Overview

Useful For
Rapid detection of respiratory infections caused by the following:

- Adenovirus
- Coronavirus (serotypes HKU1, NL63, 229E, OC43)
- Human metapneumovirus
- Human rhinovirus/enterovirus
- Influenza A (H1, H1-2009, H3)
- Influenza B
- Parainfluenza virus (serotypes 1-4)
- Respiratory syncytial virus (RSV)
- *Bordetella pertussis*
- *Chlamyphila pneumoniae*
- *Mycoplasma pneumoniae*

This test is not recommended as a test of cure.

Highlights
The FilmArray respiratory panel is a multiplex PCR test capable of qualitatively detecting DNA or RNA of 20 pathogens (bacteria and viruses) in approximately 1 hour from bronchoalveolar lavage (BAL) fluid or bronchial washings.

This test is used to diagnose infection caused by adenovirus, coronavirus (HKU1, NL63, 229E, OC43), human metapneumovirus, human rhinovirus/enterovirus, influenza A (H1, H1-2009, H3), influenza B, parainfluenza (1, 2, 3, 4), respiratory syncytial virus, *Bordetella pertussis, Chlamyphila pneumoniae*, and *Mycoplasma pneumoniae*.

Method Name
Multiplex Polymerase Chain Reaction (PCR)

NY State Available
Yes

Specimen

Specimen Type
Varies
Ordering Guidance
This assay is not predicted to detect SARS-coronavirus (CoV), MERS-CoV, or the virus (SARS-CoV-2) causing coronavirus disease-2019 (COVID-19).

It is not recommended that the following tests be concomitantly ordered if this test is ordered:

-FLUMS / Influenza Virus Type A and Type B, and Respiratory Syncytial Virus (RSV), Molecular Detection, PCR, Varies

-LADV / Adenovirus, Molecular Detection, PCR, Varies

-LENT / Enterovirus, Molecular Detection, PCR, Varies

-BPRP / Bordetella pertussis and Bordetella parapertussis, Molecular Detection, PCR, Varies

-MPRP/ Mycoplasma pneumoniae, Molecular Detection, PCR, Varies

This test is appropriate for bronchoalveolar lavage or bronchial washings only. For nasopharyngeal swab specimens, order RESPM / Respiratory Pathogen Panel, PCR, Nasopharyngeal.

Shipping Instructions
Specimens that cannot be shipped refrigerated within 3 days (72 hours) should be frozen prior to shipment. Specimens received older than 72 hours (refrigerated) or older than 30 days (frozen) will be canceled.

Specimen Required
Specimen Type: Fluid

Sources: Bronchoalveolar lavage (BAL) or bronchial washings

Container/Tube: Sterile container

Specimen Volume: 1 mL

Forms
If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Specimen Minimum Volume
0.5 mL

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Refrigerated (preferred)</td>
<td>72 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>30 days</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Information

Respiratory infections are common and generally self-limited in healthy, immunocompetent hosts. Viruses account for a significant percentage of respiratory diseases, but bacteria are also associated with respiratory infections, including pneumonia. Although respiratory illnesses are frequently mild, viruses and bacteria may cause significant morbidity and mortality in immunocompromised hosts (e.g., transplant recipients, patients with underlying malignancy); however, there is potential for prolonged shedding of microorganisms or nucleic acids in immunocompromised patients without their necessarily causing clinical disease; laboratory results should be interpreted in the context of clinical findings. Influenza viruses (type A and type B) and respiratory syncytial virus (RSV) are 2 common causes of viral respiratory illness, with peak incidence in the winter and spring months in the Northern hemisphere. Both viruses can cause a clinically indistinguishable syndrome, characterized by fever, cough, headache, and general malaise. RSV is a leading cause of respiratory illness in young children. Early diagnosis of influenza and RSV is important so that 1) necessary infection control precautions can be taken if the patient is hospitalized, and 2) antiviral therapy can be considered if the patient is hospitalized or considered at high-risk for severe disease.(1) Human metapneumovirus is a relative of RSV, and is also a cause of respiratory illness in both children and adults.

Human rhinovirus and coronavirus (serotypes HKU1, NL63, 229E, OC43) are the causative agents of the common cold, with symptoms including runny nose, sore throat, and malaise. Infections with rhinovirus and coronaviruses are common due to the large number of serotypes of these viruses. The vast majority of infections are mild and self-limiting; however, immunocompromised hosts may suffer more severe illness, including lower respiratory tract disease.

Parainfluenza viruses are a common cause of mild, self-limiting viral infections, especially in young children. Infections are most common in the spring, summer, and fall months, with symptoms including fever, runny nose, and cough; however, parainfluenza may also cause more severe lower respiratory disease, such as croup or pneumonia particularly in older adults or immunocompromised patients.

Adenoviruses may infect a range of organ systems, with sequelae ranging from cold-like symptoms (sore throat), to pneumonia, conjunctivitis (pink eye), or diarrhea. Adenoviruses generally cause mild, self-limited infections but may cause severe disease in immunosuppressed patients.

Respiratory infections may also be caused by bacterial pathogens, including Bordetella pertussis, Chlamydia pneumoniae, and Mycoplasma pneumoniae. Bordetella pertussis is the causative agent of pertussis, or whooping cough, a disease characterized by persistent cough that may be associated with an inspiratory whoop and post-tussive vomiting. Mycoplasma pneumoniae is a cause of upper respiratory infection, pharyngitis, tracheobronchitis, and pneumonia. Chlamydia pneumoniae is a rare cause of pneumonia.

Reference Values

Negative (for all targets)

Interpretation

Results of the panel are intended to aid in the diagnosis of illness and are meant to be used in conjunction with other clinical and epidemiological findings.

A negative result should not rule-out infection in patients with a high pretest probability for a respiratory infection. The assay does not test for all potential infectious agents of respiratory disease. Samples collected too early or too late in the clinical course may not yield the organism causing disease. Negative results should be considered in the context...
of a patient's clinical course and treatment history, if applicable.

Positive results do not distinguish between a viable/replicating organism and the presence of a nonviable organism or nucleic acid, nor do they exclude the potential for coinfection by organisms not contained within the panel. Nucleic acid may persist in some patients for days to weeks, even following appropriate therapy. Detection of 1 or more organisms included in this test suggests that the virus/bacterium is present in the clinical sample; however, the test does not distinguish between organisms that are causing disease and those that are present but not associated with a clinical illness. Coinfections (eg, detection of multiple viruses or bacteria or viruses and bacteria) may be observed with this test. In these situations, the clinical history and presentation should be reviewed thoroughly to determine the clinical significance of multiple pathogens in the same specimen.

**Cautions**

The detection of microbial DNA or RNA is dependent upon proper sample collection, handling, transportation, storage, and preparation. There is a risk of false-negative results due to the presence of strains with sequence variability or genetic rearrangements in the target regions of the assays.

Repeat testing should not be performed on samples collected less than 7 days apart.

This test is **not** intended for otherwise healthy, immunocompetent patients that are likely to have a mild, self-limited respiratory infection. If testing is desired, these patients should be tested by more targeted diagnostic assays based on their exposure history and clinical presentation (eg, FLUNP / Influenza Virus Type A and Type B, and Respiratory Syncytial Virus [RSV], Molecular Detection, PCR, Nasopharyngeal Swab; BPRP / Bordetella pertussis and Bordetella parapertussis, Molecular Detection, PCR, Varies; or MPRP / Mycoplasma pneumoniae, Molecular Detection, PCR, Varies).

**Adenovirus:**

Assay may variably detect nonrespiratory serotypes within species A, D, F, and G.

**Influenza A:**

Performance characteristics were established when influenza A H1-2009, A H1, and A H3 were the predominant influenza A viruses in circulation. Capability of detecting influenza A may vary if other influenza A strains are circulating or if a novel influenza A virus emerges. The performance of the FilmArray RP has not been established in individuals who received influenza vaccine. Recent administration of a nasal influenza vaccine may cause false-positive results for influenza A and/or influenza B. Some strains of human, swine or avian origin are predicted to react with influenza A assays leading to an influenza A (no subtype detected) result.

The assay detects and differentiates commonly occurring influenza A hemagglutinin subtypes based only on the hemagglutinin gene, through the use of 2 influenza A assays and 3 subtyping assays for the hemagglutinin gene. Results are reported as "detected" when at least 1 of the influenza A assays and 1 of the subtyping assays are both positive. If both of the influenza A assays are positive without a hemagglutinin subtype, results are reported as Influenza A (no subtype detected). Equivocal results are reported following repeat testing in 2 scenarios: 1) Neither of the influenza A assays are positive without a hemagglutinin gene is positive, 2) One of the influenza A assays is positive, and hemagglutinin genes are negative. The assay does not detect the influenza A neuraminidase gene.

**Influenza B:**

A new influenza B subclade (B/Victoria V 1A.3 emerged during the 2018-2019 influenza season that demonstrates a mild reduction in analytical sensitivity (estimated 10-100 fold difference in the limit of detection with this test, approximately 2000 copies per mL) compared to other Victoria strains.
Rhinovirus/Enterovirus Group:

Due to the genetic similarity of these viruses, the assay is unable to reliably differentiate the members of this group.

*Bordetella pertussis*:

Some acellular vaccines contain polymerase chain reaction (PCR)-detectable DNA. Contamination of specimens with vaccine can cause false-positive *B pertussis* PCR results. Specimens should not be collected or processed in areas that are exposed to *B pertussis* vaccine material.

Assay targets the single-copy promoter region of the pertussis toxin gene. Results of this assay may not be concordant with commonly used *Bordetella* PCR assays that target the multicopy insertions sequences (IS481). Cross reactivity could occur with high levels or rare sequence variants of other species such as *Bordetella bronchiseptica* and *Bordetella parapertussis*.

Coronavirus:

Coronavirus OC43 assay may cross-react with coronavirus HKU1. As a result, when both HKU1 and OC43 are detected in the same patient specimen, the result may be due to assay cross-reactivity. A coinfection with these 2 viruses is also possible.

**Supportive Data**

This test is FDA-approved on nasopharyngeal (NP) swabs and the manufacturer has submitted clinical performance data for this sample type. Mayo Clinic conducted a verification study of this assay using a combination of clinical and spiked bronchoalveolar lavage (BAL) and bronchial washing fluids which were collected from patients with suspected lower respiratory tract infection. These studies consisted of a retrospective comparison of the FilmArray Respiratory Panel (RP) to conventional methods (eg, routine viral cell culture, influenza A/B and RSV PCR, etc.). Spiking studies using commercially available control material (ZeptoMetrix) and prospective testing using BAL and NP swabs collected concurrently were performed. The results were compared and discordant findings were arbitrated by a third method, if possible.

For the retrospective study, 23 clinical BAL and bronchial washings that were previously tested in our laboratory were selected and tested in a blinded fashion by the FilmArray RP. Results are shown in Table 1.

**Table 1.** Retrospective comparison of the FilmArray RP to routine methods using BAL fluid.

<table>
<thead>
<tr>
<th>Samples tested by routine methods with an expected result of:</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samples tested by FilmArray RP with a result of:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>19 (A,B)</td>
<td>1 (C)</td>
<td>20</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>4</td>
<td>23</td>
</tr>
</tbody>
</table>

A. Among these 19 samples, the following analytes were represented:

Influenza A H3 (n=6)
Human metapneumovirus (n=4)
Human rhinovirus/enterovirus (n=2)
Adenovirus (n=3)
Coronavirus OC43 (n=1)
Parainfluenza 2 (n=1)
Parainfluenza 3 (n=2)
Respiratory syncytial virus (n=1)
Influenza B (n=1)

B. One sample that was positive for influenza A by virus culture was positive for influenza A H3, coronavirus (CoV) OC43, and human metapneumovirus (hMPV) by FilmArray RP. However, because routine virus culture does not detect CoV OC43 or hMPV, this result is being considered concordant for the purpose of this study. This sample was no longer available for arbitration by a third method.

C. One BAL sample that was negative by routine viral culture was positive for rhinovirus/enterovirus by the FilmArray RP. Viruses must be viable for recovery in culture, whereas the FilmArray instrument is capable of detecting nonviable nucleic acid. This sample was no longer available for discordant result resolution.

Overall agreement: 95.7% (22/23)

Spiking studies were performed with analyte-negative BAL samples spiked with diluted Zeptometrix control material "pools". The spiked BAL samples were tested in a blinded fashion and the number of expected targets was compared to the number of targets detected. The spiking studies yielded as follows: sensitivity 95.6% (215/225), specificity 97.6% (782/801) and overall agreement of 97.2% (997/1026).

Prospective studies were performed as part of a clinical study. One hundred twenty six (126) patients presenting with clinical symptoms consistent with a respiratory infection underwent concurrent collection of BAL fluid and an NP swab.

Result correlation following discordant result resolution is summarized below.

Comparison of FilmArray RP results on BAL fluid and NP swabs after discordant result resolution.

<table>
<thead>
<tr>
<th>Targets with a BAL fluid result of:</th>
<th>Number of targets with an NP swab result of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>28</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
</tr>
</tbody>
</table>

Overall agreement (following discordant result resolution): 99.2% (2376/2394)

A prospective study with 100 immunocompromised hosts (ICH) and 25 non-ICH compared results of the FilmArray Respiratory Panel on paired NP and BAL samples. The percent of positive respiratory panel results using BALs for
ICH and non-ICH were 27% (27/100) and 4% (1/25), respectively. The percent of positive respiratory panel results using NPs for ICH and non-ICH were 24% (24/100) and 8% (2/25), respectively. Most (89%) patients had concordant results between NP and BAL samples. Five (21%) ICH patients had a negative NP, but a positive BAL.

**Clinical Reference**


**Performance**

**Method Description**

The FilmArray Respiratory Panel (RP) pouch is a closed system that performs all the chemistry required to isolate, amplify, and detect nucleic acid from multiple viral and bacterial respiratory pathogens within a single lower respiratory specimen obtained from individuals suspected of respiratory tract infections. A panel contains reagents in freeze-dried form and is divided into discrete segments where the required chemical processes are carried out. Patient sample and hydration fluid are drawn by vacuum into the panel and then placed into the FilmArray instrument. The detection process operations are automated (nucleic acid purification, first stage polymerase chain reaction [PCR], second stage PCR, and melt analysis) and complete in about an hour in this closed system.

Nucleic Acid Purification: The sample is lysed by a combination of chemical and mechanical mechanisms and the liberated nucleic acid is captured, washed and eluted using magnetic bead technology.

First-Stage PCR: A reverse transcription step is performed to convert viral RNA into cDNA prior to amplification. The purified nucleic acid solution is combined with a preheated master mix to initiate the reverse transcription step and subsequent thermo cycling for multiplex PCR.

Second-Stage PCR: Products of first stage PCR are diluted and mixed with fresh PCR reagents containing an intercalating fluorescent DNA dye (LCGreen Plus, BioFire Diagnostics), which is distributed over the second stage PCR array. The individual wells of the array contain primers for different assays (in triplicate) that target specific nucleic acid sequences from each of the pathogens detected, as well as control template material.

DNA Melting Analysis: Temperature is slowly increased and fluorescence in each well of the array is monitored and analyzed to generate a melt curve.

Analysis of Melt Curves: The software evaluates the DNA melt curve for each well to determine if a PCR product was present in that well. If the melt profile indicates the presence of a PCR product, then the analysis software calculates the melting temperature of the curve, which is then compared against the expected range for the assay. When the software determines that the melt curve is positive and in range, it is called positive. When it determines that the melt curve is negative or is not in the appropriate range, it is called negative.
Analysis of Replicates: Melt curves of each of the 3 replicates for each assay are evaluated to determine the assay result. For an assay to be called positive, at least 2 of the 3 associated melt curves must be called positive, and the melting temperature (Tm) for at least 2 of the 3 positive melt curves must be similar (within 1 degree C). Assays that do not meet these criteria are called negative. (Instruction manual: FilmArray Respiratory Panel (RP). BioFire Diagnostics, LLC; RFIT-PRT-0435-03 05/2017)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

1 to 2 days

Specimen Retention Time

7 days

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test has been modified from the manufacturer’s instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

87633

87798

87581

87486

LOINC® Information

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