Seraseq®

Antepartum & Postpartum T21 Male cfDNA

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® Antepartum T21 (Trisomy 21) Male cfDNA and Postpartum T21 (Trisomy 21) Male cfDNA are intended as commutable reference materials for non-invasive prenatal testing (NIPT) of fetal Trisomy 21 in pregnant patients via cell-free DNA (cfDNA) analysis.

Each product is derived from a naturally-occurring mixture of matched (or related) maternal and fetal circulating cell-free DNA in pregnant donor blood samples whose male fetus has been diagnosed with Trisomy 21 (Down Syndrome). The antepartum cfDNA is derived from a blood sample drawn prenatally, whilst the postpartum cfDNA is derived from a blood sample drawn after birth from the same patient.

Supplied as purified cfDNA in 0.1X TE buffer with 10 mM KCl, each product can be used as Trisomy 21 reference material in assay development, validation, verification, analysis and routine monitoring of test performance as well as troubleshooting and training.

The Seraseq Antepartum and Postpartum T21 Male cfDNA products can either 1/ be used as supplied or 2/ the Seraseq Antepartum T21 male cfDNA can be diluted using the Seraseq Postpartum T21 Male cfDNA, in order to decrease the observed fetal fraction which can be useful to establish assay limit of detection (LoD).

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 clinical specimens. The use of independent reference products may provide valuable information concerning assay accuracy and bioinformatics pipeline analysis.

PRINCIPLES OF THE PROCEDURE

Seraseq Antepartum T21 Male cfDNA and Postpartum T21 Male cfDNA are designed for use in NGS, PCR or microarray-based NIPT assays in steps that follow cfDNA isolation; no further purification or DNA isolation is needed.

REAGENTS

Table 1

Material No.	Product	Format
0720-1100	Seraseq® Antepartum T21 Male cfDNA	1 vial of 25 µL (1 mM Tris, 0.1 mM EDTA, 10 mM KCl. pH 8.0)
0720-1101	Seraseq® Postpartum T21 Male cfDNA	

Each material number is available as an individual product and is provided as 1 vial, 25 µL per vial, with a nominal concentration of ~10 ng/µL (exact concentration will vary per batch and can be found in the batch-related Technical Product Report on www.seracare.com).

WARNINGS AND PRECAUTIONS

For Research Use Only. Not for use in diagnostic procedures.
CAUTION: Handle Seraseq Antepartum and Postpartum T21 Male cfDNA and all materials derived from human blood products as though they are capable of transmitting infectious agents. Seraseq Antepartum and Postpartum T21 Male cfDNA are manufactured using processed cfDNA extracted from human blood and formulated in a 1 mM Tris, 0.1 mM EDTA, 10 mM KCl, pH 8.0 aqueous buffer.

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

Do not use those products after the expiration date. Avoid contamination of the product when opening and closing the vials.

STORAGE INSTRUCTIONS

Store Seraseq Antepartum and Postpartum T21 Male cfDNA frozen at -20°C. Once opened, a vial can be thawed and re-frozen up to five (5) times. Sub-aliquoting of the product into low DNA binding tubes may be advisable to limit the number of freeze/thaw cycles to five (5) or less. When stored in this fashion, those products will be stable through the expiration indicated on the vial label.

INDICATIONS OF REAGENT INSTABILITY OR DETERIORATION

Seraseq Antepartum and Postpartum T21 Male cfDNA are derived from naturally-occurring human cfDNA supplied in 25 µL 1 mM Tris, 0.1 mM EDTA, 10 mM KCl buffer. 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 Antepartum T21 Male cfDNA is derived from cfDNA extracted from a pregnant patient source sample carrying a male fetus with confirmed Trisomy 21. Seraseq Postpartum T21 Male cfDNA is derived from cfDNA extracted from the same patient source sample collected after birth. Material is further processed to maintain natural cfDNA size profile of both fetus (when present) and maternal DNA of approximately 170 base pairs on average (Figure 1). The purified DNA is diluted in a 1 mM Tris, 0.1 mM EDTA, 10 mM KCl, pH 8.0 aqueous buffer.

Instructions for Use

Thaw the product vial on ice before use. Mix by vortexing to ensure a homogeneous solution and spin briefly. Seraseq Antepartum and Postpartum T21 Male cfDNA should be integrated into library preparation after the DNA isolation step and go through the entire library preparation and sequencing or microarray hybridization steps in parallel with test specimens. Refer to standard assay procedures in order to determine the amount of material to use.

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If the NIPT assay workflow does not allow inputting the sample after the cfDNA isolation step, the Seraseq Antepartum and Postpartum T21 Male cfDNA may be inserted into the workflow in a manner consistent with plasma fractions prior to extraction. This can be achieved by further dilution in a buffer compatible with the cfDNA extraction procedure, such as SeraCare SeraCon™ Matribase, PBS, or other suitable diluent. Refer to standard assay procedures in order to determine the total volume and minimum amount of DNA to use. Perform the additional dilution immediately before proceeding with cfDNA extraction; do not store, freeze, or thaw diluted product.

The Seraseq Antepartum and Postpartum T21 Male cfDNA products may be diluted by the user to decrease the estimated fetal fraction of the sample.

Optional Reagents Not Supplied

- SeraCon™ Matribase Negative Diluent (Material Number # 1800-0022). Available at www.seracare.com
- Phosphate buffered saline (PBS)

Quality Control

Seraseq Antepartum and Postpartum T21 Male cfDNA do not have assigned values for trisomy or fetal fraction. There are many reasons why assays may observe variations in performance, which may or may not be of significance. It is therefore recommended that each laboratory qualify the use of each lot of Seraseq Antepartum and Postpartum T21 Male cfDNA with each assay system prior to its routine use.

INTERPRETATION OF RESULTS

Detection of aneuploidy and determination of fetal fraction may vary with method used, bioinformatic parameters, test reagent lots and other parameters[2]. Since the reference material does not have assigned values, the laboratory must establish an acceptable range for each lot of Seraseq Antepartum and Postpartum T21 Male cfDNA. 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.

EXPECTED RESULTS

Specific detection of chromosomal abnormality and estimation of fetal fraction will vary among different assays, procedures, lot numbers, and laboratories[2]. Each laboratory should establish its own range of acceptable values. It is recommended that any blending of the Antepartum and Postpartum cfDNA is performed based on the fetal fraction determination established in each laboratory with the assay with which the product is intended to be used.

LIMITATIONS OF THE PROCEDURE

Seraseq Antepartum and Postpartum T21 Male cfDNA 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. Data are provided for informational purposes. LGC Clinical Diagnostics does not claim that others can duplicate test results exactly. Note that based on your particular assay and analysis parameters, a different fetal fraction value may be calculated. Seraseq Antepartum and Postpartum T21 Male cfDNA is not a calibrator and should not be used for assay calibration. Adverse shipping and storage conditions or use of outdated products may produce erroneous results.

Note that the Seraseq Antepartum and Postpartum T21 Male cfDNA may not be compatible with certain NIPT methods based on the specific assay design and methodology.

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. Becking, EC, Linthorst J, Patton S. *et al*., 2023. Variability in Fetal Fraction Estimation: Comparing Fetal Fractions Reported by Noninvasive Prenatal Testing Providers Globally. *Clinical Chemistry*, 69(2), 160–167.

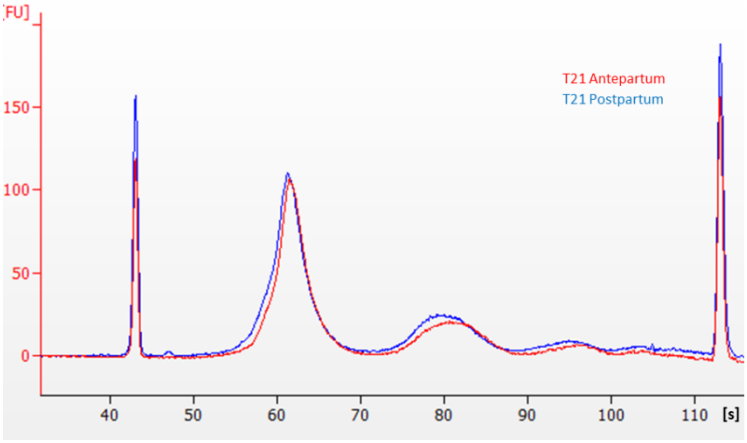

Figure 1: Representative DNA fragment size distribution for Antepartum (red) and Postpartum (blue) T21 Male cfDNA. Main cfDNA peak is present at 162 bp for both products, additional peak at approximately 330 bp.

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