Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test (Feces) Package Insert

REF IMVD-647	English

A rapid, one step test for the qualitative detection of norovirus, rotavirus, adenovirus and astrovirus in human feces.

For professional in vitro diagnostic use only.

【INTENDED USE】

The Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test (Feces) is a rapid chromatographic immunoassay for the qualitative detection of norovirus, rotavirus, adenovirus and astrovirus in human fecal specimens to aid in the diagnosis of norovirus, rotavirus, adenovirus or astrovirus infection.

【SUMMARY】

The Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test is a rapid chromatographic immunoassay for the qualitative detection of norovirus, rotavirus, adenovirus and astrovirus in human fecal specimen. The test utilizes antibody specific for norovirus, rotavirus, adenovirus and astrovirus to selectively detect norovirus, rotavirus, adenovirus and astrovirus in human fecal specimens.

The Combo Test comprises of 4 parts, viz., Norovirus, Rotavirus, Adenovirus and Astrovirus. The details for each part are given below.

For Norovirus Rapid Test (Feces): Noroviruses (NoV) are a genetically diverse group of single stranded RNA, nonenvelopped viruses belonging to the Caliciviridae family. Noroviruses are a major cause of acute gastroenteritis worldwide, often causing explosive outbreaks in institutions. Transmission is predominantly faecal-oral but may be airborne due to aerosolisation of vomitus, which typically contains abundant infectious virus particles. The illness is acute, usually mild, although it has caused fatalities among the frail elderly, and self-limiting and follows an incubation period of 24-48 hours although cases can occur within 12 hours of exposure.The symptoms of Norovirus illness usually include nausea, vomiting, diarrhea, and some stomach cramping. Sometimes people additionally have a low-grade fever, chills, headache, muscle aches, and a general sense of tiredness. The illness often begins suddenly, and the infected person may feel very sick. In most people the illness is self-limiting with symptoms lasting for about 1 or 2 days.[1]

For Rotavirus Rapid Test (Feces): Acute diarrheal disease in young children is a major cause of morbidity worldwide and is a leading cause of mortality in developing countries. Rotavirus is the most common agent responsible for acute gastroenteritis, mainly in young children.[2] Rotavirus is transmitted by oral-fecal route with an incubation period of 1-3 days. Although specimen collections taken within the second and fifth day of the illness are ideal for antigen detection, the rotavirus may still be found while diarrhea continues. Rotaviral gastroenteritis may result in mortality for populations at risk such as infants, the elderly and immunocompromised patients.[3] In temperate climates, rotavirus infections occur mainly in the winter months. With hospitalized children suffering from acute enteric disease up to 50% of the analyzed specimen were positive for rotavirus.[4]

For Adenovirus Rapid Test (Feces): Research has shown that enteric adenoviruses, primarily Ad40 and Ad41, are a leading cause of diarrhea in many of these children, second only to the rotaviruses.[5] These viral pathogens have been isolated throughout the world, and can cause diarrhea in children year round. Infections are most frequently seen in children less than two years of age, but have been found in patients of all ages. Further studies indicate that adenoviruses are associated with 4-17% of all hospitalized cases of viral gastroenteritis.[6] Rapid and accurate diagnosis of gastroenteritis due to adenovirus is helpful in establishing the etiology of gastroenteritis and related patient management.

For Astrovirus Rapid Test (Feces): Astrovirus is a type of virus that was first discovered in 1975 using electron microscopes following an outbreak of diarrhea in humans. Astroviruses are 28–35 nm diameter, icosahedral viruses that have a characteristic five- or sixpointed star-like surface structure when viewed by electron microscopy.[7] Astrovirus has a non-segmented, single stranded, positive sense RNA genome within a non-enveloped icosahedral capsid.[8] Human astroviruses have been shown in numerous studies to be an important cause of gastroenteritis in young children worldwide.

【PRINCIPLE】

The **Norovirus Rapid Test (Feces)** is a qualitative, lateral flow immunoassay for the detection of Norovirus in human feces. The assay uses Genogroup 1 and Genogroup 2 specific monoclonal antibodies coated on the test membrane. During testing, the stool specimen reacts with the conjugate antibodies. The mixture migrates upward on the membrane chromatographically by capillary action to react with Genogroup 1 and 2 antibodies on the membrane and generates a colored line at the level of the T line. The presence of a colored line in T region indicates a positive result for Genogroup 1 and/or Genogroup 2, while its absence indicates a negative result. To serve as a procedural control, a colored line will always appear in the control reaction zone (C) indicating that proper volume of specimen has been added and membrane wicking has occurred.

The **Rotavirus Rapid Test (Feces)** is a qualitative, lateral flow immunoassay for the detection of rotavirus in human feces. In this test, the membrane is pre-coated with rotavirus specific monoclonal antibody on the T line region of the test. During testing, the specimen reacts with the particle coated with rotavirus antibody. The mixture migrates upward on the membrane chromatographically by capillary action to react with rotavirus antibody on the membrane and generate a colored line. The presence of the colored line in test line region indicates a positive result, while their absence indicates a negative result. To serve as a procedural control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

The **Adenovirus Rapid Test (Feces)** is a qualitative, lateral flow immunoassay for the detection of adenovirus in human feces. In this test, the membrane is pre-coated with adenovirus specific monoclonal antibody on the T line region of the test. During testing, the specimen reacts with the particle coated with adenovirus antibody. The mixture migrates upward on the membrane chromatographically by capillary action to react with adenovirus antibody on the membrane and generate a colored line. The presence of the colored line in test line region indicates a positive result, while their absence indicates a negative result. To serve as a procedural control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

The **Astrovirus Rapid Test (Feces)** is a qualitative, lateral flow immunoassay for the detection of astrovirus in human fecess. In this test, the membrane is pre-coated with astrovirus specific monoclonal antibody on the test line region of the test. During testing, the specimen reacts with the particle coated with astrovirus antibody. The mixture migrates upward on the membrane chromatographically by capillary action to react with astrovirus antibody on the membrane and generate a colored line in the test line region. The presence of this colored line in the test region indicates a positive result, while its absence indicates a negative result. To serve as a procedural control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

【REAGENTS】

The Combo Test comprises of four parts and details of each part are given herewith.

The Norovirus rapid test contains Norovirus Genogroup 1 and Genogroup 2 monoclonal antibody coated particles and Norovirus Genogroup 1 and Genogroup 2 monoclonal antibodies coated on the membrane.

The Rotavirus rapid test contains anti-rotavirus antibody coated particles and anti-rotavirus antibody coated on the membrane.

The Adenovirus rapid test contains anti-adenovirus antibody coated particles and anti-adenovirus antibody coated on the membrane.

The Astrovirus rapid test contains anti-astrovirus antibody coated particles and anti-astrovirus antibody coated on the membrane.

【PRECAUTIONS】

Please read all the information in this package insert before performing the test.

- For professional *in vitro* diagnostic use only.
- Do not use after the expiration date. Do not reuse the test.
- Store in a dry place at 2-30 °C (36-86 °F), avoiding areas of excess moisture. If the foil packaging is damaged or has been opened, please do not use.
- Do not eat, drink or smoke in the area where the specimens or kits are handled.
- Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimens.
- The used test should be discarded according to local regulations.
- Humidity and temperature may adversely affect results.
- Wash hands thoroughly before and after handling.
- Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority.
- Use the test only once. **Keep the test upright while testing. Do not move or turn the test upside down**.
- Keep out of the reach of children.
- The kit must not be frozen or used after the expiration date printed on the package.
- Components provided in the kit are approved for use in the Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test. Do not use any other commercial kit component.

【STORAGE AND STABILITY】

The kit can be stored at room temperature or refrigerated (2-30 °C). The test is stable through the expiration date printed on the sealed pouch. The test must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

Note: It is suggested to use the test within one hour after removing it from the foil pouch.

【SPECIMEN COLLECTION AND PREPARATION】

- The fecal specimen must be collected in a clean, dry, waterproof container containing no detergents, preservatives or transport media.
- No dietary restrictions are necessary before using the Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test.
- Bring the necessary reagents and fecal specimen to room temperature before use.
- If specimens are to be shipped, they should be packed in compliance with local regulations covering the transportation of etiologic agents.

【MATERIALS PROVIDED】

- Test Cups (with dilution buffer)
- Droppers
- Package Insert

【MATERIALS REQUIRED BUT NOT PROVIDED】

- Timer
- Centrifuge
- Specimen Container
- Pipette

【DIRECTIONS FOR USE】

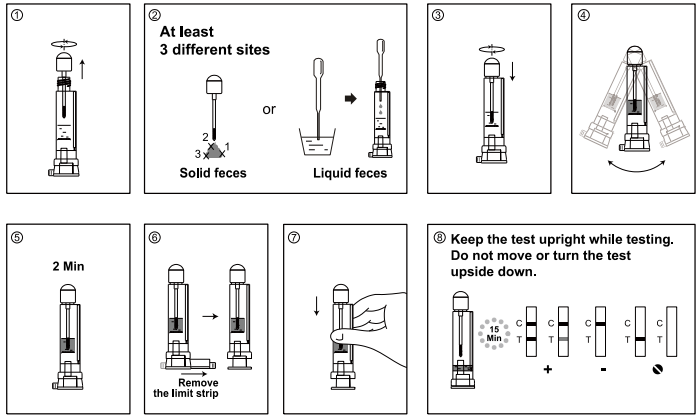
Before performing the test, allow the test specimen to reach room temperature (15-30 °C), stool samples must be collected following the instruction below.

1. Wash your hands with soap and rinse with clear water.
2. **Collect fecal specimens:**
   Collect sufficient quantity of feces (1-2 mL or 1-2 g) in a clean, dry specimen collection container. Best results will be obtained if the assay is performed within 6 hours after collection. Specimen collected may be stored for 3 days at 2-8°C if not tested within 6 hours. For long term storage, specimens should be kept below -20°C.
3. Bring the pouch to room temperature before opening it. Remove the test cup from the foil pouch and use it as soon as possible. Best results will be obtained if the test is performed immediately after opening the foil pouch.
4. **Process fecal specimens:**
   - **For Solid Specimens:**
     Unscrew the cap of the test cup and take out the specimen collection applicator.
     Randomly stab the specimen collection applicator into the fecal specimen in **at least 3 different sites**. Do not scoop the fecal specimen.
   - **For Liquid Specimens:**
     Hold the dropper vertically, aspirate fecal specimens, and then transfer **2 drops of the liquid** specimen (approximately 50 µL) into the test cup containing the dilution buffer.
5. Insert the specimen collection applicator back into the test cup and tighten the cap.
6. Shake the test cup for about **10-15 seconds** to mix well. Leave the cup for reaction for 2 minutes.
7. Remove the plastic limit strip of the test cup.
8. Put the test cup on a clean and level surface, press the cup body from the top to the bottom and start the timer.

NOTE: Keep the test cup upright during the test developing. Do not move or turn the test cup upside down.

9. **Read results at 15 minutes**. Do not read results after 20 minutes.

Note: If the specimen does not migrate (presence of particles), open a new test cup, repeat step 4 and centrifuge the diluted specimen contained in the test cup with a clean tube. Pipette 1-1.5 mL of supernatant, dispense into the test cup and insert the specimen collection applicator back into the test cup and tighten the cap. Continue from step 7-8 onwards in the above instructions for use and start the timer



【INTERPRETATION OF RESULTS】

POSITIVE:* **Two colored lines appear in the Noro/Rota/Adeno/Astro window.** One colored line should be in the control region (C) and another colored line should be in the test region (T).
This result means that there is the presence of the Noro/Rota/Adeno/Astro antigen in feces and that you should consult a physician.
***NOTE**: The intensity of the color in the test line region (T) will vary depending on the concentration of norovirus and/or rotavirus and/or adenovirus and/or astrovirus antigens present in the specimen. Therefore, any shade of color in the test line region (T) should be considered positive.

NEGATIVE: **One colored line appears in the control line region (C). No line appears in the test line region (T).**
This result means that the presence of the norovirus or rotavirus or adenovirus or astrovirus in feces was not detectable.

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

【QUALITY CONTROL】

A procedural control is included in the test. A colored line appearing in the control line region(C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

【LIMITATIONS】

1. The Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test (Feces) is for *in vitro* diagnostic use only. The test should be used for the detection of human norovirus, rotavirus, adenovirus and astrovirus in fecal specimens only. Neither the quantitative value nor the rate of increase in human norovirus, rotavirus, adenovirus and astrovirus concentration can be determined by this qualitative test.
2. The Norovirus,Rotavirus,Adenovirus and Astrovirus Combo Rapid Test (Feces) will only indicate

the presence of norovirus, rotavirus, adenovirus and astrovirus in the specimen and should not be used as the sole criteria for the conforming rotavirus and adenovirus to be etiological agent for diarrhea.

3. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
4. If the test result is negative and clinical symptoms persist, additional testing using other clinical methods is recommended. A negative result does not at any time preclude the possibility of norovirus, rotavirus, adenovirus and astrovirus infection with low concentration of virus particles.
5. For Norovirus test: fecal specimen from infant under one year old can produce a false positive result.

【PERFORMANCE CHARACTERISTICS】

Clinical performance

1. Norovirus

The performance of the Norovirus Rapid Test has been evaluated with 150 clinical specimens collected from children in comparison with Other Norovirus Rapid test. The results show that the relative sensitivity of the Norovirus Rapid Test (Feces) is 98.0% and the relative specificity is 98.0%.

Method		Other Rapid Test		Total Results
Norovirus Rapid Test	Results	Positive	Negative	
	Positive	49	2	51
	Negative	1	98	99
Total Results		50	100	150

Relative Sensitivity: 98.0% (95%CI:*89.4%-99.9%) *Confidence Intervals
Relative Specificity: 98.0% (95%CI:*93.0%-99.8%)
Relative Accuracy: 98.0% (95%CI:*94.3%-99.6%)

2. Rotavirus

The performance of the Rotavirus Rapid Test has been evaluated with 150 clinical specimens collected from children in comparison with Other Rotavirus Rapid test. The results show that the relative sensitivity of the Rotavirus Rapid Test (Feces) is 98.0% and the relative specificity is 97.0%.

Method		Other Rapid Test		Total Results
Rotavirus Rapid Test	Results	Positive	Negative	
	Positive	49	3	52
	Negative	1	97	98
Total Results		50	100	150

Relative Sensitivity: 98.0% (95%CI:*89.4%-99.9%) *Confidence Intervals
Relative Specificity: 97.0% (95%CI:*91.5%-99.4%)
Relative Accuracy: 97.3% (95%CI:*93.3%-99.3%)

3. Adenovirus

The performance of the Adenovirus Rapid Test has been evaluated with 150 clinical specimens collected from children in comparison with Other Adenovirus Rapid test. The results show that the relative sensitivity of the Adenovirus Rapid Test (Feces) is 96.0% and the relative specificity is 98.0%.

Method		Other Rapid Test		Total Results
Adenovirus Rapid Test	Results	Positive	Negative	
	Positive	48	2	50
	Negative	2	98	100
Total Results		50	100	150

Relative Sensitivity: 96.0% (95%CI:*86.3%-99.5%) *Confidence Intervals
Relative Specificity: 98.0% (95%CI:*93.0%-99.8%)
Relative Accuracy: 97.3% (95%CI:*93.3%-99.3%)

4. Astrovirus

The performance of the Astrovirus Rapid Test has been evaluated with 140 clinical specimens collected from children in comparison with Other Astrovirus Rapid test. The results show that the relative sensitivity of the Astrovirus Rapid Test (Feces) is 87.5% and the relative specificity is 99.0%.

Method		Other Rapid Test		Total Results
Astrovirus Rapid Test	Results	Positive	Negative	
	Positive	35	1	36
	Negative	5	99	104
Total Results		40	100	140

Relative Sensitivity: 87.5% (95%CI:*73.2%-95.8%) *Confidence Intervals
Relative Specificity: 99.0% (95%CI:*94.6%-99.9%)
Overall Accuracy: 95.7% (95%CI:*90.9%-98.4%)

Precision

Precision-Repeatability

Precision-repeatability has been determined by using nine specimens: negative, norovirus genogroup 1 middle positive, norovirus Genogroup 2 middle positive, rotavirus low positive, rotavirus middle positive, adenovirus low positive, adenovirus middle positive, astrovirus low positive and astrovirus middle positive specimens. The study was performed 5 replicates per day for 3 consecutive days by one operator using 1 lot of Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test, 1 lot of stool collection buffer. No difference was detected in intra lot.

Precision-Reproducibility

Precision-reproducibility has been determined by using nine specimens: negative, norovirus genogroup 1 middle positive, norovirus Genogroup 2 middle positive, rotavirus low positive, rotavirus middle positive, adenovirus low positive, adenovirus middle positive, astrovirus low positive and astrovirus middle positive specimens. The study was performed 3 replicates per day for 5 consecutive days in 3 different sites using 3 separate lots of Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test (one lot per site), and three operators per site. No difference was detected between days, sites, lots and operators.

Cross-Reactivity

Cross reactivity with following organisms has been studied at 1.0E+07 org/mL. The following organisms were found negative when tested with the Norovirus, Rotavirus, Adenovirus and Astrovirus Combo Rapid Test:

Corynebacterium diphtheria	*Neisseria gonorrhea*	*Shigella sonnei*
Pseudomonas aeruginosa	*Shigella flexneri*	*Clostridium difficile*
Enterococcus faecalis	*Enterococcus faecium*	*Gardnerella vaginalis*
Proteus vulgaris	*Shigella dysenteriae*	*Helicobacter pylori*
Candida albicans	*Proteus mirabilis*	*E.coli*

Interfering Substances

The following potentially interfering substances were added to norovirus, rotavirus, adenovirus and astrovirus negative and positive specimens. It does not interfere with the normal results.

Ascorbic acid: 20 mg/dL	Oxalic acid: 60 mg/dL	Bilirubin: 100 mg/dL
Uric acid: 60 mg/dL	Aspirin: 60 mg/dL	Urea: 2000 mg/dL
Glucose: 2000 mg/dL	Caffeine: 40 mg/dL	Albumin: 6000 mg/dL

【BIBLIOGRAPHY】

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Index of Symbols

IVD	For *in vitro* diagnostic use only	Σ	Tests per kit	REF	Catalog #
2°C 30°C	Store between 2-30°C		Use by		Do not reuse
	Do not use if package is damaged	LOT	Lot number	EC REP	Authorized representative in EU
	Manufacturer		Consult instructions for use		

Hangzhou AllTest Biotech Co.,Ltd.
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Number: 14601166501
Revision Date: 2023-05-30