# Seraseq®

## ctDNA Mutation Mix v2
## AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT

Package Insert

**PLEASE NOTE:**
THESE REAGENTS MUST NOT BE SUBSTITUTED FOR THE MANDATORY POSITIVE AND NEGATIVE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS.

### NAME AND INTENDED USE

The Seraseq® ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT is a reference material formulated for use with targeted Next Generation Sequencing (NGS) assays that detect cancer-relevant somatic mutations present in the blood stream as circulating cell-free tumor DNA. This product is intended as a quality reference material for translational and disease research testing to monitor library preparation, sequencing, and variant detection under a given set of bioinformatics pipeline parameters. *For Research Use Only. Not for use in diagnostic procedures.*

### REAGENTS

Table 1. Different variant allele frequencies (AF) for Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT. Each Item No. is available as an individual product. Information in this Package Insert applies for all 6 of these products.

| Item No. | Product |
|---|---|
| 0710-0139 | Seraseq® ctDNA Mutation Mix v2 AF2% |
| 0710-0140 | Seraseq® ctDNA Mutation Mix v2 AF1% |
| 0710-0141 | Seraseq® ctDNA Mutation Mix v2 AF0.5% |
| 0710-0142 | Seraseq® ctDNA Mutation Mix v2 AF0.25% |
| 0710-0143 | Seraseq® ctDNA Mutation Mix v2 AF0.125% |
| 0710-0144 | Seraseq® ctDNA Mutation Mix v2 WT |

For all products: 1 vial, 25 µL per vial, 10 ng/µL concentration.

### WARNINGS AND PRECAUTIONS

***For Research Use Only. Not for use in diagnostic procedures.***
CAUTION: Handle Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT as though it is capable of transmitting infectious agents. This product is formulated using DNA purified from a reference cell line, GM24385, which is a B-lymphocytic, male cell line from the Personal Genome Project offered by the NIGMS Human Genetic Cell Repository (https://catalog.coriell.org/1/NIGMS).

#### Safety Precautions

Use Centers for Disease Control and Prevention (CDC) recommended universal precautions for handling reference materials and human specimens[1]. Do not pipette by mouth. Do not smoke, eat, or drink in areas where specimens are being handled. Clean any spillage by immediately wiping with 0.5% sodium hypochlorite solution. Dispose of all specimens and materials used in testing as though they contain infectious agents.

#### Handling Precautions

Do not use Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT beyond the expiration date. Avoid contamination of the product when opening and closing the vial.

### STORAGE INSTRUCTIONS

Store Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT frozen at -20 °C or colder. Aliquoting of the product into low DNA binding tubes may be advisable to limit the number of freeze-thaw cycles.

### INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT is a mixture of human genomic DNA and synthetic DNA constructs. It should appear as a clear liquid. Alterations in this appearance may indicate instability or deterioration of the product and vials should be discarded.

### PROCEDURE

#### Materials Provided

Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT consists of DNA purified from a reference cell line, GM24385, plus constructs containing variants mixed at a defined allele frequency. Processing of the purified DNA is used to produce an average DNA fragment size of approximately 170 basepairs (Figure 1). The purified DNA is present in a 1 mM Tris, 0.1 mM EDTA, 10 mM NaCl, pH 8.0 aqueous buffer. Material is ready to use in NGS assays in steps that follow circulating cell-free DNA isolation. No further purification or DNA isolation is needed.

#### Materials Required but not Provided

Refer to instructions supplied by manufacturers of the test kits to be used.

#### Instructions for Use

Thaw the product vial on ice. Mix by vortexing to ensure a homogenous solution and spin briefly. Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT may be input directly into library preparation following procedures used for clinical specimens. Refer to your usual assay procedures in order to determine the amount of material to use.

### EXPECTED RESULTS & INTERPRETATION OF RESULTS

Table 2 indicates each of the somatic mutations represented in Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT. Detection of mutations may differ across different NGS panels and different test reagent lots. While the presence and frequency of each mutation in this product is confirmed during manufacture using functional NGS and/or digital PCR assays, there may be differences in observed allele frequencies due to assay characteristics. Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT does not have assigned values for allele frequencies of the mutations present in the product. Each laboratory must establish an assay-specific expected value for each mutation and each lot of Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT. When results for the product are outside of the established acceptance range, it may indicate unsatisfactory test performance. Possible sources of error include: deterioration of test kit reagents, operator error, faulty performance of equipment, contamination of reagents, or changes in bioinformatics pipeline parameters. Additional support documents are available online at www.seracare.com/oncology.

LGC Clinical Diagnostics, Inc. | 37 Birch Street, Milford, MA 01757 USA
Phone: +1 508.244.6400 | Toll Free (US Only) 800.676.1818
CDx-info@LGCGroup.com | www.seracare.com

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**LIMITATIONS OF THE PROCEDURE**

Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT MUST NOT BE SUBSTITUTED FOR THE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS. *TEST PROCEDURES* provided by manufacturers must be followed closely. Deviations from procedures recommended by test kit manufacturers may produce unreliable results. This product is offered for Research Use Only. Not for use in diagnostic procedures. Data are provided for informational purposes. SeraCare Life Sciences does not claim that others can duplicate test results exactly. Note that based on your particular assay protocol and regions interrogated, variants other than the 40 annotated in this product may be detected at varying allele frequencies. Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT is not a calibrator and should not be used for assay calibration. Adverse shipping and/or storage conditions or use of outdated product may produce erroneous results.

**REFERENCES**


1. Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings.


**Figure 1. Representative DNA fragment size distribution for Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT**

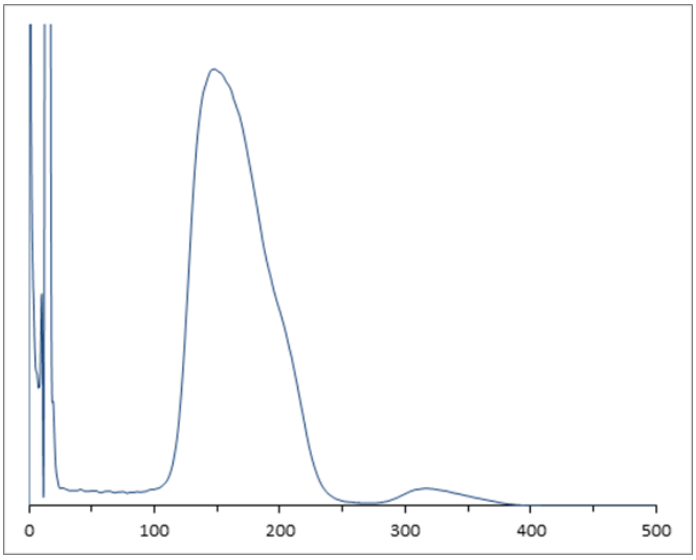



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**Table 2. Somatic mutations present in Seraseq ctDNA Mutation Mix v2 AF2%, AF1%, AF0.5%, AF0.25%, AF0.125%, & WT**

| Gene ID | COSMIC Identifier | Mutation Type | HGVS Nomenclature | Amino Acid Change |
|---|---|---|---|---|
| AKT1 | COSM33765 | Substitution | c.49G>A | p.E17K |
| APC | COSM13127 | Substitution | c.4348C>T | p.R1450* |
| APC | COSM18561 | Insertion in HP 7N | c.4666_4667insA | p.T1556fs*3 |
| ATM | COSM21924 | Deletion | c.1058_1059delGT | p.C353fs*5 |
| BRAF | COSM476 | Substitution | c.1799T>A | p.V600E |
| CTNNB1 | COSM5664 | Substitution | c.121A>G | p.T41A |
| EGFR | COSM6224 | SNV in 3N | c.2573T>G | p.L858R |
| EGFR | COSM12378 | Insertion | c.2310_2311insGGT | p.D770_N771insG |
| EGFR | COSM6225 | Deletion | c.2236_2250del15 | p.E746_A750delELREA |
| EGFR | COSM6240 | Substitution | c.2369C>T | p.T790M |
| ERBB2 | COSM682/20959 | Insertion | c.2324_2325ins12 | p.A775_G776insYVMA |
| FGFR3 | COSM715 | Substitution | c.746C>G | p.S249C |
| FLT3 | COSM783 | Substitution | c.2503G>T | p.D835Y |
| FOXL2 | COSM33661 | Substitution | c.402C>G | p.C134W |
| GNA11 | COSM52969 | Substitution | c.626A>T | p.Q209L |
| GNAQ | COSM28758 | SNV in HP 3N | c.626A>C | p.Q209P |
| GNAS | COSM27887 | Substitution | c.601C>T | p.R201C |
| IDH1 | COSM28747 | Substitution | c.394C>T | p.R132C |
| JAK2 | COSM12600 | SNV in HP 3N | c.1849G>T | p.V617F |
| KIT | COSM1314 | Substitution | c.2447A>T | p.D816V |
| KRAS | COSM521 | Substitution | c.35G>A | p.G12D |
| MPL | COSM18918 | Substitution | c.1544G>T | p.W515L |
| NCOA4-RET | N/A | Gene Fusion (DNA) | NCOA4{NC_000010.10}:r.1_1014+1312_RET{NC_000010.10}:r.2327-1437_5659 | N/A |
| NPM1 | COSM17559 | Insertion | c.863_864insTCTG | p.W288fs*12 |
| NRAS/CSDE1 | COSM584 | Substitution | c.182A>G | p.Q61R |
| PDGFRA | COSM736 | Substitution | c.2525A>T | p.D842V |
| PDGFRA | COSM28053 | Insertion | c.1694_1695insA | p.S566fs*6 |
| PIK3CA | COSM763 | Substitution | c.1633G>A | p.E545K |
| PIK3CA | COSM12464 | Insertion | c.3204_3205insA | p.N1068fs*4 |
| PIK3CA | COSM775 | Substitution | c.3140A>G | p.H1047R |
| PTEN | COSM4986 | Insertion | c.741_742insA | p.P248fs*5 |
| PTEN | COSM5809 | Deletion 6N > 5N | c.800delA | p.K267fs*9 |
| RET | COSM965 | Substitution | c.2753T>C | p.M918T |
| SMAD4 | COSM14105 | Insertion | c.1394_1395insT | p.A466fs*28 |
| TP53 | COSM10648 | Substitution | c.524G>A | p.R175H |
| TP53 | COSM10660 | Substitution | c.818G>A | p.R273H |
| TP53 | COSM10662 | Substitution | c.743G>A | p.R248Q |
| TP53 | COSM6530 | Deletion | c.723delC | p.C242fs*5 |
| TP53 | COSM18610 | Deletion 5N >4N | c.263delC | p.S90fs*33 |
| TPR-ALK | N/A | Gene Fusion (DNA) | TPR{NC_000001.10}:r.1_2185+246_ALK{NC_000002.11}:r.4125-550_6265 | N/A |