DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

August 21, 2017

R-Biopharm AG
Patricia Meinhardt
Vice President, Regulatory Affairs
870 Vossbrink Drive
Washington, MO 63090

Re: K171511
Trade/Device Name: RIDA®GENE Norovirus GI/GII
Regulation Number: 21 CFR 866.3990
Regulation Name: Gastrointestinal Microorganism Multiplex Nucleic Acid Based Assay
Regulatory Class: Class II
Product Code: PIQ, OOI
Dated: May 23, 2017
Received: May 24, 2017

Dear Ms. Meinhardt:

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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 Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Steven R. Gitterman -S for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K171511

Device Name
RIDA®GENE Norovirus GI/GII

Indications for Use *(Describe)*

The RIDA®GENE Norovirus GI/GII assay, performed on the Applied Biosystems® 7500 Fast Dx System, is a real-time RT-PCR in vitro diagnostic test for the qualitative detection and differentiation of norovirus genogroup I (GI) and II (GII) RNA from raw or unpreserved stool specimens collected from individuals with signs and symptoms of acute gastroenteritis.

The RIDA®GENE Norovirus GI/GII assay is intended for use as an aid in the differential diagnosis of norovirus genogroup I and II infections in patients symptomatic for gastroenteritis in conjunction with clinical evaluation, laboratory findings, and epidemiological information. The assay aids in the detection and identification of norovirus infections as the cause of acute gastroenteritis in sporadic cases as well as in the context of outbreaks.

Negative results do not preclude a norovirus infection and should not be used as the sole basis for diagnosis.

Type of Use *(Select one or both, as applicable)*

[X] Prescription Use (Part 21 CFR 801 Subpart D) [ ] Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

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510(k) Summary

Submitted by: R-Biopharm AG
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64297 Darmstadt
Germany

Contact: Patricia Meinhardt
R-Biopharm Inc.
870 Vossbrink Drive
Washington, MO 63090
Phone: 877-789-3033

Date of Preparation: August 11, 2017

Device:

Trade name:	RIDA®GENE Norovirus GI/GII
Common name:	RIDA®GENE Norovirus GI/GII assay
Type test:	Real-time RT-PCR intended for the *in vitro* qualitative detection and differentiation of norovirus genogroup I (GI) and II (GII) RNA
Regulation number:	21 CFR 866.3990 - Gastrointestinal microorganism multiplex nucleic acid - based assay
Product code:	PIQ, OOI
Predicate device:	Cepheid Xpert® Norovirus; (K142501)

Device Description

The RIDA®GENE Norovirus GI/GII assay, performed on the Applied Biosystems® 7500 Fast Dx System, is a real-time RT-PCR *in vitro* diagnostic test for the qualitative detection and differentiation of norovirus genogroup I (GI) and II (GII) RNA in human stool specimens. The assay also detects an internal control RNA (ICR, bacteriophage MS2) that is added to each sample prior to extraction. Sample preparation and amplification/real-time detection are completed on separate instruments. Each sample is pre-treated prior to extraction and sample processing is completed on the bioMérieux NucliSENS® easyMAG® instrument with bioMérieux NucliSENS® Nucleic Acid Extraction Reagents according to the manufacturer's instructions. The ICR serves to monitor inhibitors in the extracted specimen; it assures that adequate amplification has taken place and confirms that the nucleic acid extraction was sufficient.

Following processing, either extracted nucleic acids or extracted negative control (NC) or positive control (PC) material is added to the Master-Mix. The assay is performed on an Applied Biosystems® 7500 FAST Dx System. The detection is performed in a one-step real-time RT-PCR format where the reverse transcription is followed by the PCR in the same reaction tube under optimized conditions. The isolated RNA is transcribed into cDNA by a reverse transcriptase. Gene fragments specific for norovirus GI and GII are subsequently amplified by real-time PCR. The amplified targets (ORF1/ORF2 conserved junction region) are detected with hydrolysis (TaqMan®) probes, which are labeled at one end with a quencher and at the other end with a fluorescent reporter dye (fluorophore). In the presence of a target, the probe(s) hybridize to it and during the extension step the Taq-polymerase breaks the reporter-quencher proximity. Upon excitation by the Applied Biosystems® 7500 FAST Dx's halogen light source, the reporter emits a distinct fluorescent signal which is detected by the optical unit of the Applied Biosystems® 7500 FAST Dx System. Hence, depending on the target sequence present (genogroup GI, GII or both), one, two or none of the reporters on the norovirus specific probes emits light to be detected by the instrument. Fluorophores are chosen in a way that their excitation and emission wavelengths do not overlap and signals are readily discriminated by the software. The fluorescence signal increases with the amount of formed amplicons.

Device Intended Use

The RIDA®GENE Norovirus GI/GII assay, performed on the Applied Biosystems® 7500 Fast Dx System, is a real-time RT-PCR *in vitro* diagnostic test for the qualitative detection and differentiation of norovirus genogroup I (GI) and II (GII) RNA from raw or unpreserved stool specimens collected from individuals with signs and symptoms of acute gastroenteritis.

The RIDA®GENE Norovirus GI/GII assay is intended for use as an aid in the differential diagnosis of norovirus genogroup I and II infections in patients symptomatic for gastroenteritis in conjunction with clinical evaluation, laboratory findings, and epidemiological information. The assay aids in the detection and identification of

norovirus infections as the cause of acute gastroenteritis in sporadic cases as well as in the context of outbreaks.
Negative results do not preclude a norovirus infection and should not be used as the sole basis for diagnosis.

Substantial Equivalence

The RIDA®GENE Norovirus GI/GII assay is substantially equivalent to the Xpert® Norovirus. Both are diagnostic tests for the simultaneous qualitative detection and differentiation of norovirus genogroup I and II nucleic acid in human stool specimens. There are no differences in the intended use population, sample material or technological principle of operation between the subject and the predicate device.
A multi-center clinical study was conducted to determine the performance characteristics of the RIDA®GENE Norovirus GI/GII assay. A composite comparator method that consisted of a combination of Center for Disease Control and Prevention (CDC) RT-PCR assays and bi-directional sequencing for norovirus has been used as the reference method. The Xpert® Norovirus used the same composite comparator method in a clinical study to determine its performance characteristics. The study results showed that the RIDA®GENE Norovirus GI/GII assay is acceptable for its intended use and is as safe and effective as the predicate device.
Table 1 shows a comparison of the RIDA®GENE Norovirus GI/GII assay to the predicate device Xpert® Norovirus.

Table 1 Comparison with predicate device

Similarities		
Item	**Device**	**Predicate**
	RIDA®GENE Norovirus GI/GII (K171511)	Xpert® Norovirus (K142501)
Product code	PIQ, OOI	PIQ, OOI
Device class	II	II

Intended use	The RIDA® GENE Norovirus GI/GII assay, performed on the Applied Biosystems® 7500 Fast Dx System, is a real-time RT-PCR *in vitro* diagnostic test for the qualitative detection and differentiation of norovirus genogroup I (GI) and II (GII) RNA from raw or unpreserved stool specimens collected from individuals with signs and symptoms of acute gastroenteritis. The RIDA®GENE Norovirus GI/GII assay is intended for use as an aid in the differential diagnosis of norovirus genogroup I and II infections in patients symptomatic for gastroenteritis in conjunction with clinical evaluation, laboratory findings, and epidemiological information. The assay aids in the detection and identification of norovirus infections as the cause of acute gastroenteritis in sporadic cases as well as in the context of outbreaks. Negative results do not preclude a norovirus infection and should not be used as the sole basis for diagnosis.	The Cepheid Xpert Norovirus Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test for the identification and differentiation of norovirus genogroup I and genogroup II RNA from raw or unpreserved unformed stool specimens collected from individuals with symptoms of acute gastroenteritis. The test utilizes automated real-time reverse transcriptase polymerase chain reaction (RT-PCR) to detect norovirus RNA. The Cepheid Xpert Norovirus Assay is intended to aid in the diagnosis of norovirus infections when used in conjunction with clinical evaluation, laboratory findings, and epidemiological information. The assay also aids in the detection and identification of norovirus infectious in the context of outbreaks.
Specimen	Human stool	Same
Assay principle	Real-time reverse transcriptase polymerase chain reaction (RT-PCR)	Same

Differences		
Item	**Device**	**Predicate**
	RIDA®GENE Norovirus GI/GII (K171511)	Xpert® Norovirus (K142501)
Assay Control(s)	Bacteriophage MS2 as Internal Control RNA (ICR) in each sample. Positive control (PC) and negative controls (NC) processed with each batch of samples.	Sample processing control (SPC) and probe check control (PCC) integrated in assay/instrument system. External controls available but not provided.
Extraction	bioMérieux NucliSENS® easyMAG® instrument	Self-contained and automated in the GeneXpert Cartridge and GeneXpert Instrument Systems. No reagent preparation - all reagents are contained in the cartridge.
Analysis	Applied Biosystems®7500 FAST Dx System	Cepheid GeneXpert Instrument Systems (GeneXpert Dx, GeneXpert Infinity-48 and GeneXpert Infinity-80)

Analytical Performance:

Reproducibility

The reproducibility of the RIDA®GENE Norovirus GI/GII assay was evaluated at 3 laboratory sites. A panel of 5 samples with varying concentrations of Norovirus GI and Norovirus GII that included negative, moderate positive and low positive samples was tested in triplicates two times on each of five different days by two operators at each of the three sites (5 days x 2 times/day x 3 replicates x 3 sites). The same kit lot of RIDA®GENE Norovirus GI/GII assay was used at each of the 3 testing sites. Table 2 summarizes the results calculated over all 3 study sites.

Table 2 Reproducibility of the RIDA®GENE Norovirus GI/GII assay

Sample	Panel Member ID	Channel	n	Mean (Ct)	SD (Ct)	CV (%)
1	Negative	GI	90	0.0	0.0	n/a
2	Norovirus GI low positive	GI	90	31.3	0.8	2.6 %
3	Norovirus GII low positive	GI	90	0.0	0.0	n/a
4	Norovirus GI moderate positive	GI	90	27.9	0.9	3.1 %
5	Norovirus GII moderate positive	GI	90	0.0	0.0	n/a
1	Negative	GII	90	0.0	0.0	n/a
2	Norovirus GI low positive	GII	90	0.0	0.0	n/a
3	Norovirus GII low positive	GII	90	30.7	0.8	2.5 %
4	Norovirus GI moderate positive	GII	90	0.0	0.0	n/a
5	Norovirus GII moderate positive	GII	90	25.0	0.6	2.5 %

SD: Standard deviation, CV: Coefficient of variation

n/a: For negative samples, no coefficient of variation is calculated,

Precision

The precision of the RIDA®GENE Norovirus GI/GII assay was evaluated internally using a panel of 5 samples with varying concentrations of Norovirus GI and Norovirus GII that included negative, moderate positive and low positive samples. Experiments were performed in triplicates over 12 days with two runs per day by two operators at one study site (12 days, x 2 times/day x 3 replicates). Three independent kit lots were used for the precision study. The Inter-lot precision was calculated over those three kit lots. Results are shown in Table 3 and Table 4.

Table 3 Intra-Site Precision of the RIDA®GENE Norovirus GI/GII assay

Sample	Panel Member ID	Channel	n	Intra-Site kit lot 1			Intra-Site kit lot 2			Intra-Site kit lot 3		
				Mean (Ct)	SD (Ct)	CV (%)	Mean (Ct)	SD (Ct)	CV (%)	Mean (Ct)	SD (Ct)	CV (%)
1	Negative	GI	72	0.0	0.0	n/a	0.0	0.0	n/a	0.0	0.0	n/a
2	Norovirus GI low positive	GI	72	31.9	1.5	4.8 %	32.0	1.4	4.4 %	32.1	1.5	4.6 %
3	Norovirus GII low positive	GI	72	0.0	0.0	n/a	0.0	0.0	n/a	0.0	0.0	n/a
4	Norovirus GI moderate positive	GI	72	24.5*	0.5	2.1 %	24.8	0.5	1.9 %	24.7	0.5	2.0 %
5	Norovirus GII moderate positive	GI	72	0.0	0.0	n/a	0.0	0.0	n/a	0.0	0.0	n/a
1	Negative	GII	72	0.0	0.0	n/a	0.0	0.0	n/a	0.0	0.0	n/a
2	Norovirus GI low positive	GII	72	0.0	0.0	n/a	0.0	0.0	n/a	0.0	0.0	n/a
3	Norovirus GII low positive	GII	72	31.0*	1.9	6.1 %	31.3	1.2	3.9 %	31.3	0.9	2.8 %
4	Norovirus GI moderate positive	GII	72	0.0	0.0	n/a	0.0	0.0	n/a	0.0	0.0	n/a
5	Norovirus GII moderate positive	GII	72	23.2	0.5	2.1 %	23.3	0.6	2.4 %	23.3	0.6	2.6 %

SD: Standard deviation, CV: Coefficient of variation

n/a: For negative samples no coefficient of variation is calculated.

*1 replicate is undetermined because of a pipetting error; replicate was retested.

Table 4 Inter-Lot Precision of the RIDA®GENE Norovirus GI/GII assay

Sample	Panel Member ID	Channel	n	Inter-Lot		
				Mean (Ct)	SD (Ct)	CV (%)
1	Negative	GI	216	0.0	0.0	n/a
2	Norovirus GI low positive	GI	216	32.0	1.5	4.6 %
3	Norovirus GII low positive	GI	216	0.0	0.0	n/a
4	Norovirus GI moderate positive	GI	216	24.7*	0.5	2.0 %
5	Norovirus GII moderate positive	GI	216	0.0	0.0	n/a
1	Negative	GII	216	0.0	0.0	n/a
2	Norovirus GI low positive	GII	216	0.0	0.0	n/a
3	Norovirus GII low positive	GII	216	31.2*	1.4	4.5 %
4	Norovirus GI moderate positive	GII	216	0.0	0.0	n/a
5	Norovirus GII moderate positive	GII	216	23.3	0.6	2.4 %

SD: Standard deviation, CV: Coefficient of variation

n/a: For negative samples no coefficient of variation is calculated.

*1 replicate is undetermined because of a pipetting error; replicate was retested.

Analytical sensitivity (Limit of Detection)

The limit of detection (LoD) was performed to evaluate the analytical sensitivity of RIDA®GENE Norovirus GI/GII using a dilution series of two native fecal samples, one genogroup I and one genogroup II into a negative stool matrix.

The genogroup of the two native samples was determined by conventional RT-PCR followed by bi-directional sequencing. Norovirus RNA copy numbers in the dilution series of fecal samples were determined by using two standard curves containing either GI or GII transcripts quantified by real-time RT-PCR. Measurements for the standard curve were performed in duplicate. LoD samples were tested by RIDA®GENE Norovirus GI/GII applying the quantified standard curve described above.

The preliminary limit of detection of the RIDA®GENE Norovirus GI/GII was established based on the RNA copy number that gave a minimum of 2 out of 3 positive test results. The LoD was further verified by testing 20 replicates at the concentration determined in the preliminary studies. It was confirmed if all of those replicates yielded positive results. The RNA copy numbers per gram stool represent the mean values of the dilution series' triplicates for each dilution.

The Limits of Detection of the RIDA®GENE Norovirus GI/GII for the two genotypes are presented in Table 5.

Table 5 Limit of detection of the RIDA®GENE Norovirus GI/GII assay

	Limit of detection
Norovirus GI (GI.3B)	6.5x 10^5 RNA copies/g stool
Norovirus GII (GII.4)	2.5x 10^5 RNA copies/g stool

Cross reactivity

The analytical specificity of the RIDA®GENE Norovirus GI/GII assay was evaluated by testing a panel of 69 organisms, consisting of 56 bacteria, 1 fungus, 8 viruses, and 4 parasites representing common gastroenteritis pathogens or those potentially encountered in stool.

The analytical specificity study included testing of bacterial cultures at 10^6 to 10^9 cfu/ml, parasite and fungi cultures at 10^7 to 10^9 cfu/ml, and viral cell culture supernatants at 10^5 to 10^9 pfu/ml in the stool specimens.

The samples were extracted using the NucliSENS® easyMAG® System and tested on the Applied Biosystems® 7500 Fast Dx platform. The analytical specificity of the RIDA®GENE Norovirus GI/GII assay was 100 %. Results are shown in Table 6.

Table 6 Analytical Specificity of the RIDA®GENE Norovirus GI/GII assay

Organism	**Norovirus GI**	**Norovirus GII**	**Organism**	**Norovirus GI**	**Norovirus GII**
Acinetobacter Iwoffi	Negative	Negative	*Helicobacter pylori*	Negative	Negative
Adenovirus type 40	Negative	Negative	*Lactococcus lactis*	Negative	Negative
Adenovirus type 41	Negative	Negative	*Listeria monocytogenes*	Negative	Negative
Aeromonas caviae	Negative	Negative	*Morganella morganii*	Negative	Negative
Aeromonas hydrophila	Negative	Negative	*Pleisomonas shigelloides*	Negative	Negative
Astrovirus type 1	Negative	Negative	*Proteus mirabilis*	Negative	Negative

Astrovirus type 4	Negative	Negative
Bacillus cereus	Negative	Negative
Blastocystis hominis	Negative	Negative
Campylobacter coli	Negative	Negative
Campylobacter jejuni	Negative	Negative
Candida albicans	Negative	Negative
Citrobacter freundii	Negative	Negative
Clostridium difficile	Negative	Negative
Clostridium sordellii	Negative	Negative
Cryptosporidium parvum	Negative	Negative
Entamoeba histolytica	Negative	Negative
Enterobacter cloacae	Negative	Negative
Enterococcus faecalis	Negative	Negative
Enterococcus faecium	Negative	Negative
Enterovirus	Negative	Negative
Escherichia coli (O157:H7; EHEC)	Negative	Negative
Escherichia coli (O157; vtx1, vtx2, eae)	Negative	Negative
Escherichia coli (O26:H-; EPEC)	Negative	Negative
Escherichia coli (O26:H11; vtx2, eae)	Negative	Negative
Escherichia coli (O8; vtx1)	Negative	Negative
Escherichia coli O103	Negative	Negative
Escherichia coli O111	Negative	Negative
Escherichia coli O121	Negative	Negative
Escherichia coli O145	Negative	Negative
Escherichia coli O45	Negative	Negative
Escherichia hermannii	Negative	Negative
Giardia lamblia	Negative	Negative

Proteus vulgaris	Negative	Negative
Providencia stuartii	Negative	Negative
Pseudomonas aeruginosa	Negative	Negative
Pseudomonas fluorescens	Negative	Negative
Pseudomonas putida	Negative	Negative
Rotavirus G1	Negative	Negative
Rotavirus G2	Negative	Negative
Rotavirus G3	Negative	Negative
Rotavirus G4	Negative	Negative
Rotavirus G9	Negative	Negative
Salmonella agona	Negative	Negative
Salmonella bongori	Negative	Negative
Salmonella enteritidis	Negative	Negative
Sapovirus GI.1	Negative	Negative
Sapovirus GIV	Negative	Negative
Sapovirus GV	Negative	Negative
Serratia liquefaciens	Negative	Negative
Shigella flexneri	Negative	Negative
Shigella sonnei	Negative	Negative
Staphylococcus aureus	Negative	Negative
Steptococcus agalactiae	Negative	Negative
Steptococcus dysgalactiae	Negative	Negative
Vibrio cholerae	Negative	Negative
Vibrio parahaemolyticus	Negative	Negative
Viridans streptococci	Negative	Negative
Yersinia enterocolitica	Negative	Negative

Analytical reactivity

The analytical reactivity of the RIDA®GENE Norovirus GI/GII assay was evaluated using twenty-four genotypes representing both norovirus genogroups (GI and GII). All strains evaluated in this study were tested at low (near LoD) and at high concentration. Each norovirus genotype was extracted using the NucliSENS® easyMAG® System and tested in triplicate on the Applied Biosystems® 7500 Fast Dx platform. As shown in Table 7, all norovirus genotypes were detected at both concentration levels by the RIDA®GENE Norovirus GI/GII assay.

Table 7 Analytical Reactivity of the RIDA®GENE Norovirus GI/GII assay

Subgroup	Norovirus GI	Norovirus GII
GI.1	Positive	Negative
GI.2	Positive	Negative
GI.3	Positive	Negative
GI.4	Positive	Negative
GI.5	Positive	Negative
GI.6	Positive	Negative
GI.7	Positive	Negative
GI.8	Positive	Negative

Subgroup	Norovirus GI	Norovirus GII
GII.1	Negative	Positive
GII.2	Negative	Positive
GII.3	Negative	Positive
GII.4 Sydney	Negative	Positive
GII.4 New Orleans	Negative	Positive
GII.6	Negative	Positive
GII.7	Negative	Positive
GII.8	Negative	Positive
GII.9	Negative	Positive
GII.10	Negative	Positive
GII.12	Negative	Positive
GII.13	Negative	Positive
GII.14	Negative	Positive
GII.15	Negative	Positive
GII.16	Negative	Positive
GII.17	Negative	Positive

Interfering substances

To identify interfering substances that could affect the performance of the RIDA®GENE Norovirus GI/GII assay, an interference screen was performed. Therefore, potential interfering substances were added with appropriate concentrations (simulating either 1x or 3x the daily dose or "worst case" scenarios as appropriate) to 9 fecal samples containing the analyte (3 low positive GI, 3 low positive GII and 3 negative) For each sample, a common batch was prepared and subsequently aliquoted into 12 portions (11substances + 1 reference measurement). To each aliquot, one substance was added at the concentration stated in Table 5. To detect possible interference, the samples with and without added potential interfering substances were extracted in triplicates (each sample was extracted three times for every substance), tested and the results were compared to each other. There was no interference observed with the 11 potentially interfering substances tested (Table 8).

Table 8 Potentially interfering substances and tested final concentrations

Substance	Concentration
Acetaminophen (analgesic)	6.0 % (w/w)
Amoxicillin (antibiotic)	4.5 % (w/w)
Aspartame (artificial sweetener)	4.8 % (w/w)
Barium sulfate (radiocontrast agent	18.5 % (w/w)
Human blood (maybe found in patient stool)	5.0 % (v/w)
Ibuprofen (analgesic)	3.6 % (w/w)
Loperamide (anti-diarrhea drug)	0.02 % (w/w)
Metronidazole (antibiotic)	3.0 % (w/w)
Mucin (mucilage)	5.0 % (w/w)
Pepto-Bismol (anti-diarrheal drug)	6.3 % (v/w)
Stearic acid / Palmitic acid (1:1) (fatty acids)	40.0 % (w/w)

Carry-over and Cross-contamination study

To evaluate the carry-over and cross-contamination with the RIDA®GENE Norovirus GI/GII assay in association with the NucliSENS® easyMAG® System and PCR on the Applied Biosystems® 7500 Fast Dx platform, an internal carry-over study was performed. In this study, one high positive GII sample (Ct value between 10 and 20) was measured 47 times alternating with a negative sample measured 47 times on the same plate. This setup was repeated for a total of 5 runs (negative adjacent positive). The data showed no carry-over or cross contamination.

Clinical Performance

Performance characteristics of the RIDA®GENE Norovirus GI/GII assay were established during a prospective, multi-center study conducted at four institutions in the U.S. from February 2014 to April 2015. A total of 769 specimens were collected at the four different study sites. Of the 769 samples collected, 50 samples could not be used for study analysis.

In addition, 332 samples, prospectively collected during various previous outbreaks at two institutions, were tested from September 2016 to April 2017. Of the 332 samples, 300 samples provided valid results.

A total of 1019 study specimens consisted of raw or unpreserved stool specimens from subjects with symptoms of acute gastroenteritis. The RIDA®GENE Norovirus GI/GII assay performance was compared to a composite reference method performed at the CDC (Atlanta, GA). Specifically, specimens were tested by conventional RT-PCR followed by bi-directional sequencing for both, Region C and Region D of norovirus.

The RIDA®GENE Norovirus GI/GII assay demonstrated 91.8 % PPA and 99.1 % NPA for detection of Norovirus GI, relative to the composite reference method (Table 9). The RIDA®GENE Norovirus GI/GII assay demonstrated 94.7 % PPA and 98.0 % NPA for detection of Norovirus GII (Table 0).

Table 9 Norovirus Genogroup I vs. Composite Reference Method

	Composite Reference Method		
RIDA®GENE Norovirus GI/GII	Positive	Negative	Total
Positive	56	9	65
Negative	5	949	954
Total	61	958	1019

Positive Percent Agreement (95 % CI)	91.8 % (56/61); (81.9 % – 97.3 %)
Negative Percent Agreement (95 % CI)	99.1 % (949/958); (98.2% – 99.6 %)

Table 10 Norovirus Genogroup II vs. Composite Reference Method

	Composite Reference Method		
RIDA®GENE Norovirus GI/GII	Positive	Negative	Total
Positive	213	16	229
Negative	12	778	790
Total	225	794	1019

Positive Percent Agreement (95 % CI)	94.7 % (213/225); (90.9 % – 97.2 %)
Negative Percent Agreement (95 % CI)	98.0 % (778/794); (96.7 % – 98.8 %)

Conclusion

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the RIDA®GENE Norovirus GI/GII is substantially equivalent to the predicate device.