August 25, 2025

Precision BioLogic Inc.
Karen Black
VP of Compliance and Product Development
140 Eileen Stubbs Avenue
Dartmouth, NS B3B0A9
Canada

Re: K251440
Trade/Device Name: CRYOcheck Chromogenic Factor VIII
Regulation Number: 21 CFR 864.7290
Regulation Name: Factor deficiency test
Regulatory Class: Class II
Product Code: GGP
Dated: May 27, 2025
Received: May 27, 2025

Dear Karen Black:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Takeesha Taylor-bell -S

Takeesha Taylor-Bell
Deputy Director
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K251440

Device Name
CRYOcheck Chromogenic Factor VIII

Indications for Use *(Describe)*
CRYOcheck Chromogenic Factor VIII is for clinical laboratory use in the quantitative determination of factor VIII activity in 3.2 % citrated human plasma. It is intended to be used in identifying factor VIII deficiency and as an aid in the management of hemophilia A in individuals aged 2 years and older. For in vitro diagnostic 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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Department of Health and Human Services
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"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."

PrecisionBioLogic

Executive Summary

Proprietary Name:	CRYO*check*™ Chromogenic Factor VIII
Common Name:	Chromogenic Factor VIII Assay
Classification:	Class II
Product Code:	GGP; Test, Qualitative and Quantitative Factor Deficiency; 21 CFR 864.7290
Device Description:	CRYO*check* Chromogenic Factor VIII is used for determination of FVIII activity and contains the following four components, packaged in glass vials and provided frozen to preserve the integrity of the components: • Reagent 1: Bovine FX and a fibrin polymerization inhibitor, with activators and stabilizer. • Reagent 2: Human FIIa, bovine FIXa, calcium chloride and phospholipids. • Reagent 3: FXa substrate containing EDTA and a thrombin inhibitor. • Diluent Buffer: Tris buffer solution containing 1% BSA and a heparin antagonist. In the first stage of the chromogenic assay, test plasma (containing an unknown amount of functional FVIII) is added to a reaction mixture comprised of calcium, phospholipids, human purified thrombin and FIXa, and bovine FX (Reagent 1 and Reagent 2). This mixture swiftly activates FVIII to FVIIIa, which works in concert with FIXa to activate FX. When the reaction is stopped, FXa production is assumed to be proportional to the amount of functional FVIII present in the sample. The second stage of the assay is to measure FXa through cleavage of a FXa-specific peptide nitroanilide substrate (FXa Substrate). P-nitroaniline is produced, giving a color that can be measured spectrophotometrically by absorbance at 405 nm.
Device Intended Use:	CRYO*check* Chromogenic Factor VIII is for clinical laboratory use in the quantitative determination of factor VIII activity in 3.2% citrated human plasma. It is intended to be used in identifying factor VIII deficiency and as an aid in the management of hemophilia A in individuals aged 2 years and older. For in vitro diagnostic use.

Comparison to Predicate Device:

Similarities

Parameter	Current CRYO*check* Chromogenic Factor VIII	Changed CRYO*check* Chromogenic Factor VIII
510(k) Number	K193204	K251440
Measurand	Human Factor VIII activity	Same

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Parameter	Current CRYO*check* Chromogenic Factor VIII	Changed CRYO*check* Chromogenic Factor VIII
Applicant	Precision BioLogic Inc.	Same
Proprietary and Established Names	CRYO*check* Chromogenic Factor VIII	Same
Regulation Number	21 CFR 864.7290 Factor Deficiency Test	Same
Classification	Class II	Same
Product Code	GGP Test, Qualitative and Quantitative Factor Deficiency	Same
Panel	81 (Hematology)	Same
Intended Use	CRYO*check* Chromogenic Factor VIII is for clinical laboratory use in the quantitative determination of factor VIII activity in 3.2% citrated human plasma. It is intended to be used in identifying factor VIII deficiency and as an aid in the management of hemophilia A in individuals aged 2 years and older. For in vitro diagnostic use.	Same
Indications for Use	N/A – same as Intended Use	Same
Type of Test	Quantitative	Same
Test Principle	In the first stage of the chromogenic assay, test plasma (containing an unknown amount of functional FVIII) is added to a reaction mixture comprised of calcium, phospholipids, human purified thrombin and FIXa and bovine FX (Reagent 1 and Reagent 2). This mixture swiftly activates FVIII to FVIIIa, which works in concert with FIXa to activate FX. When the reaction is stopped, FXa production is assumed to be proportional to the amount of functional FVIII present in the sample. The second stage of the assay is to measure FXa through cleavage of a FXa-specific peptide nitroanilide substrate (FXa Substrate). P-nitroaniline is produced, giving a color that can be measured spectrophotometrically by absorbance at 405 nm.	Same

Parameter	Current CRYO*check* Chromogenic Factor VIII	Changed CRYO*check* Chromogenic Factor VIII
Expression of Results	Quantitative; results are expressed as percent activity interpreted relative to a calibration curve.	Same
Instrument	IL ACL TOP CTS Series and ACL TOP 50 CTS Series	Same

Differences

Parameter	Current CRYO*check* Chromogenic FVIII Claim	Modified CRYO*check* Chromogenic FVIII Claim
Device Description	CRYO*check* Chromogenic Factor VIII is used for determination of FVIII activity and contains the following four components, packaged in glass vials and provided frozen to preserve the integrity of the components: **Reagent 1:** Bovine FX and a fibrin polymerization inhibitor, with activators and stabilizers. **Reagent 2:** Human FIIa, human FIXa, calcium chloride and phospholipids **Reagent 3:** FXa substrate containing EDTA and a thrombin inhibitor. **Diluent Buffer:** Tris buffer solution containing 1% BSA and a heparin antagonist.	CRYO*check* Chromogenic Factor VIII is used for determination of FVIII activity and contains the following four components, packaged in glass vials and provided frozen to preserve the integrity of the components: **Reagent 1:** Bovine FX and a fibrin polymerization inhibitor, with activators and stabilizers. **Reagent 2:** Human FIIa, *bovine* FIXa, calcium chloride and phospholipids **Reagent 3:** FXa substrate containing EDTA and a thrombin inhibitor. **Diluent Buffer:** Tris buffer solution containing 1% BSA and a heparin antagonist.
Interferences	Hemoglobin: ≤500 mg/dL Intralipid: ≤500 mg/dL Bilirubin (unconjugated): ≤29 mg/dL Bilirubin (conjugated): ≤2 mg/dL von Willebrand factor: ≤20 µg/mL Unfractionated heparin: ≤2 IU/mL Low molecular weight heparin: ≤2 IU/mL Fondaparinux: ≤1.25 mg/L Lupus Anticoagulant: ≤1.8 dRVVT ratio Dabigatran and Rivaroxaban interfere with the quantification of FVIII activity.	Hemoglobin: ≤1000 mg/dL Intralipid: ≤830 mg/dL Bilirubin (unconjugated): ≤40 mg/dL Bilirubin (conjugated): ≤11 mg/dL von Willebrand factor: ≤20 µg/mL Unfractionated heparin: ≤3.3 IU/mL Low molecular weight heparin: ≤5 IU/mL Fondaparinux: ≤0.2 mg/L Lupus Anticoagulant: ≤1.8 dRVVT ratio Dabigatran and Rivaroxaban interfere with the quantification of FVIII activity. Emicizumab: ≤150 µg/mL Mim8: ≤8 µg/mL Warfarin: INR ≤7

Parameter	Current CRYO*check* Chromogenic FVIII Claim	Modified CRYO*check* Chromogenic FVIII Claim
Recovery of FVIII Replacement Therapies	The performance of this device has not been established in evaluating the potency of FVIII concentrates.	CRYO*check* Chromogenic Factor VIII accurately evaluated the potency of FVIII replacement products including ADVATE, ADYNOVATE, AFSTYLA, ALTUVIIO, ESPEROCT, HUMATE-P, JIVI, KOVALTRY, Novoeight, Nuwiq, and wilate at concentrations ranging from 0.05 to 1.0 IU/mL. It also accurately evaluated the potency of ELOCTATE, and XYNTHA from 0.05 to 0.6 IU/mL, with an over recovery observed at 0.8 and 1.0 IU/mL. There was an underestimation of OBIZUR.

Summary of Performance Testing

All studies were performed using the changed CRYO*check* Chromogenic Factor VIII on Instrumentation Laboratory ACL TOP CTS Series or TOP 50 CTS Series instruments. Precision, reproducibility, accuracy (method comparison), reference interval, shelf-life stability, in-use stability, linearity, and detection capability performance characteristics are all substantially equivalent to the current device.

Updated claims include interferences updates, and factor VIII replacement therapy recovery.

Interferences

Interference studies were conducted according to CLSI EP07-A3 using a single lot of CRYO*check* Chromogenic Factor VIII on an IL ACL TOP CTS instrument (K160276). Plasma samples were spiked with possible interferents, and 10 replicates were tested alongside 10 replicates of the corresponding blank matrix control. The following substances showed no interference up to the concentrations indicated.

Possible Interferent	Concentration
Hemoglobin	≤1000 mg/dL
Intralipid	≤830 mg/dL
Bilirubin (unconjugated)	≤40 mg/dL
Bilirubin (conjugated)	≤11 mg/dL
von Willebrand factor	≤20 µg/mL
Unfractionated heparin	≤3.3 IU/mL
Low molecular weight heparin	≤5 IU/mL
Fondaparinux	≤0.2 mg/L
Lupus Anticoagulant	≤1.8 dRVVT ratio
Emicizumab	≤150 µg/mL
Mim8	≤8 µg/mL
Warfarin	INR ≤7

Rivaroxaban and dabigatran interfered with the quantification of FVIII activity.

Recovery of Factor VIII Replacement Therapy

A recovery study was conducted using a single lot of CRYO*check* Chromogenic Factor VIII on an IL ACL TOP 550 CTS instrument (K150877). Congenital FVIII deficient plasma was spiked with 14 FVIII replacement therapies at seven concentrations and percent recovery was determined. CRYO*check* Chromogenic Factor VIII accurately evaluated the potency of FVIII concentrates including ADVATE, ADYNOVATE, AFSTYLA, ALTUVIIO, ESPEROCT, HUMATE-P, JIVI, KOVALTRY, Novoeight, Nuwiq, and wilate at concentrations ranging from 0.05 to 1.0 IU/mL. It also accurately evaluated the potency of ELOCTATE, and XYNTHA from 0.05 to 0.6 IU/mL, with an over recovery observed at 0.8 and 1.0 IU/mL. There was an underestimation of OBIZUR.

Product	Mean Percent Recovery (%)
ADVATE®	90.3
ADYNOVATE®	97.7
AFSTYLA®	89.8
ALTUVIIIO®	96.2*
ELOCTATE®	116.3
ESPEROCT®	93.2
HUMATE-P®	95.0
JIVI®	98.5
KOVALTRY®	92.0
Novoeight®	115.6
Nuwiq®	90.2
OBIZUR®	49.5
wilate®	95.2
XYNTHA®	114.7

*Per the manufacturer's recommendations, the mean percent recovery value includes dividing by a correction factor of 2.5 for chromogenic measurement.

Conclusion

The performance testing results demonstrate that the changed CRYO*check* Chromogenic Factor VIII is substantially equivalent to the predicate device, CRYO*check* Chromogenic Factor VIII (K193204), and that the assay is effective for its labeled intended use.