GeneXpert®
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Xpert® Norovirus

REF **GXNOV-10**

Cepheid®

In Vitro Diagnostic Medical Device

IVD

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Xpert® Norovirus

For In Vitro Diagnostic Use Only.

℞only

1 Proprietary Name

Xpert® Norovirus

2 Common or Usual Name

Xpert Norovirus Assay

3 Intended Use

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 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 infections in the context of outbreaks.

4 Summary and Explanation

Noroviruses are single stranded RNA, non-enveloped viruses in the genus *Norovirus*, family *Caliciviridae*, which cause acute gastroenteritis in humans and other mammals. The prototype norovirus was first identified as the cause of a gastroenteritis outbreak in Norwalk, Ohio in 1968.[1] It is estimated that norovirus may be the causative agent in over 23 million gastroenteritis cases every year in the United States, representing approximately 60% of all acute gastroenteritis cases.[2] Noroviruses can be classified into five different genogroups of which genogroup I (GI) and genogroup II (GII) cause the majority of the infections in humans.

Noroviruses are a major world-wide cause of gastroenteritis. They affect all ages, and are frequently involved in outbreaks in communal facilities, such as nursing homes, hospitals, day nurseries, prisons, and cruise ships.[3–6] Symptoms of norovirus infection are usually diarrhea, vomiting, stomach cramps, nausea, and fever. The disease is normally self-limiting and signs and symptoms may last for several days. In the young, elderly, and immunocompromised, the disease may be life threatening due to dehydration. Common names associated with norovirus gastroenteritis are winter vomiting disease, stomach flu, acute non-bacterial gastroenteritis, and viral gastroenteritis. Norovirus can only be cultured in very specialized cell culture systems.[7] Electron microscopy can be used to directly visualize norovirus in fecal specimens but has poor sensitivity.[8]

Commercially available Enzyme Immunoassays (EIAs) have proven useful during norovirus outbreak situations. However, due to low assay sensitivity, commercially available EIAs are useful only when prevalence of norovirus infection is high. In addition, current CDC guidelines recommend all negative EIA results be confirmed by molecular methods.[8] The currently available EIAs are known to have low sensitivity (36–80%) compared to RT-PCR methods and low to good specificity (47–100%) depending on the testing environment.[9–15] In Europe and Japan, where commercially available molecular assays exist, the assays require highly trained molecular technologists and, by design, force testing to be performed in a batched mode, resulting in reporting delays. Under current CDC guidelines, it is recommended that healthcare providers consider the development and adoption of facility policies to enable clinical and virological confirmation of suspected cases of symptomatic norovirus infection while implementing prompt control measures to reduce the magnitude of a potential norovirus outbreak.[16] The Xpert Norovirus Assay provides an on-demand, fast, accurate molecular test to facilitate confirmation and initiate prompt norovirus control measures, irrespective of prevalence rate.

5 Principle of the Procedure

The test is automated and utilizes real-time reverse transcriptase polymerase chain reaction (RT-PCR) to detect specific viral gene sequences associated with norovirus genogroup I and genogroup II. The stool specimens are collected from individuals with symptoms of acute gastroenteritis and transported to the laboratory in a clean container. A swab is inserted into the stool specimen and then placed in a tube containing sample reagent. Following brief vortexing, the eluted sample is transferred into the sample chamber of the disposable fluidic cartridge (the GeneXpert cartridge). The GeneXpert cartridge is loaded onto the GeneXpert Instrument System platform, which performs hands-off automated sample processing and real-time RT-PCR for identification and differentiation of norovirus genogroup I and genogroup II.

The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequences in simple or complex samples using reverse transcriptase PCR (RT-PCR) and real-time PCR assays. The systems consist of an instrument, personal computer, and preloaded software for running the tests and viewing the results. The systems require the use of single-use disposable GeneXpert cartridges that hold the RT-PCR and PCR reagents and also host the RT-PCR and PCR processes. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, see the appropriate *GeneXpert Dx Operator Manual* or *GeneXpert Infinity System Operator Manual*.

The Xpert Norovirus Assay includes reagents for the detection of nucleic acid sequences for norovirus genogroup I and genogroup II from raw or unpreserved unformed stool specimens collected from individuals with symptoms of acute gastroenteritis. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate processing of the target viruses and to monitor for the presence of inhibitors in the PCR reaction. The PCC verifies dry reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

6 Reagents and Instruments

6.1 Materials Provided

The Xpert Norovirus Assay kit contains sufficient reagents to process 10 specimens or quality control samples. The kit contains the following:

Xpert Norovirus Assay Cartridges with Integrated Reaction Tubes	**10**
• Bead 1, Bead 2, and Bead 3 (freeze-dried)	1 of each per cartridge
• Elution Reagent	1.5 mL per cartridge
• Rinse Reagent	1.0 mL per cartridge
• Binding Reagent (Guanidinium thiocyanate)	2.7 mL per cartridge
Sample Reagent (Guanidinium thiocyanate)	**10 x 2.0 mL per bottle**
CD	**1 per kit**
• Assay Definition File (ADF)	
• Instructions to import ADF into software	
• Instructions for Use (Package Insert)	

Note Safety Data Sheets (SDS) are available at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab.

Note The bovine serum albumin (BSA) in the beads within this product was produced and manufactured exclusively from bovine plasma sourced in the United States. No ruminant protein or other animal protein was fed to the animals; the animals passed ante- and postmortem testing. During processing, there was no mixing of the material with other animal materials.

7 Storage and Handling

- Store the Xpert Norovirus Assay cartridges and reagents at 2 °C - 8°C.
- Do not use reagents or cartridges that have passed the expiration date.
- Do not open the cartridge lid until you are ready to perform testing.
- Use the cartridge within 30 minutes after opening the lid.

8 Materials Required but Not Provided

- GeneXpert Dx System or the GeneXpert Infinity System (catalog number varies by configuration): GeneXpert instrument, computer with proprietary GeneXpert Software version 4.3 or higher, hand-held barcode scanner, and operator manual.
- Printer: Contact Cepheid Sales Representative to arrange for the purchase of a recommended printer.
- Vortex mixer
- Disposable transfer pipettes
- Single-use disposable dry rayon tipped swab (SDPS-120) or equivalent rayon swab for transfer of the stool specimen from the specimen container into the Sample Reagent bottle
- Clean preservative-free specimen container

9 Materials Available but Not Provided

- ZeptoMetrix NATtrol™ Rotavirus Stock (catalog # NATROTA-6MC) as external negative control.
- ZeptoMetrix NATtrol™ Norovirus GI Stock and NATtrol™ Norovirus GII Stock (catalog # NATNOVI-6MC and NATNOVII-6MC) as external positive controls.

10 Warnings and Precautions

10.1 General

- For *In Vitro* Diagnostic Use Only.
- For prescription use only.
- Treat all biological specimens, including used cartridges and reagents, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated using standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention[17] and the Clinical and Laboratory Standards Institute.[18]
- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures. If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines. Consult your institution's environmental waste personnel on proper disposal of used cartridges and unused reagents.

10.2 Specimen

- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 12, Specimen Collection, Transport, and Storage). Specimen stability, under shipping conditions other than those recommended, has not been evaluated.
- Proper sample collection, storage, and transport are essential for correct results.

10.3 Assay/Reagent

- Do not substitute Xpert Norovirus Assay reagents with other reagents.
- Do not open the Xpert Norovirus Assay cartridge lid until you are ready to add a sample.
- Do not use a cartridge that has been dropped after removing from the kit or shaken after the cartridge lid has been opened. Shaking or dropping the cartridge after opening the lid may yield false or non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.
- The Sample Reagent is a clear, colorless liquid. Do not use the Sample Reagent if it is cloudy or discolored.
- Do not use a cartridge that has a damaged reaction tube.
- Each single-use Xpert Norovirus Assay cartridge is used to process one test. Do not reuse spent cartridges.
- Good laboratory practices should be followed and gloves should be changed between handling each patient specimen in order to avoid contamination of specimens or reagents. Regularly clean the work surface/areas with 10% bleach then wipe the surface again with 70% ethanol or isopropyl alcohol before and after processing Xpert Norovirus specimens.
- Specimens may contain high levels of organisms. Ensure that specimen containers do not contact one another. Change gloves if they come in direct contact with the specimen and after the processing of each specimen to avoid contaminating other specimens.

11 Chemical Hazards[19,20]

- UN GHS Hazard Pictogram 
- Signal Word: WARNING
- **UN GHS Hazard Statements:**
  - Harmful if swallowed.
  - Causes mild skin irritation.
  - Causes eye irritation.
- **UN GHS Precautionary Statements:**
  - **Prevention**
    - Wash thoroughly after handling.
  - **Response**
    - Call a POISON CENTER or doctor/physician if you feel unwell.
    - If skin irritation occurs: Get medical advice/attention.
    - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
    - If eye irritation persists: Get medical advice/attention.

12 Specimen Collection, Transport, and Storage

1. Collect the raw or unpreserved unformed stool specimen in a clean preservative-free container. Follow your institution's guidelines for collecting samples for norovirus testing.
2. Label the stool specimen container with Patient's Name and Sample ID and send to the laboratory.
3. Store specimen at 2–8 ºC. The specimen is stable for up to two days when stored at 2–8 ºC.

13 Procedure

13.1 Preparing the Cartridge

Important **Start the test within 30 minutes of adding the sample reagent to the cartridge.**

To add the sample to the cartridge:

1. Remove the cartridge and Sample Reagent bottle from the kit.
2. Dip a swab in the raw or unpreserved unformed stool sample. See Figure 1 for the correct amount of specimen to be used for the Xpert Norovirus Assay.

Note Wrap sterile gauze around both the stem of the swab and the mouth of the bottle to minimize the risk of contamination. Do not coat the entire swab fiber tip with stool. See Figure 1. Too much stool may result in errors or invalid results.

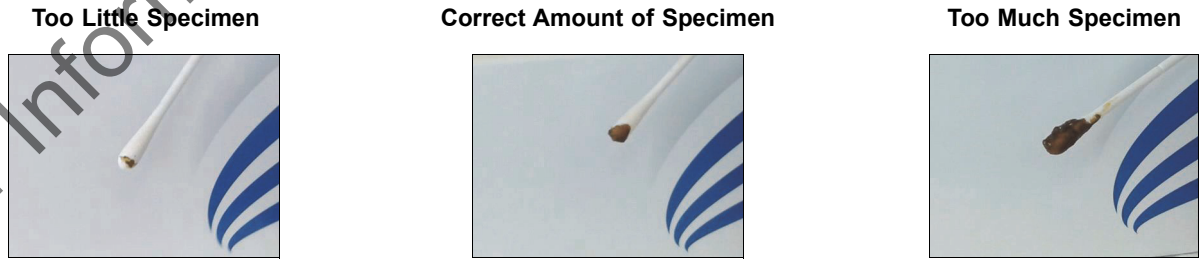

Figure 1. Sample Collection on Swab

3. After removing the cap from the Sample Reagent bottle, insert the swab with stool sample into the bottle containing the Sample Reagent.

4. Hold the swab by the stem near the rim of the bottle. Lift the swab a few millimeters from the bottom of the bottle and bend the stem over the edge of the bottle to break it off, leaving the swab short enough to allow the swab to fit into the bottle and the cap to close tightly.
5. Close the cap of the Sample Reagent bottle and vortex at high speed for ten seconds.
6. Open the cartridge lid. Using a clean transfer pipette (not supplied), transfer the entire contents of the Sample Reagent bottle to the Sample Chamber of the Xpert Norovirus Assay cartridge. See Figure 2.
7. Close the cartridge lid and start the test within 30 minutes.

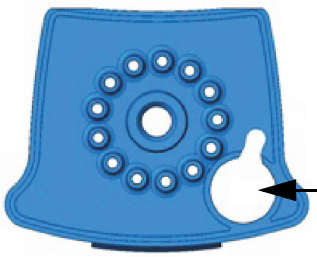

Figure 2. Xpert Norovirus Assay Cartridge (Top View)

13.2 Starting the Test

Important **Before you start the test, make sure the assay definition file for the Xpert Norovirus Assay is imported into the software. This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*, depending on the model that is being used.**

Note The steps you follow can be different if the system administrator changed the default workflow of the system.

1. Turn on the GeneXpert instrument:
   - If using the GeneXpert Dx instrument, first turn on the instrument and then turn on the computer. The GeneXpert software will launch automatically or may require double-clicking the GeneXpert Dx software icon on the Windows® desktop.

     or

   - If using the GeneXpert Infinity instrument, power up the instrument. The GeneXpert software will launch automatically or may require double-clicking the Xpertise software icon on the Windows® desktop.
2. Log on to the GeneXpert Instrument System software using your user name and password.
3. In the GeneXpert System window, click **Create Test** (GeneXpert Dx) or click **Orders** and **Order Test** (GeneXpert Infinity). The Create Test window opens.
4. Scan (or type in) the Patient ID (optional). If typing the Patient ID, make sure the Patient ID is typed correctly. The Patient ID is shown on the left side of the View Results window and is associated with the test results.
5. Scan (or type in) the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly. The Sample ID is shown on the left side of the View Results window and is associated with the test results.
6. Scan the barcode on the Xpert Norovirus Assay cartridge. Using the barcode information, the software automatically fills in the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.

Note If the barcode on the Xpert Norovirus Assay cartridge does not scan, then repeat the test with a new cartridge following the procedure in the Retest Procedure section.

7. Click **Start Test** (GeneXpert Dx) or **Submit** (GeneXpert Infinity). Type your password in the dialog box that appears.

8. For the GeneXpert Infinity System, place the cartridge on the conveyor belt. The cartridge will be automatically loaded, the test will run, and the used cartridge will be placed into the waste container.

   or

   For the GeneXpert Dx Instrument:

   A. Open the instrument module door with the blinking green light and load the cartridge.

   B. Close the door. The test starts and the green light stops blinking. When the test is finished, the light turns off.

   C. Wait until the system releases the door lock before opening the module door and removing the cartridge.

   D. The used cartridges should be disposed in the appropriate specimen waste containers according to your institution's standard practices.

14 Viewing and Printing Results

This section lists the basic steps for viewing and printing results. For more detailed instructions on how to view and print the results, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

1. Click the **View Results** icon to view results.
2. Upon completion of the test, click the **Report** button of the View Results window to view and/or generate a PDF report file.

15 Quality Control

15.1 Built-in Quality Controls

CONTROL

Each test includes a Sample Processing Control (SPC) and a Probe Check Control (PCC).

- **Sample Processing Control (SPC)**: Ensures the sample was processed correctly. The SPC contains Armored RNA® that is included in each cartridge to verify adequate processing of the sample. The SPC verifies that release of RNA from virus has occurred if the organism is present and verifies that the specimen processing is adequate. Additionally, this control detects specimen-associated inhibition of the RT-PCR and PCR reactions. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. The SPC passes if it meets the validated acceptance criteria.
- **Probe Check Control (PCC)**: Before the start of the PCR reaction, the GeneXpert Dx System or the GeneXpert Infinity System measures the fluorescence signal from the probes (SPC, QC1, and QC2, one for each of the two reagent beads) to monitor bead rehydration, reaction tube filling, probe integrity, and dye stability. Probe Check passes if it meets the assigned acceptance criteria.

15.2 External Controls

- **External Controls**: ZeptoMetrix NATtrol Rotavirus Stock (catalog # NATROTA-6MC) as external negative control and ZeptoMetrix NATtrol Norovirus GI Stock and NATtrol Norovirus GII Stock (catalog # NATNOVI-6MC and NATNOVII-6MC) as external positive controls may be used in accordance with local, state, and federal accrediting organizations, as applicable.

16 Interpretation of Results

The results are interpreted by the GeneXpert Instrument Systems from measured fluorescent signals and embedded calculation algorithms and will be shown in the View Results window. Possible results are shown in Table 1.

Table 1. Xpert Norovirus Assay Results and Interpretation

Result	Interpretation
NORO GI DETECTED, NORO GII NOT DETECTED See Figure 3.	Norovirus genogroup I (GI) RNA sequence is detected. • Norovirus genogroup I (GI) target RNA sequence has a Ct within the valid range and endpoint above the threshold setting. • SPC – NA (not applicable); SPC is ignored since norovirus target amplification may compete with this control. • PCC – PASS; all probe check results pass.

Table 1. Xpert Norovirus Assay Results and Interpretation (Continued)

Result	Interpretation
NORO GI NOT DETECTED, NORO GII DETECTED See Figure 4.	Norovirus genogroup II (GII) RNA sequence is detected. • Norovirus genogroup II (GII) target RNA sequence has a Ct within the valid range and endpoint above the threshold setting. • SPC – NA (not applicable); SPC is ignored since norovirus target amplification may compete with this control. • PCC – PASS; all probe check results pass.
NORO GI DETECTED, NORO GII DETECTED See Figure 5.	Norovirus genogroup I (GI) RNA sequence is detected and Norovirus genogroup II (GII) RNA sequence is detected. • Norovirus genogroup I (GI) target RNA sequence has a Ct within the valid range and endpoint above the threshold setting. • Norovirus genogroup II (GII) target RNA sequence has a Ct within the valid range and endpoint above the threshold setting. • SPC – NA (not applicable); SPC is ignored since norovirus target amplification may compete with this control. • PCC – PASS; all probe check results pass.
NORO GI NOT DETECTED, NORO GII NOT DETECTED See Figure 6.	Norovirus target RNA sequences are not detected. • Norovirus target RNA sequences are not detected. • SPC – PASS; SPC has a Ct within the valid range and endpoint above the endpoint threshold setting. • PCC – PASS; all probe check results pass.
INVALID See Figure 7.	Presence or absence of norovirus target RNA sequences cannot be determined. Repeat test according to the instructions in Section 17.2, Retest Procedure. • Norovirus GI – INVALID • Norovirus GII – INVALID • SPC – FAIL; SPC Ct is not within valid range and endpoint below threshold setting. • PCC – PASS; all probe check results pass.
ERROR	Presence or absence of norovirus target RNA sequences cannot be determined. Repeat test according to the instructions in Section 17.2, Retest Procedure. • Norovirus GI – ERROR • Norovirus GII – ERROR • PCC – FAIL*; one or more of the probe check results failed. * If the probe check passed, the error is caused by the maximum pressure limit exceeding the acceptable range.
NO RESULT	Presence or absence of norovirus target RNA sequences cannot be determined. Repeat test according to the instructions in Section 17.2, Retest Procedure. A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress or a power failure occurred. • Norovirus GI – NO RESULT • Norovirus GII – NO RESULT • PCC – NA (not applicable).

Figure 3. Norovirus GI Detected; Norovirus GII Not Detected

Figure 4. Norovirus GI Not Detected; Norovirus GII Detected

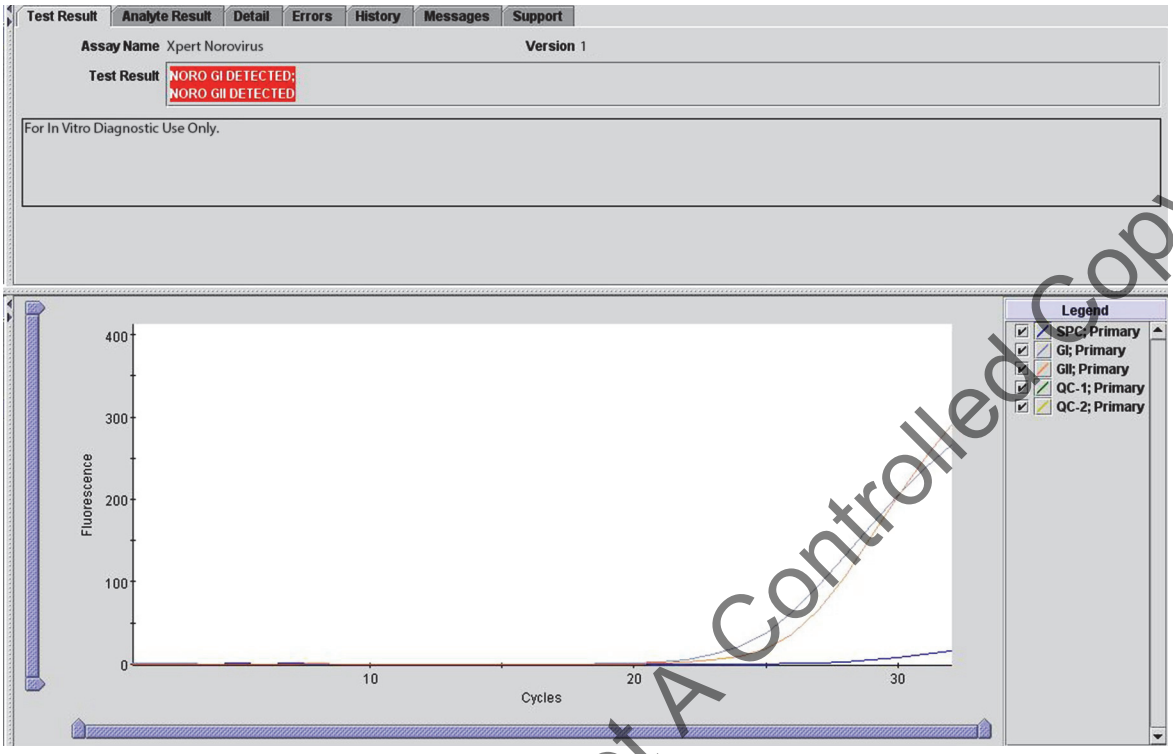

Figure 5. Norovirus GI Detected; Norovirus GII Detected

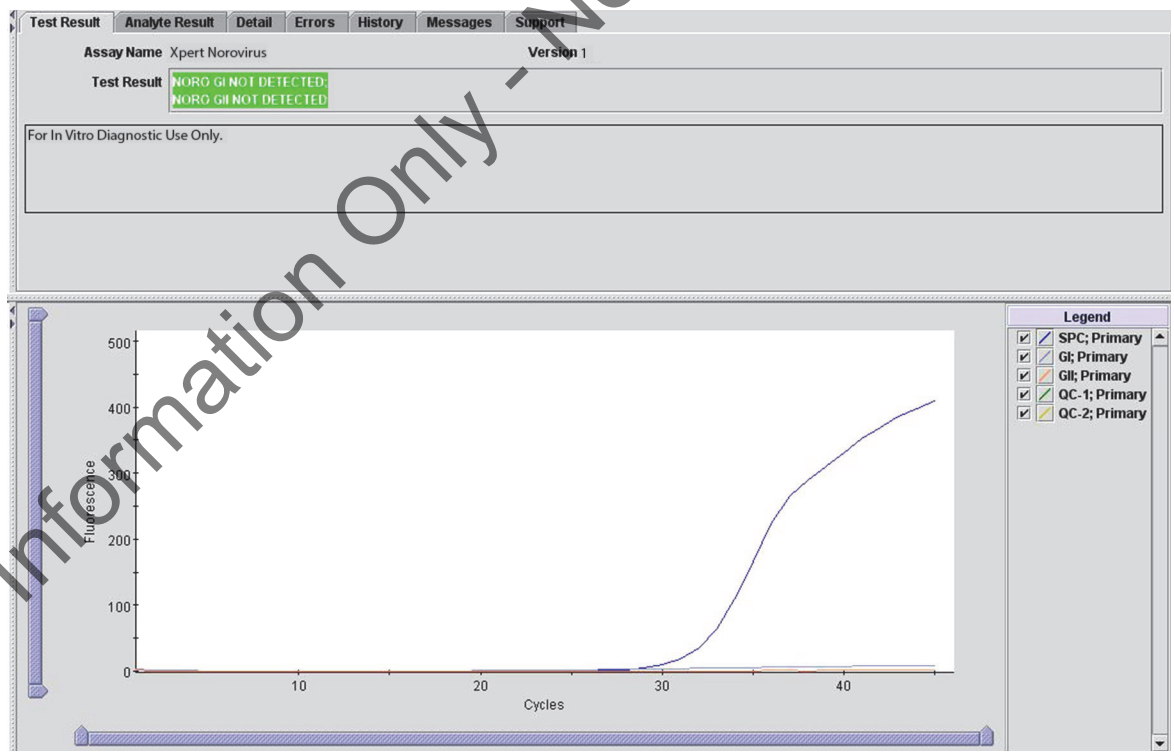

Figure 6. Norovirus GI Not Detected; Norovirus GII Not Detected

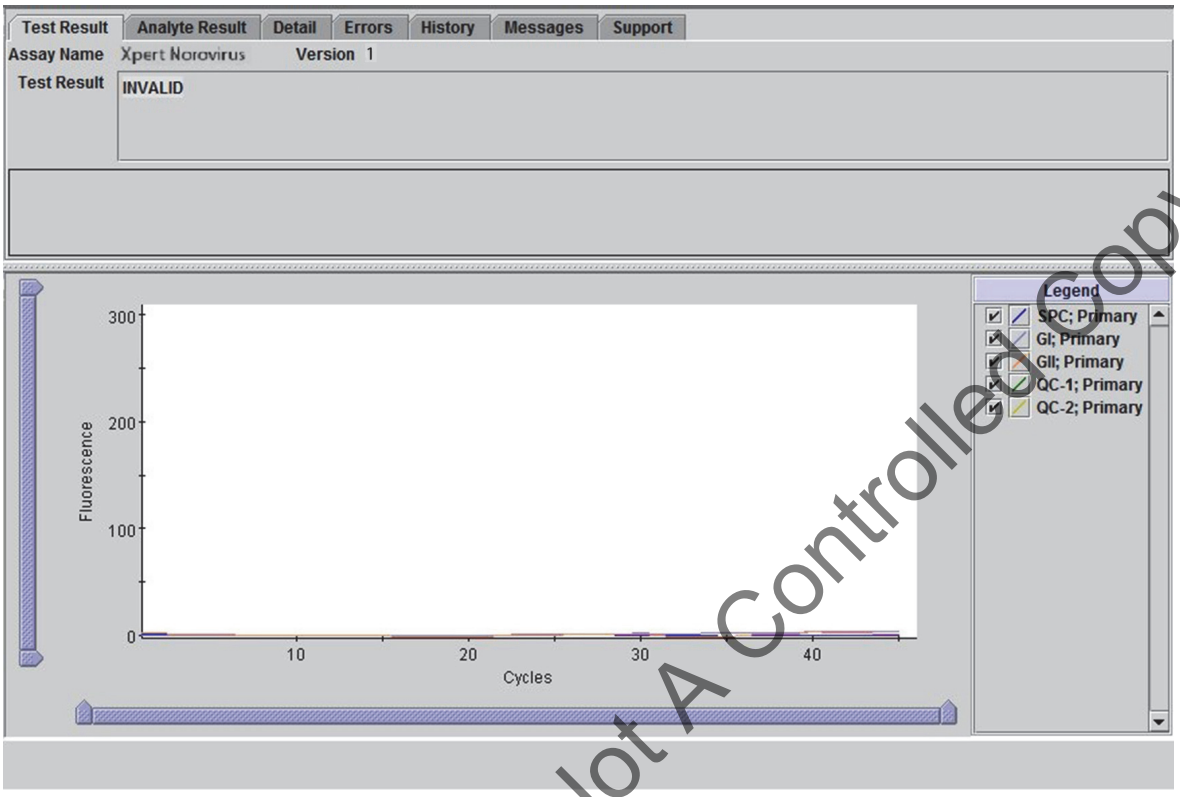

Figure 7. INVALID

17 Retest

17.1 Reasons to Repeat the Assay

If any of the test results mentioned below occur, repeat the test according to the instructions in Section 17.2, Retest Procedure.

- An **INVALID** result indicates that the SPC failed. The sample was not properly processed, PCR is inhibited, or the sample was not properly collected.
- An **ERROR** result could be due to, but not limited to, a Probe Check Control failure or the maximum pressure limits were exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress, or a power failure occurred.

17.2 Retest Procedure

For retesting of specimens with a result of **INVALID**, **ERROR**, or **NO RESULT**, use a new cartridge (do not re-use the cartridge) and new Sample Reagent bottle.

1. Remove the cartridge and Sample Reagent bottle from the Xpert Norovirus Assay kit.
2. After removing the cap from the Sample Reagent bottle, briefly dip a swab in the unformed stool sample. See Figure 8 for the correct amount of specimen to be used for the Xpert Norovirus Assay.

Note Wrap sterile gauze around both the stem of the swab and the mouth of the bottle to minimize the risk of contamination. Do not coat the entire swab fiber tip with stool. See Figure 8. Too much stool may result in errors or invalid results.

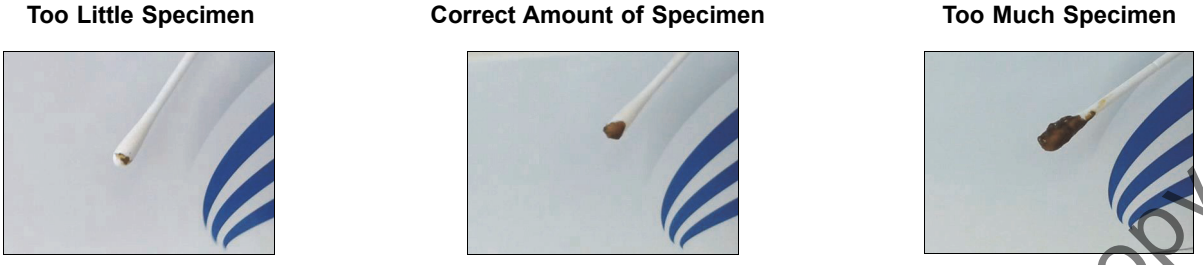

Figure 8. Sample Collection on Swab

3. After removing the cap from the Sample Reagent bottle, insert the swab with stool sample into the bottle containing the Sample Reagent.
4. Hold the swab by the stem near the rim of the bottle. Lift the swab a few millimeters from the bottom of the bottle and push the stem against the edge of the bottle to break it. Make sure the swab is short enough to allow the cap to close tightly.
5. Close the cap of the Sample Reagent bottle and vortex at high speed for ten seconds.
6. Open the cartridge lid. Using a clean transfer pipette (not supplied), transfer the entire contents of the Sample Reagent to the Sample Chamber of the Xpert Norovirus Assay cartridge. See Figure 2.
7. Close the cartridge lid and start the test within 30 minutes.

18 Limitations

- For *In Vitro* Diagnostic Use Only.
- The performance of the Xpert Norovirus Assay was validated using the procedures provided in this package insert only.
- Modifications to these procedures may alter the performance of the test. Results from the Xpert Norovirus Assay should be interpreted in conjunction with other laboratory and clinical data available to the clinician.
- Erroneous test results might occur from improper specimen collection, handling or storage, sample mix-up, or because the number of organisms in the specimen is below the limit of detection of the test. Careful compliance to the instructions in this package insert is necessary to avoid erroneous results.
- With raw or unpreserved unformed stool specimens, assay interference may be observed in the presence of Barium sulfate (≥ 1% w/w) and Benzalkonium chloride at all concentrations tested (1% w/v, 0.2%, w/v, and 0.04% w/v).
- Mutations or polymorphisms in primer or probe binding regions may affect detection of new or unknown norovirus variants resulting in a false negative result.
- In the event of a mixed Norovirus GI and GII infection where the titer of one genogroup has a higher titer than the other genogroup, the genogroup with the higher titer of the two infections will be reported as detected; the lower titer genogroup may be reported as not detected.

19 Expected Values

In the Xpert Norovirus Assay clinical study, a total of 914 prospectively collected, fresh, raw or unpreserved unformed stool specimens were included from seven study centers. The number and percentage of Norovirus GI and Norovirus GII positive cases, calculated by age group, are presented in Table 2.

Table 2. Observed Prevalence of GI and GII by Age Group

Age (Years)	No. of GI Positives	GI Observed Prevalence %	No. of GII Positives	GII Observed Prevalence %
0-1	0/8	0	0/8	0
>1-5	1/6	16.7	0/6	0
>5-12	0/10	0	1/10	10.0
>12-21	0/29	0	3/29	10.3
>21-65	9/520	1.7	35/520	6.7
>65	6/341	1.8	35/341	10.3
Total	16/914	1.8	74/914	8.1

20 Performance Characteristics

20.1 Clinical Performance

Performance characteristics of the Xpert Norovirus Assay were evaluated at seven institutions in the U.S. and E.U. The study specimens consisted of raw or unpreserved unformed stool specimens from subjects with symptoms of acute gastroenteritis. The Xpert Norovirus Assay performance was compared to a composite reference test method performed at the Centers for Disease Control and Prevention (CDC; Atlanta, GA, US).

A total of 1403 specimens were tested for Norovirus GI by the Xpert Norovirus Assay and the composite reference test. Of the 1403 specimens, 914 were fresh, prospectively collected and 489 were frozen, archived specimens. A total of 1401 specimens were tested for Norovirus GII by the Xpert Norovirus Assay and the composite reference test. Of the 1401 specimens, 914 were fresh, prospectively collected and 487 were frozen, archived specimens.

On fresh, prospectively collected specimens, the Xpert Norovirus Assay demonstrated 100% PPA and 99.6% NPA for detection of Norovirus GI, relative to the composite reference test (Table 3). The Xpert Norovirus Assay demonstrated 98.5% PPA and 98.8% NPA for detection of Norovirus GII (Table 4).

On frozen, archived specimens, the Xpert Norovirus Assay demonstrated 98.1% PPA and 94.6% NPA for detection of Norovirus GI, relative to the composite reference test (Table 5). The Xpert Norovirus Assay demonstrated 100% PPA and 96.8% NPA for detection of Norovirus GII (Table 6).

Table 3. Xpert Norovirus Assay Performance for GI vs. Composite Reference Test – Fresh Specimens

		Composite Reference Test		
		POS	**NEG**	**Total**
Xpert Norovirus	**POS**	12	4	16
	NEG	0	898	898
	Total	12	902	914
		PPA% (95% CI)	100% (95% CI: 73.5–100)	
		NPA% (95% CI)	99.6% (95% CI: 98.9–99.9)	

Table 4. Xpert Norovirus Assay Performance for GII vs. Composite Reference Test – Fresh Specimens

		Composite Reference Test		
		POS	**NEG**	**Total**
Xpert Norovirus	**POS**	64	10	74
	NEG	1	839	840
	Total	65	849	914
		PPA% (95% CI)	98.5% (95% CI: 91.7–100)	
		NPA% (95% CI)	98.8% (95% CI: 97.8–99.4)	

Table 5. Xpert Norovirus Assay Performance for GI vs. Composite Reference Test – Frozen Specimens

		Composite Reference Test		
		POS	**NEG**	**Total**
Xpert Norovirus	**POS**	101	21	122
	NEG	2	365	367
	Total	103	386	489
		PPA% (95% CI)	98.1% (95% CI: 93.2–99.8)	
		NPA% (95% CI)	94.6% (95% CI: 91.8–96.6)	

Table 6. Xpert Norovirus Assay Performance for GII vs. Composite Reference Test – Frozen Specimens

		Composite Reference Test		
		POS	**NEG**	**Total**
Xpert Norovirus	**POS**	109	12	121
	NEG	0	366	366
	Total	109	378	487
PPA% (95% CI)			100% (95% CI: 96.7–100)	
NPA% (95% CI)			96.8% (95% CI: 94.5–98.3)	

21 Analytical Performance

21.1 Analytical Sensitivity (Limit of Detection)

The limit of detection (LoD) study was performed to evaluate the analytical sensitivity of the Xpert Norovirus Assay with positive clinical stool specimens containing Norovirus GI.3 or Norovirus GII.4 diluted into a pooled negative stool matrix. The LoD is defined as the lowest concentration (copies/mL) per sample that can be reproducibly distinguished from negative samples with 95% confidence. Replicates of at least 23 were evaluated at seven concentrations for Norovirus GI.3 and Norovirus GII.4 and LoDs were estimated by probit analysis. The estimated LoDs were confirmed by testing at least 20 replicate samples with virus diluted to the estimated LoD concentrations.

The LoD point estimates and confirmed LoD for each genogroup tested are summarized in Table 7.

Table 7. Limit of Detection of the Xpert Norovirus Assay

Norovirus Genogroup/strain	Limit of Detection (95% CI)
GI.3	5.7×10^5 (copies/mL) ($4.64 \times 10^5 – 6.67 \times 10^5$)
GII.4	3.0×10^5 (copies/mL) ($1.25 \times 10^5 – 1.78 \times 10^5$)

21.2 Analytical Specificity (Cross-reactivity)

The analytical specificity of the Xpert Norovirus Assay was evaluated by testing a panel of 68 organisms, consisting of 54 bacteria, 1 fungi, 9 viruses, and 4 parasites representing common gastroenteritis pathogens or those potentially encountered in stool. A minimum of three replicates of all bacterial and fungal strains were tested at concentrations $\geq 10^6$ CFU/mL. A minimum of three replicates of all viruses were tested at concentrations $\geq 10^5$ $TCID_{50}$/mL with the exception of two viruses obtained from clinical samples with unknown concentrations. A minimum of three replicates of all parasites were tested at concentrations $\geq 10^6$ copies/mL. All organisms tested were correctly reported as **NORO GI NOT DETECTED**; **NORO GII NOT DETECTED** by the Xpert Norovirus Assay. The analytical specificity was 100%. Results are shown in Table 8.

Table 8. Analytical Specificity of Xpert Norovirus

Organism	Strain ID	Concentration
Acinetobacter baumannii	CCUG 3477	>3.0×10^8 CFU/mL
Anaerococcus prevotii[a]	ATCC 9321	6.7×10^8 CFU/mL
Bacteriocides fragilis[a]	ATCC 25285	1.4×10^9 CFU/mL
Campylobacter coli	ATCC 43478	1.8×10^8 CFU/mL
Campylobacter jejuni	ATCC 33560	1.3×10^8 CFU/mL
Campylobacter lari	ATCC 35221	3.4×10^7 CFU/mL
Citrobacter freundii	ATCC 33128	1.5×10^9 CFU/mL
Clostridium difficile[a]	ATCC 9689	2.2×10^8 CFU/mL

Table 8. Analytical Specificity of Xpert Norovirus (Continued)

Organism	Strain ID	Concentration
Clostridium sordelli[a]	DSMZ 2141	2.0 x 10^8 CFU/mL
Eggerthella lenta	ATCC 43055	>3.0 x 10^7 CFU/mL
Enterobacter cloacae	ATCC 70021	1.0 x 10^9 CFU/mL
Enterococcus casseliflavus	ATCC 25788	1.0 x 10^9 CFU/mL
Enterococcus faecalis	ATCC 29212	5.4 x 10^8 CFU/mL
Enterococcus faecium	ATCC 9756	8.2 x 10^8 CFU/mL
Enterococcus gallinarium	ATCC 49573	4.5 x 10^8 CFU/mL
Escherichiacoli O157:H7	ATCC 43888	8.4 x 10^8 CFU/mL
Escherichia coli O26:H11	CDC 033014	7.4 x 10^8 CFU/mL
Escherichia coli O45:H2	CDC 003039	3.3 x 10^8 CFU/mL
Escherichia coli O103:H11	CDC 063008	5.4 x 10^8 CFU/mL
Escherichia coli O11	CDC 201114	6.9 x 10^8 CFU/mL
Escherichia coli O121	CDC 023211	1.4 x 10^9 CFU/mL
Escherichia coli O145	CDC 993311	7.1 x 10^8 CFU/mL
Escherichia hermannii	ATCC 33650	1.5 x 10^9 CFU/mL
Fusobacterium necrophorum[a]	ATCC 31647	9.6 x 10^8 CFU/mL
Helicobacter pylori	CCUG 1784	1.5 x 10^8 CFU/mL
Klebsiella pneumoniae	ATCC 70063	1.2 x 10^9 CFU/mL
Lactobacillus jensenii	ATCC 25258	4.0 x 10^8 CFU/mL
Listeria monocytogenes	CCUG 3358	1.2 x 10^9 CFU/mL
Micrococcus luteus	ATCC 4698	1.8 x 10^8 CFU/mL
Morganella morganii	ATCC 49948	1.3 x10^9 CFU/mL
Peptostreptococcus anaerobius[a]	CCUG 7835	1.5 x 10^9 CFU/mL
Plesiomonas shigelloides	ATCC 51903	3.1 x 10^8 CFU/mL
Prevotella oralis[a]	ATCC 33269	1.2 x 10^9 CFU/mL
Proteus mirabilis	ATCC 43071	1.1 x 10^9 CFU/mL
Proteus vulgaris	ATCC 49132	1.8 x 10^9 CFU/mL
Providencia alcalifaciens	CCUG 6325	1.8 x 10^9 CFU/mL
Providencia stuartii	ATCC 49809	1.3 x 10^9 CFU/mL
Pseudomonas aeruginosa	ATCC 27853	6.3 x 10^8 CFU/mL
Pseudomonas fluorescens	ATCC 13525	>3.0 x 10^8 CFU/mL
Pseudomonas putida	ATCC 49128	5.5 x 10^8 CFU/mL
Salmonella agona	ATCC 51957	1.2 x 10^9 CFU/mL
Salmonella bongori	ATCC 43975	1.7 x 10^9 CFU/mL
Salmonella enterica	ATCC 13314	9.2 x 10^8 CFU/mL
Serratia marcescens	ATCC 43862	3.8 x 10^8 CFU/mL
Shigella flexneri	ATCC 12022	8.1 x 10^8 CFU/mL
Shigella sonnei	ATCC 25931	>3.0 x 10^8 CFU/mL
Staphylococcus aureus	ATCC 25923	8.8 x 10^8 CFU/mL
Staphylococcus epidermidis	ATCC 14990	>3.0 x 10^7 CFU/mL

Table 8. Analytical Specificity of Xpert Norovirus (Continued)

Organism	Strain ID	Concentration
Streptococcus agalactiae (GBS)	ATCC 12386	9.6 x 10^8 CFU/mL
Streptococcus dysgalactiae	ATCC 43078	7.2 x 10^8 CFU/mL
Streptococcus pyogenes	ATCC 19615	5.5 x 10^8 CFU/mL
Vibrio cholerae[b]	CCUG 9118	5.2 x 10^9 copies/µL
Vibrio parahaemolyticus	ATCC 17802	3.8 x 10^8 CFU/mL
Yersinia enterocolitica	ATCC 9610	7.1 x 10^8 CFU/mL
Adenovirus	Type 31	3.6 x 10^5 $TCID_{50}$/mL
Adenovirus	Type 40	2.8 x 10^7 $TCID_{50}$/mL
Adenovirus	Type 41	4.6 x 10^7 $TCID_{50}$/mL
Astrovirus[d]	--	Not applicable[c]
Coxsackievirus	Type B5	1.4 x 10^5 $TCID_{50}$/mL
Echovirus	11	3.3 x 10^6 $TCID_{50}$/mL
Parechovirus	Type 6	1.9 x 10^7 $TCID_{50}$/mL
Rotavirus	Type Wa	1.0 x 10^6 $TCID_{50}$/mL
Sapovirus[d]	--	Not applicable[e]
Candida albicans	ATCC 10231	>3.0 x 10^7 CFU/mL
Blastocystis hominis[b]	BT1	1.0 x 10^9 copies/mL
Cryptosporidium parvum[b]	Iowa	6.1 x 10^9 copies/mL
Giardia lamblia[b]	Portland-1	3.05 x 10^9 copies/mL
Entamoeba histolytica[b]	ATCC 30459D	4.9 x 10^6 copies/mL

a. Strictly anaerobic bacteria.
b. Tested as genomic DNA.
c. The concentration is not known for the Astrovirus clinical samples that were obtained from KUL; the Ct values according to KUL assay were in the range of 12-27.
d. Clinical sample.
e. The concentration is not known for the Sapovirus clinical samples that were obtained from KUL; the Ct values according to KUL assay were in the range of 19-23.

21.3 Analytical Reactivity (Inclusivity)

The analytical reactivity of the Xpert Norovirus Assay was evaluated against thirty-one genotypes representing both norovirus genogroups (GI and GII). The thirty-one norovirus strains evaluated in this study were tested near the LoD concentration of the assay (Table 9). Three replicates were tested for each strain.

Table 9. Analytical Reactivity Results of the Xpert Norovirus Assay

Norovirus Strain	Estimated Concentration (copies/mL)[a]	Result	
		GI	GII
GI.1	9.0 x 10^6	POS	NEG
GI.2	3.7 x 10^8	POS	NEG
GI.3	1.4 x 10^6	POS	NEG
GI.4	1.0 x 10^5	POS	NEG
GI.5[b]	2.5 x 10^5	POS	NEG
GI.6[b]	2.5 x 10^5	POS	NEG
GI.7[b]	2.5 x 10^5	POS	NEG

Table 9. Analytical Reactivity Results of the Xpert Norovirus Assay (Continued)

Norovirus Strain	Estimated Concentration (copies/mL)[a]	Result	
		GI	GII
GI.8	3.7×10^5	POS	NEG
GI.14	3.0×10^6	POS	NEG
GII.1	3.6×10^6	NEG	POS
GII.2	1.1×10^5	NEG	POS
GII.3[b]	1.3×10^3	NEG	POS
GII.4 (2006a)	1.2×10^5	NEG	POS
GII.4 (2006b)	2.4×10^5	NEG	POS
GII.4 (2008)	4.3×10^5	NEG	POS
GII.4 (2009) New Orleans	1.7×10^5	NEG	POS
GII.4 (2010)	9.6×10^4	NEG	POS
GII.4 (2012) Sydney	1.2×10^5	NEG	POS
GII.5[b]	1.3×10^3	NEG	POS
GII.6[b]	1.3×10^3	NEG	POS
GII.7	8.0×10^4	NEG	POS
GII.8[b]	1.3×10^3	NEG	POS
GII.9[b]	1.3×10^3	NEG	POS
GII.10[b]	1.3×10^3	NEG	POS
GII.11	2.6×10^5	NEG	POS
GII.12	5.7×10^5	NEG	POS
GII.13	6.9×10^5	NEG	POS
GII.14	1.5×10^5	NEG	POS
GII.15	1.7×10^5	NEG	POS
GII.16[b]	1.3×10^3	NEG	POS
GII.17[b]	1.3×10^3	NEG	POS

a. An estimated concentration or titer was provided based on a Ct value (because of the difficulty in culturing norovirus particles, an exact concentration cannot be provided). The Ct value for each clinical specimen in the inclusivity study was extrapolated to the titer obtained from the LoD study for well-characterized GI and GII samples using a standard curve at CDC.

b. Naked RNA transcripts were used for these strains, clinical samples were not available at the time of testing.

21.4 Interfering Substances Study

Potentially interfering substances that may be present in stool were evaluated directly relative to the performance of the Xpert Norovirus Assay. Potentially interfering substances included hemoglobin, mucin, cholesterol, triglycerides and whole blood, plus additional endogenous and exogenous substances listed in Table 10.

Negative samples were tested in replicates of 8 with each substance in a negative stool matrix to determine the effect on the performance of the sample processing control (SPC). Positive samples were tested in replicates of 8 per substance with one Norovirus GI and one Norovirus GII clinical isolate near the LoD.

All results were compared to positive and negative controls prepared in negative stool matrix. All valid positive and negative control samples were correctly reported using the Xpert Norovirus Assay.

Inhibition of the Xpert Norovirus Assay was observed in the presence of Benzalkonium chloride (1% w/v, 0.2% w/v, and 0.04% w/v). False-negative test results were reported for the Norovirus GII target at (1% w/v) Benzalkonium chloride. In the presence of Barium sulfate (5% w/w), a statistically significant inhibitory effect was observed on the Norovirus GII Ct in positive samples relative to the control (p-value <0.05). No statistically significant effect was observed on the Norovirus GII Ct relative to the control in the presence of Barium sulfate (1% w/w).

No other potential interfering substances were found to be inhibitory and no false-negatives were reported for these substances.

Table 10. Potentially Interfering Substances in Xpert Norovirus Assay

Endogenous substances		
Substance	**Description /Active Ingredient**	**Concentration Tested**
Cholesterol	Fecal fat/Cholesterol	5 % w/v
Hemoglobin	Hemoglobin human	12.5 % w/v
Mucin	purified Mucin protein	5 % w/v
Steric acid/ Palmitic acid (1:1)	Fatty acids/Steric acid, Palmitic acid	5 % w/w
Triglyceride	Fecal fat/Triglyceride Mix	5 % w/v
Whole Blood	Human Whole Blood	10 % v/v
Exogenous substances		
Substance	**Description /Active Ingredient**	**Concentration Tested**
Acetaminophen	Acetaminophen	5 % w/v
Amoxicillin	Antibiotic/Amoxicillin	5 % w/v
Ampicillin	Ampicillin Sodium Salt	152 µmol/L
Aspartame	Aspartame	5 % w/v
Barium sulfate	Contrast medium/Barium sulfate	5 % w/w, 1% w/w
Benzalkonium chloride Commercial alcohol	Antiseptic Towelettes/ Benzalkonium Chloride in ethanol	1 %, 0.2 %, 0.04 % w/v
Bismuth subsalicylate	Bismuth (III) Subsalicylate (an active ingredient in Peptobismol)	1 % w/v
$CaCO_3$	Calcium Carbonate	5 % w/v
Hydrocortisone	Hydrocortisone	50 % w/v
Ibuprofen	Ibuprofen	5% w/v
Imodium	Loperamide HCl	5 % v/v
Kaopectate	Attapulgite	5 mg/mL
Metronidazole	Metronidazole	5 % w/v
Mycostatin	Nystatin	50 % w/w
Naprosyn	Naproxen Sodium	2.2 µmol/mL
Novaluzid	$Mg(OH)_2$, $Al(OH)_3$ and $MgCO_3$	5 % w/v
Polymyxin B sulfate Bacitrin zinc	Polysporin/Polymyxin B Sulfate and Bacitracin Zinc	50 % w/v
Pursennid	Sennaglycosides	5 % w/v
Rexall Mineral oil laxative	Mineral Oil	50 % v/v

21.5 Carry-over Contamination Study

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples run followed by very high positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately followed by a highly positive Norovirus GII sample. This testing scheme was repeated 21 times between two GeneXpert modules for a total of 42 runs for 20 positive and 22 negative specimens. All 19 positive samples were correctly reported as **NORO GI NOT DETECTED**; **NORO GII DETECTED** and one positive sample was reported as an ERROR. All 22 negative samples were correctly reported as **NORO GI NOT DETECTED**; **NORO GII NOT DETECTED**.

22 Reproducibility

A panel of 7 specimens with varying concentrations of Norovirus GI and Norovirus GII was tested two times on five different days by two different operators, at each of three sites (7 samples x 2 time/day x 5 days x 2 operators x 3 sites). One lot of Xpert Norovirus Assay cartridges was used at each of the 3 testing sites. The Xpert Norovirus Assay was performed according to the Xpert Norovirus Assay procedure. Results are summarized in Table 11.

Table 11. Summary of Reproducibility Results

Sample ID	Site 1	Site 2	Site 3	Overall
Neg	100% (20/20)	100% (20/20)	100% (20/20)	100% (60/60)
GI - High Neg	30.0% (6/20)	15.0% (3/20)	30.0% (6/20)	25.0% (15/60)
GI - Low Pos	100% (20/20)	85.0% (17/20)	95.0% (19/20)	93.3% (56/60)
GI - Mod Pos	100% (19/19)	100% (20/20)	100% (20/20)	100% (59/59)[a]
GII - High Neg	25.0% (5/20)	30.0% (6/20)	35.0% (7/20)	30.0% (18/60)
GII - Low Pos	100% (20/20)	95.0% (19/20)	90.0% (18/20)	95.0% (57/60)
GII - Mod Pos	95.0% (19/20)	100% (20/20)	100% (20/20)	98.3% (59/60)

a. One sample 2x indeterminate

The reproducibility of the Xpert Norovirus Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-days, and between-operators for each panel member are presented in Table 12.

Table 12. Summary of Reproducibility Data

Sample	Assay Channel (Analyte)	N[a]	Mean Ct	Between-Site		Between-Day		Between-Operator		Within-Assay		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Neg	SPC	60	31.9	0.17	0.5	0.06	0.2	0.06	0.2	0.26	0.8	0.32	1.0
GI - High Neg	GI	60	39.4	0	0	0.46	1.2	0	0	1.80	4.6	1.86	4.7
GI - Low Pos	GI	59	37.9	0.29	0.8	0	0	0.36	1.0	1.03	2.7	1.13	3.0
GI - Mod Pos[b]	GI	57	34.7	0.09	0.2	0.07	0.2	0	0	0.41	1.2	1.01	1.2
GII - High Neg	GII	54	38.9	0	0	0	0	0.77	2.0	1.77	4.5	1.93	5.0
GII - Low Pos	GII	60	37.3	0	0	0	0	0.58	1.6	1.33	3.6	1.45	3.9
GII - Mod Pos[b]	GII	59	34.3	0.22	0.6	0	0	0	0	0.45	1.3	0.50	1.5

a. Results with non-zero Ct values out of 60
b. n=3 sample outliers (2 GI Mod Pos and 1 GII Mod Pos) that were more than 5 standard deviations from the mean were considered outliers and were removed from the analysis.

23 Instrument System Precision

An in-house precision study was conducted to compare the performance of the GeneXpert Dx and the GeneXpert Infinity instrument systems. A panel of 7 samples with varying concentrations of Norovirus GI and Norovirus GII was tested on 12 different days by two operators. Each operator conducted four runs of each panel samples per day on each of the two instrument systems (7 samples x 4 times/day x 12 days x 2 operators x 2 instrument systems). Three lots of Xpert Norovirus Assay cartridges were used for the study. The Xpert Norovirus Assay was performed according to the Xpert Norovirus procedure. Results are summarized in Table 13.

Table 13. Summary of Instrument System Precision Results (Dx vs. Infinity)

Sample	GeneXpert Dx			Infinity			% Total Agreement by Sample
	Op 1	Op 2	Inst	Op 1	Op 2	Inst	
Neg	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100% (48/48)	100% (96/96)	100% (192/192)
GI - High Neg	14.6% (7/48)	10.4% (5/48)	12.5% (12/96)	14.6% (7/48)	25.0% (12/48)	19.8% (19/96)	16.2% (31/192)
GI - Low Pos	100% (48/48)	97.9% (47/48)	99.0% (95/96)	97.9% (47/48)	97.9% (47/48)	97.9% (94/96)	98.4% (189/192)
GI - Mod Pos	100%[a] (47/47)	100% (48/48)	100% (95/95)	100% (48/48)	100% (48/48)	100% (96/96)	100% (191/191)
GII - High Neg	25.0% (12/48)	29.2% (14/48)	27.1% (26/96)	29.2% (14/48)	31.3% (15/48)	30.2% (29/96)	28.7% (55/192)
GII - Low Pos	89.6% (43/48)	89.6% (43/48)	89.6% (86/96)	83.3% (40/48)	95.7% (44/46)	87.5% (84/96)	88.5% (170/192)
GII - Mod Pos	100% (48/48)	100% (48/48)	100% (96/96)	100% (48/48)	100%[b] (47/47)	100% (95/95)	100% (191/191)

a. One GI Mod Pos sample not tested.
b. One GII Mod Pos sample indeterminate and not retested.

The precision of the Xpert Norovirus Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-instruments, between-lots, between-days, between-operators, and within-assays for each panel member are presented in Table 14.

Table 14. Summary of Precision Data

Sample	Assay Channel (Analyte)	N[a]	Mean Ct	Between-Instrument		Between-Lot		Between-Day		Between-Operator		Within-Assay		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Neg	SPC	192	31.8	0	0	0.44	1.4	0	0	0.08	0.2	0.39	1.2	0.59	1.9
GI - High Neg	GI	188	38.6	0.19	0.5	0.25	0.7	0.18	0.5	0	0	1.40	3.6	1.45	3.8
GI - Low Pos	GI	192	37.1	0.39	1.1	0.26	0.7	0.19	0.5	0	0	0.95	2.6	1.08	2.9
GI - Mod Pos	GI	191	34.0	0	0	0.36	1.1	0.04	0.1	0.08	0.2	0.38	1.1	0.53	1.6
GII - High Neg	GII	178	38.7	0.16	0.4	0	0	0.29	0.7	0	0	2.03	5.3	2.06	5.3
GII - Low Pos	GII	187	37.6	0.10	0.2	0	0	0	0	0.45	1.2	1.65	4.4	1.71	4.6
GII - Mod Pos	GII	191	34.3	0	0	0.09	0.2	0	0	0.17	0.5	0.42	1.2	0.46	1.3

a. Results with non-zero Ct values out of 192.

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26 Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:

- Product name
- Lot number
- Serial number of the instrument
- Error messages (if any)
- Software version and, if applicable, Computer Service Tag number

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Contact information for other Cepheid offices is available on our website at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab. Select the **Contact Us** option.

27 Table of Symbols

Symbol	Meaning
	Catalog number
	*In vitro* diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <n> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	Warning
	For prescription use only

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