K031565

510(k) SUMMARY

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Date Prepared: May 14, 2003

Device Trade Name: Xpect™ Flu A/B

Predicate Device: BD Directigen Flu A+B

Device Classification: 21 CFR 866.3330; Influenza virus serological reagents

Intended Use: REMEL's Xpect™ Flu A/B is a rapid *in vitro* immunochromatographic test for the direct, qualitative detection of influenza A and influenza B viral antigen (nucleoprotein) from nasal wash, nasal swab, and throat swab specimens from symptomatic patients. The test is intended as an aid in the rapid diagnosis of influenza A and influenza B viral infections. Negative tests should be confirmed by cell culture.

Device Description: The Xpect™ Flu A/B is a chromatographic immunoassay for the qualitative detection of influenza A and influenza B viral antigens. The test device incorporates separate membrane strips for influenza A and for influenza B. To perform the test, the patient specimen is diluted and added to the sample well of the device. The mixture moves along the membranes by capillary action. If present, influenza A or B viral antigens in the patient sample bind anti-influenza A or B conjugated antibodies. A visible line forms as a complex of antibody-antigen-antibody coated colored particles is captured in the test region (T). Antibody coated colored particles not bound at the test line are later captured in the control region (C) containing goat anti-mouse antibody. A visible line will always appear in the control region indicating that the test is working properly. The presence of a control line combined with the absence of a visible test line is interpreted as a negative test result.

A positive test is indicated by two black-colored bands; one in the (T) region and one in the (C) region. A negative test is indicated by only one black-colored band in the control (C) region. An invalid test occurs when no black-colored bands appear in the control (C) region.
A procedural control is included in the test. A colored band appearing on the control band (C) region is considered an internal positive procedural control, indicating proper performance and reactive reagents. A clear background in the results area is considered an internal negative control. If the test has been performed correctly and reagents are working properly, the background will clear to give a discernible result. It is recommended that Positive and Negative controls be run with each new test kit lot number. Each laboratory should follow their state and local requirements.

Device Comparison:

Characteristic	Directigen Flu A+B	Xpect™ Flu A/B
Intended Use	The Directigen Flu A+B test is a rapid *in vitro* immunoassay membrane test for the direct and qualitative detection of influenza A and B viral antigens from nasopharyngeal wash, nasopharyngeal aspirate, nasopharyngeal swab, lower nasal swab, throat swab and bronchoalveolar lavage specimens of symptomatic patients. The Directigen Flu A+B test is a differentiated test, and therefore influenza A viral antigens can be distinguished from influenza B viral antigens in a single test. The test is used as an aid in the diagnosis of influenza A and B viral infections. Negative test results should be confirmed by cell culture.	REMEL's Xpect™ Flu A/B is a rapid *in vitro* immunochromatographic test for the direct, qualitative detection of influenza A and influenza B viral antigen (nucleoprotein) from nasal wash, nasal swab, and throat swab specimens from symptomatic patients. The test is intended as an aid in the rapid diagnosis of influenza A and influenza B viral infections. Negative tests should be confirmed by cell culture.
Detection	Qualitative; Influenza A and B viral antigens with differentiation.	Qualitative; Influenza A and B viral antigens with differentiation.
Technology	Enzyme Immunoassay (EIA) membrane assay	Immunochromatographic membrane assay
Specimen Type	Nasopharyngeal wash, nasopharyngeal aspirate, nasopharyngeal swab, lower nasal swab, throat swab and bronchoalveolar lavage specimens	Nasal wash, nasal swab, and throat swab specimens

Summary of Performance Data:

Clinical Accuracy:
The performance of the Xpect™ Flu A/B was evaluated at three sites located in the north, south, and east regions of the United States. The clinical trial sites included a Children's hospital (pediatric population), a University hospital (primarily adult population), and a reference laboratory (adult and pediatric (60/40) population). For all

specimens evaluated, the overall sensitivity of the Xpect™ Flu A/B test when compared to culture was 92.2% (71/77) for influenza A and 97.8% (45/46) for influenza B. The overall specificity was 100% for both influenza A (314/314) and influenza B (345/345). For influenza A, there were 6 samples that were culture positive and Xpect™ Flu A/B negative. For influenza B, there was 1 sample that was culture positive and Xpect™ Flu A/B negative. Four of five discrepant samples available for analysis were positive by RT-PCR.

Nasal Wash (n=239)
Influenza A
92.5% Sensitivity (37/40); 95% CI = 79.6-98.4%
100% Specificity (199/199); 95% CI = 98.2-100%

Influenza B
100% Sensitivity; (36/36); 95% CI = 90.3-100%
100% Specificity (203/203); 95% CI = 98.2-100%

OVERALL		Culture Results		
		A+ / B-	A- / B+	A- / B-
Xpect™ Flu A/B Results	A+ / B-	37	0	0
	A- / B+	0	36	0
	A- / B-	3*	0	163

*RT-PCR was performed on the three discrepant results. One of the three specimens was negative by PCR, two were positive.

Test performance by individual site:

FLU A	Sensitivity			Specificity		
Site	#	%	95% CI	#	%	95% CI
1	0/0	NA	NA	1/1	100	NA
2	3/5	60.0	14.7-94.7	69/69	100	94.8-100
3	34/35	97.1	85.1-99.9	129/129	100	97.2-100

FLU B	Sensitivity			Specificity		
Site	#	%	95% CI	#	%	95% CI
1	0/0	NA	NA	1/1	100	NA
2	0/0	NA	NA	74/74	100	95.1-100
3	36/36	100	90.3-100	128/128	100	97.2-100

Throat Swabs (n=30)
Influenza A
100% Sensitivity (10/10); 95% CI = 69.2-100%
100% Specificity (20/20); 95% CI = 83.2-100%

Influenza B
100% Sensitivity; (4/4); 95% CI = 39.8-100%
100% Specificity (26/26); 95% CI = 86.8-100%

OVERALL		Culture Results		
		A+ / B-	A- / B+	A- / B-
Xpect™ Flu A/B Results	A+ / B-	10	0	0
	A- / B+	0	4	0
	A- / B-	0	0	16

Test performance by individual site:

FLU A	Sensitivity			Specificity		
Site	#	%	95% CI	#	%	95% CI
1	10/10	100	69.2-100	18/18	100	81.5-100
2	0/0	NA	NA	2/2	100	15.8-100
3	NA	NA	NA	NA	NA	NA

FLU B	Sensitivity			Specificity		
Site	#	%	95% CI	#	%	95% CI
1	4/4	100	39.8-100	24/24	100	85.8-100
2	0/0	NA	NA	2/2	100	15.8-100
3	NA	NA	NA	NA	NA	NA

Nasal Swab (n=122)
Influenza A
88.9% Sensitivity (24/27); 95% CI = 70.8-97.7%
100% Specificity (95/95); 95% CI = 96.2-100%

Influenza B
83.3% Sensitivity; (5/6); 95% CI = 35.9-99.6%
100% Specificity (116/116); 95% CI = 96.9-100%

		Culture Results		
		A+ / B-	A- / B+	A- / B-
Xpect™ Flu A/B Results	A+ / B-	24	0	0
	A- / B+	0	5	0
	A- / B-	3*	1*	89

*RT-PCR was performed on two of the four discrepant specimens that were available (one influenza A and one influenza B). Both specimens were positive by PCR.

Test performance by individual site:

FLU A	Sensitivity			Specificity		
Site	**#**	**%**	**95% CI**	**#**	**%**	**95% CI**
1	24/27	88.9	70.8-97.7	91/91	100	96.0-100
2	0/0	NA	NA	4/4	100	39.8-100
3	NA	NA	NA	NA	NA	NA

FLU B	Sensitivity			Specificity		
Site	**#**	**%**	**95% CI**	**#**	**%**	**95% CI**
1	5/6	83.3	35.9-99.6	112/112	100	96.8-100
2	0/0	NA	NA	4/4	100	39.8-100
3	NA	NA	NA	NA	NA	NA

Analytical Sensitivity:

The analytical sensitivity was evaluated using 12 influenza strains; 6 influenza A and 6 influenza B. Each viral strain was quantitated by $CEID_{50}$ determinations and titrated until a positive endpoint was reached using the Xpect™ Flu A/B test. The amount of virus at the endpoint dilution, expressed as $CEID_{50}$ per test, was calculated as a measure of analytical sensitivity.

Influenza Strain	Type	Detection Limit $CEID_{50}$
A/Puerto Rico/8/34 (H1N1)	A	8.9×10^3
A/Fort Monmouth/1/47 (H1N1)	A	7.9×10^1
A/New Jersey/8/76 (H1N1)	A	8.9×10^1
A/Hong Kong/8/68 (H3N2)	A	2.8×10^1
A/Victoria/3/75 (H3N2)	A	8.9×10^2
A/Port Chalmers/1/73 (H3N2)	A	4.0×10^1
B/Lee/40	B	7.9×10^3
B/Allen/45	B	4
B/Maryland/1/59	B	6
B/GL/1739/54	B	8.9×10^1
B/Taiwan/2/62	B	3
B/Hong Kong/5/72	B	1.58×10^2

Cross-Reactivity:
Thirty-six microorganisms were evaluated with the Xpect™ Flu A/B test. No cross-reactivity was observed for influenza A or influenza B. Bacteria and yeast isolates were tested at 10^8 colony-forming units per ml concentration. Viral isolates were tested at concentrations of 10^4 to 10^5 $TCID_{50}$ (tissue culture infectious dose) per ml concentration. The following organisms were tested in the Xpect™ Flu A/B test.

Acinetobacter baumanni	*Serratia marcescens*
Bordetella pertussis	*Staphylococcus aureus* (Cowan)
Candida albicans	*Staphylococcus epidermidis*
Enterococcus faecalis	*Streptococcus mutans*
Escherichia coli	*Streptococcus pneumoniae*
Gardnerella vaginalis	*Streptococcus pyogenes Group A*
Haemophilus influenzae	*Streptococcus,* Group B
Klebsiella pneumoniae	*Streptococcus,* Group C
Lactobacillus casei	*Streptococcus,* Group F
Legionella pneumophila	Adenovirus, Type 5
Listeria monocytogenes	Coronavirus
Moraxella catarrhalis	Coxsackievirus B5
Neisseria gonorrhoeae	Cytomegalovirus
Neisseria meningitidis	Parainfluenza (Sendai), Type 1
Neisseria sicca	Parainfluenza, Type 2
Neisseria subflava	Parainfluenza, Type 3
Proteus vulgaris	Respiratory Syncytial Virus, A
Pseudomonas aeruginosa	Rhinovirus, Type 14

Interfering Substances:
The following substances were tested with the Xpect™ Flu A/B test and no interference was observed in the assay for any substance tested at the indicated levels: whole blood (2%), 3 mouthwashes (25%), 3 throat drops (25%), 3 nasal sprays (25%), 4-acetamidophenol (acetaminophen) (10 mg/ml), acetylsalicylic acid (20 mg/ml), chlorpheniramine (5 mg/ml), dextromethorphan (10 mg/ml), diphenhydramine (5 mg/ml), guaiacol glyceryl ether (guaifenesin) (20 mg/ml), oxymetazoline (10 mg/ml), phenylephrine (25 mg/ml), phenylpropanolamine (20 mg/ml).

Reproducibility:
Reproducibility testing was conducted at four sites, including one in-house site, on four separate days with six blinded samples. The liquid samples consisted of diluted influenza A and influenza B antigens intended to read weakly positive or negative with the Xpect™ Flu A/B test. Ninety-nine percent of the 96 samples tested produced the expected result.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Rockville MD 20850

JUL 17 2003

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Re: k031565
Trade/Device Name: Xpect™ Flu A/B
Regulation Number: 21 CFR 866.3330
Regulation Name: Influenza Virus Serological Reagents
Regulatory Class: Class I
Product Code: GNX
Dated: May 14, 2003
Received: May 20, 2003

Dear Ms. Silvius:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE

510(k) Number (if known): K031565

Device Name: Xpect™ Flu A/B

Indications For Use: REMEL's Xpect™ Flu A/B is a rapid *in vitro* immunochromatographic test for the direct, qualitative detection of influenza A and influenza B viral antigen (nucleoprotein) from nasal wash, nasal swab, and throat swab specimens from symptomatic patients. The test is intended as an aid in the rapid diagnosis of influenza A and influenza B viral infections. Negative tests should be confirmed by cell culture.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ **OR** **Over-The-Counter Use** _____
(Per 21 CFR 801.109)

Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

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