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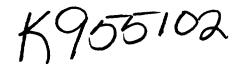
510(K) SUMMARY FOR THE BIODATA TESTOSTERONE MAIA KIT

I.   **Submitter's Name, Address, Telephone Number, and Contact Person**

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I. DESCRIPTION OF THE DEVICE

A. Intended Use

The Biodata Testosterone Maia Kit is a radioimmunoassay for the quantitative determination of testosterone in human serum or plasma. The device is intended to be used for the diagnosis of elevated or depressed levels of testosterone. It is **FOR IN VITRO DIAGNOSTIC USE ONLY.**

Neoplasms of the testes and adrenal cortex and hyperthyroidism may result in elevated levels of testosterone in the male. Elevated testosterone levels are observed in females with endometrial carcinoma, hirsutism, neoplasms of the ovaries, and Cushing syndrome. Patients with hypogonadism of pituitary origin, anorchia, gonadel dysgenesis, Klinefelter syndrome, and pseudohermaphroditism have decreased testosterone levels.

B. Radioimmunoassay Protocol

The Biodata Testosterone Maia kit is based on the competitive binding principles of radioimmunoassay. Testosterone (unlabeled antigen) in samples, standards, or controls competes with testosterone labeled with radioactive ^{125}I ("testosterone - ^{125}I") (labeled antigen) for a limited number of testosterone antibody sites. The amount of testosterone - ^{125}I bound by the antibody is inversely proportional to the amount of testosterone present in the sample, standard, or control. Testosterone Maia Separation Reagent (an antibody covalently bound to a magnetic particle capable of binding the testosterone antibody) is added to the reaction mixture to facilitate the separation of the bound and free fractions of labeled testosterone. The bound fraction of each standard, sample and control is sedimented in a magnetic separator. Each bound fraction is then counted in a gamma counter calibrated to detect ^{125}I.

The concentration of testosterone in the samples can be determined by comparing the relative percent binding of the standards with known concentrates of testosterone on the standard curve. The testosterone concentration in the sample is then compared to the reference range of testosterone concentrations established by each laboratory or the expected volumes listed in the package insert.

II. PREDICATE DEVICE

The Biodata Testosterone Maia Kit is substantially equivalent to Diagnostic Products Corporation's ("DPC") Coat-A-Count Testosterone Assay (K831342). Biodata also manufactured this device without U.S. commercialization.

III. PERFORMANCE DATA

Substantial equivalence to the Serono Immunoassay is demonstrated by the following performance data.

A. Intra-Assay Precision

Three different assays were conducted on the following controls: (1) Serotest S-18; (2) three commercially-available Lyphocheck controls; and (3) three patient pool controls, each of which had 20 replicates. The data is summarized in Table 1. The data indicates that the Biodata Testosterone Maia Kit has a high degree of precision within assays.

Table 1
Summary of Intra-Assay Data

SAMPLE	MEAN (ng/mL)	S.D.	% CV
SEROTEST S-18	1.78	0.125	7.01
LYPHOCHECK 90001	0.25	0.019	7.55
LYPHOCHECK 90002	3.57	0.154	4.31
LYPHOCHECK 90003	9.05	0.428	4.72
PATIENT POOL L	0.46	0.036	7.70
PATIENT POOL M	0.82	0.041	5.02
PATIENT POOL H	8.89	0.312	3.51

2. Inter-Assay Precision Study

Different operators conducted ten separate assays on seven controls. The inter-assay data is summarized in Table 2. The data indicates that the Biodata Testosterone Maia assay has a high degree of precision between assays.

Table 2
Summary of Inter-Assay Data

SAMPLE	MEAN (ng/mL)	S.D.	% CV
SEROTEST S-18	1.96	0.185	9.43
LYPHOCHECK 90001	0.23	0.02	7.45
LYPHOCHECK 90002	3.43	0.19	5.41
LYPHOCHECK 90003	8.87	0.25	2.77
PATIENT POOL L	0.43	0.024	5.58
PATIENT POOL M	0.83	0.044	5.30
PATIENT POOL H	8.36	0.265	3.17

C. Recovery Studies

Three patient plasma pools were made from randomly selected patient samples that had assayed values that were not greater than 7.89 ng/mL. Increasing levels of testosterone antigen were prepared in bovine serum and then were calibrated with the Biodata Testosterone Maia Kit. Aliquots of 950 µl of each pool were spiked with 50 µl of bovine serum or 50 µl of testosterone solution in bovine serum. All spiked samples were then assayed with the Biodata Testosterone Maia Kit. The recovery data is summarized in Table 3. The data indicates that the

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accuracy of the Biodata Testosterone Maia Kit is satisfactory over the range of 1.25 to 10.00 ng/mL of testosterone is satisfactory.

Table 3
Summary of Recovery Data

SPIKE VALUE NG/ML	% RECOVERY (MEAN ± 1 S.D.) n = 3 BATCH 1 REAGENTS		
10.00	108.5	±	3.90
5.00	109.3	±	1.03
2.50	104.1	±	4.89
1.25	97.6	±	9.73

4. Dilution Studies

Three patient samples were serially diluted up to a dilution factor of 32 with a low (0.70 ng/mL) testosterone standard and then assayed. The dilution data is summarized in Table 4. The data indicates that dilution using the low testosterone concentration standard is acceptable.

Table 4
Summary of Dilution Data

DILUTION FACTOR	% RECOVERY	± 1 S.D.
1	100.00	--
2	94.05	2.52
4	90.64	0.76
8	93.85	2.10
16	96.98	5.52
32	104.29	3.88

E. Sensitivity Study

Sensitivity is the smallest quantity of testosterone that can be differentiated from zero and corresponds to the count that is two standard deviations from the mean count of the zero standard. Sensitivity was evaluated by using a standard curve plus 20 further replicates of the zero standard and three replicates of first standard (0.25 ng/mL). The Minimum Detection Limit ("MDL") was calculated by linear regression. The sensitivity data is presented in Table 5. The mean detection limit for the Biodata Testosterone Maia assay was found to be 0.064 ng/mL.

Table 5
Sensitivity of the Biodata Testosterone Maia Kit

RESULTS BATCH 1 REAGENTS STANDARD "ZERO" cpm				STANDARD 1 (0.25 ng/mL) cpm
1)	67782	11)	64819	1) 57961
2)	68153	12)	65551	2) 55969
3)	66001	13)	64792	3) 55961
4)	65197	14)	65596	
5)	65095	15)	65190	
6)	65088	16)	66322	
7)	64605	17)	67674	
8)	65525	18)	67712	
9)	64041	19)	67139	
10)	65757	20)	66088	
X = 65906				X = 56630
S.D. = 1192				S.D. = 1152
CV% = 1.8				CV% = 2.0

F. Specificity Study

The specificity of the Biodata Testosterone Maia Kit was evaluated by measuring the apparent response of the assay to eight potentially cross-reactive analytes. The percentage of interference was calculated according to Abraham (x/y x 100) where x and y are respectively the weight of the testosterone and the interference compound that cause a 50% decrease in binding. The specificity data is presented in Table 6. The data indicates no significant cross-reaction with testosterone.

Table 6
Specificity of Biodata Testosterone MAIA Kit

ANTIGEN	CROSS-REACTIVITY
TESTOSTERONE	100%
DHT	15.0%
ESTRADIOL	0.007%
PROGESTERONE	0.01%
ESTRONE	0.001%
ESTRIOL	0.0005%
CORTISOL	0.002%
DHEA-S	0.006

G. Sex Hormone Binding Globulin Interference Study

Sex-hormone binding globulin ("SHBG") is the major serum binding protein of testosterone. Five serum pools were heated at 60° C for 32 minutes. Testosterone and SHBG concentrations were measured at zero, two, four, eight, sixteen, and thirty-two minutes using the Biodata Testosterone Maia Kit that is the

subject of this submission ("the new Biodata Testosterone Maia Kit") and an earlier version of the Testosterone Maia Kit ("the old Testosterone Maia Kit"). The percent change in testosterone concentration from time zero was then calculated. The data for the Biodata Testosterone Maia Kit is presented is summarized in Table 7. The data for the old Testosterone Maia Kit is summarized in Table 8. Most of the SHBG was denatured after 32 minutes. The data indicates that the SHBG Concentration does not significantly affect the measurement of testosterone in the assay.

Table 7
Summary of Sex Hormone Binding Globulis Interference Study - New Kit

% CHANGE TESTOSTERONE CONCENTRATION (MEAN +/- 1 S.D.) (n = 5)

MINUTES	AVERAGE %	$\pm$ 1 S.D.
2	99.33	5.08
4	103.12	0.99
8	104.58	2.40
16	105.49	4.22
32	103.06	6.37

Table 8
Summary of Sex Hormone Binding Globulis Interface Study - Old Kit

% CHANGE TESTOSTERONE CONCENTRATION (MEAN +/- 1 S.D.) (n = 5)

MINUTES	AVERAGE %	$\pm$ 1 S.D.
2	95.64	6.04
4	99.21	4.31
8	99.71	3.64
16	98.97	3.75
32	100.65	6.52

H. Variation of Recommended Assay Procedures

Three controls and three pools of sera were run in the assay with the recommended incubation time of 60 minutes varied by plus or minus 15 minutes, *i.e.*, 45 minutes and 75 minutes. The data for controls is presented in Table 9. The data for sera is presented in Table 10. The data indicates that a variation in the incubation time for the immunological reaction of plus or minus 15 minutes does not significantly affect the control and sample values.

Table 9
Variation of Recommend Assay Procedures - Sample

SAMPLE	45' INCUB. TIME		REFERENCE INCUB. TIME 60'	75' INCUB. TIME	
	ng/mL	%REC	ng/mL	ng/mL	%REC
SEROTEST S-18	1.85	94.4	1.96	1.82	92.9
LYPHOCHECK 90001	<0.25	--	<0.25	<0.25	--
LYPHOCHECK 90002	2.86	95.3	3.00	2.83	94.3
LYPHOCHECK 90003	8.19	104.9	7.81	7.88	100.9
POOL OF SERA 1	0.49	104.2	0.47	0.47	100.0
POOL OF SERA 2	0.77	93.9	0.82	0.77	93.9
POOL OF SERA 3	7.01	101.9	6.88	7.43	108.0
AVERAGE % RECOVERY		99.1			98.3

Table 10

Variation of Recommended Assay Procedures - Standard

STANDARD	45' STD CURVE		REFERENCE STANDARD CURVE		75' STD CURVE	
	$\%B/B_o$	$\%B/T$	$\%B/B_o$	$\%B/T$	$\%B/B_o$	$\%B/T$
1 0.25 ng/mL	85.4	67.0	84.6	67.8	86.0	68.2
2 1.00 ng/mL	62.9	49.7	62.9	50.7	63.8	51.0
3 3.00 ng/mL	48.1	38.4	48.3	39.2	48.7	39.2
4 8.00 ng/mL	32.6	26.4	32.0	26.3	34.0	27.8
5 20.00 ng/mL	19.6	16.4	19.7	16.6	20.7	17.9
NSB		1.4		1.0		1.3
B_o		76.9		78.9		77.7
TOTAL Cpm		81373		81373		81373

I. Gas Chromatography Mass Spectroscopy Tested Samples

Several control sera previously checked by Gas Chromatography Mass Spectroscopy in Germany were tested by the Biodata Testosterone Maia Kit. The data is presented in Table 11. The mean percentage recovery was found to be 75.69%. Thus, all the data fell within the range of the gas chromatography mass spectroscopy results.

Table 11

Gas Chromatography Mass Spectroscopy Tested Samples Comparison

	GCMS TARGET VALUES	GCMS RANGE	OBTAINED VALUES	RECOVERY
CONTROL SERUM	ng/mL	ng/mL	ng/mL	%
HM1/91 A	4.15	2.28 - 6.02	3.40	81.93
HM1/91 B	10.00	5.47 - 14.52	10.17	101.70
HM2/91 A	2.15	1.18 - 3.14	1.66	77.21
HM2/91 B	2.87	1.58 - 4.18	2.11	73.52
HM3/91 B	6.86	3.75 - 10.49	4.88	71.13
HM4/90 A	5.70	3.40 - 8.01	3.68	64.56
HM1/92 A	2.15	0.86 - 3.46	1.59	73.95
HM1/92 B	5.70	3.40 - 8.01	4.09	71.75
HM2/92 A	6.86	3.08 - 10.63	4.38	63.85
HM2/92 B	4.15	2.57 - 5.73	3.40	81.93
HM3/92 B	2.15	0.86 - 3.46	1.50	69.77
HM1/93 A	3.60	2.16 - 5.04	3.83	106.39
HM1/93 B	1.47	0.58 - 2.35	0.68	46.25
AVERAGE %				75.69

J. Correlation Studies

In the first correlation study, 120 samples from males were tested with the DPC Testosterone Kit, the old Testosterone Maia Kit, and the new Biodata Testosterone Maia Kit. The data comparing the DPC Testosterone Kit and the new Biodata Testosterone Maia Kit is summarized in Table 12. The data comparing the old Testosterone Maia Kit and the new Biodata Testosterone Maia Kit is summarized in Table 13. The data indicates a high degree of correlation between the new Biodata Testosterone Maia Kit and the DPC Testosterone Kit and the new Biodata Testosterone Maia Kit and the old Testosterone Maia Kit.

Table 12
Summary of Correlation Study - 120 Male Samples

TESTOSTERONE DPC (x)   /   TESTOSTERONE MAIA NEW (y)

	N. 120 MALE SAMPLES
LINEAR REGRESSION	Y = 1.0895 X - 1.034
CORRELATION COEFFICIENT	R = 0.8700
AVERAGE X	6.47 ng/mL
AVERAGE Y	6.02 ng/mL
OVER-UNDER ESTIMATION	- 7.99%

Table 13
Summary of Correlation Study - 120 Male Samples

TESTOSTERONE MAIA OLD (x)   /   TESTOSTERONE MAIA NEW (y)

	N. 120 MALE SAMPLES
LINEAR REGRESSION	Y = 0.4667 X + 1.407
CORRELATION COEFFICIENT	R = 0.8769
AVERAGE X	9.88 ng/mL
AVERAGE Y	6.02 ng/mL
OVER-UNDER ESTIMATION	- 36.43%

In the second correlation study, 63 samples from females were tested with the Testosterone DPC Kit, the old Testosterone Maia Kit, and the new Biodata Testosterone Maia Kit. The data comparing the DPC Testosterone Kit and the new Biodata Testosterone Maia Kit is summarized in Table 14. The data comparing the old Testosterone Maia and the new Biodata Testosterone Maia Kits is summarized in Table 15. The data indicates a satisfactory correlation between the new Biodata Testosterone Maia Kit and the DPC Testosterone Kit and a high degree of correlation between the new Biodata Testosterone Maia Kit and the old Testosterone Maia Kit.

Table 14
Summary of Correlation Study - 63 Female Samples

TESTOSTERONE DPC (x)   /   TESTOSTERONE MAIA NEW (y)

	N. 63 FEMALE SAMPLES
LINEAR REGRESSION	Y = 0.6061 X + 0.2471
CORRELATION COEFFICIENT	R = 0.7598
AVERAGE X	0.67 ng/mL
AVERAGE Y	0.66 ng/mL
OVER-UNDER ESTIMATION	+ 5.37%

Table 15
Summary of Correlation Study - 63 Female Samples

TESTOSTERONE MAIA OLD (x)   /   TESTOSTERONE MAIA NEW (y)

	N. 63 FEMALE SAMPLES
LINEAR REGRESSION	Y = 0.8036 X + 0.145
CORRELATION COEFFICIENT	R = 0.9322
AVERAGE X	0.64 ng/mL
AVERAGE Y	0.67 ng/mL
OVER-UNDER ESTIMATION	+ 5.66%

In the third part of the correlation study, 60 samples from pre-puberal children were assayed using the DPC Testosterone Kit, the old Testosterone Maia Kit, and the new Biodata Testosterone Maia Kit. The data is summarized in Table 16. The data indicates that the correlation between the new Biodata Testosterone Maia Kit and those devices is satisfactory.

Table 16
Summary of Correlation Study - 60 Pre-Puberal Children

KIT	NR	95 PERCENTILE (ng/mL)
NEW TESTOSTERONE MAIA	60	<0.60
OLD TESTOSTERONE MAIA	60	<0.60
TESTOSTERONE D.P.C.	60	<0.40

K. Expected Values Study

In the first part of the reference range study, 659 serum samples from males were assayed using the Biodata Testosterone Maia Kit. The males ranged in

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age from 18 to 71 years old; the mean age was 25. The data is summarized in Table 17.

Table 17
Summary of Reference Range - 659 Male Serum Sample

	N.	MEAN (ng/mL)	5-95 PERCENTILE (ng/mL)
MAN (18 TO 71 YEARS)	659	6.0	2.8 - 9.7

In the second part of the study 300 serum samples from females were assayed using the Biodata Testosterone Maia Kit. The data is summarized in Table 18.

Table 18
Summary of Reference Range - 300 Female Serum Sample

	N.	MEAN (ng/mL)	95 PERCENTILE (ng/mL)
WOMAN	300	0.65	<1.0