

K981950

NOV 3 1998

**510(k) Premarket Notification**  
**Sysmex™ Automated Reticulocyte Analyzer R-3500**  
**May 31, 1998**

**I. DEVICE NAME:**

**Trade or Proprietary Name:** Sysmex™ Automated Reticulocyte Analyzer R-3500

**Common or Usual Name:** Automated Reticulocyte Analyzer

**II. CLASSIFICATION NAMES:**

Automated Cell Counter	81 GKL
Automated Cell Dilution Device	81 GKH
Computer System Integrated with Hematology Analyzers	81 JWS

**Related Items:**

Diluent: RETSHEATH	81 GIF
RETSEARCH diluent	81 GIF
Stain: RETSEARCH dye	81 KJK
Detergent: CELLCLEAN	81JCB

**Calibrators:**

Sysmex™ Latex Particle-R	81 KSA
Sysmex™ SCS-Ret	81 KSA

**Accessories:**

Pneumatic Unit (PU-8)	NA
Sampler Unit (SU)	NA
Slide Preparation Unit (SP-100)	81GKJ
Line Controller (LC-2)	NA
Conveyor Unit (CVR-1)	NA
Rack Slider (RS)	NA
Start Yard (STY)	NA
Stock Yard (SKY)	NA
Extended Conveyor (EC-1)	NA
Turn Unit (TU-1)	NA
Data Entry Unit (DE-2)	NA

**III. ESTABLISHMENT INFORMATION:**

<i>Location</i>	<i>Registration Number</i>	
<i>Manufacturer Site</i>	<i>Owner/Operator No.</i>	<i>Manufacturer No.</i>
TOA Medical Electronics Co. Kobe, Japan	7010360	961466

*Importer & Distributor*  
Sysmex™ Corporation  
Gilmer Road 6699 RFD  
Long Grove, IL 60047-9596

*Registration Number*  
1422681

#### **IV. CLASSIFICATION INFORMATION:**

Automated reticulocyte instruments have been classified by the Hematology and Pathology Devices Panel as Class II devices.

The Immature Reticulocyte Fraction (IRF) Parameter is a Class III parameter that has already been cleared for *all* Sysmex™ R-Series Analyzers (see 510(k) submission #K971736).

#### **V. COMPLIANCE WITH PERFORMANCE STANDARDS:**

To date, no performance standards which affect this device have been finalized under Section 514 of the Food, Drug, and Cosmetic Act.

#### **VI. PROPOSED LABELING:**

A draft copy of the proposed labeling, Operator's Manual, Reagent Labeling and Sales Brochures are included.

#### **VII. SUMMARY**

Complete information on the Safety and Effectiveness Summary is included in Attachment 3.

#### **VIII. DESCRIPTION**

The Sysmex™ R-3500 is an automated reticulocyte analyzer intended for *in vitro* use in clinical laboratories.

The R-3500 provides accurate and precise test results for 8 analysis parameters in whole blood. These include RET%, RET#, RBC, IRF, LFR, MFR, HFR, and PLT.

The R-3500 processes approximately 120 samples per hour and displays and prints the data for Reticulocyte number, Reticulocyte percent, Red blood cell count, Immature reticulocyte fraction, fluorescent ratios, and platelets along with representative scattergrams. Sample abnormalities are indicated by abnormal marks, flags, and error messages which appear on the DMS display screen and on the printout. This is an indication that the sample is not within the acceptable range and requires further review and investigation.

The R-3500 uses the principle of flow cytometry for reticulocyte analysis. In the instrument, a whole blood sample is automatically aspirated, diluted and stained with a fluorescent dye (Auromine-O). The sample is hydrodynamically focused into a narrow path and passed through a flow cell, where it is illuminated by an Argon laser beam. The

cells present in the sample will fluoresce and scatter light to varying degrees. It is the analysis of the intensity of emitted fluorescent light and intensity of scattered light which allows the R-3500 analyzer to detect and enumerate reticulocytes.

A computer algorithm discriminates the different populations of cells based on the intensity of light scatter and fluorescence, and displays this on a scattergram. The red blood cells, platelets and reticulocytes are separated by means of adaptive cluster analysis of the scattergram. The reticulocyte region of the scattergram is divided into three regions based on fluorescence intensity. These areas are called the low, middle and high fluorescence ratios (LFR, MFR and HFR), and are expressed as a ratio or percentage (sum = 100) of the total reticulocyte count. The immature reticulocyte fraction (IRF) is equal to the MFR+HFR.

The R-3500 provides four modes of sample introduction: 1) Sampler (auto) Mode, 2) Closed Mode, 3) Manual Mode and 4) Capillary Mode. The Sampler mode is completely automated; closed tubes are placed in the auto mode racks, and are automatically moved through the system. Whole blood is aspirated automatically via a cap piercing system. The Closed Mode also uses the cap piercing system, but samples are analyzed one at a time. In the Manual (open) Mode, the sample tube cap is opened and the sample is aspirated through the sample probe. The Capillary Mode allows for the use of smaller volume samples such as obtained from a child. In this mode, a blood sample is diluted before analysis is performed.

Operator interface with the R-3500 is accomplished with the use of a data management system (DMS), as well as a main unit control panel keypad.

The R-3500 has a quality control (QC) program which performs statistical QC. The R-3500 maintains the reliability of analyzed data by monitoring the stability of the system (instrument and reagents) over a laboratory-defined interval. This type of QC refers to statistical calculations performed on control blood. In the QC program, QC data for each analysis parameter is obtained by analyzing control blood and storing the results in a QC file. The instrument provides 15 QC files for each test parameter, including 2 troubleshooting (alignment) parameters. Each QC file stores the latest 180 points.

There are disposables and consumables associated with the system which are required for its normal operation.

To keep the R-3500 in optimal operating conditions, periodic maintenance is required.

## **IX. SUBSTANTIAL EQUIVALENCE:**

The R-3500 is substantially equivalent in intended use and technological characteristics to the Sysmex™ SE/RAM-1 and Sysmex™ R-3000. A summary of the comparative features is presented in Table 1.

**Table 1**  
**Comparative Features between R-3500 and**  
**RAM-1/R-3000**

<b>Features</b>	<b>R-3500</b>	<b>SE/RAM-1 K964375</b>	<b>R-3000 K912494</b>
<b>FDA Clearance Date</b>	---	Mar. 13, 1997	Sept. 10, 1991
<b>Intended Use</b>	Automated reticulocyte counter for <i>in vitro</i> diagnostic use in clinical laboratories	Automated hematology and reticulocyte analyzer for <i>in vitro</i> diagnostic use in clinical laboratories	Automated reticulocyte counter for <i>in vitro</i> diagnostic use in clinical laboratories
<b>Sample Type</b>	Whole blood	Whole blood	Whole blood
<b>Sample Volume</b>	250 $\mu$ L Sampler mode 100 $\mu$ L Manual mode 40 $\mu$ L whole blood for capillary dilution	250 $\mu$ L Sampler Mode 125 $\mu$ L Manual Mode 40 $\mu$ L whole blood for capillary dilution	100 $\mu$ L Sampler Mode 100 $\mu$ L Manual Mode 40 $\mu$ L whole blood for capillary dilution
<b>Performance</b>	Similar to R-3000 and RAM-1	Proven performance; see #K964375	Proven performance; see #K912494
<b>Parameters</b>	RET%, RET#, RBC#, IRF, LFR, MFR, HFR, PLT	RET%, RET#, RBC#, IRF, LFR, MFR, HFR, PLT	RET%, RET#, RBC#, IRF, LFR, MFR, HFR
<b>Reagents</b>	RETSHEATH, RETSEARCH diluent and dye	Same	Same
<b>Principles</b>	Flow cytometry using argon laser, Auramine-O dye, sheath flow. Detection of forward fluorescence and scatter	Same	Same
<b>Dimensions (HxWxD) (mm)</b>	720x630x505	720x400x505	645x600x618
<b>Weight (kg)</b>	85.5	50	66
<b>QC System</b>	Levy-Jennings, SD,CV 15 Files per Parameter, 180data points per file	Levy-Jennings, SD,CV 12 Files per Parameter, 180data points per file	Levy-Jennings, SD,CV 6 Files per Parameter, 60 data points per file
<b>Bar Code</b>	Yes	Yes	Yes
<b>No. of Test per Hour</b>	Approximately 120	Approximately 80	Approximately 60

## X. COMPARISON TO PREDICATE DEVICE

Data to support substantial equivalence to the predicate device were generated during correlation studies performed at our research center. In these studies, the following comparative performance evaluations were conducted using the proposed device and the predicate device to evaluate specimens from apparently healthy individuals and from patients with different pathological conditions which are expected to affect the results for particular parameters. Refer to Table 2 for a summary of the correlation studies.

**Table 2**  
**Summary of Method Comparison Studies between**  
**R-3500 and RAM-1**

<b>Parameter</b>	<b>n</b>	<b>r</b>	<b>r<sup>2</sup></b>	<b>Regression Equation</b>
<b>RET#</b>	487	0.994	0.988	$y = 0.965x + 0.001$
<b>RET%</b>	487	0.997	0.994	$y = 0.964x + 0.051$
<b>RBC</b>	486	0.998	0.997	$y = 1.009x - 0.072$
<b>IRF</b>	486	0.956	0.913	$y = 0.948x + 1.409$
<b>LFR</b>	486	0.956	0.913	$y = 0.948x + 3.819$
<b>MFR</b>	486	0.923	0.852	$y = 0.917x + 1.433$
<b>HFR</b>	486	0.954	0.910	$y = 0.940x + 0.490$
<b>Platelet</b>	482	0.994	0.989	$y = 0.937x + 10.619$

## XI. HAZARD ANALYSIS:

A copy of the hazard analysis is provided as Attachment 8 of this submission.

## XII. APPLICANT ADDRESS:

Sysmex Corporation  
Gilmer Road 6699 RFD  
Long Grove, IL 60047-9596

## XIII. CONTACT PERSON:

Cathy Trester, MT(ASCP), Clinical Regulatory Specialist  
Clinical and Regulatory Affairs  
Sysmex Corporation  
Gilmer Road 6699 RFD  
Long Grove, IL 60047-9596  
Phone: 847-726-3662  
FAX: 847-726-3505  
Internet: [tresterc@sysmex.com](mailto:tresterc@sysmex.com)

**XIV. MANUFACTURING FACILITY:**

TOA Medical Electronics Co. Ltd. Japan  
Kobe, Japan

**XVI. SOFTWARE CERTIFICATION**

A copy of the software certification is included as Attachment 9.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

NOV 3 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Ms. Catherine Trester, MT (ASCP)  
Clinical and Regulatory Affairs  
SYSMEX™ Corporation  
Gilmer Road, 6699 RFD  
Long Grove, Illinois 60047-9596

Re: K981950/S1  
Trade Name: Sysmex™ R-3500 Automated Reticulocyte Analyzer  
Regulatory Class: III  
Product Code: GKL  
Dated: August 19, 1998  
Received: August 20, 1998

Dear Ms. Trester:

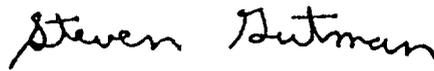
We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 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" (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 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): K981950

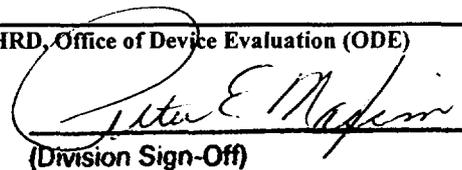
Device Name: Sysmex™ Automated Reticulocyte Analyzer R-3500

**Indications For Use:**

The intended use of the Sysmex R-3500 is as a fully automated reticulocyte analyzer for *in vitro* diagnostic use in clinical laboratories.

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

Concurrence of CHRD, Office of Device Evaluation (ODE)



(Division Sign-Off)  
Division of Clinical Laboratory Devices K981950  
510(k) Number \_\_\_\_\_

Prescription Use   
(Per 21 CFR 801.109)

OR

Over-The-Counter Use \_\_\_\_\_

(Optional Format 1-2-96)