PRODUCT SHEET

Seraseq® NIPT Reference Materials

ASSAY VALIDATION AND DAILY-RUN QC MATERIAL FOR NON-INVASIVE PRENATAL TESTING (NIPT)

HIGHLIGHTS

SINGLE-VIAL FORMAT OF PLASMA-LIKE MATERNAL-FETAL cfDNA

UNIQUE ANEUPLOIDY REFERENCE MATERIALS FOR COMMON TRISOMIES, MICRODELETIONS. NIPT-TESTED MATERIALS ASSURING PLOIDY AND FETAL FRACTION LEVELS

HIGH-QUALITY MANUFACTURED REFERENCE MATERIAL SAVES TIME AND COST PROCURING SAMPLES OR PRODUCING HOMEBREW REAGENTS WITH SPECIFIC VARIANTS

INTRODUCTION

Non-invasive Prenatal Testing (NIPT) continues to expand globally as the market shifts to covering a greater portion of the average risk population. Given the clinical implications of the test result, it is extremely critical that NIPT assays report back presence or absence of aneuploidies in an accurate and consistent manner. Reporting problems in assays are often related to low fetal fraction, process variation or bioinformatics, and can result in false negatives, false positives or no results. Matched maternal-fetal reference materials derived from pregnant maternal plasma enable accurate assessment of a broad range of NIPT assays, including those based on counting methods, SNPs, as well as differences in the length of maternal and fetal cfDNA.

The Seraseq NIPT reference materials portfolio consists of two product versions:

- Matched (or related) maternal and fetal cfDNA, derived from pregnancy plasma source samples
- Unmatched (or unrelated) fetal DNA, derived from aneuploid trophoblast cell lines, blended with maternal female genomic DNA

The portfolio of reference materials includes the most frequent chromosomal aneuploidies (such as Trisomy 21 and Trisomy 18) as well as the most frequent microdeletion – 22q11 or DiGeorge Syndrome. These materials are purpose-built to enable monitoring of a full NIPT process from extraction to reporting results. These materials are Research Use Only and not for In Vitro Diagnostic Use.

PRODUCT BENEFITS

- Develop, validate, monitor and troubleshoot your NIPT assay with a single sample
- Technology agnostic reference materials compatible with a broad range of NIPT assay methods (see Table 1)
- Save time, cost and increase QC consistency with a convenient full-process workflow control
- Eliminate need to find, source and maintain remnant samples
- Maintain regulatory compliance with a robust and consistently manufactured third-party QC material

PRODUCT FEATURES

- Collection of common chromosomal aneuploidies – trisomy 21, 18 and 13 as well as Euploid
- Assess expanded conditions such as 22q11 microdeletions (or DiGeorge Syndrome)
- Proprietary method maintains native cfDNA size profile of ~170 bp size distribution and natural maternal-fetal size difference
- Scalable technology allows for easy customization of fetal fraction, concentration and material formulation (either in plasma or fragmented DNA in buffer format)
- Long shelf life product allows for repeated use of the same lot for training, validation or assay performance assessment
- Ensure lot-to-lot consistency with materials manufactured in GMP-compliant and ISO 13485-certified facilities

PRODUCT DESIGN

Our first-generation (unmatched) products were created with a robust biosynthetic technology from unrelated maternal-fetal source materials (see Figure 1B). They are compatible with counting based assays (MPSS method) or amplification assays that do not require related maternal-fetal source samples.

However, as the NIPT assays in the market shifted towards SNP and Paired-End assays that require matched (or related) maternal-fetal source material, we developed our 2nd generation products with an in-house developed proprietary technology (See Figure 1A). This technology utilizes source plasma material obtained from pregnant patients (through an external collaboration) with a known condition as confirmed by NIPT or amniocentesis.

Both types of products are encapsulated and formulated in plasma matrix and need to be processed similarly to a patient specimen.

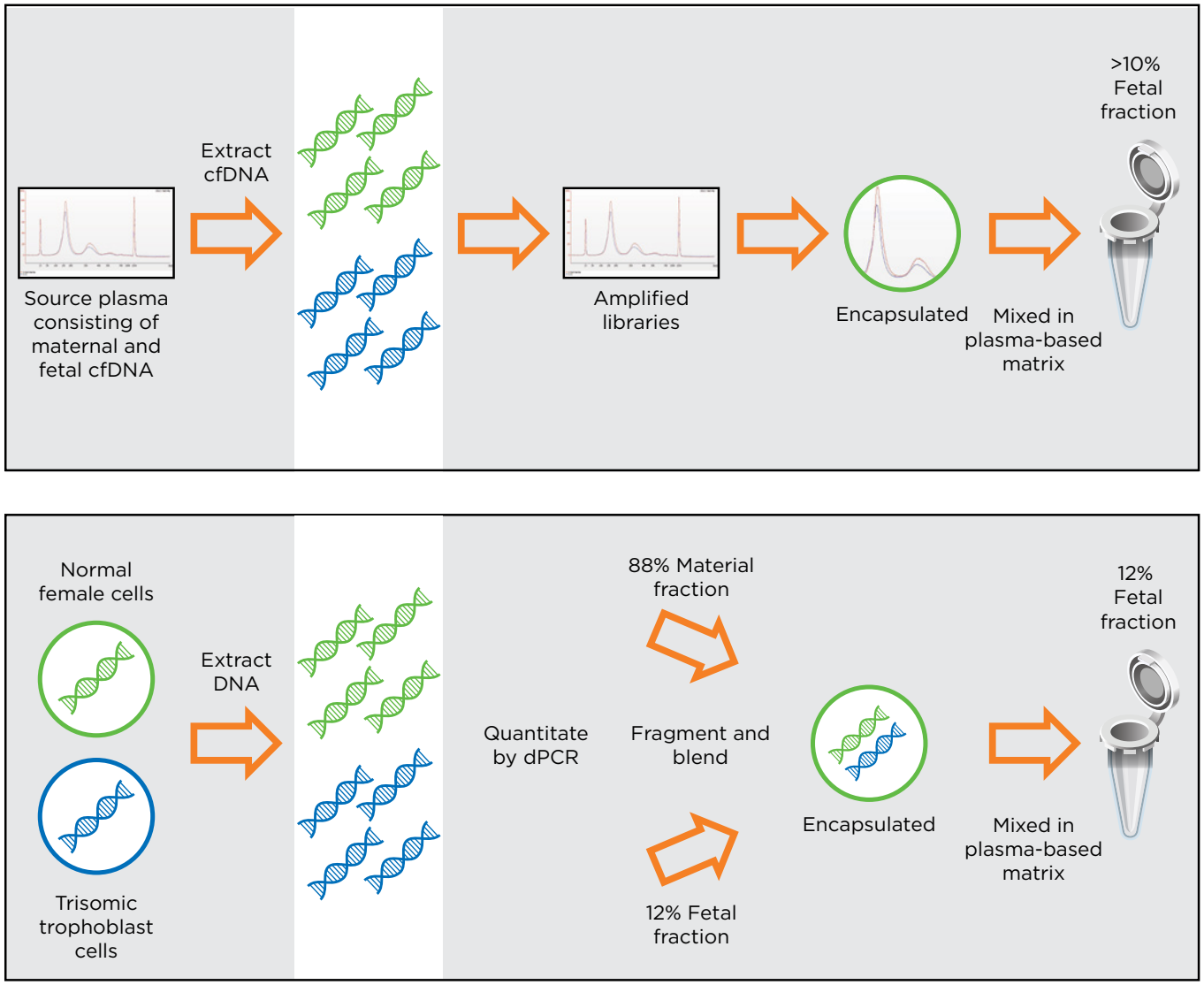
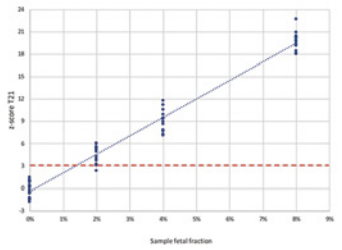


FIGURE 1: Creation of the NIPT reference materials.
Top (1A) — Matched materials prepared from a sample of maternal plasma containing maternal and fetal cfDNA. Plasma samples were collected from pregnant women, cfDNA was isolated, amplified via a proprietary method, encapsulated and formulated in a plasma matrix. Bottom (1B) – Unmatched materials were prepared by mixing fetal gDNA isolated from trophoblasts and an unrelated female (maternal) sample, then fragmented to ~170 bp size profile, encapsulated and formulated in a plasma matrix.

REAL-WORLD APPLICATION OF THE NIPT REFERENCE MATERIALS

The Seraseq NIPT reference materials have been successfully used in numerous labs across the world for a variety of applications ranging from new assay development to proficiency assessment and routine run QC:

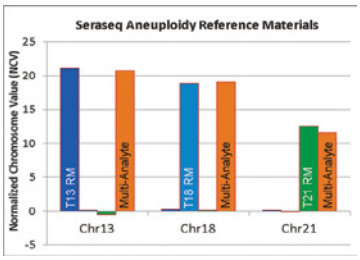
2A



Assay Development

- Enables limit of detection (LOD) studies and test range validity at varying fetal fraction levels. (Figure 2A)[1]
- Expedite new assay development and protocol optimization

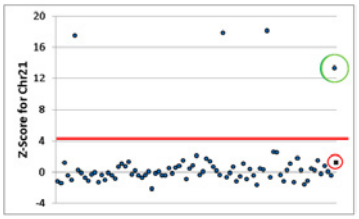
2B



Analytical Validation

- Confirm analytical performance and ability to correctly identify all the chromosomal aneuploidies (Figure 2B)
- Perform External Quality Assessment (EQA) and proficiency testing
- Conduct new assay installation and training

2C



Routine Run QC

- Produces patient-like performance for monitoring daily run performance. As shown in Figure 2C, when used as run controls, they cluster together with the patient samples (for both trisomy and euploid) providing a clear indication that these materials behave like patient samples.
- Customizable technology allows for specific volume, concentration and fetal fraction levels as required

FIGURE 2: Application of Trisomy 21 linearity panel and Multi-Analyte reference materials.
2A (Top). Trisomy 21 Reference Materials at fetal fractions 0%, 2%, 4% and 8% were analyzed to evaluate ability to measure samples with low fetal fraction (Vanadis NIPT System, PerkinElmer). 2B (Middle). Plot of multi-analyte reference material (12% T13, T18, & T21 fetal fraction in a single tube format) compared to the single analyte reference materials demonstrating excellent correlation. 2C (Bottom). Plot of samples run at Lab Cerba demonstrating majority of NIPT results being euploid with only 4 being T21 positive. The samples circled represent SeraCare T21 reference materials and their similarity to actual specimens.

COMPATIBILITY OF THE NIPT REFERENCE MATERIALS WITH EXISTING ASSAYS

	MPSS	MPSS — Pair End	Array	SNP	Non-NGS
Test examples	Verifi™, Iona®, MaterniT®	VeriSeq™	Harmony®	Panorama®	Vanadis®
Matched Maternal-fetal NIPT reference materials	✔	✔*	✔	✔	✔
Unmatched Maternal-fetal NIPT reference materials	✔	✖	✖	✖	✔

*** The 22q11 microdeletion size is approximately 2Mb, which is below the current 7Mb detection limit for VeriSeq NIPT v2[2].**
TABLE 1: NIPT tests which were shown to work with Seraseq NIPT reference materials by our customers. Blue check mark implies compatibility, while red cross mark indicates that the materials are not suitable for a given test

ABOUT SERACARE

TRUSTED SUPPLIER TO THE DIAGNOSTIC TESTING INDUSTRY FOR OVER 30 YEARS.

HIGH-QUALITY CONTROL PRODUCTS, RAW BIOLOGICAL MATERIALS, AND IMMUNOASSAY REAGENTS.

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RELIABLE, CONSISTENT REFERANCE MATERIAL

As a manufactured control reference material, developed under cGMP compliance in ISO 13485 certified facilities, Seraseq NIPT Reference Materials provide a consistent source of reference material for your NIPT assay. This not only ensures a reliable supply which is consistent from lot-to-lot; it also eliminates the need to obtain, characterize, blend, and document your own mixes of cell lines, saving you time and resources in your assay development and validation efforts.
Not for In Vitro Diagnostic Use. Research Use Only.

ORDERING INFORMATION

Matched NIPT Reference Materials

Material #	Product	Fill Size
0720-0169	Seraseq Euploid Male – Matched Reference Material	1 vial x 1 mL
0720-0170	Seraseq Euploid Female – Matched Reference Material	1 vial x 1 mL
0720-0167	Seraseq Trisomy 21 Male – Matched Reference Material	1 vial x 1 mL
0720-0168	Seraseq Trisomy 21 Female – Matched Reference Material	1 vial x 1 mL
0720-0171	Seraseq Trisomy 18 Male – Matched Reference Material	1 vial x 1 mL
0720-0172	Seraseq Trisomy 18 Female – Matched Reference Material	1 vial x 1 mL
0720-0173	Seraseq 22q11 Male - Matched Reference Material	1 vial x 1 mL
0720-0779	Seraseq Trisomy 13 Male - Matched Reference Material	1 vial x 1mL

Unmatched NIPT Reference Materials

Material #	Product	Fill Size
0720-0020	Aneuploidy Negative (Euploid) Reference Material	1 vial x 1 mL
0720-0019	Seraseq® Trisomy 21 Aneuploidy Reference Material,	1 vial x 1 mL
0720-0018	Seraseq® Trisomy 18 Aneuploidy Reference Material	1 vial x 1 mL
0720-0017	Seraseq® Trisomy 13 Aneuploidy Reference Material	1 vial x 1 mL

Custom NIPT Materials

The above products can be customized with regard to fetal fraction level, concentration, volume and format (DNA mix or plasma). Other conditions, including Sex Chromosome Aneuploidies (SCA) are available. Please contact SeraCare for any specific conditions.	Custom

LEARN MORE

To learn more about Seraseq NIPT Reference Materials and SeraCare's product offering for reproductive health, visit https://www.seracare.com/Controls---Reference-Materials-NGS-Reproductive-Health/.

Contact us at 508.244.6400 and 800.676.1881 or email info@seracare.com.

REFERENCES
1. Dahl, F et al. (2018) Imaging single DNA molecules for high precision NIPT. Scientific Reports 8:4549
2. Illumina VeriSeq https://science-docs.illumina.com/documents/RGH/veriseq-nipt-solution-v2-data-sheet-1000000032015/veriseq-nipt-solution-v2-data-sheet.pdf

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