

Clinical practice guidelines recommend that testing for fetal aneuploidy and open neural tube defects (ONTD) should be discussed with and offered to all women early in pregnancy, ideally at the first prenatal visit, regardless of maternal age. For low-risk women, maternal serum screening is often chosen as the initial testing process. Women at high-risk should consider noninvasive prenatal testing (NIPT), chorionic villus sampling (CVS), or amniocentesis instead of the tests listed below although maternal serum screening is still acceptable. High-risk factors include:

- Women ≥35 years old at delivery
- Previous pregnancy with chromosome aneuploidy
- Either parent is a known carrier of a chromosomal translocation or inversion
- Abnormal fetal ultrasound
- Increased risk of ONTD due to family history, use of specific medications (e.g. carbamazepine or valproic acid), or insulin-dependent diabetic status

Depending on the test chosen, maternal serum screening tests will report the risk of a fetus having the following conditions:

- ONTD
 - Incidence is ~1 out of every 1,000 pregnancies but varies by race and geographic location. The most common ONTDs include spina bifida and anencephaly. Risk factors include poorly controlled maternal diabetes mellitus, previous family history of an ONTD, and use of certain medications. Maternal age does not affect ONTD risk.
- Down Syndrome (trisomy 21 [T21])
 - Incidence is ~1 out of every 600 births. T21 is caused by an extra copy of chromosome 21 and causes features that include moderate to severe intellectual disability, characteristic facial features, and a several medical conditions including cardiac abnormalities. The risk of T21 increases with maternal age.
- Edwards Syndrome (trisomy 18 [T18])
 - Incidence is ~1 out of every 3,000 births. T18 is caused by an extra copy of chromosome 18 and causes features that include severe to profound intellectual disability, small birth size and growth rate, and several medical conditions more severe than T21. Most affected newborns do not survive the first year of life. The risk of T18 increases with maternal age.

TriCore offers several maternal serum screening test options. The decision on which test(s) to use should consider the gestational age at which the patient presents, the availability of a certified sonographer for nuchal translucency (NT) measurements, and patient and provider preferences.

MATERNAL SERUM SCREENING TECHNICAL INFORMATION

TEST	FIRST TRIMESTER MARKERS	SECOND TRIMESTER MARKERS	DETECTION RATE			SCREEN-POSITIVE RATE			RESULTS REPORTED
			T21	T18	ONTD	T21	T18	ONTD	
FIRST TRIMESTER SCREEN	NT, PAPP-A, hCG	N/A	85%	80%	N/A	6%	< 1%	N/A	first trimester
INTEGRATED SCREEN (without NT)	PAPP-A	AFP, hCG, uE3, DIA	85%	90%	80%	3-4%	0.01%	1-2%	second trimester
INTEGRATED SCREEN (with NT)	NT, PAPP-A	AFP, hCG, uE3, DIA	87%	90%	80%	1%	0.01%	1-2%	second trimester
SEQUENTIAL SCREEN	NT, PAPP-A, hCG	AFP, hCG, uE3, DIA	86%	90%	80%	1.6%	0.01%	1-2%	first and second trimesters
QUAD SCREEN	N/A	AFP, hCG, uE3, DIA	81%	80%	80%	4-5%	<0.5%	1-2%	second trimester

AFP = alpha-fetoprotein
 DIA = dimeric inhibin A
 hCG = human chorionic gonadotropin
 N/A = not applicable
 PAPP-A = pregnancy associated plasma protein A
 uE3 = unconjugated estriol

MATERNAL SERUM SCREENING TEST ORDERING INFORMATION EFFECTIVE 7/21/21

TEST	TRICORE TEST CODE	COLLECTION DETAILS	RECOMMENDATIONS
FIRST TRIMESTER SCREEN (first-trimester only)	MS1ST	<p>Collect blood sample between 11w0d and 13w6d gestation (CRL must be between 43 and 83.9 mm)</p> <p>Perform NT between 10w3d and 13w6d (CRL must be between 38 and 83.9 mm for usable NT value)</p>	<p>Use when patient accepts higher screen-positive rate and wants results in the first trimester</p> <p>NT measurement must be performed by an ultrasonographer certified by the Fetal Medicine Foundation (FMF) or the Nuchal Translucency Quality Review (NTQR)</p> <p>Does not screen for ONTD</p>
INTEGRATED SCREEN (combines first- and second-trimester results with risks reported after testing is completed for second-trimester sample)	<p>MSINT1 (1st sample)</p> <p>MSINT2 (2nd sample)</p>	<p>Collect first blood sample between 10w0d and 13w6d gestation (CRL must be between 32.4 and 83.9 mm)</p> <p>Perform NT between 10w3d and 13w6d (CRL must be between 38 and 83.9 mm for usable NT value)</p> <p>Collect second blood sample between 15w0d and 21w6d gestation</p>	<p>Use when patient wants the best possible detection rate with the lowest screen-positive rate and who do not mind returning for a second blood collection in the second trimester or waiting until the second trimester to receive results</p> <p>When combined with a first-trimester NT measurement, yields the best detection rate and lowest false positive rate of all maternal serum screening tests</p> <p>No results until after second trimester blood collection</p> <p>NT measurement must be performed by an ultrasonographer certified by the Fetal Medicine Foundation (FMF) or the Nuchal Translucency Quality Review (NTQR)</p> <p>Can be performed without NT at the expense of a slightly higher false positive rate</p>
SEQUENTIAL SCREEN (combines first- and second-trimester results with risks reported in both trimesters)	<p>MSSEQ1 (1st sample)</p> <p>MSSEQ2 (2nd sample)</p>	<p>Collect first blood sample between 11w0d and 13w6d gestation (CRL must be between 43 and 83.9 mm)</p> <p>Perform NT between 10w3d and 13w6d (CRL must be between 38 and 83.9 mm for usable NT value)</p> <p>Collect second blood sample between 15w0d and 21w6d gestation</p>	<p>Use when patient prefers a lower screen-positive rate (closer to that of the integrated test) but wants to know earlier if they are at higher risk and who do not mind returning for a second blood draw in the second trimester to complete the test</p> <p>An interpretation is provided after the first-trimester blood collection to identify pregnancies with very high aneuploidy risk</p> <p>NT measurement must be performed by an ultrasonographer certified by the Fetal Medicine Foundation (FMF) or the Nuchal Translucency Quality Review (NTQR)</p>
QUAD SCREEN (second-trimester only)	MSQUAD	Collect blood sample between 15w0d and 21w6d gestation (ideally between 16w0d and 18w6d)	Use when patient presents in the second trimester
AFP only screen (second-trimester only)	MSAFP	Collect blood sample between 15w0d and 21w6d gestation (ideally between 16w0d and 18w6d)	Use when patient prefers screening for only ONTD