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: K030405

1. Company/contact person:

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

Establishment registration No: 1836010

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2. Prepared: February 4, 2003

3. Device Name:

a. Proprietary Name: QMS™ / MULTIGENT™ Valproic Acid on the Abbott AEROSET® System
b. Common Name: Valproic Acid Particle Enhanced Immunoturbidmetric Assay
c. Classification Name: 862.3645 Enzyme Immunoassay, Valproic Acid

4. Legally marketed devices to which equivalency is claimed:

Seradyn QMS™ / MULTIGENT™ Valproic Acid on the Abbott AEROSET® System is substantially equivalent to the Abbott AxSYM® Valproic Acid cleared under K941615.

5. Description of Device:

The Seradyn QMS™ / MULTIGENT™ Valproic Acid Assay is a homogeneous Particle Enhanced Turbidimetric Immunoassay used for the quantitation of valproic acid in serum or plasma. The assay is intended for use on the Abbott AEROSET® System, using the Seradyn QMS™ / MULTIGENT™ Valproic Acid Calibrators.

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

The technology is based on competition between the valproic acid in the sample and valproic acid coated onto the microparticles, for the antibody-binding sites of the anti-Valproic Acid antibody reagent. In the absence of valproic acid in the sample, the specific antibody in the antibody reagent binds the valproic acid on the particle, and results in rapid agglutination of the microparticles. In the presence of valproic acid in the sample, the valproic acid 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 604 nm.

A six level Seradyn QMS™ / MULTIGENT™ Valproic Acid Calibrator set, with known valproic acid 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 valproic acid concentration and the lowest absorbance rate at the highest valproic acid concentration.

By monitoring the change in rate of a specimen with unknown valproic acid concentration, and comparing to the internal calibration curve, a sample's concentration can readily be obtained and reported as valproic acid concentration in either µg/mL or µmol/L.

6. Intended Use:

The *SERADYN **QMS™ / MULTIGENT™ VALPROIC ACID*** assay is used for the quantitation of valproic acid in human serum or plasma.

7. Comparison of Technological Characteristics:

	Device Name	
	QMS™ / MULTIGENT™ Valproic Acid	**Abbott AxSYM® Valproic Acid**
Indications for Use	The Seradyn QMS™ / MULTIGENT™ Valproic Acid assay is used for the quantitation of valproic acid in human serum or plasma on the Abbott AEROSET® System. Valproic acid is a broad-spectrum anticonvulsant drug used solely or in combination with other anticonvulsant drugs for the treatment of absence seizures. It also has demonstrated effectiveness in the management of generalized tonic-clonic and myoclonic seizures, as well as atypical absence, simple and complex partial and mixed grand mal and petit mal seizures. The capability of treating	The AxSYM® Valproic Acid assay is a reagent for the quantitative measurement of valproic acid, an anticonvulsant drug, in serum or plasma. The measurements obtained are used in monitoring levels of valproic acid to ensure appropriate therapy.

	many types of seizures with a single anticonvulsant has resulted in the wide-spread use of valproic acid, particularly in children in whom tonic-clonic and myclonic seizures are most prevalent.	
Reagent Components	Two (2) reagent system ▪ Anti-Valproic Acid Antibody reagent (R1) ▪ Valproic Acid coated Microparticle reagent (R2)	Three (3) reagent system ▪ Valproic Acid Antiserum in phosphate buffer with protein stabilizers. ▪ Pretreatment Solution, surfactant in tris buffer. ▪ Valproic Acid Fluorescein Tracer in Tris buffer containing surfactant.
Calibration	Seradyn QMS™ / MULTIGENT™ Valproic Acid Calibrators - Six levels	AxSYM® Valproic Acid Calibrators - Six levels
Assay Range	3.0 to 150.0 µg/mL (20.8 to 1039 µmol/L)	0.70 – 150.0 µg/mL (4.85 to 1039 µmol/L)
Method Principles	The Seradyn QMS™ / MULTIGENT™ Valproic Acid Assay is a homogeneous, competitive binding, Particle Enhanced Turbidimetric Immunoassay based on the principle of spectrophotometrically measuring turbidity and changes in absorbed light, which result when activated microspheres agglutinate.	The AxSYM® Valproic Acid assay utilizes Fluorescence Polarization Immunoassay (FPIA) technology.

8. Summary of Non-clinical Testing:

NONE

9. Summary of Clinical Testing:

The results of the clinical testing (Performance Characteristics) of the Seradyn QMS™ / MULTIGENT™ Valproic Acid assay were compared to results of the studies reported in the Abbott AxSYM® Valproic Acid Package Insert.

A. Specificity

Cross-reactivity was tested for the minor Valproic Acid active metabolites: 2-ethyl-2-phenylmalonamide, 2-N-propylglutaric acid and 2-N-propyl-4-pentenoic acid. In the same study, structurally related or potentially co-administered compounds were also tested using Seradyn QMS™ / MULTIGENT™ Valproic Acid reagents. Each substance was tested at 10 times the highest concentration for its therapeutic or normal range. The cross contaminants were spiked at a volume not exceeding 1% of the total volume of serum. The control sera and spiked samples were assayed in triplicate using the Seradyn QMS™ / MULTIGENT™ Valproic Acid assay on the AEROSET®. The means of the duplicate determinations were determined and used to calculate the percent cross-reactivity using the following formula:

$$\frac{\text{(Equivalent VPA conc of spiked sample – VPA conc of sample without cross reactant)}}{\text{Conc of cross reactant}} \times 100$$

Cross Reactivity Results (Refer to Table 1 of Attached Data):

Substance	Conc. of Cross-Reactant Spiked (µg/mL)	Equivalent VPA Conc. of spiked sample (µg/mL)	Conc of Serum without Cross-reactant (µg/mL	Observed Recovery (ug/mL)	% Cross-Reactivity
3-keto-valproic acid	16.67	93.66	92.86	0.80	4.80%
2-N-Propylglutaric Acid	100	101.98	95.35	6.63	6.63%
2-N-Propyl-4-pentenoic Acid	100	126.48	95.35	31.13	31.13%
2-Ethyl-2-phenylmalonamide	100	94.72	95.35	-0.63	-0.63%
Carbamazepine	140	94.27	95.35	-1.08	-0.77%
Ethosuximide	1000	95.96	95.35	0.61	0.06%
Phenobarbital	400	98.40	95.35	3.05	0.76%
Phenytoin	200	95.79	95.35	0.44	0.22%
Carbamazepine-10,11-epoxide	140	94.78	95.35	-0.57	-0.41%
Primidone	120	95.11	95.35	-0.24	-0.20%
Salicylate	100	93.86	95.35	-1.49	-1.49%

B. Accuracy by Recovery

Accuracy by analyte spike recovery was determined by adding a concentrated valproic acid solution to human serum at three 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 (µg/mL)	Mean Recovered Concentration (µg/mL)	Percent (%) Recovery
100%	144.51	144.51	100%
50%	72.25	74.15	102.6%
25%	36.13	37.83	104.7%

Acceptable Recovery: 100 ± 10% of theoretical value

The Abbott AxSYM® package insert reports accuracy by recovery throughout of the whole therapeutic range.

C. Sensitivity

The least detectable dose, defined as the lowest valproic acid concentration that can be distinguished from zero with 95% confidence, is 3.0 µg/mL (20.79 µmol/L).

The Abbott AxSYM® assay reports a lower detection limit of 0.70 µg/mL (4.85 µmol/L).

D. Accuracy & Linearity by Dilution

Accuracy and linearity by dilution was determined using a procedure described in the National Committee for Clinical Laboratory Standards (NCCLS) proposed guideline EP6-P. A 150.0 µg/mL VPA Calibrator (different from the material used to calibrate the instrument) was diluted with the 0.0 µg/mL Valproic Acid Calibrator at 80%, 60%, 40%, 20%, 10% and 2.5%. The diluted samples, as well as the 150.0 µg/mL calibrator were analyzed in duplicate on the AEROSET® using the Seradyn QMS™ MULTIGENT™ Valproic Acid assay. A mean of the duplicates for each sample was determined. 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 (µg/mL)	Mean Recovered Concentration (µg/mL)	Percent (%) Recovery
Neat	150	145.14	96.8%
80%	120	114.62	95.5%
60%	90	89.29	99.2%
40%	60	60.13	100.2%
20%	30	32.78	109.3%
10%	15	14.70	98.0%
2.5%	3.75	3.71	98.9%

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: $y = 0.9569x + 1.688$; $R = 0.999$

The Abbott AxSYM® package insert reports on accuracy and linearity by dilution.

E. Precision

Precision was determined as described in the 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 valproic acid 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		Run to Run		Total	
Sample	n	µg/mL	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
1	80	32.81	0.360	1.10%	0.512	1.56%	0.000	0.00%	0.626	1.91%
2	80	70.56	0.729	1.03%	0.637	0.90%	0.189	0.27%	0.987	1.40%
3	80	116.40	2.214	1.90%	1.598	1.37%	1.518	1.30%	3.124	2.68%

The Abbott AxSYM® assay reports the following imprecision, using an internal protocol, run to run was not reported:

		Mean	Within Run		Between Day		Total Run	
Sample	n	(µg/mL)	SD	CV(%)	SD	CV(%)	SD	CV(%)
1	80	38.82	1.32	3.4%	0.56	1.4%	1.56	4.0%
2	80	78.27	3.23	4.1%	0.40	0.5%	3.20	4.1%
3	80	127.34	4.44	3.5%	2.75	2.2%	5.93	4.7%

F. Method Comparison

Correlation Studies were performed using NCCLS Protocol EP9-A. Results from the Seradyn QMS™ MULTIGENT™ Valproic Acid assay on the AEROSET® System were compared to the Abbott VPA assay on the AxSYM®. The clinical specimens ranged from 14.65 µg/mL (101.5 µmol/L) to 131.03 µg/mL (908.0 µmol/L) by the Seradyn QMS™ / MULTIGENT™ Valproic Acid method. Results of the specimen testing are shown below.

	AxSYM®
y-intercept	3.58
Slope	0.955
Correlation Coefficient	0.986
Number of samples	53

G. Interfering Substances

Interference studies were conducted using NCCLS protocol EP7-P as a guideline document.

Abnormal bilirubin levels were prepared by using a human serum pool containing approximately 100 µg/mL of valproic acid and spiking with bilirubin. 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.

The specimens, with and without the interferents, were assayed for VPA using the QMS™/MULTIGENT™ Valproic Acid assay on the Abbott AEROSET® System

Results showed no interference at the following levels:

Interfering Substance	Interferent Concentration	n	Target (no Interferent) (µg/mL)	Mean Recovery (µg/mL)	Observed (% of Target)
Bilirubin	20 mg/dL	2	88.38	87.98	99.5%
Hemoglobin	1,000 mg/dL (10 g/L)	2	91.46	91.58	100%
Intralipid	2,000 mg/dL	2	91.59	90.64	99%

Acceptance criteria are recoveries of 100 ±10% for hemoglobin, bilirubin and lipids.

The Abbott AxSYM® package insert reports "no significant interference" up to approximately 20 mg/dL of bilirubin, approximately 1,000 mg/dL of hemoglobin, and approximately 1,100 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 valproic acid. Each of the samples were

assayed in duplicate on the Abbott AEROSET® System using the Seradyn QMS™ / MULTIGENT™Valproic Acid assay. The means of each duplicate HAMA sample were compared to the mean of the control normal human serum.

Results are as follows:

	Rep 1	Rep 2	Mean	% Recovery
Control	98.54	97.94	98.24	100%
HAMA 1	92.27	89.65	90.96	93%
HAMA 2	93.76	94.65	94.20	96%

Acceptance criteria is a recovery of 100 ±10%.

The Abbott AxSYM® package insert reports no HAMA interference study.

H. Reagent Stability Data

Instrument on-board stability
On-board stability (uncapped reagents) studies demonstrated acceptable data to make a claim of 54 days. One re-calibration was required during the study.

Abbott AxSYM® reports an instrument on-board stability of 14 days for their reagents.

I. Instrument Calibration Stability:
Instrument calibration stability study demonstrated acceptable data to make a claim of 27 days.

Abbott AxSYM® reports no calibration stability claim.

10. Conclusions:
The results of clinical testing demonstrate that the performance and effectiveness of the Seradyn QMS™ / MULTIGENT™ Valproic Acid Assay are substantially equivalent to those of the Abbott AxSYM® Valproic Acid assay.

Refer to the Abbott AxSYM® Valproic Acid 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

APR 2 8 2003

Mr. Les Padilla
Senior Scientist
Seradyn, Inc.
7998 Georgetown Road – Suite 1000
Indianapolis, IN 46268

Re: k030405
Trade/Device Name: Seradyn QMS™/Multigent™ Valporic Acid on the Abbott Aeroset® System
Regulation Number: 21 CFR 862.3645
Regulation Name: Neuroleptic drugs radioreceptor assay test system
Regulatory Class: Class II
Product Code: LEG; JIS
Dated: February 4, 2003
Received: February 6 2003

Dear Mr. Padilla:

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 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); 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). 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) 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
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE FORM

510(k) Number (if known): Not known at this time K030405

Device Name: *SERADYN QMS™ /MULTIGENT™ VALPROIC ACID ON THE ABBOTT AEROSET® SYSTEM*

Indications For Use:

The *SERADYN QMS™ / MULTIGENT™ VALPROIC ACID* assay is used for the quantitation of valproic acid in human serum or plasma on the Abbott AEROSET® System.

Valproic acid (VPA; 2-propylpentanoic acid; Depakene®) is a broad-spectrum anticonvulsant drug used solely or in combination with other anticonvulsant drugs for the treatment of absence seizures. It also has demonstrated effectiveness in the management of generalized tonic-clonic and myoclonic seizures, as well as atypical absence, simple and complex partial and mixed grand mal and petit mal seizures. The capability of treating many types of seizures with a single anticonvulsant has resulted in the wide-spread use of valproic acid, particularly in children in whom tonic-clonic and myoclonic seizures are most prevalent. Valproic acid has proven effective in the treatment of many patients otherwise refractory to other anticonvulsant treatments. Most patients receiving valproic acid do not develop a tolerance to its anticonvulsant effects.

Monitoring serum valproic acid 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.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K030405

(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)