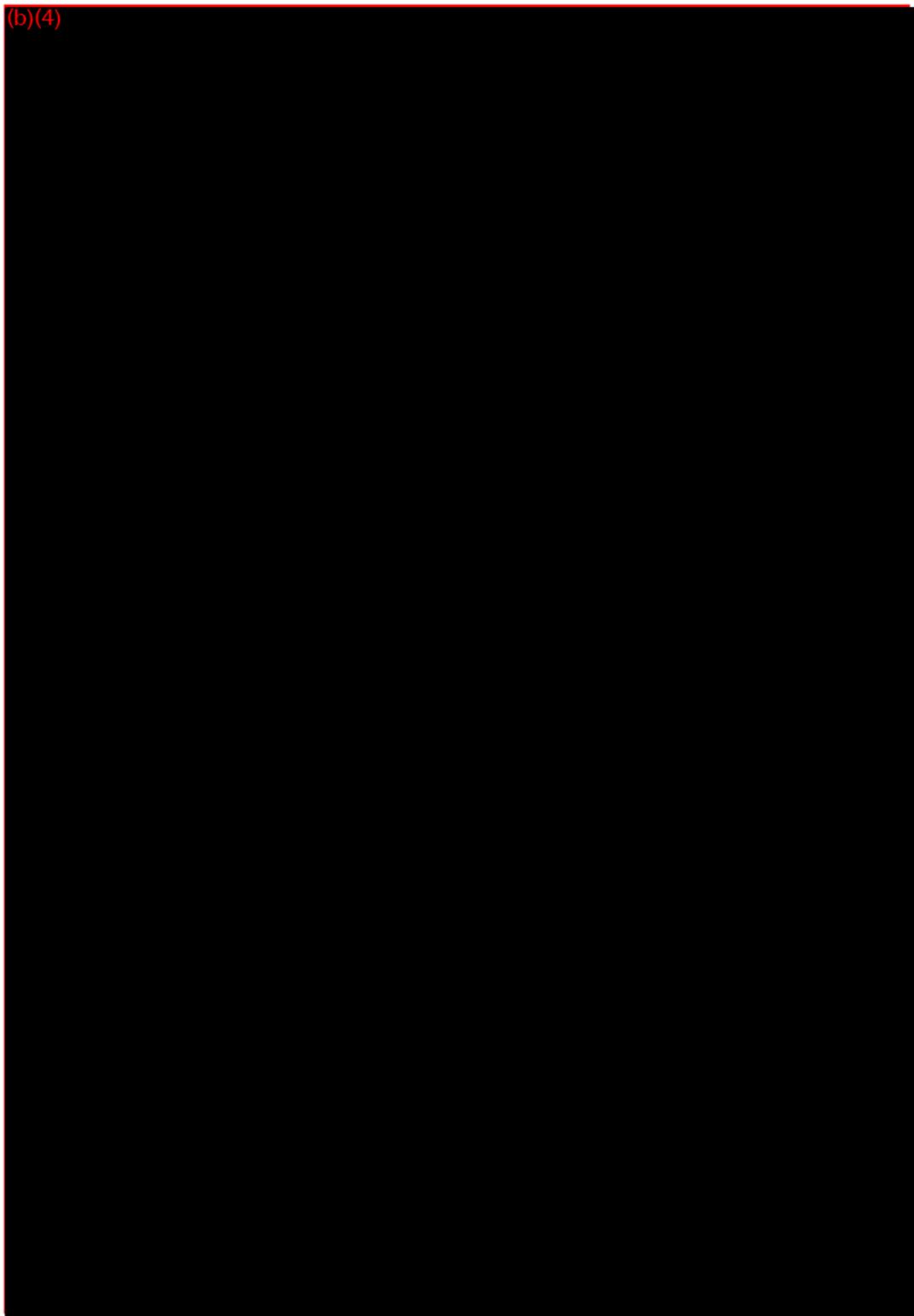
Yung W. Chan -S

Chemistry Branch Chief
FDA/CDRH/OIR/DCTD

(b)(4)

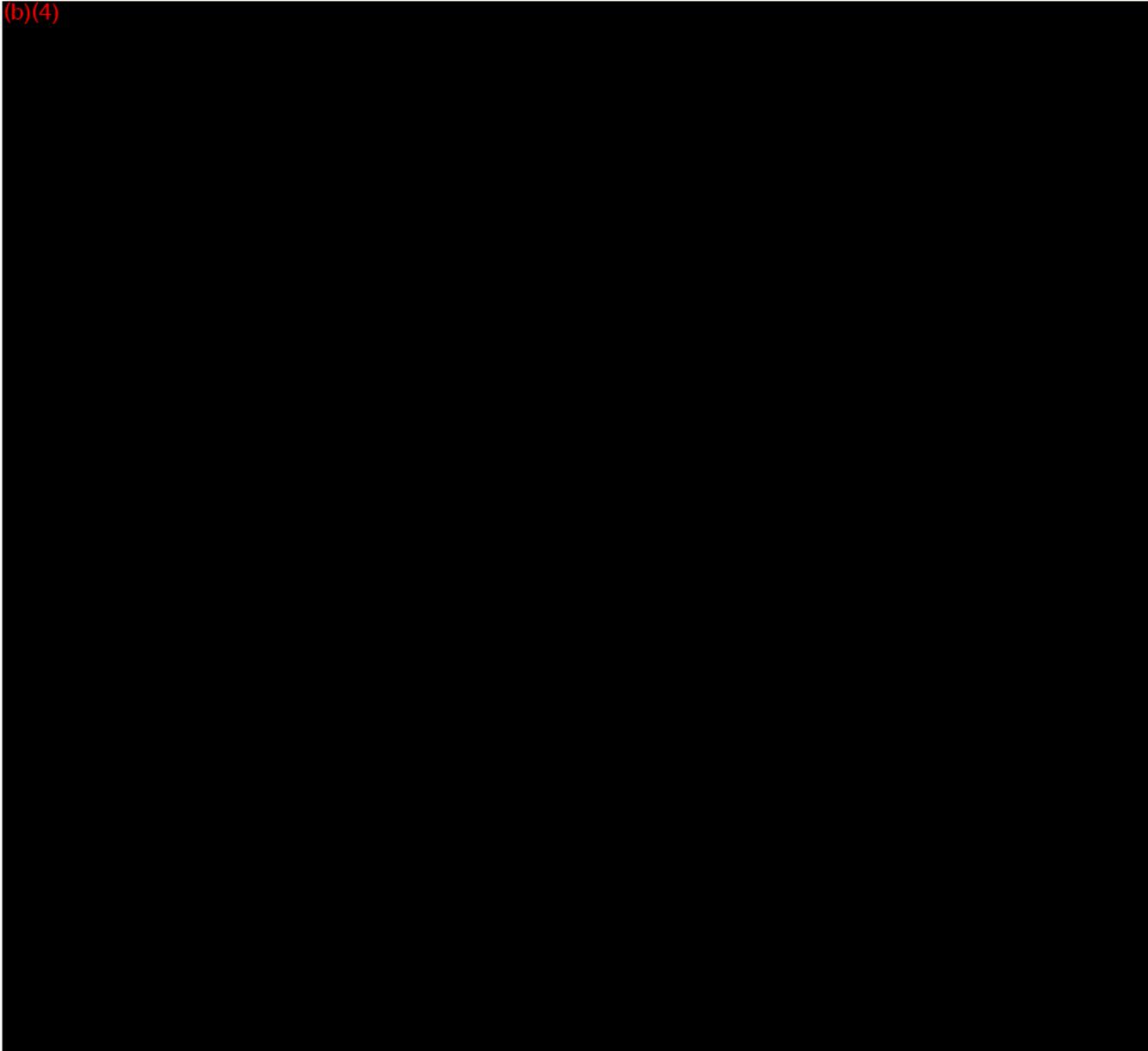


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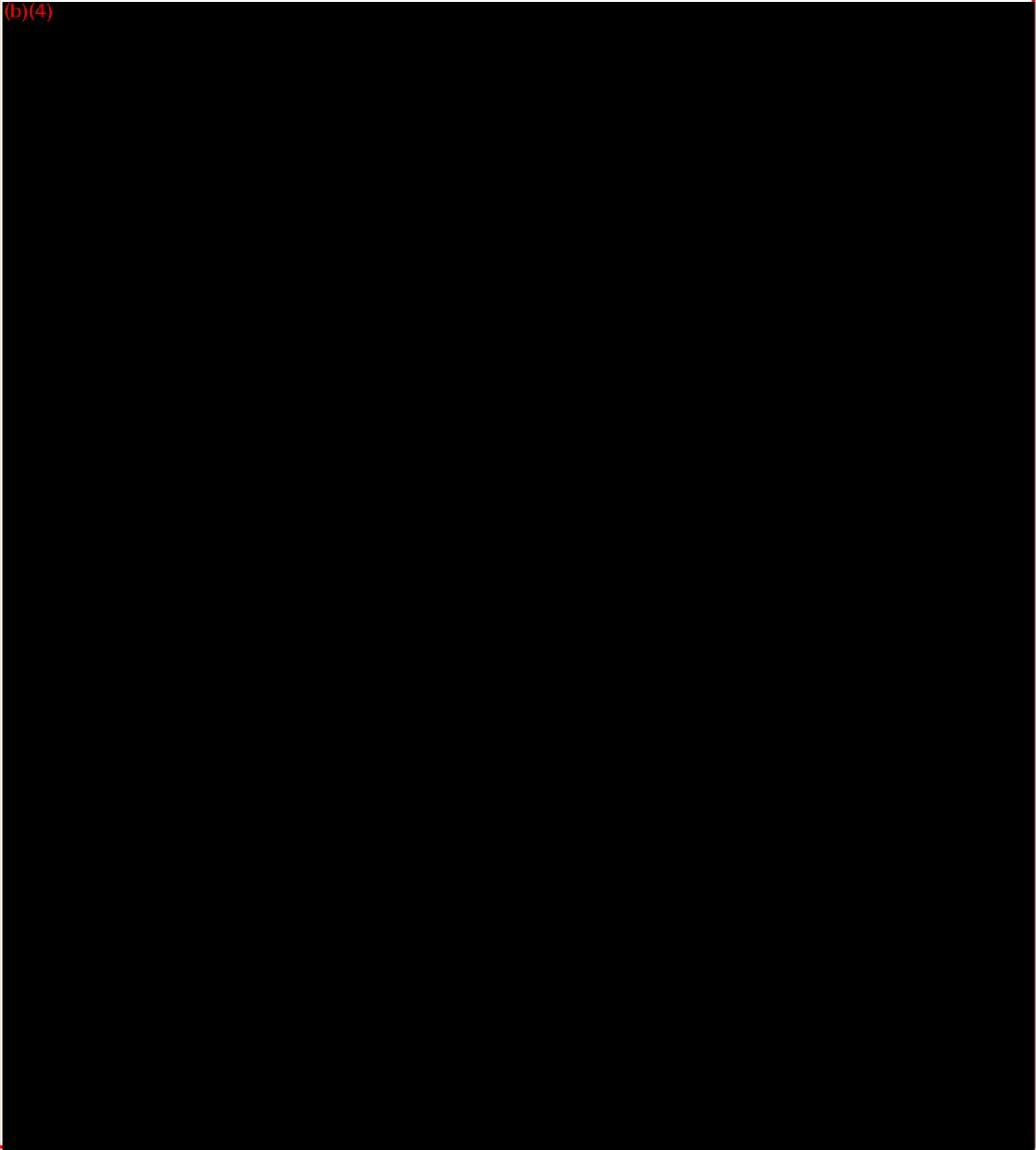
Topic: Minutes from the Submission Issue Meeting Teleconference Call
Date: Thursday, September 04, 2014 at 3:00 – 3:35 PM EST.

(b)(4)

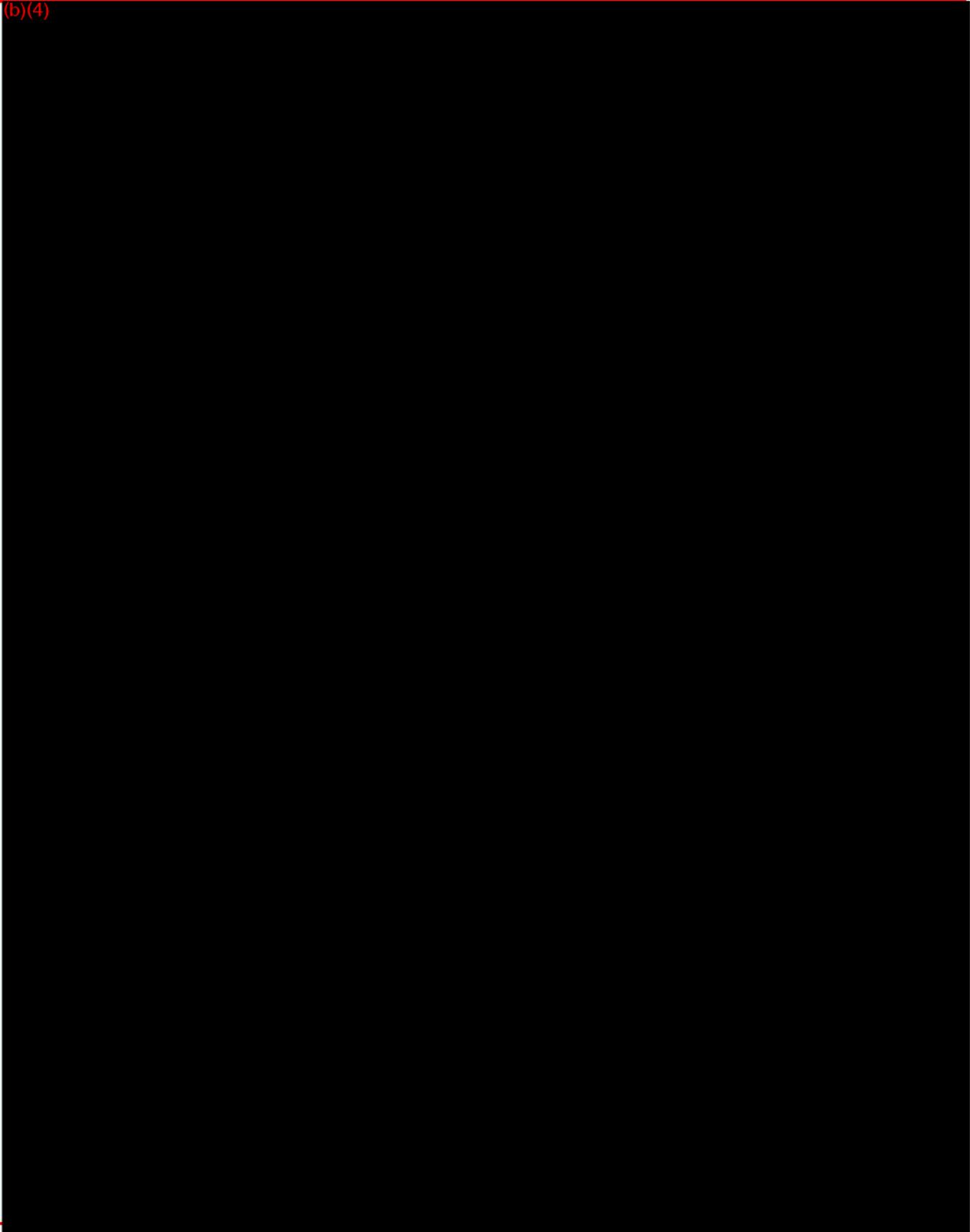


**Discussion of the Pre-Sub Questions Submitted by Bio-Rad Laboratories and
Responses delivered by FDA**

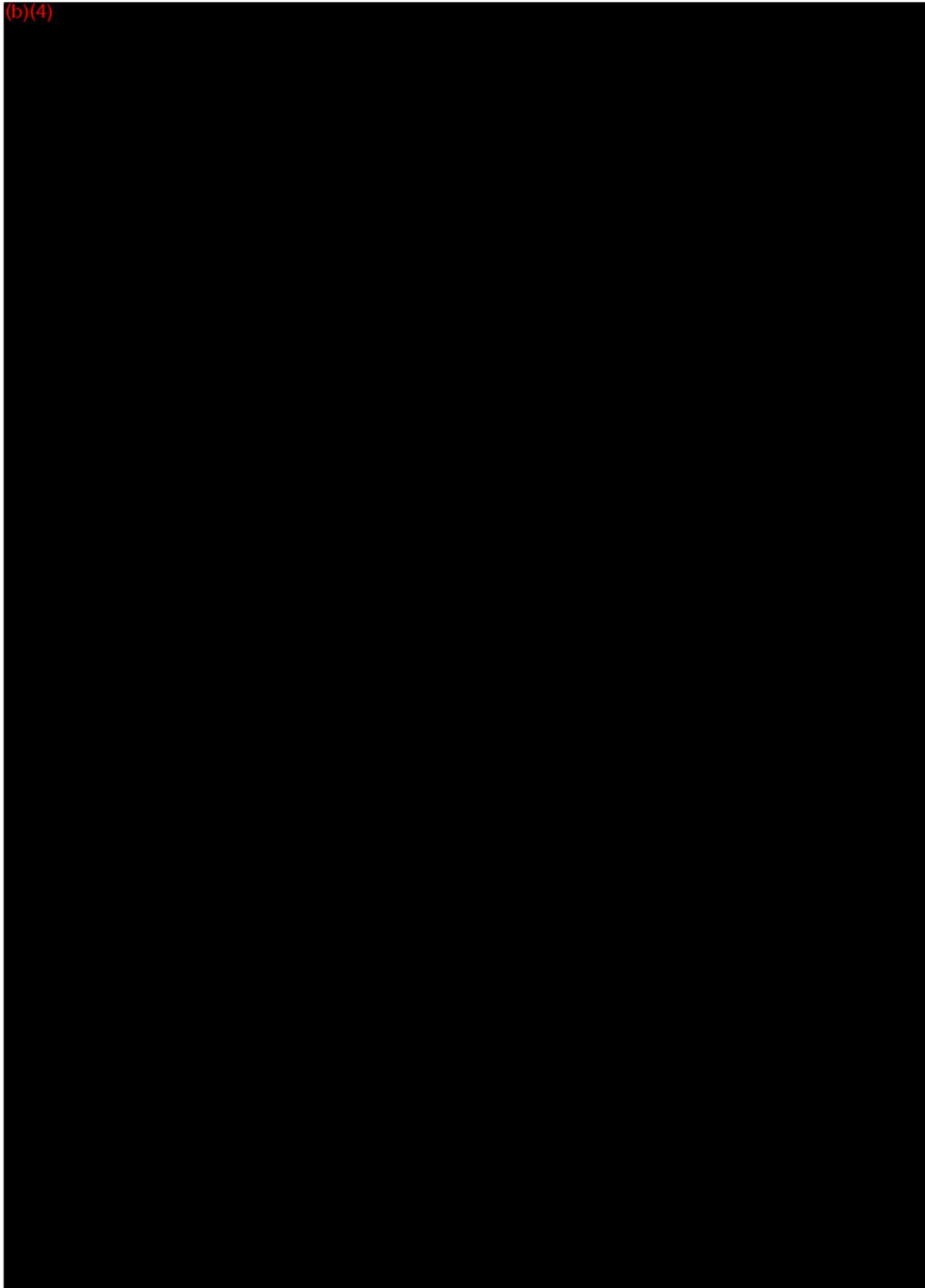
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2014.10.10 14:14:04 -04'00'

Yung Chan
Chemistry Branch Chief
FDA/CDRH/OIR/DCTD

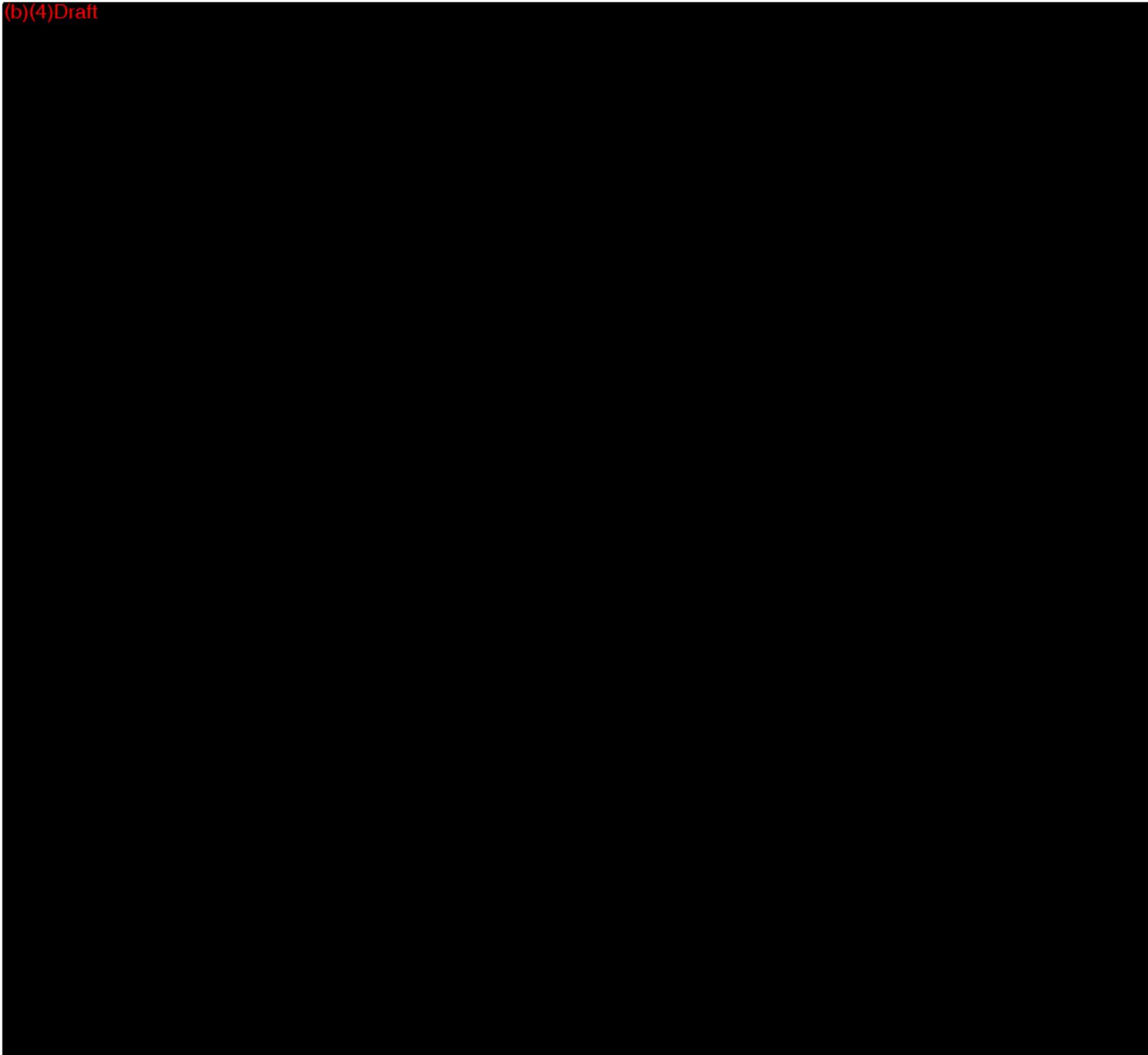
Failure to obtain the appropriate values for controls will invalidate the assay and indicates procedural error, improper sample handling or deterioration of reagents. Additional controls may be tested in accordance with local, state and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

If a control result is out of its specified range, any test results generated since the last acceptable control results must be evaluated to determine if test results may have been adversely affected. Adversely affected results are invalid, and these samples must be re-tested.

C) Load/Process Samples

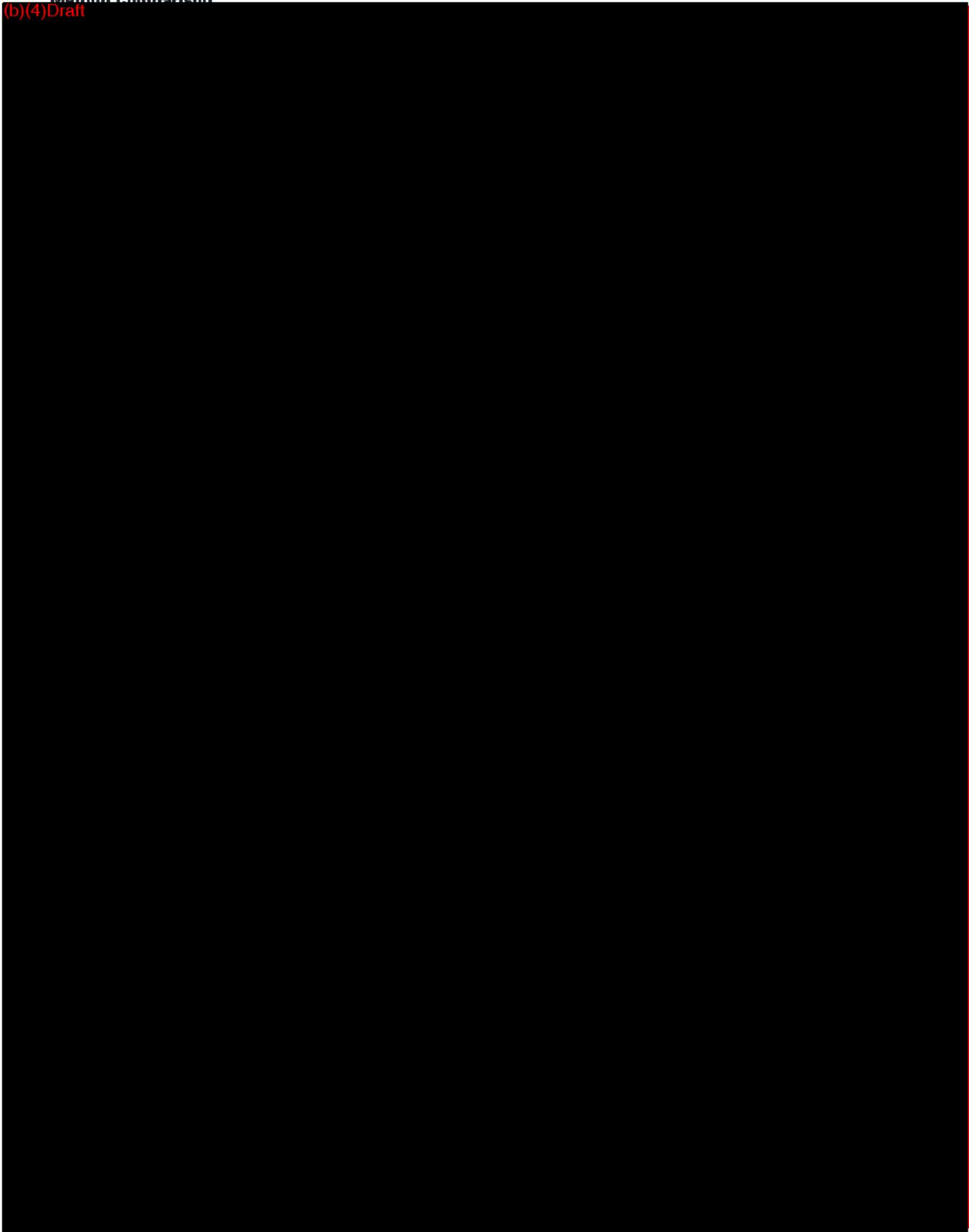
Load samples into the racks provided with the BioPlex 2200 System as indicated in the BioPlex 2200 System Operation Manual. Sample processing on the BioPlex 2200 System is fully automated. Refer to the BioPlex 2200 System Operation Manual for appropriate software setup.

(b)(4)Draft



Method Comparison

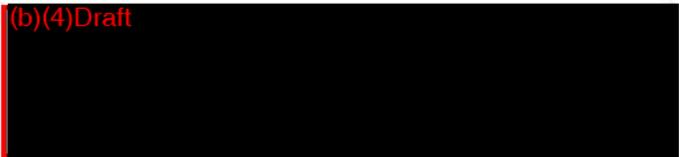
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(b)(4)Draft



(b)(4)Draft



Department of Health and Human Services
 Food and Drug Administration
STANDARDS DATA REPORT FOR 510(k)s
 (To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

Traditional Special Abbreviated

STANDARD TITLE ¹

EP9-A2IR Method Comparison and Bias Estimation Using Patient Samples, Approved Guideline, Second Edition (Interim Revision)

Please answer the following questions

Yes No

Is this standard recognized by FDA ²?

FDA Recognition number³ #7-92

Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?

Is a summary report ⁴ describing the extent of conformance of the standard used included in the 510(k)?
 If no, complete a summary report table.

Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?

Does this standard include acceptance criteria?
 If no, include the results of testing in the 510(k).

Does this standard include more than one option or selection of tests?.....
 If yes, report options selected in the summary report table.

Were there any deviations or adaptations made in the use of the standard?.....
 If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) ⁵?

Were deviations or adaptations made beyond what is specified in the FDA SIS?.....
 If yes, report these deviations or adaptations in the summary report table.

Were there any exclusions from the standard?
 If yes, report these exclusions in the summary report table.

Is there an FDA guidance ⁶ that is associated with this standard?.....
 If yes, was the guidance document followed in preparation of this 510k?

Title of guidance: _____

¹ The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

² Authority [21 U.S.C. 360d], <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm>

³ <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁴ The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and

address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

⁵ The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>

⁶ The online search for CDRH Guidance Documents can be found at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>

**EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE**

STANDARD TITLE

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A
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TYPE OF DEVIATION OR OPTION SELECTED [‡]

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

[‡] Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
1350 Piccard Drive, Room 400
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.