

K974167

Summary of Safety and Effectiveness Information  
PR-3 ANCA Test Kit

FEB 17 1998

- I. **Wieslab AB**  
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Date of preparation: Jan 19, 1998

II. **Description of Device:** The Wielisa PR-3 ANCA Test Kit is an enzyme-linked immunosorbent assay (ELISA) for the detection and semi-quantitation of IgG antibodies to Proteinase-3 (PR-3) in human sera. The assay is used to detect antibodies in a single serum specimen. The results of the assay are to be used as an aid to the diagnosis of Wegener's granulomatosis. **FOR IN VITRO DIAGNOSTIC USE.**

The wells of the microtiter strips are coated with purified proteinase 3. During the first incubation, specific antibodies in diluted serum, will bind to the antigen coating.

The wells are then washed to remove unbound antibodies and other components. A conjugate of alkaline phosphatase-labeled antibodies to human IgG binds to the antibodies in the wells in this second incubation.

After a further washing step, detection of specific antibodies is obtained by incubation with substrate solution. The amount of bound antibodies correlates to the color intensity and is measured in terms of absorbance (optical density (OD)). The absorbance is then calculated against a calibrator curve and the results are given in arbitrary units.

III. **Predicate Device**

The PR-3 ANCA test is substantially equivalent to the Immunoscan PR-3 ANCA ELISA Kit. Equivalence is demonstrated by the following comparative results:

## Performance Characteristics

**Table 1. Clinical Sensitivity and Specificity** A total of 364 frozen retrospective sera with clinical characterization were assayed. The following table summarizes the data.

Control and Disease groups	Total number	Negative <10 units	Equivocal 10-20 units	Positive >20 units
<b>Healthy Normals:</b>	120	120	0	0
<b>WG:</b>	70	5	0	65
<b>MP:</b>	55	26	3	26
<b>SLE:</b>	40	38	1	1
<b>RA:</b>	17	17	0	0
<b>Anti-GBM nephritis:</b>	62	58	0	4

WG = Wegener's granulomatosis,  
SLE = systemic lupus erythematosus

MP = microscopic polyangiitis  
RA = rheumatoid arthritis

GBM = glomerular basement membrane

### Clinical Sensitivity (Equivocal samples excluded from calculations)

WG = 65/70 = 92.9%                      95% confidence interval = 86.7-99.0%  
MP = 26/52 = 50.0%                      95% confidence interval = 36.1-63.9%

### Clinical Specificity (Equivocal samples excluded from calculations)

SLE = 38/39 = 97.4%                      95% confidence interval = 92.4-100%  
RA = 17/17 = 100%                      \*95% confidence interval = 82.7-100%  
GBM = 58/62 = 93.6%                      95% confidence interval = 87.3-99.8%  
Normals = 120/120 = 100%                      \*95% confidence interval = 97.5-100%

The 95% confidence intervals were calculated using the normal method.

\*The 95% confidence intervals were calculated assuming one false positive.

**Table 2** A total of 245 frozen retrospective sera were assayed on the Wielisa PR-3 ANCA ELISA and IFA. The following Table summarizes the relative sensitivity and specificity.

**Relative Sensitivity and Specificity of the Wielisa PR-3 ANCA  
Compared to C-ANCA IFA**

		Wielisa PR-3 ANCA			Total
		Positive	Equivocal	Negative	
C-ANCA IFA	Positive	78	0	3	81
	Negative	13	3	148	164
	Total	91	3	151	245

Sera falling in the equivocal range were excluded from the following calculations

			95% Confidence Interval
Relative Sensitivity	= 78/81	= 96.3 %	92.1 - 100.0 %
Relative Specificity	= 148/161	= 91.9 %	87.6 - 96.2 %
Relative Accuracy	= 226/242	= 93.4 %	90.2 - 96.6 %

**Table 3** A total of 120 frozen retrospective sera were assayed by the Wiesisa PR-3 ANCA ELISA and by an alternate commercial ELISA. The following table summarizes the relative sensitivity and specificity of the assay.

**Relative Sensitivity and Specificity of the Wiesisa PR-3 Kit  
Compared to an Alternate ELISA**

		PR-3 Wiesisa			Total
		Positive	Equivocal	Negative	
<b>Alternate ELISA</b>	Positive	37	0	0	37
	Equivocal	1	0	1	2
	Negative	2**	0	79	81
	Total	40	0	80	120

Sera falling in the equivocal range were excluded from the following calculations

Relative Sensitivity	= 37/37 = 100 %	95% Confidence Interval
Relative Specificity	= 79/81 = 97.5 %	92.0 -100 %*
Relative Accuracy	= 116/118 = 98.3 %	94.1 -100 %
		95.9 - 100 %

\* One false negative was included in this calculation.

\*\* Both sera were from vasculitis patients

**Table 4. Batch to batch variation.**

Batch to batch variation was determined by testing 4 different samples in duplicate. Results were obtained for four different batches.

Sample	Mean value	SD	CV %
1	25 units	2.3	9.1
2	29 units	4.1	14.3
3	68 units	8.7	12.7
4	76 units	6.7	8.9

**Table 5. Inter-assay precision.**

Inter-assay precision was determined by testing 2 different samples in duplicate. Results were obtained for six different runs.

Sample	Mean value	SD	CV %
1	75 units	2.9	3.8
2	22 units	0.5	2.5

**Table 6. Intra-assay precision.**

Intra-assay precision was determined by testing one sample in 80 wells.

Sample	Mean value	SD	CV %
1	53 units	5.6	10.5

**Table 7. Linearity**

The values were determined for serial two-fold dilutions of seven positive sera. The values were compared to log<sub>2</sub> of dilution by standard linear regression. The data in Table 7 indicates that the assay has a linear relationship with serum dilution.

Serum	Neat	1:2	1:4	1:8	1:16	1:32	1:64	r
1	168	95	57	34	15	5		0.945
2	84	43	23	13	5			0.942
3	230	80	50	31	19	7		0.851
4	200	130	81	38	19	10	6	0.935
5	269	146	64	34	20	9.5		0.908
6	276	75	46	26	12	8		0.811
7	141	73	50	30	16	8		0.931



Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

WEISLAB AB  
William L. Boteler  
c/o IMMUNO PROBE, INC.  
1306 Bailes Lane, Suite F  
Frederick, MD 21701

FEB 17 1998

Re: K974167  
Trade Name: Wielisa PR-3 ANCA Test System  
Regulatory Class: II  
Product Code: MOB 82  
Dated: January 19, 1998  
Received: January 20, 1998

Dear Mr. Boteler:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to 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). 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 (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions.

Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 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 advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>"

Sincerely yours,



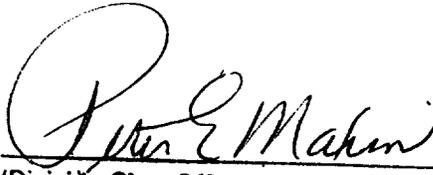
Steven I. Gutman, M.D., M.B.A.  
Director  
Division of Clinical  
Laboratory Devices  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

510(k) Number: Not known K 974167

Device Name: Wielisa PR-3 ANCA Test Kit

Indications For Use: The Wielisa PR-3 ANCA Test Kit is an enzyme-linked immunosorbent assay (ELISA) for the detection and semi-quantitation of antibodies to Proteinase-3 (PR-3) in human sera. The assay is used to detect antibodies in a single serum specimen. The results of the assay are to be used as an aid to the diagnosis of Wegener's granulomatosis.

  
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(Division Sign-Off)  
Division of Clinical Laboratory Devices  
510(k) Number K974167

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

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use   
(Per 21 CFR 801.109)

OR

Over-The Counter Use   
(Optional Format 1-2-96)