November 4, 2022

Procise Diagnostics
Kurtis Bray
Senior Director of Clinical Development and Regulatory Affairs
9449 Carroll Park Drive
San Diego, California 92121

Re: K201256
Trade/Device Name: Procise CRP Assay Kit, ProciseDx Instrument, ProciseDx Calibration Cartridge
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: Class II
Product Code: DCK
Dated: August 4, 2022
Received: August 5, 2022

Dear Kurtis Bray:

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
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K201256

Device Name
Procise CRP

Indications for Use *(Describe)*
The Procise CRP assay is a time-resolved fluorescence energy transfer immunoassay for the quantitative determination of C-Reactive Protein (CRP) levels in human scrum. The test is carried out by means of the ProciseDx Analyzer.

Measurement of CRP aids in evaluation of injury to body tissues, infection, and inflammatory disorders. The instrument and assay are for use by trained professionals in the clinical laboratory. For in vitro diagnostic use only. Not for point of care use.

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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ProciseDx

510(k) Summary

1. **Submitter**

ProciseDx, Inc.
9449 Carroll Park Drive
San Diego, CA 92121
Telephone: (619) 354-2264
Contact Person: Kurtis Bray
Date: October 24, 2022

2. **Proprietary Names**

ProciseDx Analyzer
Procise C-Reactive Protein
Procise CRP
ProciseDx Calibration Cartridge

3. **Predicate**

Orion Diagnostica QuikRead go CRP
K142993

4. **Device Description**

The Procise CRP assay is a homogeneous sandwich immunoassay assay that uses a fluorescence resonance energy transfer (FRET) signal to detect and quantify CRP. FRET is a process in which a donor molecule, in an excited state, transfers excitation energy to an acceptor fluorophore when the two are brought into close proximity. Upon excitation at a characteristic wavelength the energy absorbed by the donor is transferred to the acceptor, which in turn emits light energy. The level of light emitted from the acceptor fluorophore is directly proportional to the degree of donor/acceptor complex formation.

The Procise CRP assay format is designed as a competitive format. A monoclonal anti-CRP antibody and exogenous CRP antigen are labeled with donor and acceptor fluorophores, respectively. The monoclonal antibody specific for CRP is labelled with the donor fluorophores and the CRP antigen is labelled with the acceptor fluorophore. Similar to other competitive assay formats, as the concentration of CRP increases a proportional decrease in the signal is observed.

5. **Intended Use**

The Procise CRP assay is a time-resolved fluorescence energy transfer immunoassay for the quantitative determination of C-Reactive Protein (CRP) levels in human serum. The test is carried out by means of the ProciseDx Analyzer.

Measurement of CRP aids in evaluation of injury to body tissues, infection, and inflammatory disorders. The instrument and assay are for use by trained professionals in the clinical laboratory. For *in vitro* diagnostic use only. Not for point of care use.

6. Comparison

Device & Predicate Device(s):	K201256	K142993
Device Trade Name	Procise CRP	QuikRead Go CRP
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Procise CRP assay is a time-resolved fluorescence energy transfer immunoassay for the quantitative determination of C-Reactive Protein (CRP) levels in human serum. The test is carried out by means of the ProciseDx Analyzer. Measurement of CRP aids in evaluation of injury to body tissues, infection, and inflammatory disorders. The instrument and assay are for use by trained professionals in the clinical laboratory. For *in vitro* diagnostic use only. Not for point of care use.	The QuikRead go® CRP test is an immunoturbidimetric assay for the in vitro quantitative determination of C-reactive protein (CRP) in K2-EDTA and lithium heparin whole blood, K2-EDTA and lithium heparin plasma, and in serum samples. The test is carried out by means of the QuikRead go instrument. Measurement of C-reactive protein aids in the evaluation of injury to body tissues, and infection and inflammatory disorders. The instrument and assay are for use by trained professionals in the clinical laboratory. For in vitro diagnostic use only. Not for point-of-care use.
Product Code	DCK	Same
Assay Type	Quantitative	Same
Sample Volume	20 µL	Same
Limit of Quantitation	5 mg/L	Same

Calibrators	The reagents are pre-calibrated.	Same
Traceability	ERM® -DA474/IFCC	Same
Assay principle	Immunoassay	Same
Assay Controls	Two (2) Levels, ready to use	Same
General Device Characteristic Differences		
Sample Type	Serum	Serum Venous whole blood (K2-EDTA) Venous whole blood (Li-Heparin) Plasma
Technology	Fluorescence resonance energy transfer (FRET)	Immunoturbidimetry
Instrument	ProciseDx Analyzer	QuikRead go Analyzer
Antibody	Fab' anti-human CRP antibody	Anti-human CRP F(ab)2 fragment
Reagent Storage	Ambient (15-30°C)	Refrigerated (2-8°C)
Assay Range	5.0–150 mg/L (serum)	5–200 mg/L (plasma and serum) 5–150 mg/L (whole blood)

7. Standard/Special Control/Guidance Documents Referenced

- ANSI Standard "HL7 Messaging Standard Version 2.7.1, An Application Protocol for Electronic Data Exchange in Healthcare Environments - 2012
- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures– Third Edition - October 2014
- CLSI EP06-A: Evaluation of the Linearity of Quantitative measurement Procedures A Statistical Approach – First Edition – April 2003
- CLSI EP07-3rd Edition - Interference Testing in Clinical Chemistry - April 2018
- CLSI EP09c Measurement Procedure Comparison and Bias Estimation Using Patient Samples. Third edition – June, 2018
- CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures – Second Edition - June 2012
- CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic reagents- First Edition- September 2009
- CLSI C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical laboratory- Third Edition – November 2008

- Electrical Safety IEC 61010-1:2010 (third edition), Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 1: General requirements
- EN ISO 13485: Medical devices — Quality management systems — Requirements for regulatory purposes
- EN ISO 14971: Medical devices - Application of risk management to medical devices
- EN ISO 15223-1: Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements (ISO 15223-1:2016, Corrected version 2016-12-15)
- EN ISO 18113-1: In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling). Part 1: Terms, definitions and general requirements
- EN ISO 18113-3: In vitro diagnostic medical devices — Information supplied by the manufacturer (labelling) — Part 3: In vitro diagnostic instruments for professional use
- EN 61326-1; 2013/IEC 61326-1:2012, Electrical equipment for measurement, control and laboratory use – EMC requirements – Part 1: General requirements
- EN 62366-1: Application of usability engineering to medical devices
- General Principles of Software Validation Guidance for Industry and FDA Staff. January – 2002
- Guidance for Industry - Review Criteria for Assessment of C - Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays.
- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices Guidance for Industry and FDA Staff. May – 2005
- Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, April 2006
- IEC 62304 Medical device software — Software life cycle processes
- ISTA Procedure 2A: Partial simulation testing of individual packaged-products weighing 150 lb (68kg) or less when prepared for shipment
- Off-The-Shelf Software Use in Medical Devices. Guidance for Industry and Food and Drug Administration Staff - September 2019

8. Performance Characteristics

A Analytical Performance:

1. <u>Precision/Reproducibility:</u>

   a. Within-Laboratory Imprecision:
   The study was conducted based on CLSI guideline EP05-A3, where six serum samples were tested in duplicates per run, two runs per day for 20 days using two reagent lots on two analyzers (each lot per each analyzer). Each sample was tested to generate a total of 160 test results (2 replicates x 2 runs x 20 days x 2 lots = 160). The total SD and CV% calculation was based on the within-run, between-run, between-day, and between-lot data. The results are shown in the table below.

Sample	N	Mean (mg/L)	Within-run		Between-run		Between-day		Between-lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	160	5.9	0.4	6.2	0.0	0.0	0.1	1.2	0.2	3.8	0.4	7.4
2	160	9.2	0.6	6.4	0.0	0.0	0.1	0.7	0.5	5.7	0.8	8.6
3	160	35.5	1.4	3.9	0.7	2.0	0.0	0.0	0.3	0.8	1.6	4.4
4	160	75.1	2.8	3.7	0.8	1.1	0.9	1.2	3.4	4.6	4.6	6.1
5	160	93.5	4.3	4.6	0.0	0.0	2.3	2.5	4.2	4.5	6.4	6.8
6	160	125.6	6.8	5.4	0.0	0.0	2.3	1.9	7.0	5.5	10.0	8.0

b. Between-site imprecision:
The study was conducted at three different sites using five serum samples (3 patients and 2 QCs) with different CRP concentrations across the measuring interval. Within-run, between-run, between-day, between-operator/instrument, between-site, and total SDs and %CVs were calculated based on 180 determinations per sample performed with three replicates per run, two runs per day for five different days on two operators/instruments at three test sites using a single reagent lot (3 replicates x 2 runs x 5 days x 2 instruments x 3 sites = 180). The results are shown in the table below.

Sample	N*	Mean (mg/L)	Within-run		Between-run		Between-day		Between-instrument		Between-site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	179	7.27	0.5	6.6	0.0	0.0	0.0	0.0	0.1	1.6	0.2	2.1	0.6	7.6
2	179	25.3	1.7	6.8	0.0	0.0	0.3	1.3	0.0	0.0	0.7	2.7	2.0	7.8
3	177	72.7	6.2	8.5	0.0	0.0	0.7	0.9	0.0	0.0	0.0	0.0	6.5	9.0
QC1	179	5.53	0.5	8.9	0.0	0.0	0.0	0.0	0.1	0.8	0.3	4.6	0.6	10.0
QC2	178	48.7	4.2	8.6	0.0	0.0	0.0	0.0	0.0	0.0	1.8	3.7	4.5	9.3

* 98.3% (177/180) to 99.4% (179/180) of the test results were included in analysis.

2. Linearity:
The linearity was evaluated using a series of pooled human serum samples at 11 dilution levels prepared to evenly cover the CRP concentration range of 3.6 to 161.0 mg/L. Each sample dilution was measured in one run with three or four replicates; the mean of the three replicates or four replicates was calculated for each sample. Linear regression analysis of . expected value vs observed CRP value was performed to determine whether the sample set exhibits linearity. The linear regression results for nine samples within the measuring interval are shown in the table below.

Range (mg/L)	Slope (95%CI)	Intercept (95% CI)	R^2
3.6 – 161.0	0.99	0.05	1.00

Range (mg/L)	Slope (95%CI)	Intercept (95% CI)	R^2
	(0.97 – 1.00)	(-0.94 – 1.05)	

3. Analytical Specificity/Interference:
To investigate the test performance with presence of potential endogenous and exogenous interferents, three pooled human serum samples with various CRP concentrations (12.3, 52.9, and 89.7 mg/L) were prepared and spiked with potential interfering substances. The CRP level in the test samples was measured in three replicates and the recovery in relation to the unspiked sample without interferent was calculated. The acceptance criterion was < 10% in the mean bias for the individual recovery. No significant interference was observed at the concentration of the potential interfering substances as shown in the table below.

Endogenous Interferent	Concentration
Hemolysate	300 mg/dL
Triglycerides	37 mmol/L
Bilirubin Conjugated	43 mg/dL
Bilirubin Unconjugated	40 mg/dL
Human anti-mouse Antibodies (HAMA)	200 IU/mL
Rheumatoid Factor	400 IU/mL

Exogenous Interferent	Concentration
Acetaminophen	20 mg/dL
Ascorbic Acid	170 µmol/L
Acetylsalicylic Acid	65 mg/dL
Adalimumab	20 µg/mL
Amoxicillin	400 µmol/L
Ampicillin	500 µmol/L
Caffeine	600 µmol/L
Chloramphenicol	300 µmol/L
Erythromycin	400 µmol/L
Etanercept	0.1 µmol/L
Fluconazole	480 µmol/L
Gentamycin	120 µmol/L
Ibuprofen	2000 µmol/L
Infliximab	20 µg/mL
Methotrexate	1950 µmol/L
Penicillin	150 mg/L
Prednisone	1 µmol/L

4. Assay Reportable Range:

The analytical measuring range of Procise CRP is 5 to 150 mg/L.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   a. Traceability: The calibrators are traceable against ERM® -DA474/IFCC.

   b. Real-time Stability: The reagent stability at ambient room temperatures was evaluated by testing three serum samples (~ 5, ~ 50, and ~100 mg/L) in six replicates each, using two lots of Procise CRP at 15°C, 23°C, and 30°C. The Procise CRP is stable for 24 months at ambient room temperatures at 15-30°C.

   c. Long-term stability: The reagent stability for long-term storage was evaluated by testing ten native and three pooled human serum samples with CRP concentrations ranged 5.0 to 73.3 mg/L, using two reagent lots. The Procise CPR is stable for up to 24 months at -80°C.

   d. Shipping Stability: The shipping stability was evaluated by testing two serum samples with CRP concentrations at ~5 and ~50 mg/L , using four pouched CRP Assay kits, each containing 20 Procise CRP cartridges (regent), 20 buffer bulbs and 20 minivettes. The packed CRP Assay Kits were placed at 38°C for 72 hours and then at 60°C for six hours followed by a stress test in a sequence of compression, random vibration, drop (in carton), random vibration, low pressure, and a bubble test. The Procise CPR reagent is stable for up to 72 hours at 38°C followed by six hours at 60°C under the simulated shipping conditions.

   e. Calibration Stability: Stability of the calibration cartridge was evaluated on ProciseDx instrument by testing six calibration cartridges stored at 23°C after an initial calibration. The CRP calibration cartridge is stable at 23°C for up to 18.5 months.

   f. Sample Stability: CRP in serum is stable for 11 days at 20–25°C, 2 months at 4–8°C, and 3 years at -20°C. (Reference: Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2. 2002, p28.)

6. Detection Limit:

   For limit of blank (LoB), a set of four analyte depleted serum samples was investigated using two reagent lots over three days. Each sample was tested in five replicates per run, one run per day for three days to reach a total of 60 measurements per reagent lot. LoB was determined per CLSI EP17-A2. The higher value from both lots was taken for the LoB at 0.9 mg/L. The claimed LoB is 1.1 mg/L.

   For limit of detection (LoD), a set of five low level serum samples in the range below the measuring interval was investigated using two reagent lots. Each sample was tested in four replicates per run, one run per day for three days to reach a total of 60 measurements per

reagent lot. The LoD was determined per CLSI EP17-A2. The higher value from both lots was taken for the LoD at 1.5 mg/L.

For limit of quantitation (LoQ), a set of five low measurand content serum samples from the lower end of the measuring interval was investigated. Each sample was tested in four replicates per run, one run per day for three days using two lots to reach a total of 24 measurements. The LoQ was determined as 2.0 mg/L following CLSI EP17-A2, the sample with the highest value for the %CV in accordance with the specification for both reagent lots (<20%). The claimed LoQ is 5.0 mg/L.

7. Accuracy (Instrument):
The ProciseDx Analyzer accuracy was evaluated using ERM® -DA474/IFCC that was serially diluted with CRP-depleted human serum for preparation of 11 dilution levels, ranging 1.0 to 41.2 mg/L CRP. Each diluted serum sample was tested in three replicates while the original ERM® -DA474/IFCC (highest concentration) was tested in six replicates. The recovery bias for all samples was with ± 10% from the expected values based on dilutions of ERM® -DA474/IFCC.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A total of 81 serum samples spanning the assay measuring interval were tested by both the Procise CRP and a comparator (Orion QuikRead go® CRP). Measurement comparison between these two assays was evaluated using Passing-Bablok regression analysis and the result is shown in the table below. At the medical decision point of 5.0 mg/L, the calculated bias was 2.7%.

Sample (N)	Range (mg/L)	Slope (95%CI)	Intercept (95% CI)
81	5.3 – 134.0	0.99 (0.95 – 1.01)	0.20 (-0.56 – 1.16)

C Clinical Studies:

1. Clinical sensitivity: Not applicable
2. Clinical specificity: Not applicable
3. Other clinical supportive data (when a. and b. are not applicable): Not applicable
4. Clinical cut-off: Not applicable

D Expected Values/Reference Range:

The reference range study was conducted by testing normal healthy subjects. The subjects with chronic diseases, including obesity (BMI > 30, https://www.cdc.gov/obesity/about-obesity/index.html) were excluded in the analysis. A total of 170 samples (88 males at 18–72 years and 82 females at 21–69 years) were included in the analysis. Of 170 tested samples, 150 samples (150/170, 88.2%) had concentrations within the consensus reference interval at 5 mg/L taken from the literature reference*. The 95th percentile was 8.2 mg/L. Each laboratory should establish its own reference range.

**The expected value in the normal population aged 20 to 60 years is < 5mg/L per literature (Roberts WL, McMillin GA, Burtis CA, Bruns DE. Reference Information for the Clinical Laboratory, Tietz Textbook of Clinical Chemistry and Molecular Diagnostics; 4th Ed., Burtis CA, Ashwood ER, Bruns DE (2006): 2263).*

9. Conclusion

The submitted information in this premarket notification is complete and supports a decision of substantial equivalence to the predicate device.