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JUL 22 1996

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Date: April 1, 1996

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

Product: COULTER® STKS Analyzer with CD4 and CD8 Lymphocyte Analysis

Company: Coulter Corporation
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Common or Usual or Classification Name: Lymphocyte Immunophenotyping Using Monoclonal Antibody Reagents and Automated Differential Cell Counters

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

Intended Use: COULTER STKS Analyzer with CD4 and CD8 Lymphocyte Analysis is a complete system consisting of reagents, sample processing accessories, instrument and software. The system is intended "For In Vitro Diagnostic Use" to identify and enumerate CD4+ and CD8+ T lymphocyte percentages and absolute counts in whole blood using either of two versions of a quantitative, automated hematology analyzer and leukocyte differential counter: COULTER® STKS Analyzer or COULTER® STKS Analyzer with Reticulocyte Analysis. The system is also intended to provide the CD4/CD8 ratio, a complete blood count (CBC) and a white blood cell (WBC) differential. Reticulocyte percentage and absolute count are only available if using the COULTER® STKS Analyzer with Reticulocyte Analysis.

Substantial Equivalence: 510(k) Premarket Notification: K922745
CYTO-STAT®/COULTER CLONE® CD3(IgG1)-FITC/T4-RD1
Monoclonal Antibody Reagent (CD3/CD4)

510(k) Premarket Notification: K922744
CYTO-STAT®/COULTER CLONE® CD3(IgG1)-FITC/T8-RD1
Monoclonal Antibody Reagent (CD3/CD8)

510(k) Premarket Notification: K885093
COULTER® STKS Analyzer

510(k) Premarket Notification: K932030
COULTER® STKS Analyzer with Reticulocyte Analysis

Product Differences: The subject hematologic method, STKS with CD4 and CD8 Analysis, and the comparator method, CD3/CD4 and CD3/CD8 by Flow Cytometry, necessarily differ in some respects as a result of the technologies used to achieve the *same* intended use. The primary differences are 1) instrumentation; 2) software versus reagent controls for lymphocyte gating and non-targeted monoclonal antibody binding to irrelevant cellular populations; 3) Mab conjugation; and 4) final product form of the reagents. With respect to instrumentation, it is noteworthy that the flow cytometric method requires both a flow cytometer and the same instrument used in the subject hematologic method.

Product Testing: Product testing to assess the performance of STKS with CD4 and CD8 Analysis is described below. Studies were designed in line with performance specifications and instructions for use provided in the product manuals and package inserts. Specimens were assayed with CD3/CD4 and CD3/CD8 by Flow Cytometry for comparison purposes. The results of product testing demonstrated that STKS with CD4 and CD8 Analysis met all performance specifications and provided CD4+ and CD8+ T lymphocyte values substantially equivalent to those obtained with the comparator method, CD3/CD4 and CD3/CD8 by Flow Cytometry.

1. Accuracy:
   Normal and abnormal (i.e., HIV, organ transplant, cancer, autoimmune disease) whole blood specimens were collected from a geographically diverse population of males and females unselected as to race and ranging in age from 18 to 85 years. The specimens were divided and the samples processed and analyzed using either 1) COULTER™ CD4 or CD8 Cyto-Spheres™ Reagent on a STKS; or 2) CD3(IgG1)-FITC/T4-RD1 or CD3(IgG1)-FITC/T8-RD1 on an EPICS XL-MCL or EPICS Profile II flow ctyometer (gated on lymphocytes). A white blood cell count and 5-part differential were obtained for each whole blood specimen using the same STKS as in the subject hematologic method.

   CD4+ and CD8+ T lymphocyte percentages and absolute counts obtained with CD4 and CD8 Cyto-Spheres Reagents on the STKS represented total CD4 and total CD8 values. Values obtained with CD3(IgG1)-FITC/T4-RD1 and CD3(IgG1)-FITC/T8-RD1 on the EPICS flow cytometers represented dual-positive, CD3+/CD4+ and CD3+/CD8+ values. Values were expressed in terms of percent of the total lymphocyte count and as absolute count (cells/μL). Flow cytometric values were corrected for lymphocyte purity (Lymphocyte Gate Limits: lymphocyte recovery ≥ 90%; lymphocyte purity ≥ 85%).

   Results analyzed in terms of minimums, maximums, means ± 1 SD, regression and correlation analyses, and analyses of variance demonstrated that STKS with CD4 and CD8 Analysis and CD3/CD4 and CD3/CD8 by Flow Cytometry identify and enumerate essentially identical numbers of lymphocytes in whole blood specimens.

2. Linearity:
   Five replicate measurements were made at each of five individually prepared dilutions of a concentrated normal venous whole blood specimen to achieve a range of CD4+ or CD8+ T lymphocyte concentrations. Samples were processed with CD4 or CD8 Cyto-Spheres Reagent and analyzed on the STKS. Values were expressed in terms of absolute count (cells/μL).

   Results analyzed in terms of regression analyses and 95% confidence intervals of the data points for recovered versus expected absolute counts (cells/μL) demonstrated linearity of the assays.

3. Within Run (Intralaboratory) Precision:
   Ten replicate measurements were performed for each of three levels of CD4+ and CD8+ T lymphocyte concentrations on a STKS on the same day. A separate venous whole blood specimen was used for each CD4 or CD8 level and processed with CD4 or CD8 Cyto-Spheres Reagent prior to analysis. Values were expressed in terms of percent of the total lymphocyte count and as absolute count (cells/μL).

Results analyzed in terms of means ± 1 SD and CVs demonstrated within run (intralaboratory) precision of the assays.

5. Between Run (Run-to-Run) Precision:
Duplicate measurements were performed for CD4+ and CD8+ T lymphocyte concentrations on a STKS. A separate venous whole blood specimen was used to make both measurements. The specimen was divided and each half processed with CD4 or CD8 Cyto-Spheres Reagent prior to analysis. Values were expressed in terms of percent of the total lymphocyte count and as absolute count (cells/μL).

Results analyzed in terms of minimums, maximums, means, and mean differences between runs ± 1 SD demonstrated between run (run-to-run) precision of the assays.

6. Interlaboratory Precision:
Studies were performed for each of three levels of CD4+ and CD8+ T lymphocyte concentrations on the same day by three technicians using three different STKS instruments. Replicate measurements were made on each STKS. The same venous whole blood specimen was used to make all replicate measurements on all three instruments for a particular CD4 or CD8 percentage or absolute count level. The specimen was divided into thirds and each third processed with CD4 or CD8 Cyto-Spheres Reagent prior to analysis. Values were expressed in terms of percent of the total lymphocyte count and as absolute count (cells/μL).

Results analyzed in terms of means ± 1 SD and CVs demonstrated within run (intralaboratory) precision of the assays.

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April 1, 1996
Date

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