October 23, 2020

Precision BioLogic
Karen Black
VP of Compliance and Product Development
140 Eileen Stubbs Avenue
Dartmouth, Nova Scotia B3B 0A9 Canada

Re: K193556
Trade/Device Name: Cryocheck Hex LA
Regulation Number: 21 CFR 864.7925
Regulation Name: Partial Thromboplastin Time Tests
Regulatory Class: Class II
Product Code: GFO
Dated: December 20, 2019
Received: December 23, 2019

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 (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,

Takeesha Taylor-Bell
Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K193556

Device Name
Cryocheck Hex LA

Indications for Use *(Describe)*

Cryocheck Hex LA is for clinical laboratory use as a qualitative test kit intended to aid in the detection of lupus anticoagulants (LA) in 3.2% citrated human plasma by the application of hexagonal phase phospholipids. Cryocheck Hex LA should be used as an integrated test for lupus anticoagulant detection. For in vitro diagnostic use. The performance of this device has not been established in neonate and pediatric patient populations.

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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510(k) Summary

510(k) Summary
CRYO*check*™ Hex LA™

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is K193556

Submitter's Information	Precision BioLogic Inc. 140 Eileen Stubbs Ave. Dartmouth, Nova Scotia B3B 0A9 Canada	
Contact Person	Karen M. Black, VP of Compliance & Product Development Phone: 902-468-6422 ext. 226, or 902-706-3125 E-mail: kblack@precisionbiologic.com	
Preparation Date	14 October 2020	
Device Trade Name	CRYO*check*™ Hex LA	
Regulatory Information	Regulation Number and Description	21 CFR 864.7925 Partial thromboplastin time test
	Classification	Class II
	Product Code	GFO; Partial thromboplastin time test; 21 CFR 864.7290
	Classification Panel	Hematology
Predicate Device	Staclot LA (K923731)	
Indication for Use/ Intended Use	CRYO*check* Hex LA is for clinical laboratory use as a qualitative test kit intended to aid in the detection of lupus anticoagulants (LA) in 3.2% citrated human plasma by the application of hexagonal phase phospholipids. CRYO*check* Hex LA should be used as an integrated test for lupus anticoagulant detection. For in vitro diagnostic use. The performance of this device has not been established in neonate and pediatric patient populations.	
Device Description	CRYO*check* Hex LA is comprised of three reagents supplied in a frozen format as follows: LA Start: Pooled normal plasma with buffer and a heparin neutralizer. LA Correct: Pooled normal plasma with buffer, a heparin neutralizer, and inverted hexagonal phase phospholipid. LA APTT: Silica-based lupus sensitive APTT reagent with stabilizer.	

Comparison to Predicate		
Item	**Predicate**	**New Device**
Proprietary and Established Names	Staclot LA	CRYO*check* Hex LA
Manufacturer	American Bioproducts Inc (original applicant); Diagnostica Stago (current manufacturer)	Precision BioLogic Inc

Similarities		
	Staclot LA	**CRYO*check* Hex LA**
Measurand	lupus anticoagulant	lupus anticoagulant
Product Code	GFO Partial thromboplastin time tests	GFO Partial thromboplastin time tests
Regulation Section	21 CFR 864.7925 Partial thromboplastin time tests	21 CFR 864.7925 Partial thromboplastin time test
Classification	Class II	Class II
Panel	81 (Haematology)	81 (Haematology)
Intended Use	The Staclot LA test kit is a reagent system designed for the qualitative detection of lupus anticoagulants (LA) in plasma by the use of hexagonal H_{II} phase phospholipid molecules. (In the USA this procedure has been assigned to the high complexity category per CLIA 1988 – CDC Analyte Code 3728; CDC Test System Code 13285).	CRYO*check* Hex LA is for clinical laboratory use as a qualitative test kit intended to aid in the detection of lupus anticoagulants (LA) in 3.2% citrated human plasma by the application of hexagonal phase phospholipids. CRYO*check* Hex LA should be used as an integrated test for lupus anticoagulant detection. For in vitro diagnostic use. The performance of this device has not been established in neonate and pediatric patient populations.
Assay Type	Qualitative; hexagonal phase neutralization test	Qualitative; hexagonal phase neutralization test
Methodology	The Staclot LA test procedure is based on the following principle: the test plasma that is suspected to contain LA is first allowed to incubate at 37°C with (Tube 2) and without (Tube 1) hexagonal phase phosphatidylethanolamine (HPE) (Reagent 2); next, an APTT is performed on both tubes using an LA sensitive reagent (Reagent 4); if LA were present in the test plasma, they would be neutralized by HPE in tube 2, and this would result in a shortening of the clotting time of tube 2 compared with that of tube 1. By comparing the difference between the two clotting times, the presence of LA antibodies in the test plasma can be identified. The Reagent 3 contains a heparin inhibitor which makes the test system insensitive to heparin levels up to 1 IU/mL. Furthermore, the Staclot LA procedure calls for the addition of a normal plasma (Reagent 3) to the test system to correct a prolongation of the	CRYO*check* Hex LA is a hexagonal-phase phospholipid neutralization test (HPNT), which is an integrated test that combines screening, confirmatory and mixing test procedures into a single assay. CRYO*check* LA works on the principle that LA are neutralized by hexagonal phase phospholipids that are present in the assay's confirmatory reaction mixture and not the screening reaction mixture. The presence of LA in plasma samples is confirmed by the correction of APTT clot times in the presence of a reaction mixture containing hexagonal phase phospholipids. In the CRYO*check* Hex LA assay, the test plasma suspected to contain LA is incubated in two reaction cuvettes, both of which entail dilution with pooled normal plasma (containing a heparin

Similarities		
	Staclot LA	**CRYO*check* Hex LA**
	clotting time due to factor deficiencies that might be present. If the Staclot LA does not produce a shortening of the clotting time, then the presence of anti-factor antibodies should be suspected; in this case, use an appropriate test for anti-factor antibodies. Compare the clotting time of tube 1 (CT1) with that of tube 2 (CT2). A shortening of clotting time of 8 seconds or more of tube 2 compared with that of tube 1 is significant of a neutralization of anti-phospholipid antibodies (this 8-second cut-off in clotting times has been determined with the ST4/ST art® instrument - Diagnostica Stago).	neutralizer), thus satisfying the mixing test requirement. In the first cuvette, the screening test reaction is performed by mixing the test plasma with the LA Start reagent (pooled normal plasma). In the second cuvette, the confirmatory reaction is performed by mixing the test plasma with the LA Correct reagent (pooled normal plasma with hexagonal phase phospholipid). The LA APTT reagent is then added to each cuvette, followed by 0.025 M $CaCl_2$ to activate clotting via the intrinsic pathway. Clot times are recorded for the screening reaction mixture containing LA Start and the confirmatory reaction mixture containing LA Correct. The result is reported as the difference in clot time in seconds ("delta correction") between LA Start and LA Correct cuvettes. delta correction = (CT LA Start) – (CT LA Correct) The result is then compared to an established cut-off. A result greater than or equal to the established cut-off is considered LA positive, while a result less than the established cut-off is considered LA negative.
Expression of results	Qualitative; results are reported as clot time delta (seconds) and are interpreted as positive or negative relative to an established cut-off value.	Qualitative; results are reported as clot time delta (seconds) and are interpreted as positive or negative relative to an established cut-off value.

<table>
<tr><th colspan="3">Differences</th></tr>
<tr><th></th><th>Staclot LA</th><th>CRYOcheck Hex LA</th></tr>
<tr><td>Format</td><td>Staclot LA is comprised of three lyophilized reagents and two reconstitution liquids as follows:
Reagent 1: ready-for-use buffer
Reagent 2: lyophilized hexagonal phase phosphatidylethanolamine
Reagent 3: lyophilized normal human plasma containing a heparin inhibitor
Reagent 4: lyophilized PTT-LS reagent consisting of cephalin prepared from rabbit cerebral tissues and a particulate siliceous activator
Reagent 5: solvent for reconstitution of Reagent 4.</td><td>CRYOcheck Hex LA is comprised of three reagents supplied in a frozen format as follows:
LA Start: Pooled normal plasma with buffer and a heparin neutralizer.
LA Correct: Pooled normal plasma with buffer, a heparin neutralizer, and inverted hexagonal phase phospholipid.
LA APTT: Silica-based LA sensitive APTT reagent with stabilizer.</td></tr>
<tr><td>Storage</td><td>2-8°C until expiration</td><td>≤-70°C until expiration</td></tr>
<tr><td>Instrument</td><td>Manual (ST4/ST art®)</td><td>STA-R Evolution®</td></tr>
<tr><td>Associated Controls</td><td>STA® - Control LA 1 + 2</td><td>CRYOcheck Lupus Negative Control
CRYOcheck Weak Lupus Positive Control
CRYOcheck Lupus Positive Control</td></tr>
<tr><td>Cut-off</td><td>A shortening of clotting time of 8 seconds or more of tube 2 compared with that of tube 1 is significant of a neutralization of anti-phospholipid antibodies (this 8-second cut-off in clotting times has been determined with the ST4/ST art® instrument - Diagnostica Stago).

Each laboratory should verify this 8-second cut-off by testing the plasma of at least 20 normal individuals, using its own methodology to obtain the mean delta T + 4 SD.</td><td>The cut-off for the assay delta correction was determined using pooled data from a normal range study conducted on Stago STA-R Evolution® analyzers and calculating the mean + 4 SD, with the following results:
<table><tr><th>Delta Correction</th><th>Interpretation</th></tr><tr><td>< 6.0 seconds</td><td>LA Negative</td></tr><tr><td>≥ 6.0 seconds</td><td>LA Positive</td></tr></table>
The results were obtained using specific lots of reagent. The cut-off is calculated as the mean of the delta correction + 4 SD, consistent with accepted methods for hexagonal phase neutralization tests. This method of establishing cut-off is different than that indicated for confirmatory tests in Pengo et al., 2009.[1] Each laboratory should verify its own cut-off, by</td></tr>
</table>

[1] Pengo V, Tripodi A, Reber G, Rand JH, Ortel TL, Galli M, deGroot PG. Update of the guidelines for lupus anticoagulant detection. J. Thromb. Haemost. 2009;7(10):1737-1740.

Differences		
	Staclot LA	**CRYO*check* Hex LA**
		testing the plasma of at least 20 normal individuals.
Heparin Interference	No interference up to 1 IU/mL	Unfractionated heparin: no interference up to 2 IU/mL Low molecular weight heparin: no interference up to 2 IU/mL
Direct Thrombin and Xa Inhibitor Interference	Thrombin inhibitors (e.g., hirudin, argatroban...) present in the sample to be tested may interfere in the test and lead to falsely positive results.	Dabigatran, rivaroxaban, and fondaparinux do not interfere with the interpretation of CRYO*check* Hex LA results but may increase the delta correction of LA positive samples.
Warfarin Interference	The Staclot® LA procedure was used to test plasmas from stabilized coumadin patients (n = 29). All plasmas gave negative results with Staclot® LA.	Plasma samples with elevated INR (up to 4.5) do not interfere with the interpretation of CRYO*check* Hex LA results
Factor VIII Inhibitor Antibody Interference	The presence of anti-factor antibodies does not normally produce a correction in clotting time with the Staclot LA test procedure. However considering the heterogeneity of these antibodies, some may interfere in the test. Consequently, when these are suspected, use an appropriate test for anti-factor antibodies	Factor VIII inhibitor antibodies do not interfere with the interpretation of CRYO*check* Hex LA results, but at titers above 15 BU/mL may increase the delta correction of LA positive samples.
Factor Deficiency Interference	A total of 21 factor deficient plasmas, comprising deficiencies of F. VIII (n = 8), F. VIII with the presence of anti-F. VIII-antibodies (n = 5), F. IX (n = 4), F. XI (n = 2), F. XII (n = 1) and F. II (n = 1), were tested with the Staclot® LA procedure. The observed CT1-CT2 was found in all cases < 8 seconds.	Factor VII and factor IX deficiencies do not interfere with CRYO*check* Hex LA. Abnormally low factor X activities (below 50%) do not interfere with the interpretation of CRYO*check* Hex LA results but may increase the delta correction for LA positive samples. Abnormally low factor II activities (below 50%) may interfere with the interpretation of CRYO*check* Hex LA, potentially resulting in false negative results for weakly LA positive plasmas.
HIL interference	Unknown	Hemoglobin: ≤ 500 mg/dL Bilirubin (unconjugated): ≤ 20 mg/dL Bilirubin (conjugated): ≤ 2 mg/dL Intralipid: ≤ 500 mg/dL

Differences		
	Staclot LA	**CRYO*check* Hex LA**
C-reactive protein interference	Unknown	C-reactive protein does not interfere with the interpretation of CRYO*check* Hex LA results but at concentrations above 15 µg/mL may increase the delta correction of LA positive samples.
Elevated factor interference	Unknown	Elevated factor VIII activity (up to 180%) does not interfere with CRYO*check* Hex LA. Elevated fibrinogen concentrations do not interfere with the interpretation of CRYO*check* Hex LA results but may increase the delta correction of LA positive samples.

Performance Summary:

All studies were performed using CRYO*check* Hex LA on Diagnostica Stago STA-R Evolution® instrument(s).

Precision

An internal precision study was performed using three different lots of CRYO*check* Hex LA on a STA-R Evolution instrument in accordance with CLSI EP05-A3. Three lot numbers of CRYO*check* Hex LA were used to test three control plasmas and five plasmas with varying LA positivity, in duplicate, twice a day for 20 days. The results demonstrated a pooled precision of < 5% CV for LA Start and < 8% CV for LA Correct.

Sample	Within Laboratory Precision LA Start			Within Laboratory Precision LA Correct		
	Mean Clot Time (s)	SD	%CV	Mean Clot Time (s)	SD	%CV
CRYO*check* Lupus Negative Control	53.0	1.6	3.0	52.8	2.8	5.3
CRYO*check* Weak Lupus Positive Control	87.3	3.2	3.7	65.4	2.8	4.2
CRYO*check* Lupus Positive Control	125.4	5.2	4.2	79.8	4.5	5.7
LA Negative Plasma Sample	55.9	1.7	3.1	55.1	2.5	4.5
LA Near Cut-Off Plasma Sample	67.6	2.5	3.8	58.4	2.6	4.5
LA Weak Positive Plasma Sample	89.8	3.3	3.7	66.4	3.0	4.6
LA Moderate Positive Plasma Sample	146.5	6.0	4.1	85.9	5.8	6.7
LA Strong Positive Plasma Sample	270.7	9.6	3.6	118.0	9.0	7.6

Reproducibility

Reproducibility studies were conducted at three sites (one internal and two external) using three lots of CRYO*check* Hex LA in accordance with CLSI EP05-A3. The study tested three control plasmas as well as five plasmas with varying LA positivity. Each sample was tested in triplicate, twice a day for 5 days for each of the 3 lots of CRYO*check* Hex LA. The data across three sites demonstrated a pooled reproducibility of <5% CV for LA Start and ≤8 % CV for LA Correct as summarized in the reproducibility tables below.

Reproducibility: LA Start											
Sample	Mean Clot Time (s)	Within-Run (Repeatability)		Between-Run		Between-Day		Between-Site		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CRYO*check* Lupus Negative Control	52.8	1.4	2.7	0.3	0.6	0	0	0.4	0.7	1.6	3.0
CRYO*check* Weak Lupus Positive Control	85.6	3.3	3.9	0.5	0.6	0.5	0.6	1.9	2.2	3.9	4.6
CRYO*check* Lupus Positive Control	123.6	5.0	4.0	0	0	1.5	1.3	2.1	1.7	5.7	4.6
LA Negative Plasma Sample	55.8	1.5	2.6	0.1	0.2	0.3	0.5	0.7	1.3	1.8	3.2
LA Near Cut-Off Plasma Sample	66.9	2.3	3.5	0.4	0.6	0.8	1.2	0.8	1.2	2.7	4.0
LA Weak Positive Plasma Sample	88.3	3.7	4.1	0	0	1.1	1.3	1.8	2.0	4.3	4.8
LA Strong Positive Plasma Sample	264.9	6.9	2.6	0.3	0.1	2.3	0.9	4.5	1.7	10.3	3.9

Reproducibility: LA Correct											
Sample	Mean Clot Time (s)	Within-Run (Repeatability)		Between-Run		Between-Day		Between-Site		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CRYO*check* Lupus Negative Control	53.7	1.7	3.1	0.8	1.6	0	0	0	0	3.1	5.8
CRYO*check* Weak Lupus Positive Control	65.7	2.4	3.6	1.0	1.5	0.7	1.0	0.7	1.1	3.1	4.8
CRYO*check* Lupus Positive Control	80.2	3.2	4.0	1.5	1.8	1.4	1.7	1.8	2.2	4.8	5.9
LA Negative Plasma Sample	56.0	1.7	3.0	0.6	1.1	0.2	0.4	0	0	2.9	5.2
LA Near Cut-Off Plasma Sample	59.2	2.2	3.7	1.2	2.0	0.7	1.1	0.3	0.6	3.0	5.0
LA Weak Positive Plasma Sample	66.9	2.7	4.0	1.3	2.0	1.2	1.8	2.2	3.3	4.0	6.0
LA Strong Positive Plasma Sample	117.4	4.5	3.9	3.1	2.6	2.0	1.7	2.6	2.2	9.4	8.0

Normal Range and Assay Cut-off

A normal range study was performed in-house using on two analyzers using normal samples (Analyzer A, n = 137; Analyzer B, n = 126) according to CLSI EP28: A3c. Each sample was tested using three lots of CRYO*check* Hex LA. A pooled mean ±2 SD range was determined for delta correction results and is shown in the table below:

Normal Range	
Lower Range (s)	Upper Range (s)
-5.9	2.0

The cut-off for the assay delta correction was determined using pooled data from the normal range study and calculating the mean + 4 SD, with the following results:

Delta Correction	Interpretation
< 6.0 seconds	LA Negative
≥ 6.0 seconds	LA Positive

The cut-off results were obtained using specific lots of reagent. The cut-off is calculated as the mean of the delta correction + 4 SD, consistent with accepted methods for hexagonal phase neutralization tests. This method of establishing cut-off is different than that indicated for confirmatory tests in Pengo et al., 2009.[1] Each laboratory should verify its own cut-off, by testing the plasma of at least 20 normal individuals.

Stability

Shelf Life Stability

A shelf life stability study was conducted in accordance with CLSI EP25-A. Three lots of CRYO*check* Hex LA were stored -70 °C (-66 to -72 °C) and -80 °C (-76 to -82 °C) and tested at time = 0 and regular intervals up to 37 months. At each timepoint, 10 replicates of three controls were tested. For one lot, an additional plasma sample close to the assay cut-off was also tested. The study has been completed up to 12 months and supports a shelf-life stability claim of at least 12 months when the product is stored at -70 °C or colder.

In-Use Stability

An in-use stability study was conducted in accordance with CLSI EP25-A. Three lots of CRYO*check* Hex LA were maintained at room temperature (18–25 °C) or on-board the instrument and used to test five replicates of three control plasmas as well as four test plasmas with varying levels of LA at 0, 2, 4, 6, 7, 8 and 9 hours. The data support a 4-hour in-use stability of the product when maintained at room temperature or 8 hours when stored on-board the instrument.

Interferences

Interference studies were conducted according to CLSI EP07, 3rd ed. using a single lot of CRYO*check* Hex LA. Patient plasma samples were spiked with possible interferents and 20 replicates were tested alongside 20 replicates of the corresponding blank matrix control. The following substances showed no interference up to the concentrations indicated:

Substance Tested	Test Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 2 mg/dL
Intralipid	≤ 500 mg/dL
Unfractionated Heparin	≤ 2 IU/mL
Low Molecular Weight Heparin	≤ 2 IU/mL

- Dabigatran, rivaroxaban, and fondaparinux do not interfere with the interpretation of CRYO*check* Hex LA results but may increase the delta correction of LA positive samples.
- Elevated factor VIII activity (up to 180%) does not interfere with CRYO*check* Hex LA.
- Elevated fibrinogen concentrations do not interfere with the interpretation of CRYO*check* Hex LA results but may increase the delta correction of LA positive samples.
- C-reactive protein does not interfere with the interpretation of CRYO*check* Hex LA results but at concentrations above 15 µg/mL may increase the delta correction of LA positive samples.
- Factor VIII inhibitor antibodies do not interfere with the interpretation of CRYO*check* Hex LA results, but at titers above 15 BU/mL may increase the delta correction of LA positive samples.
- Plasma samples with elevated INR (up to 4.5) do not interfere with the interpretation of CRYO*check* Hex LA results.
- High platelet counts (>10,000 platelets/µL) showed interference with CRYO*check* Hex LA results when compared with platelet poor (<10,000/ µL, single centrifuged) or platelet free (double centrifuged) plasma samples from the same donors.
- Abnormally low factor II activities (below 50%) may interfere with the interpretation of CRYO*check* Hex LA, potentially resulting in false negative results for weakly LA positive plasmas.
- Factor VII and factor IX deficiencies do not interfere with CRYO*check* Hex LA.
- Abnormally low factor X activities (below 50%) do not interfere with the interpretation of CRYO*check* Hex LA results but may increase the delta correction for LA positive samples.

Method Comparison Studies

A method comparison study was conducted to assess the efficacy of CRYO*check* Hex LA in the qualitative detection of LA relative to a comparator assay, Staclot® LA. A total of 446 samples were included in the study: 124 known (previously characterized) LA positive samples, 75 normal (presumed LA negative) samples, 27 samples from individuals with other medical conditions including autoimmune disorders and 220 LA target screening population samples. The study was conducted at one internal and three external sites. Each site performed the investigational device assay on their assigned portion of the samples using a single lot of CRYO*check* Hex LA. One external site, acting as the central laboratory, performed the comparator device testing on all 446 samples using the Staclot LA assay on a STA-R Evolution. The data demonstrated positive

percent agreement of 95.6% (95% CI, 91-98%), negative percent agreement of 95.2% (95% CI, 92%-97%), and overall agreement of 95.3% (95% CI, 93%-97%) as summarized below.

		CRYO*check* Hex LA results		
		Negative	**Positive**	**Total**
Comparator device results	**Negative**	295	15	310
	Positive	6	130	136
	Total	301	145	446

Agreement	**Point Estimate (95% Confidence Interval)**
Positive Percent Agreement	95.6% (91% - 98%)
Negative Percent Agreement	95.2% (92% - 97%)
Overall Agreement	95.3% (93% - 97%)

Sample Integrity

A sample integrity study was conducted to assess sample stability of fresh samples at room temperature, when stored at ≤ -70 °C and after up to two freeze-thaw cycles. Sixty-four samples were measured with a single lot of CRYO*check* Hex LA. Results were compared using regression analysis and support a fresh sample stability claim of 4 hours at room temperature and a frozen storage claim of 2 months at ≤ -70 °C, including one freeze-thaw cycle.

Conclusion

The performance testing results demonstrate that CRYO*check* Hex LA is substantially equivalent to the predicate device, Staclot LA (K923731), and that the assay is effective for its labeled intended use.