K100017

PREMARKET NOTIFICATION
510(K)
SAFETY AND EFFECTIVENESS SUMMARY
(as required by 21 CFR § 807.92)

SEP 13 2010

A. 510(k)Number:
K010017

B. Purpose for Submission:
New device

C. Measurand:
Autoantibodies against glutamate receptor (type NMDA)

D. Type of Test:
Semi-quantitative indirect immunofluorescent antibody assay

E. Applicant:
EUROIMMUN US INC.

F. Proprietary and Established Names:
EUROIMMUN Anti-Glutamate receptor (type NMDA) IFA

G. Regulatory Information:

1. Regulation:
   21 CFR 866.5660 - Multiple autoantibodies immunological test system
2. Classification:
   Class II
3. Product code:
   OSK
4. Panel:
   Immunology

H. Intended Use:

1. Intended use(s):
   The EUROIMMUN Anti-Glutamate receptor (type NMDA) IFA is intended for the qualitative determination of autoantibodies against glutamate receptor (type NMDA) in human serum. It is used as an aid in the diagnosis of anti-glutamate receptor (type NMDA) autoimmune encephalitis in conjunction with other laboratory and clinical findings.
2. Indication(s) for use:
   Same as intended use.
3. Special conditions for the use statement(s):
   For prescription use only.
4. Special instrument requirements:
   Fluorescence microscope.

I. Device Description:

The EUROIMMUN IFA is an assay for standardized detection of anti-glutamate receptor (type NMDA) antibodies utilized in each laboratories familiar with indirect immunofluorescence. The non-transfected cells are used as a control to simplify differentiation of potential co-existing and non-specific reactivity such as ANA. The test kit consists of slides, which contain BIOCHIPs coated with glutamate receptor (type NMDA) transfected cells and non-transfected cells, fluorescein-labelled anti-human IgG (goat), a positive control for anti-glutamate receptor (type NMDA), a negative control, a salt for preparation of PBS, Tween 20, embedding medium, cover glasses and an instruction booklet.

95 Washington Street,
Morristown, New Jersey 07960
Tel: 973-270-0912 Fax: 973-270-0913 E-mail: kkeuroimmunus@.com

J. Substantial Equivalence Information:

1. Predicate device name (s):
   EUROIMMUN ANCA IFA Granulocyte BIOCHIP Mosaic™ Test System.
2. Predicate 510(k) number(s):
   K083850
3. Comparison with predicate:
   The EUROIMMUN ANCA IFA Granulocyte BIOCHIP Mosaic™ Test System was choosen as a device of equivalent method and technology. There is no exact predicate device available for the detection of antibodies against glutamate receptor (type NMDA).

Similarities		
Item	New device	Predicate device
Intended Use	Semi-quantitative detection of antibodies in human serum.	Same
Technology	IFA BIOCHIP TITERPLANE technology using multiple substrates	Same
Procedure	Standard IFA technique; serum incubation with tissues/cells, followed by a wash step, incubation with fluorescein–labelled anti–human globulin, wash step, embedding and reading fluorescence with a fluorescence microscope.	Same
Reagent	Fluorescein	Same
Sample type and dilution	Serum 1:10 dilution	Same
Controls	Positive control Negative control	Same
Cut Off Level	1:10 dilution	Same

Differences		
Intended Use	Detection of antibodies against glutamate receptor (type NMDA).	Detection of anti-neutrophil cytoplasmic antibodies (ANCA).
Substrates	Glutamate receptor (type NMDA) transfected cells and non-transfected cells	Human granulocytes native antigen

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

None referenced.

L. Test Principle:

The procedure follows the TITERPLANE Technique developed by EUROIMMUN as an aid in standardize immunological analyses. The TITERPLANE Technique of EUROIMMUN was cleared previously via the FDA 510(k) processes under 510(k) No. K051489, K061408, K070763 and K083850.

Patient samples, controls and in separate steps conjugate and embedding medium are applied to the reaction fields of a reagent tray. The BIOCHIP slides are then placed into the recesses of the reagent tray, where all BIOCHIPs of the slide come into contact with the fluids, and the individual reactions commence simultaneously. The fluids are confined to the recessed wells eliminating the need to use a conventional "humidity chamber".

Patient samples are diluted 1:10 in PBS-Tween, 25 µl of each diluted patient sample are added to each reaction field of the reagent tray. Reactions are started by fitting the BIOCHIP slides containing the substrates (rat hippocampus and cerebellum, glutamate receptor type NMDA transfected cells and non-transfected cells) into the corresponding recesses of the reagent tray and incubated for 30 minutes at room temperature. Specific antibodies attach to the antigens. After incubation the BIOCHIP slides are washed with PBS-Tween to remove unbound antibodies. In the meantime, 20 µl of fluorescein–labelled anti–human globulin are added to each reaction field of a clean reagent tray and the BIOCHIP slides placed into the recesses of the tray. After a

30 minutes incubation at room temperature, the BIOCHIPs are again washed with PBS-Tween to remove any unbound fluorescein-labelled reagent. 10 µl of Embedding medium are placed for each reaction field on a cover glass and the BIOCHIP slides, with the BIOCHIPs facing downwards, placed onto the prepared cover glass. Fluorescence is read with a fluorescence microscope.

M. Performance Characteristics (where applicable):

1. Analytical performance:
   a. *Precision/Reproducibility:*
   Intra-assay reproducibility
   The intra-assay reproducibility was determined by 10fold repeated measurements of 6 characterized positive and negative serum samples. The results did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level.
   Inter-assay reproducibility
   The inter-assay reproducibility was determined by repeated measurements of 6 characterized positive and negative serum samples at 5 different times. 2 slides were tested with each run. The results did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level.
   Lot to lot reproducibility
   The inter-lot reproducibility was determined by measurements of 3 characterized positive and negative serum samples using 3 different kit lots. The results did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level.
   b. *Linearity/assay reportable range:*
   Not applicable.
   c. *Traceability, Stability, Expected values (controls, calibrators or methods):*
   There is no recognized standard or reference material for autoantibodies against glutamate receptor (type NMDA).
   d. *Detection limit:*
   Not applicable.
   e. *Analytical specificity:*
   Cross-reactivity: Cross reactivity was investigated using 31 samples from patients with infectious and autoimmune encephalitis other than anti-glutamate receptor (type NMDA) encephalitis. Samples positive for anti-GluR2, anti-VGKC and anti-zic4 (cerebellar degeneration) do not react with the glutamate receptor (type NMDA).
   Interference: Three different samples are spiked with potential interfering substances in 3 different concentrations and are incubated with the test system. The recovery in relation to the original sample (not spiked) is calculated. The deviation in fluorescence intensity level did not exceed +/- 1. No interference was observed with hemolytic, lipemic or icteric samples for concentrations of up to 500 mg/dl for hemoglobin, 2000 mg/dl for triglyceride and 40 mg/dl for bilirubin.
   f. *Assay cut-off:*
   Not applicable.
2. Comparison studies:
   a. *Method comparison with predicate device:*
   Not applicable.
   b. *Matrix comparison:*
   Not applicable.

95 Washington Street,
Morristown, New Jersey 07960
Tel: 973-270-0912 Fax: 973-270-0913 E-mail: kkeuroimmunus@.com

3. Clinical studies:

a. Prevalence and specificity:

Study 1: 47 serum samples from the US from patients diagnosed with anti-gluatamate receptor (type NMDA) encephalitis and controls with other encephalopathies, including anti-VGKC and AMPA receptor encephalitis, were examined. The panel comprised samples from 7 men and 40 women with an average age of 17 years (age range: 5 to 42 years; 1 unknown). In addition, sera of 100 adult healthy blood donors of mixed age and sex from Germany were analyzed. All samples from patients with anti-glutamate receptor (type NMDA) encephalitis (29 sera) were tested positive with the transfected cells, while all disease control samples (18 sera) and healthy blood donors (100 sera) were negative.

Study 2: In a retrospective study, 2990 patients were screened for clinical symptoms of encephalitis of unknown origin. 5 of 6 samples fulfilling the criteria (6 women with an average age of 23 years, age range: 18 to 31 years; origin: Germany) were found positive for antibodies against glutamate receptor (type NMDA). The results support the fact that anti-glutamate receptor (type NMDA) encephalitis is a very frequent cause among these patients.

Study 3: 8 samples from patients with anti-glutamate receptor (type NMDA) encephalitis (origin: Germany) were investigated. The panel comprised samples from 3 men and 5 women with an average age of 25 years (age range: 16 to 39 years). All samples were found positive for anti-glutamate receptor (tpye NMDA).

Study 4: 9 samples from patients with anti-glutamate receptor (type NMDA) encephalitis and 13 samples from patients with other encephalopathies (origin: Italy) were investigated. The panel comprised samples from 8 men and 14 women with an average age of 47 years (age range: 9 to 89 years). All samples from patients with anti-glutamate receptor (type NMDA) encephalitis (9 sera) were tested positive with the transfected cells, while all disease control samples (13 sera) were negative.

Panel		n	EUROIMMUN Anti-Glutamate receptor (type NMDA) IFA		
			positive	% positive	95% C.I.
Study 1	Patients with anti-glutamate receptor (type NMDA) encephalitis	29	29	100.0%	88.1 – 100.0%
	Patients with other encephalopathies	18	0	0.0%	0.0 – 18.5%
	Healthy blood donors	100	0	0.0%	0.0 – 3.6%
Study 2	Patients with encephalitis of unknown origin	6	5	83.3%	35.9 – 99.6%
Study 3	Patients with anti-glutamate receptor (type NMDA) encephalitis	8	8	100.0%	63.1 – 100.0%
Study 4	Patients with anti-glutamate receptor (type NMDA) encephalitis	9	9	100.0%	66.4 – 100.0%
	Patients with other encephalopathies	13	0	0.0%	0.0 – 24.7%
Overall sensitivity		52	51 positive	98.1%	89.7 – 100.0%
Overall specificity		131	131 negative	100.0%	97.2 – 100.0%

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

Not applicable.

4. Clinical cut-off:

See Assay cut-off.

5. Expected values/Reference range:

The levels of the anti-glutamate receptor (type NMDA) antibodies (IgG) were analyzed with the EUROIMMUN Anti-Glutamate receptor (type NMDA) IFA in a panel of 120 sera from normal healthy adult blood donors of mixed age and gender. All samples were found negative. The reference range was determined as titer 1: < 10.

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.

Date

Signature

Kathryn Kohl, Managing Director
Typed Name, Title

95 Washington Street,
Morristown, New Jersey 07960
Tel: 973-270-0912 Fax: 973-270-0913 E-mail: kkeuroimmunus@.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food & Drug Administration
10903 New Hampshire Avenue
Building 66
Silver Spring, MD 20993

EUROIMMUN US INC.
c/o Ms. Kathryn Kohl
Managing Director
429 Rockaway Valley Road
Unit 1200
Boonton Township, NJ 07005

SEP 13 2010

Re: k100017
Trade/Device Name: EUROIMMUN Anti-Glutamate receptor (type NMDA) IFA
Regulation Number: 21 CFR§866.5660
Regulation Name: Multiple Autoantibodies Immunological Test System
Regulatory Class: Class II.
Product Code: OSK
Dated: August 4, 2010
Received: August 9, 2010

Dear Ms. Kohl:

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 class II (Special Controls), 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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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 advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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/cdrh/industry/support/index.html.

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

K100017

ATTACHMENT 2

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K100017

SEP 13 2010

Device Name: Anti-Glutamate receptor (type NMDA) IFA

Indications For Use:

The EUROIMMUN Anti-Glutamate receptor (type NMDA) IFA is intended for the qualitative determination of autoantibodies against glutamate receptor (type NMDA) in human serum. It is used as an aid in the diagnosis of anti-glutamate receptor (type NMDA) autoimmune encephalitis in conjunction with other laboratory and clinical findings.

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

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

Concurrence of CDRH, Office of Device Evaluation (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510K k100017

95 Washington Street,
Morristown, New Jersey 07960
Tel: 973-270-0912 Fax: 973-270-0913 E-mail: kkeuroimmunus@.com