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Changes: § 5
Deletions: §

LIAISON® Adenovirus (REF 318950)

1. INTENDED USE

The DiaSorin LIAISON® Adenovirus assay is an *in vitro* diagnostic chemiluminescent immunoassay (CLIA) intended for the qualitative determination of adenovirus antigen in human stool specimens. This test is used primarily as an aid for the diagnosis of acute viral gastroenteritis. Test results are to be used in conjunction with information obtained from the patient's clinical evaluation and other diagnostic procedures. The assay must be performed on the LIAISON® Analyzer Family*.

2. SUMMARY AND EXPLANATION OF THE TEST

Human adenoviruses are ubiquitous viruses consisting of at least 57 different types which cause a wide array of human diseases, including respiratory disease and gastroenteritis[1]. Adenovirus serotypes are classified within 7 known species, A – G[1], where species B1, C and E mainly cause respiratory disease, species B, D and E cause ocular disease, and species B2 causes kidney and urinary tract infections[2]. Species F contains serotypes 40 and 41 which are the serotypes primarily responsible for gastroenteritis, however other serotypes have been detected in stool to a lesser extent.

The majority of diarrheal diseases are viral in origin. In industrialized countries viral gastroenteritis is a common cause of illness, while worldwide viral gastroenteritis is responsible for several million deaths per year. Rotavirus, calicivirus, astrovirus and adenovirus are the 4 primary viruses responsible for viral gastroenteritis worldwide, with up to 15% of diarrheal disease caused by adenovirus[3].

Adenoviruses contain a double-stranded DNA genome contained in a non-enveloped icosahedral capsid. The capsid contains 240 hexon proteins located on the faces and edges of the capsid. The hexon protein is the major capsid component and plays a significant role in the immune response[2]. The LIAISON® Adenovirus assay detects the group reactive hexon antigen shared by human and other vertebrate adenoviruses.

3. PRINCIPLE OF THE PROCEDURE

The LIAISON® Adenovirus assay is a modified 2-step sandwich assay for detection of the group reactive hexon protein. The assay uses 1 monoclonal antibody for capture and detection of the hexon antigen. The assay uses 100 µL of sample consisting of a mixture of sample diluent and stool extracted adenovirus antigen, which is incubated with isoluminol conjugated antibody. Following incubation, paramagnetic particles coated with capture antibody for adenovirus antigen are added to the reaction and incubated. After the second incubation, the unbound material is removed with a wash cycle. The starter reagents are then added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of adenovirus antigen present in the calibrators, controls or samples.

4. MATERIALS PROVIDED

Reagent Integral

Magnetic Particles (2.4 mL)	SORB	Magnetic particles coated with monoclonal antibody against adenovirus antigen in phosphate buffer, BSA, surfactant, 0.1% ProClin® 300 and 0.05% gentamicin sulfate.
Conjugate (23.0 mL)	CONJ	Monoclonal antibody against adenovirus antigen conjugated to an isoluminol derivative, in phosphate buffer, BSA, surfactant, 0.1% ProClin® 300 and 0.05% gentamicin sulfate.
Number of tests		100

ProClin is a trademark of the Dow Chemical Company (Dow) or an affiliated company of Dow.

All reagents are supplied ready to use. The order of reagents reflects the layout of containers in the Reagent Integral.

*(LIAISON®, LIAISON® XL and LIAISON® XS)

Additional components not on the Reagent Integral

Calibrator 1 3 x 1 mL Lyophilized	CAL 1	Inactivated adenovirus, BSA, surfactant, 0.1% ProClin® 300 and 0.05% gentamicin sulfate. Reconstitute in 1 mL distilled or deionized water.
Calibrator 2 3 x 1 mL Lyophilized	CAL 2	Inactivated adenovirus, BSA, surfactant, 0.1% ProClin® 300 and 0.05% gentamicin sulfate. Reconstitute in 1 mL distilled or deionized water.
Rota/Adeno Sample Diluent 1 x 105 mL	DIL SPE	BSA, surfactant, 0.1% ProClin® 300 and 0.05% gentamicin sulfate. After opening, sample diluent is stable for 10 weeks when stored at 2-8 °C.
2 x 50 each	PIPETTOR	Liquid Stool Pipettors
4 x 25 each	LOOP	Inoculation Loops
LIAISON® Stool Extraction Device* 2 x 50 each part	TUBES FILTERS CAPS	Polypropylene mixing tube, conical tube and blue cap, with high-density polyethylene (HDPE) blue filter unit.

*Device does not contain Bisphenol A (BPA), latex or Di(2-ethylhexyl)phthalate (DEHP).

Standardization: The calibrator concentrations are referenced to an in-house standard preparation.

Materials required but not provided (system related)

LIAISON® XL Analyzer	**LIAISON® Analyzer**	**LIAISON® XS Analyzer**
LIAISON® Wash/System Liquid (REF 319100)	LIAISON® Wash/System Liquid (REF 319100)	LIAISON® EASY Wash Buffer (REF 319301)
-	-	LIAISON® EASY System Liquid (REF 319302)
LIAISON® XL Waste Bags (REF X0025)	LIAISON® Waste Bags (REF 450003)	LIAISON® EASY Waste (REF X0054)
LIAISON® XL Cuvettes (REF X0016)	LIAISON® Module (REF 319130)	LIAISON® Cuvettes on Tray (REF X0053)
LIAISON® XL Starter Kit REF 319200) or	LIAISON® Starter Kit (REF 319102) or	LIAISON® EASY Starter Kit (REF 319300)
LIAISON® EASY Starter Kit (REF 319300)	LIAISON® XL Starter Kit (REF 319200) or	LIAISON® Disposable Tips (REF X0055)
LIAISON® XL Disposable Tips (REF X0015) or	LIAISON® EASY Starter Kit (REF 319300)	LIAISON® EASY Cleaning Tool (REF 310996)
LIAISON® Disposable Tips (REF X0055)	LIAISON® Cleaning Kit (REF 310990)	-
-	LIAISON® Light Check 12 (REF 319150)	-

Additional required materials

LIAISON® Adenovirus Control Set (REF 318951)

5. WARNINGS AND PRECAUTIONS

FOR *IN VITRO* DIAGNOSTIC USE – Not for internal or external use in humans or animals.

GENERAL SAFETY:

- All specimens, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. Avoid contact with skin, eyes or mucous membranes. Follow good industrial hygiene practices during testing.
- Do not eat, drink, smoke or apply cosmetics in the assay laboratory.
- Do not pipet solutions by mouth.
- Avoid direct contact with all potentially infectious materials by wearing lab coat, protective eye/face wear and disposable gloves.
- Wash hands thoroughly at the end of each assay.
- Avoid splashing or forming aerosols when handling, diluting or transferring specimens or reagents. Any reagent spill should be decontaminated with 10% bleach solution (containing 0.5% sodium hypochlorite) and disposed of as though potentially infectious.

- Waste materials should be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each country.
- Do not use kits or components beyond the expiration date given on the label.

CHEMICAL HAZARD AND SAFETY INFORMATION: Reagents in this kit are classified in accordance with US OSHA Hazard Communication Standard; individual US State Right-to-Know laws; Canadian Centre for Occupational Health and Safety Controlled Products Regulations; and applicable European Union directives (see Material Safety Data Sheet for additional information).

GHS/CLP:

	ProClin®
CAS No.:	55965-84-9
Reagents:	SORB CONJ CAL 1 CAL 2 DIL SPE
Classification:	Skin sensitization, Category 1 Aquatic Chronic, Category 3
Signal Word:	Warning
Pictogram:	 GHS07 – Exclamation mark
Hazard Statements:	H317 – May cause an allergic skin reaction. H412 – Harmful to aquatic life with long lasting effects.
Precautionary Statements:	P261 – Avoid breathing mist or spray. P272 – Contaminated work clothing should not be allowed out of the workplace. P273 – Avoid release to the environment. P280 – Wear protective gloves and clothing, and eye protection.

6. PREPARATION OF THE REAGENT INTEGRAL

Please note the following important reagent handling precautions:

Resuspension of magnetic particles

6.1 Magnetic particles must be completely resuspended before the integral is placed on the instrument. Follow the steps below to ensure complete suspension:

- Before the seal is removed, rotate the small wheel at the magnetic particle compartment until the colour of the suspension has changed to brown. Gentle and careful side-to-side mixing may assist in the suspension of the magnetic particles (avoid foam formation). Visually check the bottom of the magnetic particle vial to confirm that all settled magnetic particles have resuspended.
- Repeat as necessary until the magnetic particles are completely resuspended.
- After removal of the seal carefully wipe the surface of each septum to remove residual liquid if necessary.

6.2 Foaming of reagents

In order to ensure optimal performance of the integral, foaming of reagents should be avoided. Adhere to the recommendation below to prevent this occurrence:

- Visually inspect the reagents to ensure there is no foaming present before using the integral. If foam is present after re-suspension of the magnetic particles, place the integral on the instrument and allow the foam to dissipate. The integral is ready to use once the foam has dissipated and the integral has remained onboard and mixing.

6.3 Loading of integral into the reagent area

LIAISON® Analyzer

- Place the integral into the reagent area of the analyzer with the bar code label facing left and let it stand for 30 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles.
- Follow the analyzer operator's manual to load the specimens and start the run.

LIAISON® XL Analyzer and LIAISON® XS Analyzer

- LIAISON® XL Analyzer and LIAISON® XS Analyzer is equipped with a built-in solid-state magnetic device which aids in the dispersal of microparticles prior to placement of a Reagent Integral into the reagent area of the analyzer. Refer to the analyzer operator's manual for details.
  a. Insert the Reagent Integral into the dedicated slot.
  b. Allow the Reagent Integral to remain in the solid-state magnetic device for at least 30 seconds (up to several minutes). Repeat as necessary.
- Place the integral into the reagent area of the analyzer with the label facing left and let it stand for 15 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles.
- Follow the analyzer operator's manual to load the specimens and start the run.

7. STORAGE AND STABILITY OF THE REAGENT INTEGRAL

Upon receipt, the Reagent Integral must be stored in an upright position to facilitate re-suspension of magnetic particles. When the Reagent Integral is stored unopened the reagents are stable at 2-8 °C up to the expiration date. Do not freeze. The Reagent Integral should not be used past the expiration date indicated on the kit and Reagent Integral labels. After opening, integrals may be returned to the kit box and stored upright at 2-8 °C or stored on the analyzer. Integrals properly stored have an open use stability of 8 weeks. Refer to Section 11 for calibration intervals.

8. SPECIMEN COLLECTION AND STORAGE

Collect stool specimens into a clean airtight container with no preservative. Samples should be stored at 2-8°C and tested as soon as possible upon receipt, however storage at 2-8°C for up to 48 hours is acceptable. If samples will not be tested before 48 hours, they should be stored frozen at -20°C or below immediately upon receipt. Allow stool specimens to warm to room temperature and mix as thoroughly as possible before use. Avoid repeated freeze/thaw cycles.

9. SPECIMEN EXTRACT STORAGE

Stool specimen extracts are stable for 8 hours at room temperature (18-25°C), 72 hours at 2-8°C, or 12 weeks at -20°C prior to testing. Frozen stool extracts are stable through 2 freeze thaw cycles.
Prior to long term storage in refrigerator or freezer or during transport, extract must be removed from visible debris that may be present on the bottom of the conical tube. Transfer extract to a different sample tube, do not mix visible debris at bottom of conical tube into extract.

10. CALIBRATORS LEVEL 1 AND 2

The LIAISON® Adenovirus calibrators are supplied lyophilized. Reconstitute each vial with 1.0 mL of distilled or deionized water. Allow the vials to stand for 5 minutes, at room temperature to dissolve. Mix thoroughly by gentle inversion to ensure complete reconstitution for a minimum of 10 minutes. Transfer a minimum of 600 µL (triplicate calibration) to a glass or plastic sample tube. Affix the appropriate bar code label to the tube and place in appropriate sized rack and load onto the Analyzer. Calibrate the assay as described in the Operator's Manual. LIAISON® Adenovirus calibrators have been shown to be stable for 6 hours when stored at room temperature (18-25°C).

Calibrator and reagent integral lot number are lot specific. Do not use calibrators matched with a different reagent lot in the same assay.

LIAISON® Analyzer:
Transfer the tube to the LIAISON® Analyzer "A" rack with the barcode showing outward and slide rack into LIAISON® Analyzer sample area.

LIAISON® XL Analyzer and LIAISON® XS Analyzer:
Transfer the tube to the LIAISON® XL Analyzer and LIAISON® XS Analyzer "A" rack with the barcode showing outward and slide rack into LIAISON® XL or LIAISON® XS Analyzer sample area.

11. CALIBRATION

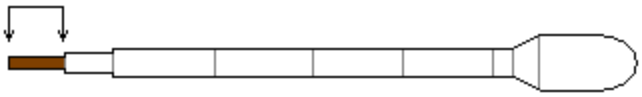
Individual LIAISON® Adenovirus Reagent Integrals contain specific information for calibration of the particular Reagent Integral lot. Renewed calibration is required:

- With each new lot of reagents (Reagent Integral or Starter Reagents)
- Every 28 days if stored according instructions in Section 7
- After each servicing of the analyzer
- If Quality Control results are out of the acceptable range

12. SPECIMEN PREPARATION

Using DiaSorin LIAISON® Stool Extraction Device:

1. Add 1.0 mL of LIAISON® Rota/Adeno Sample Diluent into LIAISON® Stool Extraction Device mixing tube.
2. Stool preparation: Mix stool as thoroughly as possible prior to withdrawing sample.
   a. ***Liquid or Semi-Solid Stools:*** Using disposable liquid stool pipettor, measure 20 µL of stool to first mark of pipettor, as shown in the diagram below, and transfer stool volume into the LIAISON® Stool Extraction Device mixing tube containing the sample diluent. Rinse the pipettor several times with stool suspension mixture if necessary to ensure as much sample as possible is removed from the Liquid Stool Pipettor.



   b. ***Solid Stools:*** Using the inoculation loop, add a sample of stool the diameter of the head of the loop, according to the diagrams below, to the mixing tube containing LIAISON® Rota/Adeno sample diluent. The solid stool on the loop should be mixed into the sample diluent well, to ensure that the solid pellet has been rinsed off the loop into the sample diluent.

Upper View without Stool

Side View with Stool

3. Firmly screw the conical blue filter unit onto the mixing tube.
4. Vortex vigorously for 20 seconds to mix stool thoroughly.
5. Centrifuge tube in a swing bucket centrifuge at a speed of ≥ 2000 x g* for 5 minutes at ambient temperature **with conical end of tube pointing DOWN.**
6. Unscrew the mixing tube and blue filter device and discard into appropriate biohazard waste receptacle. Examine liquid supernatant in conical tube, stool supernatant may be cloudy but no visible debris or bubbles should be present.
7. Place conical tube into LIAISON® analyzer sample rack type "S" or LIAISON® XL and LIAISON® XS analyzer sample rack type "H" with adapter. Load the rack onto the Analyzer for testing.
8. Clean work area with 10% bleach solution (0.5% sodium hypochlorite).

Diagrams illustrating stool preparation procedure using the DiaSorin LIAISON® Stool Extraction Device are provided at the end of the instructions for use.

13. ASSAY PROCEDURE

To ensure proper test performance, strictly adhere to the operating instructions of the Analyzer.

LIAISON® Analyzer: Each test parameter is identified via barcode on the Reagent Integral label. In the event the barcode reader cannot be read by the analyzer, the integral cannot be used. Do not discard the Reagent Integral; contact your local DiaSorin technical support for instruction.

LIAISON® XL Analyzer and LIAISON® XS Analyzer: Each test parameter is identified via information encoded in the Reagent Integral Radio Frequency Identification transponder (RFID Tag). In the even that the RFID Tag cannot be read by the analyzer, the integral cannot be used. Do not discard the reagent integral: contact your local DiaSorin technical support for instruction.

The Analyzer operations are as follows:

1. Dispense calibrators, controls or samples into the reaction module.
2. Dispense conjugate into the reaction module.
3. Incubate.
4. Dispense coated magnetic particles into the reaction module.
5. Incubate.
6. Wash with Wash/System liquid.
7. Add the Starter reagents and measure the light emitted.

Immunoassay results can be affected by temperature fluctuations. Users should be aware of variations in their laboratory environment; more frequent use of controls and subsequent recalibration may be necessary.

*$g = (1118 \times 10^{-8})(\text{radius in cm})(\text{rpm})^2$

14. QUALITY CONTROL

Quality control is required to be performed once per day of use, or according to the guidelines or requirements of local regulations or accredited organizations. It is recommended that the user refer to CLSI C24-A3[4], and 42 CFR 493.1256 (c) for guidance on appropriate quality control practices.

LIAISON® Adenovirus Control Set (REF 318951) is intended to monitor for substantial reagent failure. LIAISON® controls should be run in singlicate to monitor the assay performance. If control values lie within the expected ranges provided on the certificate of analysis, the test is valid. Whenever controls lie outside the expected ranges, calibration should be repeated, and controls and samples retested. Patient results are reportable only when control results are within expected ranges.

The performance of other controls should be evaluated for compatibility with this assay before they are used. Appropriate value ranges should be established for all quality control materials used.

The range of concentrations of each control is reported on the certificate of analysis and indicates the limits established by DiaSorin for control values that can be obtained in reliable assay runs.

15. INTERPRETATION OF RESULTS

The analyzer automatically calculates adenovirus antigen levels expressed as Index values and grades the results. For details, refer to the analyzer operator's manual.

The cut-off for the LIAISON® Adenovirus assay was determined based on the results of testing samples that represented patient populations negative and positive for adenovirus.

Samples were tested in parallel by a commercially available adenovirus assay and the LIAISON® Adenovirus assay.

The cut-off value discriminating between the presence and the absence of adenovirus was determined to have an Index value of 1.0.

Warning – If the sample result displays "invalid RLU" and an exclamation mark (!) flag, the result obtained lies below the assay signal range. The sample must be retested. If the sample upon retest still displays "invalid RLU", call DiaSorin Technical Support.

Patient results should be interpreted as follows:

Index	Results	Interpretation
< 0.90	Negative	Indicates the absence of adenovirus antigen, (or the level of adenovirus is below that which can be detected by the assay)
≥ 0.90 and < 1.10	Equivocal	Equivocal samples should be retested using a new extraction from the original sample in order to confirm the initial result. Samples that are positive (≥ 1.10) by the second test should be considered positive. Samples that are negative (< 0.90) by the second test should be considered negative. **For samples that are equivocal on retesting; a new specimen should be collected and tested.**
≥ 1.10	Positive	Indicates the presence of detectable adenovirus antigen.

16. LIMITATIONS OF THE PROCEDURE

1. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.
2. A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
3. Integrals may not be exchanged between analyzer types (LIAISON®, LIAISON® XL and LIAISON® XS). Once an integral has been introduced to a particular analyzer type, it must always be used on that analyzer until it has been exhausted.
4. Due to traceability issues resulting from the above statement, patient follow-ups may not be concluded between analyzer types. These must be accomplished on one particular analyzer type (either LIAISON®, LIAISON® XL or LIAISON® XS).

17. EXPECTED VALUES

The LIAISON® Adenovirus assay detects the presence of group reactive hexon antigen. The rate of positivity may vary with patient age, geographic location, method of specimen collection, handling of the specimen and test used for diagnosis; therefore, each laboratory should determine expected values for each population.

18. SPECIFIC PERFORMANCE CHARACTERISTICS

18.1 Method Comparison:

A total of 188 Stool samples were tested by the LIAISON® Adenovirus assay and a commercial adenovirus ELISA assay. Results are summarized in the table below.

	Comparator Adenovirus EIA			
LIAISON® Adenovirus	Positive	Equivocal	Negative	Total
Positive	41	0	0	41
Equivocal	0	0	0	0
Negative	1	0	146	147
Total	42	0	146	188

Positive Agreement =	(41/42)	97.6%	95% CI (87.7 – 99.4%)
Negative Agreement =	(146/146)	100%	95% CI (97.5 – 100%)
Overall Agreement =	(187/188)	99.5%	95% CI (97.1 – 99.9%)

18.2 Precision:

LIAISON® Analyzer: 2 kit controls and 6 adenovirus antigen buffer based samples were prepared and tested at DiaSorin Inc. twice per day in duplicate, over 12 operating days on 1 LIAISON® Analyzer, with 2 technicians using 1 reagent lot to determine repeatability and reproducibility of the LIAISON® Adenovirus assay. Samples were prepared to the following levels: 2 negative, 1 cutoff sample, and 3 positive. The testing was performed according to CLSI EP5-A2[5].

Repeatability

Sample	Neg KC	Pos KC	1	2	3	4	5	6
Number of determinations	48	48	48	48	48	48	48	48
Mean (Index)	0.03	4.72	0.34	0.75	0.96	1.24	4.70	15.67
Standard Deviation (Index)	0.00	0.06	0.01	0.01	0.02	0.03	0.09	0.23
Coefficient of Variation (%CV)	9.49	1.34	1.97	1.97	2.00	2.21	1.82	1.48

Reproducibility

Sample	Neg KC	Pos KC	1	2	3	4	5	6
Number of determinations	48	48	48	48	48	48	48	48
Mean (Index)	0.03	4.72	0.34	0.75	0.96	1.24	4.70	15.67
Standard Deviation (Index)	0.00	0.12	0.01	0.03	0.03	0.04	0.19	0.48
Coefficient of Variation (%CV)	9.49	2.58	4.02	4.18	3.62	3.60	4.02	3.05

LIAISON® XL Analyzer: 2 kit controls and 6 adenovirus antigen buffer based samples were prepared and tested at DiaSorin Inc. twice per day in duplicate, over 12 operating days on 1 LIAISON® XL Analyzer, with 2 technicians using 1 reagent lot to determine repeatability and reproducibility of the LIAISON® Adenovirus assay. Samples were prepared to the following levels: 2 negative, 1 cutoff sample, and 3 positive. The testing was performed according to CLSI EP5-A2[5].

Repeatability

Sample	Neg KC	Pos KC	1	2	3	4	5	6
Number of determinations	48	48	48	48	48	48	48	48
Mean (Index)	0.04	4.54	0.33	0.73	0.93	1.20	4.51	14.96
Standard Deviation (Index)	0.01	0.09	0.01	0.01	0.02	0.02	0.05	0.24
Coefficient of Variation (%CV)	14.38	1.88	1.72	1.43	1.64	1.66	1.17	1.59

Reproducibility

Sample	Neg KC	Pos KC	1	2	3	4	5	6
Number of determinations	48	48	48	48	48	48	48	48
Mean (Index)	0.04	4.54	0.33	0.73	0.93	1.20	4.51	14.96
Standard Deviation (Index)	0.01	0.32	0.02	0.05	0.07	0.10	0.31	0.90
Coefficient of Variation (%CV)	24.03	7.11	7.36	6.87	7.99	8.18	6.82	6.00

LIAISON® XS Analyzer: 2 kit controls and 6 adenovirus antigen buffer based samples were prepared and tested at DiaSorin Inc. once per day in replicates of 6, over 5 operating days on 3 LIAISON® XS Analyzers, using 1 reagent lot of the LIAISON® Adenovirus assay. The testing was performed according to CLSI EP15-A3.[6]

Sample ID	Mean (Index)	Intra-Run		Total	
		SD	%CV	SD	%CV
Negative Control	0.086	0.004	4.9%	0.004	5.0%
Positive Control	4.812	0.063	1.3%	0.119	2.5%
S1	0.804	0.014	1.7%	0.021	2.6%
S2	0.999	0.017	1.7%	0.027	2.7%
S3	1.130	0.021	1.9%	0.030	2.6%
S4	10.776	0.173	1.6%	0.293	2.7%
S5	14.228	0.244	1.7%	0.449	3.2%
S6	0.480	0.009	1.9%	0.017	3.6%

18.3 Interfering substances: Controlled studies of potentially interfering substances spiked into low positive and high negative adenovirus stool specimens showed no interference at the concentration for each substance listed below in the LIAISON® Adenovirus assay.

Substance	Concentration Tested
Hemoglobin	3.2 mg/mL
Whole Blood	25%
White Blood Cells	5%
Barium Sulfate	5.0 mg/mL
Stearic acid	2.65 mg/mL
Palmitic acid	1.3 mg/mL
Mucin	3.33 mg/mL
Metronidazole	12.5 mg/mL
Vancomycin hydrochloride	2.5 mg/mL
Imodium AD®	6.67×10^{-3} mg/mL
Bismuth Subsalicylate	0.87 mg/mL
Pepto Bismol®	0.87 mg/mL
Prilosec®	0.5 mg/mL
Gas-X®	0.625 mg/mL
Tums®	0.5 mg/mL
Tagamet	0.5 mg/mL
Maalox®	4.2 mg/mL
MiraLAX®	79.05 mg/mL

18.4 Cross-Reactivity

Assay specificity of the LIAISON® Adenovirus assay was determined by testing the following microorganisms. Low positive and high negative adenovirus stool specimens were spiked with each microorganism and tested by the LIAISON® Adenovirus assay. None of the organisms affected positive or negative test results.

Microorganism (in alphabetical order)	Final conc. of variant in sample		Microorganism (in alphabetical order)	Final conc. of variant in sample
Acinetobacter lwoffi	1.2×10^8 CFU/mL		*Salmonella* Group A	1.2×10^8 CFU/mL
Aeromonas hydrophila	1.2×10^8 CFU/mL		*Salmonella* Group B	1.2×10^8 CFU/mL
Campylobacter coli	1.2×10^8 CFU/mL		*Salmonella* Group C	1.2×10^8 CFU/mL
Campylobacter fetus	1.2×10^8 CFU/mL		*Salmonella* Group D	1.2×10^8 CFU/mL
Campylobacter jejuni	1.2×10^8 CFU/mL		*Salmonella* Group E	1.2×10^8 CFU/mL
Candida albicans	1.2×10^8 CFU/mL		*Serratia liquefaciens*	1.2×10^8 CFU/mL
Citrobacter freundii	1.2×10^8 CFU/mL		*Serratia marcescens*	1.2×10^8 CFU/mL
Clostridium difficile	1.2×10^8 CFU/mL		*Shigella boydii*	1.2×10^8 CFU/mL
Clostridium perfringens Type A	1.2×10^8 CFU/mL		*Shigella flexneri*	1.2×10^8 CFU/mL
Clostridium perfringens Type B	1.2×10^8 CFU/mL		*Shigella sonnei*	1.2×10^8 CFU/mL
Clostridium perfringens Type D	1.2×10^8 CFU/mL		*Staphylococcus aureus*	1.2×10^8 CFU/mL
Clostridium perfringens Type E	1.2×10^8 CFU/mL		*Staphylococcus aureus (Cowans)*	1.2×10^8 CFU/mL
Clostridium sordellii	1.2×10^8 CFU/mL		*Staphylococcus epidermidis*	1.2×10^8 CFU/mL
Clostridium sporogenes	1.2×10^8 CFU/mL		*Streptococcus agalactiae*	1.2×10^8 CFU/mL
Enterobacter aerogenes	1.2×10^8 CFU/mL		*Streptococcus dysgalactiae*	1.2×10^8 CFU/mL
Enterobacter cloacae	1.2×10^8 CFU/mL		*Streptococcus uberis*	1.2×10^8 CFU/mL
Enterococcus faecalis	1.2×10^8 CFU/mL		*Veillonella parvula*	1.2×10^8 CFU/mL
Enterococcus faecium	1.2×10^8 CFU/mL		*Yersinia enterocolitica*	1.2×10^8 CFU/mL
Escherichia coli	1.2×10^8 CFU/mL		*Chlamydia trachomatis*	$1 \times 10^{3.75}$ $TCID_{50}$/mL
Escherichia fergusonii	1.2×10^8 CFU/mL		Coxsackievirus A9	$1 \times 10^{5.34}$ $TCID_{50}$/mL
Escherichia hermannii	1.2×10^8 CFU/mL		Coxsackievirus B3	$1 \times 10^{4.70}$ $TCID_{50}$/mL
Helicobacter pylori	1.2×10^8 CFU/mL		Coxsackievirus B4	$1 \times 10^{8.68}$ $TCID_{50}$/mL
Klebsiella pneumoniae	1.2×10^8 CFU/mL		Coronavirus	$1 \times 10^{4.15}$ $TCID_{50}$/mL
Lactobacillus leichmannii	1.2×10^8 CFU/mL		Cytomegalovirus	$1 \times 10^{5.34}$ $TCID_{50}$/mL
Lactococcus lactis	1.2×10^8 CFU/mL		Echovirus 30	$1 \times 10^{6.93}$ $TCID_{50}$/mL
Listeria innocua	1.2×10^8 CFU/mL		Influenza B	$1 \times 10^{4.15}$ $TCID_{50}$/mL
Listeria monocytogenes	1.2×10^8 CFU/mL		Measles	$1 \times 10^{5.66}$ $TCID_{50}$/mL
Morganella morganii	1.2×10^8 CFU/mL		Norovirus Group I	$1 \times 10^{4.62}$ $TCID_{50}$/mL
Peptostreptococcus anaerobius	1.2×10^8 CFU/mL		Norovirus Group II	$1 \times 10^{4.15}$ $TCID_{50}$/mL
Plesiomonas shigelloides	1.2×10^8 CFU/mL		Parainfluenza Virus Type 1	$1 \times 10^{6.06}$ $TCID_{50}$/mL
Porphyromonas asaccharolytica	1.2×10^8 CFU/mL		Reovirus 3	$1 \times 10^{7.75}$ $TCID_{50}$/mL
Proteus mirabilis	1.2×10^8 CFU/mL		Rhinovirus Type 1A	$1 \times 10^{5.10}$ $TCID_{50}$/mL
Proteus vulgaris	1.2×10^8 CFU/mL		Rotavirus	$1 \times 10^{7.25}$ $TCID_{50}$/mL
Providencia stuartii	1.2×10^8 CFU/mL		Respiratory Synctial Virus B	$1 \times 10^{5.58}$ $TCID_{50}$/mL
Pseudomonas aeruginosa	1.2×10^8 CFU/mL		Simian Virus 40	$1 \times 10^{4.25}$ $TCID_{50}$/mL
Pseudomonas fluorescens	1.2×10^8 CFU/mL		Varicella Zoster	$1 \times 10^{4.39}$ $TCID_{50}$/mL
Pseudomonas putida	1.2×10^8 CFU/mL			

18.5 Carry Over

Testing was performed to determine if there was potential instrument carry over on the LIAISON® Analyzer. The obtained results showed no change in the expected value; therefore, the results demonstrate that no carry over is observed with stool samples in the LIAISON® Adenovirus assay on the LIAISON® Analyzer.
Carry over is not applicable to the LIAISON® XL Analyzer and LIAISON® XS Analyzer as disposable tips are used for sample pipetting.

19. References

1. Buckwalter SP, Teo R, Espy MJ, Sloan LM, Smith TF, Pritt, BS. Real-Time Qualitative PCR for 57 Human Adenovirus Types from Multiple Specimen Sources. Journal of Clinical Microbiology. 2012 Mar; 50(3):766-71.
2. Russell WC. Adenovirus: update on structure and function. Journal of General Virology. 2009; 90:1-20.
3. Clark B, McKendrick M. A review of viral gastroenteritis. Current Opinion in Infectious Diseases. 2004,17:461-469.
4. Clinical and Laboratory Standards Institute (CLSI) C24-A3, Vol.26, No.25, Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline - Third Edition.
5. Clinical and Laboratory Standards Institute (CLSI) EP5-A2, Vol.24, No.25, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition.
6. Clinical and Laboratory Standards Institute (CLSI) EP15-A3, Vol.34, No.13, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Third Edition

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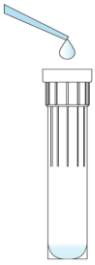
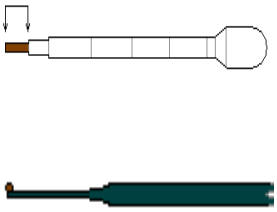
1. LIAISON® Adenovirus Sample Preparation Using LIAISON® Stool Extraction Device



Add 1.0 mL of Rota/Adeno Sample Diluent: to mixing tube



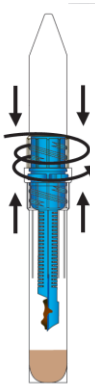
Add Sample:

Liquid or Semi-Solid Stools: Using disposable liquid stool pipettor, measure 20 µL to first mark of pipettor, see diagram.

Solid Stool: Using inoculating loop, add stool the diameter of the head of loop, see diagram of side view with stool.

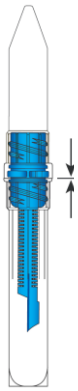
Transfer stool to mixing tube.

2. Device Assembly

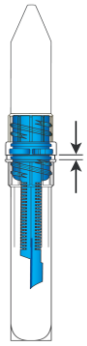


FIRMLY screw the conical blue filter unit onto the mixing tube. The outer edge of each should touch.

NOTE: No gap should be visible when device is properly assembled.

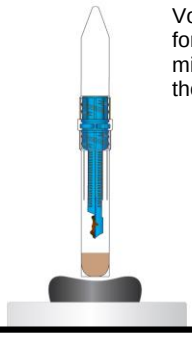


Correct:
No Gap



Incorrect:
Gap is visible

3. Mix



Vortex vigorously for 20 seconds to mix sample thoroughly.

4. Centrifugation

Centrifuge with conical tube pointing down @ ≥ 2000 x g for 5 minutes using a swing bucket centrifuge.

5. Examination and Testing

Unscrew conical tube from device.

Discard mixing tube / blue filter unit into appropriate biohazard waste receptacle according to local regulations.

Examine supernatant. Supernatant may be cloudy but no visible debris or bubbles should be present.

Place conical tube on appropriate DiaSorin Analyzer for testing or see Section 9 in Instructions for Use for recommended storage.

Clean work area with 10% bleach solution (0.5% sodium hypochlorite).

Biohazard
Single Use Device