SPECIAL 510(k): Device Modification
OIR Decision Summary

To: THE FILE **RE:** K173839

This 510(k) submission contains information/data on modifications made to the applicant's own class II or class I devices requiring 510(k). The following items are present and acceptable:

1. The name and 510(k) number of the applicant's previously cleared device:

   K120489: Pathwork Tissue of Origin Test Kit - FFPE

2. Applicant's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials.

3. A description of the device **MODIFICATION(S),** including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

   The following two changes were made: 1) the GeneChip™ 3' IVT Pico Kit is used for amplification and target labeling instead of the RampUp RNA Amplification Kit™ reagents; and 2) the Chip processing software was updated to the Genechip™ System 3000 Dx v.2 from the Genechip™ System 3000 Dx, which is no longer supported by the manufacturer. The principles of the target preparation process have not changed.

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including, intended use, equipment, reagents and limitations, are summarized in the table below:

Feature	K120489 (Predicate)	K173839
Device Name	Pathwork Tissue of Origin Test Kit-FFPE	Cancer Genetics Tissue of Origin Test Kit - FFPE
Intended use	The Pathwork Tissue of Origin Test is an in vitro diagnostic intended to measure the degree of similarity between the RNA expression patterns in a patient's formalin-fixed, paraffin-embedded (FFPE) tumor and the RNA expression patterns in a database of fifteen tumor types (poorly differentiated, undifferentiated, and metastatic cases) that were diagnosed according to then current clinical and pathological practice. This test should be evaluated by a qualified physician in the context of the patient's clinical history and other diagnostic test results. Limitations:The Pathwork® Tissue of Origin Test is not intended to establish the origin of tumors (e.g. cancer 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, 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 patterns in the database. Therefore, results cannot be used to distinguish tumor types in the database from tumor types not in the database.	Same
Microarray	Pathchip®	Same
Equipment	Hybridization oven	Same
	Scanner	Same
	Genechip™ System 3000 Dx	Genechip™ System 3000 Dx v.2
RNA isolation	Extraction Reagents	Same
Amplification Reagents	RampUp RNA Amplification Kit™	GeneChip™ 3' IVT Pico Kit
Purification of biotinylated cDNA	Ethanol precipitation	GeneChip™ 3' IVT Pico Kit
Internal Processing Quality Control	Percent Positive Overall Signal Regional Discontinuity	Same
Analysis	Algorithm as described in K092967	Same

5. A **Design Control Activities Summary** which includes:

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis

b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied

The Risk Analyses were performed to assess the impact of the modifications on the device by identifying risks, their possible causes, and appropriate control mechanisms. The Risk Analyses took into account device hazards associated with the intended use of the device. No additional hazards, no additional causes, and no required additional controls were identified. No adverse advents or reportable incidents have been associated with the device.

Based on the Risk Analyses conducted, the following studies were performed to verify and/or validate the modifications to the device:

- Changing the amplification and labeling reagents can potentially alter the expression ratios of the targets if the process does not accurately reflect the endogenous levels of these targets before amplification. As a result, the gene expression patterns may be skewed toward certain subtypes that will increase the chance of misclassification. A validation study was, therefore, performed with the modified device using 142 specimens that included all 15 subtypes in the database and that were studied in the original validation study with the predicate test. The concordance in the test results between paired specimens processed with the RampUp RNA Amplification Kit™ and the GeneChip™ 3' IVT Pico Kit was 90.8% (95% confidence interval of 83.6% to 95.3%).
- For the software modification, there are risks related to potential alterations to relative probe intensities on the array which could affect the classification results. Therefore, a validation study was performed to assess the concordance between the Genechip™ System 3000 Dx v.2 and the Genechip™ System 3000 Dx using 20 FFPE tumor specimens. All results were concordant (100% agreement with 95% confidence interval of 95.9% to 100%).

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the applicant's description of the particular modifications and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The applicant has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.