MAR 2 6 2002

K014030

APPENDIX E

As required by 21 CFR 807.3, a summary of the 510(k) safety and effectiveness information contained in this submission is provided as Appendix E.

510(k) SUMMARY

SUBMITTED BY: Diana Clive
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November 30, 2001

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.

NAME OF DEVICE:

Trade Name:	1,25-Dihydroxyvitamin D ^{125}I RIA
Common Names/Descriptions:	Immunoassay for the quantitative determination of 1,25 dihydroxyvitamin D (1,25-$(OH)_2$-D)
Classification Name:	Vitamin D test system
PREDICATE DEVICE:	DiaSorin 25-Hydroxyvitamin D ^{125}I RIA

INTENDED USE: The 1,25-Dihydroxyvitamin D ^{125}I RIA assay is a competitive equilibrium radioimmunoassay intended for the quantitative determination of 1,25 dihydroxyvitamin D (1,25-$(OH)_2$-D) in human serum or EDTA plasma to be used to assess 1,25-$(OH)_2$-D deficiency associated with renal disease. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions in adult populations.

DEVICE DESCRIPTION: The 1,25-Dihydroxyvitamin D ^{125}I RIA is a competitive radioimmunoassay intended for the quantitative determination of 1,25 Dihydroxyvitamin D (1,25-$(OH)_2$-D) in human serum or EDTA plasma. The assay consists of a two-step procedure. Serum or plasma patient samples as well as standards and kit controls are first extracted with acetonitrile to free the 1,25-$(OH)_2$ vitamin D_2 and D_3 from their vitamin D binding protein, and remove lipids that might interfere with the assay. The metabolites are then extracted by column chromatography on C_{18}OH silica cartridges using a series of organic solvent washes. Following the extraction, the treated samples are assayed using a

competitive radioimmunassay procedure. The primary antibody (rabbit anti-1,25-$(OH)_2$ vitamin D) is highly specific for both 1,25$(OH)_2$-vitamin D_3 and 1,25$(OH)_2$-vitamin D_2. During the binding reaction both sample and an ^{125}I labeled 1,25$(OH)_2$ vitamin D tracer compete for binding sites on the primary antibody. Separation of bound and unbound vitamin D_2 or D_3 is accomplished using a goat anti-rabbit (GAR) polyethylene glycol precipitating complex. After an incubation and centrifugation, sample precipitates are read in a gamma counter. The amount of radioactivity in the precipitate is inversely proportional to the concentration of 1,25-$(OH)_2$ vitamin D in the sample. Values are calculated directly from a standard curve of known calibrators and expressed as pg/ml.

TECHNOLOGICAL COMPARISON TO PREDICATE:

Feature	25-OH-D	1,25-$(OH)_2$-D
Intended Use	FOR IN VITRO DIAGNOSTIC USE. This kit is intended for the quantitative determination of 25-hydroxyvitamin D (25-OH-D) and other hydroxylated vitamin D metabolites in human serum or plasma to be used in the assessment of vitamin D sufficiency. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions in an adult population.	FOR IN VITRO DIAGNOSTIC USE. This kit is intended for the quantitative determination of 1,25-dihydroxy-vitamin D (1,25-$(OH)_2$-D) in human serum or EDTA plasma to be used to assess 1,25-$(OH)_2$-D deficiency associated with renal disease. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions in adult populations.
Assay Type	RIA	RIA
Acetonitrile Extraction	For isolation of 25-(OH)-D	For isolation of 1,25-$(OH)_2$-D
Antiserum	Polyclonal specific for 25-(OH)-D_2/D_3	Polyclonal specific for 1,25-$(OH)_2$-D_2/D_3
Tracer	^{125}I radiolabeled 25-(OH)-D analog	^{125}I radiolabeled 1,25-$(OH)_2$-D_3 analog
Precipitating Complex	20 minute incubation at 20-25° C with second antibody precipitating complex	20 minute incubation at 20-25° C with second antibody precipitating complex
Kit Controls	Two levels, human serum based, extracted identical to standards and patient samples.	Two levels, human serum based, extracted identical to standards and patient samples.
Standards	Five levels, human serum based, extracted identical to controls and patient samples.	Five levels, human serum based, extracted identical to controls and patient samples.

PERFORMANCE DATA: A clinical trial was conducted at three independent clinical laboratories. Serum values for 1,25$(OH)_2$-vitamin D were collected from two distinct populations: apparently healthy normal donors, and patients with end-stage renal disease (ESRD). Reference ranges established in the trial are summarized below.

All Sites		1,25(OH)$_2$D (pg/mL)		
Population	n	Mean	2 SD	Range
Normals	123	43.9	24.1	19.8-68.0
ESRD's	87			1.6-17.3

The equivalency of assay samples as either fresh serum or serum that has been frozen and thawed was also verified. A summary table with 95% ANOVA determined P-values is presented below.

	Normals		ESRD's	
	Frozen	Fresh	Frozen	Fresh
N	72	51	70	17
Mean	43.2	44.8	6.1	5.3
ANOVA	0.49		0.29	

Reproducibility was established both at DiaSorin and during the clinical trial. Three human serum-based samples with 1,25-(OH)$_2$-D concentrations distributed across the assay range were assayed over 25 assay days at DiaSorin, spanning more than 60 operating days. Multiple technicians, as well as multiple lot numbers for all components were included. The combined results were evaluated by analysis of variance (ANOVA) and are summarized in the following table.

			Within-run		**Between Day**		**Total**	
Sample	**n**	**Mean (pg/mL)**	**S.D.**	**%C.V.**	**S.D.**	**%C.V.**	**S.D.**	**%C.V.**
Low	25	25.8	1.76	6.8	3.8	14.6	4.0	15.3
Mid	25	41.3	3.16	7.7	4.6	11.1	5.1	12.3
High	25	105.2	11.86	11.3	11.8	11.2	14.4	13.7

These identical human serum-based controls were assayed during a clinical trial conducted at three different laboratories, over 16 different assays, spanning more than 110 days. The combined results from all three sites are summarized below.

Sample	n	Mean (pg/mL)	S.D.	%CV
Low	16	24.2	3.9	16.2
Mid	16	41.0	5.8	14.1
High	16	97.7	11.3	11.6

Similarly, kit controls included with each kit were included in each of the 16 assays above, as prescribed in the package insert instructions. The following table summarizes the precision of the controls over the course of the clinical trial.

		Site A	Site B	Site C	Total
Kit Control 1	n	7	4	8	19
	Mean	24.7	27.2	25.5	25.6
	SD	3.1	3.3	4.0	3.5
	%CV	12.5	12.2	15.8	13.7
Kit Control 2	n	7	4	7	18
	Mean	66.2	59.9	67.2	65.2
	SD	5.1	4.2	11.1	8.1
	%CV	7.8	7.1	16.6	12.4

CONCLUSION: The data collected during the clinical trial described above fully substantiates the intended use of the 1,25-Dihydroxyvitamin D ^{125}I RIA. Reference ranges established for both a healthy population and one with end stage renal disease are fully distinct. This indicates that the DiaSorin 1,25-Dihydroxvitamin D ^{125}I RIA can effectively discriminate between the two populations based on 1,25-$(OH)_2$-D serum values. Assay results can be used to assess 1,25-$(OH)_2$-D deficiency associated with renal disease.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAR 2 6 2002

Mr. David M. Ikeda
Manager, Regulatory Affairs and Quality Systems
DiaSorin Inc.
1990 Industrial Blvd.
P.O. Box 285
Stillwater, MN 55082-0285

Re: k014030
Trade/Device Name: 1,25-Dihydroxyvitamin D ^{125}I RIA Kit
Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D test system
Regulatory Class: Class II
Product Code: MRG
Dated: February 18, 2002
Received: February 20, 2002

Dear Mr. Ikeda:

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

510(k) Number (if known): K014030

Device Name: 1,25-Dihydroxyvitamin D ^{125}I RIA Kit

Indications For Use:

The 1,25-Dihydroxyvitamin D ^{125}I RIA is a competitive equilibrium radioimmunoassay intended for the quantitative determination of 1,25-dihydroxyvitamin D (1,25-$(OH)_2$-D) in human serum or EDTA plasma to be used to assess 1,25-$(OH)_2$-D deficiency associated with renal disease. Since hydroxylation of circulating 25-hydroxyvitamin D to the biologically active form 1,25-$(OH)_2$-D occurs in the kidney, renal disease may result in reduced levels of 1,25-$(OH)_2$-D and compromised calcium metabolic homeostasis. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions in adult populations.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Carol C Benson for Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K014030

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