QUICKVUE®
Influenza test

INTENDED USE

The QuickVue Influenza Test allows for the rapid, qualitative detection of influenza type A and type B antigens directly from nasal swab, nasal wash and/or nasal aspirate specimens. The test is intended for use as an aid in the rapid diagnosis of acute influenza virus infection. The test is not intended to detect influenza C antigens. Negative test results should be confirmed by cell culture.

SUMMARY AND EXPLANATION

Influenza is a highly contagious, acute, viral infection of the respiratory tract. The causative agents of the disease are immunologically diverse, single-strand RNA viruses known as influenza viruses. There are three types of influenza viruses: A, B, and C. Type A viruses are the most prevalent and are associated with most serious epidemics. Type B viruses produce a disease that is generally milder than that caused by type A. Type C viruses have never been associated with a large epidemic of human disease. Both type A and B viruses can circulate simultaneously, but usually one type is dominant during a given season.[1]

Influenza antigens may be detected in clinical specimens by immunoassay. The QuickVue Influenza Test is a lateral-flow immunoassay using highly sensitive monoclonal antibodies that are specific for influenza antigens. The test is specific to influenza types A and B antigens with no known cross-reactivity to normal flora or other known respiratory pathogens.

PRINCIPLE OF THE TEST

The QuickVue Influenza Test involves the extraction of influenza A and B viral antigens. The patient specimen is placed in the Extraction Reagent Tube, during which time the virus particles in the specimen are disrupted, exposing internal viral nucleoproteins. After extraction, the Test Strip is placed in the Extraction Reagent Tube where nucleoproteins in the specimen will react with the reagents in the Test Strip.

If the extracted specimen contains influenza antigens, a pink-to-red Test Line along with a blue procedural Control Line will appear on the Test Strip indicating a positive result. If influenza type A or type B antigens are not present, or are present at very low levels, only a blue procedural Control Line will appear.

REAGENTS AND MATERIALS SUPPLIED

2-Test Sampler Kit, Catalog Number 00325
10-Test Kit, Catalog Number 00324

- Individually Packaged Reagent Trays, 2 or 10 each containing:
  - ► Test Strip (1): Mouse monoclonal anti-influenza A and anti-influenza B antibodies
  - ► Extraction Reagent Solution (1 vial with 250 µL): Salt solution
  - ► Extraction Tube (1): Lyophilized buffer with detergents and reducing agents
  - ► Disposable Dropper (1)
  - ► Sterile Swab (1)
  - ► Procedure Card (1)
- Positive Influenza Type A Control Swab (1): Swab is coated with non-infectious recombinant influenza A antigen
- Positive Influenza Type B Control Swab (1): Swab is coated with non-infectious recombinant influenza B antigen *(not included with 2-Test Sampler)*
- Negative Control Swab (1): Swab is coated with formalin-inactivated, non-infectious *Streptococcus C* antigen *(not included with 2-Test Sampler)*
- Direction Insert (1)

25-Test Kit, Catalog Number 00317

- Shelf box containing:
  - ► Individually Packaged Test Strips (25): Mouse monoclonal anti-influenza A and anti-influenza B antibodies
  - ► Extraction Reagent Solution: (25 vials with 250 µL each): Salt solution
  - ► Extraction Tubes (25): Lyophilized buffer with detergents and reducing agents
  - ► Disposable Droppers (25)
  - ► Sterile Swabs (25)
  - ► Positive Influenza Type A Control Swab (1): Swab is coated with non-infectious recombinant influenza A antigen
  - ► Positive Influenza Type B Control Swab (1): Swab is coated with non-infectious recombinant influenza B antigen
  - ► Negative Control Swab (1): Swab is coated with formalin-inactivated, non-infectious *Streptococcus C* antigen
  - ► Direction Insert (1)
  - ► Procedure Card (1)

MATERIALS NOT SUPPLIED

- Specimen containers
- Timer or watch

WARNINGS AND PRECAUTIONS

- The QuickVue Influenza Test is for *in vitro* diagnostic use.
- Do not use the kit contents beyond the expiration date printed on the outside of the box.
- Use appropriate precautions in the collection, handling, storage, and disposal of patient samples and used kit contents.[2] Discard used material in a proper biohazard or sharps container.
- The Test Strip must remain sealed in the protective foil pouch until use.
- The Extraction Reagent Solution contains a salt solution. If the solution contacts the skin or eye, flush with copious amounts of water.
- To obtain accurate results, you must follow the Direction Insert.

KIT STORAGE AND STABILITY

Store the kit at room temperature, 59–86°F (15–30°C), out of direct sunlight. Kit contents are stable until the expiration date printed on the outer box. Do not freeze.

SPECIMEN COLLECTION

Nasal Swab Sample:
For proper test performance, use the swabs supplied in the kit.
To collect a nasal swab sample, insert the sterile swab into the nostril that presents the most secretion under visual inspection. Using gentle rotation, push the swab until resistance is met at the level of the turbinates (less than one inch into the nostril). Rotate the swab a few times against the nasal wall.

Nasal Wash or Aspirate Sample:
For Older Children and Adults:
With the patient's head hyper-extended, instill about 2.5 mL of sterile, normal saline into one nostril with a syringe. To collect the wash, place a clean, dry specimen container directly under the nose with slight pressure on the upper lip. Tilt the head forward and allow the fluid to run out of the nostril into the specimen container. Repeat for the other nostril and collect the fluid into the same specimen container.

For Younger Children:
The child should sit in the parent's lap facing forward, with the child's back against the parent's chest. The parent should wrap one arm around the child in a manner that will restrain the child's body and arms.

Fill an aspiration bulb or bulb syringe with up to 2.5 mL of sterile, normal saline (depending on the size of the child), and instill the 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 a clean, dry specimen container. Repeat the process for the child's other nostril and transfer the specimen into the same specimen container.

SAMPLE TRANSPORT AND STORAGE

Samples should be tested as soon as possible after collection. Do not use any kind of transport media to store or transport samples. Samples may be stored refrigerated (2–8°C), or at room temperature (15–30°C), in a clean, dry, closed container for up to eight hours prior to testing.

QUALITY CONTROL

Built-in Control Features

The QuickVue Influenza Test contains built-in procedural control features. The manufacturer's recommendation for daily control is to document these built-in procedural controls for the first sample tested each day.

The two-color result format provides a simple interpretation for positive and negative results. The appearance of a blue procedural Control Line provides several forms of positive control by demonstrating sufficient capillary flow has occurred and the functional integrity of the Test Strip was maintained. **If the blue procedural Control Line does not develop at 10 minutes, the test result is considered invalid.**

A built-in negative control is provided by the clearing of red background color, verifying that the test has been performed correctly. Within 10 minutes, the result area should be white to light pink and allow the clear interpretation of the test result. **If background color appears and interferes with interpretation of the test result, the result is considered invalid.** Should this occur, review the procedure and repeat the test with a new Test Strip.

External Quality Control

External controls may be also used to demonstrate that the reagents and assay procedure perform properly.

Quidel recommends that positive and negative controls be run every 25 tests, and as deemed necessary by your internal quality control procedures.

If the controls do not perform as expected, repeat the test or contact Quidel Technical Support before testing patient specimens.

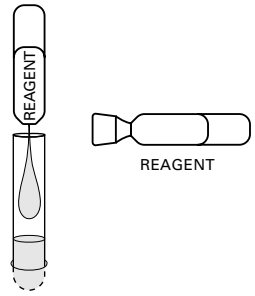
External positive and negative control swabs are supplied in the kit and should be tested using the Swab Procedure.

TEST PROCEDURES

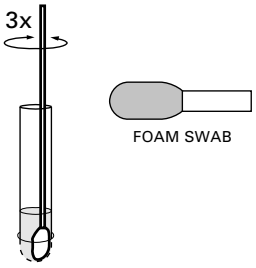
Expiration date: check expiration on each individual test package (tray or outer box) before using. *Do not use any test past the expiration date on the label.*

Nasal Swab Procedure

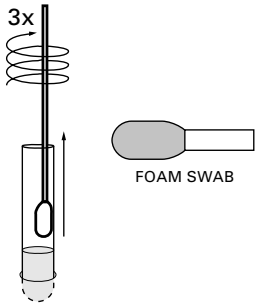
1. Dispense all of the Extraction Reagent Solution from the Reagent Tube. Gently swirl the Extraction Tube to dissolve its contents.



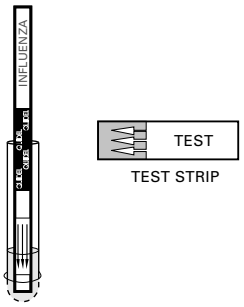
2. Place the patient swab sample into the Extraction Tube. Roll the swab at least three (3) times while pressing the head against the bottom and side of the Extraction Tube.



3. Roll the swab head against the inside of the Extraction Tube as you remove it. Dispose of the used swab in accordance with your biohazard waste disposal protocol.



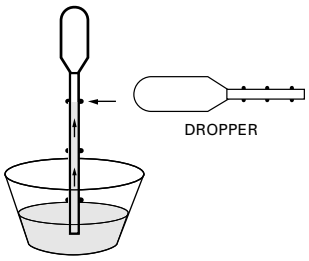
4. Place the Test Strip into the Extraction Tube with the arrows on the Test Strip pointing down. Do not handle or move the Test Strip until the test is complete and ready for reading.



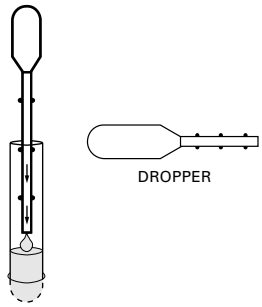
5. Read result at ten (10) minutes. Some positive results may appear sooner.

Nasal Wash/Nasal Aspirate Procedure

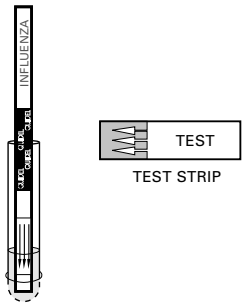
1. Fill the dropper to the top/uppermost notch with nasal wash or nasal aspirate sample.



2. Add entire contents of the dropper to the Extraction Tube. Swirl the Extraction Tube gently to dissolve its contents.



3. Place the Test Strip into the Extraction Tube with the arrows on the Test Strip pointing down. Do not handle or move the Test Strip until the test is complete and ready for reading.



4. Read result at ten (10) minutes.
Some positive results may appear sooner.

CLIA Considerations

This is a waived test under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) so long as it is used according to the instructions set in this Package Insert.

Any modification by the laboratory to the test system or the test system instructions will result in this test no longer meeting the requirements for waived categorization. A modified test is considered to be high complexity and is subject to all applicable CLIA requirements. Further, the laboratory should notify Quidel Corporation of any performance, perceived or validated, that does not meet the performance specifications as outlined in the instructions.

Under CLIA, several Consumer Precision Studies and a Consumer Accuracy Study was conducted to demonstrate that lay users with no formal laboratory training could read the package insert and perform the test with a high level of concordance with trained laboratorians. Consumer Precision Study testing was conducted using proficiency panels consisting of three hundred sixty negative, low positive and moderate positive nasal wash and nasal swab samples. Consumer Accuracy Study testing was conducted using over three hundred nasal wash samples ranging from negative through low positive samples. A similar study using nasal swab samples was not conducted.

No significant differences were observed between the lay user and the laboratorian (Consumer Accuracy Study) or between the lay user and expected results (Consumer Precision Study).

Lay User and Laboratorian Results Compared and versus Expected Results

Participant	Location	Negative % negative	High Neg Level 1 % positive	High Neg Level 2 % positive	Low Pos* Level 1 % weak pos	Low Pos* Level 1 % positive	Low Pos* Level 2 % positive
Lay User	Total 4 Sites	50/50 (100%)	0/24 (0%)	11/94 (12%)	NA	83/127 (65%)	47/50 (94%)
Trained Laboratorian	Total 1 Site	49/50 (96%)	1/25 (4%)	5/98** (5%)	32/123 (26%)	84/123*** (68%)	48/50 (96%)

NA = not applicable
***Low Positive Level 1 below assay threshold
****One sample called invalid (eliminated from result calculation)
*****One sample strip used upside down and correctly called invalid (eliminated from result calculation)

INTERPRETATION OF RESULTS

Positive Result:
At ten minutes, **ANY** shade of a pink-to-red Test Line forms **AND** the appearance of a blue procedural Control Line indicates a positive result for the presence of influenza A and/or B viral antigen.

Negative Result:
At ten minutes, the appearance of **ONLY** the blue procedural Control Line indicates the sample is negative for influenza A and B viral antigen. A negative result should be reported as a presumptive negative for the presence of influenza antigen.

Invalid Result:
If at ten minutes, the blue procedural Control Line does not appear, even if any shade of a pink-to-red Test Line appears, the result is considered invalid. If at ten minutes, the background color does not clear and it interferes with the reading of the test, the result is considered invalid. If the test is invalid, a new test should be performed with a new patient sample and a new Test Strip.

LIMITATIONS

The contents of this kit are to be used for the qualitative detection of influenza A and B antigen from nasal swab, nasal wash and nasal aspirate specimens. This test does not differentiate between influenza types A and B.

Failure to follow the Test Procedure and Interpretations of Test Results may adversely affect test performance and/or invalidate the Test Result.

Test Results must be evaluated in conjunction with other clinical data available to the physician.

A negative test result may occur if the level of antigen in a sample is below the detection limit of the test, or from improper sample collection.

Negative test results are not intended to rule-out other non-influenza viral infections.

EXPECTED VALUES

Seasonal outbreaks of influenza occur worldwide in both the northern and southern hemispheres causing widespread illness each winter. The average attack rate of influenza is 26–33 cases per 100 people per year. The risk of hospitalization is roughly 1/300 of those infected among the very young and elderly. Approximately 20,000 deaths in the U.S. are attributed to influenza or its complications each year. Ninety percent (90%) of deaths occur in those 65 years of age and older. During each of three major epidemics occurring in 1957 and 1968, more than 40,000 people died of influenza in the U.S. alone. In the 1918 pandemic, at least 20 million deaths resulted worldwide. In the multi-center clinical study conducted by QUIDEL during the 1998/1999 influenza season in North America, an illness prevalence of 24% for type A and 15% for type B influenza was observed.

PERFORMANCE CHARACTERISTICS

The performance of the QuickVue Influenza Test was compared to cell culture methods in a multi-center field clinical study. This study was conducted in pediatric, adult and geriatric patient populations at physician offices located in the Northwest, Midwest, Northeast, Mid-Atlantic, Southeast and Western regions of the United States. In this multi-center, point-of-care (POC) field trial, a combination of nasal swabs and nasal wash/aspirate specimens were collected from a total of two hundred seventy-five (275) patients.

On-site testing of the nasal swab and nasal wash or nasal aspirate specimens in the QuickVue Influenza Test was performed by physician office personnel within one hour of collection; viral transport media was added to all nasal swab specimens intended for culture transport. Swab specimens in viral transport media and nasal wash/aspirate specimens were stored at 2–8°C for up to 24 hours prior to culture. Rhesus Monkey Kidney (RMK) cells or Madin-Darby Canine Kidney (MDCK) cells were inoculated with a portion of the nasal swab specimen and nasal wash/aspirate and tested for the appearance of cytopathic effects (CPE). Infected cells were recovered from tissue culture and confirmed for influenza A or B by direct fluorescent antibody (DFA) staining.

A total of 370 specimens were tested from 275 patients [274 nasal swabs and 96 nasal wash/aspirate specimens]. The following tables summarize the results:

For Nasal Swab Specimens:

- Compared to culture and confirmed for influenza A or B by DFA, the QuickVue Influenza Test correctly identified 79/108 (73%) positive specimens and 159/166 (96%) negative specimens.

		Culture Result	
		Pos	Neg
QuickVue Influenza Test Result	Pos	79	7
	Neg	29	159

Sensitivity: 79/108 = 73% (95% C.I. 67%–78%)
Specificity: 159/166 = 96% (95% C.I. 93%–98%)
Pred. Value (+): 79/86 = 92%
Pred. Value (–): 159/188 = 85%
Accuracy: 238/274 = 87%

For Nasal Wash or Nasal Aspirate Specimens:

- Compared to culture and confirmed for influenza A or B by DFA, the QuickVue Influenza Test correctly identified 22/27 (81%) positive specimens and 68/69 (99%) negative specimens.

		Culture Result	
		Pos	Neg
QuickVue Influenza Test Result	Pos	22	1
	Neg	5	68

Sensitivity: 22/27 = 81% (95% C.I. 72%–88%)
Specificity: 68/69 = 99% (95% C.I. 93%–99%)
Pred. Value (+): 22/23 = 96%
Pred. Value (–): 68/73 = 93%
Accuracy: 90/96 = 94%

ANALYTICAL SPECIFICITY AND CROSS-REACTIVITY

The QuickVue Influenza Test was evaluated with a total of 62 bacterial and viral isolates. Bacterial isolates were evaluated at a concentration between 10^7 and 10^9 org/mL. Viral isolates were evaluated at a concentration of at least 10^4–10^8 $TCID_{50}$/mL. Adenovirus 18 and Parainfluenza virus 3 were tested at 10^2 $TCID_{50}$/mL. None of the organisms or viruses listed below gave a positive result in the QuickVue Influenza Test.

Bacterial Panel:

Acinetobacter calcoaceticus
Bacteroides fragilis
Bordetella pertussis
Branhamella catarrhalis
Candida albicans
Corynebacterium diphtheriae
Enterococcus faecalis
Escherichia coli
Gardnerella vaginalis
Haemophilus influenzae
Klebsiella pneumoniae
Lactobacillus casei
Lactobacillus plantarum
Legionella pneumophila
Listeria monocytogenes
Mycobacterium avium
Mycobacterium intracellulare
Mycobacterium tuberculosis
Mycoplasma orale
Mycoplasma pneumoniae
Neisseria gonorrhoeae
Neisseria meningitidis
Neisseria sicca
Neisseria subflava
Proteus vulgaris
Pseudomonas aeruginosa
Serratia marcescens
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus sanguis
Streptococcus sp. Gp. B
Streptococcus sp. Gp. C
Streptococcus sp. Gp. F
Streptococcus sp. Gp. G

Viral Panel:

Adenovirus 5 (Ad. 75)
Adenovirus 7 (Gomen)
Adenovirus 10 (J.J.)
Adenovirus 18 (D.C.)
Coronavirus OC43
Coxsackievirus A9 (Bozek)
Coxsackievirus B5 (Faulkner)
Cytomegalovirus (Towne)
Echovirus 2 (Cornelis)
Echovirus 3 (Morrisey)
Echovirus 6 (D'Amori)
Herpes simplex virus 1
Herpes simplex virus 2
Human Rhinovirus 2 (HGP)
Human Rhinovirus 14 (1059)
Human Rhinovirus 16 (11757)
Measles (Edmonston)
Mumps (Enders)
Parainfluenza virus 1 (Sendai)
Parainfluenza virus 2 (CA/Greer)
Parainfluenza virus 3 (C243)
Respiratory Syncytial virus (A-2)
Respiratory Syncytial virus
(Subgroup A, Long chain)
Rubella (RA 27/3)
Varicella-Zoster (Ellen)

ANALYTICAL SENSITIVITY

Analytical sensitivity was established using a total of 50 human epidemic strains of influenza viruses: 37 influenza A and 13 influenza B.

Viral Strain	Viral Type	Minimum Detectable Level (pfu/mL)	Viral Strain	Viral Type	Minimum Detectable Level (pfu/mL)
Hong Kong	A	6.60×10^{-1}	Shangdong	A	8.40×10^{3}
Beijing/32/92	A	3.30×10^{0}	Maryland/91	A	1.00×10^{4}
Duck/England	A	6.70×10^{0}	Japan/305/57	A	1.30×10^{4}
Shanghai/11	A	6.70×10^{0}	Johannesburg/94	A	1.44×10^{4}
Shanghai/16	A	1.00×10^{1}	Brazil	A	1.70×10^{4}
Duck/Alberta	A	3.30×10^{1}	Sydney	A	2.00×10^{4}
Victoria	A	3.30×10^{1}	Bangkok	A	3.30×10^{4}
Singapore/1/57	A	6.70×10^{1}	Wuhan	A	3.30×10^{4}
Port Chalmers	A	1.24×10^{2}	Equine/Miami	A	1.70×10^{5}
Gull/Maryland	A	1.30×10^{2}	Beijing/353/89	A	3.30×10^{5}
USSR	A	2.00×10^{2}	Singapore/86	A	6.60×10^{5}
Puerto Rico/8/34	A	2.60×10^{2}	Texas/91	A	1.60×10^{7}
New Jersey	A	2.70×10^{2}	Victoria	B	1.40×10^{4}
Taiwan	A	3.30×10^{2}	Taiwan	B	1.10×10^{2}
Tokyo/3/67	A	3.40×10^{2}	Panama	B	1.00×10^{0}
Bayern	A	6.60×10^{2}	Ann Arbor	B	3.30×10^{2}
Sichuan	A	6.60×10^{2}	Singapore	B	3.30×10^{2}
Beijing/352/89	A	7.70×10^{2}	Lee	B	6.60×10^{2}
NWS/33	A	1.00×10^{3}	Hong Kong	B	7.00×10^{2}
Fort Warren/1/50	A	1.70×10^{3}	Beijing/184/93	B	1.66×10^{3}
Mississippi	A	1.70×10^{3}	California	B	3.30×10^{3}
Texas/77	A	3.30×10^{3}	Maryland	B	6.60×10^{3}
Fort Monmouth/1/47	A	6.70×10^{3}	Yamagata/16/88	B	6.70×10^{3}
Duck/Ukraine	A	3.30×10^{1}	Harbin	B	1.40×10^{4}
Aichi	A	3.20×10^{3}	Stockholm	B	3.30×10^{5}

INTERFERING SUBSTANCES

Whole blood, and several over-the-counter (OTC) products and common chemicals were evaluated and did not interfere with the QuickVue Influenza Test at the levels tested: whole blood (2%); three OTC mouthwashes (25%); three OTC throat drops (25%); three OTC nasal sprays (10%); 4-Acetamidophenol (10 mg/mL); Acetylsalicylic Acid (20 mg/mL); Chlorpheniramine (5 mg/mL); Dextromethorphan (10 mg/mL); Diphenhydramine (5 mg/mL); Ephedrine (20 mg/mL); Guaiacol glyceryl ether (20 mg/mL); Oxymetazoline (10 mg/mL); Phenylephrine (100 mg/mL); and Phenylpropanolamine (20 mg/mL).

PRECISION STUDIES

The total, within-run, and between-run performance of the QuickVue Influenza Test was evaluated for precision. A panel consisting of two different levels of influenza A antigen (Johanneburg/82/96; weak positive and strong positive) and two different levels of influenza B antigen (Harbin/7/94; weak positive and strong positive) were repeated five times with a single lot of QuickVue Influenza Test on three different days. One hundred percent (100%) accuracy was obtained for all specimens tested.

PHYSICIAN OFFICE LABORATORY (POL) STUDIES

An evaluation of the QuickVue Influenza Test was conducted at three Physicians' Offices using a panel of coded specimens. Testing was performed by physician office personnel with diverse educational backgrounds and work experiences at three different locations. The proficiency panel contained negative, low positive and moderate positive specimens. Each specimen level was tested at each site in replicates of at least six over a period of three days.

The results obtained at each site agreed >99% with the expected results. No significant differences were observed within run (6 replicates), between runs (3 different days) or between sites (3 POL sites).

ASSISTANCE

If you have any questions regarding the use of this product, please call QUIDEL's Technical Support Number 800-874-1517 (toll-free) or 858-552-1100, Monday through Friday, between 7:00 a.m. and 5:00 p.m., Pacific Time. If outside the United States contact your local QUIDEL office or distributor.

REFERENCES

1. Murphy, B.R., and R.G. Webster. 1996. Orthomyxoviruses, pp. 1397–1445. In: Fields Virology, 3rd edition, B.N. Fields, D.M. Knipe, P.M. Howley, Et al. (eds.), Lippincott-Raven, Philadelphia.
2. Recommendations for the Prevention of HIV Transmission in Health Care Settings, Morbidity and Mortality Weekly Report, Centers for Disease Control, August 21 1987.

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