4/13/99

K990172

COULTER

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Coulter Electronics (A'asia) Pty. Ltd.
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Coulter electronics, Ltd.
Johannesburg, South Africa

Coulter Electronics, Ltd.
Istanbul, Turkey

Coulter Corporation
Puerto Rico

Date: January 13, 1999

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

Product:

tetraONE™ SYSTEM for EPICS® XL™ Flow Cytometry Systems
with
CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5
Monoclonal Antibody Reagent
and
CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5
Monoclonal Antibody Reagent

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

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

Telephone: 305-380-2594

Common or Usual or Classification Name: Lymphocyte Immunophenotyping System with Reagents and Software for Flow Cytometry

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

Intended Use:

The tetraONE™ SYSTEM for EPICS® XL™ Flow Cytometry Systems with CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent and CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Monoclonal Antibody Reagent combine four-color fluorescent monoclonal antibody reagents, quality control reagents, an optional absolute count reagent, and software for automated analysis of lymphocyte populations in whole blood using EPICS® XL™ flow cytometry systems with SYSTEM II™ Software. The system is intended "For In Vitro Diagnostic Use" and allows simultaneous identification and enumeration of total CD3+, total CD4+, total CD8+, dual CD3+/CD4+, dual CD3+/CD8+, CD19+, and CD3-/CD56+ lymphocyte population percentages and absolute counts. The system also provides the T4/T8 ratio when using CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent, and total lymphocyte percentage when using CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Monoclonal Antibody Reagent.

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 & CYTO-STAT®/COULTER CLONE® Mo2-RD1/KC56 (T-200)-FITC Gating Reagent

510(k) Premarket Notification: K982172

CYTO-STAT® CD3-FITC/CD56-RD1 Monoclonal Antibody Reagent with CYTO-STAT®/COULTER CLONE® MsIgG1-RD1/MsIgG1-FITC & CYTO-STAT®/COULTER CLONE® Mo2-RD1/KC56 (T-200)-FITC Gating Reagent

[**Note:** See *510(k) Premarket Notification K963263* for information pertaining to tetraONE™ SYSTEM for EPICS® XL™ Flow Cytometry Systems with CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent. The Summary of Safety and Effectiveness Information for that 510(k) Premarket Notification is not repeated here.]

[**Note:** CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5, CD3(IgG1)-FITC/B4-RD1 and CD3-FITC/CD56-RD1 will hereinafter be referred to as CD45/CD56/CD19/CD3, CD3/B4 and CD3/CD56.]

Product Comparison:
The CD45/CD56/CD19/CD3, CD3/B4 and CD3/CD56 Systems are essentially identical with respect to features and principles of operation. The New and Predicate Systems use the same, well-established, state-of-the-art technologies of immunophenotyping with monoclonal antibodies and flow cytometry to measure cellular components in whole blood via immunofluorescence analysis. Further, the intended use of the New and Predicate systems is the *same*. Also, each liquid reagent allows simultaneous identification and enumeration of more than one lymphocyte population in a single specimen using a single reagent.

The New and Predicate Systems differ in only a few respects. One difference results from the more advanced software for the tetraONE™ SYSTEM. The tetraONE™ SYSTEM software is designed to further simplify flow cytometric analysis by increasing automated modes of operation and the accuracy, precision and reliability of results. The New and Predicate Systems also differ in that the tetraONE™ SYSTEM does not require an isotypic control for monitoring and adjusting for non-specific and non-targeted monoclonal antibody binding to irrelevant cellular populations. The tetraONE™ SYSTEM software monitors and adjusts for such binding by automatically placing cursors based on the separation of positive and negative peaks. The other difference between the New and Predicate Systems is that CD45/CD56/CD19/CD3 contains a CD45 monoclonal antibody to identify a lymphocyte gate for making CD3+, CD19+ and CD3-/CD56+ measurements. CD3/B4 and CD3/CD56 require a separate reagent, CYTO-STAT®/COULTER CLONE® Mo2-RD1/KC56 (T-200)-FITC, for this purpose.

Monoclonal Antibody Conjugation:

CD45/CD56/CD19/CD3: CD45: FITC (Fluorescein Isothiocyanate); CD56: RD1 (Phycoerythrin); CD19: ECD (Phycoerythrin-Texas Red); CD3: PC5 (Phycoerythrin-Cy5)

CD3/B4 and CD3/CD56: CD3: FITC (Fluorescein Isothiocyanate); B4: RD1; CD56: RD1 (Phycoerythrin)

Product Testing:
Product testing to assess the performance of CD45/CD56/CD19/CD3 is described below. Studies were designed in line with instructions for use given in the tetraONE™ SYSTEM Guide, Package Inserts, Product Manuals, and performance specifications. Specimens were assayed with CD3/B4 and CD3/CD56 for comparison purposes. The results of product testing demonstrated that CD45/CD56/CD19/CD3 met all performance specifications and provided mature T (CD3+), B (B4+ [CD19+]) and NK [Natural Killer] (CD3-/CD56+) lymphocyte values comparable to those of CD3/B4 and CD3/CD56.

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 18 to 84 years. Specimens were divided, processed as lysed preparations and assayed in parallel with CD45/CD56/CD19/CD3, CD3/B4 and CD3/CD56. CD3+, CD19+ and CD3-/CD56+ percentages expressed in terms of the total lymphocyte count and absolute count (cells/μL) were determined with COULTER® EPICS® XL-MCL™ flow cytometers (data was gated on lymphocytes). White blood cell counts and 5-part differentials were obtained for all specimens.

   Results analyzed in terms of minimums, maximums, means ± 1 SD, confidence intervals, regression analyses and analyses of variance demonstrated that CD45/CD56/CD19/CD3, CD3/B4 and CD3/CD56 identify and enumerate essentially identical numbers of the targeted lymphocytes in whole blood specimens.

2. Linearity:
Three replicate measurements were made on a concentrated COULTER™ CYTO-TROL™ Control Cells sample serially diluted to achieve a range of CD3+, CD19+ and CD3-/CD56+ lymphocyte concentrations. Samples were assayed with CD45/CD56/CD19/CD3 and analyzed on a COULTER® EPICS® XL-MCL™ flow cytometer (data was gated on lymphocytes). Values were expressed in terms of absolute count (cells/μL).

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

3. Precision: Within Run (Intralaboratory):
Ten replicate measurements were made for each of three levels of CD3+, CD19+ and CD3-/CD56+ lymphocyte concentrations using a COULTER® EPICS® XL-MCL™ flow cytometer (data was gated on lymphocytes). Normal whole blood specimens were screened and selected to generate the various levels and assayed with CD45/CD56/CD19/CD3. Values were expressed in terms of percentage of the total lymphocyte count.

Results analyzed in terms of mean ± 1 SD and CV demonstrated Within Run (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 (data was gated on lymphocytes). All measurements were made on a single normal whole blood specimen divided and assayed with CD45/CD56/CD19/CD3. Values were expressed in terms of percentage of the total lymphocyte count.

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

Marion S. Gaide

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

January 13, 1999
Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR 13 1999

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

Re: K990172
Trade Name: tetraONE™ SYSTEM for EPICS® XL™ Flow Cytometry Systems with CYTO-STAT® tetraCHROME™ CD45-FITC/4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent and CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Monoclonal Antibody Reagent
Regulatory Class: II
Product Code: GKZ
Dated: January 13, 1999
Received: January 19, 1999

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.

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

INDICATIONS FOR USE

510(k) Number (if known): ~~Not Yet Assigned~~ K990172

Device Name: tetraONE™ SYSTEM for EPICS® XL™ Flow Cytometry Systems
with
CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent
and
CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Monoclonal Antibody Reagent

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Indications For Use:

The tetraONE™ SYSTEM for EPICS® XL™ Flow Cytometry Systems with CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent and CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Monoclonal Antibody Reagent combine four-color fluorescent monoclonal antibody reagents, quality control reagents, an optional absolute count reagent, and software for automated analysis of lymphocyte populations in whole blood using EPICS® XL™ flow cytometry systems with SYSTEM II™ Software. The system is intended "For In Vitro Diagnostic Use" and allows simultaneous identification and enumeration of total CD3+, total CD4+, total CD8+, dual CD3+/CD4+, dual CD3+/CD8+, CD19+, and CD3-/CD56+ lymphocyte population percentages and absolute counts. The system also provides the T4/T8 ratio when using CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 Monoclonal Antibody Reagent, and total lymphocyte percentage when using CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 Monoclonal Antibody Reagent.

CD3+, CD4+, CD8+, and/or CD19+ 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+, CD4+, CD8+, and/or CD19+ lymphocytes may aid in the diagnosis and/or prognosis of unidentified disease conditions in patients with altered white blood cell counts. Altered percentages of CD3+, CD4+, CD8+, and/or CD19+ lymphocytes recorded following organ (for example, kidney, heart, liver, lung) transplantation suggests T (CD3+, CD4+, CD8+) and/or B (CD19+) lymphocyte measurements may be useful as aids in monitoring these cellular populations.

Identification of abnormal levels of CD4+ immunodeficiency might also aid in the diagnosis and/or prognosis of immunodeficiency disease. For example, infection with human immunodeficiency virus (HIV), the etiologic agent of acquired immunodeficiency syndrome (AIDS), results in profound immunosuppression due predominantly to a selective depletion of the CD4+ lymphocytes that express the receptor for the virus, which is associated with the CD4+ antigen. Progressive clinical and immunologic deterioration generally correlated with a falling CD4+ lymphocyte count.

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

CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 provides the ability to comprehensively identify and enumerate an individual's major lymphocyte subsets: T, B and NK. Used as a four color Lymphocyte Immunophenotyping Panel, CYTO-STAT® tetraCHROME™ CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5 and CYTO-STAT® tetraCHROME™ CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5 also function as a quality control check for a specimen in terms of CD3+ lymphocyte measurement reproducibility within the Panel.

(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) 510i4use

(Division Sign-Off) OR Over-The-Counter Use

Division of Clinical Laboratory Devices

510(k) Number K990172