K100943

Invader® Factor II 510(k) SUMMARY

JUN - 2 2011

A. 510(k) Number:
k100943

B. Purpose for Submission:
New Device

C. Measurand:
Factor II

D. Type of Test:
Qualitative genotyping test for single nucleotide polymorphism detection.

E. Applicant:
Hologic Inc.
Third Wave Technologies
250 Campus Drive
Marlborough, MA 01752
508-263-8853
Contact Person: Randall J. Covill, Manager, Regulatory Affairs
Date of Submission: April 2010

F. Proprietary and Established Names:
Invader® Factor II

G. Regulatory Information:

1. Regulation Sections: 21 CFR 864.7280
2. Classification:
   Class II
3. Product Code:
   NPR: Test, Factor II G20210A Mutations, Genomic DNA PCR
4. Panel:
   Hematology (81)

H. Intended Use:

1. Intended Use(s):
   The Invader® Factor II test is an *in vitro* diagnostic test intended for the detection and genotyping of a single point mutation (G to A at position 20210) of the human Factor II gene in isolated genomic DNA obtained from whole blood potassium EDTA samples from patients with suspected thrombophilia.
2. Indication(s) for use:
   Same as Intended Use
3. Special Conditions for use statements(s):
   For prescription use only
4. Special instrument requirements:
   None

I. Device Description:
The Invader Factor II test consists of the following components:

Factor II Oligo Mix
Universal Buffer
Universal Enzyme Mix
No DNA Control
Factor II Wild Type Control
Factor II Heterozygous Control
Factor II Mutant Control
Invader Call Reporter™ Software
Invader® Factor II Software

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Factor II (Prothrombin) G20210A, Roche
2. Predicate 510(k) number(s):
   Roche, K033612
3. Comparison with predicate:

Table 1: Comparison with Predicate Device		
	Predicate Device	*Proposed Device*
Product Name (Manufacturer, Submission)	Factor II (Prothrombin) G20210A Kit *(Roche, K033612)*	Invader® Factor II *(Hologic, Inc., N/A)*
Intended Use	The Factor II (Prothrombin) G20210A Kit is an *in vitro* diagnostic test for the detection and genotyping of a single point mutations (G to A at position 20210) of the human Factor II gene, from DNA isolated from human whole peripheral blood. The Factor II (Prothrombin) G20210A Kit is indicated as an aid to diagnosis in the evaluation of patients with suspected thrombophilia. The test is intended to be used on the LightCycler instrument. The sample preparation must be performed according to a workflow procedure described in the package insert.	The Invader® Factor II test is an *in vitro* diagnostic test intended for the detection and genotyping of a single point mutation (G to A at position 20210) of the human Factor II gene in isolated genomic DNA obtained from whole blood potassium EDTA samples from patients with suspected thrombophilia.
Specimen Type	Purified DNA isolated from human whole peripheral blood.	Same as predicate
Indications for Use	Same as Intended Use	Same as Intended Use
Target Population	Patients with suspected thrombophilia	Same as predicate
Chemistry	The amplicon is detected by fluorescence using a specific pair of H probes. The H probes consist of two different oligonucleotides that hybridize to an internal sequence of the amplified fragment	PCR and Invader® using Fluorescence Resonance Energy Transfer (FRET) chemistry for signal reporting. Both our device and predicate device detect signal from amplicons using Fluorescence

Table 1: Comparison with Predicate Device		
	Predicate Device	*Proposed Device*
Product Name (Manufacturer, Submission)	Factor II (Prothrombin) G20210A Kit *(Roche, K033612)*	Invader® Factor II *(Hologic, Inc., N/A)*
	during the annealing phase of the PCR cycle. One probe is labeled at the 5′-end with LightCycler® Red 640-N-hydroxy-succinimide ester (Red 640-NHS ester), and to avoid extension, modified at the 3′-end by phosphorylation. The other probe is labeled at the 3′-end with fluorescein.3. Only after hybridization to the template DNA, do the two probes come in close proximity, resulting in fluorescence resonance energy transfer (FRET) between the two fluorophores. During FRET, fluorescein, the donor fluorophore, is excited by the light source of the LightCycler® 2.0 Instrument, and part of the excitation energy is transferred to LightCycler® Red 640-NHS ester, the acceptor fluorophore.	Resonance Energy Transfer (FRET).
Hardware	LightCycler® Instrument using SW 3.5	Non-specified, third-party fluorometer and thermal cycler.
Software Interface	LightCycler® Instrument using SW 3.5. Expro database and macros.	Java-based software installed on a standalone PC capable of converting raw fluorescence data into genotype calls.
Detection Method	The LightCyler® uses optical detection of stimulated fluorescence generated by the following chemistry: The H probes are also used to determine the genotype by performing a melting curve analysis after the amplification cycles are completed and the	PCR and Fluorescence Resonance Energy Transfer (FRET) chemistry for signal reporting.

Table 1: Comparison with Predicate Device		
	Predicate Device	*Proposed Device*
Product Name (Manufacturer, Submission)	Factor II (Prothrombin) G20210A Kit *(Roche, K033612)*	Invader® Factor II *(Hologic, Inc., N/A)*
	amplicon is present at increased concentration. •The Red 640-labeled H probe hybridizes to a part of the target sequence that is not mutated and functions as an anchor probe. •The Fluorescein-labeled H probe spans the mutation site (mutation probe). During the melting curve analysis, increasing temperature causes the fluorescence to decrease because the shorter of the two probes (mutation probe) dissociates first and the two fluorescent dyes are no longer in close proximity. If the Factor II (Prothrombin) G20210A mutation is present, the mismatch of the mutation probe with the target destabilizes the hybrid so the decrease in fluorescence will occur at a lower temperature. With the wild-type genotype, mismatches will not occur, and therefore, the heteroduplex DNA has a higher melting temperature (Tm). The heterozygous genotype exhibits a distinctive combination of properties.	
Sample Size	10-20ul in glass capillaries.	20ul reaction containing 0.25-4ng/ul gDNA extracted from human peripheral whole blood.
Detection Procedure	Optical detection of stimulated fluorescence using a specific pair of probes.	Multi-well fluorometer to detect raw fluorescence.

Table 1: Comparison with Predicate Device		
	Predicate Device	*Proposed Device*
Product Name (Manufacturer, Submission)	Factor II (Prothrombin) G20210A Kit *(Roche, K033612)*	Invader® Factor II *(Hologic, Inc., N/A)*
Detection Chemistry	Paired hybridization probes using fluorescence resonance energy transfer (FRET) followed by melting curve analysis.	PCR and Invader® using Fluorescence Resonance Energy Transfer (FRET) chemistry for signal reporting.
Analysis Time	A multi-step assay with different times required for each step. Detection occurs at defined intervals during PCR cycle and can be reviewed in real-time.	~90 min. amplification followed by 1 min signal detection. Software analysis post signal detection.

K. Standard/Guidance Document Referenced (if applicable):

- Guidance for Industry and FDA Staff – Class II Special Controls Guidance Document: Factor V Leiden DNA Mutation Detection Systems issued on March 16, 2004
- Guidance for Industry and FDA Staff - Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices issued May 11, 2005
- Guidance for Industry and FDA Staff – Format for Traditional and Abbreviated 510(k)s issued on August 12, 2005

L. Test Principle:

The Invader® Factor II test utilizes the Invader Plus® chemistry with DNA isolated from human whole blood, for the detection of the targeted sequence polymorphism. Specifically, the Invader Plus® chemistry utilizes a single-tube, two phase reaction, including target amplification and signal generation (mediated by Invader® chemistry). Invader Plus® reaction mixes are assembled by combining the Factor II Oligo Mix, Universal Enzyme Mix, and Universal Buffer. In a 96-well plate, reaction mix is combined with purified genomic DNA samples, as well as four (4) controls included with the test. The No DNA Control is used by the interpretive software to set the "noise" component of the run for "signal-to-noise" calculations. The genotype-specific controls (WT, HET, MUT) ensure reagents were assembled correctly and perform according to the specifications. The 96-well plate is transferred to an appropriately programmed thermal cycler for target amplification and signal generation. In the target amplification phase of the reaction, amplification is carried out using "two-step" cycling conditions (i.e. denaturation & annealing/extension). Following amplification, Taq polymerase is inactivated by a 10 minute incubation at 99°C, after which the thermal cycler proceeds to 63°C to initiate the signal generation (Invader®) phase of the reaction (see Figure 1).

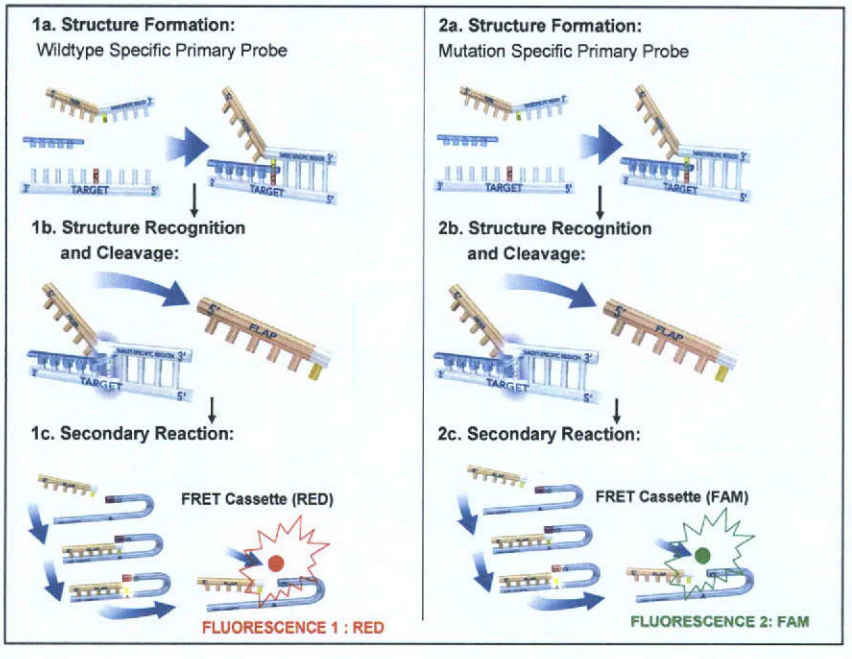

Figure 1. Invader® Signal Generation Phase

During the signal generation phase, a discriminatory Primary Probe transiently hybridizes to the amplified target sequence along with an Invader® oligonucleotide, to form an overlapping structure. The 5'-end of the Primary Probe includes a 5'-flap that does not hybridize to the target DNA. The 3'-nucleotide of the bound Invader® oligonucleotide overlaps the Primary Probe, and does not hybridize to the target DNA. The Cleavase® enzyme recognizes this overlapping structure and cleaves off the unpaired 5'-flap of the Primary Probe, releasing it as a target-specific product. The Primary Probe is designed to have a melting temperature aligned with the Invader® reaction temperature so that under the isothermal reaction conditions (~63°C) the Primary Probes cycle on and off the target DNA. This allows for multiple rounds of Primary Probe cleavage for each DNA target resulting in an accumulation of the number of released 5'-flaps. The released 5'-flap transiently hybridizes with a corresponding FRET cassette forming an overlapping structure that is recognized and the fluorophore is cleaved from the FRET cassette by the Cleavase® enzyme. The 5'-flap is designed to have a melting temperature aligned with the Invader® reaction temperature, so that the 5'-flaps cycle on and off of the corresponding FRET cassettes. This allows for multiple rounds of FRET cassette cleavage for each 5'-flap, and an accumulation of released fluorophore. When the FRET cassette is cleaved, a fluorophore and quencher are separated, generating detectable fluorescence signal. The format uses two different discriminatory Primary Probes, one for the mutant allele and one for the wild type allele (Figure 1). Each Primary Probe is assigned a unique 5'-flap, and distinct FRET cassette, with a spectrally distinct fluorophore. By design, the released 5'-flaps will bind only to their respective FRET cassettes to generate a target-specific signal, linking the wild type allele with one fluorophore (Fluorescence 1: RED) and the mutant allele with the second fluorophore (Fluorescence 2: FAM).

The Invader® Factor II software, in combination with Invader Call Reporter™ software, is a data analysis software package developed by Hologic for use with the Invader® Factor II test. The software package provides a working template for the setup of reaction mixes and sample placement, and following the import of fluorescence data, it determines results and validity for controls and samples. A summary of the Invader Call Reporter™ Invader® Factor II package workflow is shown in Figure 2.

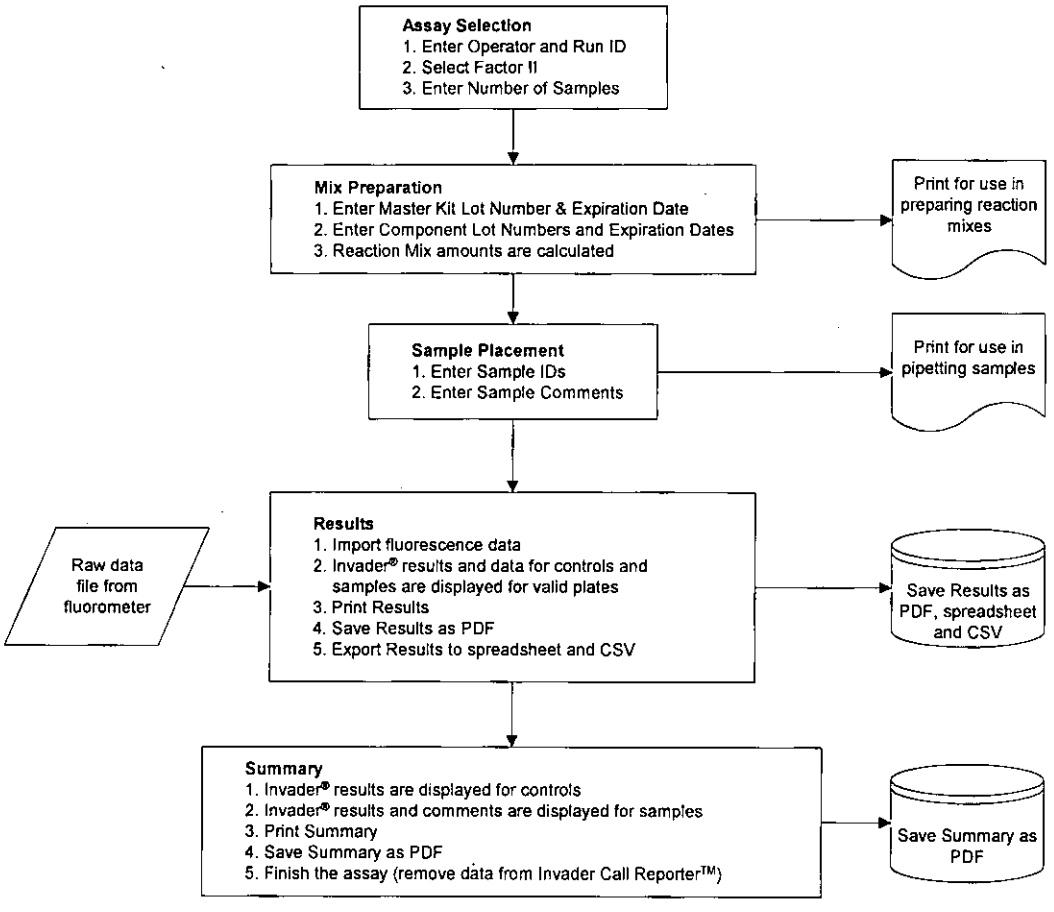

Figure 2. Invader Call Reporter™ Invader® Factor II Package Workflow

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

External Reproducibility (Study #1): Two operators each from three (3) different sites (2 external sites and 1 internal site) performed the testing, in duplicate, over five (5) non-consecutive days for a ten (10) day period using the same testing materials including a panel of nine (9) unique leukocyte depleted whole blood samples spiked cell lines specific for each of the three (3) possible genotypes (i.e. 3 wild type, 3 heterozygous, 3 homozygous mutant).

Table 2: Inter-laboratory Reproducibility of Invader® Factor II Test

Site	Operator	Samples tested	First Pass			Final			Final % Agreement
			Correct Calls	No Calls (Invalid, EQ)	Miscalls	Correct Calls	No Calls (Invalid, EQ)	Miscalls	Final Correct Calls / Samples Tested
Site 001	1	90	90	0	0	90	0	0	100%
	2	90	90	0	0	90	0	0	100%
Site 002	1	90	90	0	0	90	0	0	100%
	2	90	90	0	0	90	0	0	100%
Site 003	1	90	90	0	0	90	0	0	100%
	2	90	54	36*	0	88	2†	0	97.78%*
All	All	540	504	36*	0	538	2†	0	99.63%*

*These "No Call" results were due to an "Invalid Control" result on 2 independent runs. Upon an "Invalid Control" result, the call reporting software automatically prevents the display of all sample genotypes, which resulted in 36 "No Call" samples. Upon retraining of the Operator, and retesting of the 2 runs (see Figure 4), all controls reported "Valid". †From the 36 "No Call" samples, only 2 samples did not provide any genotype result, however upon retesting both samples were found to be in agreement with sequencing.

Lot-to-Lot Reproducibility (Study #9): A total of four (4) genomic DNA samples (three (3) wild type and one (1) heterozygous) were tested in quadruplicate using three (3) different kit lots of the Invader® Factor II test. The percent agreement between Invader® Factor II test and sequencing was 100% (n=48).

Table 3: Lot to Lot Reproducibility

Lot	# Samples Tested	First Pass Correct Calls	First Pass No Calls	Miscalls	Final Correct Calls	Final Agreement %
1	16	16	0	0	16	100
2	16	16	0	0	16	100
3	16	16	0	0	16	100
Total	48	48	0	0	48	100

b. Linearity/assay reportable range:

Refer to paragraph D below.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Real-Time Stability Study (Study #5): Three (3) lots of product in the final configuration are being stored under recommended conditions: (1) -30 to -15°C (Standard Storage of intermediate components) as well as (2) +2° to +8°C (Standard Storage of Genotype-Specific Controls). Functional testing is performed with samples representing all 3 genotypes in quadruplicate at each time point. The interim test results have demonstrated 7 months stability for the device.

Table 4: Factor II Genotype Results; Real-time Stability										
Sample/ Control	Sequencing/ Expected Factor II Genotype	T_0 Result			T_4 Result			T_7 Result		
		Lot 1	Lot 2	Lot 3	Lot 1	Lot 2	Lot 3	Lot 1	Lot 2	Lot 3
Control 1	WT	WT	WT	WT	WT	WT	WT	WT	WT	WT
Control 2	HET	HET	HET	HET	HET	HET	HET	HET	HET	HET
Control 3	MUT	MUT	MUT	MUT	MUT	MUT	MUT	MUT	MUT	MUT
gDNA 1	WT	WT	WT	WT	WT	WT	WT	WT	WT	WT
gDNA 2	WT	WT	WT	WT	WT	WT	WT	WT	WT	WT
gDNA 3	HET	HET	HET	HET	HET	HET	HET	HET	HET	HET
gDNA 4	MUT	MUT	MUT	MUT	MUT	MUT	MUT	MUT	MUT	MUT
Percent Agreement		**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Reagent Freeze-Thaw Stability Study (Study #6): Product in the final configuration was subject to 15 freeze-thaw cycles prior to the final thaw at the time of testing. Functional testing was performed using genomic DNA isolated from cell lines, representing all possible genotypes. The percent agreement between the sequencing result and the Invader® Factor II test were 100%, therefore demonstrating stability for up to fifteen (15) freeze/thaw cycles.

Table 5: Freeze/Thaw Stability of Invader Factor II																	
	Number of Freeze/Thaw Cycles																
Sample	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Total	% Agreement
Control 1 (WT)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	45	100
Control 2 (HET)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	45	100
Control 3 (MUT)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	45	100
gDNA (WT)	6	*	6	*	6	*	*	*	*	6	*	6	*	*	6	36	100
gDNA (HET)	8	*	8	*	8	*	*	*	*	8	*	8	*	*	8	48	100
gDNA (MUT)	6	*	6	*	6	*	*	*	*	6	*	6	*	*	6	36	100
Total	29	9	29	9	29	9	9	9	9	29	9	29	9	9	29	255	100
*Testing with gDNA samples did not occur at this testing point.																	

d. Detection limit/Analytical Sensitivity and Normal Range (Study #3):
Two (2) genomic DNA samples with different genotypes (i.e. WT, HET) were extracted from whole blood collected in potassium EDTA. Each sample was diluted to eight different concentrations 0.5, 5, 20, 40, 80, 200, 400, 800 ng/ µL and tested in replicates of forty (40). The recommend range of the assay was determined to be between 5-80 ng/µL of input gDNA, based on 100% concordance of all tested replicates with bi-directional sequencing.

Table 6: Analytical Sensitivity and Normal Range Percent Agreement Between Replicates		
	Sample ID (Genotype based on Sequencing)	
Input Sample Concentration	**03-4493 (HET)**	**03-4723 (WT)**
0.5 ng/µl	12.5% (5/40)	100% (40/40)
5 ng/µl	100% (40/40)	100% (40/40)
20 ng/µl	100% (40/40)	100% (40/40)
40 ng/µl	100% (40/40)	100% (40/40)
80 ng/µl	100% (40/40)	100% (40/40)
200 ng/µl	100% (40/40)	100% (40/40)
400 ng/µl	100% (40/40)	100% (40/40)
800 ng/µl	100% (40/40)	100% (40/40)

e. *Analytical specificity (Interfering Substances) (Study #4):*
Test performance was not affected by addition of the following substances to four (4) whole blood samples of different genotype (3 WT, 1 HET) prior to extraction:

- Heparin (1500 U/dL human whole blood)
- Cholesterol (300 mg/dL human whole blood)
- Bilirubin (10 mg/dL human whole blood)
- Hemoglobin (up to 0.2% in whole blood)
- Potassium EDTA (K_2EDTA) (1.8 mg/mL human whole blood)
- Ethanol-based Wash Buffer (5% in DNA sample)

Table 7: Summary, Comparison of Invader® Factor II Interfering Substance Results to Sequencing				
Interfering Substance Code	**Substance Concentration / (in blood or DNA sample)**	**% Agreement with Sequencing Genotype**	**% Agreement with Untreated Sample Invader® Factor II Genotype**	**PASS / FAIL**
A	No Addition Control (Untreated)	100% (8 of 8)	N/A	PASS
B	Bilirubin 10mg/dl (blood)	100% (8 of 8)	100% (8 of 8)	PASS
C	Cholesterol 300mg/dl (blood)	100% (8 of 8)	100% (8 of 8)	PASS
D	K_2EDTA 1.8mg/ml (blood)	100% (8 of 8)	100% (8 of 8)	PASS
E	Heparin 1500 U/dl (blood)	100% (8 of 8)	100% (8 of 8)	PASS
F1	Hemoglobin 0.2% (blood)	100% (8 of 8)	100% (8 of 8)	PASS
F2	Hemoglobin 0.1% (blood)	100% (8 of 8)	100% (8 of 8)	PASS
F3	Hemoglobin 0.05% (blood)	100% (8 of 8)	100% (8 of 8)	PASS
F4	Hemoglobin 0.025% (blood)	100% (8 of 8)	100% (8 of 8)	PASS
G	Ethanol-based wash buffer 5% (DNA)	100% (8 of 8)	100% (8 of 8)	PASS

f. *Pre-Analytical Equivalency Study/Genomic DNA Extraction Reproducibility (Study #7):* Thirty (30) human whole blood samples and ten (10) leukocyte depleted whole blood spiked with cell lines were divided and extracted using four (4), commercially available DNA extraction methods (A. Qiagen QIAamp® 96 DNA Blood Kit, B. Qiagen QIAamp® DNA Blood Mini Kit, C. Gentra Generation® Capture Column Kit (Qiagen), D. Roche MagNA Pure LC DNA Isolation Kit I). The 160 extracted DNAs were analyzed in singlicate with one (1) lot of the device. The percent agreement between the Invader® Factor II test for each extraction method and bi-directional sequencing was 100% (n=40).

Table 8: Pre-Analytical Equivalency						
Extraction Method	# Samples Tested	First Pass Correct Calls	First Pass No Calls	Miscalls	Final Correct Calls	Final Agreement %
A	40	40	0	0	40	100
B	40	39	1*	0	39*	100*
C	40	40	0	0	40	100
D	40	40	0	0	40	100
Total	160	159	1	0	159	100
*Sample was removed from study due to loss of traceability of the sample identification.						

g. Instrument Equivalency (Study #8): Twenty-nine (29) human whole blood samples and ten (10) leukocyte depleted whole blood samples spiked with cell

lines were extracted using Qiagen QIAamp® DNA Blood Mini Kit and Roche MagNA Pure LC DNA Isolation Kit I. The extracts were tested with the Invader® Factor II test using three (3) commercially available thermal cyclers (1. ABI GeneAmp® PCR System 9700 with 96-well gold block, 2. ABI Veriti™ and 3. MJ Research PTC-100) and the raw fluorescent data acquired on three (3) commercially available fluorometers (A. Tecan Infinite®, B. Tecan Genios® and C. BioTek®, FLx800). Results from the three (3) fluorometers were transferred into the interpretive software and genotype calls compared to bi-directional sequencing.

Table 9: Concordance by Instrument			
	Thermal Cycler		
Fluorometer	1	2	3
A	78 of 78 = 100%	78 of 78 = 100%	78 of 78 = 100%
B	78 of 78 = 100%	78 of 78 = 100%	78 of 78 = 100%
C	78 of 78 = 100%	78 of 78 = 100%	78 of 78 = 100%

h. Secondary Polymorphism Impact (Study #10): Samples tested included one Factor II (G20210A) homozygous normal sample, one Factor II (G20210A) heterozygous sample and four Factor II (G20210A) homozygous normal samples each with a known secondary polymorphism, A20207C, C20209T, A20218G, or C20221T. Forty replicates for each of the 6 different samples were tested.

Table 10: Invader® Factor II Concordance								
		Expected Results - Factor II (G20210A) Genotype						
		Sample 01	Sample 02	Sample 03	Sample 04	Sample 05	Sample 06	Total
Invader® Results	Normal	40	0	40	40	40	40	200
	HET	0	40	0	0	0	0	40
	MUT	0	0	0	0	0	0	0
	Total	40	40	40	40	40	40	240

2. Comparison studies:
   a. *Method comparison:* Bi-directional Sequencing (Study #2):
      Human whole blood samples (n = 336) underwent DNA extraction and subsequent bi-directional DNA sequence analysis. The same DNA samples were then analyzed using the Invader® Factor II test. The observed agreement between the Invader® Factor II test and bi-directional DNA sequencing was 100% (336/336). The overall agreement with bi-directional sequencing was 100% (336/336).

Table 10: Agreement between the Invader® Factor II Test and Bi-directional DNA Sequencing				
Factor II Genotype*	**Number tested**	**Number of Valid Results on 1st Run**	**Number of Correct genotype calls on First Run**	**Agreement**
Homozygous Wild Type (GG)	305	305	305	100%
Heterozygous (GA)	24	24	24	100%
Homozygous Mutant (AA)	7	7	7	100%
Total	336	336	336	100%
* Genotype determined through bi-directional DNA sequencing				

3. External Reproducibility studies:
   a. *Clinical Sensitivity:* please refer to section 1d above.
   b. *Clinical specificity:* please refer to section 1e above.
4. Expected values/Reference range: (Prevalence)
   Factor II: 1-2%

N. System Descriptions:

1. Modes of Operation:
   Closed System
2. Software:
   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product type. Yes___X____ or No_____
3. Specimen Identification:
   Manual Labeling
4. Specimen Sampling and Handling:
   DNA should be extracted using a validated DNA extraction method that generates DNA concentration range of greater than 5ng/µl.
5. Quality Control:
   Each test contains positive and negative controls to assure proper functioning of the system: Failure of any controls will be indicated as "Invalid" in the test results section of the report. The genotyping test result will not be reported for any sample for which a positive or negative control failure occurs.
   Positive Control: The genotype controls (WT, HET, MUT) ensure reagents were assembled correctly and perform according to the specifications.
   Negative Control: The No DNA Control is used by the interpretive software to set the "noise" component of the run for "signal-to-noise" calculations.
   Hardware and Software Controls:
   The genotyping test result will not be reported for any sample for which a positive or negative control failure occurs.

O. Proposed Labeling:
The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

P. Conclusion:
The submitted information in this 510 (k) notification is complete and supports a substantial equivalence decision.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Hologic Inc.
c/o Mr. Randall J. Covill
Manager, Regulatory Affairs
250 Campus Drive
Marlborough, MA 01752

JUN 0 2 2011

Re: k100943
Trade/Device Name: Invader® Factor II
Regulation Number: 21 CFR §864.7280
Regulation Name: Factor V Leiden DNA Mutation Detection Systems
Regulatory Class: Class II
Product Code: NPR
Dated: May 19, 2011
Received: May 26, 2011

Dear Mr. Covill:

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. 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 class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 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 Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Geeva Philip

for Maria M. Chan, Ph.D
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use Form

510(k) Number (if known): k100943

Device Name: Invader Factor II test

Indications for Use:

The Invader® Factor II test is an in vitro diagnostic test intended for the detection and genotyping of a single point mutation (G to A at position 20210) of the human Factor II gene in isolated genomic DNA obtained from whole blood potassium EDTA samples from patients with suspected thrombophilia.

Prescription Use X AND/ OR Over-The-Counter Use
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Reena Philip

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510K k100943