MAY 29 1997

K964791

Summary of Safety and Effectiveness

Beta-2-Microglobulin Method for Bayer Technicon Immuno 1® System

1. Intended Use

This is an *in vitro*, solid-phase enzyme immunoassay for the quantitative measurement of beta-2-Microglobulin in serum and urine. Measurements of beta-2-Microglobulin are used in monitoring inflammatory conditions and in diagnosing and managing patients with renal diseases.

Listed below is a comparison of the performance between the Immuno 1 beta-2-Microglobulin method and a similar device that was granted FDA clearance of substantial equivalence (The Abbott IMX beta-2-Microglobulin Assay). The information used in this Summary of Safety and Effectiveness was extracted from the Immuno 1® beta-2-Microglobulin method sheet, from data on file at Bayer Corporation, and from the Abbottt IMX beta-2-Microglobulin method sheet.

METHOD	Immuno 1 beta 2-Microglobulin		Abbott IMX (predicate Device)	
Part No.	Reagents Calibrators	T01-3669-51 T03-3670-01	2201-20	
Minimum Detectable Conc.	0.01 mg/L		0.005 mg/L	
Precision (within-run)	SERUM		SERUM	
	1.48 mg/L	1.79%	1.7 mg/L	6.0%
	2.57 mg/L	1.25%	3.9 mg/L	4.4%
	9.8 mg/L	1.89%	9.7 mg/L	4.9%
	URINE		URINE	
	0.13 mg/L	1.48%	0.10 mg/L	4.7%
	0.91 mg/L	1.10%	0.30 mg/L	5.5%
	13.56 mg/L	4.98%	0.89 mg/L	4.8%
Correlation	SERUM		URINE	
	y=0.99x+0.11		y=1.05x-0.05	
	where		where	
	y=Immuno 1		y=Immuno	
	x= Abbott IMX		x=Abbott IMX	
	n=97		n=24	
	r=0.99		r=0.99	
	Syx=0.93 mg/L		Syx=0.52 mg/L	

2. Assay Description

Beta-2-Microglobulin is an enzyme label sandwich immuno-assay using a monoclonal (mouse) capture and a polyclonal (sheep) detector antibody. The monoclonal antibody is labelled with fluorescein (R1) and the polyclonal antibody labelled with alkaline phosphatase (R2). The solid phase consists of a suspension of magnetizable particles coated with antibody to fluorescein (mIMP reagent). Sample or calibrator, R1 and R2 reagent are mixed simultaneously and incubated at 37 °C. In the presence of beta-2-Microglobulin a fluorescein-conjugate--beta-2-Microglobulin--ALP-conjugate complex is formed. After 14 minutes of incubation an aliquot of the mIMP reagent is added and the complex is captured by the anti-fluorescein antibodies on the magnetic particles. The particles are precipitated by an external magnetic field, washed and para-nitrophenolphosphate is added as the enzyme substrate. The increase in absorbance due to the formation of p-nitrophenolate is monitored spectrophotometrically at 405 nm and 450 nm. The obtained response is directly proportional to the concentration of beta-2-Microglobulin in the sample. A cubic fit through zero is used to calculate the dose response curve.
Six calibrators with beta-2-Microglobulin concentrations of 0, 0.4, 0.85, 3.0, 8.0 and 20.0 mg/L are provided.

3. Imprecision

a) Serum Samples

Imprecision data for serum samples was obtained by analyzing human serum controls on an Immuno 1 over 10 days. The concentrations of serum controls were calculated from a calibration curve genrated on day 1 of the study. (Table 1)

Table 1

specimen	Mean (mg/l)	Total SD (mg/l)	Total CV (%)	Within-Run SD (mg/l)	Within-Run CV (%)
sample 1	1.48	0.033	2.25	0.026	1.79
sample 2	2.57	0.039	1.51	0.032	1.25
sample 3	9.80	0.276	2.82	0.185	1.89
sample 4	0.27	0.005	1.89	0.005	1.85
sample 5	1.21	0.019	1.61	0.017	1.45
sample 6	3.51	0.072	2.05	0.072	2.05
sample 7	5.78	0.152	2.63	0.139	2.41
sample 8	11.06	0.325	2.93	0.254	2.30
sample 9	15.81	0.445	2.81	0.400	2.53

b) Urine Samples

Imprecision data for urine samples was obtained by analyzing human urine controls on an Immuno 1 over 5 days. The concentrations of serum controls were calculated from a calibration curve genrated on day 1 of the study. (Table 2)

Table 2

specimen	Mean (mg/l)	Total SD (mg/l)	Total CV (%)	Within-Run SD (mg/l)	Within-Run CV (%)
sample 1	0.13	0.005	3.46	0.002	1.48
sample 2	0.91	0.012	1.31	0.010	1.10
sample 3	13.56	0.676	4.98	0.676	4.98

4. Correlation

a) Serum Samples

A total of 97 serum samples were tested on the Abbott IMx (x) and the Immuno 1 (y). The correlation results are shown in Figure 1.

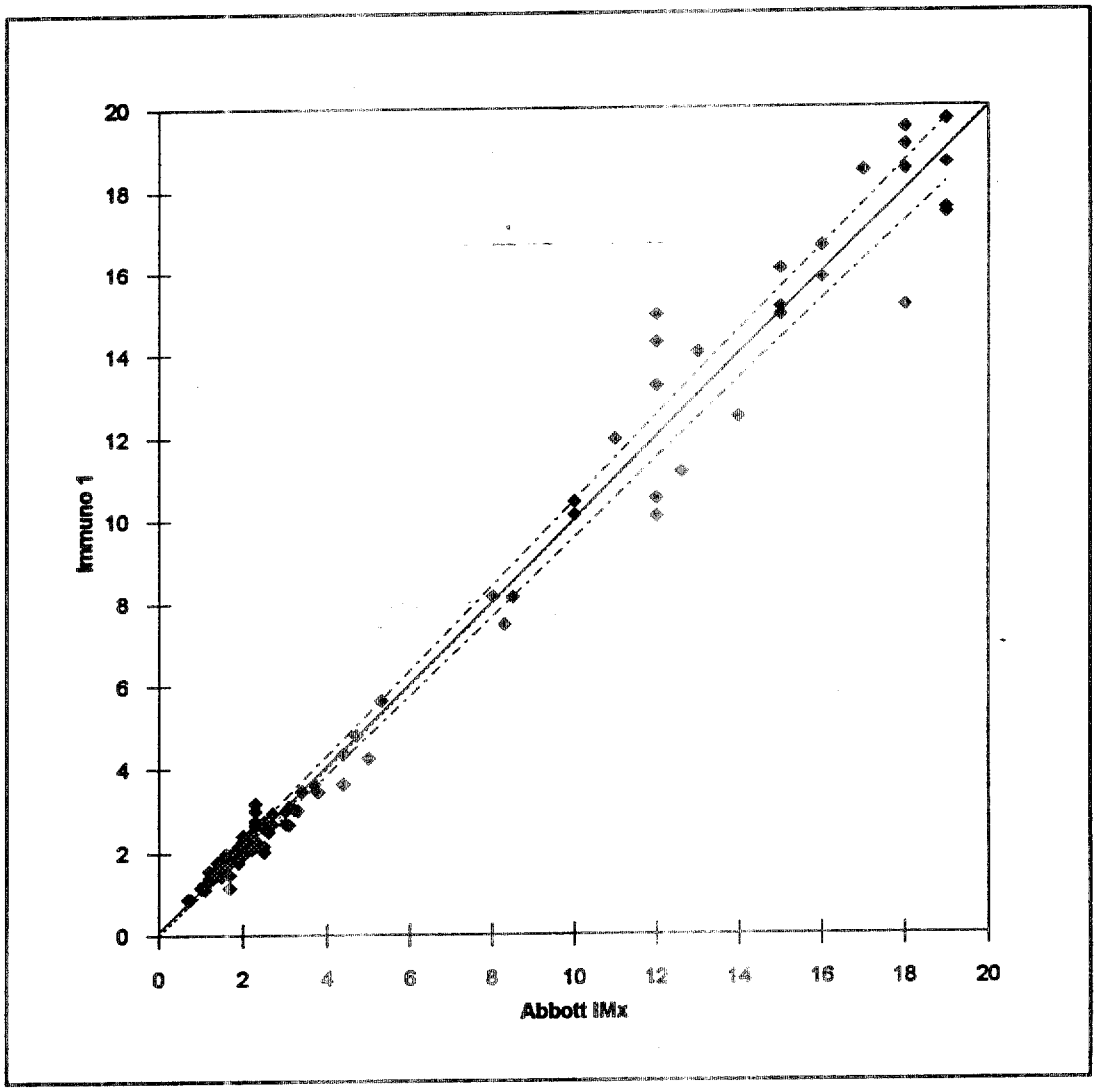

Fig 1: Serum Sample Correlation of Immuno 1 vs. Abbott IMX for beta-2-Microglobulin

The correlation equation according to Bablok-Passing was

$y = 0.99 x + 0.11$
$r = 0.9917$
$Syx = 0.93$ mg/L

b. Urine Samples

A total of 24 urine samples were tested on the Abbott IMx (x) and the Immuno 1 (y). The correlation results are shown in Figure 2.

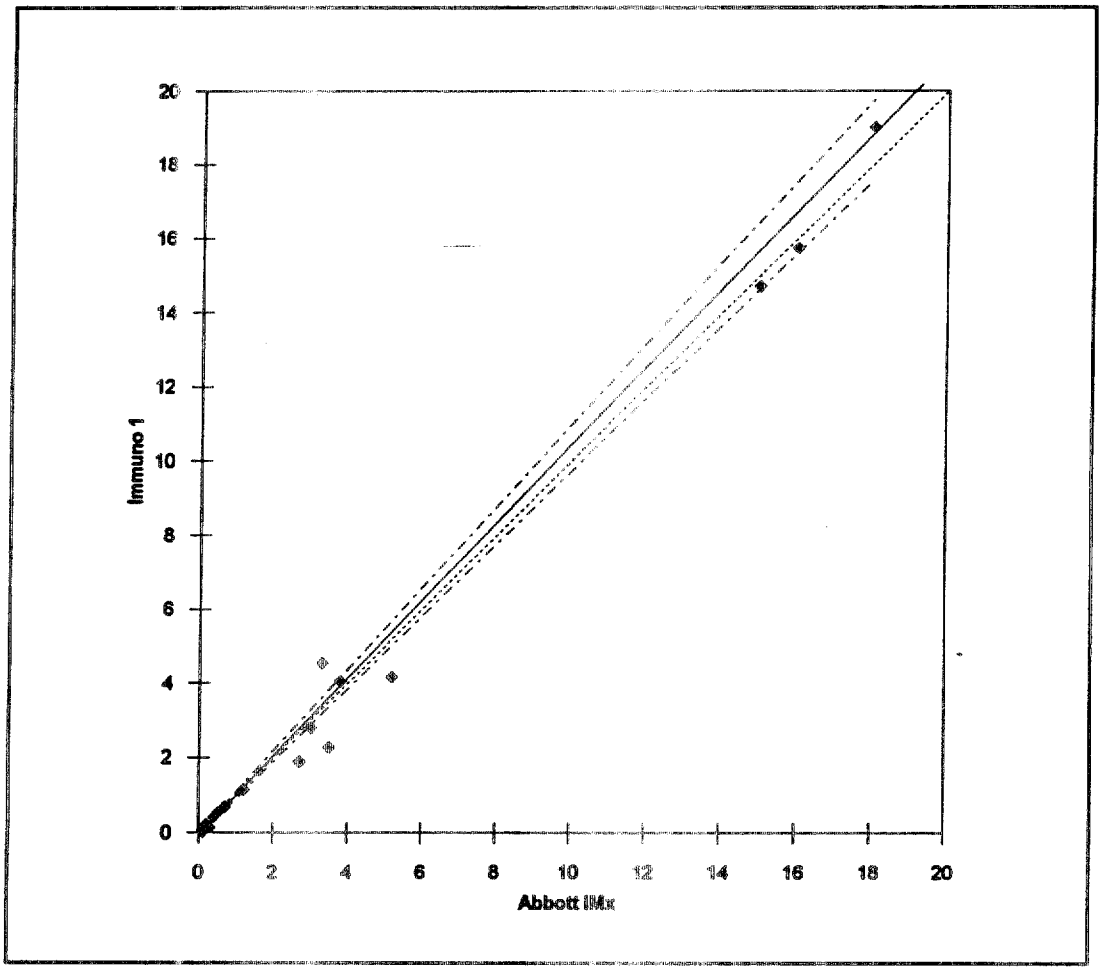

Fig 2: Urine Samples Correlation of Immuno 1 vs. Abbott IMX for beta-2-Microglobulin

The correlation equation according to Bablok-Passing was

$y = 1.05 x - 0.05$
$r = 0.9956$
$Syx = 0.52$ mg/L

5. Interferences

For all interference measurements, a pool was spiked with potentially interfering substances and cross-titered against an identical pool containing no interferants. Beta-2-Microglobulin recoveries for interference pools are summarized in Table 3.

Table 3

Interferants	Interferant Conc. (mg/dL)	B2-M Recovery mg/L
Albumin	0	2.56
	1625	2.58
	3250	2.57
	4875	2.56
	6500	2.58
Bilirubin	0	2.53
	6.25	2.46
	12.50	2.40
	18.75	2.45
	25	2.41
Urea	0	2.70
	50	2.69
	100	2.69
	175	2.70
	200	2.56
Hemoglobin	0	2.61
	300	2.60
	600	2.75
	800	2.63
	1200	2.69
Heparin	0	2.64
	12.5	2.60
	25	2.41
	37.5	2.56
	50	2.78
Human IgG	0	2.40
	1325	2.50
	2650	2.40
	3975	2.50
	5300	2.54
Triglycerides	0	3.31
	250	3.36
	500	3.56
	750	3.56
	1000	3.43

6. Sample Dilution

Serum and urine samples were diluted with beta-2-Microglobulin Calibrator Level 1 and with Sample Diluent B was carried out. For data analysis a linear regression was calculated from the results of undiluted, 10%, and 25% diluted pools. The expected results and the deviation from the measured values were calculated from this equation; these are shown in Tables 4-7.

I. Results obtained with Calibrator Level 1 as diluent

a) Serum Samples

Table 4

sample	dilution (%)	conc. (meas.)	conc. (calc.)	deviation (%)
1	0	0	0.04	-
	10	1.19	1.12	5.6
	25	2.72	2.75	-1.0
	50	5.39	5.45	-1.2
	75	8.62	8.16	5.3
	100	11.06	10.87	1.8
2	0	0	0.03	-
	10	1.16	1.10	4.8
	25	2.69	2.71	-0.8
	50	5.01	5.39	-7.6
	75	8.65	8.07	6.7
	100	11.68	10.75	8.0
3	0	0	0.08	-
	10	1.62	1.49	8.0
	25	3.56	3.61	-1.4
	50	7.10	7.15	-0.6
	75	11.64	10.68	8.2
	100	14.39	14.21	1.2
4	0	0	0.02	-
	10	1.05	1.02	2.6
	25	2.52	2.53	-0.4
	50	5.07	5.05	0.5
	75	7.95	7.56	4.9
	100	11.06	10.07	8.9
5	0	0	0.04	-
	10	1.74	1.67	4.2
	25	4.07	4.10	-0.7
	50	8.97	8.15	9.1
	75	13.4	12.2	8.9
	100	17.11	16.27	4.9
6	0	0	0.08	-
	10	2.03	1.92	5.4
	25	4.66	4.70	-0.9
	50	8.58	9.34	-8.9
	75	15.21	13.98	8.1
	100	18.89	18.61	1.4

b) Urine Samples

Table 5

sample	dilution (%)	conc. (meas.)	conc. (calc.)	deviation (%)
1	0	0	0	-
	10	0.87	0.88	-0.8
	25	2.2	2.2	0
	50	4.33	4.40	-1.6
	75	6.76	6.60	2.4
	100	9.08	8.80	3.1
2	0	0	-0.3	-
	10	1.64	1.69	-2.9
	25	4.28	4.26	0.4
	50	8.89	8.55	3.8
	75	13.59	12.84	5.5
	100	17.34	17.13	1.2
3	0	0	0.03	-
	10	1.13	1.09	3.84
	25	2.66	2.68	-0.7
	50	4.82	5.33	-10.6
	75	7.62	7.98	-4.7
	100	11.16	10.63	4.7
4	0	0	0.07	-
	10	1.53	1.41	7.7
	25	3.38	3.43	-1.4
	50	7.63	6.78	11.1
	75	11.23	10.14	9.7
	100	12.73	13.50	-6.0

II. Results obtained with Sample Diluent B

a) Serum Samples

Table 6

sample	dilution (%)	conc. (meas.)	conc. (calc.)	deviation (%)
1	0	0	-0.01	-
	10	1.45	1.44	1.0
	25	3.57	3.58	-0.2
	50	7.07	7.14	-1.0
	75	10.48	10.71	-2.2
	100	13.15	14.28	-8.6
2	0	0	-0.01	-
	10	1.11	1.14	-2.5
	25	2.88	2.87	0.4
	50	5.84	5.75	1.5
	75	8.25	8.64	-4.7
	100	11.76	11.53	2.0

b) Urine Samples

Table 7

sample	dilution (%)	conc. (meas.)	conc. (calc.)	deviation (%)
1	0	0	0.03	-
	10	1.81	1.75	3.1
	25	4.31	4.33	-0.5
	50	8.64	8.63	0.1
	75	13.12	12.93	1.4
	100	16.92	17.22	-1.8
2	0	0	0.03	-
	10	2.04	2.00	2.2
	25	4.93	4.95	-0.4
	50	9.94	9.87	0.7
	75	15.51	14.79	4.6
	100	19.31	19.71	-2.1

7. Hook Effect

A serum sample with a concentration of 126 mg/l was diluted with calibrator level 1 and the rate values and calculated concentrations were compared to L6 calibrators. It can be concluded that even very high samples do not fall back into the assay range. (Fig. 3)

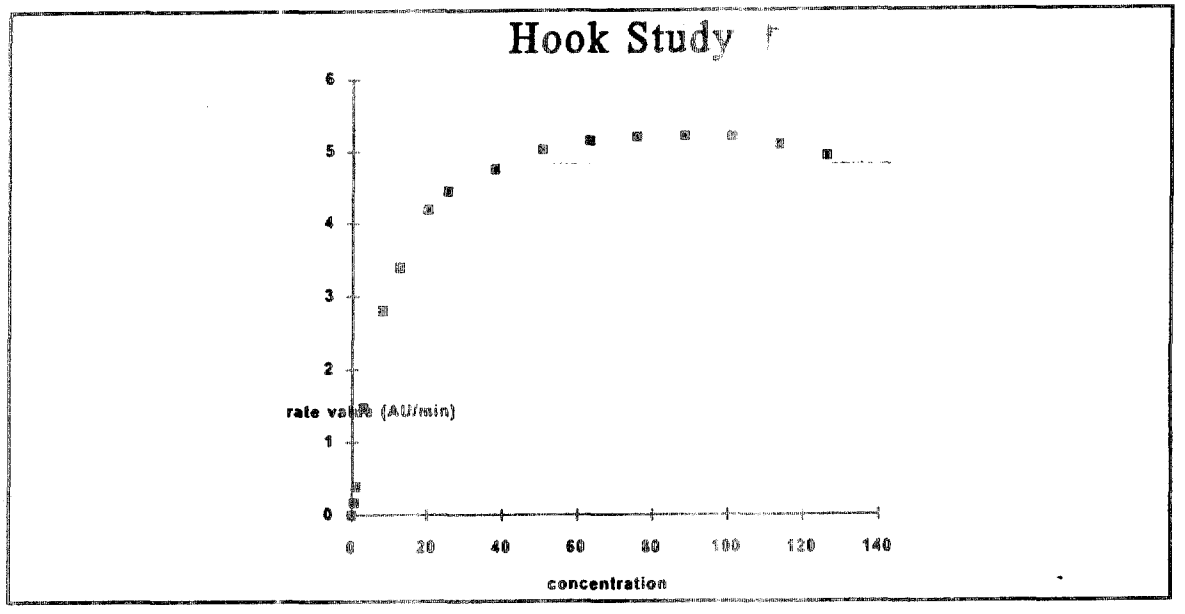

Fig. 3:

8. Recovery

Known amounts of beta-2-microglobulin were spiked into two serum and one urine samples. The recoveries cover a range of 92.5 % to 106 % are shown in Tables 8 and 9.

I. Serum Samples

Table 8

sample	conc. (calculated)	conc. (measured)	recovery (%)
sample 1 base	2.32	2.32	100
low	4.07	4.12	101.2
low-mid	5.44	5.55	102.0
mid	6.81	7.03	103.2
high-mid	8.18	7.69	94.0
high	9.55	9.89	103.6
sample 2 base	2.29	2.29	100
low	4.06	4.00	98.5
low-mid	5.43	5.32	98.0
mid	6.80	6.58	96.8
high-mid	8.17	7.56	92.5
high	9.54	9.67	101.4

II. Urine Samples

Table 9

sample	conc. (calculated)	conc. (measured)	recovery (%)
sample 1 base	0.1	0.04	-
low	1.90	2.18	114.7
low-mid	3.80	3.74	98.4
mid	5.70	5.66	99.3
high-mid	7.60	7.63	100.4
high	9.50	9.58	100.8

9. Expected Values

I. Serum Samples

Serum samples from 262 healthy individuals were measured and gave the distribution of results shown in Fig. 4.

95 % of these serum samples were found to have concentrations of 2.15 mg/L or less. The calculated mean of this distribution is 1.35 mg/L, the median is 1.28 mg/L.

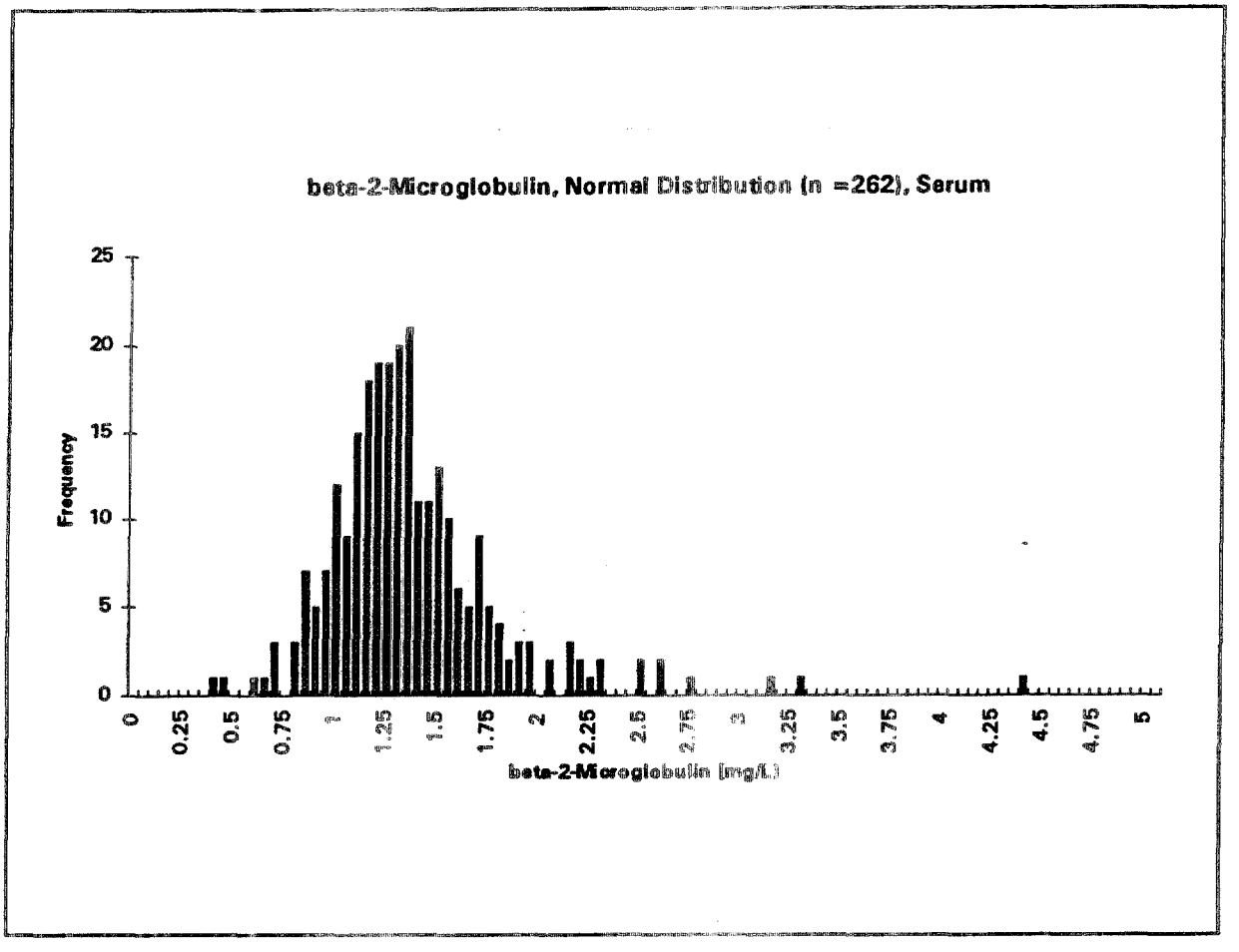

Fig. 4: Normal Distribution of beta-2-Microglobulin in Serum Samples

II. Urine Samples

Urine samples from 72 healthy individuals were measured; 95 % of these urine samples were found to have concentrations of 0.2 mg/L or less. The calculated mean of this distribution is 0.07 mg/L, the median is 0.04 mg/L. The distribution of results are shown in Fig. 5.

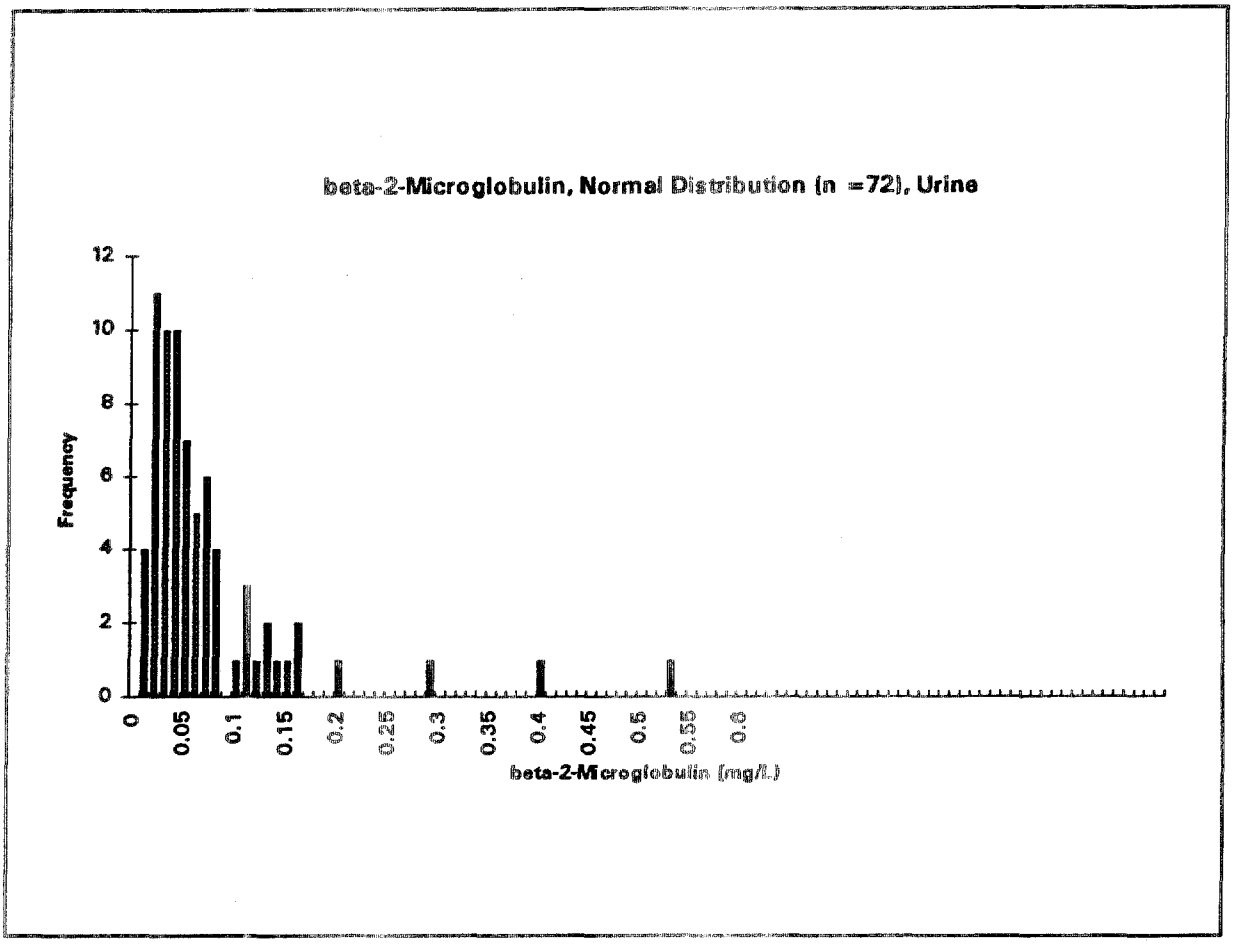

Fig. 5: Normal Distribution of beta-2-Microglobulin in Urine Samples

10. Minimum Detectable Concentration

Sensitivity or Minimum Detectable Concentration of the assay is defined as the beta-2-Microglobulin concentration that can be statistically distinguished for the zero calibrator – the mean zero absorbance + 2SD. The sensitivity measured in 32 seprate runs using 2 different lots of reagents and calibrators was determined to be 0.01 mg/L.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 29 1997

Mr. Gabriel J. Muraca, Jr.
Manager Regulatory Affairs
Bayer Corporation
Diagnostics Division
511 Benedict Avenue
Tarrytown, New York 10591

Re: K964791/S1
Trade Name: β2 Microglobulin Assay for the Technicon Immuno 1® System
Regulatory Class: II
Product Code: JZG
Dated: March 25, 1997
Received: March 26, 1997

Dear Mr. Muraca, Jr.:

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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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 I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Attachment 7

510(k) Number (if known): K964791

Device Name: Technicon Immuno 1® System β2-Microglobulin (B2S / B2U)

Indications For Use:

This *in vitro* diagnostic method is intended to quantitatively measure the concentration of β2-microglobulin in human serum and urine using the Technicon Immuno 1® system. β2-Microglobulin assay values obtained should be used in conjunction with information available from clinical and other diagnostic procedures in the management of patients with renal dysfunction and rheumatoid arthritis.

This diagnostic method is not intended for use on any other system.

Peter E Maddux

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

(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)

(Optional Format 1-2-96)