NOV - 9 1999

Attachment 4

K991907

SUMMARY OF SAFETY AND EFFECTIVENESS

C3 Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Complement C3 method and a similar device that was granted clearance of substantial equivalence (Dade Behring BNA Complement C3 method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS C3 method sheet and the BNAC3 method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure C3 in human serum on the Bayer ADVIA IMS systems. Measurements of C3 are used to aid in the diagnosis and treatment of immunologic disorders.

METHOD		**ADVIA IMS**	**BNA**
Part No.	**Reagents**	B41-3788-41	OSAP
	Calibrators	B46-4088-60	OSAU
Precision (Total)		2.1% @ 79.7 mg/dL 1.8% @ 154 mg/dL 2.1% @ 237 mg/dL	5.9% @ 72.4 mg/dL
Correlation		y=0.92x + 9.7 where y=ADVIA IMS x=BNA n=101 r=0.972 Syx=12.1 mg/dL	

Gabriel J. Murray Jr.

6/4/99

Interfering Substances

Interfering Substance	Interfering Sub Concentration	C3 Concentration	Effect (% Change)
Bilirubin, unconjugated	20 mg/dL	106 mg/dL	+1
Bilirubin, conjugated	20 mg/dL	113 mg/dL	+4
Hemoglobin	500 mg/dL	114 mg/dL	-2
Triglycerides	1000 mg/dL	107 mg/dL	-8

Analytical Range

Dilution Range	Concentration Range, mg/dL
Normal	27 - 360
Out of Range Low	6.8 - 90
Out of Range High	135 - 1800

SUMMARY OF SAFETY AND EFFECTIVENESS

C4 Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Complement C4 method and a similar device that was granted clearance of substantial equivalence (Dade Behring BNA Complement C4 method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS C4 method sheet and the BNAC4 method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure C4 in human serum on the Bayer ADVIA IMS systems. Measurements of C4 are used to aid in the diagnosis and treatment of immunologic disorders.

METHOD		**ADVIA IMS**	**BNA**
Part No.	**Reagents**	B41-3789-41	OSAO
	Calibrators	B46-4088-60	OSAU
Precision (Total)		1.9% @ 19.3 mg/dL 2.0% @ 34.8 mg/dL 1.9% @ 49.3 mg/dL	2.9% @ 15.7 mg/dL
Correlation		y=0.92x - 0.3 where y=ADVIA IMS x=BNA n=94 r=0.989 Syx=1.9 mg/dL	

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6/4/99

Interfering Substances

Interfering Substance	Interfering Sub Concentration	C4 Concentration	Effect (% Change)
Bilirubin, unconjugated	20 mg/dL	19 mg/dL	0
Bilirubin, conjugated	20 mg/dL	21 mg/dL	0
Hemoglobin	500 mg/dL	20 mg/dL	0

Analytical Range

Dilution Range	Concentration Range, mg/dL
Normal	7.2 - 96
Out of Range Low	4.0 - 53
Out of Range High	36 - 480

SUMMARY OF SAFETY AND EFFECTIVENESS

IgA Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Immunoglobulin A method and a similar device that was granted clearance of substantial equivalence (Dade Behring BNA Immunoglobulin A method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS IgA method sheet and the BNA IgA method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure IgA in human serum on the Bayer ADVIA IMS systems. Measurements of IgA are used to aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

METHOD		**ADVIA IMS**	**BNA**
Part No.	**Reagents**	B41-3791-41	OSAR
	Calibrators	B46-4088-60	OSAU
Precision (Total)		2.3% @ 122mg/dL 1.6% @ 233mg/dL 1.4% @ 344mg/dL	3.5% @ 296mg/dL
Correlation		y=1.00x - 1 where y=ADVIA IMS x=BNA n=97 r=0.994 Syx=75.6 mg/dL	

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6/4/99

Interfering Substances

Interfering Substance	Interfering Sub Concentration	IgA Concentration	Effect (% Change)
Bilirubin, unconjugated	20 mg/dL	180 mg/dL	+2
Bilirubin, conjugated	20 mg/dL	200 mg/dL	-3
Hemoglobin	500 mg/dL	191 mg/dL	+1
Triglycerides	1000 mg/dL	184 mg/dL	-8

Analytical Range

Dilution Range	Concentration Range, mg/dL
Normal	45 - 600
Out of Range Low	11.3 - 150
Out of Range High	360 - 4800

SUMMARY OF SAFETY AND EFFECTIVENESS

IgG Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Immunoglobulin G method and a similar device that was granted clearance of substantial equivalence (Dade Behring BNA Immunoglobulin G method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS IgG method sheet and the BNA IgG method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure IgG in human serum on the Bayer ADVIA IMS systems. Measurements of IgG are used to aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

METHOD		**ADVIA IMS**	**BNA**
Part No.	**Reagents**	B41-3792-41	OSAS
	Calibrators	B46-4088-60	OSAU
Precision (Total)		1.8% @ 772mg/dL 1.6% @ 1416mg/dL 3.4% @ 2141mg/dL	2.7% @ 1317mg/dL
Correlation		y=0.97 x - 3 where y=ADVIA IMS x=BNA n=97 r=0.994 Syx=118 mg/dL	

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6/4/99

Interfering Substances

Interfering Substance	Interfering Sub Concentration	IgG Concentration	Effect (% Change)
Bilirubin, unconjugated	20 mg/dL	876 mg/dL	-3.0
Bilirubin, conjugated	20 mg/dL	953 mg/dL	-3.0
Hemoglobin	500 mg/dL	897 mg/dL	+7.0
Triglycerides	1000 mg/dL	887 mg/dL	-3.0

Analytical Range

Dilution Range	Concentration Range, mg/dL
Normal	225 - 3,000
Out of Range Low	56 - 750
Out of Range High	1128 - 15,000

SUMMARY OF SAFETY AND EFFECTIVENESS

IgM Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Immunoglobulin M method and a similar device that was granted clearance of substantial equivalence (Dade Behring BNA Immunoglobulin M method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS IgM method sheet and the BNA IgM method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure IgM in human serum on the Bayer ADVIA IMS systems. Measurements of IgM are used to aid in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

METHOD		**ADVIA IMS**	**BNA**
Part No.	**Reagents**	B41-3793-41	OSAT
	Calibrators	B46-4088-60	OSAU
Precision (Total)		3.6% @ 69.0mg/dL 2.4% @ 128mg/dL 1.5% @ 177mg/dL	1.9% @ 117mg/dL
Correlation		y=1.05x - 13.4 where y=ADVIA IMS x=BNA n=89 r=0.990 Syx=123.5 mg/dL	

Gabriel J. Murray, Jr.
6/4/99

Interfering Substances

Interfering Substance	Interfering Sub Concentration	IgM Concentration	Effect (% Change)
Bilirubin, unconjugated	20 mg/dL	77 mg/dL	+3.9
Bilirubin, conjugated	10 mg/dL	85 mg/dL	+1.2
Hemoglobin	500 mg/dL	86 mg/dL	0.0

Analytical Range

Dilution Range	Concentration Range, mg/dL
Normal	30 - 400
Out of Range Low	10 - 133
Out of Range High 1	241 - 3,200
Out of Range High 2	1,203 - 16,000

SUMMARY OF SAFETY AND EFFECTIVENESS

TRF Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Transferrin method and a similar device that was granted clearance of substantial equivalence (Dade Behring BNA Transferrin method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS TRF method sheet and the BNATRF method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure TRF in human serum on the Bayer ADVIA IMS systems. Measurements of TRF are used to aid in the diagnosis and treatment of malnutrition, chronic infection, acute hepatitis, polycythemia, pernicious anemia and red blood disorders, such as iron deficiency anemia.

METHOD		**ADVIA IMS**	**BNA**
Part No.	**Reagents**	B41-3795-41	OSAX
	Calibrators	B46-4088-60	OSAU
Precision (Total)		2.2% @ 127 mg/dL 1.9% @ 268 mg/dL 3.1% @ 400 mg/dL	2.7% @ 303 mg/dL
Correlation		y=0.96x - 3 where y=ADVIA IMS x=BNA n=106 r=0.979 Syx=16.8 mg/dL	

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6/4/99

Interfering Substances

Interfering Substance	Interfering Sub Concentration	TRF Concentration	Effect (% Change)
Bilirubin, unconjugated	20 mg/dL	212 mg/dL	+2
Bilirubin, conjugated	20 mg/dL	231 mg/dL	0
Hemoglobin	500 mg/dL	261 mg/dL	0
Triglycerides	1000 mg/dL	215 mg/dL	-4

Analytical Range

Dilution Range	Concentration Range, mg/dL
Normal	54 - 720
Out of Range Low	13 - 180
Out of Range High	270 - 3,600

SUMMARY OF SAFETY AND EFFECTIVENESS

Vancomycin Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Vancomycin method and a similar device that was granted clearance of substantial equivalence (Bayer Immuno 1 Vancomycin method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS Vancomycin method sheet and the Immuno 1 Vancomycin method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure vancomycin in human serum on the Bayer ADVIA IMS systems. Measurements of vancomycin are used to aid in attaining optimum therapy in patients treated with the drug.

METHOD		**ADVIA IMS**	**Immuno 1**
Part No.	**Reagents**	B41-3767-41	T01-3705-01
	Calibrators	B46-4117-01	T03-3714-01
Analytical Range		0.4-50 µg/mL	
Precision (Total)		2.8% @ 8.6 µg/mL 3.4% @ 21.5 µg/mL 3.9% @ 35.8 µg/mL	8.9% @ 6.7 µg/mL 7.5% @ 23.3 µg/mL 8.1% @ 32.4 µg/mL
Correlation		y=1.02x + 0.68 where y=ADVIA IMS x=Immuno 1 n=55 r=0.987 Syx=1.6 µg/dL	

Interfering Substances

Interfering Substance	Interfering Substance Concentration		Vancomycin Concentration		Effect % Change
			(µmol/L)	(µg/mL)	
Bilirubin (unconjugated)	0.43 mmol/L	25 mg/dL	10.6	15.3	+0.3
Bilirubin (conjugated)	0.43 mmol/L	25 mg/dL	11.0	15.9	+0.6
Hemoglobin	10 g/L	1000 mg/dL	11.1	16.1	-7.7
Lipemia (Triglycerides)	11.4 mmol/L	1000 mg/dL	11.0	16.0	-0.2

Gabriel J. Murray Jr.
6/4/99

SUMMARY OF SAFETY AND EFFECTIVENESS

Valproic Acid Method for the Bayer ADVIA IMS Systems

Listed below is a comparison of the performance between the Bayer ADVIA IMS Valproic Acid method and a similar device that was granted clearance of substantial equivalence (Abbott TDx Valproic Acid method). The information used in the Summary of Safety and Effectiveness was extracted from the ADVIA IMS Valproic Acid method sheet and the TDx Valproic Acid method sheet.

INTENDED USE

This in vitro method is intended to quantitatively measure valproic acid in human serum on the Bayer ADVIA IMS systems. Measurements of valproic acid are used to aid in attaining optimum therapy in patients treated with the drug.

METHOD		**ADVIA IMS**	**TDx**
Part No.	**Reagents**	B41-3766-41	9514-20
	Calibrators	B46-4118-01	9514-01
Analytical Range		0.3-150 µg/mL	
Precision (Total)		3.8% @ 20.3 µg/mL	3.4% @ 37.5 µg/mL
		2.4% @ 60.2 µg/mL	3.4% @ 75 µg/mL
		2.8% @ 108.5 µg/mL	3.7% @ 125 µg/mL
Correlation		y=1.11x + 0.27 where y=ADVIA IMS x=TDx n=55 r=0.993 Syx=3.79 µg/mL	

Interfering Substances

Interfering Substance	Interfering Substance Concentration		Valproic acid Concentration		Effect % Change
			(µmol/L)	(µg/mL)	
Bilirubin (unconjugated)	0.43 mol/L	25 mg/dL	573	82.5	+6
Bilirubin (conjugated)	0.43 mol/L	25 mg/dL	542	78.1	+1
Hemoglobin	10 g/L	1000 mg/dL	557	80.2	+4
Lipemia (Triglycerides)	5.7 mmol/L	500 mg/dL	561	80.8	+3

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6/14/95

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV - 9 1999

Mr. Gabriel J. Muraca, Jr.
Manager Regulatory Affairs
Bayer Corp.
Business Group Diagnostics
511 Benedict Avenue
Tarrytown, New York 10591-5097

Re: K991907
Trade Name: 8 Additional Assays for the Bayer ADVIA® Integrated Modular System (IMS)
Regulatory Class: II
Product Code: CZW, CFQ, DBI, DDG, KTO, LEG, LEH
Dated: September 3, 1999
Received: September 7, 1999

Dear Mr. Muraca:

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 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). 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 Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS 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

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 (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

510(k) Number (if known): K991907

Device Name: **Bayer ADVIA® Integrated Modular System (IMS)**

Indications For Use:

The *Bayer ADVIA IMS* C3 assay is an *in vitro* diagnostic device intended to measure Complement C3 (C3) in human serum. Such measurements are used as an aid in the diagnosis and treatment of immunologic disorders.

The *Bayer ADVIA IMS* C4 assay is an *in vitro* diagnostic device intended to measure Complement C4 (C4) in human serum. Such measurements are used as an aid in the diagnosis and treatment of immunologic disorders.

The *Bayer ADVIA IMS* IgA assay is an *in vitro* diagnostic device intended to measure Immunoglobulin A (IgA) in human serum. Such measurements are used as an aid in the diagnosis and treatment of abnormal protein metabolism and the body's inability to resist infectious agents.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K991907

(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)

510(k) Number (if known):

Device Name: **Bayer ADVIA® Integrated Modular System (IMS)**

Indications For Use:

The *Bayer ADVIA IMS* IgG assay is an *in vitro* diagnostic device intended to measure Immunoglobulin G (IgG) in human serum. Such measurements are used as an aid in the diagnosis and treatment of autoimmune diseases, chronic or recurrent infections and abnormal protein metabolism.

The *Bayer ADVIA IMS* Immunoglobulin M (IgM) assay is an *in vitro* diagnostic device intended to measure IgM in human serum. Such measurements are used as an aid in the diagnosis and treatment of chronic or recurrent infections and abnormal protein metabolism.

The *Bayer ADVIA IMS* Transferrin assay is an *in vitro* diagnostic device intended to measure transferrin (TRF) in human serum. Such measurements are used as an aid in the diagnosis and treatment of malnutrition, chronic infection, acute hepatitis, polycythemia, pernicious anemia, and red blood cell disorders, such as iron deficiency anemia.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K991907

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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)

510(k) Number (if known):

Device Name: **Bayer ADVIA® Integrated Modular System (IMS)**

Indications For Use:

The *Bayer ADVIA IMS* Vancomycin assay is an *in vitro* diagnostic device intended to measure vancomycin, an antibiotic drug, in human serum. Measurements of vancomycin are used as an aid in the diagnosis and treatment of vancomycin overdose and in monitoring therapeutic levels of vancomycin to ensure appropriate therapy.

The *Bayer ADVIA IMS* Valproic Acid Assay is an *in vitro* diagnostic device intended to measure valproic acid, an anti-epileptic drug, in human serum. Measurements of valproic acid are used as an aid in the diagnosis and treatment of valproic acid overdose and in monitoring therapeutic levels of valproic acid to ensure appropriate therapy.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K 991907

(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)