August 2, 2023

Beckman Coulter Laboratory Systems (Suzhou) Co., Ltd.
Tracy Jin
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No. 181 West Su Hong Road, Suzhou Industrial Park
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People's Republic of China

Re: K221114
Trade/Device Name: Immunoglobulin G (IgG)
Regulation Number: 21 CFR 866.5510
Regulation Name: Immunoglobulins A, G, M, D, and E immunological test system
Regulatory Class: Class II
Product Code: CFN
Dated: February 14, 2023
Received: February 16, 2023

Dear Tracy Jin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ying Mao -S

Ying Mao, Ph.D.
Branch Chief
Division of Immunology and Hematology Devices
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Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
*See PRA Statement below.*

510(k) Number *(if known)*
K221114

Device Name
Immunoglobulin G (IgG)

Indications for Use *(Describe)*

System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma and cerebrospinal fluid on Beckman Coulter AU/DxC AU analyzers. The measurement of IgG aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

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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## 1.0 Submitted By

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## 2.0 Date of Preparation

Jul 25,2023

## 3.0 Device Name(s)

Proprietary Name: IgG
Common Name: IgG
Classification: Class II
Classification Name: Immunoglobulins A, G, M, D, E Immunological Test System
Product Codes: CFN
Regulation Number: 21 CFR §866.5510

## 4.0 Predicate Device

| Candidate | Predicate | Manufacturer |
|---|---|---|
| IgG Reagent | IgG Reagent (K162208) | Beckman Coulter, Inc. |

## 5.0 Device Description

The device consists of two reagents: R1 buffer (Tris buffer pH 7.2, polyethylene glycol 6000) and R2 (goat anti-IgG antiserum). The reagents contain sodium azide as preservative.

When a sample is mixed with R1 buffer and R2 antiserum solution, human IgG reacts specifically with anti-human IgG antibodies to yield insoluble aggregates. Immune complexes formed in solution scatter light in proportion to their size, shape, and concentration. Turbidimeters then measure the reduction of incidence light due to reflection, absorption, or scatter. The decrease in intensity of light transmitted (increase in absorbance) through particles suspended in solution is a result of complexes formed during the antigen-antibody reaction.

## 6.0 Indications for Use

System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma, and cerebrospinal fluid on Beckman Coulter AU/DxC AU analyzers. The measurement of IgG aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

For in vitro diagnostic use.

## 7.0 Comparison to the Predicate

Table 7.0 shows the similarities and differences between the candidate and predicate devices.

Table 7.0 - IgG Predicate Device Comparison Table

| Feature | Predicate Device:<br><br>IgG Reagent<br>(DxC 700 AU Clinical Chemistry Analyzer)<br><br>(K162208) | Candidate Device:<br><br>IgG Reagent<br>(DxC 500 AU Clinical Chemistry Analyzer) |
|---|---|---|
| Intended Use | System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma, and cerebrospinal fluid on Beckman Coulter AU analyzers | Same; updated instrument family branding only.<br><br>System reagent for the quantitative determination of IgG immunoglobulins in human serum, plasma, and cerebrospinal fluid on Beckman Coulter AU/DxC AU analyzers |
| Measurement | Quantitative | Same |
| Instrument Required | AU400/400$^{e}$/480, AU640/640$^{e}$ /680, AU2700/5400/AU5800 and DxC 700 AU Beckman Coulter Analyzers. | AU480, AU680, AU5800, DxC 500 AU and DxC 700 AU Beckman Coulter Analyzers. |
| Methodology | Immunoturbidimetric | Same |
| Antibody | Goat anti-IgG | Same |
| Reagent form and storage | Liquid, on-board storage | Same |

| Feature | | Predicate Device:<br><br>IgG Reagent<br>(DxC 700 AU Clinical Chemistry Analyzer)<br><br>(K162208) | Candidate Device:<br><br>IgG Reagent<br>(DxC 500 AU Clinical Chemistry Analyzer) |
|---|---|---|---|
| Specimen Type | | Serum, EDTA or Lithium heparin plasma, and cerebrospinal fluid | Same |
| Calibration | | Serum Protein Multi-Calibrator (Cat # ODR3021) | Same |
| Onboard Stability | | 90 Days | Same |
| Calibration Stability | Serum & Plasma | 90 Days | Same |
| | CSF | 2 Days | Same |
| Analytical Range | Serum & Plasma | 75 – 3000 mg/dL | Same |
| | CSF | 2 – 50 mg/dL | Same |
| Precision | Serum & Plasma | Within-run Precision:<br>≤ 3.5% CV<br><br>Total Precision:<br>< 6% CV | Same |
| | CSF | Within-run Precision:<br>≤ 6% CV or ≤0.4 mg/dL<br><br>Total Precision:<br>< 7.5% CV or <0.5mg/dL | Same |
| Sensitivity | Serum & Plasma | LoQ: <75 mg/dL using a within laboratory CV of 20% | Same |
| | CSF | LoQ: <2 mg/dL using a within laboratory CV of 20% | Same |
| Interference | Serum & Plasma | Bilirubin: NSI* up to 40 mg/dL<br>Hemolysis: NSI up to 500 mg/dL<br>Lipemia: NSI up to 1000 mg/dL<br>RF: NSI up to 1200 IU/mL | Same |
| | CSF | Bilirubin: NSI up to 36 mg/dL<br>Hemolysis: NSI up to 500 mg/dL | Same |

*NSI – No significant interference is recovery within 10% of the initial value

## 8.0 Comparison testing

Substantial equivalence is demonstrated through non-clinical (bench) studies as shown below. In accordance with FDA's *Guidance for Industry and FDA Staff - Replacement Reagent and Instrument Family Policy*, CLSI study protocols were used to verify the performance claims stated in the reagent IFU and ensure that the technological differences between the candidate and predicate analyzer models did not adversely affect safety and effectiveness.

Method Comparison
Linearity
Sensitivity
Reference Interval
Interference
Precision

## 9.0 Summary of Performance Data

The data contained in the Premarket Notification supports a finding of substantial equivalence to the measurand test systems already in commercial distribution.

### 9.1 Method Comparison with Predicate Device

Method comparison and bias estimation experiments were designed using CLSI Guideline EP09C-ED3 "Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Third Edition". These patient correlation studies demonstrate equivalence between Beckman Coulter's IgG assay on the candidate DxC 500 AU analyzer and the predicate DxC 700 AU analyzer. The results summary in Table 9.1. is based on Weighted Deming regression analysis.

Table 9.1 IgG Method Comparison Data Summary

| Sample Type | Units | N | Slope | Intercept | R |
|---|---|---|---|---|---|
| Serum | mg/dL | 147 | 1.015 | -25.422 | 0.9981 |
| CSF | mg/dL | 114 | 0.998 | 0.1141 | 0.9995 |

### 9.2 Linearity/Reportable Range:

Analytical range (linearity) studies were designed to meet the requirements of CLSI guideline EP06-A "*Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*". High and low pools were prepared and inter-diluted to achieve concentrations spanning the required linear range. Each dilution was assayed in quadruplicate on a DxC 500 AU analyzer. The performance data for the study demonstrates linearity throughout the claimed dynamic range of the IgG candidate assay, as represented in Table 9.2 below.

Table 9.2 IgG Linearity Data Summary

| Sample Type | Acceptance Criteria | | | Results | | Pass/ Fail |
|---|---|---|---|---|---|---|
| | Linear Range | Allowable Difference ± % | Allowable Difference ± units | Linear From | Linear To | |
| Serum | 75-3,000 | 8% between 375-3,000 | 30 mg/dL between 75 - 375 | 73.2868 | 3261.9190 | Pass |
| CSF | 2-50 | 10% between 2-50 | 0.5 mg/dL between 2.0 - 5 | 1.9 | 53.0 | Pass |

### 9.3 Sensitivity (Detection Limits):

LOB, LOD and LOQ studies were designed in accordance with CLSI guideline EP17-A2 "*Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures Approved Guideline - Second Edition"*. For the LOB, LOD, and LOQ determinations, the experimental design consisted of replicate measurements on blank and low-level sample pools using 2 lots of reagent across multiple days. A total of 72 blank replicates were generated per reagent lot (4 blank native serum samples 'analyte-depleted' ran n=6 for 3 days) to generate the LOB value that serves as a component of the LOD determination. For the LOD and LOQ determinations, 500 replicates were generated for each reagent lot for each application; this was comprised of 10 low-level samples for IgG which were run 10-fold for 5 days. The LOB, LOD, and LOQ sample preparation information, including the matrices of the spiking solutions, are describe in Table 9.3 below

Table 9.3 IgG Sensitivity Data Summary

| Sample Type | Units | Low End of Measuring Range | LOQ Spec | LOB | LOD | LOQ |
|---|---|---|---|---|---|---|
| Serum | mg/dL | 75 | <75 at ≤20%CV | 5.6 | 8.6 | 18.5 at 10% CV |
| CSF | mg/dL | 2 | <2 at ≤20%CV | 0.11 | 0.31 | 0.63 at 20% CV |

### 9.4 Precision:

Repeatability (within-run) and within- laboratory (total) precision studies were performed in accordance with the CLSI guideline EP05-A3 *"Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition"* using a 20-day study design. A separate 5-day study design was used to evaluate reproducibility using three DxC 500 AU analyzers. The candidate IgG assay met the performance specifications as stated in the IgG reagent IFU. The results are summarized in the Tables 9.4.1 and 9.4.2 below:

Table 9.4.1 IgG 20-day Precision Data Summary

| Sample (Units) | Sample Levels | Mean (n=80) | Repeatability (Within Run) | | Within Laboratory (Total) | |
|---|---|---|---|---|---|---|
| | | | SD | % CV | SD | % CV |
| Serum (mg/dL) | 1 | 503.99 | 5.8 | 1.2 | 6.3 | 1.2 |
| | 2 | 1797.53 | 43.1 | 2.4 | 43.2 | 2.4 |
| | 3 | 2576.22 | 86.9 | 3.4 | 94.9 | 3.7 |
| | 4 | 88.31 | 1.6 | 1.8 | 4.3 | 4.9 |
| | 5 | 835.56 | 7.2 | 0.9 | 14.8 | 1.8 |
| CSF (mg/dL) | 1 | 4.14 | 0.2 | 4.7 | 0.2 | 5.6 |
| | 2 | 11.20 | 0.2 | 2.1 | 0.4 | 3.1 |
| | 3 | 36.32 | 0.6 | 1.6 | 0.9 | 2.6 |

Table 9.4.2 IgG 5-Day Precision Data Summary

| Sample (Units) | Sample Levels | Mean (n=75) | Repeatability (Within Run) | Within Laboratory (Total) | Reproducibility |
|---|---|---|---|---|---|
| | 1 | 481.20 | 0.8% CV | 1.0% CV | 1.0% CV |
| | | | 3.67 SD | 4.63 SD | 4.63 SD |
| Serum | 2 | 1669.57 | 1.5% CV | 1.7% CV | 1.7% |
| (mg/dL) | | | 24.45 SD | 29.04 SD | 29.07 SD |
| | 3 | 2404.48 | 2.8% CV | 3.6 % CV | 3.6 % CV |
| | | | 66.69 SD | 86.08 SD | 86.08 SD |
| | 1 | 3.53 | 1.7% CV, | 4.4% CV | 4.7% CV |
| | | | 0.06 SD | 0.16 SD | 0.16 SD |
| CSF | 2 | 11.31 | 0.9% CV, | 1.9% CV | 1.9% CV |
| (mg/dL) | | | 0.10 SD | 0.22 SD | 0.22 SD |
| | 3 | 37.18 | 0.9% CV. | 1.4% CV | 1.4% CV |
| | | | 0.33 SD | 0.50 SD | 0.50 SD |

### 9.5 Interferences (Analytical Specificity):

Interference studies were designed based on the CLSI Guideline EP07, 3rd Edition "Interference Testing in Clinical Chemistry; Approved Guideline". All test samples were assayed n=5 at two analyte levels. The sample pools tested were at different levels of interferents to determine the magnitude of their effect. The data analysis involved calculating the difference in recovery of the samples with and without the potential interfering substances. The results are summarized in Table 9.5 below. The candidate IgG assay met the performance specifications as stated in the IgG reagent IFU.

Table 9.5 IgG Interferences Data Summary

| Sample | Interference Threshold | | | | |
|---|---|---|---|---|---|
| | Lipemic (Intralipid)[1] | Icteric Unconjugated[2] | Hemolytic[3] | RF | Pass/ Fail |
| Serum | Intralipid (1000 mg/dL) intf. ≤10% at IgG conc. of 1000 mg/dL & 2000 mg/dL | Bilirubin (40 mg/dL) intf. ≤10% at IgG conc. of 1000 mg/dL & 2000 mg/dL | Hemolysate (500 mg/dL) intf. ≤10% at IgG conc. of 1000 mg/dL & 2000 mg/dL | RF (1200 IU/mL) intf. ≤10% at IgG conc. of 1000 mg/dL & 2000 mg/dL | Pass |
| CSF | N/A | Bilirubin (36 mg/dL) intf. ≤10% at IgG conc. of 5 mg/dL & 20 mg/dL | Hemolysate (500 mg/dL) intf. ≤10% at IgG conc. of 5 mg/dL & 20 mg/dL | N/A | Pass |

[1] Intralipid is a 20% fat emulsion used to emulate extremely turbid samples.
[2] Unconjugated bilirubin (porcine source)
[3] Lysed human red blood cells

### 9.6 Reference Interval

The Reference Interval study utilized a transference approach in accordance with the CLSI guidelines EP028-A3c "*Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition".* The purpose of the study was to validate the acceptability of the original IgG serum reference interval for use on the candidate DxC 500 AU analyzer. Transference evaluations were not performed for the CSF sample type. The results are summarized in Table 9.6 below.

Table 9.6 IgG Reference Interval Summary

| Sample Type | Reference Range (mg/dL) | Result |
|---|---|---|
| Serum (Adult) | 635 – 1,741 | Pass |
| CSF | 15 – 20 years: 3.5 mg/dL ± 2.0 mg/dL<br>21 – 40 years: 4.2 mg/dL ± 1.4 mg/dL<br>41 – 60 years: 4.7 mg/dL ± 1.0 mg/dL | N/A* |

*Literature reference used

## 10.0 Conclusion

The IgG Reagent on the DxC 500 AU Clinical Chemistry Analyzer is identical in design and composition as the IgG Reagent on the DxC 700 AU Clinical Chemistry Analyzer cleared under K162208. Method comparison, linearity, sensitivity, reference interval, interference, and precision testing demonstrate that the assay performance is substantially equivalent between the candidate predicate test systems.

This 510(k) Summary is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and the implementing regulation 21 CFR 807.92.