Adeno Respi *K*-SeT

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***In vitro* rapid diagnostic test for the detection of Respiratory Adenovirus in nasopharyngeal secretions**

FOR IN VITRO USE ***EN***

FOR PROFESSIONAL USE ONLY

References: K-1509, 20 tests per kit, with collection set
K-1209, 20 tests per kit, without collection set

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I. INTRODUCTION

Adenoviruses cause diseases of both the respiratory tract and the eye and give rise to an estimated 5 to 10% of respiratory viral infections. These are icosahedral, non-enveloped double-stranded DNA viruses of 80 nm in diameter. These viruses cause a broad spectrum of human diseases including pharyngitis, pneumonia, conjunctivitis, hemorrhagic cystitis and diarrhoea. Amongst the 49 serotypes, divided into 6 subgroups, only serotypes 40 and 41 have been clearly associated with gastroenteritis disorders.

Adenoviruses infect most children early in life causing stuffy nose and cough whereas pharyngitis is more common in older children. These viruses are known to cause outbreaks of upper and lower respiratory tract infections probably because of crowding and stress conditions. In young adults, diseases are more characterized with pharyngitis and conjunctivitis. Several adenoviral infections, including pneumonia have been identified in immunodepressed patients.

All serotypes are endemic and some may give rise to respiratory outbreaks, which sometimes involve the eye. Of the 49 serotypes, infections by types 2, 3, 5 and 7 are the most common.

The virus is known to infect people by aerosols and by direct contact and give rise to a strong immune response. Diseases are generally mild except in immunocompromised patients in whom it may be lethal.

II. PRINCIPLE OF THE TEST

This test is ready to use and is based on a membrane technology with colloidal gold nanoparticles. A nitrocellulose membrane is sensitized with monoclonal antibodies directed against specific Adenovirus antigens. The test's specificity is due to a monoclonal antibody directed against specific Hexon antigens. It is conjugated to colloidal gold. The conjugate is immobilized on a membrane.

This test is aimed to the detection of Respiratory Adenovirus either in nasopharyngeal secretions or in culture supernatant after several days to reach a better sensitivity.

When the extraction solution of NPS (nasopharyngeal secretions) or culture extracted solution comes into contact with the strip, the solubilised conjugate migrates with the sample by passive diffusion and the conjugate and sample material come into contact with the anti-Adenovirus antibody adsorbed onto the nitrocellulose strip. If the sample contains Adenovirus, the conjugate–Adenovirus complex will remain bound to the anti-Adenovirus antibody adsorbed onto the nitrocellulose. The result is visible within 15 minutes in the form of a red line that develops on the strip. The solution continues to migrate to encounter a control reagent that binds a control conjugate, thereby producing a second red line.

III. REAGENTS AND MATERIALS

1. Adeno Respi *K*-SeT (20)

20 sealed pouches containing one device and one desiccant. Each device contains one sensitized strip.

2. HC dilution buffer (15 mL)

Saline solution buffered to pH 7.5 containing Tris, EDTA, NaN_3 (<0,1%), a detergent and blocking proteins.

3. Instruction for use (1)

4. Materials supplied with item K-1509

- HydroK Buffer for Dry swabs (15 mL). This buffer is to be used in the "dry swab" procedure VIII.2.b.
- Sampling material: 20 swabs from Copan Flock (reference 553C)

Materials to be ordered separately:

- Adenovirus positive control (Ref.: C-1082)
- Negative control (Ref.: CTR-1000)

IV. SPECIAL PRECAUTIONS

- All operations linked to the use of the test must be performed in accordance with Good Laboratory Practices (GLP).
- All reagents are for *in vitro* diagnostic use only.
- Pouch must be opened with care
- Avoid touching nitrocellulose with your fingers.
- Wear gloves when handling samples.
- Never use reagents from another kit.
- Green lines indicate immunoreagents adsorption sites. Green colour disappears during the test.
- Reagents' quality cannot be guaranteed beyond their shelf-life dates or if reagents are not stored under required conditions as indicated in the insert.

V. WASTE DISPOSAL

- Dispose of gloves, swabs, test tubes and used devices in accordance with GLP.
- Each user is responsible for the management of any waste produced, and must ensure that it is disposed of in accordance with the applicable legislation.

VI. STORAGE

- An unopened pouch may be kept at between 4 and 30°C and used until the shelf-life date indicated on the packaging. Once the pouch is opened, run the test immediately.
- Avoid freezing devices and buffer.

VII. SPECIMEN HANDLING AND COLLECTION

Specimens to be tested should be obtained and handled by standard methods for the collection of nasopharyngeal aspirates, nasopharyngeal washes or nasal/nasopharyngeal swabs.[1]

Specimens must be tested as soon as possible after collection. If they are not immediately used, they must be stored at 2-8°C or frozen at -20°C for long periods of time, depending on the transport medium used. Copan Flock swabs with Copan UTM may be stored at 2-8°C for up to 72 hours prior to testing.

The following transport media have been tested and found to be compatible with Coris BioConcept respiratory kits: M4 and M5 from Remel (Oxoid), Virocult medium (MWE), Hank's BSS used in Vircell medium and RPMI. Stuart transport medium and Amies medium are not compatible with this device.

Coris BioConcept recommends using the Flocked Swabs of Copan Flock Technologies (supplied with the K-1509) in order to guarantee the same performances as when nasopharyngeal washes or aspirates are used. The efficiency of other brands of swabs has not been established with our respiratory kits. It is strongly recommended to avoid the use of sputum or saliva as it may lead to invalid results.

Make sure that the specimens are not treated with solutions containing formaldehyde or its derivatives.

VIII. PROCEDURE

PREPARATIONS OF THE TEST:
Allow kit components, in unopened packaging, and specimens to reach room temperature (15-30°C) before performing a test.

Open the pouch and remove the device. Once opened, run the test immediately. Indicate the patient's name or specimen number on the device (one device per sample).

SPECIMEN PREPARATION PROCEDURE:
Performance claims with regard to samples types other than Nasopharyngeal Secretions have not been established. We recommend the use of fresh NPS for optimal test performance.

1. Liquid nasopharyngeal washings and/or aspirates or culture supernatant. If the sample to be tested is liquid, mix 100 µL with 100 µL or 4 droplets of the **HC dilution** buffer to reach a sample extraction ratio of 1/2.
2. Swabs. Swabs can be stored either in a tube containing a transport medium either in a device with a gel or a sponge matrix. Alternatively, Copan Flock dry swabs can be used.
   a- If the swab is stored in a liquid transport medium, it should be wiped out in the medium by pressing its matrix on the tube's wall and the resulting solution should be processed according to point 1.
   b- Dry swab procedure: When there is no dilution medium available, prepare 500 µL (15 droplets) of **HydroK** buffer (kit K-1509) or mix 250 µL (8 droplets) of **HC dilution** buffer with 250 µL of saline solution. Dry swab must be dipped in the prepared solution, twisted and wiped out by pressing swab on the tube wall. Take care not to press the swab against any surface before expressing the sample, as this could lead to virus loss and reduced sensitivity.
3. Stir thoroughly to homogenize the solution
4. Slowly dispense 100µL of diluted sample into the sample well of the device as illustrated below.
5. Leave to react for 15 minutes. The results are observed in the reading window. Positive results may be reported sooner the moment the test and control lines become visible.

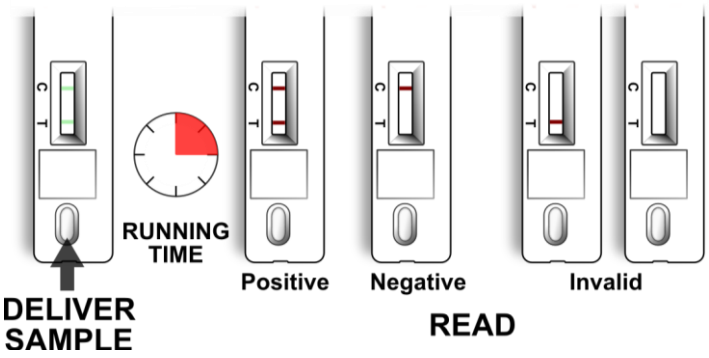
Do not take the appearance of new lines into account after the reaction time is passed.

The result must be read on still wet strip.

[1] Hall, C.B., Douglass, RG., Jr., and Geiman, M. 1975. Clinically useful method for the isolation or Respiratory Syncytial Virus. *J. Infect. Dis* 131: 1-5.

IX. INTERPRETING RESULTS

The results are to be interpreted as follows:



Negative test result: a reddish-purple line appears across the central reading window at the Control line (C) position. No other band is present.

Positive test result: in addition to a reddish-purple band at the Control line (C), a visible reddish-purple band appears at the Test line position (T). Intensity of the test line may vary according to the quantity of antigens found in the sample. Any reddish-purple line (T), even weak, should be considered as a positive result.

Invalid test result: The absence of a Control line indicates a failure in the test procedure. Repeat invalid tests with a new test device.

Note: during the drying process, a very faint shadow may appear at the Test line position. It should not be regarded as a positive result.

X. QUALITY CONTROL

In accordance with Good Laboratory Practices, we recommend checking the test's performance regularly according to the laboratory's requirements. Each control may be used once diluted twofold in the dilution buffer. 100 µL of diluted control should slowly dispense onto the device sample well.

XI. PERFORMANCE (based on Adeno Respi-Strip kit)

There is an excellent agreement (100%) between Adeno Respi *K*-SeT kit and standard Adeno Respi-Strip kit.

A. Detection Limit

The detection limit was determined with a quantified virus (Adenovirus -5 antigen) and has been evaluated at $1x10^6$ vp/mL.

B. Sensitivity - Specificity (Correlation):

The kit was validated (by a third party) in comparison with 2 other ICT competitive tests on 127 throat swab specimens. The following results were obtained:

ICT competitor 1 / Coris BioConcept	Positive	Negative	Total
Positive	48	3[b)]	51
Negative	4[a)]	72	76
Total	52	75	127

a) 3 negative cultures, 1 positive culture
b) All negatives cultures

		95 % Confidence Interval[2]
Sensitivity:	92.3 %	(80.6 to 97.5 %)
Specificity:	96 %	(88 to 99 %)
Positive Predictive value:	94.1 %	(82.8 to 98.5 %)
Negative predictive value:	94.7 %	(86.4 to 98.3 %)
Accuracy:	94.5 % (120/127)	

ICT competitor 2 / Coris BioConcept	Positive	Negative	Total
Positive	47	4[d)]	51
Negative	3[c)]	73	76
Total	50	77	127

c) All negative cultures
d) 2 positive cultures, 2 negative cultures

		95 % Confidence Interval
Sensitivity:	94 %	(82.5 to 98.4 %)
Specificity:	94.8 %	(86.5 to 98.3 %)
Positive Predictive value:	92.2 %	(80.3 to 97.5 %)
Negative predictive value:	96.1 %	(88.1 to 99 %)
Accuracy:	94.5 % (120/127)	

C. Accuracy

To check intra-batch accuracy, the same positive samples and a buffer solution were processed 15 times on kits of the same production batch in the same experimental conditions. All observed results were confirmed as expected.

To check inter-batch accuracy, some samples (positive and buffer) were processed on kits from three different production batches. All results were confirmed as expected.

D. Interference

Cross-reactivity to samples positive for the following pathogens was tested and found to be negative: Influenza A, Influenza B, Herpes virus, Rhinovirus, *Streptococcus pneumonia, Streptococcus pyogenes, Candida albicans, Aspergillus niger,* Enterovirus, *Nocardia asteroides, Moraxella catarrhalis, Legionella pneumophila*, RSV, *Mycoplasme pneumoniae*, *Parainfluenzae* type III.

Tests for cross-reactivity has been tested on *Staphylococcus aureus* and found positive at high bacteria concentrations (10^9 cfu/mL).

XII. LIMITS OF THE KIT

The test is qualitative and cannot predict the quantity of antigens present in the sample. Clinical presentation and other test results must be taken into consideration to establish diagnosis.

A positive test does not rule out the possibility that other pathogens may be present.

Kit test is an acute-phase screening test. Specimens that are collected after this phase may contain antigen titres below the reagent's sensitivity threshold. If a sample is given a negative result despite the observed symptoms, any other relevant test should be run to check the sample.

XIII. Technical problems / Complaints

If you encounter a technical problem or if performances do not correspond with those indicated in this package insert:

1. Record batch number of incriminated kit
2. If possible, keep the problematic sample in the freezer for the time lapse of complaint management
3. Contact Coris BioConcept (client.care@corisbio.com) or your local distributor

XIV. BIBLIOGRAPHIC REFERENCES

A. **Van Beers D., Chaker S., De Foor M., Viehoff R.**; *Comparison of a Rapid Immunochromatographic Diagnostic Test with Viral Culture to Detect Adenovirus in Respiratory Specimens.*; Posters/Journal of Clinical Virology 27, p. 33., 2003

B. **Renuart I., Mertens P., Leclipteux Th. :** *Adeno Respi-Strip, an Immunochromatographic Test for the Detection of Respiratory Adenovirus.*; European Biotech Crossroads, October 15-16 – Lille-Grand Palais-France, 2002.

Last update: OCTOBER 2012

REF	Catalogue number		Manufactured by
IVD	In vitro diagnostic medical device		Temperature limits
	Contains sufficient for <n> tests	DIL SPE	Diluent specimen
	Consult instructions for use		Do not reuse
	Keep dry		Use by
DIL AS	Diluent assay	CONT NaN_3	Contains Sodium azide

[2] Newcombe, Robert G. "Two-Sided Confidence Intervals for the Single Proportion: Comparison of Seven Methods," *Statistics in Medicine,* **17**, 857-872 (1998).