

RIDASCREEN® Adenovirus

REF C1001



1. Intended use

For *in vitro* diagnostic use. RIDASCREEN® Adenovirus is an enzyme immunoassay for qualitative identification of adenoviruses in human stool samples.

2. Summary and explanation of the test

Adenoviruses can be recognized by their typically icosahedral form with spiked structures on the surface. More than 50 different types of the adenovirus are known and can cause infections in the eyes, the respiratory tract, or the intestinal tract. Infections of the intestinal tract are caused by the types 40 and 41 in particular. Enteritis may also occur as a concomitant symptom of infections due to other types of the virus. Regarding viral diarrhea in children, adenoviruses and astroviruses rank equally as the next most frequent causes after rotaviruses. Adults can also become ill with this kind of infection. Because gastroenteritis caused by an adenovirus cannot be clinically differentiated from infection with a rotavirus or an astrovirus, patients should always be tested for all three pathogens. The monoclonal antibodies used in RIDASCREEN® Adenovirus are reactive to the adenovirus-specific hexon protein, and the range includes both enteral types 40 and 41 as well as most other types of the virus which cause eye infections and infections of the respiratory tract.

3. Test principle

The RIDASCREEN® Adenovirus Test employs monoclonal antibodies in a sandwich-type method. A monoclonal antibody to the hexon antigen of the adenoviruses is coated to the well surface of the microwell plate.

A pipette is used to place a suspension of the stool sample to be examined as well as control specimens into the well of the microwell plate together with biotinylated monoclonal anti-adenovirus antibodies (conjugate 1) for incubation at room temperature (20 - 25 °C). After a wash step, streptavidin poly-peroxidase conjugate (Conjugate 2) is added and it is incubated again at room temperature (20 - 25 °C). With the presence of adenoviruses in a stool sample, a sandwich complex will form which consists of immobilized antibodies, the adenovirus antigens, and the antibodies conjugated with the biotin-streptavidin-peroxidase complex. Another wash step removes the unattached streptavidin poly-peroxidase conjugate. After adding the substrate, the attached enzyme changes the colour of the previously colourless solution in the wells of the microwell plate to blue if the test is positive. Addition of a stop reagent changes the color from blue to yellow. The extinction is proportional to the concentration of adenoviruses found in the specimen.

4. Reagents provided

The reagents in the kit are sufficient for 96 determinations.

Plate	96	Microwell plate, 12 microwell strips (which can be divided) in the strip holder; coated with monoclonal anti-adenovirus antibodies (mouse)
Diluent 1	100 ml	Sample dilution buffer, protein-buffered NaCl solution; ready to use, blue color
Wash buffer	100 ml	Wash buffer, phosphate buffered NaCl solution (concentrated 10-fold); contains 0.1% thimerosal
Control +	2 ml	Positive control; inactivated adenovirus culture; ready for use
Control -	2 ml	Negative control (sample dilution buffer); ready for use
Conjugate 1	13 ml	Biotin-conjugated monoclonal anti-adenovirus antibodies (mouse) in stabilized protein solution; ready for use; green color
Conjugate 2	13 ml	Streptavidin poly-peroxidase conjugate in stabilized protein solution; ready for use; orange colored
Substrate	13 ml	Hydrogen peroxide/TMB; ready for use
Stop	12 ml	Stop reagent; 1 N sulphuric acid; ready for use

Dangerous substances are indicated according to labelling obligations. For more details, refer to Safety Data Sheets (SDS) at www.r-biopharm.com.

5. Storage instructions

All reagents must be stored at 2 - 8 °C and can be used until the expiry date printed on the label. Providing the diluted wash buffer is stored at 2 - 8 °C, it can be used for a maximum of 4 weeks. Microbial contamination must be prevented. After the expiry date, the quality guarantee is no longer valid.

The aluminum bag must be opened with scissors in such a way that the clip seal is not torn off. Any microwell strips which are not required must be returned to the aluminum bag and immediately stored at 2 - 8 °C.

The colorless substrate must also be protected from direct light to prevent it from decomposing or turning blue due to auto-oxidation. Once the substrate has turned blue, it must not be used.

6. Reagents required but not provided

6.1 Necessary reagents

The following reagents are required to perform the RIDASCREEN® Adenovirus test:

Reagents
Distilled or deionized water

6.2 Necessary laboratory equipment

The following equipment is required to perform the RIDASCREEN® Adenovirus test:

Equipment
Test tubes
Disposable pipettes (Article no.: Z0001)
Vortex mixer (optional, see 9.3.)
Micropipette for 50 - 100 µl and 1 ml volume
Measuring cylinder (1,000 ml)
Timer
Washing device for microtiter plates or multichannel pipette (300 µl).
Photometer for microtiter plates (450 nm, reference filter 620-650 nm)
Filter paper (laboratory towels)

7. Warnings and precautions for the users

For *in vitro* diagnostic only.

This test must only be carried out by trained laboratory personnel. The guidelines for working in medical laboratories must be followed. Always adhere strictly to the user instructions for this test. Specimens or reagents must not be pipetted by mouth, and contact with injured skin or mucous membranes must be prevented. Wear personal safety gear (suitable gloves, laboratory coat, safety glasses) when handling the specimens, and wash hands after finishing the test. Do not smoke, eat, or drink in areas where samples are being processed.

For more details, refer to Safety Data Sheets (SDS) at www.r-biopharm.com.

The kit includes a positive control that contains an inactivated adenovirus culture. It must be treated as potentially infectious material and handled in accordance with the national safety regulations, just like the patient samples.

The wash buffer contains 0.1 % thimerosal as preservative. This substance must not be allowed to come into contact with skin or mucous membranes.

Ensure the proper and responsible disposal of all reagents and materials after their use. For disposal, please adhere to national regulations.

8. Collection and storage of specimens

Stool samples must be taken as soon as possible within three days after occurrence of the initial symptoms of diarrhea. Until it is used, store the test material at 2 - 8 °C. If the material cannot be used for a test within three days, we recommend storage at -20 °C or colder. Avoid freezing and thawing the specimen repeatedly. After diluting a stool sample in sample dilution buffer 1:11, it can be stored at 2 - 8 °C for use within seven days (Tab. 1).

Tab. 1: Specimen storage

Undiluted stool specimen		Diluted specimen
2 - 8 °C	≤ - 20 °C	2 - 8 °C
≤ 3 days	> 3 days	≤ 7 days

Stool samples and rectal smears should not be collected in transport containers which contain transport media with preservatives, animal sera, metal ions, oxidizing agents, or detergents since these may interfere with the RIDASCREEN® Adenovirus Test. If rectal smears are used, make sure that the volume of stool material is sufficient (approx. 100 mg) for the test.

Contact tracing should include stool samples taken from contact persons who do not exhibit clinical symptoms, in order to identify asymptomatic carriers.

9. Test procedure

9.1 General information

All reagents and the microwell Plate must be brought to room temperature (20 - 25 °C) before use. The microwell strips must not be removed from the aluminum bag until they have reached room temperature. The reagents must be thoroughly mixed immediately before use. After use, the microwell strips (placed in sealed bags) and the reagents must be stored again at 2 - 8 °C. Once used, the microwell strips must not be used again. The reagents and microwell strips must not be used if the packaging is damaged or the vials are leaking.

In order to prevent cross contamination, the samples must be prevented from coming into direct contact with the kit components.

The test must not be carried out in direct sunlight. We recommend covering the microwell plate or placing plastic wrap over it to prevent evaporation losses.

9.2 Preparing the washing buffer

Mix 1 part wash buffer concentrate Wash buffer with 9 parts distilled water. Any crystals present in the concentrate must be dissolved beforehand by warming in a water bath at 37 °C.

9.3 Preparing the specimens

Fill a labelled test tube with 1 ml RIDASCREEN® sample dilution buffer **Diluent | 1**.

Use a disposable pipette (article no. Z0001) to aspirate a sample of thin stool (approx. 100 µl) to just above the second marking and add to buffer in the test tube to make a suspension. To make a suspension with a solid stool sample, add an equivalent amount (approx. 50 - 100 mg) with a spatula or disposable inoculation loop.

Homogenize the stool suspension by aspiration into and ejection from a disposable pipette or, alternatively, blend in a Vortex mixer. Let the suspension stand a short period of time (10 minutes) for the coarse stool particles to settle, and this clarified supernatant of the stool suspension can be used directly in the test. If the test procedure is carried out in an automated ELISA system, the supernatant must be particle-free. In that case, it is advisable to centrifuge the sample at 2,500 G for 5 minutes.

Note: Stool samples diluted in **Diluent | 1 can be tested in all RIDASCREEN® ELISAs for which **Diluent | 1** is used.**

9.4 First incubation

After inserting a sufficient number of wells in the strip holder, add 100 µl of the positive **Control | +**, the negative **Control | -** or the stool sample suspension to the wells. Subsequently add 100 µl of the biotin-conjugated antibody **Conjugate | 1** and blend (by tapping lightly on the side of the plate); then incubate for 60 minutes at room temperature (20 - 25 °C).

9.5 Washing

Careful washing is important in order to achieve the correct results and should therefore proceed strictly according to the instructions. The incubated substance in the wells must be emptied into a waste container for disposal in accordance with local regulations. After this, knock out the plate onto absorbent paper in order to remove the residual moisture. Then wash the plate five times using 300 µl wash buffer **Wash buffer** each time. Make sure that the wells are emptied completely by knocking them out after each wash on a part of the absorbent paper which is still dry and unused.

If you use a microplate washer or fully automated ELISA, make sure that the machine is correctly adjusted; request settings from the manufacturer, if necessary. Appliances delivered by R-Biopharm are already programmed with validated settings and work protocols. To avoid blocking the wash needles, only particle-free stool suspensions should be dispensed (see Item 9.3., Preparing the samples). Also make sure that all of the liquid is aspirated during each wash step.

9.6 Second incubation

Use a pipette to fill 100 µl streptavidin poly-peroxidase conjugate **Conjugate 2** into the wells, then incubate for 30 minutes at room temperature (20 - 25 °C).

9.7 Washing

Wash as described in Item 9.5.

9.8 Third incubation

Fill all wells with 100 µl substrate **Substrate**. Then incubate the plate for 15 minutes in darkness at room temperature (20–25 °C). Subsequently fill all wells with 50 µl stop reagent **Stop** in order to stop the reaction. After blending cautiously by tapping lightly on the side of the plate, measure the extinction at 450 nm (optional: 450/620 nm).

Note: High-positive patient samples may cause black-colored precipitates of the substrate.

10. Quality control – indication of instability or deterioration of reagents

For quality control purposes, positive and negative controls must be used each time the test is carried out, to ensure that the reagents are stable and that the test is conducted correctly. The test has been carried out correctly if the extinction rate (O.D.) for the negative control is less than 0.2 at 450 nm (less than 0.160 at 450/620 nm) and the measured value for the positive control is greater than 0.8 at 450 nm or at 450/620 nm. A value greater than 0.2 (0.160) for the negative control may indicate that washing was insufficient. Deviation from the required values, just like a turbid or blue coloration of the colorless substrate before it is filled into the wells, may indicate that the reagents have expired.

If the stipulated values are not met, the following points must be checked before repeating the test:

- Expiry date of the reagents used
- Functionality of the equipment being used (e.g. calibration)
- Correct test procedure
- Visual inspection of the kit components for contamination or leaks – a substrate solution which has turned blue must not be used.

If the conditions are still not fulfilled after repeating the test, please consult the manufacturer or your local R-Biopharm distributor.

11. Evaluation and interpretation

11.1. Calculating the cut-off

In order to establish the cut-off, 0.15 extinction units are added to the measured extinction for the negative control.

$$\text{Cut-off} = \text{extinction for the negative control} + 0.15$$

11.2. Test results

Assessment of the specimen is positive if the extinction rate is more than 10 % higher than the calculated cut-off value.

Assessment of the specimen is marginal if the extinction rate ranges from 10 % less to 10 % greater than the cut-off value. If the repeat examination with a fresh stool sample again falls within the gray zone, assessment of the sample is negative.

Samples with extinctions more than 10 % below the calculated cut-off must be considered negative.

12. Limitations of the method

The RIDASCREEN® Adenovirus Test identifies antigens of the *adenovirus* in stool samples. It is not possible to associate the determined level of extinction to the occurrence or severity of clinical symptoms. The results obtained must always be interpreted in combination with the clinical signs and symptoms.

A positive result does not rule out the presence of other infectious pathogens.

A negative result does not rule out the possibility of *adenovirus* infection. Such a result may be due to intermittent excretion of the virus, or the amount of antigen in the sample may be too small. If the patient history supports a suspicion of adenovirus infection, the examination should be repeated with another stool sample.

A borderline result may be due to non-homogeneous distribution of viruses in the stool sample.

In this case, examination should either be repeated with a second suspension from the same sample or another stool sample should be requested.

13. Performance characteristics

13.1 Test quality

RIDASCREEN® Adenovirus was validated by comparison with three commercially available adenovirus ELISAs. The sample collective that was used consisted of fresh, same-day samples taken at a routine laboratory and of prepared samples that had been frozen in advance at -20 °C for use in the comparison study. One homogeneous baseline suspension was tested by each of the ELISAs in accordance

with the manufacturers' instructions. A sample was considered positive or negative, if the results of two out of three reference tests were in agreement. The results of that study are summarized in Table 2.

Tab. 2: Correlation between RIDASCREEN® Adenovirus ELISA and three other commercial ELISAs

RIDASCREEN® Adenovirus	Competitor-ELISA		Total
	+	-	
+	21	0	21
-	0	115	115
Total	21	115	136

Sensitivität : 100 % Spezifität : 100 %

13.2 Cross-reactivity

A variety of pathogenic microorganisms from the intestinal tract were examined with the RIDASCREEN® Adenovirus ELISA and showed no cross reactivity. These studies were conducted with bacterial suspensions shown to have concentrations of 10^6 to 10^9 organisms per ml. Virus culture supernatants and toxins as well as stool samples are listed accordingly. The results of that study are summarized in Table 3.

Tab. 3: Cross reactivity with pathogenic microorganisms

Organism	Origin	Source	[OD 450 nm] mean value
<i>Acinetobacter lwoffii</i>	Culture	DSM 2403	0.063
<i>Aeromonas hydrophila anaerogenes</i>	Culture	DSM 30020	0.091
<i>Aeromonas hydrophila hydrophila</i>	Culture	DSM 30016	0.074
<i>Astrovirus</i>	Culture	Micromun	0.052
<i>Astrovirus</i>	Stool	TU Dresden	0.074
<i>C. difficile</i>	Culture	VPI 1640	0.052
<i>C. perfringens</i> 50 µg/ml	Toxoid	Kit control <i>C. perfringens</i> Enterotoxin A	0.057
<i>C. sordellii</i>	Culture	tgcBiomics	0.052
<i>Campylobacter fetus</i>	Culture	DSM 5361	0.060
<i>Campylobacter jejuni</i>	Culture	DSM 4688	0.050
<i>Campylobacter</i>	Stool	Routine lab	0.037
<i>Candida albicans</i>	Culture	ATCC 10231	0.079
<i>Citrobacter freundii</i>	Culture	DSM 30039	0.094
<i>Citrobacter spp.</i>	Culture	DSM 30047	0.070
<i>Cryptosporidium parvum</i>	Culture	Waterborne Inc.	0.051
<i>E. coli</i>	Culture	LMU München	0.078
<i>E. coli</i>	Culture	LMU München	0.074
<i>E. coli</i>	Culture	LMU München	0.062
<i>E. coli</i> (O111:H-)	Culture	LMU München	0.079
<i>E. coli</i> (O116:H21)	Culture	LMU München	0.073
<i>E. coli</i> (O157:H-)	Culture	LMU München	0.096
<i>E. coli</i> (O22:H8)	Culture	LMU München	0.095
<i>E. coli</i> (O26:H11)	Culture	LMU München	0.078
<i>E. hermannii</i>	Culture	DSM 4560	0.049
<i>Entamoeba histolytica</i>	Stool	TI Berlin	0.043
<i>Enterobacter cloacae</i>	Culture	DSM 30054	0.071
<i>Enterococcus faecalis</i>	Culture	DSM 2570	0.078
<i>Enterococcus faecium</i>	Culture	DSM 20477	0.090
<i>Giardia lamblia</i>	Stool	TI Berlin	0.039

<i>H. pylori</i>	Inaktiviertes <i>H. pylori</i> lysate	Kit control RIDASCREEN FemtoLab H. <i>pylori</i>	0.071
<i>Helicobacter pylori</i>	Culture	DSM 4867	0.051
<i>Lactococcus lactis</i>	Culture	DSM 20481	0.070
<i>Listeria innocua</i>	Culture	DSM 20649	0.060
<i>Morganella morganii</i>	Culture	DSM 6675	0.054
<i>Proteus mirabilis</i>	Culture	DSM 788	0.050
<i>Proteus mirabilis</i>	Culture	DSM 4479	0.052
<i>Proteus vulgaris</i>	Culture	DSM 30119	0.052
<i>Providencia stuartii</i>	Culture	DSM 6676	0.073
<i>Pseudomonas aeruginosa</i>	Culture	DSM 939	0.058
<i>Pseudomonas fluorescens</i>	Culture	DSM 4358	0.058
<i>Pseudomonas fluorescens</i>	Culture	DSM 50124	0.069
<i>Pseudomonas putida</i>	Culture	DSM 291	0.056
<i>Rotavirus</i>	Culture	Microbix	0.059
<i>Rotavirus</i>	Stool	TU Dresden	0.059
<i>Salmonella agona</i>	Culture	LMU München	0.052
<i>Salmonella choleraesuis</i>	Culture	DSM 4224	0.053
<i>Salmonella enteritidis</i>	Culture	DSM 9898	0.065
<i>Salmonella enteritidis</i>	Culture	Routine lab	0.065
<i>Salmonella infantis</i>	Culture	LMU München	0.053
<i>Salmonella ohio</i>	Culture	LMU München	0.053
<i>Salmonella typhimurium</i>	Culture	DSM 554	0.050
<i>Sapovirus</i>	Stool	TU Dresden	0.066
<i>Serratia liquefaciens</i>	Culture	DSM 4487	0.039
<i>Shigatoxin STX1</i>	Toxoid	Toxin Technology	0.054
<i>Shigatoxin STX2</i>	Toxoid	Toxin Technology	0.054
<i>Shigella flexneri</i>	Culture	DSM 4782	0.040
<i>Shigella sonnei</i>	Culture	DSM 5570	0.048
<i>Staphylococcus aureus</i>	Culture	DSM 20372	0.064
<i>Streptococcus agalactiae</i>	Culture	DSM 2134	0.090
<i>Streptococcus dysgalactiae</i>	Culture	DSM 20662	0.074
<i>Streptococcus uberis</i>	Culture	DSM 20569	0.071

13.3 Precision

The reproducibility of the RIDASCREEN® Adenovirus ELISA was tested with six references representing the complete measurement range from weak to high positive. To determine the intra-assay reproducibility, 40 replicates of these references were assayed. The mean values and the variation coefficients (CV) were determined for three lots.

For the inter-assay reproducibility, references from ten different working days were assayed in duplicates, with two runs per day. The measurements were determined in three lots by three technicians. The inter-lot reproducibility was determined for all three lots. The results of that study are shown in Table 4.

Tab. 4: Reproducibility and precision of the RIDASCREEN® Adenovirus ELISA

Reference	Mean value / CV (%)	Intra-assay			Inter-assay			Inter-lot
		Kit Lot 1	Kit Lot 2	Kit Lot 3	Kit Lot 1	Kit Lot 2	Kit Lot 3	Kit Lot 1-3
1	MV	2.236	2.732	3.170	2.363	2.199	2.408	2.323
	CV (%)	5.11 %	6.67 %	6.08 %	15.39 %	20.81 %	19.91 %	18.95 %
2	MV	1.359	1.590	1.975	1.411	1.368	1.559	1.446
	CV (%)	5.16 %	4.03 %	9.64 %	14.28 %	21.66 %	18.81 %	19.35 %
3	MV	1.244	1.222	1.321	1.096	1.162	1.261	1.173
	CV (%)	8.07 %	6.14 %	8.16 %	13.66 %	17.75 %	18.93 %	18.23 %
4	MV	0.813	0.899	1.014	0.794	0.822	0.862	0.826
	CV (%)	7.75 %	7.81 %	15.22 %	16.20 %	24.41 %	18.37 %	20.03 %
5	MV	0.597	0.622	0.800	0.570	0.587	0.635	0.597
	CV (%)	7.88 %	5.78 %	11.73 %	16.92 %	23.77 %	16.84 %	19.79 %
6	MV	0.368	0.394	0.588	0.407	0.434	0.462	0.434
	CV (%)	8.27 %	6.63 %	19.65 %	24.65 %	24.35 %	17.00 %	22.43 %

13.4 Analytical sensitivity

The detection limit of the RIDASCREEN® Adenovirus ELISA was determined with the serial dilution of a stool sample quantified by immunoelectron microscopy (IEM). The measurements were taken in triplicate, based on a virus titer of 1.3×10^7 particles/ml. The detection limit was defined as 3.25×10^2 virus particles/ml of the stool sample. Results of the titration series are shown in Table 5. Note that the positive OD value in ELISA is caused by intact virus particles, but also by fragments of the virus, which are not counted in the IEM.

Tab. 5: Determination of the analytical sensitivity of RIDASCREEN® Adenovirus ELISA

IEM Virus particles / ml	RIDASCREEN® Adenovirus	
	Mean value [OD 450]	Results
6.5×10^5	1.784	Positive
6.5×10^4	3.993	Positive
3.25×10^4	4.030	Positive
1.63×10^4	4.032	Positive
8.2×10^3	4.135	Positive
6.5×10^3	4.245	Positive
3.25×10^3	3.753	Positive
1.63×10^3	2.858	Positive
8.2×10^2	1.718	Positive
6.5×10^2	1.126	Positive
3.25×10^2	0.305	Positive
1.63×10^2	0.054	Negative

13.5 Interfering substances

The following list of substances showed no effects on the test results when they were blended into adenovirus positive and adenovirus negative stool samples in the described concentrations:

Mucins	5.0 % w/w	Diclofenac	0.00263 % v/w
Human blood	5.0 % v/w	Cyclamate	5.0 % v/w
Barium sulfate	5.0 % w/w	stearic acid and palmitic acid combination	40 % w/w (1:1)
Loperamide	5.0 % w/w		
Pepto-Bismol	5.0 % v/w	Metronidazole 0.5 % solution	5.0 % v/w

14. Version history

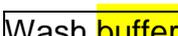
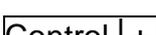
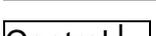
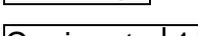
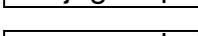
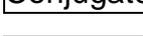
Version number	Chapter and designation
2017-04-20	Previous version
2019-07-09	General revision 4. Reagents provided 8. Collection and storage of specimens 9.2 Preparing the washing buffer 9.5 Washing

15. Explanation of symbols

General symbols

	For in vitro diagnostic use
	Consult instructions for use
	Lot number
	Expiry
	Store at
	Article number
	Number of tests
	Date of manufacture
	Manufacturer

Test specific symbols

	Microtiter plate
	Sample dilution buffer
	Washing buffer
	Positive control
	Negative control
	Conjugate 1
	Conjugate 2
	Substrate
	Stop reagent

16. References

1. Horwitz, M.S.: Adenoviral Diseases. In B.N. Fields, ed. Virology, Raven Press, New York, 477-495.
2. Wigand, R. and Th. Adrian: Die Diagnostik von Adenovirus-Infektionen. Internist 26, 109-112 (1985).
3. Wigand, R.: Klinische Relevanz von Adenovirusinfektionen. Laboratoriumsblätter 30, 118 -123 (1980).
4. Brandt, C.D., H.W.Kim, A.J. Vargosdo, B.C. Jeffries, J.O. Arrobio, B.Rindge, R.H. Parrot and R.M. Chanock: Infections in 18.000 infants and children in a controlled study of respiratory tract disease. I. Adenovirus pathogenicity in relation to serologic type and illness syndrome. Am. J. Epidemiol. 90, 484-500 (1969).
5. Mallet, R., M. Riberre, F. Bonnenfant, B. Labrune and L. Reyrole: Les pneumopathies graves a adeno-virus. Arch. Fr. Pediatr. 23, 1057-1073 (1966).
6. Kemp, M.C., J.C. Hierholzer, C.P. Cabradilla and J.F. Obijesti: The changing etiology of epidemic keratoconjunctivitis: Antigenic and restriction enzyme analysis of adenovirus types 19 and 37 isolated over a 10 year period. J. Infect. Dis. 148, 24-33 (1983).
7. Foy, H.M., M.K. Cooney and J.B. Hatlen: Adenovirus type 3 epidemic associated with intermittend chlorination of a swimming pool. Arch. Environ. Health 17, 795-802 (1968).
8. De Jong, P.J., G. Valderrama, I. Spigland and M.S. Horwitz: Adenovirus isolates from the urines of patients with the acquired immunodeficiency syndrome. Lancet 1, 1293-1296 (1983).
9. Takiff, H.F., S.E. Straus and C.F. Garon: Propagation and in vitro studies of previously non-cultivable enteric adenoviruses in 293 cells. Lancet 2, 832-834 (1981).
10. Herrmann, J.E., D.M. Perron-Henry, D. Stobbs-Walro and N.R. Blacklow: Preparation and characterization of monoclonal antibodies to enteric adenovirus types 40 and 41. Arch. Virology 94, 259-265 (1987).
11. Uhnoo, I., G. Wadell, L. Svensson and M.E. Johansson: Importance of enteric adenoviruses 40 and 41 in acute gastroenteritis in infants and young children. J. Clin. Microbiol. 20, 365-372 (1984).
12. Kidd, A.H., E.H. Harley and M.J. Erasmus: Specific detection and typing of adenovirus types 40 and 41 in stool specimens by dot-blot hybridization. J. Clin. Microbiol. 22, 934-939 (1985).
13. Cukor G. and N.R. Blacklow: Human viral gastroenteritis. Microbiological Reviews 48, 157 -179 (1984).
14. Mogabgab, W.J.: Mycoplasma pneumonia and adenovirus respiratory illnesses in military and university personnel, 1959-1966. Am. Rev. Respir. Dis. 97, (345 - 358) (1968).

15. Richmond, S.J., E.O. Caul, S.M. Dunn, C.R. Ashley, S.K.R. Clarke: An outbreak of gastroenteritis in young children caused by adenoviruses. *Lancet* 1, 1178-1180 (1979).
16. Chiba, S., S. Nakata, I. Nakamura, K. Taniguchi, S. Urasawa, K. Fujinaga and T. Nakao: Outbreak of infantile gastroenteritis due to type 40 adenovirus. *Lancet* 2, 954-957 (1983).
17. E.H. Lennette and N.J. Schmidt: *Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections*, Fifth edition, 1979, American Public Health Associates, Inc., Washington, D. C., 241 - 242, 229-255.
18. Cepko, C.L., C.A. Whetstone and P.A. Sharp: Adenovirus hexon monoclonal antibody that is group specific and potentially useful as a diagnostic reagent. *J. Clin. Microbiol.* 17, 360-364 (1983).