Norovirus Rapid Test

Cat. No.:DTS694
Pkg.Size:

Intended use

One-step immunochromatographic test for the differential detection of Norovirus Genogroups I and II in human faeces.
The Norovirus chromatographic immunoassay is a procedure for the qualitative detection, in separate bands, of Genogroup I (GI) and Genogroup II (GII) of Norovirus in human feces. A positive signal in either test band provides a good indication that we may be in presence of a Norovirus infection which should draw the attention of the clinician.

General Description

Description of Norovirus:
Noroviruses are a type of single-stranded, positive-sense RNA viruses belonging to the family Caliciviridae (Sapoviruses also belong to this family, among others). They are highly contagious viruses whose main routes of transmission are: person-to-person contact and through contaminated food/water (in the U.S. is estimated that they account for 50% of gastrointestinal outbreaks by food poisoning). They often cause large outbreaks in closed communities in a variety of environments such as hospitals, nursing homes, schools, kindergarten, restaurants, cruises,... where, once the virus has been introduced, the infection spreads very quickly.
Several studies show that Noroviruses are responsible for almost 50% of gastroenteritis outbreaks worldwide (considering all outbreaks of any aetiology).
Human Noroviruses have been very difficult to study because of their high diversity and the lack of an efficient cell culture for "in vitro" replication as well as a suitable animal model.
The cloning of genomes of Norovirus and expression of the viral capsid proteins in baculovirus and other expression systems, have allowed to obtain "virus-like particles" (VLP) which, once assembled, are able to recreate the actual structure of the virus. Norovirus capsid is composed of a single major structural protein, the capsid protein (VP1) which can be divided into two main domains: the shell (S) and the protruding domains (P). The expression of VP1 in a eukaryotic system allows to obtain empty structural particles similar to the native present in the virus (VLP) that have been used as a substitute for native Norovirus for many years in any research process.
Classification of Noroviruses:
Noroviruses are grouped into five Genogroups (GI to GV), of which GI and GII are involved in most acute cases of viral gastroenteritis in humans.
Within each Genogroup viruses are classified into Genotypes (GI.1, GII.1,...). Over 25 different Genotypes have been described within Genogroups I and II. Of these, GII.4 is the most common Genotype representing around 60-80% of cases worldwide. Following are GII.2, GII.3 and GII.7 within GII and GI.1, GI.3 or GI.4 within GI4 although, in general, this Genogroup is rather less common than GII, representing less than 5%.
Recent studies have shown that in recent years new variant strains of GII. have been identified, which arise as a result of genetic changes that, in some cases, affect only one amino acid in the sequence of the capsid protein but this is enough to make them different from previous GII.4 strains. This means that any type of immunity that an individual would have generated against GII.4 could be useless against these new strains. In short, a single Genotype is presented as a whole family, tremendously complex and variable over time.
Characteristics of Norovirus Infection:
Although Noroviruses can be detected throughout the year, it has been clearly observed that there is a seasonal prevalence with

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

peaks during autumn and winter. Norovirus infection has an incubation period of 24-48 hrs. and is characterized by nausea, vomiting, abdominal pain, fever,... Acute symptoms usually appear for 1-3 days, although safety hygiene actions must be maintained for a minimum of two weeks (the elimination of the virus in faeces may continue for days, even weeks); the patient may remain asymptomatic from third or fourth day after onset of symptoms. After overcoming the infection, immunity to Norovirus is usually incomplete and temporary (about 6 months) as well as specific for a particular Genotype. Given the high genetic variability of Noroviruses, individuals are likely to be infected several times throughout their lifetime. This may explain the high rates of infection that occur in all ages at an outbreak level. Recent studies suggest that susceptibility to Norovirus infection may be genetically determined.

Principle Of The Test

The test is based on the immunological capture of coloured microbeads during its passage along a membrane on which specific monoclonal antibodies against GI and GII have been immobilized in two separate bands.
Norovirus test uses a combination of:
1) red latex particles conjugated to specific antibodies against GII which cooperates with another antibodies specific for GII located on the membrane under the control band.
2) other red latex particles conjugated to specific antibodies against GI which cooperates with another antibodies specific for GI located on the membrane above the control band.
3) blue latex particles conjugated to an antigen recognized by an antibody specific for this antigen bound to the membrane forming the so called test control band. In this test the sample is treated first with the sample diluent buffer (included in the kit) to achieve the extraction of the virus from the stool matrix. After the extraction, you just need to add a certain volume of supernatant onto the test strip and wait for 15 minutes. When the extracted sample flows through the test membrane, the coloured particles migrate. In the case of a positive sample, specific antibodies on the membrane will capture the coloured particles covered by the antigen. Depending on the virus content of the sample, different coloured lines will be visible. These lines are used for interpretation of results, following a 15-minute incubation at room temperature.

Test Formats

Norovirus test is available in two different formats:
1. Stick format: is a reaction strip packaged in an aluminium pouch or in a tube. A test tube (included in the kit) or a flat bottom well of a 96-well microplate (to deposit the extracted sample and run the test) is required.
2. Simple format: is a reaction strip inside a plastic device or casing. The extracted samples are added directly to the sample window of the casing marked with an arrow.
Both formats have the same features, the only difference is related to the method for running the test.

Reagents And Materials Provided

1. Reaction devices (Simple or Stick formats)
2. Sample dilution buffer.
3. Non-graduated disposable plastic pipettes (yellow).
4. Graduated disposable plastic pipettes.
5. Wooden applicators for solid samples.
6. 1.5 ml plastic micro-tubes with lid.
7. Test tubes.
8. Stands for the above test tubes allowing to keep them in an upright, stable position.

Materials Required But Not Supplied

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

1. Centrifuge for the 1.5 ml micro-tubes.
2. Vortex
3. Stopwatch

Storage

Product may be stored at any temperature between +2 and +25°C.
The expiry date is printed on the tubes or aluminium packages.

Specimen Collection And Preparation

SAMPLES:
1. This test is designed for the analysis of human faecal samples.
2. It is recommended to collect the stool sample as soon as symptoms appear (diarrhoea and vomiting, especially) as the elimination of virus in faeces is greatest during the first three days from the onset of symptoms.
3. Do not use samples collected in transport media or added with preservatives (such as formalin, SAF, PVA or similar) or enrichment media as their presence could interfere with the proper performance of the test.
4. The use of fresh untreated samples is recommended. If they have to be stored for some time, they can be stored in the refrigerator (+2-8°C) for 1 or 2 days. For a longer storage, they should be frozen at -20°C, considering that some samples lost immunoreactivity after being frozen.
5. In case of freezing, thaw the samples completely at room temperature prior to analysis.
6. Avoid freezing-thawing cycles for the faecal samples as the immunological recognition of virus can be altered.
PREPARATION OF FECAL SAMPLES:
General Note: disposable gloves should be used throughout the test procedure due the handling of infectious samples. Once the work is concluded, do not forget to comply with the hygiene procedures detailed in point 4 of the “Precautions” section.
The protocol for faecal samples preparation is the same for Simple and Stick formats:
1. For liquid or semi-liquid faeces add 100 µl of sample to a labelled 1.5-ml micro-tube. When using the disposable non-graduated pipettes (yellow) included in the kit, take 2- 3 drops of sample (3 drops for a liquid sample and 2 drops for a semi-solid sample). For solid samples, take a portion of approximately 75 mg (a small ball of about 4 mm in diameter) with the wooden applicator and added it to a labelled 1.5-ml micro-tube.
Important: homogenize the sample and take a portion of at least three different sites of the sample to obtain a sample as representative as possible.
2. Add 1 ml of sample diluent to the above 1.5-ml microtube or the appropriate volume to keep a ratio of 100 µl (or 75 mg) of sample in 1 ml of sample dilution buffer.
3. Vortex for 30 seconds or the time required to ensure complete resuspension of the sample in the buffer. If a vortex is not available, shake vigorously by hand until complete resuspension of the stool sample in the buffer.
4. Centrifuge the 1.5-ml micro-tubes for 5 minutes at 700xg (about 3000 rpm) in a small centrifuge adapted for these micro-tube to sediment the solid particles. If a suitable centrifuge is not available, wait for 3-5 minutes until the solid particles have settled to the bottom of the tube. In any case, optimum test performance is achieved with a clear solution of a sample extracted following centrifugation.

Assay Procedure

SIMPLE NOROVIRUS PROCEDURE:
Once the samples have been prepared as described in previous sections, the procedure is as follows:
1. Remove the reaction device from the aluminium pouch. Discard the desiccant bag as it only serves to preserve the test from moisture.

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

2. Take the sample supernatant, after centrifugation, with a new disposable yellow pipette and add 4 drops (or 100 µl) to the sample area of the reaction device (round window marked with an arrow).
3. Wait for 15 minutes, read and interpret the results.
STICK NOROVIRUS PROCEDURE:
Once the samples have been prepared as described in previous sections, the procedure is as follows:
1. Remove the test strip from the aluminium pouch or the corresponding tube (close it again immediately to avoid damage due to humidity).
2. When using the test tube included in the kit, insert the tube into the holder included in the kit. Take a volume of 265 µl (fourth mark on the graduated disposable pipette) of the sample supernatant, after centrifugation, and deposit inside the test tube.
3. When using a flat bottom 96-well microplate, take a volume of about 150 µl (third mark on the graduated disposable pipette) per well, of sample supernatant after centrifugation.
4. Insert the strip into the test tube (placed onto the stand-up holder) or into the well of the microplate with the arrows upper pointing down.
5. Incubate and read the results at 15 minutes on the white central area of the strip.

Interpretation of Results

The five strips are an example of the different results that can be obtained with the Norovirus test.
Three different coloured bands can be distinguished:
Blue band: is the control band indicating a proper test performance.
Upper red band: indicates the presence of Norovirus Genogroup I in the sample.
Lower red band: indicates the presence of Genogroup II in the sample.
The control blue band should always appear. The additional presence of any red band, indicates the presence of Norovirus in the sample.
Strip 1: NEGATIVE result: a single transverse BLUE line appears in the middle area of reaction device (in SIMPLE format aligned with the letter “C” marked on the plastic cassette or casing). This band is the control band and should always appear indicating that chromatography takes place normally.
Strips 2-4: POSITIVE results
Strip 2. Detection of GII: a BLUE band (control) and a RED band 3 mm below the control band (in Simple format aligned with the label "T1" marked on the casing) appear.
The band intensity depends on virus concentration in the sample.
Strip 3. Detection of GI: a BLUE band (control) and a RED band 3 mm above the control band (in Simple format aligned with the label "T2" marked on the casing) appear.
The band intensity depends on virus concentration in the sample.
Strip 4. Detection of GII and GI:a BLUE band (control) along with two RED bands (one above -GI- and one below -GII- the control band) appear.
Strip 5: INVALID result: the blue control band is not visible regardless the presence of any red band. This indicates a malfunction of the test. Some of the causes that may explain this fact can be:
some of the reagents have deteriorated or the test hasexpired.
sample has not been prepared according to the instructions of use.
a sample diluent other than that provided by the kit has been used.
In the case of an invalid result, it is recommended to repeat the test with a new strip strictly following the instructions of use in this manual.
Any line that appears beyond 15 minutes because of the nature of the sample, has no diagnostic value.
NOTE: the final and definitive diagnosis is established by the clinician. This test only detects Norovirus in a sample, but is not an

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

argument to conclude that the person has an infection with Norovirus.

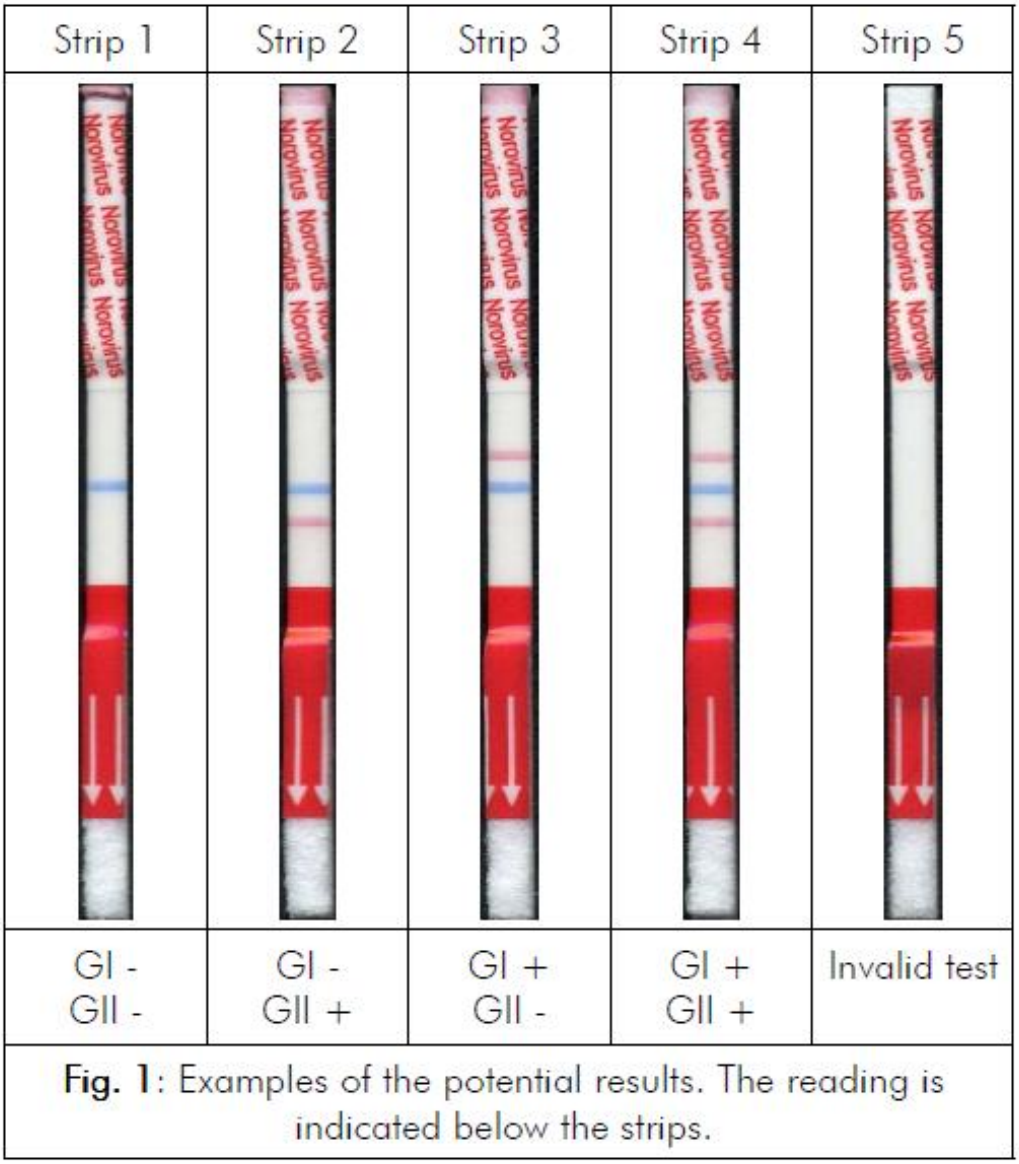


Fig. 1: Examples of the potential results. The reading is indicated below the strips.

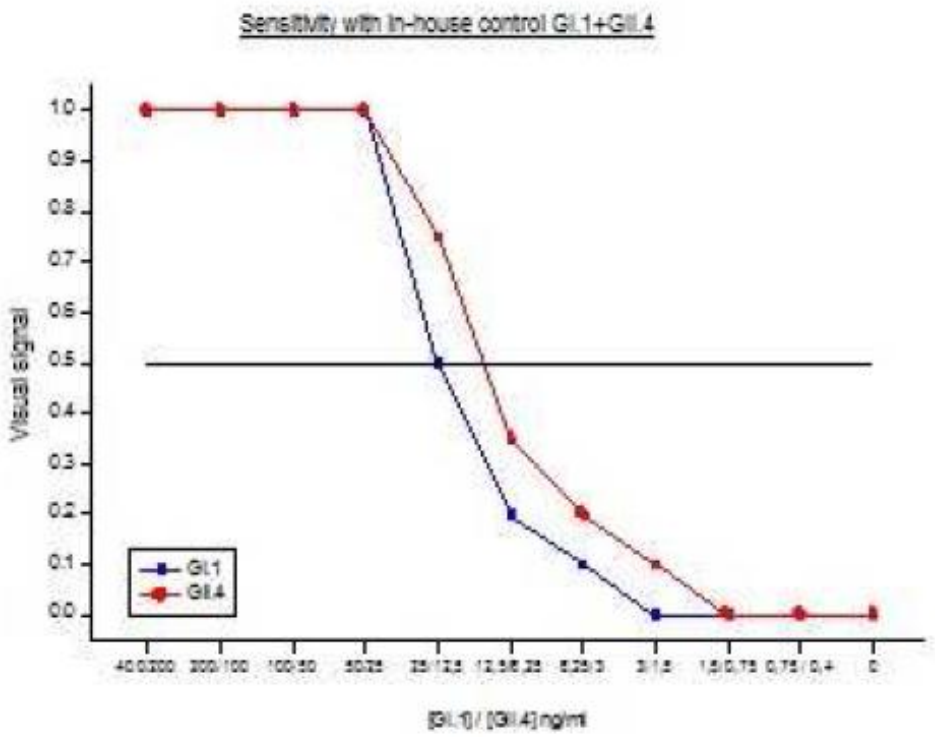
Sensitivity

ANALYTICAL SENSITIVITY

For the determination of the analytical sensitivity of Norovirus test, recombinant “virus like particles” (VLP) belonging to different Genotypes such as GI.1, GI.3, GI.6, GII.1, GII.2, GII.3, GII.4, GII.7 y GII.17 were used. The mean sensitivity values obtained were very different depending on the VLP assessed. We have included the results obtained with GI.1 and GII.4, as they are the most representative and common Genotypes within each Genogroup. For this reason, our internal control to validate all manufactured lots of Norovirus test is a mixture of GI.1 + GII.4. This internal control is diluted in sample dilution buffer of Norovirus test to a concentration of 400 ng/ml for GI.1 and 200 ng/ml for GII.4. From this point, two-fold dilutions are prepared in

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

the same buffer to complete a sensitivity curve with 10 points + blank (buffer).
Detection limit for GI.1 = 25 ng/ml
Detection limit for GII.4 = 10 ng/ml
Both values are below the LPC value established for each Genotype (50 ng/ml for GI.1 and 25 ng/ml for GII.4). It is important to note that the detection limit of the test was also analyzed using real stool samples. Values were consistent with those obtained from pure VLPs. These results demonstrate the robustness of the test.



Diagnostic Sensitivity and Specificity

A. Internal Evaluation.
A comparison between the Norovirus test and two other commercial EIA for Norovirus detection, one ELISA and one immunoenzimatic rapid test, was done. The study included the analysis of 52 negative samples, 11 positive samples for Genogroup I and 66 positive samples for Genogroup II. All them are frozen samples characterized by RT-PCR in the original hospitals. The results obtained were seen in Diagnostic Sensitivity and Specificity Image.

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

	Negative Samples	GII Samples	GI Samples
DTS694	51	51	9
Rapid EIA	51	51	1
ELISA	52	50	1

All the comparative assays have very high specificities (ranging between 98 and 100%) and a sensitivity GII very similar, around 77%; however, the great advantage of the test is related to Genogroup I detection which is situated around 82% while GI sensitivity of any of the other two commercial test is below 10%.

B. External evaluation by the Health Protection Agency (HPA, London).

The study involves the analysis of 33 negative samples, 10 positive samples for GI and 121 positive samples for GII. All samples were characterized by RT-PCR and selected based on its Ct value (Ct<31) due to recent studies13 indicate that those samples with Norovirus Ct<31 are associated with Norovirus symptomatic infections, whereas if the Ct value is >31, it is more probable that the infection would be asymptomatic or the sample has been collected after the acute phase of the disease when the patient is sufficiently recovered due to Norovirus infection involves severe symptoms during 1-2 days. All the positive samples for RT-PCR with Ct>31 were excluded from this analysis.

Sensitivity= 83.2 % (75.7-89.2%)*

Sensitivity GI = 90.0 % (55.5-99.7%)

Sensitivity GII = 82.6 % (74.7-88.9%)

Specificity ≈100 % (89.4-100%)

* these ranges refer to the 95% confidence interval

The Norovirus testhas a very high specificity with respect to the reference technique (RTPCR).

Regarding sensitivity, Genogroup I detection is high which correlates with the results of the previous internal evaluation. The Genogroup II sensitivity is slightly lower while approaching other commercial EIA assays.

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

164 samples		RT-PCR		
		pos GI	pos GII	neg
Norovirus	pos GI	9		0
	pos GII		100	0
	neg	1	21	33
		10	121	33

Hook Effect

The maximum amount of Norovirus that a person can eliminate during the acute phase of disease is about 1012 particles/gr of stool, which is equivalent to 7.5*1010 particles/ml taking into account that the Norovirus test uses a sample extraction of 75 mg of stool in 1 ml of buffer. Considering an approximate equivalence between VLPs and mass of 1 µg = 5.87*1010 VLPs/ml, 7.5*1010 particles/ml are about 1280 ng/ml of VLP. As the idea is to know the effect of a very high concentration of VLPs, well above the values that can be found among the population, a maximum concentration of 40000 ng/ml of both GI.1 and GII.4 was measured with the Norovirus test. This concentration is 800-fold the test limit of GI.1 and 1600- fold the test limit of GII.4.

Repeatability

INTRA-ASSAY PRECISION

Ten replicates of each of the three concentrations established as PC, LPC and NC with our internal standard were measured on the same day by the same person. A 100% repeatability was obtained with these three critical concentrations indicating a high intra-assay precision of the test.

Reproducibility

INTER-DAY PRECISION

Using a single lot of Norovirus test the sensitivity curve described above is measured through four days spaced in time. The results were very reproducible (we obtained the same sensitivity for both GI and GII through the four days of measurement).

INTER-OPERATOR PRECISION

Five operators with no prior training measured in duplicate the sensitivity curve described in the section “Analytical Sensitivity”. Differences were observed that in no case exceeded one two-fold dilution.

INTER-LOT PRECISION

Using three different lots of Norovirus test a sensitivity curve was measured in duplicate. The analysis was performed by the same person on the same day. Only differences below to one two-fold dilution were observed, acceptable and tolerable for the assay.

The differences found in the different “Precision” sections are acceptable for a qualitative immunochromatographic technique with its inherent variability.

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

Interferences

The substances indicated in the table at the concentration specified did not interfere with the results when added to stool samples (positive and negative ones):

Atropine	0,1 mg/ml	Ibuprofen	25 mg/ml
Cimetidine	8 mg/ml	Acetylsalicylic acid	40 mg/ml
Loperamide	10 mg/ml	Sweetener	50 mg/ml
Metronidazol	30 mg/ml	Palmitic acid	90 mg/ml
Neomicyn	25 mg/ml	Barium Sulfate	50 mg/ml
Ampicillin	30 mg/ml	Mucin	50 mg/ml
Omeprazole	10 mg/ml	Whole blood	30% (v/v)

Precautions

1. Patient specimens (faeces) should be handled with caution as they may contain infectious agents. The use of disposable gloves throughout the entire procedure is required.
2. The sample dilution buffer contains sodium azide as anti-microbial agent. Avoid direct contact with skin and mucous membranes. Dispose of appropriately. Do not use the buffer if signs of contamination or precipitation are present.
3. Do not eat, drink, smoke or prepare or store food in areas where reagents or samples are handled.
4. Once completed the procedure, clean work surfaces with soap and water and finish disinfecting with a suitable solution. Finally, discard the gloves and then wash hands first with soap and water rubbing them well for 30 seconds.
5. Do not exchange components from one kit lot to another.
6. Before use, allow all kit components and stool samples to reach room temperature, as cold reagents and/or samples can reduce test functionality. Twenty to 30 minutes are recommended to reach room temperature.
7. All reagents are for in vitro use exclusively.
8. Do not use kit components beyond their expiration date.
9. In case of package damage, the product may be used if none of its components has been damaged.
10. For the Simple format, is very important to add the correct volume of extracted sample to the reaction device. If the amount is lower than required, the chromatography may not be completed as the sample does not reach the reaction area, if it is bigger, brown lines may appear instead of red or blue lines.
11. Used product should be disposed of according to applicable laws.
12. Do not use the test if any coloured lines appear in the result area before using the test.
13. It is very important to take the adequate sample amount: about 75 mg for solid samples (a small ball of about 4 mm in diameter) or 100 µl for liquid or semiliquid samples; these amounts are extracted in 1 ml of sample diluent included in the kit. If a greater amount of sample is taken, just maintain the ratio of 75 mg (or 100 µl) of sample in 1 ml of sample diluent. An excess of sample relative to the amount of buffer
added, prevents the chromatography to perform correctly, this is especially critical in the case of solid samples since it is not so simple to take the appropriate amount of sample.

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

14. In order to ensure an adequate chromatography it is very important to centrifuge the 1.5 ml microtubes prior to extracting the specific quantity of supernatant. Correct results cannot be guaranteed if the solid particles are left to settle rather than being centrifuged. This is particularly true in the case of solid stool samples, as the greater number of suspended particles can interfere with the chromatography.
15. For the Stick format packaged in a tube, is very important to recap it immediately once the reaction strip has been taken out, as a high relative humidity could damage the remaining strips inside the can.

Limitations

1. The Norovirus test is intended for the differential identification of Norovirus Genogroups I and II by detecting its presence in human faeces provided that the viral load is equal to or higher than the detection limit of the assay.
2. This is a qualitative, not quantitative test, although the intensity of positive bands relates to the amount of detectable virus in the stool sample.
3. Over 200 stool samples were assessed to ensure proper test performance. The correlation of results with other techniques (RT-PCR, ELISA and rapid tests) was good. However, this study does not exclude potential interference in test performance when analysing other faecal samples.
4. Norovirus test has not been validated with all Genotypes able to infect humans and, therefore, the test may fail to detect Norovirus due to the high antigenic diversity of the circulating strains.
5. Insufficient sample amount may lead to extremely weak positive results. In this case, repeat the test with a larger amount of sample while maintaining the recommended ratio to the volume of sample diluent. On the other hand, a sample excess can cause the test to run very slowly and even prevent the test to perform properly (the control line is not visible). In this event, the test must be repeated with a lower sample amount
6. A negative result does not exclude the possibility of a Norovirus infection. The failure in the detection of Norovirus may be the result of factors such as: taking the sample at an incorrect time of disease (when a low amount of virus is eliminated in the faeces), an incorrect sample storage, an inadequate handling of the sample, the presence of a Norovirus Genotype not detected by the strip (as the test has not been validated with all Genotypes able to infect humans and may fail to detect any of them).
7. A positive result does not exclude the presence of other pathogens; furthermore, a co-infection of Norovirus with other microorganisms may occur. In this regard, note that the most common co-infections of Norovirus often occur with parasites, specially with Giardia lamblia followed by Cryptosporidium parvum. In any case, co-infections can only be clarified by a differential diagnosis.
8. Test results should be interpreted in conjunction with information available from epidemiological studies, patient clinical evaluation and other diagnostic procedures.

REFERENCES

1. Atmar RL and Estes MK. Diagnosis of noncultivatable gastroenteritis viruses, the human caliciviruses. Clinical Microbiology Reviews, 2011. Vol: 14 (pp: 15-37).
2. Ribes Fernández JM and Buesa Gómez J. Infecciones por Norovirus. Enferm Infecc Microbiol Clin, 2010. Vol: 28 (pp: 51-55).
3. Patel MM, Hall AJ, Vinjé J and Parashar UD. Noroviruses: a comprehensive review. Journal of Clinical Virology, 2009. Vol: 44 (pp: 1-8).
4. Xerry J, Gallimore CI, Iturriza-Gómara M and Gray JJ. Genetic characterization of Genogroup I Norovirus in outbreaks of gastroenteritis. Journal of Clinical Microbiology, 2010. Vol: 48 (pp: 2560-2562).
5. Ausar SF, Foubert TR, Hudson MH, Vedvick TS and Middaugh CR. Conformational stability and disassembly of Norwalk virus-like particles. The Journal of Biological Chemistry, 2006. Vol: 281 (pp: 19478-19488).
6. Buesa J, Montava R, Abu-Mallouh R, Fos M, Ribes JM, Bartolomé R, Vanaclocha H, Torner N and Domínguez A. Sequential evolution of Genotype GII.4 Norovirus variants causing gastroenteritis outbreaks from 2001 to 2006 in Eastern Spain. Journal of Medical Virology, 2008. Vol: 50 (pp: 1288-1295).
7. Siebenga J, Kroneman A, Vennema H, Duizer E and Koopmans M. Food-borne viruses in Europe network report: the norovirus GII.4 2006b (for US named Minerva-like, for Japan Kobe034-like, for UK V6) variant now dominant in early seasonal surveillance. Eurosurveillance, Jan-Mar 2008. Vol: 13 (Issues 1-3).
8. Okame M, Akihara S, Hansman G, Hainian Y, Tran HT, GiaPhan T, Yagyu F, Okitsu S and Ushijima H. Existence of multiple

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com

Genotypes associated with acute gastroenteritis during 6-year survey of Norovirus infection in Japan. Journal of Medical Virology, 2006. Vol: 78 (pp: 1318-1324).
9. Furuya D, Kuribayashi K, Hosono Y, Tsuji N, Furuya M, Miyazaki K and Watanabe N. Age, viral copy number, and immunosuppressive therapy affect the duration of norovirus RNA excretion in inpatients diagnosed with norovirus infection. Jpn. J. Infect. Dis, 2011. Vol: 64 (pp: 104-108).
10. Reeck A, Kavanagh O, Estes MK, Opekun AR, Gilger MA, Graham DY and Atmar RL. Serological correlate of protection against Norovirus-induced gastroenteritis. Journal Infection Disease, 2010. Vol: 202 (pp: 1212- 1218).
11. Waqas Nasir. A study of Norovirus-HBGA interactions. Chalmers University of Technology. University of Gothenburg, Sweden. December 2009.
12. Arias Castellanos I and González Quiceno M. Determinación de la coinfección entre enterobacterias, parásitos y Norovirus en niños de edades entre tres meses y cinco años con enfermedad diarreica aguda en los barrios arabia y Jerusalén de la localidad de ciudad Bolivar. Universidad Pontificia Javeriana. Facultad de Ciencias, 12 Bogotá.
13. Phillips G, Lopman B, Tam CC, Iturriza-Gomara M, Brown D and Gray J. Diagnosis Norovirus associated infectious intestinal disease using viral load. BMC Infectious Diseases, 2009. 9:63.
14. Hoonmo L. Koo and Herbert L. DuPont. Noroviruses as a potential cause of protracted and lethal disease in immunocompromised patients. Clinical Infectious Disease, 2009. Vol: 49 (pp: 1069-71).

45-16 Ramsey Road Shirley, NY 11967, USA
Tel: 631-624-4882 ·Fax:631-614-7828
E-mail: info@creative-diagnostics.com
www.creative-diagnostics.com