GEN-2-043 Attachment I- AfpTest (for ONTDs) Instruction Manual

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NTD Labs SOP ID	GEN-2-043 (Att I)	**Division**	1-D Clinical Diagnostics Services
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		Functional Area	QM - Quality Management

Written by	Elizabeth Sylander
Functional Document Owner	Eurofins D CDS US Quality Management Department; Eurofins D CDS US Laboratory Management; Eurofins D CDS US Quality Control Department
Review and Approval	• Reviewers: Stephanie Zichi; Margaret Palladino; David Krantz; Norman Moore; Lisa Schmitt; Jonathan Hayden • Approver (Laboratory Director Only): Terrence Hallahan
Reason for Revision	Remove specimen collection section

Revision Log

Date	Rev.	Author	Description
May 18, 2018	1	Eurofins D CDS US Quality Management Department; Eurofins D CDS US Laboratory Management; Eurofins D CDS US Quality Control Department	

Electronic Signatures

Jonathan Hayden;Review;Jul 6, 2018 4:59 PM EDT
Stephanie Zichi;Review;Jul 9, 2018 10:06 AM EDT
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Lisa Schmitt;Review;Jul 11, 2018 10:32 AM EDT
Norman Moore;Review;Jul 11, 2018 1:47 PM EDT
Terrence Hallahan;Approval;Jul 18, 2018 9:53 AM EDT

Reporting Title: AFP Test for ONTDs

Test Definition: SECTRIAFP
Testing Location: Melville, NY
Reporting Location: Melville, NY

Description:

Alpha-fetoprotein (AFP) values are compared to the median value of the unaffected population at a given gestational age and the multiple of the median (MoM) is obtained and classified as either Within Range, Borderline elevated or significantly elevated. In addition, risks for open spina bifida, anencephaly, and ventral wall defects are provided.

Analytical Method(s):
Serum Specimens: AFP is measured on the AutoDELFIA machine using PerkinElmer's solid phase 2-site sandwich fluorometric assay (product number: PKI B079-201).

Dried Blood Specimens: AFP is measured on the AutoDELFIA machine using a lab developed solid phase 2-site sandwich fluorometric assay.

Specimen Requirements:

Specimen Type: Serum

Container/Tube: Red-top Vacutainer® tube or Serum Separator Tube (Red/Grey or Gold Top SST)

Specimen Volume: 0.5 ml of spun serum or 5 ml of unspun whole blood

Specimen Stability: Serum samples are stable at ambient temperature for 6 days.

Specimen Rejection Criteria: hemolysis, lipemia, incorrect tube type

Specimen Type: Dried Blood

Container/Tube: Dried Blood Spot Card

Specimen Volume: Minimum: 2 Spots, Preferred: 5 spots

Specimen Stability: Dried blood spots are stable at ambient temperature for 30 days.

Specimen Rejection Criteria: insufficient volume, layering, insufficient drying time

Specimen Collection Instructions

See Blood Specimen Collection from Venipuncture Instruction Manual or Dried Blood Specimen Collection Instruction Manual as applicable

Additional Information:

1. Indications for Testing: General population screening of pregnant women

2. GA at draw date is calculated by EDC or by Ultrasound. If data is entered for both methods, gestational age will be calculated based on Ultrasound. This comment relates to Ask on Entry questions (EDC, EDCUS, GAUS and USDATE).
3. Special Timing: Draw blood between 15 weeks, 0 days and 21 weeks, 6 days.
4. Do not draw blood after performing amniocentesis, as that may lead to an artificially increased serum alpha-fetoprotein level and unreliable results.
5. Specimen Stability: Serum specimens are stable at ambient temperature for 6 days. Dried blood specimens are stable at ambient temperature for 30 days.
6. Rejection Criteria Serum: hemolysis, lipemia, incorrect tube type
7. Rejection Criteria Dried Blood: insufficient volume, layering, insufficient drying time

CPT Code: 1 x 82105

Reference Values:

Total ONTDs/VWD
AFP MoM < 2 MoM are Within Range
AFP MoM 2-2.49 MoM are Borderline Elevation
AFP MoM ≥ 2.5 MoM are Significant Elevation

An Interpretive Report will be provided.

Supplemental Report:
No

Testing Algorithm:

Follow up testing:
1. MSAFP Borderline Elevation and GA<19 weeks: Repeat blood or serum.
2. MSAFP Borderline Elevation and GA>=19 weeks: Genetic Counseling, Ultrasound and offer of amniocentesis.
3. MSAFP Significant Elevation: Genetic Counseling, Ultrasound and offer of amniocentesis.

Consents/Authorizations:
Patient signature on patient authorization/assignment on requisition form is required.

Disclaimers:

Serum Specimens:
The PerkinElmer AFP assay has been approved by the FDA for testing for Open neural tube defects.

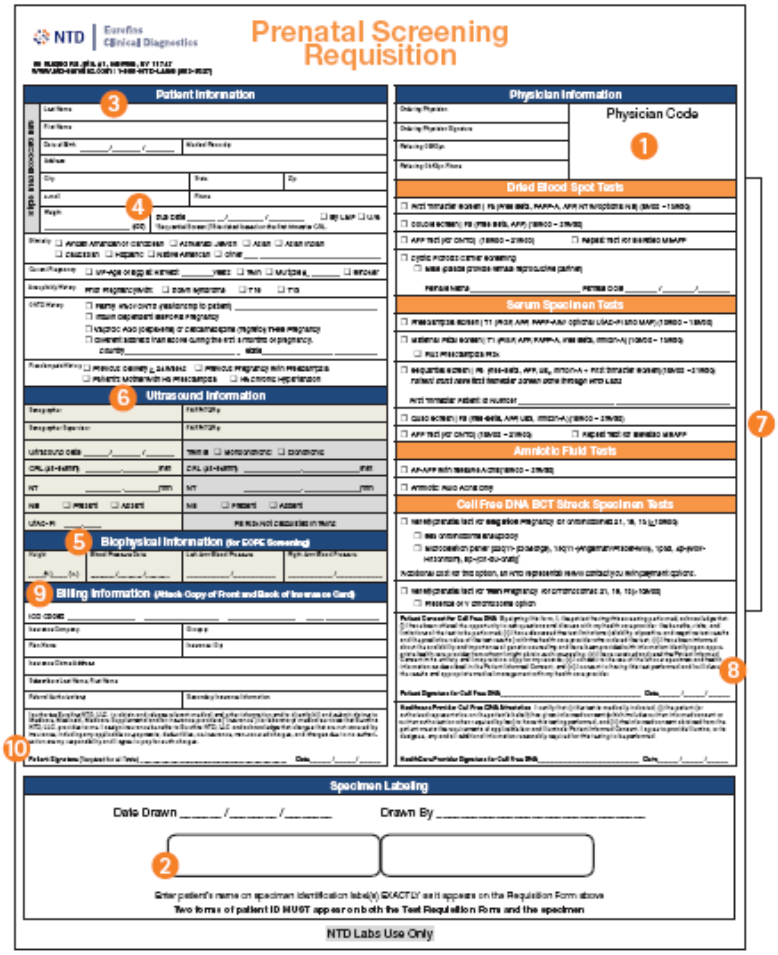
Dried Blood Specimens:
The test was developed and its performance characteristics determined by Eurofins NTD, LLC. It has not been cleared or approved by the U.S. Food and Drug Administration. The methods and performance characteristics have been reviewed and approved by the New York State Department of Health.

Test Requisition Instructions

NTD | Eurofins Clinical Diagnostics

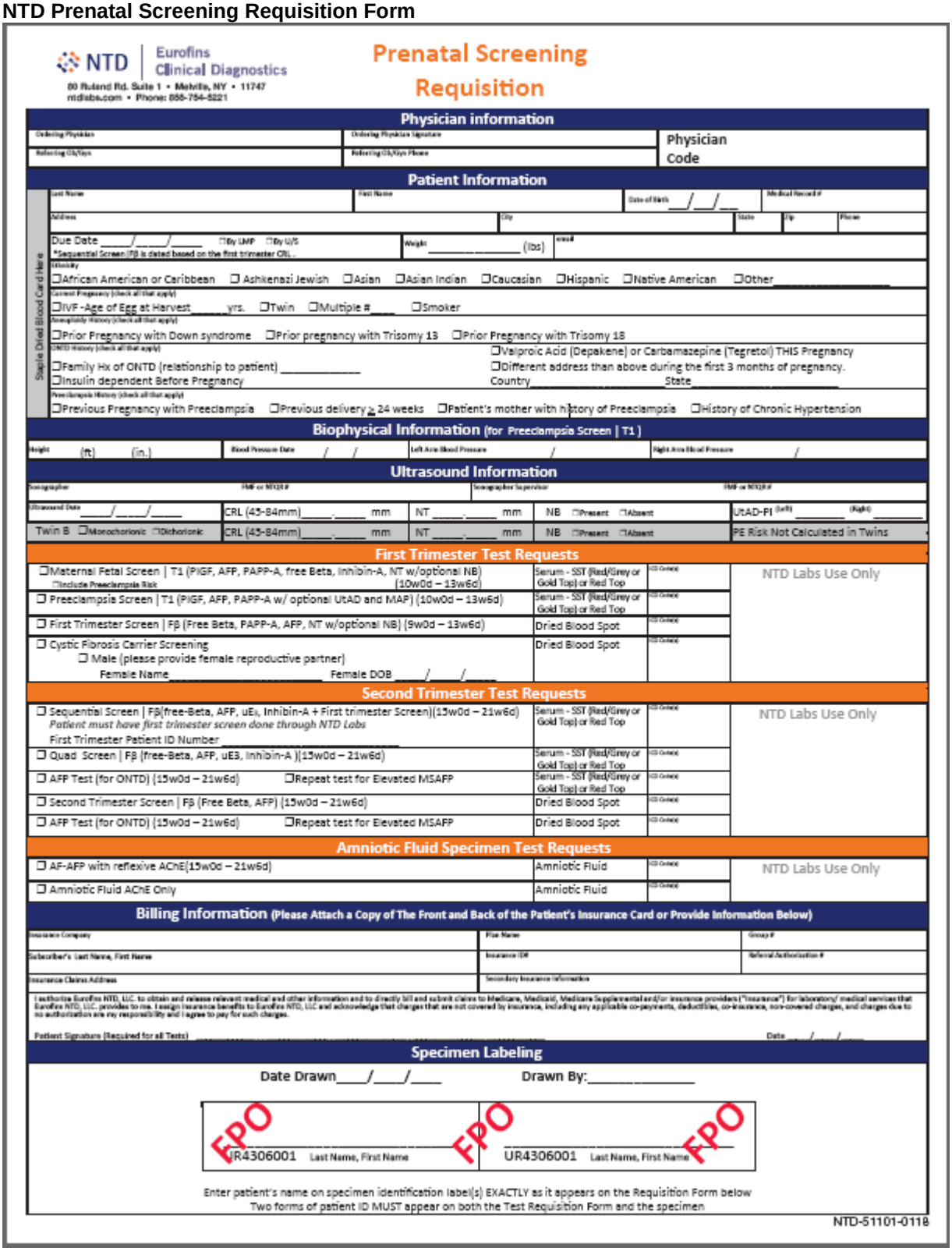
Prenatal Screening Test Requisition Form Instructions

1. **Account Information** – Please enter Ordering Physician name and Referring Ob/Gyn name and phone number, if applicable. A provider signature is required for patients with Medicaid.
2. **Specimen Labels** – Preprinted with the requisition number. Please enter the patient's last and first name EXACTLY as they appear on the requisition form. Affix label(s) to patient specimen(s). Please complete date drawn and drawn-by fields.
3. **Patient Information** – For all tests, please complete patient weight, ethnicity and current pregnancy information. Complete additional patient history as appropriate for test(s) ordered. *Please note, all patient information requested is used to ensure the most accurate risk assessment possible for your patient.*
4. **Gestational Age** – Complete for tests other than First Trimester Screen | Fβ, Sequential Screen | Fβ, PreeclampsiaScreen℠ | T1 or Maternal Fetal Screen℠ | T1 which require CRL (see section 6).
5. **Biophysical Information** – Complete this section for preeclampsia screening only.
6. **Ultrasound Information** - Please provide sonographer and supervisor names and credentialing numbers. Enter all ultrasound information as appropriate for test(s) ordered.
7. **Test Requests** - Tests are ordered by specimen type. Check all tests that apply and provide appropriate ICD codes.
8. **Cell Free DNA** - BOTH the physician and patient signatures are required.
9. **Billing Information** – Provide photocopy of front and back of insurance card or print the information in the required fields.
10. **Patient Signature** - Required for all tests.



Please call 1-888-NTD-LABS (683-5227) for further assistance.

NTD Prenatal Screening Requisition Form



NTD | Eurofins Clinical Diagnostics
80 Ruland Rd. Suite 1 • Melville, NY • 11747
ntdlabs.com • Phone: 888-754-5221

Prenatal Screening Requisition

Physician information

Ordering Physician | Ordering Physician Signature | Physician Code
Referring OB/Gyn | Referring OB/Gyn Phone

Patient Information

Staple Dried Blood Card Here

Last Name | First Name | Date of Birth ___/___/___ | Medical Record #
Address | City | State | Zip | Phone
Due Date ____/____/____ ☐By LMP ☐By U/S
*Sequential Screen (Fβ is dated based on the first trimester CRL.
Weight _____ (lbs) | email
Ethnicity
☐African American or Caribbean ☐ Ashkenazi Jewish ☐Asian ☐Asian Indian ☐Caucasian ☐Hispanic ☐Native American ☐Other _____
Current Pregnancy (check all that apply)
☐IVF -Age of Egg at Harvest _____ yrs. ☐Twin ☐Multiple #___ ☐Smoker
Anuegnicity History (check all that apply)
☐Prior Pregnancy with Down syndrome ☐Prior pregnancy with Trisomy 13 ☐Prior Pregnancy with Trisomy 18
ONTD History (check all that apply)
☐Family Hx of ONTD (relationship to patient) _____
☐Insulin dependent Before Pregnancy
☐Valproic Acid (Depakene) or Carbamazepine (Tegretol) THIS Pregnancy
☐Different address than above during the first 3 months of pregnancy.
Country _____ State _____
Preeclampsia History (check all that apply)
☐Previous Pregnancy with Preeclampsia ☐Previous delivery ≥ 24 weeks ☐Patient's mother with history of Preeclampsia ☐History of Chronic Hypertension

Biophysical Information (for Preeclampsia Screen | T1)

Height (ft) (in.) | Blood Pressure Date ___/___/___ | Left Arm Blood Pressure ___/___ | Right Arm Blood Pressure ___/___

Ultrasound Information

Sonographer | NMD or NP/LP # | Sonographer Supervisor | NMD or NP/LP #
Ultrasound Date ____/____/____ | CRL (45-84mm)____.____ mm | NT ____.____ mm | NB ☐Present ☐Absent | UtAD-PI (Left) _____ (Right) _____
Twin B ☐Monochorionic ☐Dichorionic | CRL (45-84mm)____.____ mm | NT ____.____ mm | NB ☐Present ☐Absent | PE Risk Not Calculated in Twins

First Trimester Test Requests

☐Maternal Fetal Screen | T1 (PlGF, AFP, PAPP-A, free Beta, Inhibin-A, NT w/optional NB) (10w0d – 13w6d) ☐Include Preeclampsia Risk	Serum - SST (Red/Grey or Gold Top) or Red Top	CD Code(s)	NTD Labs Use Only
☐ Preeclampsia Screen | T1 (PlGF, AFP, PAPP-A w/ optional UtAD and MAP) (10w0d – 13w6d)	Serum - SST (Red/Grey or Gold Top) or Red Top	CD Code(s)	
☐ First Trimester Screen | Fβ (Free Beta, PAPP-A, AFP, NT w/optional NB) (9w0d – 13w6d)	Dried Blood Spot	CD Code(s)	
☐ Cystic Fibrosis Carrier Screening ☐ Male (please provide female reproductive partner) Female Name_____ Female DOB ____/____/____	Dried Blood Spot	CD Code(s)	

Second Trimester Test Requests

☐ Sequential Screen | Fβ(free-Beta, AFP, uE3, Inhibin-A + First trimester Screen)(15w0d – 21w6d) *Patient must have first trimester screen done through NTD Labs* First Trimester Patient ID Number _____	Serum - SST (Red/Grey or Gold Top) or Red Top	CD Code(s)	NTD Labs Use Only
☐ Quad Screen | Fβ (free-Beta, AFP, uE3, Inhibin-A)(15w0d – 21w6d)	Serum - SST (Red/Grey or Gold Top) or Red Top	CD Code(s)	
☐ AFP Test (for ONTD) (15w0d – 21w6d) ☐Repeat test for Elevated MSAFP	Serum - SST (Red/Grey or Gold Top) or Red Top	CD Code(s)	
☐ Second Trimester Screen | Fβ (Free Beta, AFP) (15w0d – 21w6d)	Dried Blood Spot	CD Code(s)	
☐ AFP Test (for ONTD) (15w0d – 21w6d) ☐Repeat test for Elevated MSAFP	Dried Blood Spot	CD Code(s)	

Amniotic Fluid Specimen Test Requests

☐ AF-AFP with reflexive AChE(15w0d – 21w6d)	Amniotic Fluid	CD Code(s)	NTD Labs Use Only
☐ Amniotic Fluid AChE Only	Amniotic Fluid	CD Code(s)	

Billing Information (Please Attach a Copy of The Front and Back of the Patient's Insurance Card or Provide Information Below)

Insurance Company | Plan Name | Group #
Subscriber's Last Name, First Name | Insurance ID# | Referral Authorization #
Insurance Claims Address | Secondary Insurance Information

I authorize Eurofins NTD, LLC. to obtain and release relevant medical and other information and to directly bill and submit claims to Medicare, Medicaid, Medicare Supplemental and/or insurance providers ("Insurance") for laboratory/ medical services that Eurofins NTD, LLC. provides to me. I assign insurance benefits to Eurofins NTD, LLC and acknowledge that charges that are not covered by insurance, including any applicable co-payments, deductibles, co-insurance, non-covered charges, and charges due to no authorization are my responsibility and I agree to pay for such charges.

Patient Signature (Required for all Tests) _____ Date ___/___/___

Specimen Labeling

Date Drawn____/____/____ Drawn By:_____

FPO UR4306001 Last Name, First Name | FPO UR4306001 Last Name, First Name

Enter patient's name on specimen identification label(s) EXACTLY as it appears on the Requisition Form below
Two forms of patient ID MUST appear on both the Test Requisition Form and the specimen

NTD-51101-0118

EMR Ask at Order Entry (AOE) Questions:

Test ID	Question ID	Description	Type	Required
SECTRIAFP	REPEAT	Repeat Specimen for Elevated MSAFP • No • Yes	Answer List	No
SECTRIAFP	MATWT	Maternal Weight	Plain Text	YES
SECTRIAFP	MWLBSKGS	Units • LBS • KGS	Answer List	YES
SECTRIAFP	ETHNIC	Ethnicity • African American/Caribbean • Asian • Asian Indian • Caucasian • Hispanic • Native American • Other	Answer List	YES
SECTRIAFP	HXNTD	Family History of ONTD • None • Prev Child • Patient's Sister's Child • Patient's Brother's Child • Patient's Sister • Patient's Brother • Patient's Aunt • Patient's Uncle • Partner's Prev Child • Partner's Brother	Answer List	YES
SECTRIAFP	IVFAGE	IVF-Age of Egg (years)	Plain Text	NO
SECTRIAFP	NOF	Number of Fetuses • 1 • 2	Answer List	YES
SECTRIAFP	SMOKE	Is Patient a Smoker • No • Yes	Answer List	YES
SECTRIAFP	VALPRO	Valproic Acid or carbamazepine used during preg • No • Yes	Answer List	YES
SECTRIAFP	IDDM	Insulin dependent diabetic Prior to pregnancy • No	Answer List	YES

		• Yes		
SECTRIAFP	EDD	Due Date	Plain Text	NO
SECTRIAFP	EDDUS	Due Date Confirmed By U/S • No • Yes	Answer List	NO
SECTRIAFP	GAUS	GA at U/S (Weeks.Days)	Plain Text	NO
SECTRIAFP	USDATE	U/S Date	Plain Text	NO
SECTRIAFP	CO3MO	Address-Country(If different 1st 3 mos. of preg)	Plain Text	NO
SECTRIAFP	ST3MO	Address-State(If different 1st 3 mos. Of preg)	Plain Text	NO

EMR Result Codes:

Data Type	Code	LOINC	Name	Contains Result	Comments
CE	RSKTBL		Risk Table	No	Included if disorders are available
ST	TONTD	59462-2	Total ONTDs/VWD	Yes	Risk result information contained in NTEs
ST	TONTD-B	59462-2	Total ONTDs/VWD Twin B	Yes	Risk result information contained in NTEs
CE	MKRANA		Markers/Analytes	No	Included if any 1T markers are available
CE	2T		2nd Trimester	No	
CE	AFP2	19176-7	AFP	Yes	Measurements contained in NTEs
CE	DGD		Demographic Data	Yes	Included if demographic data is available (contained in NTEs)
CE	2TD		2nd Trimester Data	Yes	Included if test-specific data is available (contained in NTEs)
CE	REC		Recommendations	Yes	Only displayed if recommendations are available
CE	REC-B		Recommendations Twin B	Yes	Displayed for twin B, Only displayed if recommendations are available
CE	COM	55107-7	Comments	Yes	Only displayed if comments are available
CE	COM-B	55107-7	Comments Twin B	Yes	Displayed for twin B, Only displayed if comments are available
CE	FTR		Footer	Yes	Only displayed if footer is available
CE	FTR-B		Footer Twin B	Yes	Displayed for twin B, Only displayed if footer is available
CE	NOT		Notification	Yes	Included for Unsatisfactory Specimens Only
CE	NOT-B		Notification Twin B	Yes	Included for Unsatisfactory Specimens Only, Displayed for twin B

Example Report

NTD Eurofins Clinical Diagnostics 60 Ruland Rd. Suite 1 • Melville, NY • 11747 • (631) 425-0800 • Fax (631) 425-0864 • reporting@ntd-eurofins.com

Afp Test (for ONTDs)

Physician ID #: 24328
Physician Tel #: (000) 000-0000
OB SPECIALISTS
100 ANYWHERE ST
MELVILLE, NY 11747

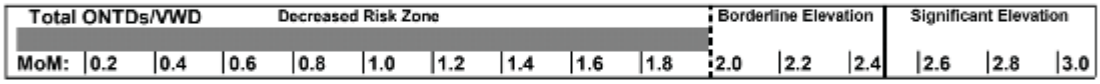
Patient Name: BORDERLINE, AFPONLY
Client ID #:
Patient ID #: 17SE0099992
Date of Birth: 05/29/72
Age at EDC: 45
Mat. Weight: 225 lbs
Ethnicity: Caucasian
Prev Chrom Hx: None
Multi. Preg: No
Smoker: No
EDC: 09/01/17

2nd Trimester data
Insulin Rx: No
Fam Hx ONTD: No
State: NY
Draw Date: 03/11/17
GA @ Draw: 15w1d
GA by: EDC By U/S
Date Received: 03/13/17
Report Date: 03/14/17

2nd Trimester

Marker/Analyte	Value	MoM	%ile
AFP	42.27 (IU/ml)	2.03	98

Risk Table	Cut-Off	Risk Before Screening	Risk After Screening	Result
Total ONTDs/VWD	2 MoM	1 in 588	1 in 323	**BORDERLINE ELEVATION**
Open Spina Bifida	--	1 in 2,000	1 in 536	---
Anencephaly	--	1 in 1,429	1 in 1,350	---
Ventral Wall Defect	--	1 in 2,000	1 in 2,040	---



Recommendations:
• Repeat blood or serum.

Jonathan B. Carmichael, Ph.D
Laboratory Director,
Eurofins NTD, LLC

Terrence W. Hallahan, Ph.D
Laboratory Director,
Eurofins NTD, LLC

CAUTION: These results do not eliminate the possibility that this pregnancy may be associated with birth defects including open neural tube defects, ventral wall defects, or other disorders not detectable by this screening test. This report contains Protected Health Information. The recipient shall not disclose this information without the permission of the patient unless required to provide appropriate medical care. **Any recommendations or comments on specific analytes are provided as a courtesy to the ordering physician and do not constitute medical advice.**

This report was generated on: 03/14/2017 05:03:55 PM

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Physician Information Brochure

Enhance Prenatal Screening with MSAFP

NTD Labs' second-trimester MSAFP screening, available via dried blood spot:

A simple solution for ONTD risk assessment

ACMG* guidelines recommend that all pregnant women, regardless of medical background and family history, be offered **maternal serum alpha-fetoprotein (MSAFP) screening** between **16 to 18 weeks'** gestation.[1]

Cell-free DNA non-invasive prenatal testing (NIPT) has not negated the continued need for open neural tube defect (ONTD) screening.

Second-trimester MSAFP identifies pregnancies at risk for the following:

- Open neural tube defects (ONTDs)
- Anencephaly
- Ventral wall defects

MSAFP may also be used to predict increased risk for:

- Low birth weight
- Macrosomia
- Placenta accreta
- Preeclampsia
- Preterm birth
- Spontaneous abortion
- Stillbirth

Why MSAFP screening from NTD Labs?

- Supports ACOG** recommendations
- Provides high detection rates for ONTDs[2]
  - 90% detection rate for spina bifida
  - 98% detection rate for anencephaly
- Offers fast turnaround time (24–48 hours)
- Low out-of-pocket costs for patients
  - NTD Labs is well-contracted with third-party payers
- Offers flexibility, convenience and ease of use
  - Flexible sample types—available on dried blood spot (DBS) or whole blood
  - Same requisition form as other NTD Labs' prenatal screening tests
  - Simple, easy-to-read reports, available through online portal (eReports)

For more than 30 years, NTD Labs has pioneered the research and development of prenatal testing protocols for ONTDs, Down syndrome, trisomy 18 and trisomy 13. Today, NTD Labs is a proven leader in prenatal testing, serving universities, medical centers, hospitals, laboratories, obstetricians and maternal fetal medicine specialists worldwide.

Count on NTD Labs for your prenatal screening needs.

For more information, please contact your local Genetic Accounts Executive, or call us at **1-888-NTD-LABS** (683-5227).

NTD | Eurofins Clinical Diagnostics

80 Ruland Road, Suite 1, Melville, NY 11747
www.ntdlabs.com | 1-888-NTD-LABS (683-5227)

1. Driscoll, DA. ACMG Policy Statement: second-trimester maternal serum screening for fetal open neural tube defects and aneuploidy. ACMG. July 10, 2004.
2. Milunsky A, Jick SS, Bruell CL, et al. Predictive values, relative risks and overall benefits of high and low maternal serum-fetoprotein screening in singleton pregnancies: new epidemiologic data. Am J Obstet Gynecol. 1988;161(2):291-297.

* American College of Medical Genetics ** The American Congress of Obstetricians and Gynecologists

Pursuant to applicable federal and/or state laboratory requirements, NTD Labs has established and verified the accuracy and precision of its testing services. Testing has not been cleared or approved by the FDA.

 NTD-011110-05/17 Printed in USA

Patient Information Brochure

N/A