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SUMMARY OF SAFETY AND EFFECTIVENESS

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SUMMARY OF SAFETY AND EFFECTIVENESS

This premarket notification is to add the qualitative measurement of IgM antibodies to *Toxoplasma gondii* in human serum to the Bayer Immuno 1 analyzer system. The performance of the Bayer IMMUNO 1 Toxoplasma IgM assay has been established by comparison to a predicate device, Abbott IMx Toxoplasma IgM assay. The information presented in this Summary of Safety and Effectiveness was derived from Analytical Laboratory Studies and Clinical studies comparing the performance of the Bayer IMMUNO 1 Toxoplasma IgM assay and the Abbott IMx Toxoplasma IgM assay.

I. Intended Use

This in vitro diagnostic method is intended to qualitatively measure IgM antibodies to *Toxoplasma gondii* in human serum using the Bayer Immuno 1 analyzer. Measurements of anti-Toxoplasma IgM antibodies are presumptive for the diagnosis of recent Toxoplasma infection. Anti-Toxoplasma IgM antibody measurements must be performed in conjunction with a commercially available method to quantitatively measure the level of anti-Toxoplasma IgG antibodies.

This method has not been cleared or approved by the FDA for blood or plasma donor screening.

This method is intended for in vitro diagnostic use only on the Bayer Immuno 1 analyzer.

II. Background

The obligate intracellular parasite, *Toxoplasma gondii (T. gondii)*, has emerged as an important opportunistic pathogen in man. Infection occurs by ingesting oocysts in uncooked meat, from hands contaminated with soil or cat feces containing oocysts, by organ transplantation, blood transfusion, or perinatal. Infection in adults is typically mild or asymptomatic, and may be clinically difficult to diagnose. However, toxoplasmosis acquired in utero produces severe congenital neurologic and ophthalmic defects and even death. Further, infection of immunocompromised individuals such as cancer patients, organ transplant recipients, and AIDS (Acquired Immune Deficiency Syndrome) patients results in serious complications. Importantly, Toxoplasma meningoencephalitis is the most common opportunistic infection of the central nervous system of AIDS patients.

Acute Toxoplasma infection can be confirmed by the presence of Toxoplasma specific IgM antibodies or by the demonstration of a rise in Toxoplasma specific IgG antibody levels in paired serum samples taken at the acute phase and 10-20 days thereafter. In congenital Toxoplasma infection, Toxoplasma specific IgM may be detectable at birth in the neonate. Rapid detection of Toxoplasma specific IgM antibodies is critical in the diagnosis of maternal exposure to Toxoplasma and the diagnosis of congenital

Toxoplasma. Early detection of *T. gondii* infection is critical for effective antibiotic treatment.

Description of Disease

Toxoplasmosis is the clinical and/or pathological disease manifestation of *T.gondii* infection. A wide spectrum of disease is associated with infection, including acute, latent or chronic, reactivated and congenital.

The primary route of infection by *T. gondii* is by ingestion. At this point, the encysted oocytes emerge and infect mucosal cells where maturation into tachyzoites occurs. The tachyzoites can then infect additional cells. With a tropism for the retina, brain, skeletal muscle, heart, and lymph nodes, the parasite may spread further. In immunocompetent individuals acute infection is rarely symptomatic and the cellular and humoral immune response control the infection. However, lymphoadenopathy and clinical symptoms resembling infectious mononucleosis may occur. Following this acute phase, the parasite remains encysted and/or dormant (latent or chronic infection). In immunocompromised individuals, a reactivation may occur with the reemergence of tachyzoites from the tissue cysts. These individuals may develop toxoplasmic encelphalitis, myocarditis, myositis and other CNS complications. Likewise, acute infection in the immunocompromised individual can lead to rapid dissemination of the parasite and the development of toxoplasmic encelphalitis, myocarditis, and myositis (1, 2, 3, 5, 6, 7, 8, 11).

Congenital toxoplasmosis, associated with maternal parasitemia and infection of the placenta and subsequent infection of the fetus, can lead to severe consequences. Congenital toxoplasmosis is characterized by ocular and neurologic damage including, chorioretinitis, hydrocephaly, optic nerve atrophy, microcephaly and mental retardation. However, approximately 70 percent of infected infants are asymptomatic at birth. These asymptomatic individuals later develop the neurologic complications. The clinical manifestations of disease following fetal infection is dependent upon the time of infection. The severity of disease is greatest if infection occurs early in pregnancy (spontaneous abortion and severe disease). Infection late in pregnancy often results in subclinical asymptomatic disease (1, 3, 6, 7, 8).

III. Device Description

The Bayer IMMUNO 1 Toxoplasma IgM assay is a qualitative, heterogeneous IgM antibody capture magnetic separation sandwich immunoassay. A 5 µL patient serum sample (calibrator or control) and 20 µL of mIMP (monoclonal ImmunoMagnetic Particle) Reagent are mixed in the reaction cuvette and incubated with 150 µL of Reagent 1 (R1) containing fluorescein labeled monoclonal anti-human IgM antibody. After 15 minutes, the particles are washed and 100 µL of a binary reagent (R2), consisting of purified Toxoplasma antigen and monoclonal $F(ab)_2$ anti-Toxoplasma alkaline

phosphatase conjugate, is added. The binary reagent reacts with the bound Toxoplasma specific IgM from the sample. After a 12 minute incubation, the particles are washed to remove unbound conjugate and the substrate (pNPP) is added. The rate of hydrolysis of the substrate is measured at 405 nm and is proportional to the concentration of Toxoplasma specific IgM in the sample. The patient results are reported as index values relative to the cut-off (index) calibrator. Time to first result is 38 minutes.

IV. Clinical Impact of False Positive and False Negative Results

False positive results may result in therapeutic abortion or unnecessary therapy.

False negative results may result in disease in the newborn and/or a delay in antibiotic treatment regimes.

V. Merits and Limitations of the Methodology

As with any immunochemical reaction, users should be alert to the possible effects on test results of potential interference from medications or unknown endogenous substances. All patient results should be evaluated in the light of the total clinical status of the patient.

Samples from patients recieving preparation of mouse monoclonal antibodies for therapy or diagnosis can contain Human Anti-Mouse Antibodies (HAMA). Such samples may show either falsely elevated or falsely depressed values when tested with this assay (12,13).

Patient samples containing significant levels of Rheumatoid Factor (RF) or heterophilic antibodies may produce falsely elevated or falsely depressed values when tested with this assay (13).

Potential interference caused by the presence of these substances should be considered when interpreting assay results which are inconsistent with the total clinical status of the patient.

Patients undergoing retinal fluorescein angiography may retain amounts of fluorescein in the body for up to 48 hour post-treatment. In the case of patients with renal insufficiency, including many diabetics, retention may be much longer. Such samples may produce falsely elevated or falsely depressed values when tested with this assay until the fluorescein is cleared (14).

Only serum specimens have been validated for this method.

A serum specimen taken during the acute phase of infection may contain undetectable levels of IgM antibodies.

Results obtained from immunocompromised patients should be interpreted with caution.

VI. Summary of Studies

The Analytical Laboratory Studies and the Clinical Studies were performed with two lots of the Bayer Immuno 1 Toxoplasma IgM Reagents (Product Number T01-3566-01) using two lots of the Bayer Immuno 1 Toxoplasma IgM Controls and Calibrators (Product Number T03-3567-01) manufactured at Bayer Corporation, Diagnostics Division, Middletown, Virginia. All samples were tested over twenty days using the Abbott Toxo IgM IMx comparative method.

A. Analytical Laboratory Studies

The analytical laboratory studies were performed at Bayer Corporation, Diagnostics Division, Tarrytown, New York. The studies included; Validation of Cut-off, Prevalence, Expected Values, Clinical Sensitivity and Specificity, Interference Studies, Precision and Reproducibility. The, Expected Values, Clinical Sensitivity and Specificity, Precision and Reproducibility studies are included in the Clinical Studies section (IX.B.).

1. Validation of Cut-off

Sensitivity is defined clinically as the percent test positive in a population of patients with the disease. Specificity is defined as the percent negativity in a population without the disease. As in most immunoassays of this type, there is an overlap of test results between samples from infected and uninfected populations, and a cut-off point has to be established. The selection of a cut-off value takes into consideration sensitivity, specificity and predictive value. In the case of Toxoplasma, the highest predictive values are desired since inappropriate treatment has serious consequences, i.e. therapeutic abortion.

The assay cut-off was evaluated by testing a population of 400 serum samples consisting of 287 normal donor samples, 98 samples from patients with potentially interfering substances and 15 sequential samples from a Toxoplasma infected patient. The interference samples included samples from patients with RF, HAMA, multiple myeloma, anti-nuclear antibody, acute viral infections (EBV and CMV) and hemolyzed, lipemic and icteric samples.

The cut-off was set at greater than 7 standard deviations (SD) above the mean of the negative population; asymptomatic donor samples and patient samples containing potentially interfering substances. The 20% equivocal zone, index values between 0.80 and 1.0 corresponds to approximately 5 SD above the negative population mean. This reduces the probability of a false positive result.

2. Prevalence of Toxoplasma IgM

The prevalence of IgM antibody to Toxoplasma from a population with no apparent symptoms of Toxoplasma infection was established by testing 287 random donor samples using two lots of reagent in comparison with the Abbott Toxo M IMx assay. The results are summarized in the table below, with overall correlation to the Abbott Toxo M IMx assay of 99.65 %.

NORMAL DONOR SAMPLE TOXOPLASMA IgM RESULTS

Result	Exp. 2	Trial 1	TOXO IMx
Positive	1	1	0
Equivocal	1	1	1
Negative	285	285	286
Total	287	287	
% Agreement	99.65% (285/286)	99.65% (285/286)	

The prevalence of Toxoplasma IgM antibodies normal donor serum samples was 0.35% for Experimental 1 and Trial 1 reagents. The % agreement between the two lots was 100%.

3. Interference Studies

A. Potentially problematic sera were tested with two lots of Immuno 1 reagents in comparison with the Abbott Toxo M IMx assay. These samples included sera from patients with acute EBV and CMV viral infections, from patients with Rheumatoid Factor, anti-nuclear antibodies, HAMA and multiple myeloma and from hemolyzed, lipemic and elevated bilirubin samples. The results of this study demonstrate that this group of potentially problematic sera did not adversely affect method performance.

B. Specificity of IgM class antibody detection by the Immuno 1 Toxoplasma IgM assay was confirmed by reducing IgM antibody in samples with dithiothreitol (2.5 mM for 60 min. at 37°C) and by fractionating the sample into IgG and IgM before testing.

The 2.5 mM DTT treatment is relatively mild and may not completely destroy high levels of IgM. Eight samples reactive for Toxoplasma IgM and three Toxoplasma negative samples were tested with the Immuno 1 Toxoplasma IgM assay before and after treatment with DTT. All of the positive samples were reduced after DTT treatment. The results of this study indicate that the Immuno 1 Toxoplasma IgM assay is specific for IgM class antibody.

To further demonstrate the antibody class specificity of the Toxoplasma IgM assay, Toxoplasma IgM activity was tested in Toxoplasma positive patient samples before and after fractionation of IgM and IgG. Nine Toxoplasma serum or plasma samples were

separated into IgM and IgG fractions using Quik-Sep column system. During separation, IgM fractions are diluted 1:20 and IgG fractions 1:91. Fractions were concentrated using Amicon filters/centrifugation system. Final volumes of the concentrated samples ranged from 1 to 5 times the original volume. Serum/plasma samples and their IgG and IgM fractions were tested for Toxoplasma IgG and IgM with the Bayer IMMUNO 1 Toxoplasma IgG and IgM assays.

After fractionation, no IgM activity was present in the IgG fraction and all Toxoplasma IgM activity, as measured with the Immuno 1 Toxoplasma IgM assay, was located in the IgM fraction. Thus, the results demonstrate that the Immuno 1 Toxoplasma IgM assay is class specific for IgM.

B. Clinical Studies

The clinical studies were performed at two external investigator sites, University of Texas Medical Branch, Galveston, Texas, and San Francisco General Hospital Medical Center, San Francisco, California and at one research and development laboratory, Bayer Corporation, Diagnostics Division, Tarrytown, New York. The studies included; Prevalence, Clinical Sensitivity and Specificity, Precision and Reproducibility.

1. Expected Values

The prevalence of IgM antibody to the Toxoplasma parasite will vary with age and geographic location. A total of 701 serum samples from prenatal and hospital patients were tested to determine the prevalence of Toxoplasma IgM antibodies. In these studies, performed with the Bayer IMMUNO 1 system in Texas and California, the prevalence of Toxoplasma IgM antibodies was 1.4 %. The distribution of index values for these samples is shown in the following tables.

San Francisco and University of Texas Combined: Expected Results

TECHNICON IMMUNO 1	NUMBER OF SPECIMENS		% OF TOTAL	
TOXOPLASMA IgM INDEX	EXP2	TRIAL 1	EXP2	TRIAL 1
0-0.09	0	0	0	0
0.1-0.19	5	44	0.7	6.3
0.2-0.29	162	250	23.1	35.7
0.3-0.39	230	207	32.8	29.5
0.4-0.49	147	109	21	15.5
0.5-0.59	85	40	12.1	5.7
0.6-0.69	31	19	4.4	2.7
0.7-0.79	17	12	2.4	1.7
0.8-0.89	10	6	1.4	0.9
0.9-0.99	3	4	0.4	0.6
GREATER THAN OR EQUAL TO 1.00	11	10	1.6	1.4
TOTAL	701	701	100%	100%

2. Clinical Sensitivity and Specificity versus Abbott IMx

Clinical sensitivity and specificity were evaluated by testing 1121 samples at the three clinical sites. The patient population consisted of 988 prenatal, hospital and blood donor samples and 133 samples from toxoplasmosis patients. The Danish (D) toxoplasmosis patient samples were obtained from the State Serum Laboratory. The French (F) toxoplasmosis patient samples were obtained from Rangueil University Hospital Center, Laboratory of Parasitology-Mycology. The Polish (P) toxoplasmosis patient samples were obtained from the National Institute of Hygiene, Parasitology Department. The prenatal and hospital samples were provided by the investigators at the University of Texas Medical Branch and at San Francisco General Hospital. The blood donor samples were obtained from Bioclinical Partners, Franklin, MA. Each specimen was also tested in parallel with the Abbott IMx Toxoplasma IgM assay.

Definitions:

Discordant sample - Any sample with a disagreement between the Immuno-1 Trial 1 qualitative result (positive, negative or equivocal) and the Abbott IMx qualitative result was considered a discordant sample.

Resolution - A second Toxoplasma IgM EIA method was used to reconcile the discordant samples. The other EIA method was the Denmark in-house method (for samples provided by the State Serum Institute, Copenhagen, Denmark) or the Sanofi

Platelia method (for all other samples). If the IMx value and the second EIA value disagreed, then the second EIA value was substituted. Otherwise, the IMx value was retained. IMMUNO 1 values were not changed. Sensitivity and specificity were then recalculated.

A. Combined Data

Based upon these results, the sensitivity and specificity relative to the Abbott IMx method at each site were as follows:

Clinical Site	Relative Sensitivity	Relative Specificity
San Francisco	38/45 (84.4%)	350/354 (98.9%)
University of Texas	53/57 (93.0%)	333/338 (98.5%)
Tarrytown	2/2 (100%)	292/300 (97.3%)
Total	93/104 (89.4%)	975/992 (98.3%)

Combined Sites Patient Sample Summary

Combined (n = 1121)

		ABBOTT		
		+	+/-	-
IMMUNO 1	+	93	8	17
	+/-	6	0	10
	-	11	1	975

% Agreement = (1068/1096) 97.4%
% Relative Specificity = (975/992) 98.3%
% Relative Sensitivity = (93/104) 89.4%

Discrepant samples were resolved by means of the Sanofi Platelia or a Denmark EIA method. The resolved sensitivity and specificity after retesting are as follows:

Clinical Site	Resolved Sensitivity	Resolved Specificity
San Francisco	45/49 (91.8%)	353/356 (99.2%)
University of Texas	54/56 (96.4%)	335/340 (98.5%)
Tarrytown	9/9 (100%)	292/293 (99.7%)
Total	108/114 (94.7%)	980/989 (99.1%)

After Resolution (n = 1121)

		Resolved		
		+	+/-	-
IMMUNO 1	+	108	1	9
	+/-	6	0	10
	-	6	1	980

Resolved Specificity = (980/988) 99.1%
Resolved Sensitivity = (108/114) 94.7%

B. Individual Site Data

Tarrytown Patient Sample Summary

Sample Type	Result	Exp. 2	Trial 1	IMx
Donor Samples	Positive	1	1	0
	Equivocal	1	1	1
	Negative	285	285	286
Toxoplasmosis Patients	Positive	9	9	2
	Equivocal	1	0	0
	Negative	7	8	15

		ABBOTT		
		+	+/-	-
IMMUNO 1	+	2	0	8
	+/-	0	0	1
	-	0	1	292

Relative Sensitivity = 2/2 (100%)
Relative Specificity = 292/300 (97.3%)
Percent Agreement = 294/302 (97.4%)

		Resolved		
		+	+/-	-
IMMUNO 1	+	9	0	1
	+/-	0	0	1
	-	0	1	292

Resolved Sensitivity = 9/9 (100 %)
Resolved Specificity = 292/293 (99.7 %)

University of Texas Medical Branch Patient Sample Summary

Sample Type	Result	Exp. 2	Trial 1	IMx
Prenatal Samples	Positive	5	5	1
	Equivocal	1	0	0
	Negative	331	332	336
Toxoplasmosis Patients	Positive	52	52	55
	Equivocal	3	3	1
	Negative	5	5	4

		ABBOTT		
		+	+/-	-
IMMUNO 1	+	53	1	5
	+/-	3	0	0
	-	4	0	333

Relative Sensitivity = 53/57 (93.0%)
Relative Specificity = 333/338 (98.5%)
Percent Agreement = 386/395 (97.7%)

		Resolved		
		+	+/-	-
IMMUNO 1	+	54	0	5
	+/-	3	0	0
	-	2	0	335

Resolved Sensitivity = 54/56 (96.4%)
Resolved Specificity = 335/340 (98.5 %)

San Francisco General Hospital Patient Sample Summary

Sample Type	Result	Exp. 2	Trial 1	IMx
Prenatal Samples	Positive	6	5	2
	Equivocal	11	7	1
	Negative	347	352	361
Toxoplasmosis Patients	Positive	44	44	46
	Equivocal	3	3	6
	Negative	7	7	2

		ABBOTT		
		+	+/-	-
IMMUNO 1	+	38	7	4
	+/-	3	0	9
	-	7	0	350

Relative Sensitivity = 38/45 (84.4%)
Relative Specificity = 350/354 (98.9%)
Percent Agreement = 388/399 (97.2%)

		Resolved		
		+	+/-	-
IMMUNO 1	+	45	1	3
	+/-	3	0	9
	-	5*	0	352

* 2 samples drawn from same patient

Resolved Sensitivity = 45/49 (91.8 %)
Resolved Specificity =353/356 (99.2 %)

3. Precision

The imprecision results below are pooled across the three clinical trial sites and across Experimental 2 and Trial 1 reagent, calibrator and control lots. Index values used to generate the table below were calculated by applying the Experimental 2 calibrator rate from an initial calibration run (or the mean calibrator rate from day 1 in Tarrytown) to all sample index value calculations in the imprecision study (except at the University of Texas where a second off-line calibration was performed since the period of data collection exceeded 30 days).

MONTHLY CALIBRATION

Sample	Number	Mean Index Value	Within Run SD	Within Run %CV	Total SD	Total %CV
Negative Control	1420	0.22	0.03	15.1	0.04	16.2
Positive Control	914	3.21	0.15	4.7	0.18	5.5
Index Calibrator	931	0.93	0.07	7.3	0.07	7.7
Positive 1	478	1.83	0.10	5.5	0.12	6.6
Positive 2	324	4.61	0.14	3.1	0.21	4.5

PRECISION AND CALIBRATION FREQUENCY

IMMUNO 1 Toxoplasma IgM precision performance was examined by application of two methods of calibration: run-by-run and monthly (i.e., once every 30 days). A performance summary is given below. The results of the imprecision study indicate that:

1. Calibration of the Toxoplasma IgM assay once every 30 days is an acceptable alternative to run-by-run calibration.

2. For both methods of calibration, the within-run and total precision were in close agreement.

3. There was less than a 4% negative bias between the monthly calibrated and run-by-run calibrated index values, on the average. This difference was not clinically significant.

4. Reproducibility

Reproducibility was evaluated by testing a 20 member panel of negative samples and positive samples. The positive samples were prepared by dilution of single positive samples into a pool of negative serum. The samples were stored frozen until use. There was no significant difference in recovery of the samples across the sites. The results from this testing is illustrated in the following table.

<-SAN FRANCISCO->			<------- TEXAS -------->			<--TTN IMMUNO 1 --->		
SAMPLE	**EXP2**	**TRL1**	**SAMPLE**	**EXP2**	**TRL1**	**SAMPLE**	**EXP2**	**TRL1**
PS1	0.50	0.38	**PS1**	0.30	0.27	**PS1**	0.31	0.29
PS2	4.90	5.31	**PS2**	5.15	5.63	**PS2**	4.64	4.98
PS3	0.47	0.41	**PS3**	0.30	0.28	**PS3**	0.38	0.27
PS4	2.42	2.55	**PS4**	2.53	2.66	**PS4**	2.21	2.37
PS5	1.30	1.34	**PS5**	1.25	1.25	**PS5**	1.13	1.18
PS6	1.63	1.73	**PS6**	1.64	1.74	**PS6**	1.47	1.56
PS7	6.73	7.42	**PS7**	7.26	7.98	**PS7**	6.51	7.22
PS8	3.19	3.44	**PS8**	3.33	3.59	**PS8**	3.01	3.25
PS9	1.54	1.66	**PS9**	1.60	1.68	**PS9**	1.50	1.51
PS10	0.34	0.30	**PS10**	0.31	0.26	**PS10**	0.32	0.27
PS11	0.31	0.26	**PS11**	0.31	0.26	**PS11**	0.32	0.26
PS12	5.73	6.46	**PS12**	6.34	6.81	**PS12**	5.65	6.15
PS13	2.78	2.96	**PS13**	2.98	3.20	**PS13**	2.68	2.78
PS14	1.81	1.92	**PS14**	1.92	2.04	**PS14**	1.76	1.86
PS15	1.36	1.40	**PS15**	1.41	1.50	**PS15**	1.32	1.34
PS16	1.19	1.23	**PS16**	1.22	1.23	**PS16**	1.07	1.12
PS17	0.34	0.28	**PS17**	0.28	0.24	**PS17**	0.27	0.24
PS18	0.29	0.24	**PS18**	0.24	0.19	**PS18**	0.25	0.20
PS19	1.81	1.95	**PS19**	1.84	1.97	**PS19**	1.72	1.82
PS20	4.45	4.92	**PS20**	4.77	5.25	**PS20**	4.42	4.75

5. Receiver Operating Characteristic Curve Analysis

Receiver Operating Characteristic Curve (ROC) analyses were conducted as a means to compare the IMMUNO 1 Toxoplasma IgM method with the Abbott Toxoplasma IgM IMx method. The ROC analysis compares the accuracy (i.e., minimum false negative and false positive results) obtained by continuously varying the decision threshold over the entire range of results observed. The ROC curve analysis and graphs obtained from the two clinical trial sites computes the accuracy of the IMMUNO 1 Toxoplasma IgM assay using Experimental 2 reagents relative to the IMx method across all decision thresholds. The analysis below is based upon the assumption that the IMx method is the reference method; all diagnoses are based upon the IMx results. This is summarized by the areas under the curve:

San Francisco General Hospital:
IMMUNO 1 Toxoplasma IgM Experimental 2 reagents:

Abbott IMx Positive group sample size	= 48
Abbott IMx Negative group sample size	= 365
Area under the ROC curve:	= 0.942
Standard error:	= 0.024
95% Confidence interval:	= 0.915 to 0.963

University of Texas Medical Branch:
IMMUNO 1 Toxoplasma IgM Experimental 2 reagents:

Abbott IMx Positive group sample size	= 60
Abbott IMx Negative group sample size	= 339
Area under the ROC curve:	= 0.967
Standard error:	= 0.016
95% Confidence interval:	= 0.945 to 0.982

VII. Stability

Stability studies were performed at Bayer Corporation, Diagnostics Division, Tarrytown, New York with the Bayer IMMUNO 1 Toxoplasma IgM assay reagents (Product Number T01-3566-01) and the Bayer SETpoint Toxoplasma IgM Calibrator and Controls (Product Number T03-3567-01).

A. Reagent Stability

SHELF-LIFE: To determine the shelf-life of unopened product at the proper storage temperature (2-8°C). The data substantiates a stability claim of at least a 12 month shelf-life at 2-8°C.

ON SYSTEM: To determine the shelf-life of the product after it is opened and placed on the Bayer IMMUNO 1 analyzer. The data substantiates an on system stability of at least 30 days when stored on the Bayer IMMUNO 1 analyzer.

SHIPPING: To determine the storage temperature required for shipping the product. The data indicates that the product must be shipped under refrigeration (2-8°C).

B. Controls and Calibrator

SHELF-LIFE: To determine the shelf-life of unopened product at the proper storage temperature (2-8°C). The data substantiates a stability claim of at least a 12 month shelf-life at 2-8°C.

OPEN VIAL: To determine the shelf-life of the product after it is opened and stored at the proper storage temperature (2-8°C). The data substantiates an open vial stability of at least 90 days when stored at the proper storage temperature (2-8°C).

SHIPPING: To determine the storage temperature required for shipping the product. The data indicates that the product must be shipped under refrigeration (2-8°C).

VIII. Conclusions

The conclusions drawn from these studies are based upon valid scientific evidence. Data was gathered following a well designed protocol at three sites. The Bayer Immuno1 Toxoplasma IgM Assay clinical performance, including Validation of Cut-off, Prevalence, Expected Values, Clinical Sensitivity and Specificity, Interference Studies, Precision and Reproducibility met accepted specifications for an assay of this type. The method concordance studies confirm the substantial equivalence of the Bayer Immuno1 Toxoplasma IgM Assay with the Abbott IMx Toxoplasma IgM assay. Therefore, based upon the concordance established in these studies, the Bayer Immuno1 Toxoplasma IgM Assay and the Abbott IMx Toxoplasma IgM assay are equivalent with respect to clinical utility and the method safety and effectiveness.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Re: K971989
Trade Name: Toxoplasma IgM Assay for the Bayer Immuno1™ System
Regulatory Class: II
Product Code: LGD
Dated: August 21, 1997
Received: August 26, 1997

Dear Mr. Muraca:

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 requirement, 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.

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 Gutman

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 (if known): K971989

Device Name: Toxoplasma IgM (TXM)

Indications For Use:

This *in vitro* diagnostic method is intended to qualitatively measure IgM antibodies to *Toxoplasma gondii* in human serum using the *Bayer Immuno* 1™ system. Measurements of anti-Toxoplasma IgM antibodies are presumptive for the diagnosis of recent Toxoplasma infection. Anti-*Toxoplasma gondii* IgM antibody measurements must be performed in conjunction with an anti-*Toxoplasma gondii* IgG antibody assay.

This method has not been cleared or approved by the FDA for blood or plasma donor screening.

The use of the Bayer Immuno 1 Toxoplasma IgM method has not been validated for testing of cord blood or neonatal serum.

This method is intended for *in vitro* diagnostic use only on the Bayer Immuno 1 system.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Jean Cooper
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number OR K971989

Prescription Use ✓ (Per 21 CFR 801.109)

Over-The-Counter Use ____

Optional Format 1-2-96)