K091657

510(k) Summary

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Date of preparation: June 5, 2009
Revised: November 5, 2009

II. Device/Trade name: Immunoscan CCPlus®
Common name: Anti-CCP test
Governing regulation: 21 CFR 866.5775
Device classification: Class II
Classification panel: Immunology
Product code: NHX

III. Description of Device: The Immunoscan CCPlus® test kit is a modification of the Immunoscan RA anti-CCP Test kit, K052133. It is an enzyme-linked immunosorbent assay (ELISA) for qualitative and semi-quantitative determination of IgG antibodies to Cyclic Citrullinated Peptides (CCP) 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 Rheumatoid Arthritis (RA), in conjunction with other laboratory and clinical findings. The analysis should be performed by trained laboratory professionals. "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.

IV. Legally marketed device to which equivalence is claimed: Immunoscan RA anti-CCP Test kit, K052133.

V. Intended use of the device: The intended use of the modified device has not changed. The Immunoscan CCPlus® test kit is an enzyme-linked immunosorbent assay (ELISA) for qualitative and semi-quantitative determination of IgG antibodies to Cyclic Citrullinated Peptides (CCP) 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 Rheumatoid Arthritis (RA), in conjunction with other laboratory and clinical findings. The analysis should be performed by trained laboratory professionals. "For in vitro diagnostic use".

VI. Comparison of technological characteristics:

Table 1. Similarities and differences between Immunoscan CCPlus® and Predicate Device, Immunoscan RA anti CCP Test kit, K052133

Similarities

Item	Modified Device Immunoscan CCPlus®	Predicate Device Immunoscan RA anti-CCP
Intended use	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 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.
Intended user	For use by health care professionals	For use by health care professionals
Method	ELISA	ELISA
Type of test	Qualitative and semi-quantitative	Qualitative and semi-quantitative
Analyte measured	Anti-CCP	Anti-CCP
Coated antigen	Synthetic CCP	Synthetic CCP
Conjugate	Anti-human IgG	Anti-human IgG
Substrate	TMB (3, 3', 5, 5'-tetramethylbenzidin)	TMB (3, 3', 5, 5'-tetramethylbenzidin)
Wavelength	450 nm	450 nm
Incubation time	60 min + 30 min + 30 min	60 min + 30 min + 30 min
Cut-off	≥25 U/mL	≥25 U/mL
Sample	Serum	Serum
Sample preparation	Dilute 1:50	Dilute 1:50
Microtitre plate	Material: Polystyrene Surface: MaxiSorp	Material: Polystyrene Surface: MaxiSorp

Differences

Item	Modified Device Immunoscan CCPlus®	Predicate Device Immunoscan RA anti-CCP
Microtiter plate	96 individual wells plate Note: The material and surface of the microtitre plate are the same	8 strips x 12 wells plate Note: The material and surface of the microtitre plate are the same
Calibrator curve	25 U/mL, 50 U/mL, 200 U/mL, 800 U/mL, 3200 U/mL Note: The same material is used to produce the calibrator	25 U/mL, 50 U/mL, 200 U/mL, 800 U/mL, 1600 U/mL Note: The same material is used to produce the calibrator

VII. Summary of performance: The modified device, Immunoscan CCPlus®, is substantially equivalent to the Immunoscan RA anti-CCP Test kit. Equivalence is demonstrated by the following comparative results.

Table 2. Percent agreement of the Immunoscan CCPlus® compared to the Immunoscan RA anti-CCP Test kit. A total of 628 frozen retrospective sera were assayed. 368 were obtained from RA patients and 260 samples were from apparently healthy blood donors.

		Predicate device Immunoscan RA anti-CCP	
Immunoscan CCPlus®	N = 628	Positive	Negative
	Positive	275	5
	Negative	2	346

Positive Percent Agreement: 275/277 = 99.3% 95% CI = 97.4 - 99.9%
Negative Percent Agreement: 346/351 = 98.6% 95% CI = 96.7 - 99.5%
Overall Percent Agreement: 621/628 = 98.9% 95% CI = 97.7 - 99.6%

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

Table 3. Clinical sensitivity and specificity. A total of 1180 frozen retrospective sera with clinical characterisation were assayed. The following table summarizes the results.

	n	negative	positive	Sensitivity
Patients with clinically defined RA	399	90	309	77.4%

Clinical sensitivity
RA 309/399 = 77.4% 95% CI = 73.3 - 81.5%

Clinical specificity for the Immunoscan CCPlus® for non-RA diseased patients and asymptomatic individuals (healthy blood donors).

Control and Disease groups	Total number	Negative < 25 U/mL	Positive ≥ 25 U/mL
Blood donors	260	257	3
RA	399	90	309
WG	20	18	2
MP	20	20	0
SLE	66	64	2
Sjögren's syndrome	13	13	0
IBD	98	95	3
Osteoarthritis	21	21	0
Thyroiditis	20	20	0
Epstein Barr Virus	5	5	0
Parvovirus	5	5	0
Mycoplasma	9	9	0
Toxoplasma	6	6	0
Tuberculosis	5	5	0
Yersinia	8	8	0
Salmonella	3	3	0
Chlamydia	5	4	1
Malaria	4	4	0
Borrelia	9	9	0
Syphilis	5	5	0
Infectious endocarditis	3	3	0
Legionella	4	4	0
AST	3	3	0
Schistomiasis	4	4	0
Rubella	5	5	0
Chaga's syndrome	3	3	0
Scleroderma	17	16	1
Multiple Sclerosis	20	20	0
IDDM	20	20	0
PM/DM	20	20	0
MCTD	20	19	1
Routine samples	80	78	2

RA = rheumatoid arthritis
WG = Wegener's granulomatosis
MP = microscopic polyangiitis
SLE = systemic lupus erythematosus
PM/DM = Polymyositis/Dermatomyositis
IBD = inflammatory bowel disease
AST = anti-Streptolysine test
IDDM = insulin dependent diabetes mellitus
MCTD = mixed connective tissue disease

Clinical specificity

Blood donors	= 257/260 = 98.8%	95% CI = 96.7 - 99.8%
WG	= 18/20 = 90.0%	95% CI = 68.3 – 98.8%
MP	= 20/20 = 100%	95% CI = 83.2 - 100%
SLE	= 64/66 = 97.0 %	95% CI = 89.5 - 99.6%
Sjogren's	= 13/13 = 100 %	95% CI = 75.3 - 100%
IBD	= 95/98 = 96.9%	95% CI = 91.3 - 99.4%
Osteoarthritis	= 21/21 = 100%	95% CI = 83.9 - 100%
Thyroiditis	= 20/20 = 100%	95% CI = 83.2 - 100%
Infectious Disease	= 85/86 = 98.8%	95% CI = 93.7 - 100%
Scleroderma	= 16/17 = 94.1%	95% CI = 71.3 - 99.8%
Multiple Sclerosis	= 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 = 95.0%	95% CI = 75.1 - 99.9%
Routine samples	= 78/80 = 97.5 %	95% CI = 91.3 - 99.7 %

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

Table 4. Intra-assay precision was determined by testing six different samples eight times each.

	High		**High**		**High**	
	U/mL	OD	U/mL	OD	U/mL	OD
Mean.	2672	1.421	2685	1.432	1150	1.664
S.D.	138	0.01	205	0.01	55.3	0.02
% C.V.	5.2	0.4	7.6	0.4	4.8	0.9
	Medium		**Low**		**Low**	
	U/mL	OD	U/mL	OD	U/mL	OD
Mean	239	1.014	56	0.421	28	0.232
S.D.	2.3	0.01	2.1	0.01	0.5	0.01
%C.V.	1.0	0.4	3.8	2.8	3.6	1.3

Table 5. Inter-assay precision was determined by testing six different samples eight times each. Results were obtained for three different runs.

	High		**High**		**High**	
	U/mL	OD	U/mL	OD	U/mL	OD
Mean.	2696	1.426	2600	1.422	1168	1.706
S.D.	328	0.01	299	0.01	101.7	0.07
% C.V.	12.2	0.7	11.5	0.8	8.7	3.8
	Medium		**Low**		**Low**	
	U/mL	OD	U/mL	OD	U/mL	OD
Mean	242	1.031	59	0.428	28	0.232
S.D.	5.0	0.03	3.1	0.02	0.5	0.01
%C.V.	2.1	2.5	5.2	3.8	1.8	0.9

Table 6. Lot to lot variation was determined by testing six different samples eight times each. Results were obtained for three different lots.

	High		High		High	
	U/mL	OD	U/mL	OD	U/mL	OD
Mean.	2896	1.408	2870	1.408	1530	1.807
S.D.	405	0.02	335	0.02	260.4	0.03
% C.V.	14.0	1.4	11.7	1.5	17.0	1.6
	Medium		**Low**		**Low**	
	U/mL	OD	U/mL	OD	U/mL	OD
Mean	259	1.100	60	0.462	62	0.471
S.D.	21.8	0.04	4.2	0.02	6.6	0.04
%C.V.	8.4	3.9	6.9	4.4	10.8	8.2

Table 7. Dilution recovery was determined by testing five serial dilutions for three different samples.

Sample	Dilution	Mean Measured Concentration (U/mL)	Calculated Concentration (U/mL)	Dilution Corrected % Recovery
1	1/50	395	395	100
	1/100	195	198	98
	1/200	104	99	105
	1/400	53	50	106
	1/800	26	25	104
Sample	**Dilution**	**Mean Measured Concentration (U/mL)**	**Calculated Concentration (U/mL)**	**Dilution Corrected % Recovery**
2	1/50	921	921	100
	1/100	486	461	105
	1/200	257	230	112
	1/400	124	115	107
	1/800	63	58	109
Sample	**Dilution**	**Mean Measured Concentration (U/mL)**	**Calculated Concentration (U/mL)**	**Dilution Corrected % Recovery**
3	1/50	2962	2962	100
	1/100	1496	1481	101
	1/200	771	741	104
	1/400	349	370	94
	1/800	194	185	105

Detection Limit
The detection limit of the assay was determined by running the zero standard 14 times on three different lots. The detection limit of 1.6 U/mL was calculated by finding the mean plus two standard deviations.

Interference Study
Three low positive samples were spiked with bilirubin at 0.2 mg/mL, haemoglobin at 400 mg/dl, lipid at 15 mg/mL and rheumatoid factor at 200 IU/mL. The data indicates that the assayed concentrations do not interfere with the anti-CCP results.

Summary performance characteristics:

Clinical sensitivity

Immunoscan CCPlus®	77.4%
Predicate device	75.1%

Clinical specificity

Immunoscan CCPlus®	Between 94.1% - 100%
Predicate device	Between 94.1% - 100%

Intra-assay precision

Immunoscan CCPlus®	Anti-CCP: 28 - 2685 U/mL	%C.V.: 1.0-7.6
Predicate device	Anti CCP: 34 - 1007 U/mL	%C.V.: 4.3-12.8

Inter-assay precision

Immunoscan CCPlus®	Anti-CCP: 28 - 2696 U/mL	%C.V.: 2.1-12.2
Predicate device	Anti CCP: 33 - 1106 U/mL	%C.V.: 6.0-17.7

Lot to lot precision

Immunoscan CCPlus®	Anti-CCP: 60 - 2896 U/mL	%C.V.: 6.9-17.0
Predicate device	Anti CCP: 29 - 1117 U/mL	%C.V.: 3.8-12.2

Detection Limit

Immunoscan CCPlus®	1.6 U/mL
Predicate device	1.6 U/mL

VIII. Conclusion
The modified device Immunoscan CCPlus® is similar in intended use and performance characteristics to the originally cleared, K052133, Immunoscan RA anti-CCP Test kit. The modification does not alter the fundamental scientific technology of the device.

- same material and surface of ELISA plate
- same production procedure
- performance characteristics are equal or better compared to predicate device

We trust that the information provided in this 510(k) will support a decision of substantial equivalence to the predicate Immunoscan RA anti-CCP Test kit.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-G609
Silver Spring, MD 20993-0002

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Euro-Diagnostica AB
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Regulatory Affairs Manager
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Re: k091657
Trade/Device Name: Immunoscan CCPlus®
Regulation Number: 21 CFR §866.5775
Regulation Name: Rheumatoid factor immunological test system
Regulatory Class: Class II
Product Code: NHX
Dated: September 28, 2009
Received: October 1, 2009

Dear Dr. 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 (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 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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

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 (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan, 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: k091657

Device Name: Immunoscan CCPlus®

Indication For Use: The Immunoscan CCPlus® test kit is an enzyme-linked immunosorbent assay (ELISA) for qualitative and semi-quantitative determination of IgG antibodies to Cyclic Citrullinated Peptides (CCP) 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 Rheumatoid Arthritis (RA), in conjunction with other laboratory and clinical findings. The analysis should be performed by trained laboratory professionals. "For in vitro diagnostic use".

Prescription Use ___X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K091657