



**CPAL**

Central Pennsylvania Alliance Laboratory

**Technical Bulletin**

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**KRAS Mutational Analysis (Companion Diagnostic)  
- Method Change -**

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**Effective Date:**

**March 11, 2013**

**Method Change:**

**This method replaces the Sanger DNA sequencing method.**

CPAL will be performing all KRAS testing using the *therascreen*® KRAS RGQ PCR Kit. The *therascreen*® KRAS RGQ PCR Kit is an FDA approved *in vitro* assay intended to aid in the identification of colorectal cancer patients for treatment with Erbitux® (cetuximab) based on a KRAS “*no mutation detected*” test result. Performance of this assay has been verified against Sanger DNA sequencing and may provide useful clinical information in other clinical circumstances.

There are no changes in specimen requirements.

**NOTE:** KRAS and BRAF mutational analysis can be performed from a single slide series specimen submission.

**Summary:**

KRAS encodes for a GTP-binding protein that acts as a signal transducer, and is one of several downstream signaling pathways of the epidermal growth factor receptor (EGFR). This pathway is involved in regulating apoptosis, cell proliferations, cell differentiation, and angiogenesis. Oncogenic mutation of the KRAS gene leads to a constitutively activated protein which is commonly found in many carcinomas,

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including 30-50% of colorectal carcinomas and 15-30% of lung non-small cell adenocarcinoma. Several studies have indicated that the presence of mutant KRAS in colorectal tumors correlates with a poor prognosis and is associated with a lack of response to EGFR tyrosine kinase inhibitors.

This assay tests for seven KRAS mutations:

<b>Mutation</b>	<b>Base Change</b>
GLY12ALA (G12A)	GGT>GCT
GLY12ASP (G12D)	GGT>GAT
GLY12ARG (G12R)	GGT>CGT
GLY12CYS (G12C)	GGT>TGT
GLY12SER (G12S)	GGT>AGT
GLY12VAL (G12V)	GGT>GTT
GLY13ASP (G13D)	GGC>GAC

This assay has single digit sensitivity that varies by mutation. Please note that there may be other mutations of the EGFR pathway that are contributory to poor prognosis and/or drug insensitivity that are not detected by this test. Results should be interpreted in conjunction with clinical and other laboratory findings for the most accurate interpretation.