Seraseq™

Trisomy 21 Aneuploidy Linearity Panel (FF1-8) 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™ Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is a four member panel intended to challenge the lower limits of detection for whole genome or targeted Next Generation Sequencing (NGS) assays or Microarray assays that screen for Trisomy 21 chromosomal abnormalities in cell-free fetal DNA (cfDNA). The Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is intended as a quality reference material for researchers and Non-Invasive Prenatal Testing (NIPT) labs, and monitors library preparation, sequencing, and detection performance. *For Research Use Only. Not for use in diagnostic procedures.*

SUMMARY
A well-designed quality control program can provide added confidence in the reliability of results obtained for unknown specimens. The use of independent reference products may provide valuable information concerning assay sensitivity and bioinformatics pipeline analysis.

PRINCIPLES OF THE PROCEDURE
Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is ready to use in NGS or Microarray assays starting with DNA extraction with no further purification needed (similar to an actual sample). One (1) mL is provided per vial and each vial contains human genomic DNA at a concentration of 20 ng/mL. Four vials are provided per panel, and the vials represent a range of fetal fraction amounts. The product is formulated in a commutable matrix (simulated plasma) that is compatible with both PCR-based target amplification and hybridization-based target selection methods following extraction.

REAGENTS
Item No. 0720-0052*. 4 vials, 1 mL per vial, 20 ng/mL concentration.

Tube name	Target fetal fraction
Fetal fraction 8%	8%
Fetal fraction 4%	4%
Fetal fraction 2%	2%
Fetal fraction 1%	1%

* Patent Pending and manufactured under exclusive license from University of California San Francisco (UCSF).

WARNINGS AND PRECAUTIONS
For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) and all materials derived from human blood products as though they are capable of transmitting infectious agents. Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is manufactured using human genomic DNA, and unrelated fetal DNA derived from cultured human trophoblast progenitor cell lines. Purified genomic DNA mixture is formulated in a commutable matrix (simulated plasma) containing human protein isolates.

Safety Precautions
Use Center 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 Trisomy 21 Aneuploidy Linearity Panel (FF1-8) refrigerated at 2 – 8 ºC. Do not freeze. Samples are designed to be single use.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION
Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is a mixture of human genomic DNA (maternal and fetal). It should appear as a clear to pale yellow liquid. Alterations in this appearance may indicate instability or deterioration of the product and vials should be discarded.

PROCEDURE
Materials Provided
Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is a mixture of human genomic DNA in a commutable matrix (simulated plasma). One (1) mL is provided per vial at a concentration of 20 ng/mL. A total of four (4) vials are provided per panel.

Materials Required but not Provided
Refer to instructions supplied by manufacturers of the test kits to be used.

Instructions for Use
Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) may be inserted into workflows in a manner consistent with plasma fractions prior to extractions. Mix by vortexing to ensure a homogeneous solution. Do not centrifuge. Following extraction, Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) must go through the entire library preparation and sequencing steps in parallel with the test specimens. Refer to standard assay procedures in order to determine the amount of material to use. Each vial is intended for a single-use.

Quality Control
Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) does not have assigned values for trisomy or fetal fraction. However, the product is formulated using digital PCR quantitation to target the cell-free fetal DNA for each trisomy to be present at 12% of the total DNA amount. There are many reasons why assays may observe deviation from this target, which may or may not be of significance. It is therefore recommended that each laboratory qualify the use of each lot of Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) with each assay system prior to its routine use.

INTERPRETATION OF RESULTS
Detection of aneuploidy may vary with different NGS and Microarray assays and different test reagent lots. Since the reference material does not have an assigned value, the laboratory must establish an acceptable range for each lot of Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8). 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 Trisomy 21 Aneuploidy Linearity Panel (FF1-8) 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. Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) is not a calibrator and should not be used for assay calibration. These materials are also not whole process controls and do not evaluate the methods used for specimen extraction.

Adverse shipping and storage conditions or use of outdated product may produce erroneous results.

EXPECTED RESULTS

Specific detection of chromosomal abnormality will vary among different assays, different procedures, different lot numbers, and different laboratories. Each laboratory should establish its own range of acceptable values. 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].

REFERENCES

1. CDC Recommendations for prevention of HIV transmission in health care settings. MMWR 36 (supp.2), 1987.

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

SPECIFIC PERFORMANCE CHARACTERISTICS

Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) has been designed for use with whole genome or targeted NGS assays or Micro-Array assays for the purposes of assessing assay characteristics. The product is manufactured from purified human genomic DNA. Although the product is formulated with a 8%, 4%, 2% and 1% target fetal fraction for trisomy 21 as determined by digital PCR (as shown in Table 1), Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8) 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.

TABLE 1: Digital PCR analysis of fetal fraction % in Seraseq Trisomy 21 Aneuploidy Linearity Panel (FF1-8)

Target fetal fraction (%)	Average dPCR estimate* (%)
1	1.1
2	2.1
4	4.2
8	8.5

*Based on calculated copy number variation for chromosome Y using a digital PCR (dPCR) assay