

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K052499

B. Purpose for Submission:

New device(s)

C. Measurand:

Influenza A and B nucleoprotein antigens

D. Type of Test:

Rapid chromatographic immunoassay that differentiates influenza A from influenza B virus

E. Applicant:

Genzyme Corporation

F. Proprietary and Established Names:

® Influenza OSOM A&B Test

G. Regulatory Information:

1. Regulation section: 21CFR 866.3330; Influenza Virus Serological Reagents
2. Classification: Class: I
3. Product code: GNX, Antigens, CF, including CF controls, Influenza A, B, and C.
4. Panel: 83 Microbiology

H. Intended Use:

The OSOM Influenza A&B Test is an in vitro diagnostic immunochromatographic assay intended for the qualitative detection of influenza A and influenza B viral antigens from nasal swab specimens. It is intended to aid in the rapid differential diagnosis of influenza A and/or B viral infections. A negative test is presumptive and should be confirmed by cell culture.

Cross-reactivity with other respiratory viruses in this assay has not been

evaluated. The user is responsible for determining the cross-reactivity of other respiratory viruses with this test.

2. Indication(s) for use:

The OSOM Influenza A&B Test is an in vitro diagnostic immunochromatographic assay intended for the qualitative detection of influenza A and influenza B viral antigens from nasal swab specimens. It is intended to aid in the rapid differential diagnosis of influenza A and/or B viral infections. A negative test is presumptive and should be confirmed by cell culture.

Cross-reactivity with other respiratory viruses in this assay has not been evaluated. The user is responsible for determining the cross-reactivity of other respiratory viruses with this test.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

None

I. Device Description:

The OSOM Influenza A&B Test consists of a test stick that separately detects influenza A and B. The test procedure requires the solubilization of the nucleoproteins from a swab by mixing the swab in Extraction Buffer. The test stick is then placed in the sample mixture, which then migrates along the membrane surface. If influenza A and/or B viral antigens are present in the sample, it will form a complex with mouse monoclonal IgG antibodies to influenza A and/or B nucleoproteins conjugated to colloidal gold. The complex will then be bound by another mouse anti-influenza A and/or B antibody coated on the nitrocellulose membrane. A pink to purple control line must appear in the control region of the stick for results to be valid. The appearance of a second and possibly a third light pink to purple line will appear in the test line region indicating an A, B or A and B positive result.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Viral cell culture, Quidel QuickVue® Influenza A+B Test

2. Predicate 510(k) number(s):

Comparison with predicate:

Table 1: Summary of Device Similarities and Differences

	OSOM Influenza A&B Test	Quidel QuickVue® Influenza A+B Test
Intended use	Intended for the qualitative detection of influenza A and influenza B viral antigens from nasal swab specimens. It is intended to aid in the rapid differential diagnosis of influenza A and/or B viral infections. The test is for use in clinical laboratories, health clinics, and physician office laboratories.	Intended for the rapid, qualitative detection of influenza type A and influenza type B antigens from nasal swab, nasal wash and/or nasal aspirate specimens. This test is intended for use as an aid in the rapid differential diagnosis of acute influenza type A and type B virus infection.
Assay Format	Lateral flow immunoassay	Lateral flow immunoassay
Specimen	- nasal swabs	- nasal swabs - nasal wash - nasal aspirate
Antibodies (labeled and capture)	Mouse monoclonals	Mouse monoclonals
Conjugate	Colloidal gold	Latex
Objective Test Line	Pink to purple line	Red line
Internal Control	Yes – red line	Yes – blue line
Time To Result	10 minutes	10 minutes

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

Immunochromatographic assay

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Assay Reproducibility

A reproducibility proficiency study was conducted to demonstrate that the OSOM Influenza A&B Test will perform acceptably in the hands of nurses, nurse practitioners and physicians' office personnel. A panel of swabs including negative (no virus), strong negative (below the limit of detection), low (near the limit of detection) and mid viral levels for influenza A and B were coded and masked to the operators. This study was conducted with three operators at three health centers in the eastern United States (2 physician's offices and 1 clinic site) and at Genzyme Diagnostics. The overall accuracy was 97% for flu A and 94% for flu B. Two invalid tests were considered as incorrect results in each analysis.

	Correct Response for Flu A		Lower 95% Confidence Interval	Upper 95% Confidence Interval
A - Strong Neg	12/12	100.0%	73.0%	100.0%
A – Low	23/24*	95.8%	78.9%	99.9%
A – Med	11/12*	91.7%	61.5%	99.8%
B - Strong Neg	12/12	100.0%	73.0%	100.0%
B – Low	23/24	95.8%	78.9%	99.9%
B – Med	11/12	91.7%	61.5%	99.8%
AB – Med	12/12	100.0%	73.0%	100.0%
Negative	48/48	100.0%	92.5%	100.0%
Total	152/156*	97.4%	93.6%	99.3%

	Correct Response for Flu B		Lower 95% Confidence Interval	Upper 95% Confidence Interval
A - Strong Neg	12/12	100.0%	73.0%	100.0%
A – Low	23/24*	95.8%	78.9%	99.9%
A – Med	11/12*	91.7%	61.5%	99.8%
B - Strong Neg	11/12	91.7%	61.5%	99.8%
B – Low	21/24	87.5%	67.6%	97.3%
B – Med	11/12	91.7%	61.5%	99.8%
AB - Med	12/12	100.0%	73.0%	100.0%
Negative	46/48	95.8%	85.7%	99.5%
Total	147/156*	94.2%	89.3%	97.3%

*invalids due to insufficient volume or no control line.

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Not applicable

d. *Detection limit:*

Analytical Sensitivity

Dilutions of influenza A Kitakyushu/159/93 (H3N2) and for influenza B Lee/40 virus were run in triplicate on three lots of the OSOM Influenza A&B Test. The approximate detection limits of the OSOM Influenza A&B Test are 4.4×10^4 TCID₅₀/test for influenza A and 1.44×10^5 TCID₅₀/test for influenza B.

Not applicable

e. *Analytical specificity:*

The OSOM Influenza A&B Test was evaluated with 25 bacterial isolates. Bacterial isolates were tested at a concentration of approximately 10^8 cfu/mL. Very high levels of *Staphylococcus aureus* ($>9 \times 10^8$ cfu/mL) produced a positive result. All other bacteria listed gave negative responses. Cross-reactivity with other known respiratory viruses was not evaluated. Only influenza isolates were tested.

Bacterial Panel:

Acinetobacter calcoaceticus

Bordetella pertussis

Candida albicans

Corynebacterium diphtheriae

Enterococcus faecalis

Enterococcus gallinarum

Escherichia coli

Haemophilus influenza

Klebsiella pneumoniae

Legionella pneumophila

Moraxella catarrhalis

Mycobacterium avium

Mycobacterium tuberculosis

Neisseria meningitidis

Proteus mirabilis

Proteus vulgaris

Pseudomonas aeruginosa

Serratia marcescens

Staphylococcus aureus

Staphylococcus epidermidis

Streptococcus Group A

Streptococcus Group B

Streptococcus mutans

Streptococcus pneumoniae

Torulopsis glabrata

Influenza A/B Panel testing

A total of 46 human and animal influenza strains were tested with the OSOM Influenza A&B test. Viral titers (TCID₅₀) for A/Kitakyushu/159/93 (H3N2) and B/Lee/40 were determined by inoculating MDCK cells, followed by standard procedures for cell culture viral assays. Aliquots of these controls with known TCID₅₀ were then used to establish a standard curve in an ELISA assay. The concentrations of other influenza viruses were determined indirectly using the ELISA assay after the viruses had been inactivated. Influenza viruses were tested at an ELISA estimated TCID₅₀ as listed in the table below.

All influenza virus isolates gave positive results with the test line at the expected location for the A, B and animal (positive for influenza A) isolates.

Influenza A strains:	Sub-type	Estimated ELISA TCID₅₀/mL
<i>Beijing/262/95</i>	H1N1	8.25E+07
<i>Brazil/11/78</i>	H1N1	NA
<i>Chile/1/83</i>	H1N1	NA
<i>New Jersey/8/76</i>	H1N1	2.78E+08
<i>Taiwan/1/86</i>	H1N1	3.47E+07
<i>Guizhou/54/89</i>	H3N2	7.54E+07
<i>OMS/5389/88</i>	H3N2	NA
<i>Beijing/32/92</i>	H3N2	3.97E+06
<i>England/427/88</i>	H3N2	4.73E+07
<i>Johannesburg/33/94</i>	H3N2	1.61E+07
<i>Leningrad/360/86</i>	H3N2	2.50E+06
<i>Mississippi/1/85</i>	H3N2	NA
<i>Philippines/2/82</i>	H3N2	9.75E+07
<i>Shangdong/9/93</i>	H3N2	1.67E+08
<i>Shanghai/16/89</i>	H3N2	3.49E+08
<i>Shanghai/24/90</i>	H3N2	NA
<i>Sichuan/2/87</i>	H3N2	NA
<i>Kitakyushu/159/93</i>	H3N2	3.19E+08
<i>Akita/1/94</i>	H3N2	2.90E+08
<i>Beijing/262/95</i>	H1N1	1.71E+08
<i>Yamagata/32/89</i>	H1N1	7.28E+07
<i>New Caledonia/20/99</i>	H1N1	6.86E+07
<i>Panama/2007/99</i>	H3N2	1.40E+08
<i>Wyoming/03/03</i>	H3N2	7.40E+06
<i>Fujian/411/02</i>	H3N2	6.12E+07

Influenza B strains:	Sub-type	Estimated ELISA TCID₅₀/mL
<i>Ann Arbor/1/86</i>		NA
<i>Beijing/1/87</i>		1.04E+07
<i>Guangdong/120/2000</i>		6.44E+07
<i>Hongkong/8/73</i>		1.74E+07
<i>Panama/45/90</i>		3.79E+07
<i>Singapore/222/79</i>		4.84E+07
<i>Yamagata/16/88</i>		1.78E+07
<i>Lee/40</i>		2.13E+08
<i>Mie/1/93</i>		4.84E+07
<i>Guangdong/05/94</i>		1.27E+07
<i>Johannesburg/5/99</i>		5.87E+07
<i>Shandong/7/97</i>		4.41E+07
<i>Shanghai/361/2002</i>		NA

Animal influenza strains:	Sub-type	Estimated ELISA TCID₅₀/mL
<i>A/Duck/Singapore-Q/F119-3/97</i>	H5N3	1.65E+08
<i>A/Equine/Prague/56</i>	H7N7	5.37E+06
<i>A/Duck/Wisconsin/1120/82</i>	H5N3	2.30E+08
<i>A/Hong Kong/483/97</i>	H5N1	1.06E+08
<i>A/Hong Kong/213/2003</i>	H5N1	1.84E+08
<i>A/Turkey/Ontario/71</i>	H7N3	8.12E+07
<i>A/Mallard/Wisconsin/479/79</i>	H7N3	2.08E+08
<i>A/Mallard/Saskatchewan</i>	H7N3	2.46E+08

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with gold standard:* See clinical studies.

b. *Matrix comparison :*

Not applicable

3. Clinical studies : A clinical trial was conducted during the 2004-2005 flu season in the United States at sites located in the east, central and west regions to establish the clinical sensitivity and clinical specificity of the OSOM Influenza A&B Test in detecting influenza A and influenza B antigens in nasal swab specimens. Sites included family practice and pediatric offices, emergency departments and clinics. All clinical samples were collected from patients with flu-like symptoms including fever, dry cough and myalgia. Nasal swab specimens were collected from a total of 383 subjects enrolled in the study. Of the 383 samples, 132 samples were from pediatric subjects (2-19 years) and 251 samples were from adults (≥ 20 years). The OSOM Influenza A&B Test was compared to cell culture to determine the comparative clinical sensitivity and clinical specificity for detection of influenza A and influenza B in nasal swab specimens

a. *Clinical Sensitivity and specificity:*

Comparison of OSOM Influenza A&B Test to Cell culture: Nasal Swab

Flu A OSOM Influenza A&B	Culture			Total
	A+	Negative		
A+	79	9 ¹		88
A+B+	0	1 ²		1
Negative	28 ³	266		294
Total	107	276		383

Clinical sensitivity: 73.8% (79/107)
(95% CI 64.4% - 81.9%)

Clinical specificity: 96.4%. (266/276)
(95% CI 93.4% - 98.2%)

Flu B OSOM Influenza A&B	Culture			Total
	B+	Negative		
B+	30	11 ⁴		41
A+B+	0	1 ⁵		1
Negative	20 ⁶	321		341
Total	50	333		388

Clinical sensitivity: 60.0% (30/50)
(95% CI 45.2-73.6%)

Clinical specificity: 96.4% (321/333)
(95% CI 93.8% - 98.1%)

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.