CONSULT®
diagnostics

McKESSON

INFLUENZA A&B TESTS

A rapid qualitative test that detects Influenza type A and type B antigens directly from nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens. For professional and laboratory use only. For *in vitro* diagnostic use only. Rx Only. For use with MFR # 181-36025.

CLIA Complexity: Moderate Complexity when Used with Nasopharyngeal Wash/Aspirate Samples. CLIA Waived when Used with Nasal and Nasopharyngeal Swabs.

INTENDED USE

McKesson Consult® Influenza A&B Test is an *in vitro* rapid qualitative test that detects influenza type A and type B nucleoprotein antigens directly from nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens obtained from patients with signs and symptoms of respiratory infection. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections.

Negative test results are presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other management decisions.

The test is intended for professional and laboratory use.

Performance characteristics for influenza A and B were established during the 2007-2009 and the 2014-2016 influenza seasons when influenza A/H1N1, A/H1N1 pandemic, A/H3N2, influenza B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the Flu Activity & Surveillance reports from the CDC. When other influenza viruses are emerging, performance characteristics may vary.

If infection with a novel influenza virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

SUMMARY AND EXPLANATION

Influenza is a highly contagious acute viral infection of the respiratory tract. It is a communicable disease easily transmitted from person to person through aerosol droplets excreted when sneezing and coughing. Common symptoms include high fever, chills, headache, cough, sore throat and malaise. The type A influenza virus is more prevalent and is the primary pathogen associated with serious epidemics. The type B virus causes a disease that is generally not as severe as that caused by the type A virus.

An accurate diagnosis of influenza based on clinical symptoms is difficult because the initial symptoms of influenza are similar to those of numerous other illnesses. Therefore, it can be confirmed only by laboratory diagnostic testing.[1] Early differential diagnosis of influenza type A or type B can allow for proper treatment with appropriate antiviral therapy while reducing the incidence of inappropriate treatment with antibiotics. Early diagnosis and treatment is of particular value in a clinical setting where accurate diagnosis can assist the healthcare professional with management of influenza patients who are at risk for complications.[2] McKesson Consult Influenza A&B Tests are a rapid immunoassay to be used as an aid for the differential diagnosis of influenza type A and type B.

PRINCIPLE OF PROCEDURE

McKesson Consult Influenza A&B Tests utilize the chemical extraction of viral antigens followed by solid-phase immunoassay technology for the detection of extracted antigen, influenza A and/or B. In the test procedure, a specimen is collected and placed for one minute into the Extraction Well of the test cassette containing extraction solution, during which time antigen is extracted from disrupted virus particles. The test cassette is then raised, tapped and laid back down onto a level surface to allow the solution in the Extraction Well to migrate through the pads containing detector antibodies conjugated to gold dye and then through the test membrane. If influenza antigens are present in the specimen, they will react with anti-influenza antibody coupled to gold dye particles, migrate through the membrane as antigen-antibody-dye complexes, bind to the immobilized anti-influenza antibody on the membrane, and generate a colored line in the test line position (A and/or B). The rest of the sample and unbound/bound dye complexes continue to migrate to the control line position (C), where antibody to the anti-influenza antibody is immobilized, and forms the control line. Formation of the control line serves as an internal control to demonstrate that antibodies in the dye pad have been hydrated and that sufficient sample has been applied to allow for migration to the test line and beyond. If the control line does not appear within the designated incubation time, the result is invalid and the test should be repeated.

McKesson Consult Influenza A&B Tests have two test lines, one for influenza A and one for influenza B. The two test lines allow for the separate and differential identification of influenza A and/or B from the same specimen. If either test line appears in the test result window, together with the control line, the test result is positive for influenza.

REAGENTS

Materials Provided

Each McKesson Consult Influenza A&B Test kit contains enough reagents and materials for 25 tests. The following components are included in a kit.

- McKesson Consult Influenza A&B test cassettes (25): The test strip in each cassette contains mouse monoclonal antibodies to nucleoprotein (NP) of influenza A and influenza B. The cassette is individually pouched.
- Extraction Reagent in capsules (25): For use with swab samples, 300 µL of Phosphate buffer with detergents and preservative
- Sterile Swabs (25): For swab samples
- Positive Control Swab (1): Influenza A and B antigens (non-infective recombinant nucleoprotein)
- Negative Control Swab (1): Inactivated Group B Streptococcus antigen (non-infective)
- Package Insert /Instructions for use (1)
- Procedure Card (1)

Materials Required, But Not Provided

For Aspirate Samples only (available separately: MFR # 181-36026)

- Extraction Reagent in a bottle (5 mL): Phosphate buffer with detergents and 0.09% sodium azide
- Disposable Transfer Pipettes (50): Buffer and sample transfer
- Procedure card for aspirate samples

For All Sample types:

- Timer
- Latex gloves

PRECAUTIONS/WARNINGS

- For *in vitro* diagnostic use only.
- Do not use after the expiration date.
- Use only the swabs provided for collecting swab samples. Other swabs may not work properly.
- Two forms of Extraction Reagent are available. Use Extraction Reagent in capsules to test swab samples, and Extraction Reagent in a bottle to test nasopharyngeal wash/aspirate samples.
- Do not smoke, eat or drink in areas in which specimens or kit reagents are handled.
- Extraction Reagent is slightly caustic. Avoid contact with eyes, sensitive mucous membranes, cuts, abrasions, etc. If the reagent comes in contact with skin or eyes, flush with a large volume of water.
- Wear disposable gloves while handling kit reagents or specimens and thoroughly wash hands afterwards.
- All specimens should be handled as if they are capable of transmitting disease. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimens and test cassettes.
- The McKesson Consult Influenza A&B test cassette should remain in its original sealed pouch until ready for use. Do not use the test if the seal is broken or the pouch is damaged.
- Performance characteristics for influenza A were established when influenza A/H3 and A/H1 were the predominant influenza A viruses in circulation. When other influenza A viruses emerge, performance characteristics may vary.

- If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimen should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

STORAGE AND STABILITY

The McKesson Consult Influenza A&B Test may be stored at 35-86°F (2-30°C) in the original sealed pouch, away from direct sunlight. Kit contents are stable until the expiration date printed on the pouch or box.

SPECIMEN COLLECTION AND PREPARATION

- Inadequate or inappropriate specimen collection, storage, and transport are likely to yield false negative test results. Training in specimen collection is highly recommended because of the importance of specimen quality.
- To collect nasopharyngeal or nasal swab specimens, the swab provided in the McKesson Consult Influenza A&B test kit should only be used.
- Using 2.5 mL of sterile saline solution is recommended to collect wash/aspirate specimens.
- Use fresh samples for best performance. Freshly collected specimens should be tested immediately. If necessary, aspirate specimens may be stored for up to 8 hrs at room temperature or up to 24 hrs at 2-8°C, and swab samples for up to 4 hrs at room temperature or up to 8 hrs at 2-8°C. Aspirate samples can be frozen for up to 7 days.
- If transport of the samples is required, the following transport media have been tested and shown not to interfere with the performance of the test.

BD™ Universal Viral Transport medium	Bartel ViraTrans™ medium
Saline Solution	Puritan Amies Transport medium
Veal Infusion Broth	Puritan UTM medium
Copan UTM-RT medium	Hank's Balanced Salt Solution
Tryptose Phosphate Broth	M4 medium
M5 medium	M6 medium
PBS	PBS + 0.5% BSA
BD™ Eswab collection kit (Buffer only)	

NOTE: Using one milliliter (1 mL) or less of transport media is recommended for optimal test performance, as dilution of the sample may result in decreased test sensitivity.

Flu A&B Specimen Collection Procedures

Good sample collection is the most important first step for an accurate test result. Therefore, follow below instruction carefully to obtain as much secretion as possible.

Nasal Swab Specimen:

Using a flocked swab provided in the McKesson Consult Influenza A&B Test Kit, gently insert the swab approximately 1/4" into the anterior nares (just inside the nasal orifice). Rotate the swab a few times, and repeat in the second nostril, using the same swab.

Nasopharyngeal Swab Specimen:

Using a flocked swab provided in the McKesson Consult Influenza A&B Test kit, insert the swab into the nostril, gently rotating the swab inward until resistance is met at the level of the turbinates. Rotate the swab a few times against the nasopharyngeal wall and then withdraw the swab.

Nasopharyngeal Aspirate Specimen:

With the patient's head slightly hyper-extended, instill 2.5 mL or less (the minimal volume of saline required per patient's size and age) of sterile saline into the patient's nostril. Gently thread the tube through the external nostril, into the nasopharynx. Aspirate wash solution by gentle suction with rotating movement.

NOTE: Catheter should remain in nasopharynx no longer than 10 seconds. Repeat the procedure until adequate sample volume (2.5ml) is obtained.

Nasopharyngeal Wash Specimen:

Adults and Older Children:

Position the patient comfortably in a sitting position, with the neck slightly hyper-extended. Prior to the procedure, have the patient blow their nose.

Using a sterile syringe, introduce 2.5 ml of sterile saline into one nostril. If possible, have the patient retain the saline for a few seconds. Place specimen container directly under the nose with slight pressure on the upper lip. Tilt the head forward and allow the fluid to flow into the specimen container. Repeat the procedure on other nostril, collecting fluid into the same container.

Infants and Younger Children:

The parent should wrap one arm around the child in a manner that will restrain the child's body and arms. Fill a bulb syringe with 2.5 ml of sterile saline, depending on the size of the patient, and instill saline into one nostril, while the head is tilted back. Release the pressure on the bulb to aspirate the specimen back into the bulb. Transfer the specimen into specimen container. Repeat the procedure on other nostril, transferring the second specimen into the same specimen container.

TEST PROCEDURE

Procedural Notes

- The test procedure below must be followed to obtain accurate and reproducible results.
- Reagents, specimens, and cassettes must be at room temperature (18-30°C) for testing.
- Do not open the foil pouch until you are ready to perform the test.
- Several tests may be run at one time.
- Label the cassette with the patient identification or control to be tested.
- Place test cassette on a level surface.

Swab Sample Procedure

1. Tear the tab off the Extraction Reagent capsule.
2. Squeeze the Extraction Reagent capsule to dispense all of the solution into the Extraction Well of the test cassette.
3. Insert the specimen swab on the Swab Stand in the Extraction Well. Rotate swab 3 times to mix the specimen.
4. Incubate 1 minute with the swab in Extraction Well.
5. Rotate swab 3 times to mix the specimen. Remove and discard the swab.
6. Raise the cassette upright (see picture).
7. Let it stand for 1-2 seconds. Gently tap the cassette to ensure that the liquid flows into the hole.
8. Lay the cassette back down onto the flat surface. Start timing.
9. Read test results at 10-15 minutes. Confirm negative results at 15 minutes.

Nasopharyngeal Wash/Aspirate Sample Procedure (Purchase of MFR # 181-36026 required)

1. Draw nasal wash or nasopharyngeal aspirate sample to the first (lowest) mark of the graduated transfer pipette.
2. Dispense the entire sample in the transfer pipette into the Extraction Well of the test cassette.
3. Remove the cap from the Extraction Reagent bottle.
4. Using a new transfer pipette, draw Extraction Reagent Solution to the first (lowest) mark.
5. Dispense all of the solution in the transfer pipette into the Extraction Well of the test cassette.
6. Incubate 1 minute. Re-cap the Extraction Reagent bottle.
7. Raise the test cassette upright (see picture).
8. Let it stand for 1-2 seconds. Gently tap the cassette to ensure that the liquid flows into the hole.
9. Lay the cassette back down onto the flat surface. Start timing.
10. Read test results at 10-15 minutes. Confirm negative results at 15 minutes.

Swab Sample in Transport Media Procedure

To test transport media with a swab sample, remove swab by vigorously rotating the swab in the liquid media (or vortex), then use the media for testing by following the Nasopharyngeal Wash/Aspirate Sample Procedure.

WARNING: The performance of the McKesson Consult Influenza A&B test kit has not been evaluated with swab samples collected in transport media.

(continued)

Influenza Type	Viral Strain	$TCID_{50}$/mL	Influenza Type	Viral Strain	$TCID_{50}$/mL
A	A/CA/08/2009 (H1N1)	9.31×10^3	B	B/R75	2.94×10^3
A	A/NY/18/2009 (H1N1)	2.5×10^3	B	B/Russia/69	3.16×10^3
A	A/Mexico/ 4108/2009 (H1N1)	8.51×10^3	B	B/Hong Kong/5/72	2.88×10^1
A	A/CA/07/2009 NYC, X-179A (H1N1)	1.08×10^3	B	B/Texas/39/2006**	2.34×10^4

*Clinical isolate cultured and titered. Culture confirmed positive for 2009 H1N1 Influenza A strain using proFLU+ Influenza A Subtyping.

**Although this test has been shown to detect these viral strains cultured from positive human respiratory specimens, the performance characteristics of this cassette with clinical specimens that are positive for these viruses have not been established.

Influenza Type	Viral Strain#	EID_{50}/mL	Influenza Type	Viral Strain#	EID_{50}/mL
A	A/Anhui/1/2013 (H7N9)	7.94×10^6	A	A/Texas/50/2012	2.03×10^4
A	A/Vietnam/1194 /2004 (H5N1)	1.60×10^6	A	A/California/07/2009	1.01×10^6
A	A/Anhui/01/2005 (H5N1)	1.60×10^7	A	A/Washington /24/2012	2.02×10^4
A	A/Northern/Pintail/ Washington /40964/2014 (H5N2)	8.04×10^5	B	B/Brisbane/60/2008	3.19×10^6
A	A/Gyrfalcon / Washington /410886/2014 (H5N8)	2.03×10^5	B	B/Montana/05/2012	4.02×10^5
A	A/Brisbane /59/2007	1.01×10^5	B	B/Wisconsin/1/2010	2.54×10^3
A	A/Fujian Gulou /1896/2009	8.06×10^4	B	B/Massachusetts /02/2012	1.01×10^5
A	A/Perth/16/2009	2.54×10^5			

#Although this test has been shown to detect these viral strains cultured from positive human respiratory specimens, the performance characteristics of this cassette with clinical specimens that are positive for these viruses have not been established.

The performance of McKesson Consult Influenza A&B Tests were evaluated with nasal and nasopharyngeal swab samples obtained from patients infected with the 2009 H1N1 influenza virus consisting of sixty six (66) frozen clinical Nasal and Nasopharyngeal samples that had previously tested positive for 2009 H1N1 by FDA-cleared CDC RT-PCR test. The McKesson Consult Influenza A&B Test detected 71% (47/66) of the CDC RT-PCR test positive specimens. The detection rate was 91% with the higher titered specimens and 38% with the lower titered specimens.

ANALYTICAL SPECIFICITY

Cross-Reactivity

The potential cross-reactivity of the non-influenza respiratory pathogens and other microorganisms with which the majority of the population may be infected was tested using the McKesson Consult Influenza A&B Test at medically relevant levels, 10^6 cfu/mL for bacteria and 10^5 pfu/mL for non-flu viruses. None of the organisms or viruses listed in the table below gave a positive result with McKesson Consult Influenza A&B Tests at the tested concentration.

Viruses Tested	
Adenovirus*	Measles**
Human coronavirus**	Human metapneumovirus**
Cytomegalovirus**	Mumps virus**
Enterovirus**	Respiratory syncytial virus; Type B*
Epstein Barr Virus**	Rhinovirus; Type 1A**
Human parainfluenza; Type 1, 2 and 3*	

*In the study the virus was confirmed using FDA approved immuno-fluorecence assay

**In the study the virus was confirmed using commercially available PCR (not approved by FDA).

Bacteria Tested	
Bordetella pertussis	*Mycoplasma pneumoniae*
Chlamydia pneumoniae	*Neisseria meningitides*
Corynebacterium sp.	*Neisseria sp.*
Escherichia coli	*Pseudomonas aeruginosa*
Hemophilus influenzae	*Staphylococcus aureus: Protein A Producer*
Lactobacillus sp.	*Staphylococcus epidermidis*
Legionella sp.	*Streptococcus pneumoniae*
Moraxella catarrhalis	*Streptococcus pyogenes*
Mycobacterium tuberculosis avirulent	*Streptococcus salivarius*

Interference

The interference study was conducted using medically relevant concentrations of the potentially interfering substances listed below with two strains each of influenza type A and type B to assess the potential interference of the substances on the performance of the McKesson Consult Influenza A&B Test.

The test was conducted by spiking each substance into samples containing the lowest detectable virus level of influenza Type A or Type B for the positive interference testing and into samples without influenza virus for the negative interference testing. Each substance had no inhibitory effect on the McKesson Consult Influenza A&B Test at the concentration listed in the table below.

Substances Tested	Concentration Tested
Mucin	1 mg/ml
Whole Blood	1%
Phenylephrine	10 mg/mL
Oxymetazoline	10 mg/mL
Sodium Chloride with preservative	20%
Beclomethasone	1 mg/mL
Dexamethasone	1 mg/mL
Flunisolide	1 mg/mL
Triamcinolone	1 mg/mL
Budesonide	1 mg/mL
Mometasone	1 mg/mL
Fluticasone	0.5 mg/mL
Luffa opperculata, sulfur	1%

(continued)

Galphimia glauca	1%
Histaminum hydrochloricum	1%
Live intranasal influenza virus vaccine	1%
Benzocaine	1 mg/mL
Menthol	1 mg/mL
Zanamivir	1 mg/mL
Mupirocin	1 mg/mL
Tobramycin	1 mg/mL

CLIA WAIVER STUDY

Clinical Study at CLIA Waived Sites

To evaluate the expected performance of the McKesson Consult Influenza A&B Test when used by operators at CLIA-waived sites, a prospective clinical study was performed using nasopharyngeal and nasal swab specimens at seven CLIA waived sites (non-laboratory study sites) from December 2014 to May 2016. A total of sixteen operators from seven intended user sites in the USA were involved in the study. All collected samples were tested with both McKesson Consult Influenza A&B Tests and an FDA-cleared NAAT. The total number of samples tested was 455, of which 148 samples were archived samples which were confirmed by PCR as Influenza A or Influenza B.

The combined data from all sites of the prospective study and archived samples are presented in the table below.

	Comparator (PCR) Results			
McKesson Consult	Flu A Positive	Flu A Negative	Total	Performance
Flu A Positive	124	2	126	PPA: 89.2% 95% CI: 83.0-93.4%
Flu A Negative	15	314	329	NPA: 99.4% 95% CI: 97.7-99.8%
Total	139*	316	455	

*The total number of Influenza A positive includes 27 archived samples.

	Comparator (PCR) Results			
McKesson Consult	Flu B Positive	Flu B Negative	Total	Performance
Flu B Positive	133	3	136	PPA: 86.4% 95% CI: 80.1-90.9%
Flu B Negative	21	298	319	NPA: 99.0% 95% CI: 97.1-99.7%
Total	154*	301	455	

*The total number of Influenza B positive includes 121 archived samples.

Performance with Near Cutoff Concentrations at CLIA Waived Sites

To determine the performance of operators at CLIA waived sites with the McKesson Consult Influenza A&B Test when tested with samples near the cutoff, this study was conducted using a sample panel consisting of high negative (C_5), weak positive (C_{95}) and moderate positive (3 x C_{95}) samples for influenza type A and B, and samples negative for both flu A and B (true negative). For influenza A and B positive samples, A/Denver/1/57 (H1N1) and B/Maryland/1/59 were used. The testing was performed over a period of 10 days using 90 coded samples for each of 6 operators (True negative: 50, High Negative: 15, Low Positive; 15, Moderate Positive; 10 samples respectively). The results are summarized in below table.

	Sample	Site 1 (2 operators)	Site 2 (2 operators)	Site 3 (1 operator)	Site 4 (1 operator)	Agreement	95% CI
Flu A	Negative	100% (100/100)	97.0% (97/100)	100% (50/50)	100% (50/50)	99.0% (297/300)	97.1% -99.7%
	High Negative C_5	96.7% (29/30)	100% (29/29*)	93.3% (14/15)	100% (15/15)	97.8% (87/89*)	92.2% -99.4%
	Low Positive C_{95}	96.7% (29/30)	100% (30/30)	100% (15/15)	93.3% (14/15)	97.8% (88/90)	92.3% -99.4%
	Moderate Positive	100% (20/20)	100% (20/20)	100% (10/10)	100% (10/10)	100% (60/60)	94.0% -100%
Flu B	Negative	100% (100/100)	100% (99/99*)	100% (50/50)	100% (50/50)	100% (299/299*)	98.7% -100%
	High Negative C_5	100% (30/30)	96.7% (29/30)	93.3% (14/15)	100% (15/15)	97.8% (88/90)	92.3% -99.4%
	Low Positive C_{95}	100% (30/30)	93.3% (28/30)	93.3% (14/15)	100% (15/15)	96.7% (87/90)	90.7% -99.0%
	Moderate Positive	100% (20/20)	95.0% (19/20)	100% (10/10)	100% (10/10)	98.3% (59/60)	91.2% -99.7%

*One test result out of 30 tests was invalid affecting the total number.

Annual analytical reactivity testing results with CDC influenza panel and other information can be found on our web site at mms.mckesson.com.

REFERENCES

1. Shaw MW, Arden NH and Massab HF. New aspects of influenza viruses. Clin. Microbiol. Rev. 5: 74-92 (1992)
2. WHO recommendations on the use of rapid testing for influenza diagnosis, July 2005.
3. Design Considerations for Pivotal Clinical Investigations for Medical Devices: Guidance for Industry, Clinical Investigators, Institutional Review Boards and Food and Drug Administration Staff, November 7, 2013 (Page 45)

SYMBOLS

SYMBOL	TITLE	STANDARD	REFERENCE NUMBER	DESCRIPTION
	Consult instructions for use	ISO 15223-1 Medical Devices -Symbols to be used with medical device labels - General requirements	Section 5.4.3	Indicates the need for the user to consult the instructions for use.
	Caution	ISO 15223-1 Medical Devices -Symbols to be used with medical device labels - General requirements	Section 5.4.4	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
IVD	*In vitro* diagnostic medical device	ISO 15223-1 Medical Devices -Symbols to be used with medical device labels - General requirements	Section 5.5.1	Indicates a medical device that is intended to be used as an *in vitro* diagnostic medical device.
	Do not reuse	ISO 15223-1 Medical Devices -Symbols to be used with medical device labels - General requirements	Section 5.4.2	Indicates a medical device that's intended for one use, or for use on a single patient during a single procedure.
LOT	Batch code	ISO 15223-1 Medical Devices -Symbols to be used with medical device labels - General requirements	Section 5.1.5	Indicates the manufacturer's batch code so that the batch or lot can be identified.
EXP	Use-by date	ISO 15223-1 Medical Devices -Symbols to be used with medical device labels - General requirements	Section 5.1.4	Indicates the date after which the medical device is not to be used.

Technical Support? Call 1-800-526-2125
General Questions? Call 1-800-777-4908

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If you are not completely satisfied with any McKesson Brands product, you may return it for a full refund or credit.

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