

JUN 7 1999

K990814

510(k) Summary for Cryo✓Check™ Factor 2 Deficient Plasma

1. Submitter's Address and Contact Information

a) Address

Precision BioLogic Incorporated
900 Windmill Rd.
Unit # 100
Dartmouth, Nova Scotia
Canada
B3B 1P7

b) Contact

Mr. Sandy Morrison
Manager, Technical Operations
Phone: (902) 468-6422
Fax: (902) 468-6421
E-mail: smorrison@precisionbiologic.com

c) Date Prepared: February 16, 1999

2. Device Name

a) Proprietary (trade) name: Cryo✓Check™ Factor 2 Deficient Plasma

b) Common name: Factor II (2) Deficient Plasma (human)

c) Classification name: Coagulation Factor Deficient Plasma

d) Classification information: Regulatory Class II
Hematology Panel
Product Code - 81 GJT

3. Device Description:

Cryo✓Check™ Factor 2 Deficient Plasma is frozen human plasma deficient in the Factor II coagulation protein. It is prepared from citrated pooled normal human plasma which has been depleted of Factor II by immunoabsorption. Activity levels of Factor II are assayed at less than 1% normal levels while all other coagulation factors are within normal levels.

4. Intended Use

Cryo✓Check™ Factor 2 Deficient Plasma is recommended for use as a substrate in clot-based factor II assays using the one stage prothrombin time (PT) assay.

5. Substantially Equivalent Device

- a) 510(k) number: K900906
- b) Trade Name: Factor II Deficient Plasma
- c) Manufacturer: Sigma
- d) Substantial Equivalence Comparison

Cryo✓Check™ Factor 2 Deficient Plasma is similar to the predicate device in that they both have the same “indications for use”, target population, and are both made from human plasma.

Cryo✓Check™ Factor 2 Deficient Plasma differs from the predicate device in that it is a frozen liquid preparation and not a lyophilized product. Additionally, **Cryo✓Check™** Factor 2 Deficient Plasma is prepared from normal human plasma from which Factor II has been immunoabsorbed, while the predicate device is derived from human donors with a congenital Factor II deficiency.

To our knowledge, these differences do not affect the intended use or performance of the device.

6. Non-Clinical Performance Data - 24 Hour Open Vial Stability :

- a) Testing Performed:
 - i) Prothrombin Time (PT) assays and Activated Partial Thromboplastin Time (APTT) assays were performed on vials of **Cryo✓Check™** Factor 2 Deficient Plasma at 0 hours, 8 Hours and 24 hours. No anomalous results were detected.
 - ii) Factor II assays were performed on a known reference plasma using vials of **Cryo✓Check™** Factor 2 Deficient Plasma as a substrate. Recovered Factor II values were measured at 0 hours, 8 Hours and 24 hours. (see table S1 for results)
 - iii) Inter- and intra-lot reproducibility testing on normal and abnormal samples using two lot numbers of factor II deficient plasma. (see tables S2 for results)

- iv) Correlation study with a predicate device using samples with factor II levels in the normal, borderline, and pathological ranges. (see table S3 for results)
 - v) Normal donor study using healthy male and female donors. (see table S4 for results)
- b) Conclusions:
- i) Factor II level for **Cryo✓Check™** Factor 2 Deficient Plasma is less than 1%
 - ii) All other coagulation factors are within normal limits
 - iii) No anomalous results for PT and APTT assays were observed during a 24 hour open vial stability study
 - iv) Factor II values were within expected levels following factor II assays over a 24 hour open vial stability study
 - v) Inter and intra-lot CV's of < 4 % were recovered
 - vi) Correlation studies showed an R² value of 0.997 with the predicate device
 - vii) Normal donor studies showed a normal range based on 95% confidence interval of 92.7% - 133.5%

Table S1
Open Vial Stability of Cryo✓Check™
Factor 2 Deficient Plasma

| | Summary Statistics (% Recovery) | | | 24Hr. Average |
|--------------------|---------------------------------|---------|----------|---------------|
| | 0 Hours | 8 Hours | 24 Hours | |
| MEAN | 83.2 % | 82.8 % | 83.2 % | 83.07 % |
| MAXIMUM | 85 % | 85 % | 87 % | 87 % |
| MINIMUM | 82 % | 82 % | 80 % | 80 % |
| S.D. | 1.64 | 1.30 | 2.77 | 1.87 |
| 2 S.D. | 3.29 | 2.61 | 5.55 | 3.74 |
| SAMPLE SIZE | 5 | 5 | 5 | 15 |
| C.V.% | 1.97 | 1.57 | 3.34 | 2.25 |

Note: Reference Value = 85% Factor II
 Acceptable values are: Mean (+/-) 5% of reference value; and %C.V. < 5%

Table S2

Intra Lot Reproducibility of Cryo✓Check™
Factor 2 Deficient Plasma

Normal Sample
Factor II Deficient – Lot 1

| | |
|---------------------------|--------------|
| Number | 10 |
| Mean (sec) | 102.2 |
| Standard Deviation | 1.398 |
| C.V. (%) | 1.4 |

Normal Sample
Factor II Deficient –Lot 2

| | |
|---------------------------|--------------|
| Number | 10 |
| Mean (sec) | 103.5 |
| Standard Deviation | 0.850 |
| C.V. (%) | 0.8 |

Abnormal Sample
Factor II Deficient –Lot 1

| | |
|---------------------------|--------------|
| Number | 10 |
| Mean (sec) | 36.9 |
| Standard Deviation | 0.738 |
| C.V. (%) | 2.0 |

Abnormal Sample
Factor II Deficient –Lot 2

| | |
|---------------------------|--------------|
| Number | 10 |
| Mean (sec) | 36.7 |
| Standard Deviation | 1.252 |
| C.V. (%) | 3.4 |

Table S2

Inter Lot Reproducibility of Cryo✓Check™
Factor 2 Deficient Plasma

Normal Sample

| | |
|---------------------------|--------------|
| Number | 20 |
| Mean (sec) | 102.9 |
| Standard Deviation | 1.309 |
| C.V. (%) | 1.3 |

Abnormal Sample

| | |
|---------------------------|--------------|
| Number | 20 |
| Mean (sec) | 36.8 |
| Standard Deviation | 1.005 |
| C.V. (%) | 2.7 |

Table S3

Correlation Study of Cryo✓Check™
Factor 2 Deficient Plasma

| Sample Type | % Activity Equivalent Device Factor II Def. | | | % Activity Predicate Device Factor II Def. | | |
|------------------------------|--|-----------------|-------------|---|-----------------|-------------|
| | Result 1 | Result 2 | Mean | Result 1 | Result 2 | Mean |
| Normal Range | 106 | 106 | 106 | 98 | 98 | 98 |
| Normal Range | 103 | 105 | 104 | 98 | 98 | 98 |
| Borderline Range | 36 | 37 | 37 | 38 | 37 | 38 |
| Borderline Range | 40 | 38 | 39 | 38 | 32 | 35 |
| Pathological Range | 8 | 8 | 8 | 8 | 9 | 9 |
| Factor VIII Deficient | 84 | 85 | 85 | 87 | 85 | 86 |
| Factor X Deficient | 92 | 92 | 92 | 85 | 83 | 84 |
| Factor XII Deficient | 108 | 111 | 110 | 103 | 106 | 105 |
| Factor II Deficient | 0 | 0 | 0 | 1 | 0 | 1 |
| Factor II Deficient | 0 | 0 | 0 | 1 | 1 | 1 |

Regression analysis gave an $R^2 = 0.997$

Table S4

Normal Donor Study with Cryo✓Check™
Factor 2 Deficient Plasma

| | |
|---|-------------------|
| Number | 21 |
| Mean | 113.1 |
| Standard Deviation | 10.195 |
| Reference Range (95% Conf. Limits) | 92.7-133.5 |



DEPARTMENT OF HEALTH & HUMAN SERVICES

JUN 7 1999

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. Sandy Morrison
Manager, Technical Operations
Precision BioLogic Inc.
900 Windmill Road, Suite 100
Dartmouth, Nova Scotia
Canada
B3B 1P7

Re: K990814
Trade Name: Cryo^v CheckTM Factor 2 Deficient Plasma
Regulatory Class: II
Product Code: GJT
Dated: May 6, 1999
Received: May 13, 1999

Dear Mr. Morrison:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895.

A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

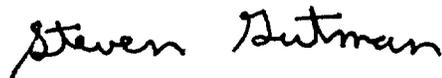
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597, or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive style.

Steven I. Gutman, M.D, M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number: K990814

Device Name: Cryo✓Check™ Factor 2 Deficient Plasma

Indications for Use

Deficiencies in coagulation factors may have congenital or acquired etiologies and can compromise *in vivo* hemostasis. Factor II (also known as prothrombin) is a serine protease located in the “common coagulation pathway” and is essential to normal hemostasis. Factor II deficiency is commonly diagnosed *in vitro* through the use of a modified prothrombin time (PT) assay.

Cryo✓Check™ Factor 2 Deficient Plasma is human plasma deficient in the Factor II coagulation protein while having all other coagulation factors within normal limits. It is recommended for use as a substrate in clot-based Factor II assays using the one stage prothrombin time (PT).



(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K990814

Prescription ✓