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ProSpecT Adenovirus Microplate Assay

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1. INTENDED USE

The ProSpecT™ Adenovirus Microplate Assay is a qualitative enzyme immunoassay for the detection of adenovirus in human faeces or infected cell culture monolayers.

2. SUMMARY

Adenoviruses are non-enveloped DNA viruses of icosahedral symmetry. The family Adenoviridae comprises two genera, mammalian adenoviruses (Mastadenovirus) and avian adenoviruses (Aviadenovirus)[1]. To date at least 51 adenovirus serotypes have been discovered. They are grouped into six sub-groups A-F, and have been identified and characterised by haemagglutination, neutralisation tests, DNA hybridisation tests and restriction endonuclease analysis of adenoviral DNA[1,2,3,4,31].

Human adenoviruses are associated with a wide range of clinical disease in immunocompetent and immunocompromised individuals including infections of the respiratory tract, conjunctiva and gastrointestinal tract[3,5]. Infections are common in children and can occur sporadically or in outbreaks. Approximately 5% of acute respiratory disease in children and 10% of febrile illnesses and childhood pneumonias have been associated with adenovirus infections[3,6,7]. Adenovirus infections of the eye may lead to pharyngoconjunctival fever, follicular conjunctivitis or epidemic keratoconjunctivitis[3,8]. Adenovirus serotypes 40 and 41 are commonly associated with viral gastroenteritis in infants and reported to be responsible for 4-15% of nosocomial infections in paediatric wards[3,9,10]. In immunocompromised patients (e.g. transplant or AIDS patients) severe systemic infections can occur which can be life threatening[3].

The laboratory diagnosis of adenovirus infections plays an important role in patient management and enables effective management and control of outbreaks. Diagnostic methods include direct detection of the virus or viral proteins in clinical specimens, isolation of viable virus in cell culture monolayers inoculated with respiratory, conjunctival or faecal specimens, or by detection of adenovirus specific immunoglobulins[3,5].

Isolation of adenoviruses from clinical specimens can be accomplished in continuous cell lines of mainly epithelial origin including HeLa, Hep2, KB and 293 cell lines, in which adenoviruses may exhibit a characteristic cytopathic effect[3,5]. A range of techniques have been used to confirm the identification of adenovirus isolates including neutralisation tests, radioimmunoassay, DNA hybridisation, electron microscopy and DNA electrophoretyping[11,12,13,14,15]. These techniques can be complex, laborious, time consuming and often inappropriate for routine use.

Adenoviruses associated with viral gastroenteritis can be detected directly in faecal specimens using electron microscopy[11,16]. However this facility is only available in specialised laboratories.

More recently direct immunofluorescence (e.g. IMAGEN Adenovirus) or enzyme immunoassays, using specific monoclonal or polyclonal antibodies, have been described for the direct detection of adenovirus in clinical specimens or cell culture monolayers[15,17,18].

Enzyme immunoassay offers a rapid, sensitive and specific method for the detection and confirmation of adenovirus isolates in cell culture monolayer or faecal specimens.

The ProSpecT Adenovirus Microplate Assay is an immunoassay for the detection of all human adenovirus serotypes in faecal specimens or cell culture monolayers. The test utilises a genus-specific monoclonal antibody to detect an epitope of the adenovirus hexon antigen which is present in all human serotypes[19].

3. PRINCIPLE OF THE TEST

The ProSpecT Adenovirus Microplate Assay utilises a monoclonal antibody in a solid phase sandwich enzyme immunoassay to detect a genus-specific hexon epitope of adenovirus. Break-apart microwells are coated with an adenovirus specific monoclonal antibody. Faecal suspension or undiluted cell culture fluid is added to the microwell and incubated simultaneously with an Adenovirus specific monoclonal antibody conjugated to horseradish peroxidase. Adenovirus antigen present in the sample is captured between antibody on the solid phase and the enzyme conjugated antibody. After 60 minutes incubation at room temperature, the microwells are washed with working strength washing buffer to remove excess specimen and any unbound enzyme labelled antibody. A chromogen is added to the microwells and incubated for 10 minutes at room temperature. The presence of specifically bound enzyme labelled antibody in the microwells results in a colour change which is stopped by the addition of acid. Colour intensity significantly above background levels is indicative of the presence of adenovirus antigen in the specimen or control.

4. SYMBOL DEFINITIONS

The following symbols have been used throughout the product information.

REF	Catalogue number
	Consult the instructions for use
Σ N	Contains sufficient for 'N' tests
	Manufacturer
IVD	In vitro diagnostic medical device
	Use by
LOT	Batch Code
8°C 2°C	Storage temperature limitations

5. KIT CONTENTS

Σ 96 - Each kit contains sufficient materials for 96 determinations.

- The shelf life of the kit is as indicated on the outer box label.

Store all components at 2-8°C.

Before use bring all reagents to room temperature (20-25°C) and mix gently. Store all unused reagents at 2-8°C after use.

All reagents except the Wash Buffer are supplied ready to use. If reagents are poured out for use with multichannel pipettes do not pour excess reagent back into the bottle.

Instructions for use
Transfer pipettes
Microplate cover
Certificate of contents
Procedure card

MICROTITRATION PLATE — One 96 well microtitration plate of twelve, 8 microwell break-apart strips coated with an adenovirus specific monoclonal antibody. A resealable foil pouch containing desiccant is provided for storage of unused microwells. Microwells may be used for up to 16 weeks after initial opening, provided they are stored correctly in the pouch.

One bottle of each of the following unless indicated otherwise:

SAMPLE DILUENT — 120ml Sample Diluent: tris buffered saline containing antimicrobial agent and red dye

CONTROL + — 4ml Positive Control: inactivated adenovirus type 7 in buffer containing antimicrobial agent

CONTROL − — 4ml Negative Control: tris buffered saline containing antimicrobial agent and red dye

CONJUGATE — 12ml Conjugate: adenovirus specific monoclonal antibody conjugated to horseradish peroxidase in a buffered protein solution containing antimicrobial agent and blue dye

WASH BUFFER (x10) — 120ml Wash Buffer concentrate (x10): phosphate buffered solution containing antimicrobial agent and detergent

Dilute 10x Wash Buffer concentrate by adding 1 part concentrate to 9 parts distilled or deionised water. Diluted Wash Buffer is stable for up to 30 days when stored at 2-8°C.

SUBSTRATE TMB — 12ml Substrate: 3,3'-5,5'-tetramethylbenzidine in a mildly acidic buffer

STOP SOLUTION — 12ml Stop Solution: 0.46mol/L sulphuric acid

6. PRECAUTIONS

IVD - For *in vitro* diagnostic use. Anyone performing an assay with this product must be trained in its use and must be experienced in laboratory procedures.

Please refer to the Safety Data Sheet (SDS) and product labelling for information on potentially hazardous components.

HEALTH AND SAFETY INFORMATION

6.1. The Positive Control contains inactivated Adenovirus type 7 which has been shown to be non infectious in cell culture. However, the control must be handled and disposed of as though potentially infectious.

6.2. Stop Solution contains sulphuric acid (0.46mol/L).

6.3. Wash Buffer contains potential skin sensitiser (<1% v/v). Avoid skin contact. Wear disposable vinyl or nitrile gloves.

6.4. Do not eat, drink, smoke, store or prepare foods, or apply cosmetics within the designated work area.

6.5. Do not pipette materials by mouth.

6.6. Wear disposable gloves while handling clinical specimens and reagents. Always wash hands after working with infectious materials.

6.7. Dispose of all clinical specimens in accordance with local legislation.

6.8. ProSpecT Adenovirus reagents contain a proprietary antimicrobial agent which presents no hazard to the user if normal laboratory safety precautions are followed.

6.9. Due to the affinity of some adenoviruses for the ocular area, hand to eye contact must be carefully avoided at all stages when testing samples.

ANALYTICAL PRECAUTIONS

6.10. Components must not be used after the expiry date printed on the labels. Do not mix or interchange the following reagents as performance may be compromised:- Plate, Conjugate and Controls.

6.11. The following common reagents may be used across the ProSpecT product range:- Wash Buffer, TMB Substrate and Stop Solution.

6.12. Avoid contamination of reagents.

6.13. When using the dropper bottle method ensure all controls and reagents are added in the same way. (Performance of the kit may be adversely affected if a combination of pipette and dropper methods are used).

6.14. Use separate disposable pipettes or pipette tips for each sample, control or reagent (if not using dropper bottles) in order to avoid cross contamination of either samples, controls or reagents which could cause erroneous results.

6.15. Store deionised or distilled water for dilution of concentrated reagent in clean containers to prevent microbial contamination.

6.16. Avoid contamination with metal ions and oxidising agents.

6.17. Do not use substrate showing a blue colour prior to its addition to the microwells.

6.18. Protect Substrate from light.

6.19. Microwells cannot be re used.

6.20. Unused working strength Wash Buffer can be stored for up to 30 days at 2-8°C for subsequent use. When not in use Wash Buffer reservoirs should be rinsed in deionised or distilled water and left to dry.

6.21. Manual or automated washing equipment must be free of microbial contamination, be correctly calibrated and maintained according to the manufacturer's instructions.

6.22. When using reagent dropper bottles, hold the bottles vertically with the nozzle approximately 5mm above the microwell. Squeeze the bottle **gently** and ensure that the drops fall freely into the microwells without touching the sides of the well. Avoid contamination of all the dropper nozzles.

7. COLLECTION OF FAECAL AND CELL CULTURE SPECIMENS

COLLECTION OF FAECAL SPECIMENS

Faecal specimens should be collected as soon as possible following the onset of symptoms.

Peak excretion of adenovirus in faeces from patients with gastroenteritis is reported to occur 3-13 days after the onset of symptoms[3].

Faecal specimens for direct testing should be collected into containers that do not contain media, preservatives, animal sera, metal ions, oxidising agents or detergents, as all of these additives may interfere with the ProSpecT Adenovirus test.

If rectal swabs are collected they must contain sufficient faecal material to obtain a 10% suspension of faeces (see section 8 A).

Specimens may be stored for 8 days at 2-8°C prior to testing. For long term storage of faecal specimens, store at -20°C.

COLLECTION OF CELL CULTURE SPECIMENS

The collection of specimens is of fundamental importance in the diagnosis of adenovirus by cell culture. Specimens must be collected from the site of infection during the time of peak viral excretion so that they contain as much infected material as possible. Conjunctival swabs, nasal and/or throat swabs, or other types of swabs collected, should be placed into viral transport medium routinely used for virus isolation and sent to the laboratory immediately. The optimum time for specimen collection is as soon as possible after onset of symptoms. Nasopharyngeal aspirates or secretions should be collected into a mucus extractor through a size 8 feeding tube. The mucus extractor and tubing should be sent to the laboratory immediately for processing.

8. PROCEDURE

REQUIRED MATERIALS PROVIDED

See Kit Contents, section 5

MATERIALS REQUIRED BUT NOT PROVIDED

Faecal specimen collection containers
Clean screw-capped disposable containers (minimum 3ml capacity) for preparation of faecal specimen
Clean absorbent paper (onto which microwells can be tapped dry)
Precision micropipettes and disposable tips to deliver 50µl, 100µl and 1000µl
Waste discard container with suitable fresh disinfectant
Timer
Wash bottle for Wash Buffer
Distilled or deionised water

OPTIONAL MATERIALS NOT PROVIDED

Microplate reader capable of reading 450nm (with 620-650nm reference optional)
Vortex mixer with plate adapter or plate shaker incubator
Automated plate washer or suitable equipment for washing 8 microwell strips

PROCEDURE

8.1. Open the foil pouch, remove the required number of microplate strips and place into a microplate strip holder. Use one well for the Negative Control and one well for the Positive Control. If using less than 8 wells break off the required number of wells from a strip and return the unused wells to the foil pouch with desiccant. RESEAL POUCH TIGHTLY TO EXCLUDE MOISTURE AND RETURN TO STORAGE AT 2-8°C.

A. DILUTON OF FAECAL SAMPLES

Add 1ml of Sample Diluent to a suitable labelled container and use to prepare a 10% suspension or dilution of faecal specimen by addition of approximately 0.1g of solid faeces (small pea-sized portion) or approximately 100µl of liquid faeces using transfer pipettes. Mix thoroughly and leave transfer pipette in container for later use.

Rotate rectal swabs in 1ml of Sample Diluent whilst squeezing swab against the side of the container to release faecal material. Mix thoroughly.

Faecal suspensions previously preserved in formalin should be further diluted in ProSpecT Adenovirus Sample Diluent to prepare a 10% suspension of faeces before testing.

Specimens suspended/diluted in ProSpecT Adenovirus Sample Diluent may be stored at 2-8°C for up to 8 days prior to testing.

NOTE: Faecal specimens prepared in ProSpecT Astrovirus, ProSpecT Rotavirus and ProSpecT Norovirus Sample Diluent can also be tested in the ProSpecT Adenovirus test. Alternative Sample Diluents have not been validated for use.

B. DILUTION OF CELL CULTURE SPECIMENS

Cell culture specimens can be tested directly in the ProSpecT Adenovirus test. Specimens collected for cell culture should be inoculated into the cell lines routinely used in the laboratory for the isolation of adenoviruses eg Hep2 or HeLa cells. Cell cultures should be examined regularly for the appearance of a cytopathic effect (CPE) characteristic of adenovirus. Adenovirus CPE can develop within 2-7 days after inoculation of cell lines, but in some instances may require up to 28 days to develop. Culture fluid from cell monolayers exhibiting a CPE can be harvested and tested directly for the presence of adenoviruses using the ProSpecT Adenovirus test.

Cell culture harvests should be stored at 2-8°C and must be tested within 72 hours of harvesting. For long term storage of cell culture harvests, store at –20°C or colder.

8.2. Add 2 drops (or 100µl) of each diluted specimen, cell culture fluid, Negative Control or Positive Control to the separate microwells. At least one Negative Control and one Positive Control should be included in each batch of tests.

8.3. After addition of all specimens and controls, add 2 drops (or 100µl) of Conjugate to each microwell and mix gently for 20-30 seconds.

8.4. Cover the plate and incubate at 20-30°C for 60 +/- 5 minutes.

8.5. Shake out or aspirate the contents of the wells. Wash by completely filling each well with diluted Wash Buffer (~350-400µl per well). Shake out or aspirate all fluid from wells after each wash. Wash a total of 5 times. After the last wash remove contents and strike plate on clean paper towels or aspirate. If using an automated washer, this should be programmed to complete 5 wash cycles. Washers must be correctly calibrated to ensure complete filling and emptying of microwells between each wash. After the final wash, the plate should be inverted and tapped on absorbent paper to remove the last traces of wash buffer.

8.6. Add 2 drops (or 100µl) of Substrate to each microwell.

8.7. Cover the plate and incubate at 20-30°C for 10 minutes.

8.8. Microwells can be read visually immediately after the second incubation (See sections 9 and 10).

8.9. Alternatively, stop the Substrate reaction by adding 2 drops (or 100µl) of Stop Solution to each microwell. Ensure thorough mixing of the microwells before reading the results. The coloured product is stable for up to 30 minutes after addition of Stop Solution.

8.10. Read spectrophotometrically at 450nm (see sections 9 and 10).

9. QUALITY CONTROL

At least one Positive Control and one Negative Control should be included each time the test is performed.

VISUAL DETERMINATION

All Negative Control microwells should be colourless. If this is not the case the test results should not be determined visually.

The Positive Control microwell should show a distinct blue colour clearly distinguishable from the Negative Control.

SPECTROPHOTOMETRIC DETERMINATION

The Negative Control value, or mean of the Negative Control values, should be less than 0.150 absorbance units.

The Positive Control value must be greater than 0.500 absorbance units.

10. RESULTS

VISUAL DETERMINATION

Any specimens giving a blue colour more intense than that of the Negative Control is positive. Any specimen giving colour equal to or less than the Negative Control is negative. Microwells in which the colour intensity is difficult to interpret when compared to the Negative Control should be read photometrically after addition of Stop Solution or retested.

SPECTROPHOTOMETRIC DETERMINATION

10.1. The microwells should be read photometrically within 30 minutes of addition of the Stop Solution.

10.2. Mix the contents of the microwells and read the absorbance of each microwell using a spectrophotometer set at 450nm. Ensure the bottoms of the microwells are clean before reading. The reader should be blanked on air before the plate is scanned.

10.3. If the spectrophotometer allows for the use of a reference wavelength (at 620 to 650nm), dual wavelength reading should be performed.

10.4. Calculate the cut-off value by adding 0.100 absorbance units to the Negative Control value, or mean value when more than one Negative Control is included.

10.5. Interpret the test results:

Positive:	clinical sample absorbance value > the cut-off value
Negative:	clinical sample absorbance value < the cut-off value
Equivocal:	clinical sample absorbance value within 0.010 absorbance units of the cut-off value. These samples should be retested or the patient resampled

11. PERFORMANCE LIMITATIONS

11.1. The validity of results with the ProSpecT Adenovirus Microplate Assay depends on the control reactions performing as expected. See Quality Control section 9.

11.2. A negative result does not exclude the possibility of adenovirus infection in the patient. Failure to detect adenovirus may be a result of factors such as collection of specimen at an improper time in the disease when too few virions are present, improper sampling, handling of the specimen or failure of cell culture.

11.3. ProSpecT Adenovirus test detects a genus specific hexon antigen which is present in all human serotypes. The test cannot be used to differentiate serotypes.

11.4. The reagents are provided at fixed working concentrations. Test performance will be adversely affected if reagents are modified or stored under conditions other than those detailed in section 5.

11.5. A negative result for a faecal specimen may not preclude the presence of infection with non enteric adenoviruses in other body sites. If respiratory or ophthalmic infection is suspected, specimens from the site of infection should be cultured.

11.6. All positive results must be interpreted in conjunction with patient related clinical information since adenovirus is capable of latency and recrudescence. Asymptomatic excretion of virus may occur up to 18 months after infection[20]. Enteric adenoviruses may be found in faecal specimens from asymptomatic children[21].

11.7. The use of ProSpecT Adenovirus Microplate Assay for direct testing of specimens other than faecal specimens is not recommended as either the presence of insufficient antigen or inadequate specimen collection may cause misleading negative results. A positive result in faecal specimens, in association with diarrhoea, is highly suggestive of adenoviral gastroenteritis[10]. Adenovirus types 40, 41 and occasionally 31 are most commonly associated with viral gastroenteritis.

11.8. A positive result does not preclude the presence of other enteric pathogens. Whilst the relationship between adenovirus and gastroenteritis is well established, concurrent infection with other microbial pathogens is possible.

11.9. Meconium samples have not been validated for use with the ProSpecT Adenovirus Microplate Assay.

11.10. Test results should be interpreted in conjunction with information available from epidemiological studies, clinical assessment of the patient and other diagnostic procedures[20].

12. EXPECTED VALUES

Positivity rates may vary according to the prevalence of adenovirus in different populations, geographical location, specimen collection, handling, storage, and transportation of specimens, cell culture system used and the general health environment of the patient populations under study.

The frequency of adenovirus infection will vary with the clinical syndrome and the age of the individual. In children under 5 years, approximately 5% of acute respiratory disease is due to adenovirus[22].

Approximately 10% of childhood pneumonias may be caused by adenoviruses[6]. Acute haemorrhagic cystitis in children may be caused by adenoviruses in 20-70% of cases[23,24]. Enteric adenoviruses (types 40 and 41) have been implicated as the causative organism in approximately 10% of cases of paediatric gastroenteritis and appear most frequently in children under 2 years of age[10].

In adults, adenoviruses have been implicated at times in cervicitis[25], and in acute respiratory disease especially in military recruits[26]. Ocular infections such as epidemic keratoconjunctivitis and so called "swimming pool conjunctivitis" due to adenoviruses may occur in any age group[27,28]. All groups of patients who are immunosuppressed may become infected with adenovirus[29,30].

13. PERFORMANCE CHARACTERISTICS

SENSITIVITY AND SPECIFICITY

ProSpecT Adenovirus Microplate Assay was evaluated in clinical studies performed at four centres. Studies were conducted on faecal specimens taken from patients presenting with gastroenteritis and on cell culture monolayers inoculated with clinical specimens collected from patients with suspected adenovirus infection. The results of the ProSpecT Adenovirus Microplate Assay were compared with Electron Microscopy (EM) for faecal specimens and with viral neutralisation for cell culture samples.

A total of 176 faecal specimens and 153 cell culture samples were tested. The results of these studies are shown in Tables 13.1. and 13.2.

13.1. Faecal specimens

When faecal specimens were tested, the ProSpecT Adenovirus test showed a correlation of 95.5% (168/176) with Electron Microscopy. The overall sensitivity and specificity of the ProSpecT Adenovirus test when compared to EM, was 90.1% (64/71) and 99.0% (104/105) respectively.

Table 13.1 Comparison of ProSpecT Adenovirus with Electron Microscopy for faecal specimen testing

METHOD		EM	
		+	-
ProSpecT Adenovirus	+	64	1*
	-	7**	104
Sensitivity		90.1 %	
Spesifisitet		99.0 %	
Specificity		95.5 %	

* Insufficient specimen for repeat testing.

** All samples were reported to have occasional virus particles by EM and non-fastidious Adenovirus strains were isolated from 5 samples (types 2, 4 and 5).

13.2. Cell culture samples

When cell culture samples were tested, the ProSpecT Adenovirus test showed a correlation of 98.0% (150/153) with viral neutralisation in cell culture. The overall sensitivity and specificity of the ProSpecT Adenovirus test, when compared to viral neutralisation was 97.6% (82/84) and 98.6% (68/69) respectively.

Table 13.2 Comparison of ProSpecT Adenovirus with viral neutralisation tests on cell culture isolates

METHOD		EM	
		+	-
ProSpecT Adenovirus	+	82	1
	-	2	68
Sensitivity		97.6%	
Spesifisitet		98.6%	
Specificity		98.0%	

LIMIT OF DETECTION

An adenovirus positive faecal specimen with estimated virus particle counts per ml determined by EM was serially diluted and tested in the ProSpecT Adenovirus test to determine the limit of detection (see Table 13.3). The results show that adenovirus particle counts as low as 3.0 x 10^5 per ml can be detected by the ProSpecT Adenovirus test.

Table 13.3 Absorbance values (A_{450}) obtained with titrations of a faecal specimen known to contain Adenovirus

Viral Particles/ml (EM)	Mean absorbance reading using ProSpecT Adenovirus
$1.9x10^7$	1.85
$4.8x10^6$	1.75
$1.2x10^6$	0.84
$5.9x10^5$	0.45
$3.0x10^5$*	0.21
$7.4x10^4$	0.10

* Endpoint concentration of adenovirus detected by ProSpecT Adenovirus.

PRECISION

Intra assay precision

The intra-assay precision was assessed with three faecal specimens and three cell culture samples. Each specimen was tested in a single assay 32 times and the mean and coefficient of variation determined (n=32).

Table 13.4 Intra-assay precision of the ProSpecT Adenovirus test

Specimen status	Cell Culture samples		Faecal specimens	
	Mean Au	%CV	Mean Au	%CV
Negative	0.05	5.5	0.05	10.8
Positive	0.36	5.6	0.42	10.5
Positive	2.89	4.2	2.34	8.4

Inter assay

The inter-assay precision was assessed with three faecal specimens and three cell culture samples. Each specimen was tested in 12 different assays and the mean absorbance values and coefficient of variation determined (n=24).

Table 13.5 Inter-assay precision of the ProSpecT Adenovirus test

Specimen status	Cell Culture samples		Faecal specimens	
	Mean Au	%CV	Mean Au	%CV
Negative	0.05	7.3	0.05	7.6
Positive	0.24	8.6	0.33	5.4
Positive	2.02	5.3	1.75	7.9

CROSS REACTIVITY

The following micro-organisms were tested and shown to be negative in the ProSpecT Adenovirus test. Cross-reactivity tests were performed either on clinical specimens for which the microbial status had been determined, or on laboratory cultures of known organisms, containing approximately 10^7-10^8 viable organisms/ml.

Viruses
Astrovirus
Coronavirus
Cowpox virus
Coxsackie virus A16, B2, B3, B4, B5
Cytomegalovirus
Echovirus 9, 11, 22, 32
Enterovirus
Epstein-Barr-virus
Foamy virus
Herpes simplex virus types 1 and 2
Influenzavirus A and B
Parainfluenza 1, 2, 3, 4a, 4b
Polio virus types 1, 2 and 3
Measles virus
Mumps virus
Respiratory syncytial virus
Rhinovirus
Rotavirus
Sendai virus
Small round structured virus

Bacteria
Acholeplasma laidlawii
Aeromonas spp
Bacillus spp
Bordetella pertussis
Branhamella catarrhalis
Campylobacter spp
Chlamydia trachomatis
Chlamydia pneumoniae
Clostridium difficile (toxin)
Clostridium perfringens (toxin)
Clostridium spp
Corynebacterium sp
Escherichia coli
Enteropathogenic E. coli
Enterotoxigenic E. coli
Haemophilus influenzae
Klebsiella pneumoniae
Lactobacillus spp
Legionella spp
Listeria monocytogenes
Mycobacterium avium
Mycobacterium intracellulare
Mycobacterium tuberculosis
Mycoplasma arginini
Mycoplasma hominis
Mycoplasma hyorhinis
Mycoplasma orale
Mycoplasma pneumoniae
Mycoplasma salivarium
Neisseria flavascens
Neisseria lactamica
Neisseria meningitidis A, B, C and D
Neisseria mucosa
Neisseria perflava
Neisseria pharyngis
Plesiomonas shigelloides
Pseudomonas aeruginosa
Salmonella agona
Salmonella enteritidis
Salmonella typhimurium
Salmonella virchow
Shigella dysenteriae
Shigella sonnei
Staphylococcus aureus
Streptococcus pneumoniae
Streptococcus spp
Vibrio alginolyticus
Vibrio cholerae
Vibrio haemolyticus

Protozoa
Cryptosporidium sp
Giardia lamblia

Other micro-organisms
Candida spp
Microsporum spp
Pneumocystis carinii
Trichuris trichiura

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