



1196 Borregas Avenue  
Suite 200  
Sunnyvale, CA 94089

**SECTION 6  
510(k) SUMMARY**

**JUL 30 2008**

This 510(k) Summary is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is **K080896**.

**807.92 (a)(1):**      **Name:**                      Pathwork® Diagnostics, Inc.  
                         **Address:**                      1196 Borregas Avenue  
                                                              Suite 200  
                                                              Sunnyvale, CA 94089  
  
                         **Phone:**                              408-400-0828 x103  
                         **Contact:**                              Glenda G. Anderson  
                                                              Founder and CTO

**807.92 (a)(2): Device Name – trade name and common name, and classification**

**Trade name:**                      Pathwork® Tissue of Origin Test  
  
**Common name:**                      Microarray and software system kit for gene expression-based  
                                                              diagnostics  
  
**Classification:** 21 CFR § 862.3100, Amphetamine Test System  
                                                              Class II, Product Code NVI (diagnostic software)

**807.92 (a)(3): Identification of the legally marketed predicate device**

The Tissue of Origin Test is substantially equivalent to the BioPlex 2200 Medical Decision Support software (MDSS) on the BioPlex 2200 Multi-Analyte Detection System, (Bio-Rad Laboratories, Hercules, CA), cleared under premarket notification K043341 on October 27, 2005.

**807.92 (a)(4): Device Description**

The Pathwork® Tissue of Origin Test is a microarray and analytics “kit” that quantifies the similarity of tumor specimens to 15 cancer types representing 60 morphologies. Frozen biopsy specimens are processed by the clinical laboratory as described in the User Guide. In brief, mRNA is extracted, amplified, labeled and hybridized to the Pathchip® microarray, which is then scanned using one of the instrument systems validated for use with this test. The resulting data file is transmitted via secure internet transfer protocol to the Pathwork® System Software for data quality control and analysis. Test results are available for clinical interpretation via a secure password protected website.

**Components included in the kit**

Microarray: Pathchip microarrays, packaged in boxes of 5 or 10.

Tissue of Origin Test Report produced by the Pathwork System Software (by licensed agreement): The Pathwork® System Software receives data from the scanned Pathchip™ microarray and performs data quality control and analysis. The System Software then generates a Pathwork® Tissue of Origin Test Report which provides a Similarity Score for each of the 15 tissues on the test panel. The test report is accessible for clinical interpretation via a secure password protected website.

Tissue of Origin Test Reagents: Reagents for specimen processing and RNA extraction.

**807.92 (a)(5): Intended Use**

**Indications for Use:** The Pathwork® Tissue of Origin Test is intended to measure the degree of similarity between the RNA expression pattern in a patient’s fresh-frozen tumor and the RNA expression patterns in a database of tumor samples (poorly differentiated, undifferentiated and metastatic cases) that were diagnosed according to then current clinical and pathological practice. The database contains examples of RNA expression patterns for fifteen common malignant tumor types: bladder, breast, colorectal, gastric, hepatocellular, kidney, non-small cell lung, ovarian, pancreatic, prostate, and thyroid carcinomas, melanoma, testicular germ cell tumor, non-Hodgkins lymphoma (not otherwise specified), and soft tissue sarcoma (not otherwise specified). The Pathwork® Tissue of Origin Test result is intended for use in the context of the patient’s clinical history and other diagnostic tests evaluated by a qualified clinician.

**Limitations:** The Pathwork Tissue of Origin Test is not intended to establish the origin of tumors that cannot be diagnosed according to current clinical and pathological practice, (e.g. carcinoma of unknown primary). It is not intended to subclassify or modify the classification of tumors that can be diagnosed by current clinical and pathological practice, nor to predict disease course or survival or treatment efficacy, nor to distinguish primary from metastatic tumor. Tumor types not in the Pathwork Tissue of Origin Test database may have RNA expression patterns that are similar to RNA expression patterns in tumor types in the database, leading to indeterminate results or misclassifications.

**807.92 (a)(6): Technological Similarities and Differences to Predicate**
**Similarities/Differences between the Tissue of Origin Test and the Predicate**

CHARACTERISTIC	Tissue of Origin Test K080896	Bioplex 2200 Medical Decision Support Software K043341
Intended Use	<p>Indications for Use: The Pathwork® Tissue of Origin Test is intended to measure the degree of similarity between the RNA expression pattern in a patient's fresh-frozen tumor and the RNA expression patterns in a database of tumor samples (poorly differentiated, undifferentiated and metastatic cases) that were diagnosed according to then current clinical and pathological practice. The database contains examples of RNA expression patterns for fifteen common malignant tumor types: bladder, breast, colorectal, gastric, hepatocellular, kidney, non-small cell lung, ovarian, pancreatic, prostate, and thyroid carcinomas, melanoma, testicular germ cell tumor, non-Hodgkins lymphoma (not otherwise specified), and soft tissue sarcoma (not otherwise specified). The Pathwork® Tissue of Origin Test result is intended for use in the context of the patient's clinical history and other diagnostic tests evaluated by a qualified clinician.</p>	<p>The Bioplex 2200 Medical Decision Support Software (MDSS), used in conjunction with the ANA Screen, is an optional laboratory tool that associates patient antibody results with predefined MDSS profiles that have been correlated with the following systemic autoimmune diseases: SLE, Mixed Connective Tissue Disease, Sjogren's Syndrome, Scleroderma, and Polymyositis</p>
Principle of Operation	<p>The frozen biopsy specimen is processed by the clinical laboratory and is then hybridized to the Pathchip microarray. The Pathchip is scanned and the resulting intensity data file is processed by the Pathwork System Software. The results are presented to the laboratory as a Pathwork Tissue of Origin Test Report (secure internet access; pdf file) that quantifies the similarity of the RNA expression pattern found in a tumor specimen (poorly or un-differentiated primary tumors, as well as metastatic tumors) to expression patterns found in tumor specimens from 15 known tissues of origin.</p>	<p>The autoantibody results from the chemistry assay are compared to the MDSS database that contain results for over 1,400 sera/plasma, representing test results from patients with systemic autoimmune diseases and from healthy individuals. If one or more results are obtained from a serum or plasma sample, the results are associated with the most appropriate MDSS profiles. When the MDSS result is positive, the MDSS produces two outputs that BioPlex 2200 can display in its User Interface. The first output is a text result containing the specific disease association(s) results. The second output is a graph of the specific disease association(s) and the patient's analyte results.</p>

**Similarities/Differences (continued)**

CHARACTERISTIC	Tissue of Origin Test K080896	Bioplex 2200 Medical Decision Support Software K043341																		
Sample Preparation	Frozen biopsy tissues	Serum or plasma																		
Required Platform	Affymetrix GeneChip® Scanner GCS3000Dx, or equivalent	BioPlex 2200 Multi-Analyte Detection System																		
Output	Similarity of RNA expression patterns found in tumor specimens to 15 known tissues of origin	Results of MDSS analysis fall into one of three categories: Negative, No Association, or Association with Disease																		
Testing Environment	Professional use, CLIA High Complexity Laboratory	Professional use, CLIA High Complexity Laboratory																		
Precision	Reproducibly studies were conducted at four sites with multiple specimens (n = 3 or n = 6) from all 15 tissue types offered on the Pathwork Tissue of Origin Test panel (n = 60 specimens across all tissue types). Aliquots from each specimen were processed, scanned, and interpreted by all four sites, and each site was compared to each other. The overall site- to-site concordance among the four sites for Tissue of Origin Test results was approximately 93%.	Reproducibly studies were conducted at three sites with 11 eleven panel samples and three lots of reagents. Each sample was tested in duplicate, two “runs” per day for 10 days. The data were analyzed for intra-assay precision and inter-assay precision. For intra-assay precision, the percent coefficients of variation (%CVs) ranged from 1.7% to 11.1% across the three sites. For inter-assay precision, the %CVs ranged from 2.8% to 12.8% across the three sites.																		
Accuracy	The accuracy, defined as positive and negative percent agreement against the available diagnosis was as follows. The positive percent agreement across all 15 tissues was approximately 90% The negative percent agreement across all 15 tissues was approximately 99%.	Percent agreements of the MDSS outputs when a specific positive antibody was present, to the available diagnosis, ranged from 71% to 100%.																		
Interfering Substances	Studies were conducted that evaluated the effect from potential interfering substances found in biopsy specimens, such as adipose tissue, RNases, fibrous tissue, and necrotic tissue. The data showed that there was no effect from high levels of adipose tissue (as found in breast specimens), fibrous tissue (as found in skin specimens), or necrotic tissue, when up to 20% of the biopsy specimen. The test demonstrated adequate performance with pancreas- related specimens, although performance is lower than for other tissues on the panel. The lower performance is ostensibly due to elevated levels of RNases in these specimens.	No significant interference was found from the following substances when challenges were made at high concentrations:  <table data-bbox="971 1437 1365 1749"> <thead> <tr> <th>Substance</th> <th>Concentration</th> </tr> </thead> <tbody> <tr> <td>Hemoglobin</td> <td>≤ 500 mg/dl</td> </tr> <tr> <td>Bilirubin (unconjugated)</td> <td>≤ 20 mg/dl</td> </tr> <tr> <td>Triglycerides</td> <td>≤ 3000 mg/dl</td> </tr> <tr> <td>Protein (total)</td> <td>≤ 12 g/dl</td> </tr> <tr> <td>Cholesterol</td> <td>≤ 500 mg/dl</td> </tr> <tr> <td>Red blood cells</td> <td>≤ 0.4% concentrate</td> </tr> <tr> <td>Gamma-globulin</td> <td>≤ 2.5 g/dl</td> </tr> <tr> <td>Ascorbic acid</td> <td>≤ 3.0 mg/dl</td> </tr> </tbody> </table>	Substance	Concentration	Hemoglobin	≤ 500 mg/dl	Bilirubin (unconjugated)	≤ 20 mg/dl	Triglycerides	≤ 3000 mg/dl	Protein (total)	≤ 12 g/dl	Cholesterol	≤ 500 mg/dl	Red blood cells	≤ 0.4% concentrate	Gamma-globulin	≤ 2.5 g/dl	Ascorbic acid	≤ 3.0 mg/dl
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**807.92 (b)(1): Brief Description of Non-clinical data**

Studies were conducted that evaluated the effect from potential interfering substances found in biopsy specimens, such as adipose tissue, RNases, fibrous tissue, and necrotic tissue. The data showed that there was no effect from high levels of adipose tissue (as found in breast specimens), fibrous tissue (as found in skin specimens), or necrotic tissue up to 20% of the biopsy specimen. The Tissue of Origin Test demonstrates adequate performance with pancreas-related specimens, although performance is lower than for other tissues on the TOO panel. The lower performance is ostensibly due to elevated levels of RNases in these specimens.

Reproducibility studies were conducted at four sites with multiple specimens (n = 3 or n = 6) from all 15 tissue types offered on the Pathwork Tissue of Origin Test panel (n = 60 specimens across all tissue types). Aliquots from each specimen were processed, scanned, and interpreted by all four sites, and each site was compared to each other. The overall site-to-site concordance among the four sites for Tissue of Origin Test results was approximately 93%.

**807.92 (b)(2): Brief Description of Clinical Data**

The clinical study was performed at four laboratory sites and included 545 frozen specimens. The accuracy, defined as positive and negative percent agreement against the available diagnosis was as follows. The positive percent agreement across all 15 tissues was 89.4 (487/545), with a confidence interval of 86.5% to 91.8%. The negative percent agreement across all 15 tissues was 99.6% (507/509) with a confidence interval of 98.6% to 100.0%.

**807.92 (b)(3): Conclusions from Clinical Testing**

The results of the clinical validation demonstrated that the Pathwork Tissue of Origin Test is safe and effective for its intended use.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Pathwork Diagnostics, Inc.  
c/o Ms Erika B. Ammirati  
Regulatory Consultant  
1196 Borregas Ave,  
Suite 200  
Sunnyvale, CA 94089

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

Re: k080896

Trade/Device Name: Pathwork® Tissue of Origin Test  
Regulation Number: 21 CFR 862.3100  
Regulation Name: Amphetamine test system  
Regulatory Class: II  
Product Code: OIW  
Dated: July 21, 2008  
Received: July 22, 2008

JUL 30 2008

Dear Ms. Ammirati:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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 and the limitations described below. 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.

The Office of In Vitro Diagnostic Device Evaluation and Safety has determined that there is a reasonable likelihood that this device will be used for an intended use not identified in the proposed labeling and that such use could cause harm. Therefore, in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear under the Indications for Use section of the device's labeling and the patient test report:

The Pathwork® Tissue of Origin Test is not intended to establish the origin of tumors (e.g. carcinoma of unknown primary) that cannot be diagnosed according to current clinical and pathological practice. It is not intended to subclassify or modify the classification of tumors that can be diagnosed by current clinical and pathological practice, nor to predict disease course or survival or treatment efficacy, not to distinguish primary from metastatic tumor. Tumor types not in the Pathwork® Tissue of Origin Test database may have RNA expression patterns that are similar to patterns in the database.

Please note that the above labeling limitations are required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) is required before these limitations are modified in any way or removed from the device's labeling.

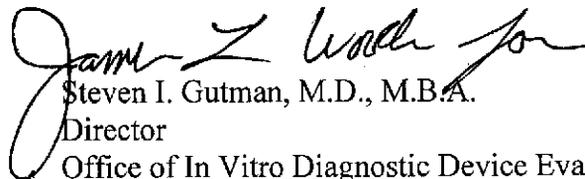
The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification if the limitation statement described above is added to your labeling.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations (CFR), Title 21, Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific information about the application of other labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address <http://www.fda.gov/cdrh/industry/support/index.html>.

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.

Director

Office of In Vitro Diagnostic Device Evaluation and Safety  
Center for Devices and Radiological Health

Enclosure

**Indications for Use**

510(k) Number (if known): k080896

Device Name: Pathwork® Tissue of Origin Test

FDA's Statement of the Indications For Use for device:

The Pathwork® Tissue of Origin Test is intended to measure the degree of similarity between the RNA expression pattern in a patient's fresh-frozen tumor and the RNA expression patterns in a database of tumor samples (poorly differentiated, undifferentiated and metastatic cases) that were diagnosed according to then current clinical and pathological practice. The database contains examples of RNA expression patterns for fifteen common malignant tumor types: bladder, breast, colorectal, gastric, hepatocellular, kidney, non-small cell lung, ovarian, pancreatic, prostate and thyroid carcinomas, melanoma, testicular germ cell tumor, non-Hodgkins lymphoma (not otherwise specified), and soft tissue sarcoma (not otherwise specified). The Pathwork® Tissue of Origin Test result is intended for use in the context of the patient's clinical history and other diagnostic tests evaluated by a qualified clinician.

Limitations:

The Pathwork® Tissue of Origin Test is not intended to establish the origin of tumors (e.g. carcinoma of unknown primary) that cannot be diagnosed according to current clinical and pathological practice. It is not intended to subclassify or modify the classification of tumors that can be diagnosed by current clinical and pathological practice, nor to predict disease course or survival or treatment efficacy, not to distinguish primary from metastatic tumor. Tumor types not in the Pathwork® Tissue of Origin Test database may have RNA expression patterns that are similar to patterns in the database.

Prescription Use    
 (Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use \_\_\_\_\_   
 (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

*Maria M. Chan*   
 **Division Sign-Off**

**Office of In Vitro Diagnostic   
 Device Evaluation and Safety**

510(k) k080896