Norovirus/Rotavirus/Adenovirus Combo Rapid Test Package Insert

REF VINRA-647	English

INTENDED USE

The VivaDiag™ Norovirus/Rotavirus/Adenovirus Combo Rapid Test is a rapid chromatographic immunoassay for the qualitative detection of norovirus, rotavirus and adenovirus and in human feces specimens. It is intended to be used as an aid in the diagnosis of infection with norovirus, rotavirus and adenovirus. For *in vitro* diagnostic use only.

SUMMARY

Norovirus, sometimes referred to as the winter vomiting bug, is the most common cause of gastroenteritis. Infection is characterized by diarrhea, vomiting, and stomach pain. Blood is not usually present. Fever or headaches may also occur. This usually develops 12 to 48 hours after being exposed. Recovery typically occurs within 1 to 3 days. Complications may include dehydration.

The virus is usually spread by the fecal-oral route. This may be by contaminated food or water or person-to-person contact. It may also spread via contaminated surfaces or through the air. Risk factors include unsanitary food preparation and sharing close quarters. Diagnosis is generally based on symptoms. Confirmatory testing may be done for public health purposes. Norovirus results in about 685 million cases of disease and 200,000 deaths globally a year. It is common both in the developed and developing world. Those under the age of five are most often affected and in this group it results in about 50,000 deaths in the developing world. Disease more commonly occurs in winter months. It often occurs in outbreaks, especially among those living in close quarters. In the United States, it is the cause of about half of food borne disease outbreaks. The disease is named after Norwalk, Ohio, where an outbreak occurred in 1968.

Rotavirus is the most common agent responsible for acute gastroenteritis, mainly in young children. Its discovery in 1973 and its association with infantile gastro-enteritis represented a very important advancement in the study of gastro-enteritis not caused by acute bacterial infection. Rotavirus is transmitted by orofacial 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 Ag detection, the rotavirus may still be found while diarrhoea continues. Rotaviral gastroenteritis may result in mortality for populations at risk such as infants, the elderly, and immunocompromised patients. In temperate climates, rotavirus infections occur mainly in the winter months. Endemics as well as epidemics affecting some thousand people have been reported. With hospitalized children suffering from acute enteric disease up to 50% of the analysed specimen were positive for rotavirus. The viruses replicate in the cell nucleus and tend to be host species specific producing a characteristic cytopathic effect (CPE). Because rotavirus is extremely difficult to culture, it is unusual to use isolation of the virus in diagnosing an infection. Instead, a variety of techniques have been developed to detect rotavirus in feces.

Acute diarrheal disease in young children is a major cause of morbidity worldwide and is a leading cause of mortality in developing countries. 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. 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 4-15% of all hospitalized cases of viral gastroenteritis.

Rapid and accurate diagnosis of gastroenteritis due to adenovirus is helpful in establishing the etiology of gastroenteritis and related patient management. Other diagnostic techniques such as electron microscopy (EM) and nucleic acid hybridization are expensive and labor-intensive. With the self-limiting nature of adenovirus infection, such expensive and labor-intensive tests may not be necessary.

PRINCIPLE

The Rota/Adeno Ag Rapid Test is a lateral flow chromatographic immunoassay. The test device consists of: 1) a burgundy colored conjugate pad containing mouse-anti-adenovirus monoclonal antibody 1 and mouse-anti- rotavirus monoclonal antibody 1 conjugated with colloidal gold (antibody conjugates), 2) a nitrocellulose membrane strip containing two test lines (R line and A line) and a control line (C line). The R line is pre-coated with mouse-anti-rotavirus monoclonal antibody 2, the A line is pre-coated with mouse-anti-adenovirus monoclonal antibody 2, and the C line is pre-coated with goat anti-mouse IgG antibody.

During testing, the specimen reacts with antibody conjugated with coloured particles and pre-coated on the sample pad of the test. The mixture then migrates along the membrane by capillary action and interacts with components on the membrane. If there is sufficient rotavirus in the specimen, a coloured line will form in the test line (R line) region of the membrane. If there is sufficient adenovirus in the specimen, a coloured line will form in the test line (A line) region of the membrane. The presence of this coloured line indicates a positive test result, while its absence indicates a negative test result. The appearance of a coloured line in the control line region serves as a procedural control indicating that the proper volume of specimen has been added and membrane wicking has occurred.

The Norovirus GI/GII Rapid Test has been designed to detect norovirus GI and GII through visual interpretation of color development in the internal strip. The membrane was immobilized with anti-norovirus GI antibodies and anti-norovirus GII antibodies on the test region.

During the test, the specimen reacts with colored anti-norovirus GI antibodies colloidal gold conjugates and anti-norovirus GII antibodies colloidal gold conjugates, which were precoated on the conjugate pad of the test. The mixture then moves on the membrane by a capillary action, and interact with reagents on the membrane. If there were enough norovirus GI in specimens, a colored band will form at the T1 region of the membrane. Similarity, if there were enough norovirus GII in specimens, a colored band will form at the T2 region of the membrane. Presence of colored band(s) indicates a positive result, while its absence indicates a negative result. Appearance of a colored band at the control region serves as a procedural control. This indicates that proper volume of specimen has been added and membrane wicking has occurred.

WARNINGS AND PRECAUTIONS

- For professional *in vitro* diagnostic use only.
- For single use. Do not reuse tests.
- Do not interchange or mix reagents from different lots.
- Do not use the test if its foil pouch is damaged.
- Do not use the test after the expiration date.
- This test contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not completely guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious and handled by observing usual safety precautions (e.g. do not ingest or inhale).
- Avoid cross-contamination of specimens by using a new specimen collection container for each specimen obtained.
- Do not eat, drink or smoke in the area where the specimens or kits are handled. Protective clothing such as laboratory coats, disposable gloves and eye protection are recommended. Observe established precautions against microbiological hazards throughout testing. Follow standard procedures for proper disposal of specimens in accordance with local regulations.
- Humidity and temperature can adversely affect results.
- The components of the test (e.g. antibodies/chemicals) do not cause any danger if the test is used according to the instructions.
- Do not perform the test in a room with strong air flow, i.e. an electric fan or strong air-conditioning.
- Follow the instructions for use carefully. Inform the patients of the procedures of the collection and dilution of the stool sample.
- Used testing materials should be discarded according to local regulations.

COMPOSITION

Materials provided and available for purchase:

1. Test Device in foil pouch
2. Specimen collection container with buffer
3. Package insert
4. Dropper

Materials required but not provided:

1. Timer
2. Personal protective equipment, such as protective gloves, medical masks, lab coats, etc.
3. Appropriate biohazardous waste containers and disinfectants.

STORAGE AND STABILITY

- Store the test kit in a cool, dry place between 36-86°F (2-30°C). Keep away from light. Exposure to temperature and/or humidity outside the specified conditions may cause inaccurate results.
- Do not freeze. Use the test kit at temperatures between 59-86°F (15-30°C).
- Use the test kit between 10-90% humidity.
- Do not use the test kit beyond the expiration date (printed on the foil pouch and box).
- Do not remove the test device from the pouch until ready to use. The test device should be used within 1 hour once opened.

Note: *All expiration dates are printed in Year-Month-Day format. 2022-06-18 indicates June 18, 2022.*

SPECIMEN COLLECTION AND HANDLING

The Norovirus/Rotavirus/Adenovirus Combo Rapid Test is intended only for use with human feces specimens.

1) Specimen collection

Specimen collection and pre-treatment:

Use the specimen collection tube for specimen collection. Best results will be obtained if the assay is performed within 6 hour after collection.

For solid specimens:

1. Unscrew and remove the applicator stick attached on the cap. Be careful not to spill or spatter solution from the tube. Collect specimen by inserting the applicator stick into at least 6 different sites of the feces to collect approximately 50 mg of feces (equivalent to 1/4 of a pea).
2. Place the applicator back into the tube and screw the cap tightly.
3. Shake the specimen collection tube vigorously to mix the specimen and buffer.

For liquid specimens:

1. Hold the dropper vertically, aspirate feces specimens, and then transfer 2 drops (approximately 50 μL) into the specimen collection tube containing buffer.
2. Place the applicator back into the tube and screw the cap tightly.

Solid Specimen　　Liquid Specimen

2) Specimen handling

Perform the testing immediately after the specimen collection. Do not leave the specimens at room temperature for prolonged periods. Specimens may be stored at 2-8°C for up to 72 hours. Specimens prepared in the specimen collection tube may be stored for 12 months at -20°C if not tested within 1 hour after preparation.

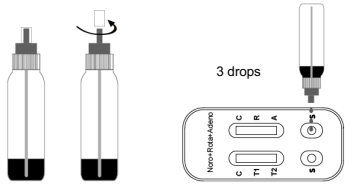
Note:

- *Patients should not collect samples during their menstrual period, if they have bleeding hemorrhoids, blood in the urine, or if they have strained during bowel movement.*
- *The excretion peak of Rv from gastroenteritis patients' feces is 3-5 days after symptom appears. Positive results will not occur if the feces are collected long time after the diarrhea appears.*
- *A sample must be collected in a clean and dry container.*

TEST PROCEDURE

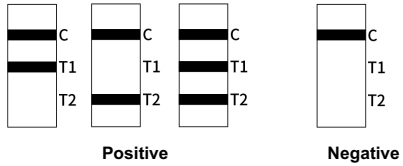
Please read the instructions carefully before testing. Allow equipment, buffers, and samples to equilibrate to room temperature (15°C to 30°C) prior to testing.

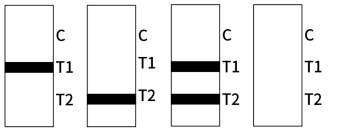
1. Take out a test device from sealed foil pouch and put it on a clean and level surface.
2. Hold the specimen collection tube upright and open the cap onto the specimen collection tube. Apply 3 drops of the extracted specimen into the specimen well. Please avoid bubbles during applying.
3. Wait for the red line(s) to appear. Read the test result at **10 minutes**. Don't read the result after 20 minutes.



INTERPRETATION OF TEST RESULTS

Fo Norovirus GI/GII





Positive*:

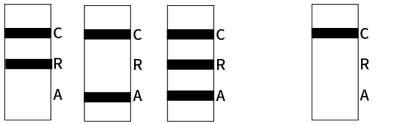
- **Norovirus GⅠPositive:** Two distinct colored lines appear. One line should be in the control line region (C) and another line should be in the test line region (T1).
- **Norovirus GⅡ Positive:** Two distinct colored lines appear. One line should be in the control line region (C) and another line should be in the test line region (T2).
- **Norovirus GⅠand GⅡ Positive:** Three distinct colored lines appear. One line should be in the control line region (C) and two lines should be in the test line region (T1 and T2).

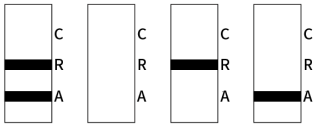
***Note:** The intensity of the color in the test line region (T) may vary depending on the concentration of Norovirus present in the specimen. Therefore, any shade of color in the test line region (T) should be considered positive.*

Negative: One red line appears in the control region(C). No apparent red or pink line appears in the test region (T).

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.

For Rota/Adeno





Invalid

Positive*:

Rotavirus Positive: Two distinct colored lines appear. One line should be in the control line region (C) and another line should be in the test line region (R), the test result indicates the presence of Rotavirus.
Adenovirus Positive: Two distinct colored lines appear. One line should be in the control line region (C) and another line should be in the test line region (A), the test indicates the presence of Adenovirus.
Rotavirus and Adenovirus Positive: Three distinct colored lines appear. One line should be in the control line region (C) and two lines should be in the test line region (R and A), the test indicates the presence of Rotavirus and Adenovirus.

Note: *The intensity of the color in the test line region (R and A) may vary depending on the concentration of Rotavirus and Adenovirus present in the specimen. Therefore, any shade of color in the test line region (R and A) should be considered positive.*

Negative: One colored line appears in the control line region (C). No apparent colored line appears in the test line region (*R and A*).

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. Control standards are not supplied with this kit; however, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

LIMITATIONS

- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore, recommended that these products be treated as potentially infectious, and handled observing the usual safety precautions (do not ingest or inhale).
- Avoid cross-contamination of specimens by using a new specimen collection container for each specimen obtained.
- Read the entire procedure carefully prior to performing any tests.

PERFORMANCE

1. Accuracy

The performance of the VivaDiag™ Norovirus/Rotavirus/Adenovirus Combo Rapid Test has been evaluated with 330 clinical specimens collected from children and young adults in comparison with the other rapid test. The results are summarized in the following table:

1.1 Accuracy of Rota

VivaDiag™ Norovirus/Rotavirus/Adenovirus Combo Rapid Test	Other rapid test		
	Positive	Negative	Total
Positive	121	0	121
Negative	0	209	209
Total	121	209	330
Sensitivity	＞99.9% (121/121, 95%CI, 96.9%~100%)		
Specificity	＞99.9% (209/209, 95%CI, 98.2%~100%)		
Accuracy	＞99.9% (330/330, 95%CI, 98.9%~100%)		

1.2 Accuracy of Adeno

VivaDiag™ Norovirus/Rotavirus/Adenovirus Combo Rapid Test	Other rapid test		
	Positive	Negative	Total
Positive	103	0	103
Negative	0	227	227
Total	103	227	330
Sensitivity	＞99.9% (103/103, 95%CI, 96.4%~100%)		
Specificity	＞99.9% (227/227, 95%CI, 98.3%~100%)		
Accuracy	＞99.9% (330/330, 95%CI, 98.9%~100%)		

A total of 382 samples from susceptible subjects were tested by the Norovirus GI/GII Rapid Test for Norovirus GI Test and by a Latex Agglutination. Comparison for all subjects is showed in the following table:

1.3 Clinical Performance For GI Test:

VivaDiag™ Norovirus/Rotavirus/Adenovirus Combo Rapid Test	Latex Agglutination		
	Positive	Negative	Total
Positive	224	0	224
Negative	2	156	158
Total	226	156	382
Sensitivity	99.1% (224/226, 95%CI, 96.8%-99.9%)		
Specificity	>99.9% (156/156, 95%CI, 97.7%-100.0%)		
Accuracy	99.5% (380/382, 95%CI, 98.1%-99.9%)		

1.4 Clinical Performance For GⅡ Test:
A total of 239 samples from susceptible subjects were tested by the Norovirus GI/GII Rapid Test for Norovirus GⅡ Test and by a Latex Agglutination. Comparison for all subjects is showed in the following table:

VivaDiag™ Norovirus/Rotavirus/Adenovirus Combo Rapid Test	Latex Agglutination		
	Positive	Negative	Total
Positive	82	1	83
Negative	0	156	157
Total	82	157	239
Sensitivity	>99.9% (82/82, 95%CI, 95.6%-99.9%)		
Specificity	99.4% (156/157, 95%CI, 96.5%-99.9%)		
Accuracy	99.6% (238/239, 95%CI, 97.7%-99.9%)		

2. Cross-Reactivity

The following organisms showed no cross-reactivity when tested with the Rota/Adeno rapid test at the concentration of 1.0 x 10^9 organisms/mL.

Acinetobacter calcoaceticus	*Group C rotavirus*
Astrovirus	*Hemophilus influenzae*
Branhamella catarrhalis	*Klebsiella pneumoniae*
Candida albicans	*Neisseria gonorrhea*
Chlamydia trachomatis	*Neisseria meningitides*
E.coli	*Proteus mirabilis*
Enterovirus	*Proteus vulgaris*
Enterococcus faecalis	*Pseudomonas aeruginosa*
Group B streptococcus	*Salmonella choleraesius*
Group C streptococcus	*Staphylococcus aureus*
Group B rotavirus	/

3. Interference Substances:

There was no interference for potential interfering substances listed below.

Interfering substance	Concentration in specimen	Interfering substance	Concentration in specimen
Bilirubin	600 μmol/L	Hemoglobin	10 mg/mL
Triglyceride	5 g/L	Oxalic acid	10 mg/mL
Ascorbic acid	100 mg/dL	Atropine	40 mg/dL

REFERENCES

1. Wadell, G. Laboratory Diagnosis of Infectious Diseases: Principles and Practices. New York: Springer-Verlag, Volume II, 1988: 284-300.
2. WILHELMI I, ROMAN E, SANCHEZ-FAUQUIER A. Viruses causing gastroenteritis. Clin Microbiol Infect. April. 2003, vol.9:247-262
3. Cubitt, WD (1982) Rotavirus Infection: An Unexpected Hazard in Units Caring for the Elderly. Geriatric Medicine Today 1: 33-38
4. Wood, D. J., K. Bijlsma, J. C. de Jong, and C. Tonkin. "Evaluation of a Commercial Monoclonal Antibody-Based Enzyme Immunoassay for Detection of Adenovirus Types 40 and 41 in Stool Specimens." Journal of Clinical Microbiology, June 1989; 27(6): 1155-1158.
5. Thomas, Eva. E., D. Roscoe, L. Book, B. Bone, L. Browne, and V. Mah. "The Utility of Latex Agglutination Assays in the Diagnosis of Pediatric Viral Gastroenteritis." Am. J. Clin. Pathol. 1994; 101:742-746.
6. Norovirus (vomiting bug). nhs.uk. 2017-10-19. Retrieved 8 June 2018.
7. Norovirus Symptoms. CDC. 24 June 2016. Retrieved 29 December 2017.
8. Brunette GW (2017). CDC Yellow Book 2018: Health Information for International Travel. Oxford University Press. p. 269. ISBN 9780190628611.
9. Norovirus Worldwide. CDC. 15 December 2017. Retrieved 29 December 2017.
10. Global Burden of Norovirus and Prospects for Vaccine Development (PDF). CDC. August 2015. p. 3. Retrieved 29 December 2017.
11. Nguyen GT, Phan K, Teng I, Pu J, Watanabe T (October 2017). A systematic review and metaanalysis of the prevalence of norovirus in cases of gastroenteritis in developing countries". Medicine. 96 (40): e8139. doi:10.1097/MD.0000000000008139. PMC 5738000. PMID 28984764.
12. Thomas, Eva. E., D. Roscoe, L. Book, B. Bone, L. Browne, and V. Mah. "The Utility of Latex Agglutination Assays in the Diagnosis of Pediatric Viral Gastroenteritis." Am. J. Clin. Pathol. 1994; 101:742-746.
13. Conly J, Johnston B (January 2003). "Norwalk virus - Off and running". The Canadian Journal of Infectious Diseases. 14 (1): 11–3. doi:10.1155/2003/702517. PMC 2094906.PMID 18159419.
14. Norovirus: The perfect pathogen. Knowable Magazine.

INDEX OF SYMBOLS

	Consult instructions for use		Use by	Σ	Contains sufficient for <n> tests
IVD	For *in vitro* diagnostic use only	LOT	Lot number	REF	Catalog number
2°C-30°C	Storage temperature limitations		Manufacturer		Do not reuse
EC REP	Authorized Representative				

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CE
IVD

Number: 1624073201
Effective date: 2024-06-10