DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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June 23, 2017

ROCHE DIAGNOSTICS
KELLI TURNER
REGULATORY AFFAIRS PRINCIPAL
9115 HAGUE RD.
INDIANAPOLIS IN 46250

Re: K162678
Trade/Device Name: Elecsys Toxo IgM, Elecsys Toxo IgM PreciControl
Regulation Number: 21 CFR 866.3780
Regulation Name: *Toxoplasma gondii* serological reagents
Regulatory Class: II
Product Code: LGD, JJX
Dated: May 19, 2017
Received: May 22, 2017

Dear Ms. Turner:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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 Parts 801 and 809); 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 regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education 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. 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 Industry and Consumer Education 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,

Ribhi Shawar -S For

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
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and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k162678

Device Name
Elecsys Toxo IgM Immunoassay

Indications for Use *(Describe)*

Elecsys Toxo IgM Immunoassay

The Elecsys Toxo IgM immunoassay is for the in vitro qualitative detection of IgM antibodies to Toxoplasma gondii in human serum and plasma. This assay may be used as an aid in the diagnosis of an acute or recent Toxoplasma gondii infection in suspected patients and pregnant women. Patient testing must be performed in conjunction with an anti-Toxoplasma gondii IgG antibody assay.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and cobas e immuno-assay analyzers. This assay has not been cleared by the FDA for blood/plasma donor screening.

PreciControl Toxo IgM

PreciControl Toxo IgM is used for quality control of the Elecsys Toxo IgM immunoassay on the Elecsys and cobas e immunoassay analyzers.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Elecsys Toxo IgM
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	**Roche Diagnostics**
Address	9115 Hague Road Indianapolis, IN 46250
Contact	Kelli Turner Phone: (317) 521-4515 FAX: (317) 521-3080 Email: kelli.turner@roche.com
Date Prepared	June 21, 2017
Proprietary Name	1) Elecsys Toxo IgM 2) PreciControl Toxo IgM
Common Name	1) Toxo IgM 2) PreciControlToxo IgM
Classification Name	1) Toxoplasma gondii serological reagents 2) Single (specified) analyte controls (assayed and unassayed)
Product Codes	1) LGD, 866.3780 2) JJX, 862.1660
Predicate Device	1) VIDAS TOXO IgM Test System (k923166)
Establishment Registration	Roche Diagnostics GmbH in Mannheim, Germany, is 9610126 Roche Diagnostics GmbH in Penzberg, Germany, is 9610529 Roche Diagnostics in the United States is 1823260

1. DEVICE DESCRIPTION

The Elecsys Toxo IgM is a two-step sandwich immunoassay with streptavidin microparticles and electrochemiluminescence detection. In the first incubation10 µL of sample are automatically prediluted 1:20 with Elecsys Diluent Universal and *T. gondii*-specific recombinant antigen labeled with a ruthenium complex is added. Anti-Toxo IgM antibodies present in the sample react with the ruthenium-labeled *T. gondii*-specific recombinant antigen. Then biotinylated monoclonal human-IgM- specific antibodies and streptavidin-coated microparticles are added. The complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined automatically by the Elecsys software by comparing the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cutoff value previously obtained by Toxo IgM calibration.

1.1. Reagents

The reagent working solutions include:

- rackpack (kit placed on instrument)
  - Streptavidin coated microparticles,
  - Reagent 1 (Toxoplasma-Ag~ Ru(bpy)2+3) and
  - Reagent 2 (Anti human IgM Ab~biotin).
  - Included with the kit:
    - Calibrator 1 (negative calibrator) Human serum non-reactive for anti Toxo IgM
    - Calibrator 2 (positive calibrator) Human serum reactive for anti Toxo IgM

1.2. Control

PreciControl Toxo IgM is a ready for use control serum based on human serum. The controls are used for monitoring the accuracy of the Elecsys Toxo IgM immunoassay.

The PreciControl Toxo IgM includes:

- PC Toxo IgM 1 (Human serum negative for Toxo IgM antibodies, preservatives)
- PC Toxo IgM 2 (Human serum positive for Toxo IgM antibodies, preservatives)

2. INDICATIONS FOR USE

The Elecsys Toxo IgM immunoassay is for the in vitro qualitative detection of IgM antibodies to *Toxoplasma gondii* in human serum and plasma. This assay may be used as an aid in the diagnosis of an acute or recent *Toxoplasma gondii* infection in suspected patients and pregnant women. Patient testing must be performed in conjunction with an anti-*Toxoplasma gondii* IgG antibody assay. The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and **cobas e** immunoassay analyzers. This assay has not been cleared by the FDA for blood/plasma donor screening.

Comparison with the predicate device

The Elecsys Toxo IgM immunoassay was compared to a commercially marketed kit VIDAS TOXO IgM Test System (k923166) by Biomerieux. Both kits have the same intended use and use the same methodology. Below are tables comparing the reagents and the procedures of the two devices.

Similarities		
Item	Device	Predicate
Intended Use	The Elecsys Toxo IgM immunoassay is for the in vitro qualitative detection of IgM antibodies to *Toxoplasma gondii* in human serum and plasma. This assay may be used as an aid in the diagnosis of an acute or recent *Toxoplasma gondii*	The VIDAS® TOXO IgM (TXM) assay is intended for use with a VJDAS® (Vitek ImmunoDiagnostic Assay System) instrument as an automated enzyme-linked fluorescent immunoassay (ELFA) for the presumptive qualitative

Similarities		
Item	Device	Predicate
	infection in suspected patients and pregnant women. Patient testing must be performed in conjunction with an anti-*Toxoplasma gondii* IgG antibody assay. The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and cobas e immuno-assay analyzers. This assay has not been cleared by the FDA for blood/plasma donor screening. PreciControl Toxo IgM is used for quality control of the Elecsys Toxo IgM immunoassay on the Elecsys and cobas e immunoassay analyzers.	detection of anti-*Toxoplasma gondii* IgM antibodies in human serum, as an aid in the diagnosis of acute, recent, or reactivated *Toxoplasma gondii* infection. This assay must be performed in conjunction with an anti-*Toxoplasma gondii* lgG antibody assay. VIDAS TXM assay performance has not been established for prenatal screening or newborn testing. This assay has not been cleared by the FDA for blood/plasma donor screening.
Calibrator	Included with the kit	Same
Assay type	Sandwich ELISA	Same
Instrument Platform	Fully automated system	Same
Differences		
Item	Device	Predicate
Assay Protocol	Electrochemiluminescence Immunoassay (ECLIA)	Enzyme-linked fluorescent immunoassay (ELFA)
Sample type	Serum, lithium heparin plasma, potassium EDTA plasma and sodium citrate plasma	Serum
Calibrators	Two	One

3. NON-CLINICAL PERFORMANCE EVALUATION

3.1. Precision

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision was determined at one site using Elecsys reagents, human sera and controls in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days (n = 60). The following results were obtained:

			Repeatability		Between-run		Intermediate precision	
Sample	N	Mean [s/co]	SD [s/co]	CV (%)	SD [s/co]	CV (%)	SD [s/co]	CV (%)
PC[d)] Toxo IgM 1	60	0.146	0.004	2.5	0.003	1.9	0.005	3.2
PC Toxo IgM 2	60	1.61	0.037	2.3	0.045	2.8	0.059	3.6
Serum Pool 1	60	0.147	0.003	2.3	0.005	3.1	0.006	3.9
Serum Pool 2	60	2.06	0.075	3.7	0.031	1.5	0.082	4.0
Serum Pool 3	60	3.49	0.173	4.9	0.060	1.7	0.183	5.2

d) PC = PreciControl

Note: intermediate precision is within lab precision data.

3.2. Reproducibility

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Reproducibility was determined at two sites using Elecsys reagents and human sera in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days at each site (n = 120). The following results were obtained:

			Repeatability		Between-run		Intermediate precision	
Sample	N	Mean [s/co]	SD [s/co]	CV (%)	SD [s/co]	CV (%)	SD [s/co]	CV (%)
Serum Pool 1	120	0.161	0.003	1.9	0.006	3.5	0.006	4.0
Serum Pool 2	120	2.01	0.065	3.3	0.03	1.5	0.072	3.6
Serum Pool 3	120	3.37	0.135	4.0	0.073	2.2	0.153	4.6

			Between site		Total precision	
Sample	N	Mean [s/co]	SD [s/co]	CV (%)	SD [s/co]	CV (%)
Serum Pool 1	120	0.161	0.021	13.0	0.022	13.6
Serum Pool 2	120	2.01	0.067	3.3	0.098	4.9
Serum Pool 3	120	3.37	0.174	5.2	0.232	6.9

3.3. Cross-reactivity

A total of 218 potentially cross-reacting samples were collected and tested with the Elecsys Toxo IgM assay. The results are shown in the table below.

Antibody or Disease State	# Tested	Elecsys Toxo IgM Positive	% Cross-reactivity
AMA	15	1	6.7
ANA	26	0	0
Chlamydia	5	0	0
CMV	13	0	0
EBV	10	1	10
Gonorrhea	5	0	0
HAV	10	0	0
HBV*	21	0*	4.8
HCV	12	0	0
HIV	13	0	0
HSV	9	0	0
Influenza	16	0	0
Malaria*	25	1*	8
Parvo B19	11	0	0
Rubella*	10	0*	10
Syphilis	5	0	0
TPHA	4	0	0
VZV	8	0	0

*contains 1 HBV sample repeatedly equivocal by Elecsys and negative with reference, 1 Malaria sample repeatedly equivocal by Elecsys and positive with reference, 1 Rubella sample reactive in Elecsys and initially equivocal with reference (no repetition possible due to low sample volume). Equivocal samples are counted as positive.

3.4. Matrix equivalency study

Studies were conducted to evaluate the suitability of the following 5 types of blood collectin tubes; serum/gel separation tubes, lithium heparin plasma, K_2-EDTA plasma, K_3-EDTA plasma and sodium citrate plasma. A minimum of 49 sample pairs were drawn into serum and plasma collection tubes. The recovery of the analyte in the presence of the anti coagulant was compared to serum. All results met the acceptance criteria.

3.5. Limitations – interference

The assay is unaffected by:

Compound	Concentration
Bilirubin	< 684 µmol/L or < 40 mg/dL
Hemoglobin	< 1.24 mmol/L or < 2 g/dL
Intralipid	< 2000 mg/dL
Biotin	< 246 nmol/L or < 60 ng/mL

Criterion: Samples ≤ 0.5 COI*: recovery within ± 0.25 COI and Samples > 0.5 COI recovery ± 20 %.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. >5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 3720 IU/mL.

The high-dose hook effect does not lead to false-negative results in the Elecsys Toxo IgM assay.

In vitro tests were performed on 18 commonly used pharmaceuticals and in addition on spiramycine, sulfadiazine, folinic acid and pyrimethamine. No interference with the assay was found.

As with many µ-capture assays an interference with unspecific IgM is observed. Increasing amounts of unspecific IgM may lead to a decrease in the recovery of positive samples with the Elecsys Toxo IgM assay.

In rare cases, interference due to extremely high titers of antibodies to immunological components, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

*COI= cut off index

3.6. Hook Effect

For verification of this claim and due to the fact that spiking of the analyte is not possible, three high positive serum samples (single donors), with a COI value of 30.5, 31.9 and 64.5 COI, (based on the measured Elecsys Toxo IgM result) were used for this experiment. It was diluted with native human negative serum in decreasing gradients. All dilution steps were measured in three-fold determination. The median of the signals for each dilution is calculated and, in relation to the dilution factor shown for each dilution in a diagram.

Acceptance criterion: For the Elecsys Toxo IgM assay it is claimed that High-dose Hook effect does not lead to false-negative results

3.7. Assay Cut-off

The cut-off for the Elecsys Toxo IgM immunoassay was established by the use of sample collectives characterized with commercially available assays.

The classification of samples, based on the cut-off establishment, verification, and validation, is as follows:

- Sample results < 0.8 COI = Non-reactive sample
- Sample results ≥ 0.8 to < 1.0 COI = Indeterminate (Border) sample
- Sample results ≥ 1.0 COI = Reactive sample

4. CLINICAL PERFORMANCE EVALUATION

Summary of clinical performance

To characterize the performance of the Elecsys Toxo IgM immunoassay, relative to an FDA cleared method, multicenter studies in US and EU were performed. In total, 601 samples were tested as detailed below.

4.1. Study 1

A total of 440 prospective specimens were obtained from US reference laboratory. All specimens represented samples for whom anti Toxo testing had been ordered per clinical routine. The patient population consisted of 162 males and 278 females. There were 158 pregnant women among the females. The patient's age ranged from 2 to 86. The performance of the Elecsys Toxo IgM immunoassay, relative to an FDA cleared method is presented in the table below.

US prospectively collected overall patient population

		Reference Toxo IgM Method			
		Positive	**Equivocal**	**Negative**	**Total**
Elecsys Toxo IgM	Reactive	2	0	2	4
	Equivocal	0	0	4	4
	Non-reactive	0	1	431	432
	Total	2	1	437	440

Agreement Classification	Numerator/ Denominator	Percent Agreement	95 % Confidence Interval
Positive agreement	2/3	66.7	9.43 - 99.2
Negative agreement	431/437	98.6	97.0 - 99.5

Equivocals are counted as discrepant results against the Elecsys.

4.2. Study 2

A total of 60 retrospective samples were obtained from a US commercial sample vendor. The patient population consisted of 4 males and 56 females. There were 50 pregnant women among the females. All specimens represented samples from whom anti-Toxo testing had been ordered per clinical routine. The performance of the Elecsys Toxo IgM immunoassay, relative to an FDA cleared method is presented in the table below.

US retrospectively collected overall patient population

Reference Toxo IgM Method

		Positive	Equivocal	Negative	Total
Elecsys Toxo IgM	Reactive	0	0	0	0
	Equivocal	0	0	1	1
	Non-reactive	0	0	59	59
	Total	0	0	60	60

Agreement Classification	Numerator/ Denominator	Percent Agreement	95 % Confidence Interval
Positive agreement	0/0	NA	NA
Negative agreement	59/60	98.3	91.1 - 100

4.3. Study 3

One hundred one (101) samples collected prospectively were obtained from the general population in Europe under suspicion of Toxoplasmosis consisting of 5 males and 96 females with an age range of 22 to 69. The agreement results are shown below.

EU prospectively collected overall patient population

Reference Toxo IgM Method					
		Positive	**Equivocal**	**Negative**	**Total**
Elecsys Toxo IgM	Reactive	81	1	5	87
	Equivocal	0	1	1	2
	Non-reactive	4	1	7	12
	Total	85	3	13	101

Agreement Classification	Numerator/ Denominator	Percent Agreement	95 % Confidence Interval
Positive agreement	81/86	94.2	87.0 - 98.1
Negative agreement	7/14	50.0	23.0 - 77.0

Equivocals are counted as discrepant results against the Elecsys. In case of unanimously equivocal samples, samples will not be considered for agreement calculation.

Of the 101 prospectively collected European specimens described above, 87 were from pregnant women. The agreement results are shown below.

EU prospectively collected pregnant women

		Reference Toxo IgM Method			
		Positive	**Equivocal**	**Negative**	**Total**
Elecsys Toxo IgM	Reactive	68	0	5	73
	Equivocal	0	1	1	2
	Non-reactive	4	1	7	12
	Total	72	2	13	87

Agreement Classification	**Numerator/ Denominator**	**Percent Agreement**	**95 % Confidence Interval**
Positive agreement	68/73	93.2	84.7 - 97.7
Negative agreement	7/13	53.9	25.1 - 80.8

Equivocals are counted as discrepant results against the Elecsys. In case of unanimously equivocal samples, samples will not be considered for agreement calculation.

5. CONCLUSIONS

The information provided in this Premarket Notification [510(k)] shows that the device Elecsys Toxo IgM is safe and effective and will support a substantial equivalence determination to the predicate device, VIDAS TOXO IgM Test System (k923166).