MAY 30 1997

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Appendix C

510(k) Summary of Substantial Equivalence
MicroVision Medical Systems, Inc.
(MD_x 2000 Digital Analyzer)

This summary of substantial equivalence information is furnished in accordance with 21 CFR 807.92 as follows:

21 CFR 807.92(a):

21 CFR 807.92(a)(1):

* Submitter's name and address:

MicroVision Medical Systems, Inc.
33171 Paseo Cerveza
San Juan Capistrano, California
92675

* Submitter's telephone number: (714) 443-3366

* Contact person:

Mr. Michael Schneider
MicroVision Medical Systems, Inc.
33171 Paseo Cerveza
San Juan Capistrano, California
92675

* Date this 510(k) summary was prepared: March 4, 1997

21 CFR 807.92(a)(2):

* Trade/proprietary name of the device: MD_x 2000 Digital Analyzer

* Classification name: Automated microscopy cell locating workstation

21 CFR 807.92(a)(3): Legally marketed predicate devices to which substantial equivalence is claimed:

* Nikon *Biostation*

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* Intelligent Imaging, Inc. Model IMS-200 automated cell locating device.

* Sigma Diagnostics' alkaline phosphatase reagent system *FAST VIOLET B SALT* catalog No. 85-1.

21 CFR 807.92(a)(4): Description of the device that is the subject of this premarket notification:

The MD_X 2000 Digital Analyzer is an automated intelligent microscope cell locating device that detects, by color and pattern recognition techniques, cells stained with alkaline phosphatase reagent system *FAST VIOLET B SALT*. The system consists of software resident in computer memory and includes keyboard, color monitors, microscope, printer, and an automatic slide handling and scanning mechanism controlled and operated by a health care professional.

21 CFR 807.92(a)(5): Intended use and labeled indications for use:

Automated scanning microscopy work station for histological identification of the enzyme leucocyte alkaline phosphatase in neutrophilic granulocytes to differentiate:

* Granulocytic leukemia; a malignant disease characterized by excessive overgrowth of granulocytes in bone marrow, and

* Reactions that resemble true leukemia, such as those occurring in severe infections.

21 CFR 807.92(a)(6): Technological characteristics:

The design, construction, energy source, and other characteristics of the MD_X 2000 candidate device are considered to be substantially equivalent to the relevant features of the predicate devices. A summary of the

technological characteristics of the MD_x 2000 candidate device in comparison to those of the predicate devices follows:

* **Reagent system:** The reagent system is identical to Sigma Diagnostics' alkaline phosphatase reagent system *FAST VIOLET B SALT*, catalog No. 85-1.

* **Method of cell detection:** The same as the predicate devices; i.e., colorimetric pattern recognition by microscopic examination of prepared cells by size, shape, hue, and intensity as observed by an automated computer controlled microscope and/or by visual observation by a health care professional.

* **System components:** The system components comprising the candidate device are the same as those in the Intelligent Medical Imaging, Inc. and/or Nikon predicate devices; i.e., computer, microscope, color monitor(s), keyboard, printer, automatic loading and positioning of prepared sample on microscope stage, automatic focusing of microscope, and automatic storage of acquired images.

* **Energy source:** The electrical service is 120 VAC 60 HZ, the same as the Intelligent Medical Imaging, Inc. and Nikon predicate devices.

21 CFR 807.92(b): 510(k) summaries for those premarket submissions in which a determination of substantial equivalence is also based on performance data shall contain the following information:

21 CFR 807.92(b)(1): Brief discussion of the non-clinical tests submitted, referenced, or relied upon in this premarket notification submission:

There were no nonclinical tests submitted, referenced, or

relied upon in this submission.

21 CFR 807.92(b)(2): Brief discussion of the clinical tests submitted, referenced, or relied upon in this premarket notification submission:

This premarket notification relies on both referenced literature and clinical tests performed. A brief discussion of the results and conclusions of the performance of naphthol as phosphate as a reagent in the cytochemical demonstration of alkaline phosphatase activity on thin smears of human blood is first discussed. This discussion is followed by a brief discussion of the results and conclusions from clinical trials conducted:

1. Referenced literature:

Cytochemistry of Leukocyte Alkaline Phosphatase; Use of Complex Naphthol as Phosphates in Azo Dye-Coupling Technics.

Leonard S. Kaplow, M.D.
With the technical assistance of Mrs. Charlotte Ladd, M.T. (ASCP)
Department of Pathology, Medical College of Virginia

The American Journal of Clinical Pathology
Vol. 39, No. 5, pp. 439-449, May 1963

Summary:

Upon preparation of blood smear slides as described in the literature, examination of negative and positive controls at 100X magnification disclosed the theoretical sites of enzyme activity were represented by distinct pink granulations varying in color from very pale pink to a brilliant ruby red. The precipitation took the form of minute dots or larger granules or rod shaped structures. The contrast of the red cytoplasm with the blue-black nuclei was striking. Localization appeared far more precise, although similar in pattern, than that seen with older technics.

A scoring procedure was established from ratings from zero

to 4+ on the basis of quantity and intensity of precipitated dye within the cytoplasm of the cells. The sum of the reading of 100 observed cells was regarded as the "score" for a given blood smear. The ratings were based on the number, size, and intensity of staining of the granules.

Conclusion:

The value of assessing leukocyte alkaline phosphatase activity as an aid in the diagnosis of certain hematologic diseases is now well established. Such assessment is particularly valuable in distinguishing chronic granulocytic leukemia from leukemoid reactions and from other myeloproliferative diseases as well as in distinguishing polycythemia vera from secondary polycythemia.

Cytochemical technics are suitable staining methods and have been used in many laboratories as routine procedures. By means of these staining methods and in conjunction with a "scoring" procedure, it is possible to obtain a numerical representation of the degree of enzyme activity of leukocytes on a given blood smear and thus to compare enzyme activity disease states with the normal.

2. Clinical trials:

* Description of clinical sites and devices used:

The results of clinical trials were used to obtain data to compare the analytical performance, accuracy, and precision of the MD_x 2000 candidate device to that of the predicate devices. The clinical trials were conducted in accordance with a written MicroVision Medical Systems, Inc. protocol and were conducted on a model MD_x 2000 device (three different devices; not the same device) at three different sites.

*** Description of the scientific methods used:**

The following characteristics of the clinical trials

conducted were carefully selected to help ensure the clinical trials were objective and statistically valid:

- The number of clinical sites
- The quantity of patient samples per site
- The quantity of stained smears examined
- The number of times a smear stained slide was examined
- The number of qualified medical technologists examining the slides
- The design of the double blind study
- The number of times the same "control" slide(s) was run on each of the three devices to determine the expected value for each "control" slide
- The number of times the same "control" slide(s) was run on each of the three devices to establish the standard deviation of the neutrophil alkaline phosphatase (NAP)
- Running the "control" slide(s) on each device at the beginning and end of each daily run on each of the three MD_x 2000 candidate devices to evaluate the consistency of the devices

*** Methods of statistical analysis:**

Statistical analyses of the data included:

- The use of parametric and/or non-parametric statistical methods to analyze the data
- Pooling/combining data from the three clinical sites only if statistically justified based on equivalent results

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- Assessment of bias (accuracy) and imprecision as generally described in the National Committee for Clinical Laboratory Standards (NCCLS) documents EP9-A and EP5-T

- Bias of the MD_x 2000 candidate device compared with the predicate devices was based on the use of linear regression comparison of the averages of the devices versus the average manual count.

- Statistical assessment of the estimated bias using the appropriate t-test.

- Analysis of variance of the data to estimate the variance contributions of the technologists, slides, replication, and other variables.

21 CFR 807.92(b)(3): The conclusion drawn from the non-clinical and/or clinical tests that demonstrate the MD_x 2000 candidate device is as safe, is as effective, and performs as well or better than the predicate devices:

The MD_x 2000 Digital Analyzer candidate device was found to provide neurophilic alkaline phosphatase (NAP) measurements that had similar precision within site over 125 patients tested at 3 clinical sites. Use of the candidate device provided more between-site consistency in reported results than that for the comparative Sigma NAP kit manual method, and eliminated the considerable between-technologist variability that occurred at each of the study sites.

The accuracy of the MD_x 2000 Digital Analyzer candidate device data was assessed by method comparison linear regression against the manual method. At two study sites, the results were directly comparable with little clinical bias between the two methods. At one of the study sites, there was considerable negative bias of the candidate device against the manual method, but this was consistent and characterizable, and is assumed to be removable by adjustment (calibration) of the local reference range.

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The candidate device was proved comparable to the candidate devices at the other sites by cross-validation with control slides. The difference in bias relationship at the different sites was not unanticipated, based on the labeling of the Sigma Diagnostics predicate device/kit and the National Committee for Clinical Laboratory Standards publication H-22P, *Histological Method for Leukocyte Alkaline Phosphatase*, that warn of considerable subjective differences in technologist and site expected values.

.... END OF 510(k) SUMMARY ....

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. Michael Schneider
Official Correspondent
MicroVision Medical Systems, Inc.
33171 Paseo Cerveza
San Juan Capistrano, California 92675

MAY 30 1997

Re: K970824
Trade Name: MD_x 2000 Digital Analyzer
Regulatory Class: II
Product Code: JOY
Dated: March 5, 1997
Received: March 6, 1997

Dear Mr. Schneider:

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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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 at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/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

510(k) number (if known): Unknown; not yet assigned by FDA.

Device name: Model MD_X 2000 Digital Analyzer

Indications for use for the device:

Automated scanning microscopy work station for histological identification of the enzyme leucocyte alkaline phosphatase in neutrophilic granulocytes to differentiate:

* Granulocytic leukemia, a malignant disease characterized by excessive overgrowth of granulocytes in bone marrow, and

* Reactions that resemble true leukemia, such as those occurring in severe infections.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K970824

(Please do not write below this line. Continue on another page if needed.)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ or Over-the-Counter Use ____
(Per 21 CFR 801.109)

(Optional format 1-2-96)

K2C