MAR 1 3 2001

The assigned K# is: K003503

Summary of Safety and Effectiveness Information

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.

Submitter's Name: Rebecca S. Ayash
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Date of Preparation: 1/31/01

Device Name: N Latex Cystatin C Test Kit

Classification Name: Not yet classified

Predicate Device: Roche (Boehringer Mannheim) Creatinine

Device Description: Polystyrene particles coated with antibodies to cystatin C are agglutinated when mixed with samples containing cystatin C. The intensity of the scattered light is measured using immunonephelometry and depends on the concentration of the analyte in the sample. This concentration is determined by comparison with dilutions of a standard of known concentration.

N Cystatin C Control is a lyophilized product of polygeline containing urine proteins of human origin. The concentration of cystatin C was standardized with reference to purified cystatin C. It is an assayed control intended to monitor and evaluate the precision and accuracy of the N Latex Cystatin C Test Kit. The control is provided as a single level. A second level is prepared from a 1:2 dilution with N Diluent.

N Cystatin C Supplementary Reagent is used to prevent nonspecific agglutination of latex enhanced reagents by rheumatoid factors (RF).

Substantial Equivalence: The N Latex Cystatin C test kit is substantially equivalent in intended use and performance to creatinine assays such as the Roche (Boehringer Mannheim) Creatinine and Creatinine/Rate-Blanked assays (K921661) for the Hitachi family of analyzers. Both N Latex Cystatin C and the Roche Creatinine assays are *in vitro* assays used for the diagnosis and treatment of renal diseases.

Intended Use: N Latex Cystatin C is an *in vitro* diagnostic assay for the quantitative determination of cystatin C in human serum and heparinized plasma by means of particle enhanced immunonephelometry. Cystatin C measurements are used in the diagnosis and treatment of renal diseases.

Comparison to Predicate Device:

Table 1

Comparison of N Latex Cystatin C with Roche Creatinine Rate Blanked and Creatinine Assays

Item	N Latex Cystatin C	BM Creatinine/ Rate-Blanked	BM Creatinine
Intended Use	*In vitro* diagnostic assay for the quantitative determination of cystatin C in human serum and heparinized plasma. Cystatin C measurements are used in the diagnosis and treatment of renal diseases.	*In vitro* diagnostic assay for the quantitative determination of creatinine in serum, plasma, and urine. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for other urine analytes.	*In vitro* diagnostic assay for the quantitative determination of creatinine in serum, plasma, and urine. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for other urine analytes.
Principle	Polystyrene particles coated with antibodies to cystatin C are agglutinated when mixed with samples containing cystatin C. The intensity of the scattered light is measured using immunonephelometry and depends on the concentration of the analyte in the sample. This concentration is determined by comparison with dilutions of a standard of known concentration.	In an alkaline medium, creatinine forms a yellow-orange colored complex with picric acid. The rate of color formation is proportional to the concentration of creatinine present and may be measured photometrically. Rate-blanked measurement minimizes "pseudo" creatinine and bilirubin interferences.	In an alkaline medium, creatinine forms a yellow-orange colored complex with picric acid. The rate of color formation is proportional to the concentration of creatinine present and may be measured photometrically.
Measuring Range	Approx. 0.23 to 8 mg/L	Serum/plasma = 0.1 to 25.0 mg/dL	Serum/plasma = 0.1 to 25.0 mg/dL
Sample	Serum or plasma	Serum, plasma, or urine	Serum, plasma, or urine
Instrumentation	BN™ Systems	Automated clinical chemistry analyzers	Automated clinical chemistry analyzers

Comments on Substantial Equivalence: Split sample comparison between the N Latex Cystatin C Test Kit and Roche (Boehringer Mannheim) Creatinine are shown in Table 2.

Table 2
Summary of Method Comparison Regression Analysis

	Slope (95% CI)	Intercept (95% CI)	R	Syx	Cystatin C Range	n
Site A	0.52 ± 0.03 (0.46, 0.58)	1.11 ± 0.12 (0.87, 1.35)	0.891	0.89	0.57-7.58	100
Site B	0.70 ± 0.02 (0.66, 0.74)	0.39 ± 0.04 (0.31, 0.47)	0.833	0.41	0.46-4.83	499
Site C	0.79 ± 0.05 (0.69, 0.89)	0.30 ± 0.15 (0.01, 0.59)	0.843	0.86	0.54-6.34	99

Five hundred subjects were recruited from patients undergoing an Iothalamate Clearance procedure for evaluation of GFR. Of these, 363 (73%) were found to have an abnormal GFR based on the Iothalamate Clearance results. In addition to the Iothalamate clearance testing, samples were assayed using N Latex Cystatin C and the comparative creatinine assay.

N Latex Cystatin C and creatinine demonstrated similar specificities (p=0.170, not significant). The specificity of N Latex Cystatin C was 82% compared to only 88% for creatinine. However, a significantly higher sensitivity was observed for N Latex Cystatin C than for creatinine (p<0.001). The sensitivity of N Latex Cystatin C was 94% compared to only 81% for creatinine. A difference between sensitivities of 13% (95% CI 8%; 17%) and a difference of - 6% (95% CI -14%; 3%) between specificities was observed. The area under the ROC curve was estimated to be 0.881 (95% CI 0.842; 0.920) for N Latex Cystatin C and for creatinine to be 0.847 (95% CI 0.808; 0.886).

Table 3
Clinical Sensitivity and Specificity

Cystatin C	**Observed (%)**	**95% Confidence Interval**
Sensitivity	94	(91, 96)
Specificity	82	(76, 89)
Positive Predictive Value	93	(91, 96)
Negative Predictive Value	83	(77, 89)
Creatinine		
Sensitivity	81	(77, 85)
Specificity	88	(83, 94)
Positive Predictive Value	95	(92, 97)
Negative Predictive Value	64	(57, 71)

Conclusion: The N Latex Cystatin C Test Kit is substantially equivalent in principle and performance to the Roche (Boehringer Mannheim) Creatinine and Creatinine/Rate-Blanked assays based on the data summarized above. The N Latex Cystatin C Test Kit has demonstrated the ability to determine the concentration of cystatin C in human serum and plasma and to act as an aid in the diagnosis and treatment of renal diseases.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAR 1 3 2001

Ms. Rebecca S. Ayash
Director, Regulatory Affairs, Biology
Dade Behring Inc.
P.O. Box 6101
Newark, Delaware 19714

Re: K003503
Trade Name: N Latex Cystatin C Test Kit
Regulatory Class: II
Product Code: NDY
Dated: February 1 2001
Received: February 2, 2001

Dear Ms. Ayash:

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 have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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 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 Statement

510(k) Number (If known) K003503

Device Name: N Latex Cystatin C Test Kit

Indications for Use: The N Latex Cystatin C Test Kit is an *in vitro* diagnostic test kit for the quantitative determination of cystatin C in human serum and heparinized plasma by means of particle enhanced immunonephelometry. Cystatin C measurements are used in the diagnosis and treatment of renal disease.

Ian Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K003503

Rebecca S. Ayash
Rebecca S. Ayash
Director, Regulatory Affairs
Biology
Date: 11/10/00

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓
(Per 21 CFR 801.109)

Over-The-Counter-Use____
(Optional Format 1-2-96)