

K970326

Attachment B*Summary of Safety and Effectiveness*

NOV 21 1997

Submitter Information (21 CFR 807.92(a)(1))

Submitter: Becton Dickinson Immunocytometry Systems
2350 Qume Drive
San Jose, CA 95131-1807

Contact: Anna Longwell, Esq.
Director, Regulatory Affairs - Corporate
(408) 954-2254

Summary date: November 19, 1997

Name of Device and Classification (21 CFR 807.92(a)(2))

Name: Becton Dickinson TriTEST™ reagent CD3 FITC/CD8 PE/CD45 PerCP; TRUCOUNT™ Absolute Count Tubes

Classification: Class II

Predicare Device (21 CFR 807.92(a)(3))

The BDIS TriTEST™ CD3 FITC/CD8 PE/CD45 PerCP reagent, when used to enumerate percentages of lymphocytes is substantially equivalent to IMK-Lymphocyte Tube E that was cleared to market under 510(k) K913192. When the TriTEST reagent is used with TRUCOUNT Absolute Count Tubes, it is substantially equivalent to the BDIS FACSCount system cleared under 510(k) K933486.

Description of the Device (21 CFR 807.92(a)(4))

The BDIS TriTEST CD3 fluorescein isothiocyanate (FITC)/CD8 phycoerythrin (PE)/CD45 peridinin chlorophyll protein (PerCP) reagent is a three-color, direct immunofluorescence reagent for identifying and enumerating percentages of T lymphocytes (CD3+) and T-suppressor/cytotoxic (CD3+CD8+) cells in erythrocyte-lysed whole blood (LWB). When used with TRUCOUNT Absolute Count Tubes, the product will yield absolute counts in cells/μL. The Becton Dickinson TriTEST/TRUCOUNT system for immunophenotyping consists of a flow cytometer (either from BDIS or from another manufacturer), conjugated monoclonal reagent (TriTEST CD3 FITC/CD8 PE/CD45 PerCP) and TRUCOUNT Absolute Count Tubes.

The process to obtain lymphocyte subset percentages includes: 1) obtaining a whole blood sample, 2) cell-surface antigen staining with three-color monoclonal antibody reagents, 3) erythrocyte lysis, and 4) flow cytometric acquisition and analysis of list mode data. Analysis involves computing the

Summary of Safety and Effectiveness

ratio of reagent-positive events to the CD45 positive events, and expressing the ratio as a percentage.

To obtain absolute counts, the TriTEST reagent and whole blood are added directly to an Absolute Count Tube prior to lysis. The remaining process, until analysis, is identical to that for percentages. Analysis for absolute counts requires that an additional region, the bead region, be identified and the events in this region counted. The proportion of reagent positive events to bead events (P) is computed. The absolute count is $P \times (\text{beads/pellet}) / (\text{volume of blood sample})$.

When monoclonal antibody reagents are added to human whole blood, the fluorochrome-labeled antibodies bind specifically to antigens on the surface of leukocytes, thus identifying lymphocyte populations. The patient blood sample is added to the counting bead pellet and is treated with fluorochrome-labeled antibodies and the erythrocytes are lysed with FACS® Lysing Solution. The flow cytometer is set up so that cell populations for most samples occupy approximately the same region of fluorescence space. The sample is then introduced into the flow cytometer and the stained cells and beads fluoresce when excited by a laser beam.

The three-color reagent permits identification of lymphocyte subsets using fluorescence gating instead of forward scatter gating. This three-color reagent allows direct gating on the CD45-positive population using a combination of fluorescence and side scatter parameters. By gating on the CD45-positive population, a maximum number of lymphocytes may be captured in the gate and non-lymphocyte contamination may be minimized.

Intended Use (21 CFR 807.92(a)(5))

For in vitro diagnostic use to identify and enumerate percentages and absolute counts of CD3+ and CD3+CD8+ lymphocytes in blood.

Indications for Use

- For use with any flow cytometer equipped with a 488 nm laser and capable of detection in the ranges: 515-545 nm, 562-607 nm, and > 650 nm
- For use with erythrocyte lysed whole blood
- For use with or without an isotype control
- To characterize and monitor forms of autoimmune diseases, such as lupus
- To characterize and monitor congenital or acquired immunodeficiencies, such as SCID or AIDS

Summary of Safety and Effectiveness

Clinical Utility

The determination of CD3+ and CD3+CD8+ lymphocytes has been found useful in monitoring some forms of immunodeficiency and autoimmune disease.

Comparison to Predicate Device (21 CFR 807.92(a)(6))

The CD3 FITC/CD8 PE/CD45 PerCP TriTEST reagent, when used to enumerate percentages of lymphocytes, is substantially equivalent to the IMK-Lymphocyte Tube E that was cleared to market under 510(k) K913192. When used with TRUCOUNT Absolute Count Tubes to enumerate absolute counts, it is substantially equivalent to the FACSCOUNT System (K933486) for CD3+ and CD3+CD8+. Both the TriTEST product and the predicate devices yield equivalent results for the same analytes, and both are intended for use as an in vitro diagnostic test using a flow cytometer-based instrument and recommended computer hardware and software. The products differ in the steps used to determine analysis gates to identify the lymphocyte population.

Performance Data (21 CFR 807.92(b)(2))

Performance of the product was established by testing at Cleveland Clinic, Johns Hopkins Hospital, Institute of Tropical Medicine, University of North Carolina, and at Becton Dickinson Immunocytometry Systems laboratories in San Jose, California.

Several studies were performed:

- Accuracy was determined by comparison to both IMK-Lymphocyte Tube E and the FACSCOUNT system. Accuracy data demonstrated the TriTEST and TriTEST/TRUCOUNT product's equivalence to IMK-Lymphocyte Tube E and FACSCOUNT, respectively.
- Use of isotype control was studied. Data were analyzed for percent CD3+ and percent CD3+CD8+ first using a control to set gates and markers and then using only the stained sample to set gates and quadrant markers. Data indicated that the reagent may be used with or without an isotype control.
- Reference range studies were performed. Many variables, such as sex, age and geographical location may influence the reference range. Each site must determine its own reference range.
- A stability study was conducted to assess the time effect relating to age of blood (time-from-draw) and the time effect relating to the age of the stain (time-from-sample preparation), as well as the

Summary of Safety and Effectiveness

combined effect of both. Stability was determined for both percentages and absolute counts. Stability was determined for whole blood samples at 6, 24, 48 and 72 hours post draw. Additionally, stability was measured for stained samples at 6 and 24 hours from time of staining. A combination of the two, time from draw plus time from sample preparation, was studied. Results indicated that either 1) staining the samples within 24 hours of draw and analyzing samples within 24 hours of staining or alternatively, 2) staining the samples with 48 hours of draw and analyzing them within 6 hours is recommended.

- Within-specimen reproducibility was performed at BDIS and at three clinical sites for both percentage enumeration and absolute counts. Results demonstrated acceptable within-sample reproducibility.
- Linearity was determined using blood samples from three normal donors diluted to five concentrations, ranging from 16,700 to 200 lymphocytes/ μL and from 31,000 to 2,500 WBC/ μL . Results indicate the product gives linear results over this range.
- Cross reactivity of these clones is reported in the literature. Conjugation and product formulation have not changed their specificity.
- Results from a cross platform reproducibility study indicated 1) for absolute count results there was a small (< 20%) non-zero bias, but good correlation between results on a Becton Dickinson flow cytometer versus a Coulter cytometer. Therefore, users will be advised that they must validate performance characteristics for absolute counts. 2) For determining percent positive results or absolute counts, TriTEST reagent with TRUCOUNT Absolute Count Tube may be used with flow cytometers not made by Becton Dickinson.

Performance Data - Conclusions (21 CFR 807.92(b)(3))

The results of the clinical studies demonstrate that the device is as safe and effective as the predicate devices.



Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Ms. Anna Longwell, Esq.
Director, Regulatory Affairs - Corporate
Becton Dickinson Immunocytometry Systems
2350 Qume Drive
San Jose, California 95131-1807

NOV 21 1997

Re: K970326
Trade Name: Becton Dickinson TriTEST™ Reagent CD3 FITC/CD8
PE/CD45 PerCP; TRUCOUNT™ Absolute Count Tubes
Regulatory Class: II
Product Code: GKZ
Dated: August 28, 1997
Received: September 2, 1997

Dear Ms. Longwell:

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 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 requirement, 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.

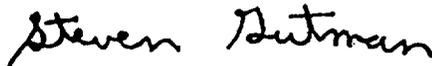
Page 2

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 at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/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

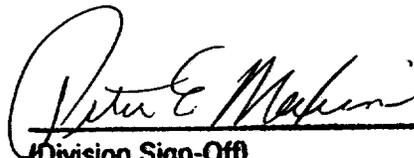
Attachment A
TriTEST CD3/CD8/CD45 with TRUCOUNT Control Beads & Absolute Count Tubes
K970326

Indications for Use Statment

- For use with any flow cytometer equipped with a 488 nm laser and capable of detection in the ranges: 515-545 nm, 562-607 nm, and > 650 nm
- For use with erythrocyte lysed whole blood
- For use with or without an isotype control
- To characterize and monitor forms of autoimmune diseases, such as lupus
- To characterize and monitor congenital or acquired immunodeficiencies, such as SCID or AIDS

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

Concurrence of CDRH, Office of Device Evaluation (ODE)



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

Prescription Use _____
(Per 21 CFR 801.109)

OR

Over-The-Counter Use _____

(Optional Format 1-2-96)