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### 13. 510(k) Summary of Safety and Effectiveness Information Supporting a Substantially Equivalent Determination

The following information as presented in the Premarket Notification 510(k) for the Cell-Dyn® 3500R System Hematology Analyzer constitutes data supporting a substantially equivalent determination.

Substantial equivalence has been demonstrated between the Cell-Dyn 3500R System and the Becton Dickinson FACScan™ Flow Cytometer RetiCOUNT™ Reticulocyte Enumeration Software, Premarket Notification #K872166/A.

#### Intended Use

The Cell-Dyn 3500R System is a multi-parameter, automated hematology analyzer designed for in vitro diagnostic use in clinical laboratories.

#### Device Description

The Cell-Dyn 3500R System is a table-top analyzer consisting of the main analyzer, data station, and printer. The instrument has two sampling modes: Open Sample Aspiration Mode and Closed Sample Aspiration Mode. The Cell-Dyn 3500R System is available with a manual Closed Sampler (3500R, CS) or an automated Sample Loader (3500R, SL). The instrument has the capability of processing a whole-blood specimen to provide a CBC, including a 5-part WBC differential for a total of 22 parameters. The 22 reportable parameters are as follows:

White blood cells (WBC), red blood cells (RBC), platelets (PLT), percent of neutrophils (%N), number of neutrophils (NEU), percent of lymphocytes (%L), number of lymphocytes (LYM), percent of monocytes (%M), number of monocytes (MONO), percent of eosinophils (%E), number of eosinophils (EOS), percent of basophils (%B), number of basophils (BASO), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW) mean platelet volume (MPV).

In addition, the Reticulocyte software allows the instrument to process stained, diluted specimens in the Open Mode to provide a Reticulocyte percent (RETIC %), and number of Reticulocytes Absolute Number (Retic Abs). A Retic Scatter Index is provided for Laboratory Use Only and is not reportable.

### Principles of Operation

The Reticulocyte software is designed to configure the instrument to process stained, diluted whole blood specimens. When the Reticulocyte Package is turned ON, the instrument automatically selects the appropriate configuration file and adjusts the instrument settings to the values in this file. This configuration is retained until the Reticulocyte Package is turned OFF. The instrument then returns to the standard hematology settings.

The Cell-Dyn<sup>®</sup> 3500R method uses the thiazine dye New Methylene Blue N. The Reticulocyte assay is performed in the WOC channel of the instrument. Sample preparation is performed manually by adding 20  $\mu$ L of blood to a tube of Cell-Dyn Reticulocyte Reagent. At room temperature, staining of the reticulum is complete within approximately 15 minutes. The stained sample is aspirated in the Open Mode.

After the stained sample is aspirated, it is diluted approximately 50 fold with Sheath Reagent. Once diluted with Sheath, the RBCs sphere due to the influence of the nonionic detergent incorporated into the staining solution. Sphering is necessary to eliminate optical orientational noise that would otherwise be introduced into the scatter measurements. The usual lytic action of the Sheath Reagent is prevented by electrolytes contained in the staining solution and the lack of the usual incubation period used in the channel during WBC analysis. In addition, the high New Methylene Blue concentration in the staining reagent exerts a stabilizing effect on RBCs. During data acquisition, 20 and 90 degree scatter are collected. The 0 degree threshold is set high enough to exclude most platelets. Histogram data are used to differentiate Reticulocytes, mature RBCs, platelet clumps and nucleated cells. Reticulocytes have similar 10 degree scatter to mature RBCs, but differ from them by exhibiting greater 90 degree scatter. Reticulocytes are reported in percent. If an RBC count is available, the instrument will automatically calculate the Reticulocyte Absolute Number. The RBC value may be automatically obtained from the standard Hematology Data Log, or manually entered by the operator.

A Reticulocyte Scatter Index is a calculation in which Reticulocytes are divided into three categories (low, middle, and high), depending on the amount of scatter they produce. This classification relates to cell maturity, with the more immature cells producing the higher scatter. The Reticulocyte Scatter Index is displayed on the RETIC SCATTER PROFILE screen and is for laboratory use only.

### Similarities and Differences

The Cell-Dyn 3500R System Reticulocyte Method and the Becton Dickinson FACScan<sup>™</sup> Reticulocyte Method are similar in that they both provide quantitation of Reticulocytes in K<sub>3</sub>EDTA- anticoagulated human whole blood. They use optical light scatter to provide a Reticulocyte percent. Both systems provide data input by keyboard and output to a data

display computer screen and printer. Both systems utilize a microprocessor for system control, data acquisition and data reduction. Both systems require off-line dilution and staining of whole blood with a reagent to obtain the Reticulocyte parameters. Finally, both systems aspirate the prepared specimen into the instrument for automated processing.

The two systems are dissimilar in that the Cell-Dyn® 3500R System uses reagent containing New Methylene Blue and a sphering agent, while the Becton Dickinson FACScan™ Reticulocyte Method uses Thiazol Orange reagent (no sphering of RBCs). Additionally, the CELL-DYN 3500R uses Optical Laser Light Scatter while the BD FACScan uses Fluorescence and Light Scatter technology. The Cell-Dyn 3500R System allows for bar code reader input not available on the Becton Dickinson FACScan.

#### Equivalency Data

The data compiled to support the claim that the Cell-Dyn 3500R System is substantially equivalent to the Becton Dickinson FACScan includes accuracy, precision, linearity, and carryover.

The data supports the claim that the Cell-Dyn 3500R System is substantially equivalent to the Becton Dickinson FACScan Flow Cytometer RetiCOUNT™ Reticulocyte Enumeration Kit. The accuracy, precision and linearity data shows performance to manufacturer's specifications.

#### Conclusion

The CELL-DYN 3500R System shows an evolution of the technology used to enumerate Reticulocytes that is similar to the technology used on the Becton Dickinson FACScan Flow Cytometer RetiCOUNT Reticulocyte Enumeration Kit.

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