# RSV *K*-SeT

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Produced in BELGIUM

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

***FOR IN VITRO USE*** ***EN***

**FOR PROFESSIONAL USE ONLY**

**References: K-1506, 20 tests per kit, with collection set**
**K-1206, 20 tests per kit, without collection set**

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## I. INTRODUCTION

RSV, Respiratory Syncytial Virus, is the major cause of respiratory illness in all ages. It represents the most frequent cause of serious respiratory tract infections in infants and children younger than 4 years of age but is also responsible for severe problems in elderly and immunocompromised patients giving rise to high death rates. Pneumonia and bronchiolitis are the two most frequent severe infections prevalent in infants aged 2 to 6 months. Infection of older children and adult may be mild, usually self-limiting, causing nasal stuffiness and discharge not distinguishable from a common cold.

Every year, up to 50% of infants are infected. RSV disease causes about 70% of bronchiolitis and results in 80,000 to 125,000 hospitalisations in the US. Those children who require hospitalisation are newborns and children suffering from asthma, lung disorders or heart problems. Moreover, RSV bronchiolitis in the first year of life is one of the most important risk factors for the subsequent development of asthma.

It is a highly contagious disease through contact with respiratory secretions. It is also a common cause of nosocomial infections whose prevalence increases during community outbreaks through casual contacts. RSV affects both the upper and lower respiratory tracts, but pneumonia and bronchiolitis are the most prevalent lower respiratory illnesses. Bronchiolitis is diagnosed by coughing, wheezing, and the onset of dyspnoea, increase of respiratory rate up to 40 breaths per minute and bluish discoloration of the skin around the mouth. Rattling in the chest and respiratory distress are common symptoms of pneumonia.

## 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 a monoclonal antibody directed against one epitope of the F protein of the Respiratory Syncytial Virus. Another monoclonal antibody directed against a second epitope of the F protein is conjugated to colloidal gold particles. This conjugate is dried on a membrane.

This test is aimed to the detection of RSV either in nasopharyngeal secretions or in supernatant after several days of culture in order 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 both the conjugate and sample material come into contact with the anti-RSV antibody that it is adsorbed onto the nitrocellulose strip. If the sample contains RSV, the conjugate–RSV complex will remain bound to the anti-RSV 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. RSV *K*-SeT (20)**
20 sealed pouches containing one device and one desiccant. Each device contains one sensitized strip.

**2. Extraction buffer (15 mL)**
Saline solution buffered to pH 7.5 containing Borate, $NaN_3$ (<0,1%) and a detergent.

**3. Instruction for use (1)**

**4. Materials supplied with K-1506**
Sampling material: 20 swabs from Copan Flock (reference 553C)

Materials to be ordered separately:
- RSV positive control (Ref.: C-1086)
- 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-1506) 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 extraction buffer to reach a sample dilution 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, dry swab must be dipped in 15 droplets or 500 µL of extraction buffer, 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

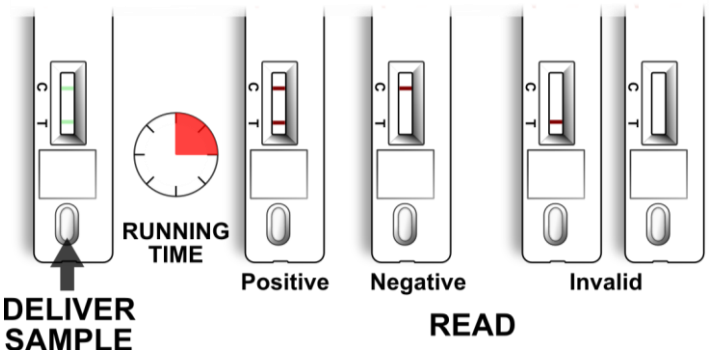
The results are to be interpreted as follows:

**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 extraction buffer. 100 µL of diluted control should slowly dispense onto the device sample well.

## XI. PERFORMANCE

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

### A. Detection Limit

The detection limit was determined with a quantified virus (RS Virus Strain A-2) and has been evaluated at 3.7 X $10^5$ vp/mL (based on RSV Respi-Strip kit).

### B. Sensitivity - Specificity (Correlation):

The RSV kit was validated by comparison with a cell culture method in a routine laboratory lab (Belgium).

| Culture / Coris BioConcept | Positive | Negative | Total |
|---|---|---|---|
| **Positive** | 48 | 17 [(a)] | 65 |
| **Negative** | 2 | 170 | 172 |
| **Total** | 50 | 187 | 237 |

(a) Of the 17 Coris RSV false-positive results 15 were positive by RT-PCR (RT-PCR method[2])

| | | 95 % Confidence Interval[3] |
|---|---|---|
| Sensitivity: | 96 % | (85.1 to 99.3 %) |
| Specificity: | 90.9 % | (85.6 to 94.5 %) |
| Positive Predictive value: | 73.8 % | (61.2 to 83.6 %) |
| Negative predictive value: | 98.8 % | (95.4 to 99.8 %) |
| Accuracy: | 92 % (218/237) | |

Results corrected by RT-PCR approach:

| | | 95 % Confidence Interval |
|---|---|---|
| Sensitivity: | 96.9 % | (88.4 to 99.5 %) |
| Specificity: | 98.8 % | (95.4 to 99.8 %) |
| Positive Predictive value: | 96.9 % | (88.4 to 99.5 %) |
| Negative predictive value: | 98.8 % | (95.4 to 99.8 %) |
| Accuracy: | 98.3 % (233/237) | |

### 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: *Adenovirus, HSV, Parainfluenza, Enterovirus, Influenza A, Influenza B, Rhinovirus, Nocardia asteroides, Streptococcus pneumoniae, Moraxella catarrhalis, Streptococcus pyogenes, Aspergillus niger, Legionella pneumophilae, Candida albicans, Haemophilus influenzae*.

Tests for cross-reactivity has been tested on *Staphylococcus aureus* and found positive at a high bacteria concentration ($10^9$ 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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| **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] Steven J. Read and John B. KurtZ; Laboratory Diagnosis of Common Viral Infections of the Central Nervous System by Using a Single Multiplex PCR Screening Assay. *J. Clin. Microbiol* 1999 37, No 5: p.1352-1355.

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