

# Diagnostic Kit and Device Validation Support

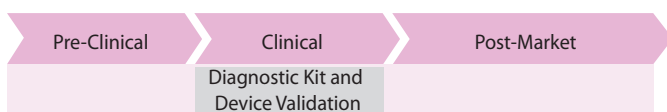
## Providing the Highest Quality Sequencing Data in Support of 510(k) Submissions



Beckman Coulter Genomics has more than 20 years of experience in bidirectional sequencing used as a reference method for pre-market approval applications (PMA) and pre-market notification 510(k) submissions for pharmacogenetic and other human tests in accordance with applicable GLP and GMP regulations.

Beckman Coulter Genomics has performed multiple successful studies for our clients in support of 510(k) applications for diagnostic kits and devices. Based on individual client's needs, we can design custom studies to support validation of client's assays by proving testing starting with nucleic acid extractions, template amplification followed by a "gold standard" reference method\*\* such as bidirectional sequencing in accordance with applicable GLP and GMP regulations that would identify SNPs and/or other mutations in the gene of interest and provide consensus sequences for microorganisms identification.

For cases in which bi-directional sequencing may not be the appropriate method (i.e., for large deletion, rearrangement or insertion mutations), Beckman Coulter Genomics offers a multitude of alternative sequencing and genotyping solutions to address these needs.



### Project Planning and Technology

Beckman Coulter Genomics provides a truly personalized outsourcing partnership, letting you focus on your core competencies. Our Study Managers maintain open and continuous communication throughout the project, and are available for consultation on developing appropriate study designs. These include project-specific protocols, sample types used, selection criteria, and other project needs.

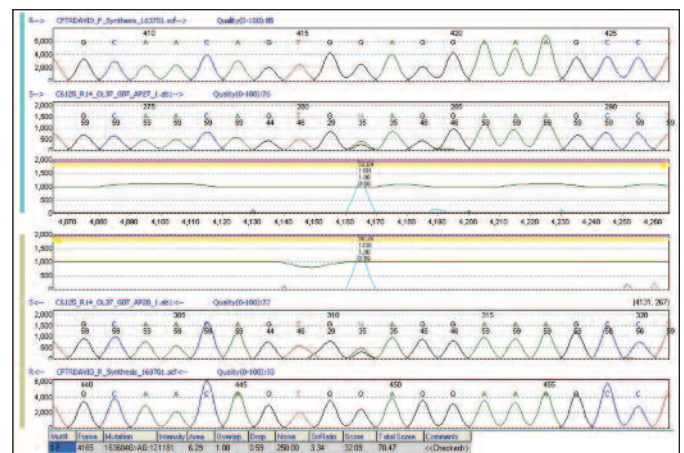
Beckman Coulter Genomics utilizes ABI\* 3730xl DNA Analyzer systems and provides assay design, validation and custom data analysis and reporting. This allows Beckman Coulter

Genomics to offer reliable and sensitive methods to test for pharmacogenetic polymorphisms and other genetic mutations, as well as generation of consensus sequences used for comparison in microorganism identification.

Sequence detection software reads DNA sequencer trace data, calls bases, assigns quality values to the bases, and writes the base calls and quality values to output files. Beckman Coulter Genomics uses these quality values to monitor operational performance ensuring that our systems are running optimally at all times. Our quality standard for regulatory submission sequencing projects is the equivalent of Phred 30 for individual read raw data which indicates 99.99% accuracy. This provides quality levels that exceed the FDA's Phred 40 consensus requirements.

### Assay Development, Validation and Technology Transfer

Beckman Coulter Genomics offers many optimized assays and can also develop an assay specific to our client's target. Client-specific assay validation can be performed in accordance with ICH guidelines to assess specificity, accuracy, linearity, precision, range, and robustness for the sequencing assays.



Mutation analysis for the presence of SNPs by DNA sequencing using Mutation Surveyor\* (SoftGenetics, LLC). Heterozygous genotype AVG is detected.

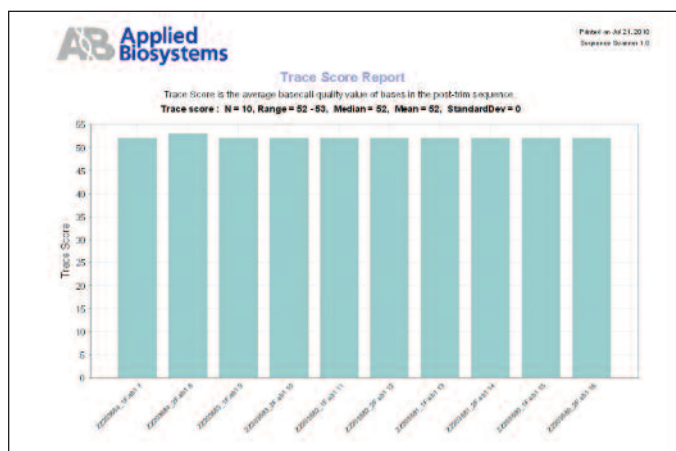
Beckman Coulter Genomics can provide expertise in assay validation for protocol generation or execute validation in accordance with a client's developed protocol.

Beckman Coulter Genomics also has a proven record of success in performing technology transfer to our facility for customer developed assays and methods. Customer specific SOPs and continuous personnel proficiency testing can be incorporated into our quality systems.

### Validated Data Assembly and Analysis

Beckman Coulter Genomics utilizes validated software, including Sequencher\* (Genecodes), Mutation Surveyor (ABI), and Variant Reporter\* (ABI) anti-correlation technologies which rapidly locates all differences between the wild type sequence and sample traces with excellent accuracy and sensitivity.

A BLAST (Basic Local Alignment Search Tool) analysis can also be performed, which is a sequence comparison algorithm, optimized for speed, which is used to search sequence databases for optimal local alignments to a query.



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† The PCR process is covered by patents owned by Roche Molecular Systems, Inc., and F. Hoffman-La Roche, Ltd. Beckman Coulter and the stylized logo are registered trademarks of Beckman Coulter, Inc.

For more information, please visit our website at [www.beckmangenomics.com](http://www.beckmangenomics.com) or contact your local sales representative.

### Final Report

In addition to the raw data, Beckman Coulter Genomics can provide a standard or custom data analysis and reporting format to support specific client expectations. A dedicated Ph.D-level Study Manager will prepare a comprehensive custom report which will include:

- Alignment of the expected vs. actual sequence
- Graphical overview of contig assemblies
- Consensus sequence data text file
- Quality scores
- Mutations detected
- Quality Assurance statement

### \*\* Examples of Relevant Guidance

- Guidance for Industry and FDA Staff - Pharmacogenetic Tests and Genetic Tests for Heritable Markers, issued on June 19, 2007
- Guidance for Industry and FDA Staff: Establishing the Performance Characteristics of In Vitro Diagnostic Devices for the Detection or Detection and Differentiation of Influenza Viruses, draft guidance issued February 15, 2008
- Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Respiratory Viral Panel Multiplex Nucleic Acid Assay, issued on October 9, 2009

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