OCT 2 4 2002

510K SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K023058

1. Company/contact person:

Seradyn, Inc
7998 Georgetown Road,
Suite 1000
Indianapolis, IN 46268

Establishment registration No: 1836010

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Director of Quality
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2. Prepared: September 12, 2002

3. Device Name:

a. Proprietary Name: QMS™ Digoxin on the Abbott AEROSET® System
b. Common Name: Digoxin Particle Enhanced Immunoturbimetric Assay
c. Classification Name: 862.3320 Enzyme Immunoassay, Digoxin

4. Legally marketed devices to which equivalency is claimed:

Seradyn QMS™ Digoxin on the Abbott AEROSET® System is substantially equivalent to the Roche Tina-quant Digoxin cleared under K953239.

5. Description of Device:

The Seradyn QMS™ Digoxin Assay is a homogeneous Particle Enhanced Turbidimetric Immunoassay used for the quantitation of digoxin in serum or plasma. The assay is intended for use on the Abbott AEROSET® System, using the Seradyn QMS Digoxin Calibrators (previously cleared as Digoxin Immunoassay K983323.

The reagent system components are 1) digoxin coated microparticle reagent, and 2) the antibody reagent which consists of a mouse monoclonal antibody specific for digoxin.

The technology is based on competition between the digoxin in the sample and digoxin coated onto the microparticles, for the antibody-binding sites of the anti-digoxin antibody reagent. In the absence of digoxin in the sample, the specific antibody in the antibody reagent binds the digoxin on the particle, and results in rapid agglutination of the microparticles. In the presence of digoxin in the sample, the digoxin in the sample competes for antibody binding sites of the specific antibody in the antibody reagent, and partially inhibits the agglutination of the microparticles. The rate of agglutination (turbidity) is directly proportional to the rate in absorbance change of incident light and is measured spectrophotometrically by the Abbott AEROSET® System at a wavelength of 700 nm.

A six level Seradyn QMS™ Digoxin Calibrator set, with known digoxin concentrations is used to quantitate the assay. An internal concentration-dependent calibration curve is generated by the AEROSET® System, by measuring the rate of absorbance change of each calibrator level. Maximum absorbance rate is at the lowest digoxin concentration and the lowest absorbance rate at the highest digoxin concentration.

By monitoring the change in rate of a specimen with unknown digoxin concentration, and comparing to the internal calibration curve, a sample's concentration can readily be obtained and reported as digoxin concentration in either ng/ml or nmol/L.

6. Intended Use:

The *SERADYN* ***QMS™ DIGOXIN*** assay is used for the quantitation of digoxin in human serum or plasma.

7. Comparison of Technological Characteristics:

	Device Name	
	QMS™ Digoxin	**Tina-quant® Digoxin**
Indications for Use	The Seradyn QMS™ Digoxin assay is used for the quantitation of digoxin in human serum or plasma on the Abbott AEROSET® System. Digoxin is a potent cardiac glycoside widely prescribed for the treatment of patients suffering from congestive heart failure, as well as some types of cardiac arrhythmias. Digoxin intoxication is a common and serious problem in the clinical setting. Monitoring serum digoxin levels combined with other clinical data can provide the physician with useful information to aid in adjusting patient dosage, achieving optimal therapeutic effect while avoiding useless subtherapeutic or harmful toxic dosage levels.	The Tina-quant Digoxin method is used for the quantitative determination of digoxin, a cardioactive drug, in human serum and plasma on the Hitachi® analyzers. Measurements are used in the diagnosis and treatment of digoxin overdose and in monitoring levels of digoxin to ensure proper therapy.

	Device Name	
	QMS™ Digoxin	**Tina-quant® Digoxin**
Reagent Components	Two (2) reagent system ▪ Anti-digoxin Antibody reagent (R1) ▪ Digoxin coated Microparticle reagent (R2)	Two (2) reagent system ▪ Anti-digoxin Antibody reagent (R1) ▪ Digoxin coated Microparticle reagent (R2)
Calibration	Seradyn QMS™ Digoxin Calibrators - Six levels	Preciset Digoxin Calibrators - Six levels
Assay Range	0.05 to 5.0 ng/mL (0.06 to 6.40 nmol/L)	0.15 to 7.5 ng/mL (0.19 to 9.6 nmol/L)
Method Principles	The Seradyn QMS™ Digoxin Assay is a homogeneous Particle Enhanced Turbidimetric Immunoassay based on the principle of spectrophotometrically measuring turbidity and changes in absorbed light, which result when activated microspheres agglutinate. The microspheres (R2) are coated with digoxin, which in the presence of an anti-digoxin antibody (R1), rapidly agglutinate. The sample is incubated with the Antibody reagent. The microparticles are added and allowed to incubate. In the absence of any digoxin in the sample, rapid agglutination occurs, resulting in a turbid solution. When a sample containing digoxin is introduced, the agglutination is partially inhibited, slowing down the agglutination process. Thus the Abbott AEROSET® analyzer can measure the resulting turbidity and generate a classic inhibition curve (calibration curve), with respect to concentration, with maximum rate of agglutination at the lowest digoxin concentration, and minimum rate of agglutination at the highest digoxin concentration. By monitoring the change in rate of specimen agglutination (absorbance rate), and comparing to the internal calibration curve, a sample's concentration can readily be obtained and reported as digoxin concentration in either ng/ml or nmol/L.	The Tina-quant® Digoxin is also a homogeneous Particle Enhanced Turbidimetric Immunoassay with exactly the same principles as the Seradyn QMS™ Digoxin Assay. The only difference is that the turbidity (change in absorbance) is measured spectrophotometrically on the Hitachi® analyzers. The digoxin concentration can also be reported in ng/ml or nmol/L.

Tina-quant® and Hitach® are registered trademarks of Roche Diagnostics Corp.

8. Summary of Non-clinical Testing:

NONE

9. Summary of Clinical Testing:

The results of the clinical testing (Performance Characteristics) oof the Seradyn QMS Digoxin assay were compared to results of the studies reported in the Roche Tina-quant Digoxin Package Insert.

A. Specificity

Cross-reactivity was tested on the AEROSET using the Seradyn QMS Digoxin assay. The major digoxin active metabolites, digoxigenin bis-digitoxoside, digoxigenin mono-digitoxoside, and digoxigenin, as well as digitoxin, another cardiac glycoside, and its common analogue, digitoxigenin, were tested.

Cross reactivity was calculated using the following formula:

$$\frac{\text{(Equivalent digoxin conc of spiked sample – Dgoxin conc of sample without cross reactant)}}{\text{Conc of cross reactant}} \quad X \quad 100\%$$

The % cross reactivity on the AEROSET was compared to the reported Roche Tina-quant cross reactivity.

	AEROSET		Tina-quant	
Compound	Conc. of Cross-Reactant Spiked (ng/mL)	% Cross-Reactivity	Conc. of Cross-Reactant Spiked (ng/mL)	% Cross-Reactivity
Digitoxigenin	500	0.5%	Not Reported	<1%
Digitoxin	50	3.1%	51	4.1%
Digoxigenin	50	4.0%	33	6.4%
Digoxigenin bis-digitoxoside	5	112%	1.75	120%
Digoxigenin mono-digitoxoside	5	78.2%	1.9	111%

Spironolactone and Canrenone

Aldosterone inhibitors, spironolactone and canrenone have been reported to interfere with digoxin recovery in other commercially available immonoassays. These compounds were tested on the Abbott AEROSET® System using the Seradyn QMS™ Digoxin assay. The effect of spironolactone and canrenone were assessed in both the presence and absence of digoxin in the sample.

Percent cross reactivity was calculated and compared to the Tina-quant reported results.

	AEROSET		Tina-quant	
Compound	Conc. of Interferent Spiked (ng/mL)	% Cross-Reactivity	Conc. of Interferent Spiked (ng/mL)	% Cross-Reactivity
Spironolactone	800	0.0%	Not Reported	<1%
Canrenone	3,000	<0.002%	Not Reported	Not Reported

B. Accuracy by Recovery

Accuracy by analyte spike recovery was determined by adding a concentrated digoxin solution to human serum at four different concentrations. Percent recoveries for each level were calculated using the following formula:

% Recovery = ("mean recovered concentration" divided by "theoretical concentration") x 100%

Data summary are shown below.

% Analyte Added	Added (Theoretical) Concentration (ng/mL)	Mean Recovered Concentration (ng/mL)	Percent (%) Recovery
100%	4.85	4.85	100%
75%	3.64	3.73	102%
50%	2.43	2.37	98%
25%	1.21	1.14	94%

Acceptable Recovery: 100 ± 10% of theoretical value

The Roche Tina-quant package insert has no reported study of accuracy by recovery

C. Sensitivity

The least detectable dose, defined as the lowest Digoxin concentration that can be distinguished from zero with 95% confidence, is 0.05 ng/mL (0.064 nmol/L).

The Roche Tina-quant assay reports a lower detection limit of 0.15 ng/mL (0.19 nmol/L).

D. Accuracy & Linearity by Dilution

Accuracy and linearity by dilution was determined using a slightly modified procedure described in National Committee for Clinical Laboratory Standards (NCCLS) proposed guideline EP6-P. The 5.0 ng/mL Digoxin Calibrator was diluted with the 0.0 ng/mL Digoxin Calibrator at 80%, 60%, 40%, and 20%. The diluted samples, as well as the 5.0 ng/mL calibrator were analyzed on the AEROSET® using the Seradyn QMS™ Digoxin assay.

Percent recoveries for each level were calculated using the following formula:

% Recovery = ("mean recovered concentration" divided by "theoretical concentration") x 100%

Representative data are shown below.

Dilution	Theoretical Concentration (ng/mL)	Mean Recovered Concentration (ng/mL)	Percent (%) Recovery
Neat	5.00	4.92	98%
80%	4.00	4.2	105%
60%	3.00	3.14	105%
40%	2.00	2.05	103%
20%	1.00	1.05	105%

Acceptable Recovery: 100 ± 10% of theoretical value.

Linearity was assessed by performing linear regression analysis using the least squares method. The expected values were plotted on the x-axis against the observed values on the y-axis. Linear regression statistics yielded: $y = 1.0066x - 0.0923$; $R^2 = 0.9955$

The Roche Tina-quant assay reported "acceptable linearity" when serially diluting a with a digoxin concentration of 6.8 ng/mL with Digoxin Calibrator 1. It is acknowledged that concentration levels this high are extremely rare.

E. Precision

Precision was determined as described in National Committee for Clinical Laboratory Standards (NCCLS) protocol EP5 (including an additional estimate of between day precision). A tri-level human serum based commercial control containing digoxin was was assayed in duplicate twice a day for twenty days. The between run, within run, and total sd and %CVs were calculated.

The following are representative results from pooled data:

		Mean	Within Run		Between Day		Total Run	
Sample	n	(ng/mL)	SD	CV(%)	SD	CV(%)	SD	CV(%)
1	80	0.59	0.0128	2.17%	0.0047	0.80%	0.0137	2.31%
2	80	1.48	0.0145	0.98%	0.0042	0.28%	0.0151	1.02%
3	80	4.81	0.0372	0.77%	0.0227	0.47%	0.0436	0.91%

The Roche Tina-quant assay reports the following imprecision, using an internal protocol:

		Within Run			Between Day		
Sample	N	Mean (ng/mL)	SD	CV(%)	Mean (ng/mL)	SD	CV(%)
Control	63	1.17	0.06	5.1	1.81	0.07	3.6
Control	63	2.09	0.05	2.3	4.85	0.13	2.7
Human Serum	63	---	---	---	1.9	0.09	4.5

F. Method Comparison

Correlation Studies were performed using NCCLS Protocol EP9-A. Results from the Seradyn QMS™ Digoxin assay on the AEROSET® System were compared to the Tina-quant® assay on the Hitachi® 717. The clinical specimens ranged from 0.33 ng/mL (0.42 nmol/L) to 3.06 ng/mL (3.92 nmol/L). Results of the specimen testing are shown below.

	Hitachi
y-intercept	1.06
Slope	-0.13
Correlation Coefficient	0.99346
Number of Samples	55

G. Interfering Substances

Digoxin assay on the Abbott AEROSET® System at the concentrations indicated. Interference studies were conducted using NCCLS protocol EP7-P as a guideline document.

Abnormal bilirubin levels were prepared by adding to human serum pool containing approximately 0.8 ng/mL of digoxin. Abnormal hemoglobin levels were prepared by addition of red blood cell lysate to the same human serum pool. Abnormal lipid levels were prepared by addition of Intralipid® to the same human serum pool.

Results showed no interference at the following levels:

Interfering Substance	Interferent Concentration		N	Target (no Interferent) (ng/mL)	Mean Recovery (ng/mL)	Observed (% of Target)
Bilirubin	20 mg/dL	(342 umol/L)	2	0.84	0.83	99%
Hemoglobin	1,000 mg/dL	(10 g/L)	2	0.80	0.88	110%
Intralipid	2,000 mg/dL	(22.6 mmol/L)	2	0.84	0.89	106%

Acceptance criteria are recoveries of 100 ±12% for hemoglobin, 100 ±10% for hemoglobin, 100 ±20% for lipids

The Roche Tina-quant package insert reports "no significant interference" up approximately 60 mg/dL of bilirubin, approximately 1,000 mg/dL of hemoglobin, and approximately 1700 mg/dL of triglyceride.

HAMA Interference

As with any assay employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample, which could cause falsely elevated results. A normal human serum pool (control), and HAMA type 1 and HAMA type 2

samples were spiked with the same amounts of digoxin. Each of the samples were assayed in duplicate on the Abbott AEROSET® System using the Seradyn QMS™ Digoxin assay. The means of each duplicate HAMA sample were compared to the mean of the control normal human serum. Acceptance criteria is a recovery of 100 ±10% of the control serum.

Results are as follows:

	Rep 1	Rep 2	Mean	% Recovery
Control	0.83	0.81	0.82	100
HAMA 1	0.83	0.83	0.83	101
HAMA 2	0.88	0.88	0.88	107

The Roche Tina-quant package insert reports no HAMA interference study.

H. Reagent Stability Data

Real Time Stability

The long-term stability is on going. Two months real time stability is collected so far.

Instrument on-board stability

The reagents were left uncapped on-board and controls were assayed twice weekly for a period of 60 days. Control recoveries at subsequent time points were compared to Day 0 recovery. Data showed that the control recoveries to be acceptable, demonstrating reagents on board stability for 70 days. Based on this data, an on-board stability claim of at least 60 days is made. No re-calibration was required during the study.

Roche Tina-quant reports an instrument on-board stability of 90 days for their reagents.

I. Instrument Calibration Stability:

Data used in the on-board stability is used to claim instrument calibration stability of 60 days, since no re-calibration was required during the period under study.

Roche Tina-quant reports no calibration stability claim.

10. Conclusions:

The results of clinical testing demonstrate that the performance and effectiveness of the Seradyn QMS™ Digoxin Assay are substantially equivalent to those of the Roche Diagnostic Systems Tina-quant® Digoxin assay.

Refer to the Roche Diagnostic Systems Tina-quant® Digoxin Package Insert for Specific Performance data.

11. Other Information:

None

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville, MD 20850

OCT 24 2002

Ms. Lisa Brown
Director of Quality
Seradyn, Inc.
7998 Georgetown Road, Suite 1000
Indianapolis, IN 46268

Re: k023058
Trade/Device Name: Seradyn QMS™ Digoxin on the Abbott Aeroset® System
Regulation Number: 21 CFR 862.3320
Regulation Name: Digoxin test system
Regulatory Class: Class II
Product Code: KXT; DLJ
Dated: September 12, 2002
Received: September 13, 2002

Dear Ms. Brown:

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 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" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/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

INDICATIONS FOR USE FORM

510(k) Number (if known): K023058

Device Name: *SERADYN QMS™ DIGOXIN ON THE ABBOTT AEROSET® SYSTEM*

Indications For Use:

The *SERADYN QMS™ DIGOXIN* assay is used for the quantitation of digoxin in human serum or plasma on the Abbott AEROSET® System.

Digoxin is a potent cardiac glycoside widely prescribed for the treatment of patients suffering from congestive heart failure, as well as some types of cardiac arrhythmias. Digoxin intoxication is a common and serious problem in the clinical setting. This is, in part, a result of the fact that cardiac glycosides have a low therapeutic ratio (a very small difference between therapeutic and tissue toxic levels). Coupled with the narrow therapeutic range is a marked patient variability in response to the same dosage of drug, often resulting in unpredictable serum drug levels. Intoxication symptoms are often indistinguishable from the original condition for which the drug was prescribed. It may not be immediately apparent whether the patient has been under or overdosed.

Monitoring serum digoxin levels combined with other clinical data can provide the physician with useful information to aid in adjusting patient dosage and achieving optimal therapeutic effect while avoiding useless sub-therapeutic or harmful toxic dosage levels.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____
(Per 21 CFR 801.109)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K023058