Seraseq®

ctDNA Extraction Reference Material
20 ng/mL, 50 ng/mL, 80 ng/mL

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 Extraction Reference Material is intended for use in verifying the functionality of plasma cfDNA extraction workflows and downstream analysis of pathogenic variants present in ctDNA. The Seraseq ctDNA Extraction Reference Material is intended as a quality reference material for translational and disease research testing and monitors cfDNA extraction efficiency, library preparation, sequencing, and variant allele detection under a given set of bioinformatics pipeline parameters. *For Research Use Only. Not for use in diagnostic procedures.*

REAGENTS

Table 1. Seraseq CtDNA Extraction Reference Material

Material No.	Product
0710-3294	Seraseq® ctDNA Extraction Reference Material 20 ng/mL
0710-3295	Seraseq® ctDNA Extraction Reference Material 50 ng/mL
0710-3296	Seraseq® ctDNA Extraction Reference Material 80 ng/mL

Each Material No. is available as an individual product. Information in this Package Insert applies to all products.

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq ctDNA Extraction Reference Material and all materials derived from human blood products as though it is capable of transmitting infectious agents. Seraseq CtDNA Extraction Reference Material is manufactured using genomic DNA extracted from the human 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 up with 0.5% sodium hypochlorite solution. Dispose of all specimens and materials used in testing as though they contain infectious agents.

Handling Precautions

Avoid contamination of the product when opening and closing the vials.

STORAGE INSTRUCTIONS

Store Seraseq ctDNA Extraction Reference Material frozen at -20 °C or colder. When stored at -20 °C or colder the material will be usable until the expiration date indicated on the vial label. Repeated freeze-thawing of this product is not recommended.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq ctDNA Extraction Reference Material 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 Extraction Reference Material is derived from DNA purified from a reference cell line, GM24385, plus constructs containing variants mixed at a defined allele frequency. Purified DNA is utilized to produce an average DNA fragment with a peak size in the range of 150-200 base pairs. The DNA is introduced into a dilution of SeraCare's SeraCon™ Matribase to the concentration indicated on the label claim as determined using Thermo Fisher Qubit™ dsDNA BR Assay Kit. Material must undergo extraction prior to input into NGS library preparation or most other DNA analysis workflows. Each vial is intended to be used as a single-use aliquot for extraction of cfDNA from 1 mL plasma. QIAGEN QIAamp® Circulating Nucleic Acid Kit with carrier RNA (extraction) and Qubit dsDNA BR Assay Kit (quantification) were utilized to extract ctDNA from a 1 mL volume, in triplicate (each concentration), and yielded the concentration in ng/mL of DNA indicated on the label claim. Note: Yield may vary depending on extraction and quantification method used.

Materials Required but not Provided

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

Instructions for Use

Allow the product vial to come to room temperature before use. Mix by vortexing to ensure a homogeneous solution and spin briefly. Seraseq ctDNA Extraction Reference Material may be input into workflows in a manner consistent with plasma fractions prior to extraction. Seraseq ctDNA Extraction Reference Material may be processed through library preparation and sequencing in parallel with test specimens. Refer to standard assay procedures in order to determine the amount of material to use.

Quality Control

Although Seraseq ctDNA Extraction Reference Material is designed to simulate a cfDNA sample with EGFR variants present at 1%, the product does not have assigned values for mutation frequencies. There are many reasons why assays may observe deviation from the representative data which may or may not be of significance. It is therefore recommended that each laboratory qualify the use of Seraseq ctDNA Extraction Reference Material with each assay system prior to its routine use.

INTERPRETATION OF RESULTS

Detection of the variants within Seraseq ctDNA Extraction Reference Material may vary with different types of tests and different test kit lots. Since the reference material does not have an assigned value, the laboratory must establish a range for each lot of Seraseq ctDNA Extraction Reference Material. 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 change in bioinformatics pipeline parameters.

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LIMITATIONS OF THE PROCEDURE

Seraseq ctDNA Extraction Reference Material MUST NOT BE SUBSTITUTED FOR THE CONTROL REAGENTS PROVIDED WITH MANUFACTURED TEST KITS.

TEST PROCEDURES and *INTERPRETATION OF RESULTS* provided by manufacturers of test kits must be followed closely. Deviations from procedures recommended by test kit manufacturers may produce unreliable results. Seraseq ctDNA Extraction Reference Material is not a calibrator and should not be used for assay calibration. Adverse shipping and storage conditions or use of outdated product may produce erroneous results.

EXPECTED RESULTS

Specific detection of variants and variant allele frequencies will vary among different assays, different procedures, different lot numbers, and different laboratories. Each laboratory should establish its own acceptance criteria. For example, the acceptable range for each variant might include all values within two standard deviations of the mean of 20 data points obtained in 20 runs[2]. Table 2 lists the variants in the product which are present at approximate 1% VAF (verified by digital PCR and reported on the batch specific technical product report).

Table 2: List of mutations present in Seraseq Extraction Reference Material.

Gene	Nucleotide Change	Protein Change
EGFR	c.2236_2250del	p.E746_A750del
EGFR	c.2155G>A	G719S
EGFR	c.2369C>T	p.T790M
EGFR	c.2573T>G	p.L858R

SPECIFIC PERFORMANCE CHARACTERISTICS

Seraseq ctDNA Extraction Reference Material has been designed for use with NGS sequencing procedures for the purposes of evaluating assay performance. Seraseq ctDNA Extraction Reference Material does not have assigned values. Procedures for implementing a quality assurance program and monitoring test performance on a routine basis must be established by each individual laboratory.

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.
2. Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline-Second Edition. NCCLS document C24-A2, 1999.

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