

# Laboratory Bulletin

Important News from DCL Medical Laboratories



September 1, 2009

## DCL begins performing Prenatal Screening tests in-house

*Single AFP, Triple and Quad Screens assess risk for Down syndrome, open neural tube defects or trisomy 18*

As a full-service medical laboratory with a strong focus on women's health, DCL is proud to announce the capability to perform Triple and Quad Screen testing in-house. This testing is performed between the 15th and 22nd weeks of pregnancy to screen for fetal risk of Down syndrome (trisomy 21), open neural tube defects (open spina bifida or anencephaly) or trisomy 18.

This Laboratory Bulletin contains important information regarding specimen collection, test ordering and results interpretation for this testing. If you have any questions, please contact DCL Client Services at (317) 874-1334 or toll free at (866) 874-1334.

### Prenatal Screening

Prenatal screening is performed to assist in the identification of fetal development with increased risk of certain birth defects, including open neural tube defects (NTD) such as spina bifida and anencephaly, and chromosomal disorders such as Down syndrome and trisomy 18.

Screening tests are designed to identify those individuals with increased risk who might benefit from additional diagnostic testing. Prenatal screening is not diagnostic.

Risk assessment for neural tube defects is based on Alpha-fetoprotein (AFP) alone. Down syndrome and trisomy 18 risk assessments are based on multiple marker combinations that include AFP, total beta-human chorionic gonadotropin (hCG), unconjugated Estriol (uE3) and inhibin A.

Quantitative alpha-fetoprotein concentrations are correlated with a greater risk of a fetus with a neural tube defect if increased, and if decreased, are correlated with an higher risk of Down syndrome.

<b>Prenatal Screen, Single Marker-NTD</b>	
<b>AFPM-NTD</b>	<b>DCL #: 8001</b>
<b>Tests Included:</b> Alpha-fetoprotein (AFP)	
<b>Prenatal Screen, Triple Marker</b>	
<b>PREN RISK3</b>	<b>DCL #: 8002</b>
<b>Tests Included:</b> Alpha-fetoprotein (AFP) Unconjugated Estriol (uE3) Beta-hCG (hCG)	
<b>Prenatal Screen, Quadruple Marker</b>	
<b>PREN RISK4</b>	<b>DCL #: 8003</b>
<b>Tests Included:</b> Alpha-fetoprotein (AFP) Unconjugated Estriol (uE3) Beta-hCG (hCG) Inhibin A (DIA)	
<b>Collection Container:</b> SST - Serum	
<b>Storage/Stability:</b> <b>AFP:</b> 3 days refrigerated <b>uE3:</b> 7 days at refrigerated <b>hCG:</b> 7 days at refrigerated <b>DIA:</b> 24 hours refrigerated or 30 days frozen	
<b>Turnaround Time:</b> 1-3 days	
<b>Days Run:</b> Mon - Fri	
<b>Preferred amount:</b> 4.0 mL	
<b>Minimum amount:</b> 2.0 mL	
<b>Centrifuge required?:</b> Yes	
<b>Special Instructions:</b> The serum specimens should be collected between 15 and 22 weeks of gestation. Provide required patient demographic information by submitting a completed Prenatal Screening Patient Information Form.	
<b>Method:</b> <b>AFP, hCG and UE3:</b> Immunochemiluminescence assay <b>DIA:</b> Enzyme Immunoassay	
<b>Reference Range:</b> See chart on page two.	
<b>Clinical Utility:</b> <ul style="list-style-type: none"> <li>• Prenatal risk assessment for neural tube defect</li> <li>• Prenatal risk assessment for Down syndrome (trisomy 21)</li> <li>• Prenatal risk assessment for Edwards syndrome (trisomy 18)</li> </ul>	
<b>CPT AFPM-NTD (8001): 82105</b>	Medicare Reimbursement: \$24.49
<b>CPT PREN RISK3 (8002): 82105, 82677, 84702</b>	Medicare Reimbursement: \$24.49, \$35.31, \$10.20
<b>CPT PREN RISK4 (8003): 82105, 82677, 84702, 86336</b>	Medicare Reimbursement: \$24.49, \$35.31, \$10.20, \$21.89

\* Per Jan. 2009 Clinical Diagnostic Laboratory Fee Schedule for Indiana.

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*Continued on the next page*

Maternal beta-hCG is elevated in pregnancies with a fetus with Down syndrome. Decreased levels of uE3 and AFP are associated with Down syndrome and trisomy 18. The addition of inhibin A appears to make the test more accurate in detecting pregnancies at risk of Down syndrome. In Down syndrome pregnancies, inhibin A levels are two-fold greater than in unaffected pregnancies, leading to the detection of approximately 40% of Down syndrome cases with a 5% false positive rate. However, when combined with maternal AFP, hCG and uE3, the detection rate increases to approximately 75%. Addition of inhibin A improves the detection rate by approximately 10% relative to commonly used marker combinations. Multiple marker screening is typically performed at 15-17 weeks gestation. Although it can be performed at 14-22 weeks gestation, risk calculation for open neural tube defects (OSB) cannot be calculated if the specimen is collected prior to the 15th week of gestation.

### Method and Interpretation of Results

For interpretation of results, pre-analytical information provided by the patient's health provider is crucial in addition to analyte values. A completed copy of the Prenatal Screening Patient Information Form included with this Laboratory Bulletin must be provided with the completed requisition.

The following patient information MUST be provided for accurate interpretation of results:

- Maternal date of birth (mm/dd/yy)
- Maternal weight
- Patient's ethnicity
- Number of fetuses in the pregnancy
- Insulin-dependent diabetic status
- Estimated date of delivery as determined by ultrasound, LMP or physical exam
- Indication of any family history of neural tube defects
- Whether or not a repeat specimen is being submitted

Serum concentrations of AFP, hCG and uE3 are determined using Immunochemiluminescence assay and inhibin A is determined using Enzyme Immunoassay. The multiple of the median (MoM) is calculated for each. Different MoM values are used for African American and Asian populations. MoM values for all analytes are adjusted for maternal weight; however, only the AFP MoM is adjusted for insulin dependent diabetes status. All four MoM values are combined with maternal age at time of delivery to determine the Down syndrome risk. Trisomy 18 risk is based on maternal age and AFP, hCG and uE3 MoMs. Neural tube defect risk is based on the AFP MoM only.

### Reference Ranges (Please note that risk assessment is for mid-term only.)

Open neural tube defect		Normal risk	Increased risk
	Singleton Pregnancy	AFP MoM < 2.5	AFP MoM ≥ 2.5
	Twin Pregnancy	AFP MoM < 4.0	AFP MoM ≥ 4.0
	Triplet Pregnancy	AFP MoM < 4.5	AFP MoM ≥ 4.5
	Insulin-dependent diabetic	AFP MoM < 1.9	AFP MoM ≥ 1.9
	Insulin-dependent diabetic Twin Pregnancy	AFP MoM < 3.5	AFP MoM ≥ 3.5
<b>Down syndrome Risk Cutoff = 1 : 270</b>			
<b>Trisomy 18 Risk Cutoff = 1 : 100</b>			

### References:

1. Canick JA, MacRae AR. Second trimester serum markers. Semin Perinatol. 2005 Aug;29(4):203-8. Review.
2. Cleary-Goldman J, Morgan MA, Malone FD, Robinson JN, D'Alton ME, Schulkin J. Screening for Down syndrome: practice patterns and knowledge of obstetricians and gynecologists. Obstet Gynecol. 2006 Jan;107(1):11-7.
3. Wald NJ, Huttly WJ, Hackshaw AK. Antenatal screening for Down's syndrome with the quadruple test. Lancet. 2003 Mar 8;361(9360):835-6.
4. Renier MA, Vereecken A, Van Herck E, Straetmans D, Ramaekers P, Buytaert P. Second trimester maternal dimeric inhibin-A in the multiple-marker screening test for Down's syndrome. Hum Reprod. 1998 Mar;13(3):744-8.
5. Benn PA, Fang M, Egan JF, Horne D, Collins R. Incorporation of inhibin-A in second-trimester screening for Down syndrome. Obstet Gynecol. 2003 Mar;101(3):451-4.
6. Arben Paralloi and Dr. Celia De Lozier. Second Trimester Maternal Screening Programs for the Detection of Down's Syndrome. Geneva Foundation for Medical Education and Research.