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K062045

Revised Summary of Safety and Effectiveness Information
EDIA™ anti-CCP kit

I. Euro-Diagnostica AB, Medeon, SE-205 12 Malmo, Sweden
Contact person: Ms. Annika Andersson
Telephone: +46 40 32 11 55
Fax: +46 40 92 31 50
Date of preparation: October 16, 2006

II. Description of Device: The EDIA™ anti-CCP test kit is an enzyme-linked immunosorbent assay (ELISA) for detection and semi-quantitation of IgG antibodies to Cyclic Citrullinated Peptides (CCP) in human sera and plasma. The assay is used to detect antibodies in a single specimen. The results of the assay are to be used as an aid to the diagnosis of Rheumatoid Arthritis (RA), in conjunction with other laboratory and clinical findings. Trained laboratory professionals should perform the analysis.
"For in vitro diagnostic use".

The wells are coated with Cyclic Citrullinated Peptides. 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 labelled 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 colour 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 EDIA™ anti-CCP test is substantially equivalent to the. Immunoscan RA anti-CCP test kit. Equivalence is demonstrated by the following comparative results:

Table 1. Percent agreement of the EDIA™ anti-CCP compared to the Immunoscan RA anti-CCP test kit. A total of 678 frozen retrospective sera were assayed. 416 from RA patients and 262 samples were apparently healthy blood donors.

New device	N = 678	Predicate device (Immunoscan RA anti-CCP) Positive	Negative
EDIA™ anti-CCP	Positive	317	2
	Negative	5	354

Positive Percent Agreement: 317/322 = 98.4% 95% CI = 96.4 - 99.5%
Negative Percent Agreement: 354/356 = 99.4% 95% CI = 98.0 - 99.9%
Overall Percent Agreement: 671/678 = 99.0% 95% CI = 97.9 - 99.6%

The 95% confidence interval (CI) was calculated using the exact method.

Figure 1 Linear correlation between anti-CCP titres of 174 sera from RA patients with values <50 U/mL for the EDIA anti-CCP and <250 U/mL for the Immunoscan RA anti-CCP.

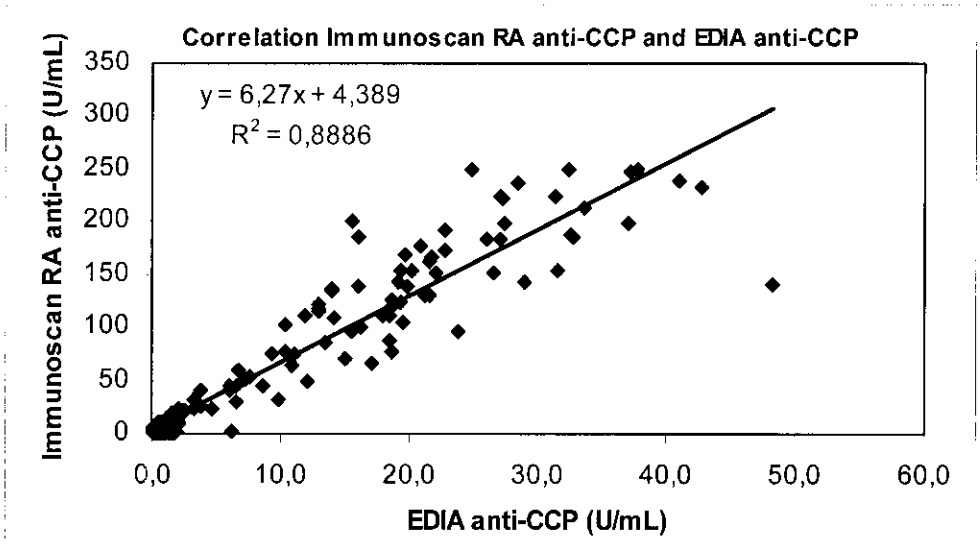

Table 2. Clinical sensitivity and specificity. A total of 1209 frozen retrospective sera with clinical characterisation were assayed. The following table summarises the results.

Sensitivity of EDIA™ anti-CCP for 416 sera from established RA patients

	n	negative	positive	Sensitivity
Patients with clinically defined RA	416	99	317	76%

Clinical Sensitivity: RA 317/416 = 76.2% 95% CI = 72.1-80.3

Clinical specificity for the EDIA™ anti-CCP for non-RA diseased patients and asymptomatic individuals (healthy blood donors).

	n	negative	positive	Specificity
Healthy blood donors	262	260	2	99%
Crohn's disease	10	10	0	100%
Colitis ulcerosa	10	10	0	100%
Systemic lupus erythematosus	30	30	0	100%
Sjögren's syndrome	17	16	1	94%
EBV	5	5	0	100%
Parvo	5	5	0	100%
Mycoplasma	9	9	0	100%
Toxoplasma	6	6	0	100%
Yersinia	8	8	0	100%
Chlamydia	5	4	1	80%
Malaria	4	4	0	100%
Borrelia	9	9	0	100%
Lues	5	5	0	100%
Rubella	5	5	0	100%
TPO-AB (anti-thyroid peroxidase ab)	20	20	0	100%
Osteoarthritis	21	21	0	100%
Endocarditis	3	3	0	100%
Tuberculosis	5	5	0	100%
Legionella	4	4	0	100%
Salmonella	3	3	0	100%
AST/ASH (anti-streptococcal ab)	3	3	0	100%
Schistosomiasis	4	4	0	100%
Chaga's disease	3	3	0	100%
Scleroderma	17	16	1	94%
Multiple sclerosis	20	20	0	100%
Insulin dependent diabetes mellitus	20	20	0	100%
Polymyositis / Dermatomysositis	20	20	0	100%
Mixed connective tissue disease	20	19	1	95%
MPO-ANCA positive. MP	20	20	0	100%
PR3-ANCA positive. WG	20	20	0	100%
Ds-DNA positive	40	38	2	95%
Inflammatory bowel disease	80	79	1	99%
nonRA autoimmune patients	80	78	2	98%
TOTAL	793	782	11	98.6%

MP = Microscopic polyangiitis
WG = Wegener's granulomatosis

Clinical specificity

Blood donors	260/262	= 99.2%	95% CI = 97.3 - 99.9%
Crohn's disease	10/10	= 100%	95% CI = 69.2 - 100%
Colitis ulcerosa	10/10	= 100%	95% CI = 69.2 - 100%
SLE	30/30	= 100%	95% CI = 88.4 - 100%
Sjorgen's syndrome	16/17	= 94.1%	95% CI = 71.3 - 99.8%
EBV	5/5	= 100%	95% CI = 47.8 - 100%
Parvo	5/5	= 100%	95% CI = 47.8 - 100%
Mycoplasma	9/9	= 100%	95% CI = 66.4 - 100%
Toxoplasma	6/6	= 100%	95% CI = 54.1 - 100%
Yersinia	8/8	= 100%	95% CI = 63.1 - 100%
Chlamydia	4/5	= 80%	95% CI = 28.4 - 99.5%
Malaria	4/4	= 100%	95% CI = 39.8 - 100%
Borrelia	9/9	= 100%	95% CI = 66.4 - 100%
Lues	5/5	= 100%	95% CI = 47.8 - 100%
Rubella	5/5	= 100%	95% CI = 47.8 - 100%
TPO-AB	20/20	= 100%	95% CI = 83.2 - 100%
Osteoarthritis	21/21	= 100%	95% CI = 83.9 - 100%
Endocarditis	3/3	= 100%	95% CI = 29.2 - 100%
Tuberculosis	5/5	= 100%	95% CI = 47.8 - 100%
Legionella	4/4	= 100%	95% CI = 39.8 - 100%
Salmonella	3/3	= 100%	95% CI = 29.2 - 100%
AST/ASH	3/3	= 100%	95% CI = 29.2 - 100%
Schistosomiasis	4/4	= 100%	95% CI = 39.8 - 100%
Chaga's disease	3/3	= 100%	95% CI = 29.2 - 100%
Scleroderma	16/17	= 94.1%	95% CI = 71.3 - 99.8%
Multiple Sclreosis	20/20	= 100%	95% CI = 83.2 - 100%
IDDM	20/20	= 100%	95% CI = 83.2 - 100%
PM/DM	20/20	= 100%	95% CI = 83.2 - 100%
MCTD	19/20	= 95%	95% CI = 75.1 - 99.9%
MP	20/20	= 100%	95% CI = 83.2 - 100%
WG	20/20	= 100%	95% CI = 83.2 - 100%
ds-DNA positive	38/40	= 95%	95% CI = 83.1 - 99.4%
IBD	79/80	= 98.6%	95% CI = 93.2 - 100%
nonRA autoimmune	78/80	= 97.5%	95% CI = 91.3 - 99.7%

The 95% confidence interval (CI) was calculated using the exact method.

Table 3. Intra-assay precision was determined by testing six different samples eight times each.

	High (U/mL)	**Medium** (U/mL)	**Low** (U/mL)
Mean	173.9	34.0	9.9
S.D.	13.8	0.6	0.2
% C.V.	7.9	1.9	2.1
	Low (U/mL)	**Low** (U/mL)	**Low** (U/mL)
Mean	11.8	7.8	9.7
S.D.	0.5	0.1	0.4
%C.V.	4.0	1.9	4.4

Table 4. Inter-assay precision was determined by testing six different samples eight times each. Results were obtained for three different runs.

	High (U/mL)	**Medium** (U/mL)	**Low** (U/mL)
Mean.	183.8	36.6	9.3
S.D.	19.5	3.0	0.9
% C.V.	10.6	8.2	9.8
	Low (U/mL)	**Low** (U/mL)	**Low** (U/mL)
Mean	11.9	7.8	10.6
S.D.	0.8	0.7	0.9
%C.V.	6.3	9.5	8.9

Table 5. Batch to batch variation was determined by testing six different samples eight times each. Results were obtained for three different batches.

	High (U/mL)	**Medium** (U/mL)	**Low** (U/mL)
Mean	232.5	41.6	11.5
S.D.	30.9	4.5	1.3
% C.V.	13.3	10.8	11.2
	Low (U/mL)	**Low** (U/mL)	**Low** (U/mL)
Mean	14.1	9.8	13.0
S.D.	1.2	1.0	1.2
%C.V.	8.3	10.4	9.3

Table 6. Dilution recovery was determined by testing five serial dilutions of three different patient samples.

Sample	Dilution	Mean Measured Concentration (U/mL)	Calculated Concentration (U/mL)	Dilution Corrected % Recovery
1	1/100	205.0	205.0	100
	1/200	110.5	102.5	108
	1/400	47.3	51.3	92
	1/800	24.8	25.6	97
	1/1600	10.8	12.8	84
Sample	**Dilution**	**Mean Measured Concentration (U/mL)**	**Calculated Concentration (U/mL)**	**Dilution corrected % recovery**
2	1/100	138.9	138.9	100
	1/200	70.3	69.5	101
	1/400	40.4	34.7	116
	1/800	18.3	17.4	105
	1/1600	8.7	8.7	100
Sample	**Dilution**	**Mean Measured Concentration (U/mL)**	**Calculated Concentration (U/mL)**	**Dilution corrected % recovery**
3	1/100	47.3	47.3	100
	1/200	26.7	23.6	113
	1/400	13.0	11.8	110
	1/800	6.3	5.9	107
	1/1600	3.0	3.0	103

Limit of detection

The detection limit of the assay was determined by running the zero calibrator 12 times on three different lots. The detection limit of 0.5 U/mL was calculated by finding the mean plus two standard deviations.

Interference study

Three low positive samples were spiked to the following concentrations in diluted serum samples; Bilirubin F at 0.188 mg/dL, Bilirubin C at 0.2 mg/dL, Haemoglobin at 453 mg/dL, Chyle at 0.24 U/dL and Rheumatoid Factor at 200 IU/mL. The data indicates that the assayed concentrations do not interfere with the anti-CCP results.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Euro-Diagnostica AB
c/o Ms. Annika Andersson
Regulatory Affairs Specialist
Medeon
SE-205 12 Malmö
Sweden

DEC - 4 2006

Re: k062045
Trade/Device Name: EDIA™ Anti-CCP
Regulation Number: 21 CFR 866.5775
Regulation Name: Rheumatoid Factor Immunological Test System
Regulatory Class: Class II
Product Code: NHX
Dated: July 14, 2006
Received: July 19, 2006

Dear Ms. Andersson:

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 the Code of Federal Regulations, Title 21, Parts 800 to 898. 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 Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k062045

Device Name: EDIA™ anti-CCP

Indications For Use: The EDIA™ anti-CCP test kit is an enzyme-linked immunosorbent assay (ELISA) for detection and semi-quantitation of IgG antibodies to Cyclic Citrullinated Peptides (CCP) in human sera and plasma. The assay is used to detect antibodies in a single specimen. The results of the assay are to be used as an aid to the diagnosis of Rheumatoid Arthritis (RA), in conjunction with other laboratory and clinical findings. The analysis should be performed by trained laboratory professionals.

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Maria M Chan
Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K062045