

SEP 24 1998

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**COULTER**

COULTER CORPORATION  
P.O. BOX 169015  
Miami, Florida 33116-9015 USA

**Date:** June 17, 1998

Customer Service: (800) 526-7694  
Product Information: (800) 526-6932  
(800) 327-6531 (305) 327-6531  
www.coulter.com

**Title:** Summary of Safety and Effectiveness Information For 510(k) Premarket Notification

**Product:** CYTO-STAT® CD3-FITC/CD56-RD1 Monoclonal Antibody Reagent  
with  
CYTO-STAT®/COULTER® CLONE® MsIgG1-RD1/MsIgG1-FITC Isotypic Control

Coulter Corporation  
Miami, Florida USA

**Company:** Coulter Corporation  
11800 SW 147 Avenue  
Miami, FL 33196-2500

Coulter Leasing Corporation  
Miami, Florida USA

Coulter Electronics Pty Ltd  
Sydney, Australia

Coulter Electronics Ind. & Com. Ltda.  
Rio de Janeiro, Brazil

**Contact:** Dr. Marion S. Gaide (M/C: 31-B06)  
Senior Regulatory Affairs Specialist  
Corporate Regulatory Affairs

Coulter Electronics of Canada, Ltd.  
Burlington, Ontario, Canada

Coulter Electronics, Ltd.  
Luton Bedfordshire, England

**Telephone:** (305) 380-2594

Coultronics France, S.A.  
Marseilles, France

**Common or Usual or Classification Name:** Lymphocyte Immunophenotyping Monoclonal Antibody Reagent with Isotypic Control

Coulter Electronics GmbH  
Krefeld, Germany

**Product Classification:** Product Code: GKZ; C.F.R. Section: 864.5220; Classification Panel: Hematology and Pathology Devices; Device Class: II

Coulter Electronics (HK), Ltd.  
Hong Kong

Coulter K. K.  
Tokyo, Japan

**Intended Use:**

Coulter de Mexico S.A., DE C.V.  
Mexico City, Mexico

CYTO-STAT® CD3-FITC/CD56-RD1 is a two-color fluorescent reagent comprised of two murine monoclonal antibodies. Each antibody is labeled with a different color fluorochrome. The reagent allows simultaneous identification and enumeration of total CD3+ and CD3-/CD56+ lymphocytes in whole blood by flow cytometry. An isotypic control, CYTO-STAT®/COULTER® CLONE® MsIgG1-RD1/MsIgG1-FITC, is used to monitor nonspecific staining.

Coulter Electronics, Ltd.  
Mijdrecht, Netherlands

Coulter Electronics, Pty. Ltd.  
Auckland, New Zealand

CYTO-STAT®/COULTER® CLONE® MsIgG1-RD1/MsIgG1-FITC is a two-color fluorescent reagent comprised of two murine monoclonal antibodies. Each antibody is labeled with a different color fluorochrome. This product is intended for use as a quality control reagent to monitor the levels of nonspecific antibody binding in cell surface staining procedures which use CYTO-STAT® OR CYTO-STAT®/COULTER® CLONE® Monoclonal Antibody Reagents comprised of two monoclonal antibodies of the MsIgG1 subclass conjugated to RD1 and FITC.

Coulter Electronics Sales of P.R., Inc.  
San Juan, Puerto Rico

Coulter Electronics, Ltd.  
Johannesburg, South Africa

Coulter Electronics, Ltd.  
Istanbul, Turkey

Coulter Electronics, S.A.  
Caldas, Venezuela

**Substantial Equivalence:** 510(k) Premarket Notification: K926124

CYTO-STAT®/COULTER CLONE® CD3(IgG1)-FITC/B4-RD1 Monoclonal Antibody Reagent with CYTO-STAT®/COULTER CLONE® MsIgG1-RD1/MsIgG1-FITC Isotypic Control

**Product Comparison:**

The CD3/CD56 and CD3/B4 systems are essentially identical with respect to features and principles of operation. Each liquid reagent allows simultaneous identification and enumeration of more than one T lymphocyte population (CD3+ and CD3-/CD56+ or CD19+) in a single specimen using a single reagent. Each system also requires an isotypic control to monitor nonspecific binding. The difference between the systems is that CD3/CD56 contains the CD56 monoclonal antibody to identify and enumerate NK (Natural Killer) lymphocytes whereas CD3/B4 contains the CD19 monoclonal antibody to identify and enumerate B lymphocytes. CD3/CD56 and CD3/B4 both require a separate reagent, CYTO-STAT®/COULTER CLONE® Mo2-RD1/KC56 (T-200)-FITC, to identify a lymphocyte gate.

Mab Conjugation: CD3: FITC (Fluorescein Isothiocyanate). CD56: RD1 (Phycoerythrin).

**Product Testing:** Product testing to assess the performance of CD3/CD56 is described below. Studies were designed in line with instructions for use in the product package insert and performance specifications. Specimens were assayed with CD3/B4 for comparison purposes. The results of product testing demonstrated that CD3/CD56 meets all performance specifications and provides mature T (CD3+) lymphocyte values comparable to those of CD3/B4. CD3/CD56 and CD3/B4 also provide appropriate values for NK (CD3-CD56+) and B (CD19+) lymphocytes.

1. Accuracy:

Normal and abnormal whole blood specimens were collected from geographically diverse populations of males and females unselected as to race and ranging in age from 19 to 84 years. Specimens were divided, processed as lysed preparations and assayed in parallel with CD3/CD56 and CD3/B4. CD3+, CD3-/CD56+ and CD19+ percentages expressed in terms of the total lymphocyte count and absolute counts (cells/ $\mu$ L) were determined with COULTER® EPICS® XL-MCL™ flow cytometers gated on lymphocytes. White blood cell counts and 5-part differentials were obtained for all specimens.

Results analyzed in terms of minimums, maximums, means  $\pm$  1 SD, confidence intervals, regression analyses and analyses of variance demonstrated that CD3/CD56 and CD3/B4 identify and enumerate appropriate numbers of the targeted lymphocytes in whole blood specimens.

2. Linearity:

Three replicate measurements were made on a concentrated COULTER™ CYTO-TROL Cells sample serially diluted to achieve a range of CD3+ and CD3-/CD56+ lymphocyte concentrations. Samples were assayed with CD3/CD56 and analyzed on a COULTER® EPICS® XL-MCL™ flow cytometer gated on lymphocytes. Values were expressed in terms of absolute count (cells/ $\mu$ L).

Results analyzed in terms of regression and correlation analyses for recovered vs. expected absolute counts demonstrated Linearity of the assay.

3. Precision: Within Run (Intralaboratory):

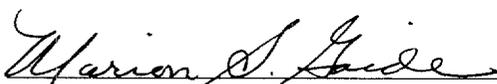
Ten replicate measurements were made for each of three levels of CD3+ and CD3-/CD56+ lymphocyte concentrations on the same day using a COULTER® EPICS® XL-MCL™ flow cytometer gated on lymphocytes. Levels were obtained by selective screening of normal whole blood specimens and assayed with CD3/CD56. Values were expressed in terms of percentage of the total lymphocyte count.

Results analyzed in terms of mean  $\pm$  1 SD and CV demonstrated Within Day (Intralaboratory) Precision of the assay.

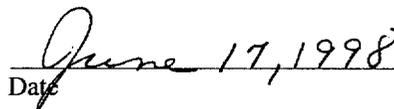
4. Precision (Interlaboratory):

Ten replicate measurements were made on the same day using different laboratories and COULTER® EPICS® XL-MCL™ flow cytometers. All measurements were made on a single normal whole blood specimen divided and assayed with CD3/CD56. Values were expressed in terms of percentage of the total lymphocyte count.

Results analyzed in terms of mean  $\pm$  1 SD and CV demonstrated Interlaboratory Precision of the assay.



Marion S. Gaide, Ph.D.  
Senior Regulatory Affairs Specialist  
Corporate Regulatory Affairs

  
Date



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

SEP 24 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Marion S. Gaide, Ph.D.  
Senior Regulatory Affairs Specialist  
Coulter Corporation  
11800 SW 147 Avenue  
Miami, Florida 33196-2500

Re: K982172/S1  
Trade Name: CYTO-STAT® CD3-FITC/CD56-RD1 Monoclonal Antibody  
Reagent with CYTO-STAT®/COULTER® CLONE® MsIgG1-  
RD1/MsIgG1-FITC Isotypic Control  
Regulatory Class: II  
Product Code: GKZ  
Dated: August 19, 1998  
Received: August 21, 1998

Dear Dr. Gaide:

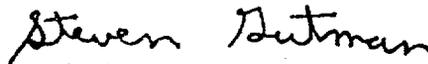
We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28,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

# INDICATIONS FOR USE

510(k) Number (if known): Not Yet Assigned

Device Name: CYTO-STAT® CD3-FITC/CD56-RD1 Monoclonal Antibody Reagent  
with  
CYTO-STAT®/COULTER® CLONE® MsIgG1-RD1/MsIgG1-FITC Isotypic Control

## Indications For Use:

CYTO-STAT® CD3-FITC/CD56-RD1 Monoclonal Antibody Reagent is a two-color fluorescent reagent comprised of two murine monoclonal antibodies. Each antibody is labeled with a different color fluorochrome. The reagent allows simultaneous identification and enumeration of total CD3+ and CD3-/CD56+ lymphocytes in whole blood by flow cytometry. An isotypic control, CYTO-STAT®/COULTER CLONE® MsIgG1-RD1/MsIgG1-FITC, is used to monitor nonspecific staining.

CYTO-STAT®/COULTER CLONE® MsIgG1-RD1/MsIgG1-PC5 Isotypic Control is a two-color fluorescent reagent comprised of two murine monoclonal antibodies. Each antibody is labeled with a different color fluorochrome. This product is intended for use as a quality control reagent to monitor the levels of nonspecific antibody binding in cell surface staining procedures which use CYTO-STAT® or CYTO-STAT®/COULTER CLONE® Monoclonal Antibody Reagents comprised of two MsIgG1 subclass monoclonal antibodies conjugated to RD1 and FITC.

CD3+ lymphocyte percentages and absolute counts may be used as aids to evaluate immune competency underlying known or unknown disease states and to monitor lymphocyte levels following organ transplantation.

To illustrate, identification of abnormal levels of CD3+ lymphocytes may aid in the diagnosis and/or prognosis of unidentified disease conditions in patients with low white blood cell counts. Measurement of CD3+ lymphocytes, in conjunction with CD4+ (inducer) and CD8+ (suppressor/cytotoxic) T lymphocytes and corresponding T4/T8 ratios, may aid in the diagnosis and/or prognosis of immunodeficiency disease such as infection with human immunodeficiency virus (HIV), the etiologic agent of acquired immunodeficiency syndrome (AIDS). Altered percentages of CD3+ lymphocytes recorded following organ (for example, kidney, heart, liver, lung) transplantation suggests T lymphocyte quantitation may be useful as an aid in monitoring these cellular populations.

NK (Natural Killer) lymphocyte populations have been functionally defined as a lymphocyte population capable of mediating non-MHC restricted cytotoxicity against targets such as certain tumor and virus-infected cells.

As part of a Two Color Lymphocyte Immunophenotyping Panel which includes the B lymphocyte reagent, CYTO-STAT®/COULTER® CLONE® CD3(IgG1)-FITC/B4-RD1, CYTO-STAT® CD3-FITC/CD56-RD1 provides the ability to comprehensively identify and enumerate an individual's major lymphocyte subsets: T, B and NK. The reagent also functions as a quality control check for a specimen in terms of total lymphocyte percentage and CD3+ lymphocyte measurements across the panel.

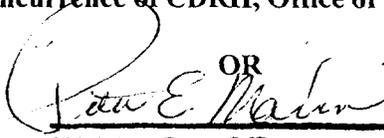
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Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use   
(Per 21 CFR 801.109)

OR

Over-The-Counter Use



(Division Sign-Off)

Division of Clinical Laboratory Devices  
510(k) Number

1987172