NEW YORK
state department of
HEALTH

Nirav R. Shah, M.D., M.P.H.
Commissioner

Sue Kelly
Executive Deputy Commissioner

New York State FEDM – Proficiency Testing Program

TO: Laboratory Directors

CATEGORY: Fetal Defect Markers (FEDM)

MAILOUT: January 24, 2012

FROM: Dr. G.J. Mizejewski, Director of FEDM Program

DUE DATE: February 8, 2012

Samples:
There are five (5) vials labeled **MS276** to **MS280**, each containing various predetermined amounts of alpha-fetoprotein (**AFP**), human chorionic gonadotropin (**hCG**), unconjugated estriol (**uE3**) and Dimeric **Inhibin A**. Also, five additional vials (AF 276 to AF 280) containing AFP in amniotic fluid have also been included. In addition, five extra vials **FT 276 to FT 280** containing human chorionic gonadotropin (**hCG**) and **PAPP-A** are added for ***optional*** testing. Please note that you do not have an option if you offer First Trimester and or Integrated Testing but the results of **FT 276 to FT 280** will ***not be graded***. Please analyze for all of those markers tested in your laboratory the same way as you would with a patient sample. If your lab is also measuring Amniotic fluid AFP, you are also required to measure those samples provided. Maternal serum samples are in human-derived serum base, sterile filtered and dispensed. Please **keep refrigerated** until use, but do ***not*** freeze. Before analyzing, make sure samples are mixed completely.

Reporting of Results:
All laboratories **must** submit their proficiency testing results electronically through the electronic proficiency testing reporting system (**EPTRS**) on the Department's Health Commerce System (HCS). The HCS is a secure website and requires all users to obtain an account ID in order to access the HCS and EPTRS application. The portal's URL is https://commerce.health.state.ny.us. Questions regarding the entry and submission of proficiency test results or the account application process can be directed to clepeptrs@health.state.ny.us. If your laboratory does not have an HCS account, you must request one as soon as possible before the next PT event by contacting the Clinical Laboratory Evaluation Program at 518-486-5410. Also, please also **see attached January 2012 bulletin**.

For help with logins, password problems and reactivating HCS accounts, contact the Commerce Account Management Unit (CAMU) at (866) 529-1890.

Results must be reported for all 5 Maternal Sera and/or Amniotic fluid samples; otherwise a zero grade will be applied to the missing data. Please enter your mass unit results in the spaces provided with one or two decimals accordingly. If a result exceeds your analytical range, indicate this with a "less than (<)"or "greater than (>)" sign if similar results from patient samples are reported in the same manner. If such samples are routinely retested after dilution, you may do so provided the result is identified accordingly. Select the instrument and reagent/kit used for each analyte using the drop-down menus. Please note that the risk factor and further action (not graded) for each of the samples has also been placed in the EPTRS. All applicable fields must be completed. Missing entries will result in a failing grade for the missing results.

If CLEP is contacted for permission to submit results via paper, this request may be approved under extenuating circumstances. However, the lack of active HCS accounts, the lack of submission roles, or the lack of Internet access will not excuse a laboratory from having to submit results electronically. Without such approval, mailed or faxed proficiency test results will not be accepted. Note that such approvals will not be given on the due date! If you have any questions, please call Ms. Helen Ling at (518) 474-0036.

Please Turn Over

Special Instructions:
In order to achieve uniformity among our labs in reporting gestational age results, please report gestational week in "**decimal weeks (weeks + day/7)**" for the maternal serum samples.

Example: 18,3 weeks in the Ultrasound dating means 18 weeks + 3 days or 18.4 weeks (18 weeks + 3/7 weeks) ***not*** ~~**18.3**~~, i.e. **18.4 should be reported**

Note: We recommend the use of LMP (ultrasound dating when available) in calculating the gestational age, please note that the use of EDD is not an accepted standard of patient care.

Caution:
All human derived specimens should be handled as biohazard materials using Universal Precautions.

Only extra correspondence and information about **new kits** may be mailed to**:**

Fetal Defect Markers Proficiency Testing c/o Helen Ling
Wadsworth Center
Empire State Plaza, Room E610
PO BOX 509
Albany, NY 12201-0509

Please let us know immediately if you do not receive the samples in satisfactory condition by calling Ms. Helen Ling at (518) 474-0036.

DUE DATE: Results must be submitted electronically before 11:59 PM of February 8, 2011.
*Test results will not be evaluated if the results are **submitted** after the due date and a Failing Grade will be assigned.*

The next Proficiency Test mail-out for 2012 has been tentatively scheduled for:

Ship-out date	**Due date**
May 8, 2012	May 23, 2012
September 11, 2012	September 26, 2012

Demographic Data:

Specimen	Maternal Date of Birth	Race[1] W,B,H,A	Maternal Weight (lbs)	IDD[2] Presence	Gravida	Parity	LMP[3]	Draw Date
MS 276	1/31/1982	A	150	None	1	0	9/13/2011	1/24/2012
MS 277	1/30/1987	W	140	None	1	0	9/20/2011	1/24/2012
MS 278	**1/29/1991**	**H**	**135**	**None**	**2**	**1**	**10/11/2011**	**1/24/2012**
MS 279	1/31/1981	B	170	None	1	0	9/27/2011	1/24/2012
MS 280	**1/31/1983**	**W**	**155**	**None**	**3**	**1**	**9/6/2011**	**1/24/2012**

Specimen	GA[4]
AF 276	17.0
AF 277	18.0
AF 278	**15.0**
AF 279	19.0
AF 280	**20.0**

***Note: MS278 and MS280** are the serum sample matched to the amniotic fluid sample **AF278 and AF280, respectively**. (Dating by ultrasound)

[1]Race: W = White, not of Hispanic origin; B = Black, not of Hispanic origin; H = Hispanic; A = Asian

[2]IDD = Insulin-Dependent Diabetic
[3]LMP = Last Menstrual Period
[4]GA = Gestational Age in Decimal Weeks

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Fetal Defect Marker Proficiency Test Mailout[1]
January 2012

Dear Laboratory Director,

Below you will find a summary and critique of the Proficiency Testing mail-out from January 24, 2012, for Fetal Defect Markers, which included samples for first and second trimester screening, as well as amniotic fluids. Your laboratory's results and grades are printed on a separate sheet; also included are the grades from the previous two PT events. These will be mailed to you separately. Please review and sign your evaluation. Retain the signed evaluation in your files. You will need it for your next laboratory survey to demonstrate participation in the NYSPT program.

I. Graded Results Section: Table 1: Second Trimester Maternal Serum: Summary of All Lab Results

Samples *N = 27	**Sample #**	**MS 276**	**MS 277**	**MS 278**	**MS 279**	**MS 280**
	Gestational Age (weeks)	19.0	18.0	15.0	17.0	20.0
Maternal Race	Ethnic Group	Asian	White	Hispanic	Black	White
Maternal Weight	Pounds (lbs)	150	140	135	170	155
Maternal Age	Years	30	25	21	31	29
Alpha-Fetoprotein (AFP)	Mean ng/ml ± Std. Dev.	57.7 ± 4.3	157.8 ± 13.7	16.3 ± 1.6	39.3 ± 3.3	159.0 ± 10.9
	MOM ± Std. Dev.	1.13 ± 0.11	3.41 ± 0.39	0.54 ± 0.06	1.00 ± 0.12	2.79 ± 0.27
Unconjugated Estriol (uE3)	Mean ng/ml ± Std. Dev.	1.36 ± 0.09	1.19 ± 0.09	0.36 ± 0.03	0.71 ± 0.06	1.39 ± 0.09
	MOM ± Std. Dev.	0.98 ± 0.21	1.03 ± 0.23	0.64 ± 0.22	0.86 ± 0.26	0.84 ± 0.23
human Chorionic Gonadotrophin (hCG)	Mean IU/ml ± Std. Dev.	16.04 ± 1.77	55.17 ± 7.39	63.98 ± 10.55	18.03 ± 2.04	18.76 ± 2.15
	MOM ± Std. Dev.	0.87 ± 0.10	2.59 ± 0.31	1.60 ± 0.26	0.77 ± 0.10	1.12 ± 0.10
Dimeric Inhibin-A (DIA)	Mean pg/ml ± Std. Dev.	193.43 ± 13.64	405.28 ± 33.07	356.34 ± 29.93	212.24 ± 16.02	411.84 ± 30.26
	MOM ± Std. Dev.	1.08 ± 0.16	2.27 ± 0.32	1.80 ± 0.28	1.32 ± 0.17	2.13 ± 0.28
Neural Tube Screen (Positive, Negative) Percent	Pos. (+) or Neg. (-)	(-) (100%)	(+) (100%)	(-) (100%)	(-) (100%)	(+) (96.3%)
	Further Action G,U,A	NFA	FA	NFA	NFA	FA
	NTD Risk 1 in	5,660	34	10,000	10,000	116
Trisomy-21 Screen (Positive, Negative) Percent 1. Triple test	Pos. (+) or Neg. (-)	(-) (100%)	(-) (100%)	(+) (71%)	(-) (100%)	(-) (100%)
	Recommended Action**	NFA	NFA	G = 57% U = 36% A = 57%	NFA	NFA
	Risk Est. 1 in	5,000	5,956	137	5,000	5,250
2. Quad Test	Pos. (+) or Neg. (-)	(-) (96%)	(-) (100%)	(+) (93%)	(-) (100%)	(-) (100%)
	Recommended Action **	NFA	NFA	G = 77% U = 62% A = 81%	NFA	NFA
	Risk Est. 1 in	6,490	5,505	73	3,460	10,500
Trisomy-18 Screen (Positive, Negative) Percent	Pos. (+) or Neg. (-)	(-) (100%)	(-) (100%)	(-) (100%)	(-) (100%)	(-) (100%)
	Recommended Action**	NFA	NFA	NFA	NFA	NFA
	Risk Est. 1 in	23,900	59,500	5,500	9,735	20,600

*N = total numbers may vary since some labs do not test all analytes. The values represent the all-lab consensus based on the arithmetic mean ± Std. Dev.;
(B) = borderline positive or negative, risk reflects central tendency (Median number for NTD/Down positive or negative/borderline screen). NFA = no further action; FA = further action; G = genetic counseling; U = ultrasound, A = amniocentesis, and R = repeat.
**This percentage is normalized to labs requesting further action. ‡ Insulin Dependent Diabetic pregnancy.
The use of brand and/or trade names in this report does not constitute an endorsement of the products on the part of the Wadsworth Center or the New York State Department of Health.

1) Second Trimester Maternal Serum Analytes:

A. Narrative Evaluation of Second Trimester Screening Results:

N = 27 all-lab Consensus Values.

Sample #	Summary Comments (Mock specimens):
MS 276 Wk 19.0	This specimen was obtained from a 30 year old Asian woman (Gravida = 1, Parity = 0) in her 19th week of gestation with a body weight of 150 lbs. A race correction may be indicated. She had no personal history of pregnancy loss. Her specimen was negative for NTD and for both Trisomies and all labs were in agreement. Thus, no recommendations for further action were noted. This specimen had no amniotic fluid counterpart.
MS 277 Wk 18.0	This specimen was obtained from a 25 year old White woman (Gravida = 1, Parity = 0) in her 18th week gestation with a body weight of 140 lbs. She had a family history of pregnancy complications and her specimen resulted in a positive screen for NTD with no body weight correction indicated. The labs were also in agreement that both Trisomy screens were negative. Specimen MS277 was not paired with an amniotic fluid specimen. See critique for more discussion on this sample.
MS 278 Wk 15.0	This specimen was obtained from a 21 year old Hispanic woman (Gravida = 2, Parity = 1) in her 15th week of gestation with a body weight of 135 lbs. She had a family (sibling) history of pregnancy complications. Her sample screened negative for NTD; however, her aneuploidy screen was positive for Trisomy-21 (93% by quad, 71% by triple) on the basis of low AFP and uE3, and moderately elevated hCG and inhibin-A levels. Recommendations for further action from labs performing the T21 quad screen were: genetic counseling, 77%, ultrasound, 62% and amniocentesis, 81%; while the triple tests were: genetic counseling, 57%; ultrasound, 36% and amniocentesis, 57%. Specimen MS278 resulted in a negative T18 screen in 100% of the participating labs. The sample was paired to an amniotic fluid specimen which had a low AFAFP level (MOM = 0.54).
MS 279 Wk 17.0	This specimen was obtained from a 31 year old Black woman (Gravida = 1, Parity = 0) in her 17th week of gestation with a body weight of 170 lbs. She had a family history that was unremarkable. Her sample screened negative for NTD; as did her aneuploidy screen for Trisomies-21 and 18. This sample was not paired to an amniotic fluid specimen.
MS 280 Wk 20.0	This specimen was obtained from a 29 year old white Woman (Gravida = 3, Parity = 1) in her 20th week of gestation with a body weight of 155 lbs. She had a family (sibling) history of reproductive complications. Her sample screened positive for NTD, and her aneuploidy screens were negative for both Trisomy-18 and Trisomy-21. The MS280 sample was paired to an amniotic fluid specimen, which was elevated (AFAFP MOM = 2.90). Please see Critique for further discussion of these samples.

Notice of Gravida/Parity Clarification for Present and Future Mail outs;

Instructional Note:

This notice regards the demographic data provided for the mock patients in the FEDM program. For the sake of this program, it will be understood that gravida indicates the pregnant status of a woman and parity is the state of having given birth to a completed term infant or infants. Thus, a gravida = n, indicates number (n) of times pregnant including the present one; a gravida = 2 indicates that the women was pregnant once before in addition to her present pregnancy. Parity = 1 indicates the patient already has one child; however, multiple birth is also considered as a single parity.

Example: A woman of gravida = 3, parity = 2 indicates that the pregnant woman has been pregnant twice before, and has two children.

2) AMNIOTIC FLUID AFP (NTD-analysis):

N=27; all-lab Consensus Values

Sample#	Values	Summary Comments:
AF 276 Wk 17.0	AFP = 8.71 ± 1.28 µg/ml MOM = 0.76 ± 0.10	The AF276 sample was targeted for a normal AFAFP value in the lower gestational age range. All labs called AF276 a normal MOM AFAFP specimen. The AFAFP sample was not matched to a maternal serum specimen.
AF 277 Wk 18.0	AFP = 8.13 ± 1.24 µg/ml MOM = 0.87 ± 0.12	The AF277 sample was targeted for a negative NTD screen for AFAFP in the mid-gestational screening window. All labs categorized this as an NTD screen negative specimen. This sample was not matched to a maternal serum specimen.
AF 278 Wk 15.0	AFP = 8.99 ± 1.13 µg/ml MOM = 0.54 ± 0.08	The AF278 sample was targeted for a low AFAFP value in the lower gestational age screening range. All labs called AF278 a non-elevated specimen for NTD. This AFAFP sample was matched to maternal serum specimen MS278 which was also low (MOM = 0.54).
AF 279 Wk 19.0	AFP = 5.66 ± 0.98 µg/ml MOM = 0.74 ± 0.12	The AF279 sample was targeted as an NTD negative screen in the upper gestational screening window. All labs categorized AF279 as a negative NTD screen specimen. This specimen had no maternal serum counterpart.
AF 280 Wk 20.0	AFP = 18.50 ± 2.28 µg/ml MOM = 2.90 ± 0.33	The AF280 sample was targeted for a screen positive AFAFP value in the upper gestational age screening range. All labs reported this specimen as a screen positive AFAFP value. The AF280 specimen was paired with maternal serum sample MS280, which was positive (MOM = 2.79) for NTD. Please see Critique for further discussion of samples MS280 and AF280.

II. Non-Graded Results Section:

Table 2: First Trimester Maternal Serum all-lab Results

Samples *N = 17	**Sample #**	**FT 276**	**FT 277**	**FT 278**	**FT 279**	**FT 280**
	Gestational Age (weeks)	11.2	11.9	13.0	11.9	11.4
Maternal Race	Ethnic Group	Hispanic	Asian	Black	White	White
Maternal Weight	Pounds (lbs)	140	120	160	150	125
Maternal Age	Years	28	30	29	25	21
Nuchal Translucency (NT)-Associated Measurements	Crown Rump Length (mm)	45	53	67	53	47
	NT Thickness (mm)	1.10	1.24	1.60	2.90	1.09
	NT – MOM	0.96 ± 0.07	0.93 ± 0.07	0.98 ± 0.06	2.20 ± 0.17	0.91 ± 0.06
Human Chorionic Gonadotrophin (hCG) Total	Mean IU/mL ± Std. Dev.	55.10 ± 7.78	51.91 ± 10.64	48.09 ± 6.36	121.63 ± 25.76	41.11 ± 6.19
	MOM ± Std. Dev.	0.67 ± 0.09	0.62 ± 0.11	0.75 ± 0.07	1.63 ± 0.25	0.48 ± 0.07
Pregnancy-Associated Plasma Protein–A (PAPP-A)	Mean ng/mL*** ± Std. Dev.	920.45 ± 115.21	1471.23 ± 142.85	2749.12 ± 298.12	458.71 ± 51.61	620.11 ± 75.65
	MOM ± Std. Dev.	1.93 ± 1.09	2.10 ± 1.29	2.79 ± 1.61	0.74 ± 0.32	1.00 ± 0.43
Trisomy-21 Screen (Positive, Negative) Percent	Pos (+) or Neg. (-)	(-) (100%)	(-) (100%)	(-) (100%)	(+) (93%)	(-) (100%)
	Recommended Action NFA**	NFA	NFA	NFA	G = 93% U = 40% A = 47% C = 53%	NFA
	Risk Estimate 1 in	10,000	10,000	10,000	18	15,800
Trisomy-18 Screen (Positive, Negative) Percent	Pos (+) or Neg. (-)	(-) (100%)	(-) (100%)	(-) (100%)	(-) (90%)	(-) (100%)
	Recommended Action	NFA	NFA	NFA	NFA	NFA
	Risk Estimate 1 in	10,000	10,000	10,000	1,860	10,000

*N = total numbers may vary since some labs do not test all analytes. (B) = borderline negative or positive; NFA = no further action; G = genetic counseling; U = ultrasound; A = amniocentesis; C = chorionic villus sampling; N = number of labs participating; FT = First Trimester.
**This percentage is normalized to labs requesting further action.
***Results from methods that give IU/ml were converted to ng/ml as described in section D.1 below.

1) First Trimester Maternal Sera Only:

B. Narrative Evaluation of First Trimester Screening Results:

N = 17 all-lab Consensus Values.

Sample#	Summary Comments:
FT 276 Wk 11.2	This specimen was obtained from a 28 year old Hispanic woman of average body weight (140 lbs.). Her gestational age at the time of screening was 11.2 weeks. She had no prior history of pregnancy complications and/or adverse outcomes. This FT specimen was screen negative with all testing labs in agreement. The FT276 risk estimate for Trisomy-21 was 1 in 10,000, and the Trisomy-18 risk was also 1 in 10,000.
FT 277 Wk 11.9	This specimen was procured from a 30 year old Asian woman of average body weight (120 lbs.). Her gestational age at the time of screening was 11.9 weeks. She had no prior history of any pregnancy complications. This FT specimen was screen negative for Trisomy-21 and all testing labs were in agreement. The FT277 risk estimate for Trisomy-21 was 1 in 10,000 as was the Trisomy-18 risk.
FT 278 Wk 13.0	This specimen was obtained from a 29 year old Black woman with a body weight of 160 lbs. Her gestational age at the time of screening was 13.0 weeks. She had no prior history of pregnancy complications or difficulties. This FT specimen was screen negative and all testing labs were in agreement. The FT278 risk estimate for Trisomy-21 was 1 in 10,000 and the Trisomy-18 risk was 1 in 10,000.
FT 279 Wk 11.9	This specimen was procured from a 25 year old White woman of average body weight (150 lbs.). Her gestational age at the time of screening was 11.9 weeks. She had a prior family history of pregnancy complications and adverse outcomes. This FT specimen was screen positive for Trisomy-21 and 93% of testing labs were in agreement (see Critique). The FT279 risk estimate for Trisomy-21 was 1 in 18, while the Trisomy-18 risk was 1 in 1,860 with 90% of testing labs in agreement that it was negative.
FT 280 Wk 11.4	This specimen came from a 21 year old White woman of average body weight (125 lbs.). Her gestational age at the time of screening was 11.4 weeks. She reported no prior family history of pregnancy problems. This FT specimen was screen negative for Trisomy-21 and Trisomy-18. The Trisomy-21 risk estimate for FT280 was 1 in 15,800, and the Trisomy-18 risk was 1 in 10,000. All labs were in agreement with both screen assessments.

III. Critique and Commentary:

Critique:

A) Second Trimester Maternal Serum and Amniotic Fluid:

In general, the all-lab results were consistent with the targeted values for the NTD and the Trisomy Screens for risks and outcomes. The Caucasian maternal serum sample **MS280** was targeted as a positive specimen for NTD (Figs. 1 and 3) and was matched to an elevated **AF280** sample (Fig. 2). Most labs (96.3%) agreed that specimen **MS280** was screen positive for NTD and negative for both Trisomy screens. The **MS280** sample generated recommendations for further action. Follow-up recommendations for the **MS280** consisted of the following: genetic counseling, 78%; ultrasound, 89%; amniocentesis, 78%; and repeat sample, 0%. This mock patient had been referred to a tertiary care medical center for amniocentesis due to a family history of pregnancy difficulties in both extended and close family members. A maternal serum sample was obtained prior to the amniocentesis; the post procedure AF specimen (untainted by color) together with the prior MS sample were subsequently analyzed. The final outcome in this mock patient showed that level-II diagnostic ultrasound demonstrated the presence of a neural tube defect and a diagnostic Ache band was present following polyacrylamide gel electrophoresis.

Sample **MS278** was obtained from a white woman with a prior sibling history of pregnancy complications. The T21 MOM results for specimen **MS278** (MSAFP-MOM = 0.54, MSuE3-MOM = 0.64, MShCG-MOM = 1.60, DIA-MOM = 1.80) were consistent with a T21 positive screen; thus, most labs (71% triple and 93% quad) classified this specimen as T21 screen positive and recommended further action. The T21-related recommended actions for **MS278** triple screen were genetic counseling, 57%; ultrasound, 36%; and amniocentesis, 57%; while the quad test action was genetic counseling, 77%; ultrasound, 62% and amniocentesis was 81%. The **MS278** sample produced a risk from the quad test of 1 in 73 and a triple test risk of 1 in 137 (Figs. 5,6).

The specimen **MS278** was designed to represent a positive screen for Down Syndrome with a typical profile of low MSAFP, low MSuE3, and elevated MShCG and MSDIA. With the addition of MS-DIA in second trimester screening, the detection rate in the literature has been reported to increase from 65% to 75% while maintaining a 5% false positive rate (50). In the case of specimen **MS278**, the MS-DIA MOM value of 1.80 increased the patient risk value from 1 in 137 (triple test) to a greater risk of 1 in 73 (quad

test). This increased risk was further reflected by the "further actions" recommended by the participating laboratories, as well as the percent positive screens. Thus, the all-lab consensus for **MS278** using the quad test was 93% compared to 71% with triple test.

Two other specimens, **MS276**, and **MS279** produced negative screens for NTD, T21, and T18, and no corrections for body weight and race were indicated.

The **MS277** specimen was a special case involving elevated levels of three protein analytes. Sample **MS277** was screen positive for NTD, but negative for T-21 and T-18; however the elevated MSAFP was of special interest because two other placental protein markers were also elevated. The follow-up actions recommended for **MS277** were genetic counseling, 78%; ultrasound, 96%; amniocentesis, 74%; and repeat, 11%. The **MS277** sample was determined to have elevated MSAFP (MOM = 3.41), elevated MShCG (MOM = 2.59), normal uE3 (MOM = 1.03), and elevated DIA (MOM = 2.27) values, which were obtained by all participating laboratories. However, the AFAFP values turned out to be normal. This mock patient had been referred to a tertiary care medical center for a consultation due to a family history of adverse pregnancy outcomes among several extended and close family members. Although a maternal serum sample was procured at the tertiary care center following the initial consultation, an amniocentesis had not yet been performed. When completed, the lab amniocentesis and ultrasound results in this mock patient showed a normal karotype and level-II diagnostic sonography revealed no presence of NTD or T21-associated image defects, nor were other structural or anatomic anomalies detected.

Due to the elevation of more than two biomarkers in the prenatal screen, a perinatologist suggested that this mock patient undergo Doppler velocimetric measurement at GA week 22. The obtained Doppler waveform diastolic notch suggested that patient **MS277** was a possible candidate for pregnancy complications and/or poor term outcome. The addition of the Doppler velocimetric measurement to the fetoplacental marker screening results has been shown to be clinically beneficial. In a study of 118 women at 22-24 weeks gestation, both the uterine mean pulsatility index (PI) and the levels of MSDIA and beta MShCG were significantly increased (22). The combination of the Doppler ultrasound measurement and the biochemical markers detected 92% of patients that subsequently developed preeclampsia with a false positive rate of 10%. A prior study of 689 patients had shown that second trimester MSDIA alone or combined with uterine artery Doppler measurements improved the screening efficacy for the prediction of preeclampsia; this was especially true when preterm delivery was involved (23). Thus, Doppler waveform analysis was found to vastly improve the clinical value of adverse outcome predictions when combined with fetoplacental markers. In a study of 56 women with preeclampsia at 22 weeks gestation, the combination of maternal serum markers combined with abnormal Doppler waveform (diastolic notch) examination were found to improve the identification of women at risk of pregnancy difficulties (24). Using Doppler ultrasound alone (without biomarkers), aberrant uterine artery waveforms proved to be good predictors of the onset of preeclampsia and the presence of intrauterine growth restriction in 74 affected women in the second trimester (25). Thus, Doppler waveform analysis at 22-24 weeks gestation, when combined with the fetoplacental triple/quad test results from 15-21 weeks can identify women who subsequently develop pregnancy complications at time of delivery (25-28). It can readily be observed in Table A (see below) that various fetoplacental markers alone or in combination can predict the onset of multiple adverse pregnancy outcomes or conditions at term. However, only by combining the biochemical marker results with Doppler waveform analysis is it possible to encompass all the conditions listed in Table A.

The specimen **MS277** is of special interest in that three of the four fetoplacental analytes of the Down Syndrome quad test were elevated; that is, MSAFP MOM was 3.4, MShCG MOM was 2.6, and MSDIA MOM was 2.3. The biomarker levels of this mock patient were modeled after a case history from a previous real-time prenatal screening laboratory. Extreme levels of two or more fetoplacental markers usually reflect impaired placental functions, and have been associated with adverse outcomes and abnormal pregnancy states (1-7). Such outcomes do not usually include fetal anatomical defects and malformations, but rather encompass abnormal pregnancy conditions of well-being such as small-for-gestational age (SGA), intra-uterine growth restriction (IGR), late miscarriage, preeclampsia, gestational diabetes, preterm delivery, stillbirths, low birthweight (LBW), placental separations, and gestational hypertension. However, identifying women at risk for adverse pregnancy outcomes using fetoplacental markers is limited by low sensitivity and specificity (8-11). To assist in these deficiencies, Doppler waveform velocimetry has recently been added as an adjunct to the biomarker screening to enhance detection and prediction of possible adverse outcomes at term (12). At some tertiary care medical centers, women with one or more extreme levels of fetoplacental markers are offered to undergo Doppler waveform examinations at 22-24 weeks gestation in accordance with previously published protocols (13). Unfortunately, in the case of the real specimen mimicked by **MS277**, the patient miscarried at 25 weeks of pregnancy. Miscarriage and fetal death are some of the disorders predicted by extreme levels of fetoplacental markers. To the patient's benefit, her MSAFP returned to normal after a few weeks. Thus, the elevation of MSAFP was not attributed to an abnormal condition present in the mother.

The associations between unexplained elevations of MShCG at 16-20 weeks and pregnancy complications at term have long been known. One study involving 6,011 pregnant women showed that 4.7% of patients exhibited elevated levels of MShCG greater than 2.5 MOMs (14). These pregnant women had displayed high risk predictors for both gestational hypertension and fetal growth restrictions, while women with MShCG levels greater than 4.0 MOMs had an even greater risk for preterm delivery. Thus, women with unexplained elevated MShCG values were deemed as high risk pregnancies and were counseled to be managed with the established standards of care. In a later study of 638 women screened with elevated MShCG levels (>2.0 MOM), 19% were found to deliver SGA infants as opposed to 3.9% in patients displaying normal MShCG levels (15). Various mothers in this study with elevated MShCG had significantly higher risks for fetal death, premature membrane rupture, and placental separations. In a further study, it was shown that an elevated MShCG together with a low MSuE3 were associated with intra-uterine growth restriction; such

cases received close surveillance in their subsequent follow-up toward term delivery(16). Interestingly, MSAFP levels in this study were only weakly correlated with adverse perinatal outcomes.

The combination of both elevated MShCG and MSAFP has proved useful for predicting pregnancy complications. In a study involving 438 pregnant women, the combination of both elevated MSAFP and MShCG levels has substantially improved the identification of mothers at high risk for adverse pregnancy outcomes (17). In groups of women with serum marker levels of MShCG MOMs exceeding 3.0 and MSAFP MOMs of 2.5, significantly higher incidences were found in disorders such as fetal/neonatal deaths, preterm birth (<37 weeks), LBW, and preeclampsia as compared to control groups. In another report with 650 women with only second trimester MSAFP levels exceeding 2.0 MOMs, associations were linked to multiple term pregnancy complications (18). Such pregnancy outcomes included premature membrane rupture, preterm birth, and LBW. Of these outcomes, premature rupture of membranes proved to be the most detrimental. However, no associations were found with preeclampsia, oligohydramnios, and polyhydramnios in this study.

Inhibin-A (MSDIA) is a dimeric glycoprotein initially secreted to in the maternal circulation during the first trimester of pregnancy. The MSDIA circulates at higher levels in pregnant women with gestational hypertension, preeclampsia, and fetal growth restriction (19). The addition of elevated MShCG results to those of highly elevated MSDIA levels considerably enhanced the prediction of preeclampsia in a study of 685 pregnant women at 15-19 weeks gestation (20). There was also a significant correlation found in women who subsequently developed preterm preeclampsia (prior to 37 weeks) in contrast to full-term preeclampsia. The addition of MShCG levels to the MSDIA results did not improve the screening efficacy suggesting that both analytes were markers of the same underlying pathological process. In a further study involving preeclampsia in 96 pregnant women of 15-22 weeks gestation, MSDIA and total MShCG (or beta MShCG) levels were combined with MSAFP measurements to determine their screening power for the detection of preeclampsia (8). In that report, women that developed preeclampsia at term displayed MShCG (total or beta) and MSDIA levels that were significantly elevated, while MSAFP values were not notably raised. This study further demonstrated that the use of two or more of the quad test protein analytes enabled detection of 34% of the pregnancies that subsequently developed preeclampsia and did so with a 5% false-positive rate. It was determined that the screening performance to detect preeclampsia using the quad test protein biomarkers was materially better than that using only hCG and AFP of the triple marker test.

It has been suggested that the ability of fetoplacental proteins to predict adverse pregnancy outcomes could likely be attributed to placental dysfunction and fetal growth. Since the biomarker constituents of the triple and quad tests are already employed in the identification of chromosomal abnormalities, the dual use of these markers to predict pregnancy complications at term serves as an added advantage. Using triple test constituents to identify high-risk pregnancies in a study of 60,040 women, the combination of screening results of elevated levels (>2.5 MOMs) of MSAFP and MShCG revealed associations with multiple adverse pregnancy outcomes (21). Such conditions included gestational hypertension, miscarriage, preterm delivery, and fetal death. After the FASTER Down Syndrome clinical trials were published, a study utilizing 33,145 pregnancies confirmed that extremely elevated triple and quad analyte levels produced a somewhat low, but significant risk of adverse outcomes such as preterm birth, intrauterine growth restriction, preeclampsia, and fetal loss (11). These data suggested that combining marker analytes of the quad test may prove useful in predicting risk for adverse pregnancy outcomes and demonstrated that the total number and specific combinations of the analytes are important factors to consider for such screening protocols.

It is noteworthy that some prenatal screening laboratories are already preparing to use commercial and in-house developed algorithms to incorporate the “soft” ultrasound markers of nuchal translucency and nasal bone. In the near future, additional sonogram markers could be included such as uterine artery pulse index, tricuspid flow, ductus venus flow, facial angle, and others. Thus, the time of employing Doppler waveform measurement in conjugation with the “classical” fetoplacental screening markers to monitor pregnancy progression in the clinic is fast approaching and may already be in place at some tertiary care medical centers.

Aberrant levels of multiple screening biomarkers in the same specimen using triple and quad testing have always been a concern for the prenatal screening laboratory. Aside from neural tube defects and aneuploidies, isolated or combined elevated and/or reduced levels of MSAFP and its supplemental biomarkers do not yet have an algorithm-based risk calculation for pregnancy complications and adverse outcomes following the prenatal screen. However, abnormal levels of MSAFP and its combined biomarkers have already been reported to be associated with such conditions as demonstrated in Table A. In contrast to the anatomical malformations and chromosomal disorders, the adverse pregnancy outcomes and complications can be involved at all levels of maternal, fetal, and placental anatomical structures. As shown in Table A, the elevated analyte levels alone or in various combinations together with Doppler ultrasound can serve as indicators of various pregnancy difficulties and problems. At present, pregnant women displaying such biomarker combination patterns receive no follow-up in the screening laboratory, as these patterns of analyte profiles/combinations have not been definitively determined to be associated with adverse perinatal outcomes. Nonetheless, very low or high levels of pregnancy biomarkers normally require prenatal consultations following their detection in the prenatal screen. These patterns have not been sufficiently studied; hence, no specific treatments are available. Until treatments for such conditions are developed and implemented, no screen follow-up or further action (other than Doppler) is warranted and such patterns are still considered research or investigational in nature.

Table A. Elevated fetoplacental biomarkers alone or in various combinations are listed versus the adverse pregnancy outcomes whose risk they can predict indicated as a + sign. Data were extracted and collated from references 1 to 29 of the text.

Elevated Biomarker (>2.0 MOM)	**Adverse Pregnancy Outcome or Condition**								
	Fetal Death, Miscarriage	Preterm Birth	Gestational Hypertension	Fetal Growth Restriction	Small-for-Gestation Age	Membrane Rupture	Placental Separation	Pre- and Term Preeclampsia	Low Birth Weight
1. MShCG alone	+		+	+	+	+	+		
2. MShCG + MSAFP	+	+	+					+	+
3. MSAFP alone	+	+				+			+
4. MSDIA alone			+	+				+	+
5. MSDIA + MShCG		+	+					+	
6. Doppler alone				+	+		+	+	
7. Doppler + Biomarkers	+	+	+	+	+	+	+	+	+

MShCG = maternal serum human gonadotropin
MShAFP = maternal serum alpha-fetoprotein
MSDIA = maternal serum dimeric inhibin-A
Doppler = wavelength analysis of uterine artery diastolic notch

B) Assay Kit Performance:

The performances of the various kits for maternal serum analytes (AFP, uE3, hCG, and Inhibin A) are presented in a bar-graph format (Figs. 7-10) for each of the five MS samples. As shown in Figs. 7A and 8A, AFP and uE3 mass measurements in serum among the individual kits mostly agreed, although the values from the Siemens Immulite kits were about 10% lower for AFP, and 5-10% higher for uE3 than those obtained with Beckman instruments. In contrast, when the kit specific uE3 MOMs were compared, values from Siemens Immulite 2000/2500 ranged from 40 to 60% higher than those from Beckman (Fig. 8B). Regarding the hCG kits (Fig. 10), the two Beckman instruments (Access2 and UNICEL DXL) yielded similar mean hCG values, while the Siemens Immulite/2000 results were 10-30% lower than those from the other assay platforms. Finally, the method comparison for Inhibin-A displayed in Fig. 9A shows that the results from the Beckman Access/2 or Unicel were similar and that the of Diagnostic Systems Lab (DSL) assay platform was 20-25% lower; this was also true for the MS inhibin MOM values (Fig. 9B).

Interestingly, when the AFP measurements in amniotic fluid were compared, the differences among the various methods appeared somewhat larger than in serum (Fig. 7B). In particular, results from the Abbott Axsym were 15-25% higher, Beckman Unicel DXL instrument was about 10-20% lower, with the results from the other instruments somewhere in between. Since these specimens are derived from actual AF samples, these levels would be comparable to real patient testing**.**

C) Second Trimester Screening Software Utilized:

The alpha and Benetech software packages were each used by 30% and 22%, of the labs, respectively; Robert Maciel (RMA) software was employed by 30%; and in-house and "other" softwares comprised 18%. Labs using programs classified as "other" are presumably proprietary software packages.

D) First Trimester Screen:

Five first trimester maternal serum mock samples were provided in the present mailout. All laboratories that are **validation-approved** and presently perform first trimester Down syndrome screening are **REQUIRED** to test and report screen results; however, the laboratory results will **not** be graded at this time. Those laboratories not presently offering the test, nor planning to implement the test, can request that no further samples be sent to them. The FT sample (FT = first trimester) information provided to participating labs included maternal age, nuchal translucency NT (measurements in millimeters), last menstrual period (LMP), crown-rump length (CRL) measurements, race, maternal body weight, and date of blood draw.

As demonstrated in Section II, Table 2, the all lab measurement of the 11.2 week Hispanic **FT276** specimen for total hCG resulted in a mass mean of 55.10 IU/ml $\pm$ 7.78, with a MOM of 0.67 $\pm$ 0.09. Furthermore, the all-lab mass mean for PAPP-A was 920.45 $\pm$ 115.21 ng/ml with a MOM of 1.93 $\pm$ 1.09. This resulted in an all-lab T21 risk assessment of 1 in 10,000 for the **FT276**

specimen and a negative screen (Fig. 13). Thus, the **FT276** sample resulted in a 100% T21 negative screen assessment and a T18 risk assessment of 1 in 10,000 (Fig. 14).

As shown in Table 2 for the **FT277** Asian specimen, the gestational age all-lab mean was reported as 11.9 weeks. Assay measurements resulted in an all-lab total hCG mass measurement of 51.91 $\pm$ 10.64 IU/ml (MOM = 0.62 $\pm$ 0.11); the all-lab PAPP-A mass measurement was 1471.23 ± 142.85 ng/ml (MOM = 2.10 $\pm$ 1.29). The all-lab T21 screen consensus for **FT277** was negative with a risk assessment of 1 in 10,000 (Fig. 13). No further actions were recommended by the labs. Finally, the **FT277** specimen screened negative for T18 (1 in 10,000 Fig. 14).

In the **FT278** Afro-American specimen, the gestational age all-lab mean was reported as 13.0 weeks. Assay measurements for **FT278** resulted in an all-lab total hCG mass measurement of 48.09 $\pm$ 6.36 IU/ml (MOM = 0.75 $\pm$ 0.07), while the all-lab PAPP-A mass assessment was 2749 $\pm$ 298.12 ng/ml (MOM = 2.79 $\pm$ 1.61). All labs agreed that the **FT278** sample was screen negative for T21 with a risk of 1 in 10,000 (Fig. 13). The all-lab T18 risk assessment for **FT278** was also 1 in 10,000; hence, the **FT278** specimen resulted in a negative screen for T18 (Fig. 14).

The all lab measurement of the 11.9 week Caucasian **FT279** specimen for total hCG resulted in a mass mean of 121.63 $\pm$ 25.76 IU/ml, with a MOM of 1.63 $\pm$ 0.25; the all-lab mass mean for PAPP-A was 458.71 $\pm$ 51.61 ng/ml with a MOM of 0.74 $\pm$ 0.32. As a result, the all-lab T21 risk assessment for FT279 was 1 in 18(Fig. 13). The **FT279** sample displayed a 93% consensus T21 positive screen assessment. Further action was indicated which included genetic counseling, 93%, ultrasound, 40%, amniocentesis, 47%, and chorionic sampling, 53%. 90% of labs considered the **FT279** specimen screen negative for T18 (1 in 1,860) using a cutoff of 1 in 100 (Fig.14).

For the Caucasian **FT280** specimen, the gestational age all-lab mean was reported as 11.4 weeks. Assay measurements resulted in an all-lab total hCG concentration of 41.11 $\pm$ 6.19 IU/ml (MOM = 0.48 $\pm$ 0.07) while the all-lab PAPP-A concentration was 620.11 $\pm$ 75.65 ng/ml (MOM = 1.00 $\pm$ 0.43). The all-lab FT T21 risk assessment was 1 in 15,800 and all labs agreed that the **FT280** sample was negative for T21 (Fig. 13). The **FT280** specimen was also screen negative for T18 with an all-lab risk assessment of 1 in 10,000 (Fig.14).

D. 1.) First Trimester Assay Kit Performance:

In order to compare the new Beckman Access 2/Unicel assays (60% users) for PAPP-A with those of the older Siemens Immulite and DSL assay platforms, a conversion factor was calculated from participating labs using data from the last five PT mailouts (Note: this conversion factor may not be applicable to real patient samples because of potential matrix effects in the PT samples). Hence, Beckman Access 2/Unicel (y-axis) data for PAPP-A in ug/ml were plotted versus Siemens Immulite 2000 (x-axis) data in mIU/ml yielding a linear correlation with an R^2 value of 0.9753, a slope of 0.1407 and an intercept of essentially 0 (Fig. 15A). In Fig. 15B, Beckmann Access2/Unicel PAPP-A values (y-axis) were plotted against DSL PAPP-A values (x-axis) yielding a second degree polynomial correlation with an R^2 value of 0.988. Using the respective correlation equation allowed us to convert mIU/ml values into ng/ml and to directly compare Beckman Access 2/Unicel PAPP-A mass units of ng/ml to the mIU/mL mass units generated by Siemens Immulite and DSL (Fig. 12A). However, for grading purposes, each lab's results were compared to their own peer group without conversion.

The performance of the kits used for first trimester maternal serum analytes (hCG and PAPP-A) are presented in Figs. 11 and 12A for each of the five FT samples. As shown in Fig. 11, hCG measurements between the two Beckman instruments were similar (within 10%), while the Siemens Immulite instruments measured approximately 15-30% below the Beckman Access 2/Unicel instruments. The results from the three PAPP-A kits, when converted to the same mass units, were relatively consistent among each other. In contrast, when the PAPP-A kit MOMs were compared, Siemens Immulite were more than double those from DSL and Beckman (Fig. 12B).

E) First Trimester Screening Software Utilized:

The alpha and Benetech software packages were each used by 31% and 19% of the labs, respectively; Robert Maciel (RMA) software was employed by 31%; and in-house software comprised 19%. None of the labs used programs classified as "other" which are proprietary software packages.

G.J. Mizejewski, Ph.D.

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Immunological Aspects of AFP:

Section - 2.

The immunoregulatory functions of HAFP have long been studied [1]. In brief, full-length HAFP has been found immunosuppressive in both B- and T-cell lectin blast cell stimulations [2]; Mizejewski, 2006 #1216]. However, recent studies have reported that not all self versus non-self AFP-specific T-cell clones are deleted during ontogeny, and that potential AFP antigenic sites persist and are recognized by both murine and human T-cells. During the last several years, multiple research groups have succeeded in mapping T-cell immunodominant epitope sites on HAFP [3-7]. These research groups have determined that four major HLA-A epitotopic sites and several more minor epitopic determinants can be localized throughout the three domain structure of HAFP.

The proposed concept that normal human pregnancy is actually a controlled state of inflammation has recently been validated in the biomedical literature [8]. The human conceptus has classically been viewed as a foreign (non-self) object in the mother's body and has long been considered a tissue allograft residing in the maternal uterus. Investigators have recently shown that the conceptus resides in an immunologically privileged site situated in juxtaposition to the placental cells (barrier) which are in direct contact with uterine tissue containing NK (natural killer) cells of the maternal innate immune system. In turn, the maternal NK cells secrete cytokines that attract maternal lymphocytes to the placental boundary causing the maternal tissues to view the foreign cell clusters as tissue inflammatory sites. Such lymphocytes wall off intruder cells from the maternal tissues at the placental/uterine interface and the cells of the conceptus are viewed by maternal cells as sites of tissue inflammation. Obviously, any fetal protein that contains cell surface proteins resembling the many cytokines of the immune system would have a definitive advantage in sustaining and maintaining the foreign tissue as a site of inflammation. AFP is such a protein consisting of a series of successive modular cassette-like peptides serving as immune system cytokine mimics, substitutes, and back-up immunoregulatory peptides [9]. Since the first reports emerged in the 1970s, AFP has long been recognized as both a B- and T- cell immunoregulatory protein [10]

AFP influence on Genital Function:

Mammalian AFP has been shown to affect postnatal and adult genital function including the onset of puberty, menstrual cycling, and spermatogenesis. AFP concentrations are low in prepubertal mammals, but supplemental injections of purified rodent AFP have been shown to inhibit follicular maturation and ovulation in the ovary and

spermatogenesis in the testis [11]. Rodent AFP was found to reduce the number of gonocytes during fetal and postnatal life rather than stopping oocyte meiosis at the diplatene stage as previously proposed [12]. During pregnancy, follicular maturation could be blocked by administration of purified rodent AFP at the antral stage; the follicles at this stage contain degenerating oocytes that are AFP-positive following immunofluorescent staining [13]. AFP was first proposed and then confirmed to play a blocking role in genital cycling as well as the induction of follicular atreas [14]. Prior to that report, AFP had been localized both in the ovary and hypophysis of prepubertal rats [15]. During postnatal rat development, it is known that AFP serum levels drop to adult (low) concentrations coincident with achievement of ovarian maturity on postnatal day-35 and administration of supplemental AFP alters reproductive events at this time [16]. Finally, studies now suggest that high fetal AFP levels during human pregnancy may contribute to congenital disorders which can include cryptorchidism in term pregnancies [17].

Studies in rodents have further demonstrated that neonatal AFP prevents circulating estrogens from accessing the brain, thus defending it from masculinization and defeminization [18-20]. Such events occur in the first week of life in rodents and in late third trimester of humans. Rodent AFP, which binds E2 with high affinity, has been proposed to either prevent entry of the estrogens into the brain or to actively transport estrogens in the developing female brain [20]. Using AFP gene-knockout mice, investigators have demonstrated that these mice displayed both defeminization and masculization traits. Injections of the aromatose inhibitor 1, 46- androstene-3, 17- dione into the rat brain rescued the animals from defeminization indicating that AFP may serve to protect the rodent female brain from such effects [21]. These same investigators had earlier demonstrated that female AFP-knockout mice were sterile at birth due to underexpressed genes of the gonadotrophin–releasing peptide hormone resulting in down-regulation of the pituitary hormone pathways [22]. Since HAFP binds little or no E2 and rodent AFP is a high affinity estrogen binder, it is difficult to reconcile the relevance of these results to the human state. However, if the basis of estrogen brain protection is based on cell regulatory signal transduction cascades rather than E2 binding to AFP, then steroid ligand binding is not the crucial event in these studies.

d) Alpha-fetoprotein (AFP) and AFP Receptor Expression in the normal human placenta

The authors of several studies have investigated the role of the placenta in the transport and possible synthesis of ATP in situ [23-26] since an earlier report showed that AFP was synthesized by the first trimester human placenta [27]. The objective of these investigators was to probe for the placental expression of AFP and its receptor in trophoblast cells of normal pregnancies at full term. Lafuste et al had previously [28] reported that AFP was synthesized in the first

trimester placenta but not the term placenta; nonetheless, the presence of AFP could be histochemically localized in the villous tissue of the term placenta presumably in the course of transplacental passage. Also, they found no evidence of mRNA AFP in the placental tissues or maternal serum in term pregnancies. Since they also detected the presence of the AFP receptor in the placental villous tissue, the authors proposed a receptor-mediated transport mechanism for AFP placental transfer to maternal tissues. Similar to albumin, AFP transplacental passage might involve a temperature-sensitive process which does not depend on an intact cell cytoskeleton but is associated with a megalin/clathrin-mediated receptor endocytosis pathway which was localized to the villous trophoblast cells [29]. Thus, the presence of the AFP receptor in the term placenta signified a means of transplacental passage of AFP to the maternal decidual tissues. Knowledge of the presence of AFP in the placenta is deemed important since fetomaternal hemorrhages can occur during chorionic villus sampling in the first trimester [30].

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ABSTRACTS

A) Screening Abstract "Picks-of-the-Month":

(1) Title: Alpha-1-Fetoprotein (AFP): international proficiency study with different test systems

Source: *Clin Lab* **2011,** *57* (9-10), 669-675.9-10

Authors: Oremek, G.M., Oertl, A., Bertsch, T., Bewarder, N., Burger, V., Dannenberg, R., Dibbelt, L., Gerstmeyer, A., Grunow, G., Irmer-Vorpeil, A., Klapdor, R., Klemm, M., Krengel, G., Lerahn, A., Marivoet, S., Misianik, J., Ortin, V., Peeters, V., Roder, B., Schauer, I., Schneider, A., Schweiger, A.M., Seefried, D., Straetmans, D., Trommer, A. and Weinhold, A.

Abstract: BACKGROUND: The present proficiency study aimed to elucidate the comparability and reliability of test systems for the determination of AFP concentrations.
METHODS: 25 laboratories using 8 different commercial test systems used liquid BIOREF-AFP control serum in their routine internal quality control over a period of one year. For statistical analysis the results were collected centrally.
RESULTS: The statistical analysis of the test results revealed considerable variation for the different laboratories. The deviations of the mean values of different laboratories from the overall mean value varied between 0.1 and 26.1%, and for most of the laboratories the deviation was round about 10%. The precision of measured values in the individual laboratories was in most cases acceptable: Nevertheless, the coefficients of variation of the individual laboratories ranged from 13 to 16.1%.
CONCLUSIONS: In conclusion, this study indicates that AFP results vary between different laboratories albeit an international standard for AFP is available. Therefore, every laboratory should participate in external ring studies and should use a quality control serum independent of the test kit manufacturer for the internal quality control.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22029181.

(2) Title: Proteomic analysis of amniotic fluid of pregnant rats with spina bifida aperta

Source: *J Proteomics* **2011**

Authors: Shan, L., Fan, Y., Li, H., Liu, W., Gu, H., Zhou, F. and Zhengwei, Y.

Abstract: Congenital spina bifida aperta is a common congenital malformation in children and has an incidence of 1 per thousand to 5 per thousand in China. However, we currently lack specific biomarkers for screening or prenatal diagnosis and there is no method to entirely cure or prevent such defects. In this study, we used two-dimensional gel electrophoresis (2-DE)/mass spectrometry (MS) to characterize differentially expressed proteins in amniotic-fluid samples (AFSs) of embryonic day (E) 17.5 rat fetuses with spina bifida aperta induced by retinoic acid (RA). We identified five proteins differentially expressed in AFSs of spina bifida aperta, including three upregulated proteins (transferrin, alpha-1 antiproteinase and signal recognition particle receptor, B subunit [SRPRB] 55kDa), two downregulated proteins (apolipoprotein A IV [APO A4] and Srprb 77kDa). Specifically, we found 11 alpha-1 fetoprotein (AFP) fragments that were downregulated and 35 AFP fragments that were upregulated in AFSs from embryos with spina bifida aperta. Of the downregulated AFP fragments, 72.7% (8/11) were confined to the AFP N-terminus (amino acids [aas] 25-440) and 77.1% (27/35) of upregulated AFP fragments were confined to the AFP C-terminus (aas 340-596). We also confirmed APO A4 and AFP by immunoblot analysis. This is the first comparative proteomic study of AFSs from rat fetuses with spina bifida aperta. We demonstrate proteomic alterations in the AFS of spina bifida aperta, which may provide new insights in neural tube defects and contribute to the prenatal screening.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22108047

(3) Title: Association between uterine leiomyomas and the biochemical screening test results in the first and second trimester of pregnancy: a pilot study

Source: *J Matern Fetal Neonatal Med* **2011,** *24* (7), 904-906.7

Authors: Sieroszewski, P., Wierzbicka, D., Bober, L. and Perenc, M.

Abstract: OBJECTIVES: The presence of the uterine leiomyomas may change the concentrations of the screening serum markers and so after the risk calculation of the fetal chromosomal abnormalities.
PURPOSE: To estimate the influence of the uterine leiomyomas on the first and second trimester serum markers concentrations.

MATERIAL AND METHODS: The studied group consisted of 127 women between 11 and 20 weeks of normal singleton pregnancy. In each patient, the uterine leiomyomas were diagnosed - over 20 mm in the diameter and located in the uterine wall. Seventy-seven patients had undergone the first trimester screening, 50 patients the second trimester screening. The control group consisted of 1020 women between 11 and 20 weeks of normal singleton pregnancy without uterine leiomyomas. RESULTS: In the first trimester group, the pregnancy-associated plasma protein A serum concentrations were not different from the controls. The median concentrations of free beta-human chorionic gonadotrophin (beta-hCG) were significantly higher (1.43 MoM). In the second trimester group, no significant differences in AFP and estriol median concentrations were observed, while the median value for free beta-hCG was significantly higher (2.01 MoM) than in control group.
CONCLUSIONS: The presence of the uterine leiomyomas may increase maternal serum concentration of the beta-hCG and so after the rate of the false positive results of the prenatal screening tests.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21463216

(4) Title: [Assessment of AFP in amniotic fluid: comparison of three automated techniques]

Source: *Ann Biol Clin (Paris)* **2011,** *69* (4), 441-446.4

Authors: Leguy, M.C., Tavares Sdos, R., Tsatsaris, V., Lewin, F., Clauser, E. and Guibourdenche, J.

Abstract: Ultrasound scanning is useful to detect neural tube defect (NTD) but scarcely distinguished between closed NTD and open NTD, which had very different prognosis. An amniotic fluid punction is thus mandatory to search for an increase in alpha foeto protein (AFP) levels and for the presence of acetylcholinesterase which identified open NTD. However, AFP levels fluctuate both with the gestational age and the assay used. Our aim was to establish normative values for AFP in amniotic fluid in the second half of pregnancy using three different immunoassays and to improve their clinical relevance. Amniotic fluid punctions were performed on 527 patients from 9 week of gestation (WG) to 37 WG either for maternal age, Trisomy 21 screening, increase in nucal translucency (control group, n = 527) or for suspicion of neural tube defect or abdominal defect (n = 5). AFP was measured using the immunoassay developed for serum AFP on the Access 2 system, the Immulite 2000 and the Advia Centaur. Results were expressed in ng/ml, multiple of the median (MoM) and percentiles. AFP decrease by 1.5 fold between 9 and 19 WG. When NTD was suspected, an increase in anmniotic AFP was observed (from 2.5 MoM to 9.3 MoM) confirming an open NTD. In conclusion, the assay developed on those 3 automates is suitable for the measurement of AFP in amniotic fluid.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21896409

B) Case History Screening "Picks-of-the-Month":

(1) Title: Pediatric reference intervals for serum alpha-fetoprotein

Source: *Clin Chim Acta* **2012,** *413* (1-2), 352.1-2

Authors: Coakley, J.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21993184

(2) Title: Biochemical screening of fetal aneuploidies and neural tube defects by "double-test" in Croatia: a 10 years' experience

Source: *Coll Antropol* **2011,** *35* (3), 957-962.3

Authors: Tislaric-Medenjak, D., Kosec, V., Tonkovic-Durisevic, I., Zec, I., Sabolovic-Rudman, S., Kuna, K., Herman, R., Ivicevic-Bakulic, T., Soljacic-Vranes, H., Tuckar, N., Muzinic, D., Butorac, D., Bolanca, I., Kosec, A. and Stipoljev, F.

Abstract: The aim of the study is to investigate the efficiency of the second-trimester biochemical screening, with maternal serum alpha-fetoprotein (MS-AFP) and free beta-subunit of human chorionic gonadotropin (free beta-hCG), during the ten-year period. The study included 11,292 of pregnant women between the 15th and 18th gestational week, who underwent screening from November 1996 to December 2006. The risk for trisomy 21 and trisomy 18 were calculated by computer software, based on a model which generated the final risk for fetal aneuploidies from the pregnant woman's a priori age risk and the likelihood ratio of the distribution of the biochemical markers, according to the second-trimester gestation. With the cut-off value of the final risk > or = 1:250, the detection rate for trisomy 21 was 75% (21/28). In women less than or equal to 35, the detection was 57.1% (8/14) and 92.9% (13/14) in those over 35 years, respectively. The detection

rate of trisomy 18 was 50% (2/4). The results confirmed that the implementation of double-test, as non-invasive screening for fetal aneuploidies, should be accepted as a complementary method of antenatal care.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22053587

(3) Title: A Novel Sandwich Electrochemical Immunosensor Based on the DNA-Derived Magnetic Nanochain Probes for Alpha-Fetoprotein

Source: *J Autom Methods Manag Chem* **2011,** *2011*, 957805

Authors: Gan, N., Jia, L. and Zheng, L.

Abstract: One novel electrochemical immunosensor was constructed by immobilizing capture antibody of alpha-fetoprotein (AFP Ab(1)) on a nafion/nanogold-particle modified glassy carbon electrode. With a sandwich immunoassay, one DNA-derived magnetic nanoprobe, simplified as DNA/(ZMPs-HRP-AFP Ab(2))(n), was employed for the detection of AFP. The fabricated procedure of the proposed biosensor was characterized by cyclic voltammetry and electrochemical impedance spectroscopy. The performance and factors influencing the performance of the biosensor were also evaluated. Under optimal conditions, the developed biosensor exhibited a well-defined electrochemical behavior toward the reduction of AFP ranging from 0.01 to 200 ng/mL with a detection limit of 4 pg/mL (S/N = 3). The biosensor was applied to the determination of AFP in serum with satisfactory results. It is important to note that the sandwich nanochainmodified electro-immunosensor provided an alternative substrate for the immobilization of other tumor markers.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22013390

(4) Title: Neuropathology in classical and variant ataxia-telangiectasia

Source: *Neuropathology* **2011**

Authors: Verhagen, M.M., Martin, J.J., van Deuren, M., Ceuterick-de Groote, C., Weemaes, C.M., Kremer, B.H., Taylor, M.A., Willemsen, M.A. and Lammens, M.

Abstract: Ataxia-telangiectasia (A-T) is classically characterized by progressive neurodegeneration, oculocutaneous telangiectasia, immunodeficiency and elevated alpha-fetoprotein levels. Some patients, classified as variant A-T, exhibit a milder clinical course. In the latter patients extrapyramidal symptoms, instead of cerebellar ataxia, tend to be the dominating feature and other classical disease hallmarks, like telangiectasia, appear later or even may be absent. Some patients with variant disease have clinically pronounced anterior horn cell degeneration. Neuropathological studies of genetically proven A-T patients are lacking. The aims of our study were to describe the neuropathology of three A-T patients; in two of them the diagnosis was genetically confirmed. The neuropathological findings were compared with those of all known published autopsy findings in A-T patients up to now. Two classical A-T patients aged 19 and 22 and a 33-year-old patient with variant disease were autopsied. In line with previous reports, our patients had severe cerebellar atrophy, less pronounced degeneration of the dentate nucleus and inferior olive, degeneration of the posterior columns and neurogenic muscular atrophy. In addition, all three had anterior horn cell degeneration, which was most prominent at the lumbar level. Compared to the literature, the degenerative changes in the brain stem of the variant A-T patient were somewhat less than anticipated for his age. Degenerative changes in the cerebellum and spinal cord were comparable with those in the literature. Progeric changes were lacking. In conclusion, compared to classical A-T, the variant A-T patient showed essentially the same, only slightly milder neuropathological abnormalities, except for anterior horn degeneration.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22017321

C) News of Note: Abstracts of New Markers:

(1) Title: Inflammatory cytokines and antioxidants in midtrimester amniotic fluid: correlation with pregnancy outcome

Source: *Am J Obstet Gynecol* **2011,** *204* (2), 155 e151-157.2

Authors: Pressman, E.K., Thornburg, L.L., Glantz, J.C., Earhart, A., Wall, P.D., Ashraf, M., Pryhuber, G.S. and Woods, J.R., Jr.

Abstract: OBJECTIVE: Elevated interleukin-6 (IL-6) level in midtrimester amniotic fluid is associated with preterm delivery. We hypothesized that, in patients with elevated IL-6, vitamin C and alpha-fetoprotein may provide protection from spontaneous preterm delivery through antioxidant functions. STUDY DESIGN: Antioxidant potential of alpha-fetoprotein was assessed in vitro. Amniotic fluid was collected from a prospective cohort of patients who underwent midtrimester

amniocentesis. In patients with IL-6 >600 pg/mL, alpha-fetoprotein, vitamin C, tumor necrosis factor-alpha, tumor necrosis factor receptors, and antioxidant capacity were compared between subjects with spontaneous preterm and term deliveries. RESULTS: Alpha-fetoprotein demonstrated 75% the antioxidant capacity of albumin in vitro. Of 388 subjects, 73 women had elevated IL-6 levels. Among these subjects, alpha-fetoprotein, but not vitamin C, was significantly lower in 9 women with preterm birth. Antioxidant capacity correlated with vitamin C and tumor necrosis factor receptors, but not with alpha-fetoprotein or pregnancy outcome. CONCLUSION: Amniotic fluid alpha-fetoprotein, but not vitamin C, may protect against preterm birth in patients with elevated midtrimester IL-6 levels.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=20950789

(2) Title: Placental characteristics as a proxy measure of serum hormone and protein levels during pregnancy with a male fetus

Source: *Cancer Causes Control* **2011**,

Authors: Trabert, B., Longnecker, M.P., Graubard, B.I., Klebanoff, M.A., Stanczyk, F.Z. and McGlynn, K.A.

Abstract: OBJECTIVE: In utero exposure to steroid hormones may be related to risk of some cancers such as testicular germ cell tumors (TGCT). To determine whether placental characteristics are good surrogate measures of maternal biomarker levels, we evaluated the correlations in mothers of sons at higher (whites, n = 150) and lower (blacks, n = 150) risk of TGCT. Associations with birth weight were also examined. METHODS: All mothers, participants in the Collaborative Perinatal Project, were primigravidas who gave birth to male singletons. Associations between placental weight and placental thickness and third-trimester biomarker levels were evaluated using linear regression. Partial correlation coefficients for placental characteristics and birth weight were also estimated. RESULTS: Placental weight was positively correlated with alpha-fetoprotein (AFP), sex hormone-binding globulin (SHBG), testosterone, estradiol and estriol in whites, and AFP and estriol in blacks. Placental thickness was not associated with any biomarker. After adjustment for placental weight, birth weight was not correlated with any biomarker. CONCLUSIONS: In these data, placental weight was modestly correlated with third-trimester biomarker level; however, it appeared to be a better surrogate for third-trimester biomarker level than birth weight. Placental thickness had limited utility as a surrogate measure for biomarker levels.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21336590

(3) Title: Pediatric reference intervals for serum alpha-fetoprotein

Source: *Clin Chim Acta* **2012,** *413* (1-2), 352.1-2

Authors: Coakley, J.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21993184

(4) Title: Improvement and multicenter evaluation of the analytical performance of an automated chemiluminescent immunoassay for alpha fetoprotein

Source: *Int J Biol Markers* **2011**, 0

Authors: Morota, K., Komori, M., Fujinami, R., Yamada, K., Kuribayashi, K., Watanabe, N., Sokoll, L.J., Elliott, D., Chan, D.W., Martens, F., Heijboer, A.C., Blankenstein, M.A., Hershberger, S.J., Pfeiffer, Z.A., Vaidya, S.V. and Dowell, B.L.

Abstract: Background: A new ARCHITECT(R) alpha fetoprotein (AFP) assay was developed to improve the linearity at the upper end of the calibration curve and to enhance other performance characteristics. In addition, this reformulation eliminated the possibility of falsely depressed samples at high AFP concentrations. The purpose of this study was to evaluate its analytical performance at multiple sites.
Methods: The assay configuration, the diluent formulation, and the manufacturing process were redesigned. Analytical performance was evaluated at Abbott Laboratories, Sapporo Medical University, VU University Medical Center, and Johns Hopkins University.
Results: The limit of quantitation of the assay was 1.00-1.30 ng/mL. Total precision (%CV) across the assay range varied between 1.41 and 3.52. The assay was linear from 1.19 to 2535 ng/mL, and the range of the assay was expanded from 200 ng/mL to 2000 ng/mL. Comparison of this assay with the on-market ARCHITECT, AxSYM, ADVIA Centaur, DxI, AIA-1800, and E 170 systems yielded regression slopes of 0.91-1.08 and correlation coefficients of =0.99 for serum samples. No falsely depressed results were observed in 174 serum samples with AFP concentrations of 2018-1,196,856 ng/mL and in a spiked sample containing up to 10 mg/mL of purified AFP.

Conclusions: The new AFP assay has improved an issue of the on-market ARCHITECT AFP assay and demonstrated excellent assay performance.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22020369

D) News of Note: Abstracts of New Testing Agents/Methods:

(1) Title: Potential biomarkers for hepatoblastoma: Results from the SIOPEL-3 study

Source: *Eur J Cancer* **2011**,

Authors: Purcell, R., Childs, M., Maibach, R., Miles, C., Turner, C., Zimmermann, A., Czauderna, P. and Sullivan, M.

Abstract: Hepatoblastoma (HB) is a rare malignant liver tumour found in infants. Many heterogenous histological tumour subtypes exist. Although survival rates have improved dramatically in recent years with the use of platinum-based chemotherapy, there still exists a subset of HB that does not respond to treatment. There are currently no tumour biomarkers in use and in this study we aim to evaluate potential biomarkers to aid identification of relapse cases that would otherwise be overlooked by current prognostication. This may identify patients that would benefit from more aggressive therapy and could improve overall survival rates. We used immunohistochemistry to analyse the expression of beta-catenin, E-cadherin, Cyclin D1, Ki-67 and alpha-fetoprotein (AFP) protein in tumours from 91 patients prospectively enroled into the SIOPEL 3 clinical trial. The relationship between these biomarkers and clinicopathologic features and patient survival were statistically analysed. We identified one biomarker, Cyclin D1, which has a correlation with mixed epithelial/mesenchymal HB approaching significance (P=0.07). Survival analysis using these markers has revealed two potential prognostic indicators; Cyclin D1 and Ki-67 (P=0.01, 0.01).

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22137595

(2) Title: Triploidy in a fetus following amniocentesis referred for maternal serum screening test at second trimester

Source: *Indian J Hum Genet* **2010,** *16* (2), 94-96.2

Authors: Bagherizadeh, E., Oveisi, M., Hadipour, Z., Saremi, A., Shafaghati, Y. and Behjati, F.

Abstract: Amniocentesis was carried out at 17 weeks gestation in a 27-year-old woman, following an abnormal maternal serum screening (MSS) test. MSS test was carried out primarily to estimate the risk of trisomy for chromosome 21. The maternal serum markers used were alpha-fetoprotein (AFP), human chorionic gonadotrophin (hCG), and unconjugated estriol (uE3), together with maternal age. The fetus was identified as screen-positive for Edward's syndrome (trisomy 18), with low uE3, normal AFP and hCG levels. The calculated risk for trisomy 18 was more than 1:50. To identify any possible chromosomal abnormality, cytogenetic investigation was carried out on the amniotic fluid sample. The fetus's karyotype showed triploidy with 69, XXX chromosome complement in all the metaphase spreads obtained from three different cultures, using GTG banding technique. Upon termination of the fetus, gross abnormalities indicative of triploidy were present in the fetus.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21031058

(3) Title: Normalization of maternal serum alpha-fetoprotein levels after 23 weeks' gestation in an NPHS1 nephrotic syndrome carrier pregnancy

Source: *Prenat Diagn* **2011,** *31* (13), 1314-1316.13

Authors: Brady, T.B. and Mitra, A.G.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22030743

(4) Title: Prenatal diagnosis and molecular cytogenetic characterization of a derivative chromosome der(18;18)(q10;q10)del(18)(q11.1q12.1)del(18)(q22.1q22.3) presenting as apparent isochromosome 18q in a fetus with holoprosencephaly

Source: *Taiwan J Obstet Gynecol* **2011,** *50* (2), 182-187.2

Authors: Chen, C.P., Kuo, Y.K., Su, Y.N., Chern, S.R., Tsai, F.J., Wu, P.C., Chen, Y.T., Town, D.D. and Wang, W.

Abstract: OBJECTIVE: To present prenatal diagnosis and molecular cytogenetic characterization of a derivative chromosome der(18;18)(q10;q10)del(18)(q11.1q12.1)del(18)(q22.1q22.3).
MATERIALS, METHODS, AND RESULTS: A 32-year-old woman was referred for genetic counseling of prenatally detected isochromosome 18q [i(18q)]. She had undergone amniocentesis at 19 gestational weeks because of a trisomy 18 risk of 1/39 derived from abnormally low levels of maternal serum unconjugated estriol, inhibin A, alpha-fetoprotein, and total beta-human chorionic gonadotropin. Amniocentesis revealed a karyotype of 46,XX,i(18)(q10). Parental karyotypes were normal. Prenatal ultrasound showed alobar holoprosencephaly. Repeated amniocentesis was requested and performed at 21 gestational weeks. Array-comparative genomic hybridization analyses revealed a 14-Mb deletion of 18p11.32-p11.21, a 37.8-Mb duplication of 18q12.1-q22.1, and a 6.9-Mb duplication of 18q22.3-q23. Metaphase fluorescence in situ hybridization study showed the absence of an 18q12.1-specific probe signal in one arm and the absence of an 18q22.2-specific probe signal in the other arm of the derivative chromosome. Quantitative fluorescent polymerase chain reaction analysis determined a paternal origin of the derivative chromosome. The cytogenetic result was 46,XX,der(18;18)(q10;q10)del(18)(q11.1q12.1)del(18)(q22.1q22.3). The fetus postnatally manifested cebocephaly.
CONCLUSION: Concomitant monosomy 18p and trisomy 18q can be associated with holoprosencephaly and abnormal maternal serum screening results. Array-comparative genomic hybridization, fluorescence in situ hybridization, and quantitative fluorescent polymerase chain reaction are useful in genetic counseling of prenatally detected isochromosomes by providing information on the origin and genetic components of the isochromosome.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21791305

E) Special Abstract Selection:

(1) Title: Reasons for adult referrals for genetic counseling at a genetics center in Izmir, Turkey: analysis of 8965 cases over an eleven-year period

Source: *J Genet Couns* **2011,** *20* (3), 287-293.3

Authors: Cogulu, O., Ozkinay, F., Akin, H., Onay, H., Karaca, E., Durmaz, A.A., Durmaz, B., Aykut, A., Pariltay, E., Kirbiyik, O., Gunduz, C. and Ozkinay, C.

Abstract: A limited numbers of published studies evaluate the referral reasons for genetic counseling services in the literature. These studies are focused on prenatal genetic counseling services, in particular, prenatal diagnosis. In order to provide the most effective and helpful genetic counseling services, genetics professionals need adequate knowledge about the profile of individuals referred for these services. In addition, physicians need increased awareness of the nature of genetic issues in order to make appropriate referrals. This study was intended to provide a descriptive analysis of the referral reasons of patients that received genetic counseling at a genetics center in Izmir, Turkey during an 11-year period. A total of 8965 records generated between 1998 and 2008 from one genetic center (which consists of The Department of Medical Genetics and Division of Pediatric Genetics) were evaluated retrospectively. Of these, 6,258 involved referrals for prenatal reasons, and 2,707 involved referrals for postnatal reasons. Both prenatal and postnatal records were further classified into more specific categories of referral reasons. The most common reason for genetic counseling among the prenatal patients was advanced maternal age (42.0%), followed by high risk results on prenatal biochemical screening tests such as second trimester double test [(serum concentration of alphafetoprotein (AFP), beta-human chorionic gonadotropin (beta-HCG)], triple test (serum concentration of AFP, beta-HCG, oestriol) and integrated test (26.5%). The most common indications for postnatal patients were recurrent miscarriages (28.2%) and infertility (19.7%). A significant increase in number of specific categories of referrals for genetic counseling was observed for the last 3 years after the establishment of the Medical Genetics Department. These data provide useful information about the frequency of referrals to the genetics department, and the feasibility of genetic services. Organization of genetic services and systematic procedures for genetic counseling and genetic testing may improve the public's awareness of genetics and ensure a high standard of patient care.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21221751

(2) Title: Biochemical amniotic fluid pattern for prenatal diagnosis of esophageal atresia

Source: *Pediatr Res* **2011,** *70* (2), 199-202.2

Authors: Czerkiewicz, I., Dreux, S., Beckmezian, A., Benachi, A., Salomon, L.J., Schmitz, T., Bonnard, A., Khen-Dunlop, N. and Muller, F.

Abstract: Prenatal diagnosis of esophageal atresia (EA) may improve the outcome of affected neonates by allowing optimization of both prenatal and postnatal care. Prenatal sonographic detection is based on polyhydramnios and/or nonvisualization of the fetal stomach bubble, two signs with a large number of etiologies. We evaluated a biochemical approach to improving diagnostic efficiency. We compared amniotic fluid biochemical markers in 44 EA cases with 88 polyhydramnios and 88 nonpolyhydramnios controls. Both matched for GA with cases. Total proteins, alpha-fetoprotein (AFP), and digestive enzyme activities were assayed, including gamma-glutamyl transpeptidase (GGTP). We defined an EA index (AFP multiplied by GGTP). A significant difference ($p < 0.0001$) was observed for total protein, AFP, GGTP, and EA index between the EA group and each of the two control groups. No statistical difference was observed for any marker between the two most frequent EA subgroups (type I and type III) or between the two control groups. Using a cutoff of 3 for the EA index, 98% sensitivity and 100% specificity were observed for amniotic fluid prenatal diagnosis of EA, whatever the anatomical type. A large prospective series is required to confirm these results.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21522036

(3) Title: Paper-based chemiluminescence ELISA: Lab-on-paper based on chitosan modified paper device and wax-screen-printing

Source: *Biosens Bioelectron* **2011**,

Authors: Wang, S., Ge, L., Song, X., Yu, J., Ge, S., Huang, J. and Zeng, F.

Abstract: A novel lab-on-paper device combining the simplicity and low-cost of microfluidic paper-based analytical devices (muPADs) and the sensitivity and selectivity of chemiluminescence ELISA (CL-ELISA) for the high-throughput, rapid, stable and reusable point-of-care testing is presented here. Chitosan was used to modify muPADs to covalently immobilize antibodies on muPADs. Thus, sandwich CL-ELISA on muPADs can be easily realized for further development of this technique in sensitive, specific and low-cost application. The paper device was fabricated by a low-cost, simple, and rapid wax-screen-printing method. Using tumor markers and paper microzone plate as model, the application test of this paper-based CL-ELISA was successfully performed with a linear range of 0.1-35.0ngmL(-1) for alpha-fetoprotein, 0.5-80.0UmL(-1) for cancer antigen 125 and 0.1-70.0ngmL(-1) for carcinoembryonic antigen. Since the cutoff values of the three tumor markers in clinical diagnosis are 25ngmL(-1), 35UmL(-1) and 5ngmL(-1), the sensitivity and linear ranges of the proposed method were enough for clinical application. In addition, this lab-on-paper immunodevice can provide reproducible results upon storage at 4 degrees C (sealed) for at least 5 weeks. Ultimately, this novel chitosan modification and wax-screen-printing methodology for muPADs can be readily translated to other signal reporting mechanism including electrochemiluminescence and photoelectrochemistry, and other receptors such as enzyme receptors and DNA receptors for determination of DNA, proteins and small molecules in point-of-care testing.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22051546

4) Title: Quantum dot-based immunochromatography test strip for rapid, quantitative and sensitive detection of alpha fetoprotein

Source: *Biosens Bioelectron* **2011,** *30* (1), 145-150.1

Authors: Yang, Q., Gong, X., Song, T., Yang, J., Zhu, S., Li, Y., Cui, Y., Zhang, B. and Chang, J.

Abstract: Rapid, quantitative detection of tumor markers with high sensitivity and specificity is critical to clinical diagnosis and treatment of cancer. We describe here a novel portable fluorescent biosensor that integrates quantum dot (QD) with an immunochromatography test strip (ICTS) and a home-made test strip reader for detection of tumor markers in human serum. Alpha fetoprotein (AFP), which is valuable for diagnosis of primary hepatic carcinoma, is used as a model tumor marker to demonstrate the performance of the proposed immunosensor. The principle of this sensor is on the basis of a sandwich immunoreaction that was performed on an ICTS. The fluorescence intensity of captured QD labels on the test line and control line served as signals was determined by the home-made test strip reader. The strong luminescence and robust photostability of QDs combined with the promising advantages of an ICTS and sensitive detection with the test strip reader result in good performance. Under optimal conditions, this biosensor is capable of detecting as low as 1ng/mL AFP standard analyte in 10min with only 50muL sample volume. Furthermore, 1000 clinical human serum samples were tested by both the QD-based ICTS and a commercial electrochemiluminescence immunoassay AFP kit simultaneously to estimate the sensitivity, specificity and concordance of the assays. Results showed high consistency except for 24 false positive cases (false positive rate 3.92%) and 17 false negative cases (false negative rate 4.38%); the error rate was 4.10% in all. This demonstrates that the QD-based ICTS is capable of rapid, sensitive, and quantitative detection of AFP and shows a great promise for point-of-care testing of other tumor markers.

URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21963096

VI. Potentially helpful website connections/locations:

1) http://health.allrefer.com/health/alpha-fetoprotein-info.html

2) www.healthopedia.com/alpha-fetoprotein

3) http://pregnancy.about.com/cs/afp/a/afptesting.htm

4) http://www.webmd.com/baby/alpha-fetoprotein-afp-in-blood

5) http://pregnancy.about.com/od/afp/Alphafetoprotein_Testing.htm

6) http://www.americanpregnancy.org/prenataltesting/afpplus.html

Figure 1

Maternal Sera AFP MoM

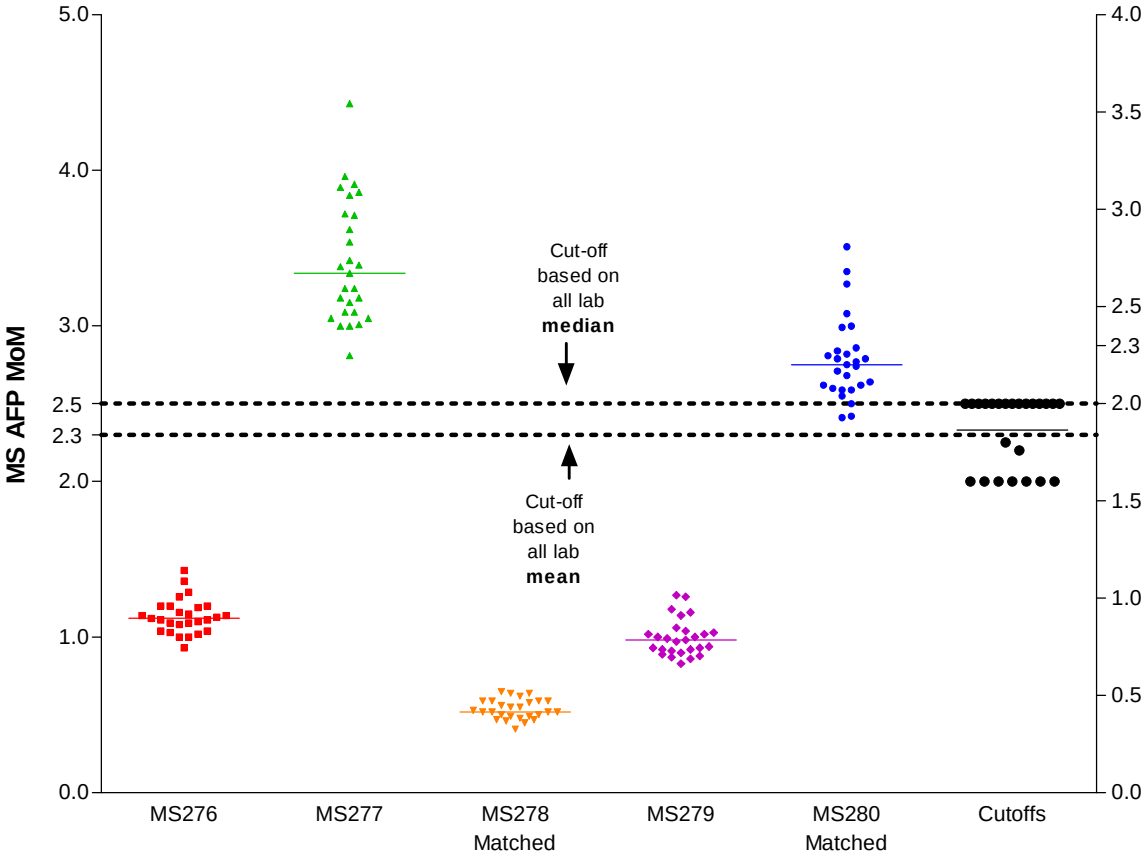


Figure 2

Amniotic Fluid AFP MoM

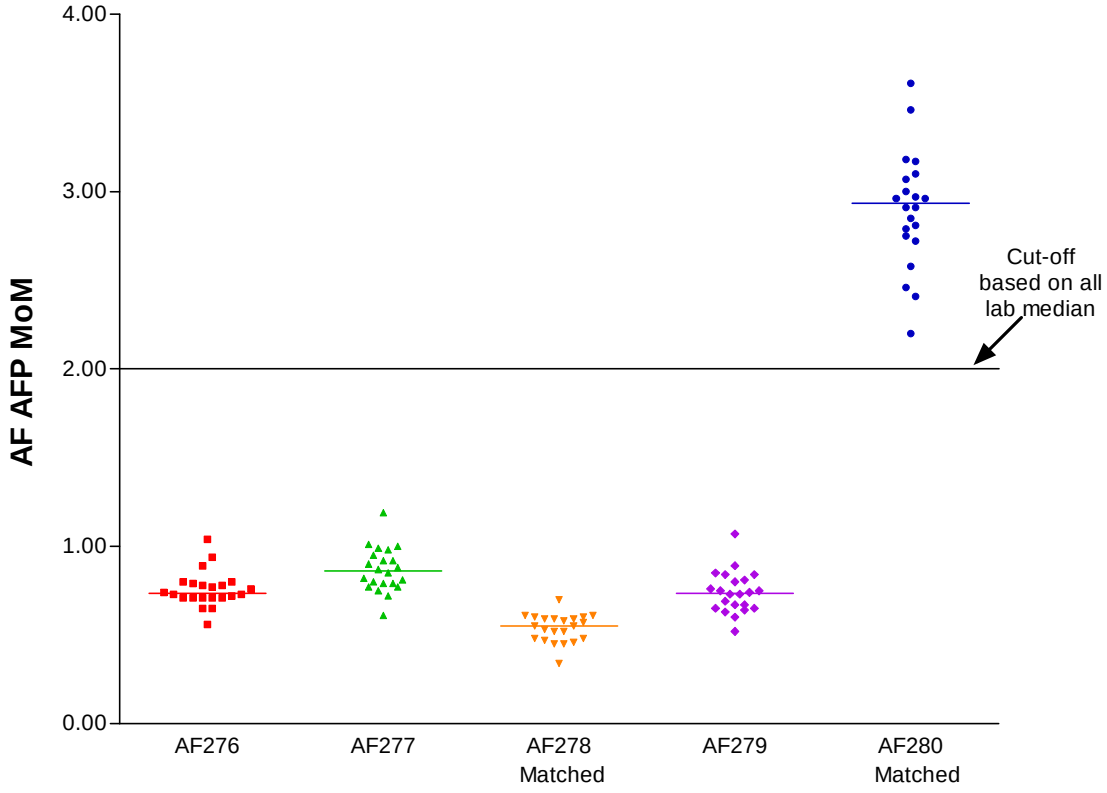


Figure 3

Graphic Distribution of Second Trimester Neural Tube Defect Risk Estimates

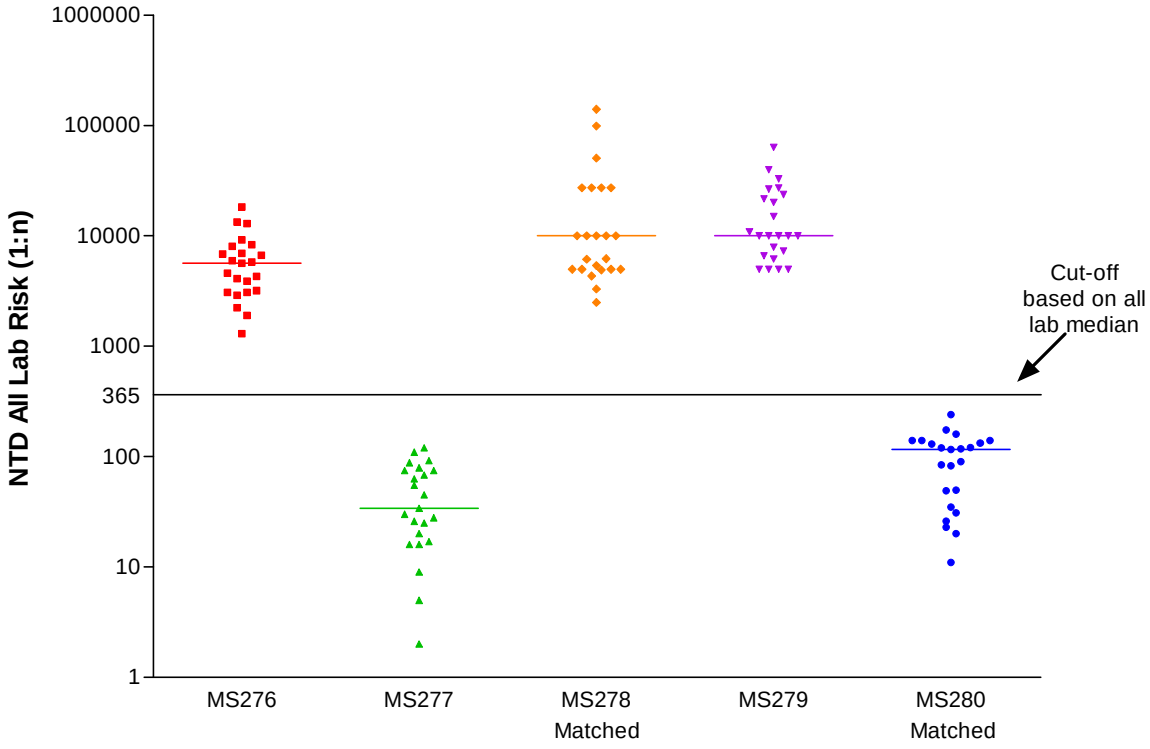


Figure 4

Graphic Distribution of Second Trimester Trisomy 18 Risk Estimates

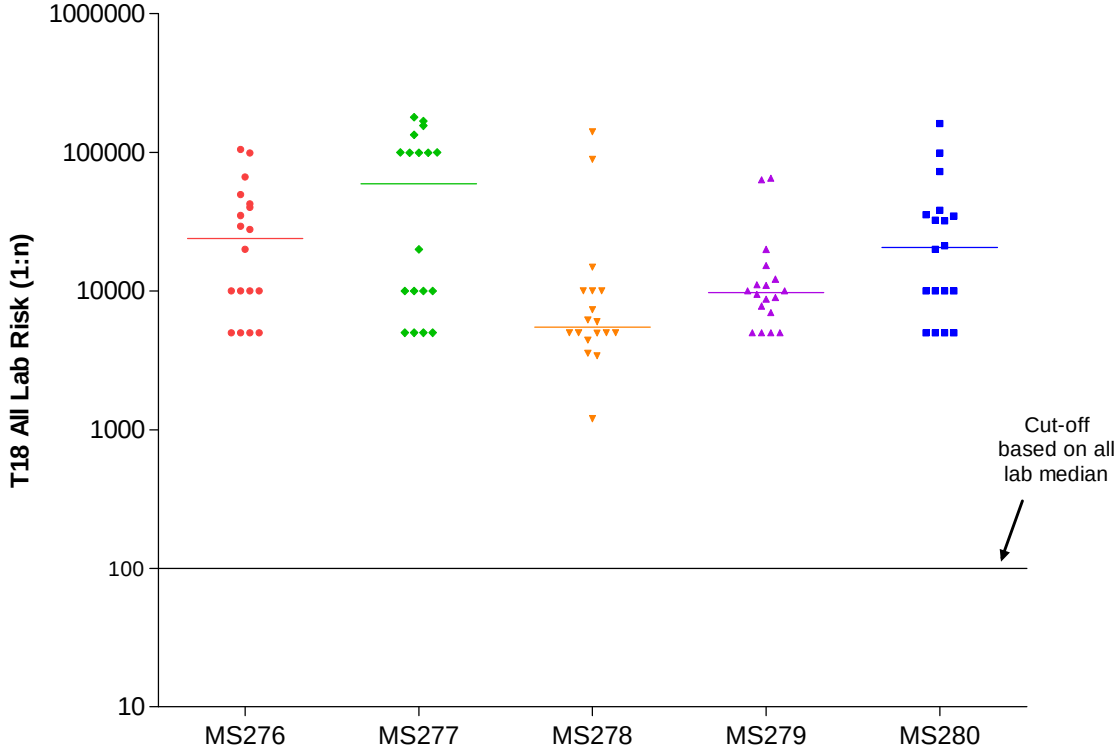


Figure 5

Graphic Distribution of Second Trimester Trisomy 21 Triple Risk Estimates

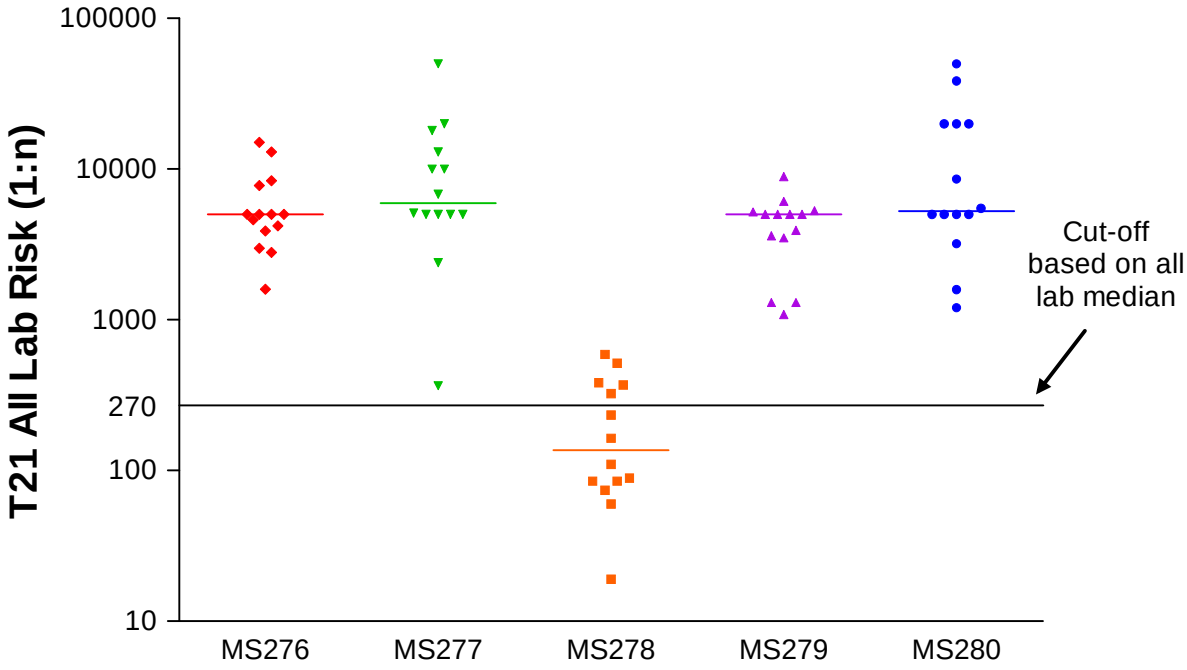
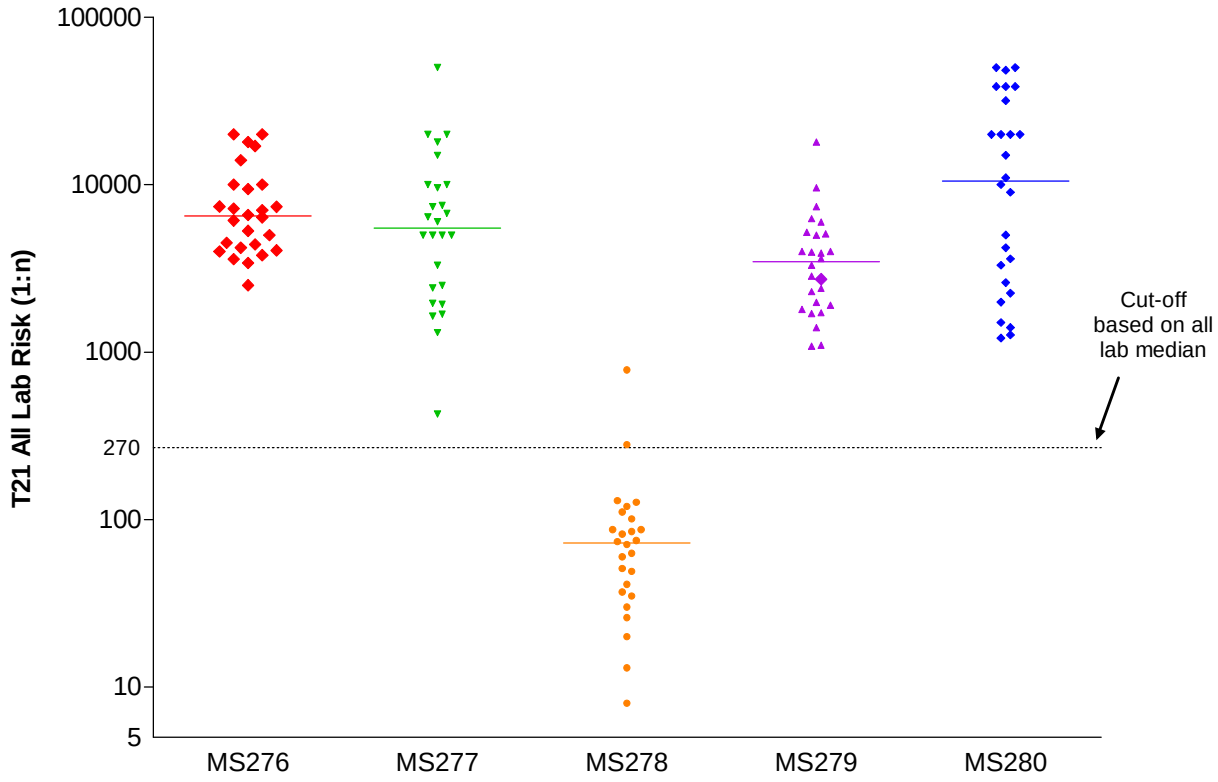


Figure 6

Graphic Distribution of Second Trimester Trisomy 21 Quadruple Risk Estimates



NYS FEDM PT 1/12

Figure 7A

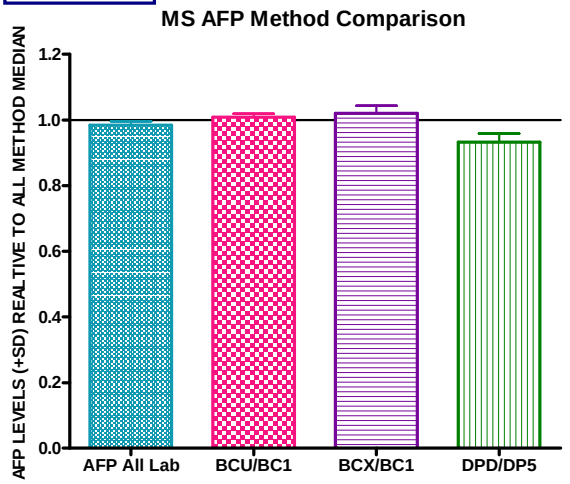


Figure 7B

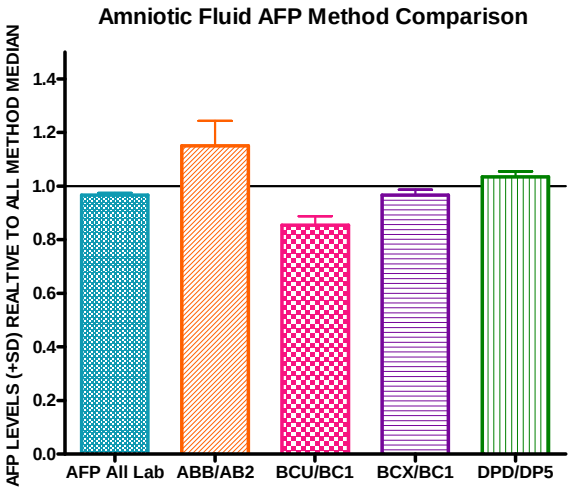


Figure 8A

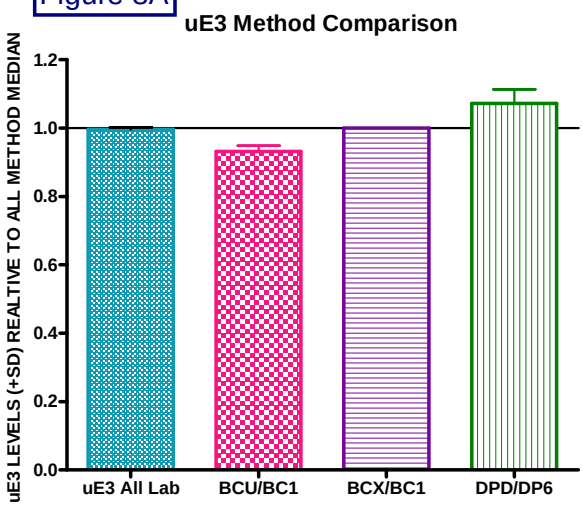


Figure 8B

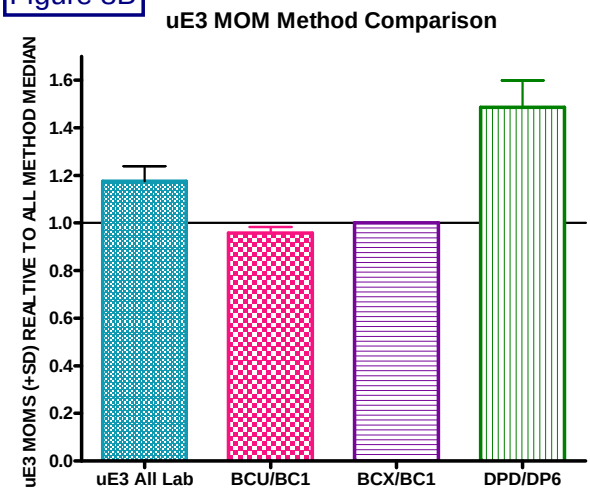


Figure 9A

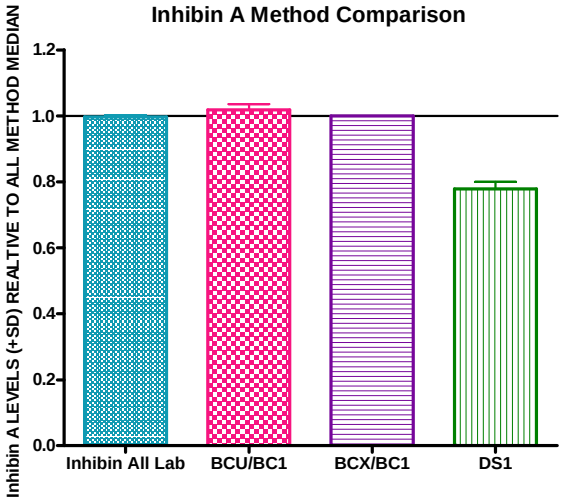


Figure 9B

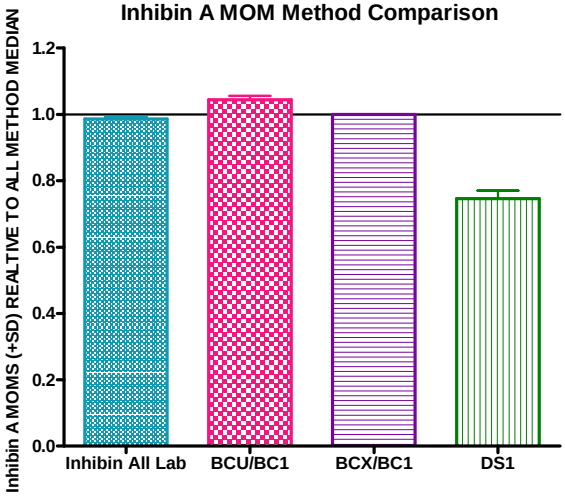


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Figure 10

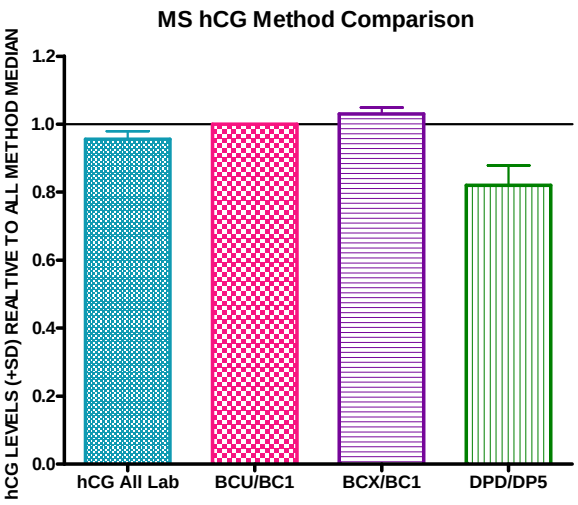


Figure 11

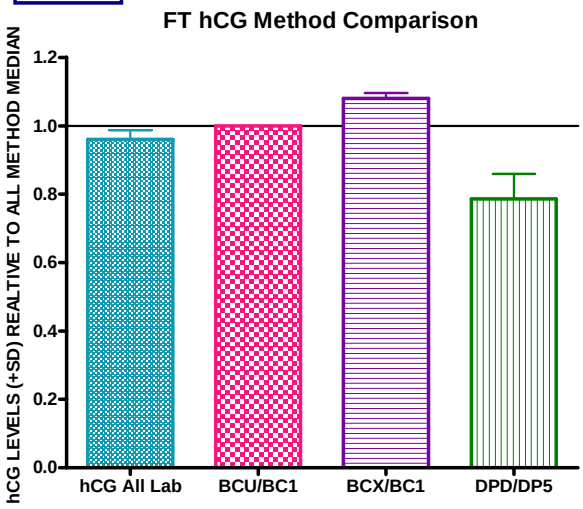


Figure 12A

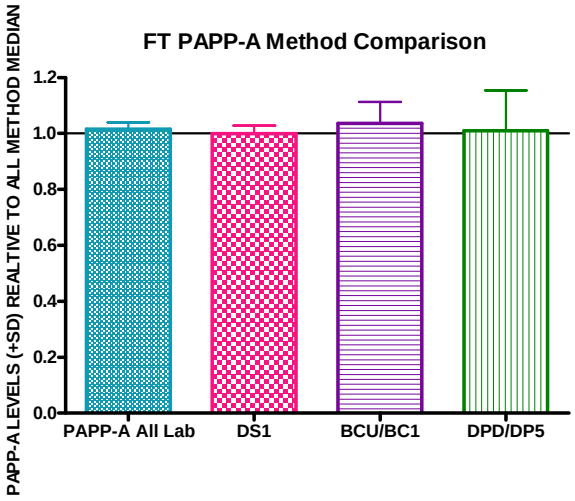
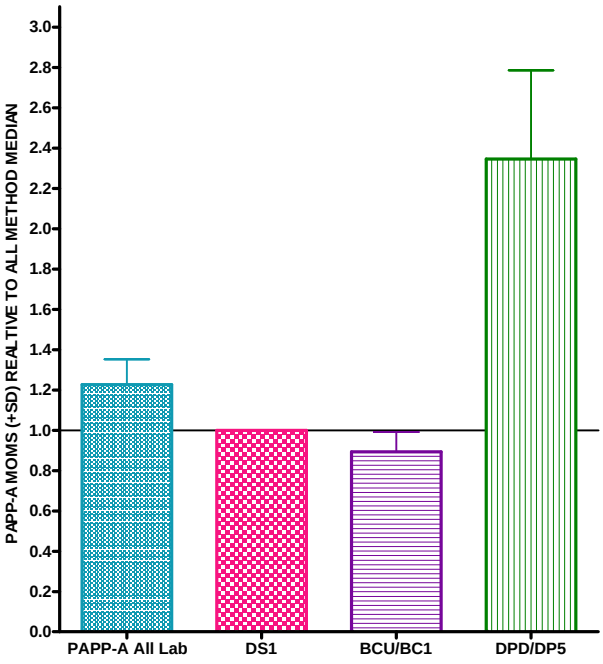


Figure 12B



ABB/AB1 = Abbott Asxym
BCX/BC1 = Beckman Access/2
BCU/BC1 = Beckman Unicel
DPD/DP5 = Siemens Immulite 2000
DS1 = Diagnostic Systems Labs

Figure 13

Graphic Distribution of First Trimester
Trisomy 21 Risk Estimates

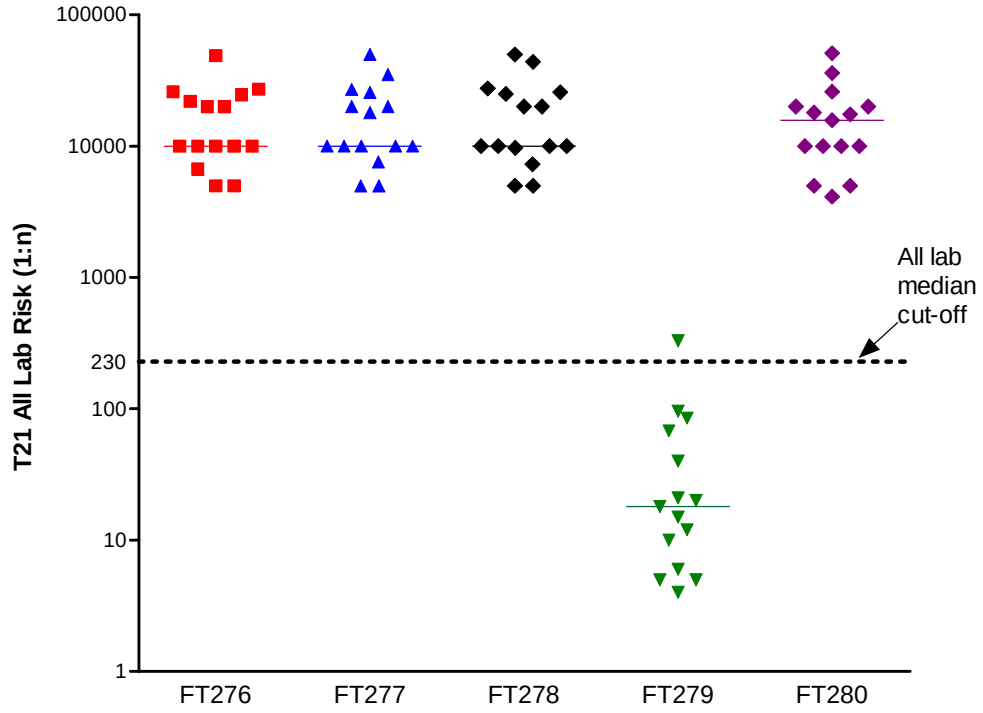


Figure 14

Graphic Distribution of First Trimester
Trisomy 18 Risk Estimates

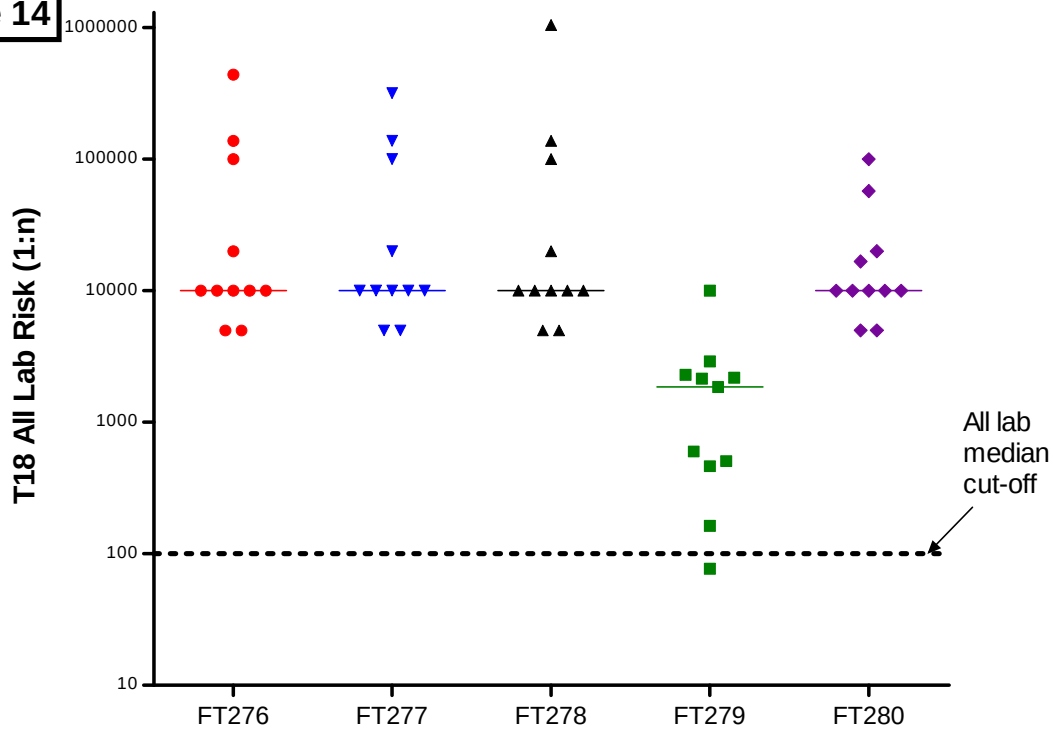


Fig. 15A

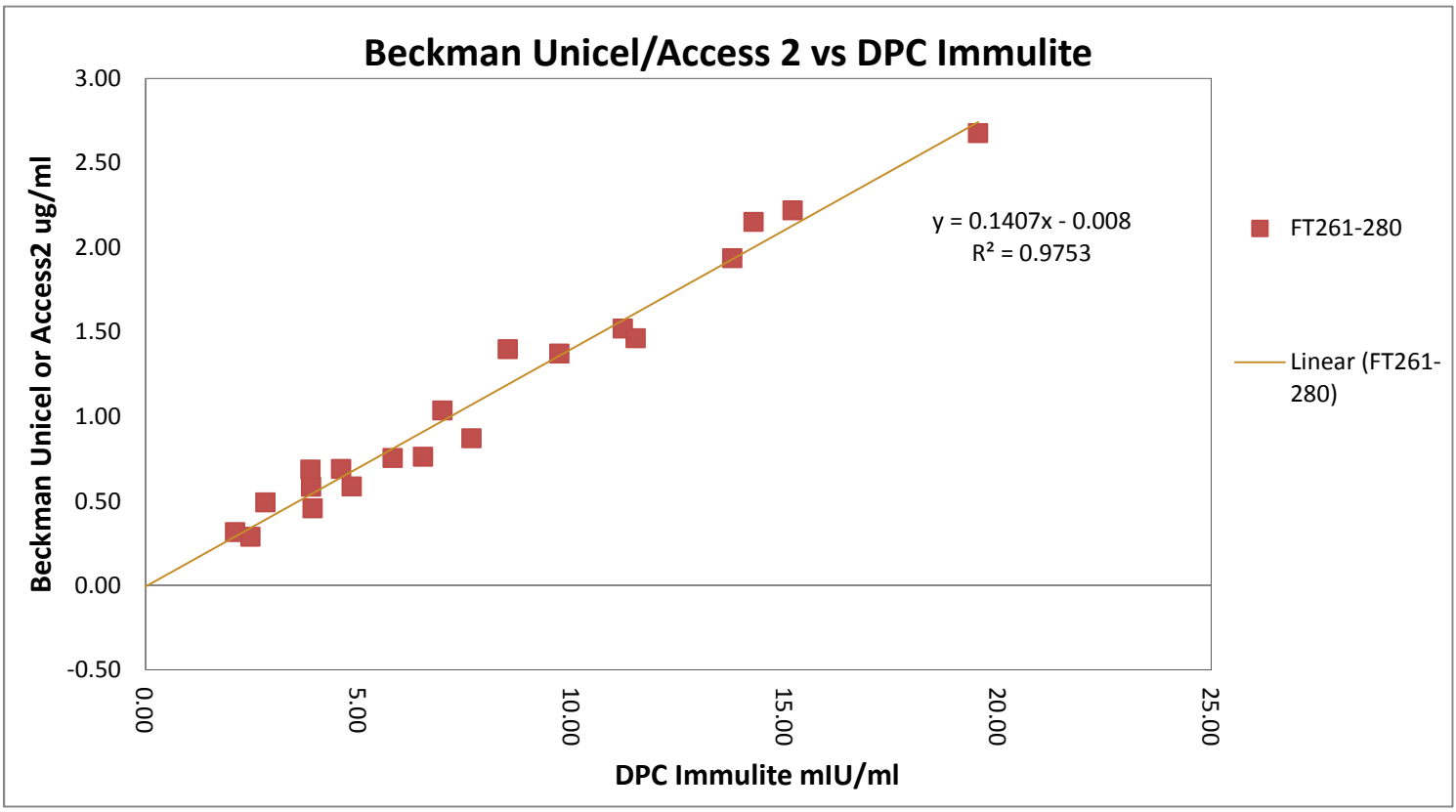
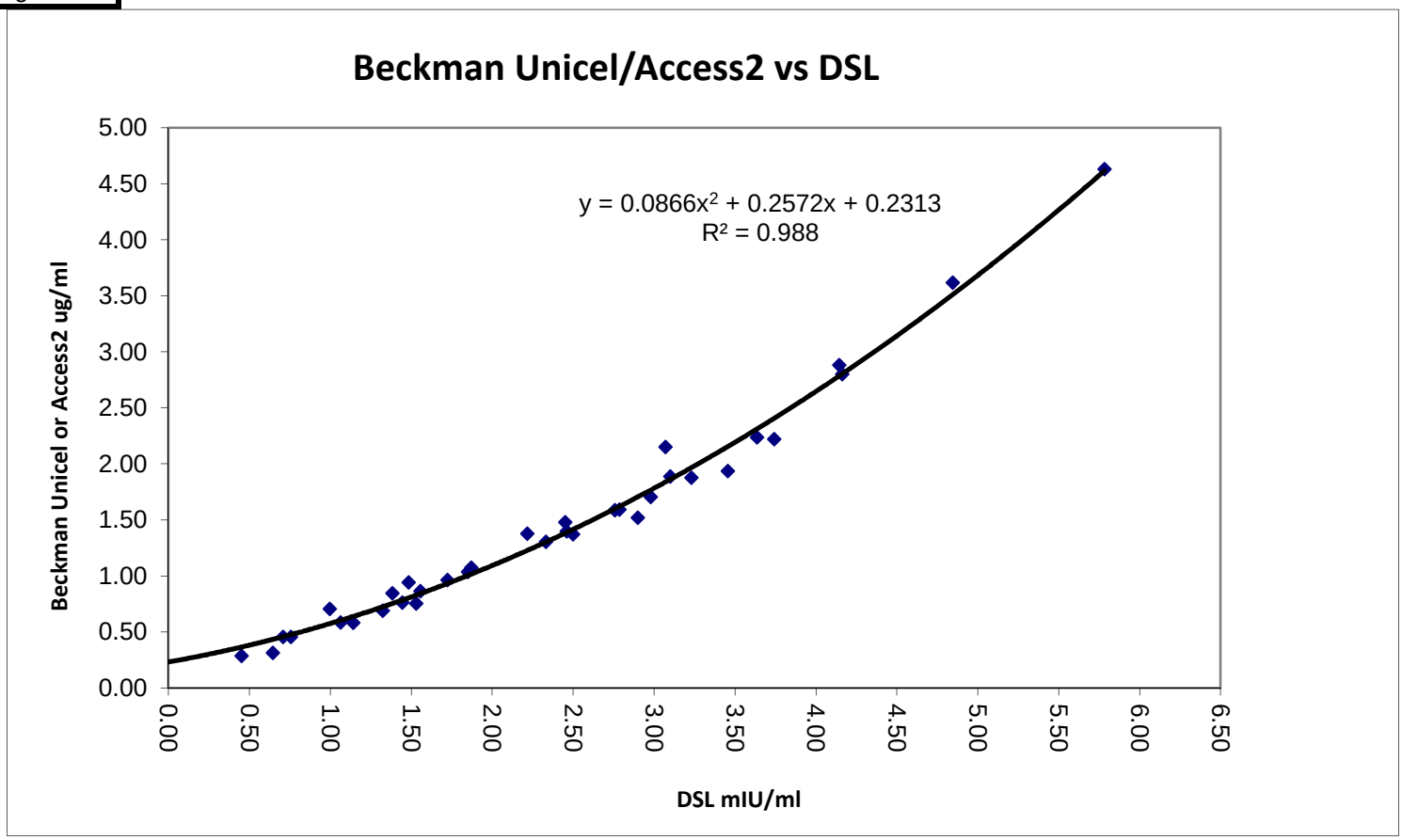


Fig. 15B



New York State Fetal Defect Markers Proficiency Test,
January 2012
Summary of Results

	MS 276	MS 277	MS 278	MS 279	MS 280
Gestational Age All Lab Mean:					
Mean	19.0	18.0	15.0	17.0	20.0
SD	0.00	0.00	0.00	0.00	0.00
%CV	0.0%	0.0%	0.0%	0.0%	0.0%
X+3*SD	19.0	18.0	15.0	17.0	20.0
X-3*SD	19.0	18.0	15.0	17.0	20.0
N	27	27	27	27	27

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP All Lab Mean:					
mean	57.7	157.8	16.3	39.3	159.0
SD	4.3	13.7	1.6	3.3	10.9
%CV	7.5%	8.7%	9.6%	8.3%	6.9%
mean+3SD	70.7	198.9	21.0	49.1	191.7
mean-3SD	44.7	116.7	11.6	29.5	126.3
N	27	27	27	27	26
median	56.9	155.0	16.1	39.6	157.15
mean/all kit median	1.00	0.97	0.98	0.98	0.99

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP Beckman Access (BCX/BC1) mean:					
mean	59.7	162.1	16.7	40.6	167.4
SD	4.9	18.9	2.0	3.9	16.8
%CV	8.1%	11.6%	12.0%	9.6%	10.1%
mean+3SD	74.3	218.7	22.7	52.3	217.9
mean-3SD	45.1	105.4	10.7	28.8	116.8
N	9	9	9	9	9
median	58.1	160.6	17.0	40.6	161.0
mean/all kit median	1.04	1.00	1.00	1.01	1.05

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP Beckman Unicel (BCU/BC1) mean:					
Mean	57.6	164.5	17.0	40.2	160.0
SD	4.4	7.4	1.4	2.9	11.5
%CV	7.6%	4.5%	8.3%	7.2%	7.2%
mean + 3SD	70.7	186.8	21.2	48.8	194.4
mean - 3SD	44.5	142.3	12.8	31.5	125.5
N	8	8	8	8	8
Median	57.2	166.1	17.0	40.6	161.1
mean/All kit median	1.00	1.02	1.02	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP DPC Immulite 2000 (DPD/DP5) mean:					
mean	55.7	147.4	15.3	36.7	151.8
SD	3.4	5.3	0.8	1.6	7.3
%CV	6.1%	3.6%	5.1%	4.3%	4.8%
mean+3SD	65.9	163.4	17.6	41.5	173.7
mean-3SD	45.6	131.3	12.9	31.9	129.8
N	8	8	8	8	8
median	55.6	147.0	15.1	36.5	151.5
mean/all kit median	0.97	0.91	0.92	0.91	0.95

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP MoMs All Lab Mean:					
mean	1.13	3.41	0.54	1.00	2.79
SD	0.11	0.39	0.06	0.12	0.27
%CV	9.9%	11.5%	11.9%	11.8%	9.6%
mean+3SD	1.47	4.59	0.73	1.35	3.60
mean-3SD	0.80	2.23	0.35	0.64	1.98
N	27	27	27	27	27

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP kit average:					
mean	57.7	158.0	16.3	39.1	159.7
SD	2.0	9.3	0.9	2.1	7.8
all kit median	57.6	162.1	16.7	40.2	160.0

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 All Lab Mean:					
mean	1.36	1.19	0.36	0.71	1.39
SD	0.09	0.09	0.03	0.06	0.09
%CV	6.9%	7.5%	9.5%	8.5%	6.7%
mean+3SD	1.65	1.46	0.46	0.89	1.67
mean-3SD	1.08	0.92	0.25	0.53	1.11
N	25	26	25	25	26
mean/all kit median	1.00	0.99	1.00	1.00	0.99

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 Beckman Unicel (BCU/BC1) mean:					
Mean	1.32	1.12	0.33	0.66	1.30
SD	0.05	0.03	0.03	0.02	0.05
%CV	3.7%	3.0%	7.6%	3.0%	4.0%
mean+3SD	1.46	1.22	0.41	0.72	1.46
mean-3SD	1.17	1.02	0.26	0.60	1.14
N	8	8	8	8	8
Median	1.32	1.12	0.34	0.66	1.32
mean/all kit median	0.96	0.92	0.93	0.93	0.92

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 BeckmanAccess (BCX/BC1) mean:					
mean	1.37	1.21	0.36	0.71	1.41
SD	0.11	0.07	0.04	0.05	0.06
%CV	7.7%	5.7%	9.9%	7.4%	4.4%
mean+3SD	1.68	1.41	0.46	0.87	1.60
mean-3SD	1.05	1.00	0.25	0.55	1.22
N	9	9	9	9	9
median	1.33	1.21	0.36	0.70	1.39
mean/all kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 DPC Immulite 2000 (DPD/DP6) mean:					
Mean	1.44	1.24	0.40	0.79	1.46
SD	0.15	0.10	0.05	0.11	0.08
%CV	10.3%	8.2%	13.2%	14.6%	5.3%
mean+3SD	1.89	1.55	0.56	1.13	1.70
mean-3SD	1.00	0.94	0.24	0.44	1.23
N	9	9	9	9	9
Median	1.45	1.25	0.38	0.77	1.48
mean/All Kit Median	1.06	1.03	1.12	1.11	1.04

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 kit average:					
mean	1.38	1.19	0.36	0.72	1.39
SD	0.06	0.07	0.03	0.06	0.08
all kit median	1.37	1.21	0.36	0.71	1.41

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoMs All Lab Mean:					
Mean	0.98	1.03	0.64	0.86	0.84
SD	0.21	0.23	0.22	0.26	0.23
%CV	21.4%	22.0%	34.7%	30.3%	27.4%
X+3SD	1.61	1.71	1.31	1.64	1.54
X-3SD	0.35	0.35	-0.03	0.08	0.15
N	26	26	27	27	27
mean/All Kit Median	1.13	1.11	1.26	1.22	1.16

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoMs (BCU/BC1) Mean:					
Mean	0.85	0.86	0.50	0.68	0.68
SD	0.05	0.06	0.04	0.04	0.03
%CV	5.4%	6.6%	8.4%	6.5%	4.7%
X+3SD	0.98	1.03	0.63	0.81	0.77
X-3SD	0.71	0.69	0.37	0.55	0.58
N	8	8	8	8	8
mean/All Kit Median	0.98	0.93	0.98	0.97	0.93

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoMs (BCX/BC1) Mean:					
Mean	0.87	0.93	0.51	0.70	0.73
SD	0.09	0.09	0.07	0.07	0.06
%CV	10.5%	9.8%	12.8%	10.3%	7.6%
X+3SD	1.14	1.20	0.71	0.92	0.89
X-3SD	0.59	0.65	0.31	0.49	0.56
N	9	9	9	9	9
mean/All Kit Median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoM (DPD/DP6) Mean:					
Mean	1.21	1.29	0.84	1.11	1.05
SD	0.19	0.18	0.19	0.21	0.20
%CV	15.7%	13.9%	22.8%	18.7%	18.8%
X+3SD	1.78	1.83	1.41	1.73	1.64
X-3SD	0.64	0.75	0.26	0.49	0.46
N	9	9	9	9	9
mean/All Kit Median	1.39	1.39	1.64	1.57	1.44

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoM kit average:					
mean	0.97	1.03	0.62	0.83	0.82
SD	0.20	0.23	0.19	0.24	0.20
all kit median	0.87	0.93	0.51	0.70	0.73

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG All Lab Mean:					
mean	16.04	55.17	63.98	18.03	18.76
SD	1.77	7.39	10.55	2.04	2.15
%CV	11.0%	13.4%	16.5%	11.3%	11.4%
mean+3SD	21.4	77.3	95.6	24.1	25.2
mean-3SD	10.7	33.0	32.3	11.9	12.3
N	26	26	26	26	26
mean/all kit median	0.98	0.94	0.93	0.95	0.98

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG Beckman Access (BCX/BC1) mean:					
mean	17.0	59.7	70.9	19.2	20.3
SD	1.5	5.5	5.9	1.3	0.8
%CV	9.0%	9.3%	8.4%	6.8%	4.0%
mean+3SD	21.6	76.3	88.7	23.1	22.8
mean-3SD	12.4	43.1	53.1	15.2	17.8
N	9	9	9	9	9
median	16.9	60.4	71.1	19.1	20.4
mean/all kit median	1.03	1.02	1.03	1.01	1.06

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG Beckman Unicel (BCU/BC1) mean:					
mean	16.44	58.63	68.74	19.00	19.21
SD	1.76	4.35	7.65	1.05	2.09
%CV	10.7%	7.4%	11.1%	5.5%	10.9%
mean+3SD	21.56	76.31	88.66	23.08	22.76
mean-3SD	12.35	43.07	53.09	15.25	17.84
N	8	8	8	8	8
median	16.35	58.20	66.65	19.45	19.45
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG DPC Immulite 2000 (DPD/DP5) mean:					
mean	14.6	46.6	51.1	15.7	16.4
SD	1.3	4.0	4.7	1.6	1.3
%CV	8.7%	8.6%	9.2%	10.1%	8.0%
mean+3SD	18.3	58.6	65.2	20.4	20.4
mean-3SD	10.8	34.5	37.1	10.9	12.5
N	8	8	8	8	8
median	14.3	44.6	51.0	15.9	16.2
mean/all kit median	0.89	0.79	0.74	0.82	0.86

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG MoMs All Lab Mean:					
mean	0.87	2.59	1.60	0.77	1.12
SD	0.10	0.31	0.26	0.10	0.10
%CV	11.3%	11.8%	16.0%	12.5%	9.3%
mean+3SD	1.16	3.51	2.37	1.06	1.44
mean-3SD	0.57	1.68	0.83	0.48	0.81
N	26	26	26	26	26

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG kit average:					
mean	16.0	55.0	63.6	17.9	18.7
SD	1.3	7.3	10.8	2.0	2.0
all kit median	16.4	58.6	68.7	19.0	19.2

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A all lab mean:					
Mean	193.43	405.28	356.34	212.24	411.84
SD	13.64	33.07	29.93	16.02	30.26
%CV	7.1%	8.2%	8.4%	7.5%	7.3%
mean + 3SD	234.4	504.5	446.1	260.3	502.6
mean- 3SD	152.5	306.1	266.5	164.2	321.1
N	25	25	25	25	25
All Lab Median	195.1	411.3	365.6	213.6	416.5
mean/all kit median	0.99	1.00	1.00	0.99	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A Beckman Access (BCX/BC1) mean:					
Mean	195.8	405.8	356.0	214.2	413.7
SD	9.8	20.7	22.1	14.9	29.9
%CV	5.0%	5.1%	6.2%	7.0%	7.2%
mean + 3SD	225.1	467.9	422.4	259.0	503.3
mean- 3SD	166.5	343.7	289.5	169.4	324.1
N	13	13	13	13	13
median	197.1	418.4	365.6	214.3	419.0
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A Beckman Unicel (BCU/BC1) mean:					
Mean	195.5	418.1	369.3	215.1	420.6
SD	14.1	33.7	25.0	14.1	20.9
%CV	7.2%	8.1%	6.8%	6.5%	5.0%
mean + 3SD	237.9	519.3	444.2	257.3	483.3
mean- 3SD	153.2	316.9	294.4	172.9	357.9
N	10	10	10	10	10
median	194.6	417.7	366.1	214.3	417.0
mean/all kit median	1.00	1.03	1.04	1.00	1.02

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A Diagnostic System Labs (DS1) Mean:					
Mean	151.5	309.4	271.3	172.6	328.4
SD	28.9	49.2	42.7	23.5	49.4
%CV	19.1%	15.9%	15.7%	13.6%	15.1%
mean + 3SD	238.0	456.9	399.3	243.2	476.7
mean- 3SD	64.9	161.9	143.3	102.0	180.0
N	3	3	3	3	3
median	161.2	332.0	277.3	177.5	344.0
mean/all kit median	0.77	0.76	0.76	0.81	0.79

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A kit average:					
mean	180.9	377.8	332.2	200.6	387.6
SD	25.5	59.5	53.1	24.3	51.4
all kit median	195.5	405.8	356.0	214.2	413.7

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM All Lab Mean:					
mean	1.08	2.27	1.80	1.32	2.13
SD	0.16	0.32	0.28	0.17	0.28
%CV	14.5%	13.9%	15.7%	12.8%	13.3%
mean+3SD	1.56	3.21	2.65	1.83	2.99
mean-3SD	0.61	1.32	0.95	0.82	1.28
N	26	26	26	26	26
mean/All kit median	0.98	0.99	0.98	0.99	0.99

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM Beckman Unicel (BCU/BC1) mean:					
Mean	1.14	2.40	1.90	1.41	2.26
SD	0.14	0.24	0.23	0.14	0.20
%CV	12.6%	9.9%	12.0%	10.2%	9.0%
X + 3SD	1.58	3.10	2.58	1.84	2.87
X - 3SD	0.71	1.69	1.21	0.98	1.65
N	10	10	10	10	10
Kit Median	1.08	2.28	1.81	1.34	2.18
mean/All kit median	1.04	1.04	1.03	1.06	1.05

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM Beckman Access (BCX/BC1) mean:					
Mean	1.10	2.30	1.84	1.33	2.15
SD	0.09	0.18	0.21	0.09	0.17
%CV	8.0%	8.0%	11.3%	6.5%	8.1%
X + 3SD	1.37	2.85	2.47	1.59	2.67
X - 3SD	0.84	1.75	1.22	1.07	1.63
N	13	13	13	13	13
Kit Median	1.09	2.30	1.84	1.35	2.18
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM Diagnostic System Labs (DS1) Mean:					
Mean	0.81	1.70	1.32	1.01	1.67
SD	0.19	0.47	0.33	0.20	0.48
%CV	23.0%	27.4%	24.8%	19.8%	29.1%
X + 3SD	1.36	3.10	2.30	1.61	3.12
X - 3SD	0.25	0.30	0.34	0.41	0.21
N	3	3	3	3	3
Kit Median	0.72	1.56	1.27	1.00	1.51
mean/All kit median	0.73	0.74	0.72	0.76	0.78

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM kit average:					
mean	1.0	2.1	1.7	1.3	2.0
SD	0.2	0.4	0.3	0.2	0.3
all kit median	1.1	2.3	1.8	1.3	2.1

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	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP All Lab Mean :					
mean	8.71	8.13	8.99	5.66	18.50
SD	1.28	1.24	1.13	0.98	2.28
%CV	14.7%	15.2%	12.6%	17.2%	12.3%
mean+3SD	12.6	11.8	12.4	8.6	25.3
mean-3SD	4.9	4.4	5.6	2.7	11.7
N	22	22	22	22	22
All kit median	9.2	8.4	9.3	5.8	19.1
mean/All kit mean	0.95	0.97	0.97	0.97	0.97

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP Beckman Unicel (BCU/BC1) mean:					
Mean	7.5	7.1	8.2	4.8	16.9
SD	0.6	0.5	0.7	0.5	1.2
%CV	7.6%	7.6%	9.0%	10.0%	6.8%
X+3SD	13.1	11.9	13.6	8.3	28.4
X-3SD	4.4	4.2	4.4	2.9	9.8
N	7	7	7	7	7
median	7.6	7.2	8.0	4.9	17.3
mean/All kit median	0.82	0.84	0.89	0.83	0.89

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP MoMs All Lab Mean:					
mean	0.76	0.87	0.54	0.74	2.90
SD	0.10	0.12	0.08	0.12	0.33
%CV	13.3%	14.4%	14.5%	15.9%	11.3%
mean+3SD	1.06	1.24	0.77	1.09	3.89
mean-3SD	0.46	0.49	0.30	0.39	1.91
N	22	22	22	22	21

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP Beckman Access (BCX/BC1) mean:					
mean	8.8	8.0	9.0	5.6	19.1
SD	1.5	1.3	1.5	0.9	3.1
%CV	16.7%	16.0%	16.9%	16.2%	16.2%
mean+3SD	13.1	11.9	13.6	8.3	28.4
mean-3SD	4.4	4.2	4.4	2.9	9.8
N	7	7	7	7	7
median	8.5	8	9.3	5.7	19
mean/all kit median	0.95	0.95	0.97	0.96	1.00

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP DPC Immulite 2000 (DPD/DP5) mean:					
mean	9.7	8.8	9.5	6.1	19.0
SD	0.7	0.7	0.6	0.4	1.8
%CV	7.3%	7.5%	6.1%	7.3%	9.7%
mean+3SD	11.8	10.8	11.2	7.4	24.5
mean-3SD	7.5	6.8	7.8	4.7	13.5
N	5	5	5	5	5
median	9.4	8.7	9.5	5.9	18.4
mean/all kit median	1.05	1.05	1.03	1.04	1.00

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP Abbott Axsym (ABB/AB2) mear:					
mean	10.1	10.1	10.2	7.6	20.3
N	2	2	2	2	2
mean/all kit median	1.09	1.20	1.10	1.29	1.07
AF AFP kit average:					
mean	9.0	8.5	9.2	6.0	18.8
SD	1.1	1.3	0.8	1.1	1.4
all kit median	9.2	8.4	9.3	5.8	19.1

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	FT276	FT277	FT278	FT279	FT280
FT Gestational Age All Lab Mean:					
Mean	11.2	11.9	13.0	11.9	11.4
SD	0.13	0.11	0.05	0.11	0.10
%CV	1.2%	0.9%	0.4%	0.9%	0.8%
mean+3*SD	11.6	12.2	13.1	12.2	11.7
mean-3*SD	10.8	11.6	12.8	11.6	11.1
N	17	17	17	17	17

	FT276	FT277	FT278	FT279	FT280
FT NT MoMs All Lab Mean:					
Mean	0.96	0.93	0.98	2.20	0.91
SD	0.07	0.07	0.06	0.17	0.06
%CV	7.0%	7.6%	5.8%	7.7%	6.8%
X+3SD	1.16	1.14	1.15	2.71	1.10
X- 3SD	0.76	0.72	0.81	1.69	0.73
N	16	16	16	16	16
All Median	0.97	0.92	0.98	2.14	0.90

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	FT276	FT277	FT278	FT279	FT280
FT hCG All Lab Mean:					
mean	55.10	51.91	48.09	121.63	41.11
SD	7.78	10.64	6.36	25.76	6.19
%CV	14.1%	20.5%	13.2%	21.2%	15.1%
X+3SD	78.4	83.8	67.2	198.9	59.7
X-3SD	31.8	20.0	29.0	44.3	22.5
N	16	16	16	16	16
mean/All kit median	0.99	0.95	0.98	0.92	0.96

	FT276	FT277	FT278	FT279	FT280
FT hCG Beckman Unicel (BCU/BC1) mean:					
mean	55.53	54.57	49.15	131.63	42.85
SD	2.73	2.05	2.01	4.89	1.41
%CV	4.9%	3.8%	4.1%	3.7%	3.3%
X+3SD	78.06	74.10	62.22	171.64	58.63
X-3SD	43.52	45.87	43.58	109.13	31.89
N	4	3	4	4	4
median	55.00	54.60	48.95	129.65	42.70
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	FT276	FT277	FT278	FT279	FT280
FT hCG DPC Immulite 2000(DPD/DP5) mean:					
mean	46.8	44.5	40.5	87.4	33.9
SD	5.4	3.6	4.6	11.2	3.8
%CV	11.5%	8.2%	11.3%	12.8%	11.3%
X+3SD	62.9	55.4	54.2	120.8	45.5
X-3SD	30.7	33.6	26.8	53.9	22.4
N	5	5	5	5	5
median	44.6	43.1	40.0	84.1	33.3
mean/All kit median	0.84	0.82	0.82	0.66	0.79

	FT276	FT277	FT278	FT279	FT280
FT hCG Beckman Access (BCX/BC1) mean:					
mean	60.8	60.0	52.9	140.4	45.3
SD	5.8	4.7	3.1	10.4	4.5
%CV	9.5%	7.8%	5.9%	7.4%	9.8%
X+3SD	78.1	74.1	62.2	171.6	58.6
X-3SD	43.5	45.9	43.6	109.1	31.9
N	7	7	7	7	7
median	61.8	60.8	52.7	141.0	45.3
mean/All kit median	1.09	1.10	1.08	1.07	1.06

	FT276	FT277	FT278	FT279	FT280
FT hCG MoMs All Lab Mean:					
Mean	0.67	0.62	0.75	1.63	0.48
SD	0.09	0.11	0.07	0.25	0.07
%CV	12.9%	17.5%	9.5%	15.0%	14.6%
mean+3*SD	0.94	0.95	0.96	2.37	0.69
mean - 3*SD	0.41	0.30	0.54	0.90	0.27
N	15	15	15	15	15
All Median	0.69	0.63	0.77	1.62	0.47

	FT276	FT277	FT278	FT279	FT280
FT hCG kit average:					
mean	54.4	53.0	47.5	119.8	40.7
SD	7.1	7.9	6.3	28.4	6.0
all kit median	55.5	54.6	49.2	131.6	42.9

New York State Fetal Defect Markers Proficiency Test,
January 2012
Summary of First Trimester Results

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A All Lab Mean:					
Mean	920.45	1471.23	2749.12	458.71	620.11
SD	115.21	142.85	298.12	51.61	75.65
%CV	12.5%	9.7%	10.8%	11.3%	12.2%
mean + 3SD	1266.08	1899.78	3643.47	613.53	847.07
mean- 3SD	574.82	1042.67	1854.77	303.89	393.15
N	14	14	14	14	14
All Lab Median	895.60	1476.20	2760.00	476.64	646.03
mean/All kit median	1.03	1.01	1.00	0.99	1.05

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A DPC Immullite 2000 (DPD/DP5) Mean:					
Mean	1069.29	1610.05	2740.34	388.77	537.45
SD	101.91	73.11	296.58	36.80	22.61
%CV	9.5%	4.5%	10.8%	9.5%	4.2%
X + 3SD	1375.03	1829.38	3630.09	499.17	605.29
X - 3SD	763.56	1390.72	1850.59	278.38	469.60
N	3	3	3	3	3
Kit Median	1111.97	1652.26	2904.49	405.66	528.07
mean/All kit median	1.20	1.10	1.00	0.84	0.91

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A Beckman Unicel(BCU/BC1) Mean:					
Mean	870.43	1461.58	2674.82	490.73	685.10
SD	58.84	96.31	156.60	27.67	25.73
%CV	6.8%	6.6%	5.9%	5.6%	3.8%
X + 3SD	1046.96	1750.53	3144.61	573.75	762.29
X - 3SD	693.91	1172.64	2205.03	407.72	607.91
N	6	6	6	6	6
Kit Median	892.6	1470.2	2723.4	496.5	677.3
mean/All kit median	0.98	1.00	0.98	1.06	1.16

	FT276	FT277	FT278	FT279	FT280
***FT PAPP-A Diagnostic Systems Lab (DS1) Mean:**					
Mean	891.16	1399.50	2843.55	462.25	591.71
SD	110.35	176.15	441.27	42.42	71.06
%CV	12.4%	12.6%	15.5%	9.2%	12.0%
X + 3SD	2.26	3.24	5.55	1.06	1.53
X - 3SD	1.02	1.70	2.83	0.38	0.54
N	5	5	5	5	5
Kit Median	891.45	1394.92	3059.98	480.69	601.24
mean/All kit median	1.00	0.96	1.04	1.00	1.00

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A kit average:					
mean	943.63	1490.38	2752.90	447.25	604.75
SD	109.32	108.19	85.07	52.61	74.69
all kit median	891.16	1461.58	2740.34	462.25	591.71

***Note: The above 2 tables contain converted values (mIU/ml->ng/ml) from equations obtained based on in house correlation data.**
(see critique)

New York State Fetal Defect Markers Proficiency Test,
January 2012
Summary of First Trimester Results

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM All Lab Mean:					
Mean	1.93	2.10	2.79	0.74	1.00
SD	1.09	1.29	1.61	0.32	0.43
%CV	56.6%	61.3%	57.8%	44.0%	42.5%
mean + 3SD	5.19	5.97	7.62	1.70	2.28
mean- 3SD	-1.34	-1.77	-2.05	-0.23	-0.28
N	14	14	14	14	14
All Lab Median	1.49	1.64	2.34	0.67	0.90
mean/ All kit median	1.35	1.34	1.25	1.10	1.09

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM DPC Immulite 2000 (DPD/DP5) Mean:					
Mean	3.88	4.40	5.40	1.28	1.71
SD	0.37	0.65	1.37	0.12	0.10
%CV	9.7%	14.7%	25.4%	9.0%	5.6%
X + 3SD	5.00	6.34	9.52	1.63	2.00
X - 3SD	2.75	2.45	1.28	0.94	1.42
N	3	3	3	3	3
mean/All kit median	2.72	2.80	2.43	1.92	1.86

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM Beckman Unicel(BCU/BC1) Mean:					
Mean	1.43	1.57	2.22	0.67	0.92
SD	0.21	0.17	0.50	0.06	0.14
%CV	14.4%	10.7%	22.7%	8.5%	14.9%
X + 3SD	2.04	2.08	3.73	0.84	1.33
X - 3SD	0.81	1.07	0.71	0.50	0.51
N	6	6	6	6	6
Kit Median	1.39	1.56	2.16	0.67	0.91
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM Diagnostic System Labs (DS1) Mean:					
Mean	1.42	1.46	2.15	0.53	0.73
SD	0.31	0.29	0.57	0.12	0.17
%CV	22.0%	19.7%	26.7%	23.6%	23.5%
X + 3SD	2.35	2.33	3.87	0.90	1.25
X - 3SD	0.48	0.60	0.43	0.15	0.21
N	4	4	4	4	4
Kit Median	1.39	1.51	2.25	0.51	0.72
mean/ All kit median	0.99	0.93	0.97	0.79	0.79

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM kit average:					
mean	2.24	2.48	3.26	0.83	1.12
SD	1.42	1.66	1.86	0.40	0.52
all kit median	1.43	1.57	2.22	0.67	0.92

Figure 1

Maternal Sera AFP MoM

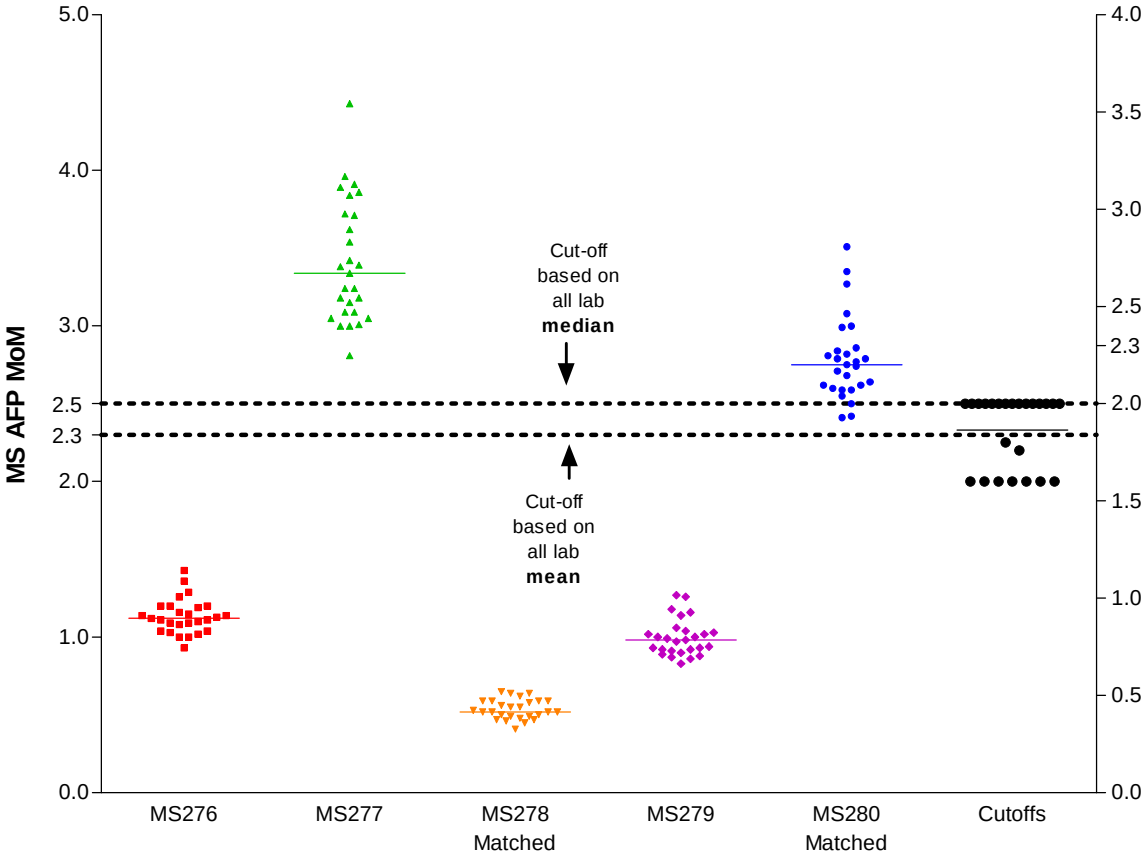

Figure 2

Amniotic Fluid AFP MoM

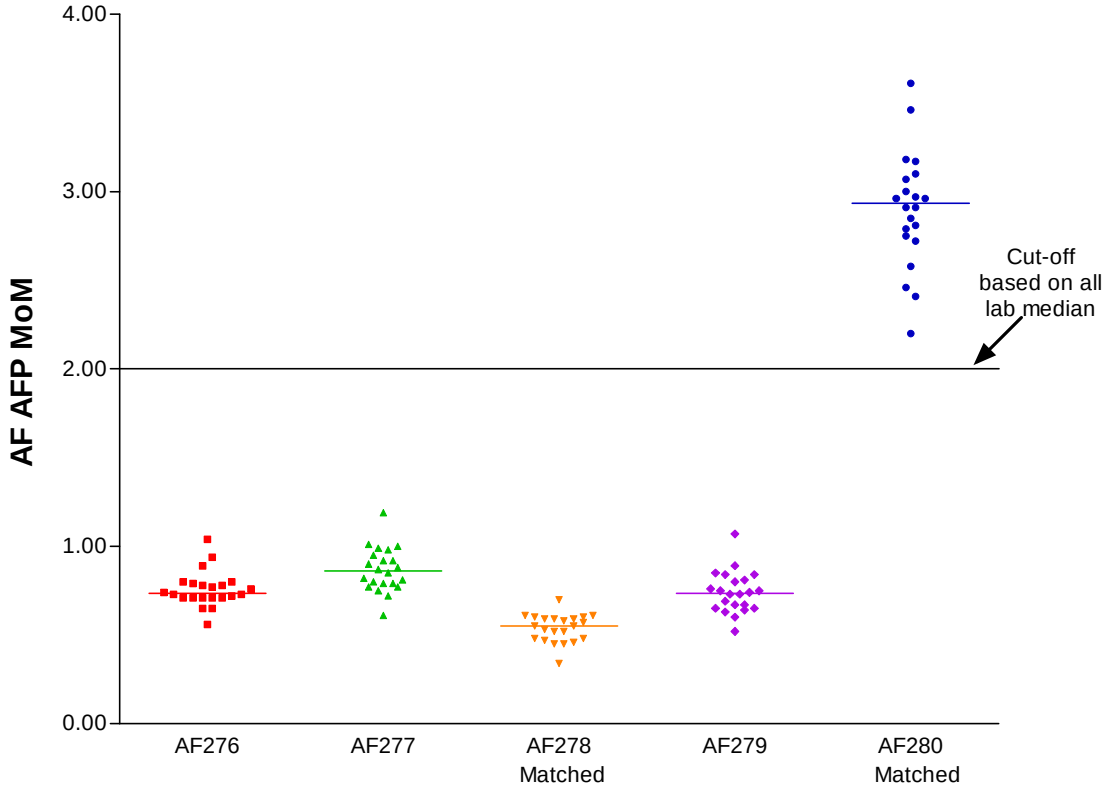

Figure 3

Graphic Distribution of Second Trimester Neural Tube Defect Risk Estimates

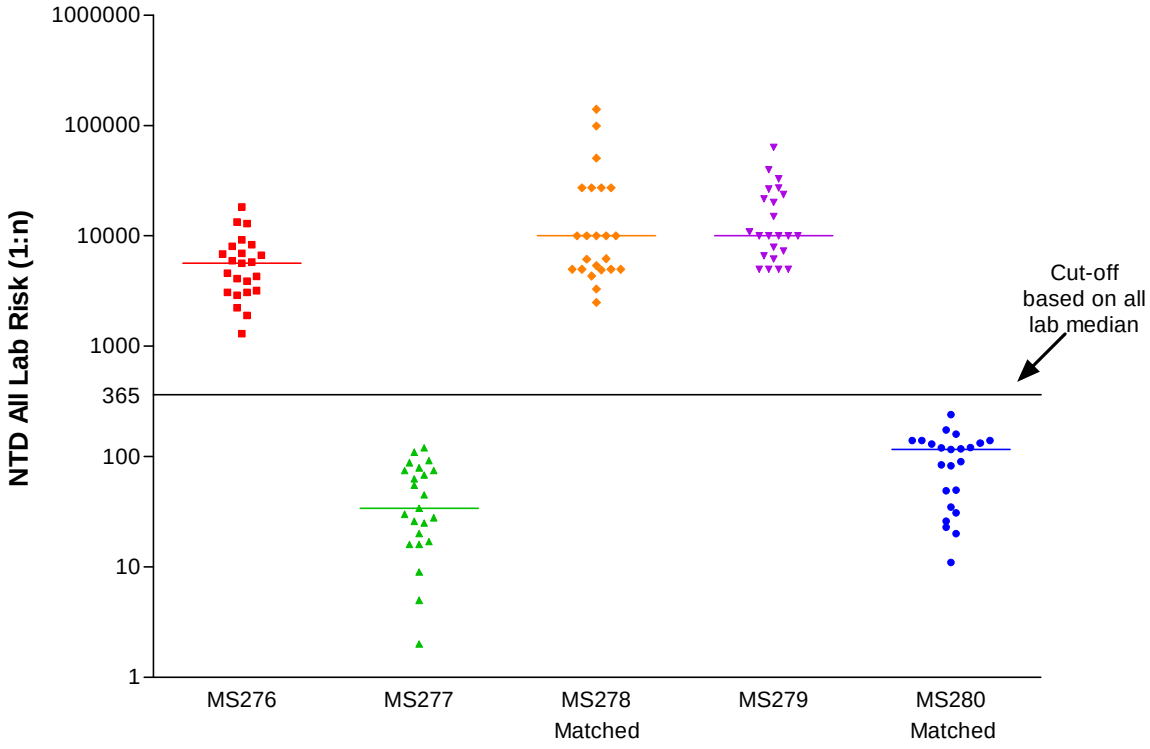

Figure 4

Graphic Distribution of Second Trimester Trisomy 18 Risk Estimates

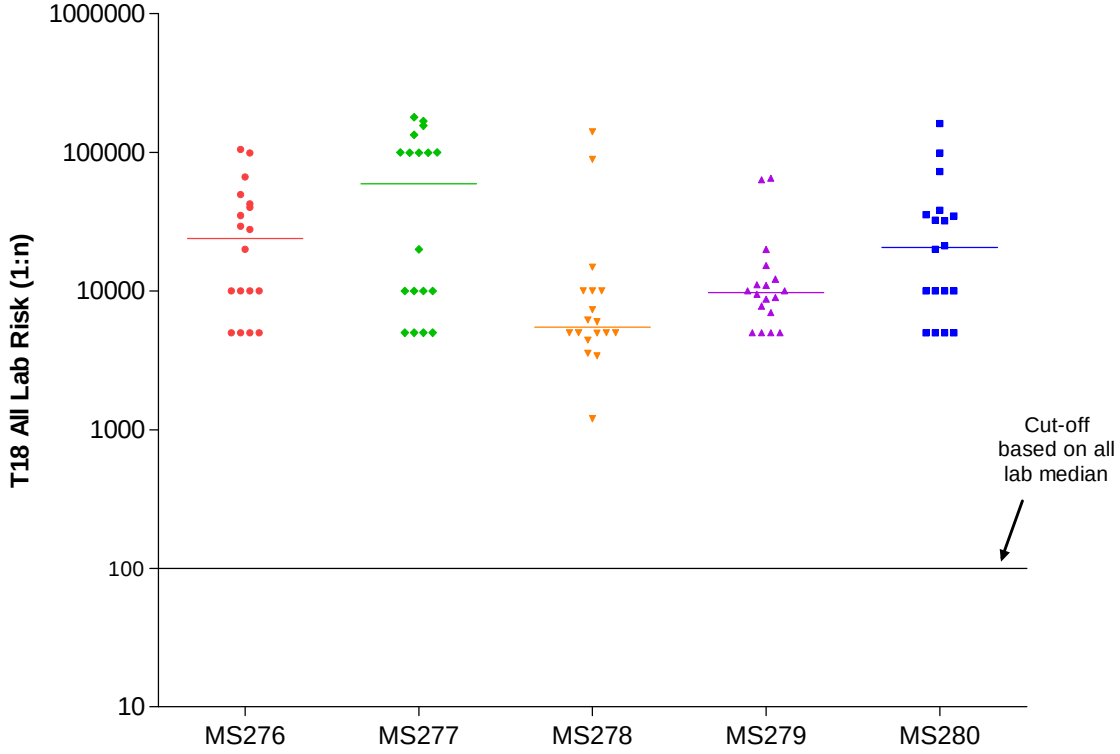

Figure 5

Graphic Distribution of Second Trimester Trisomy 21 Triple Risk Estimates

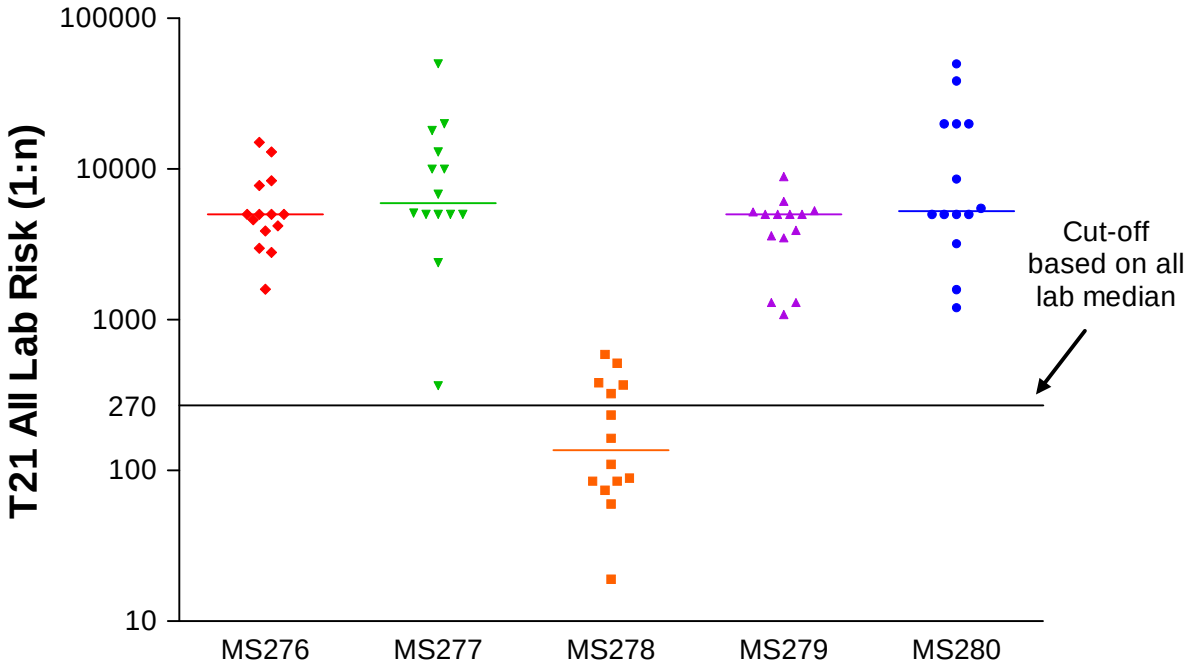

Figure 6

Graphic Distribution of Second Trimester Trisomy 21 Quadruple Risk Estimates

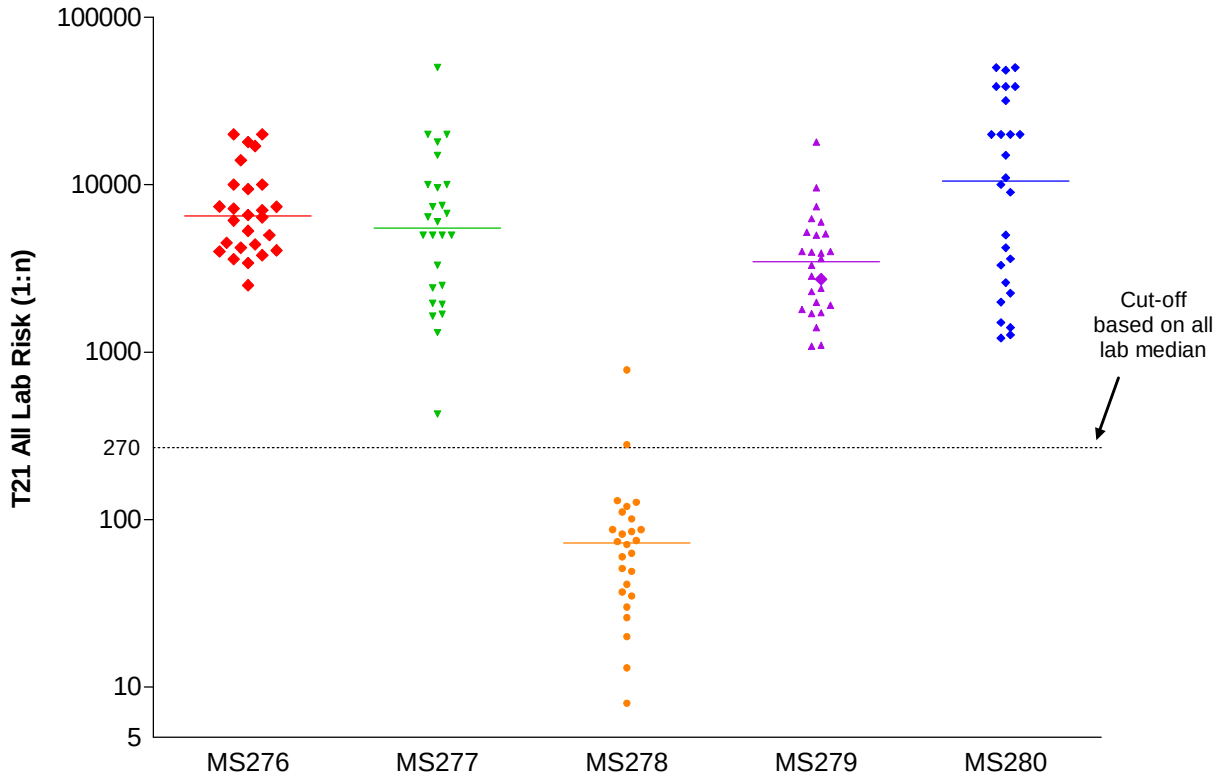

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Figure 7A

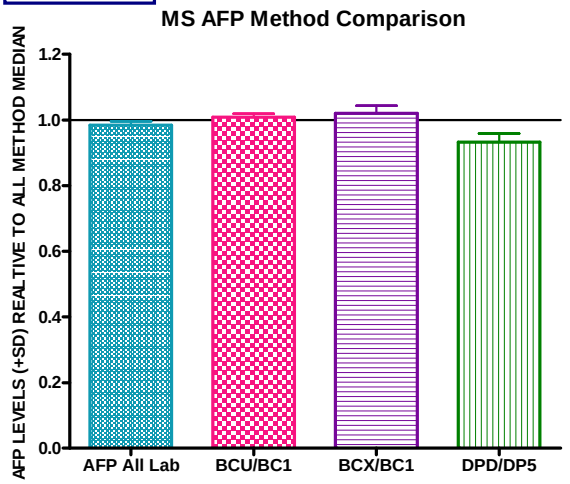

Figure 7B

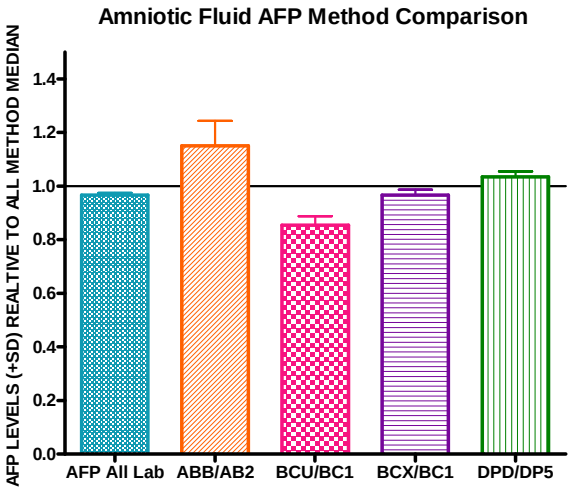

Figure 8A

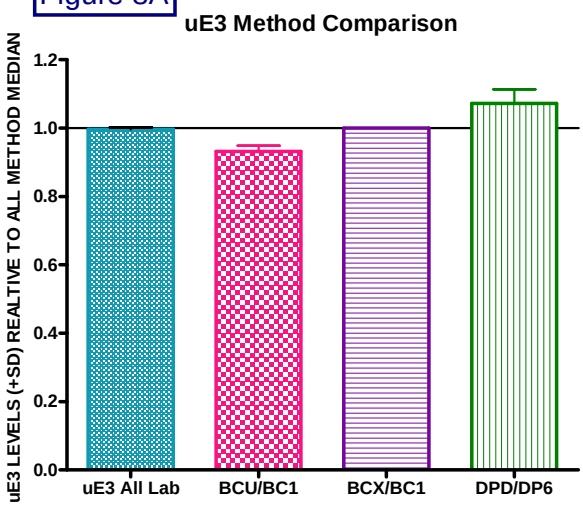

Figure 8B

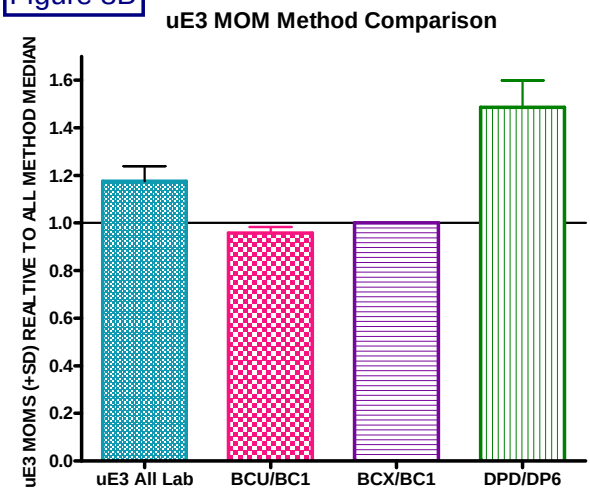

Figure 9A

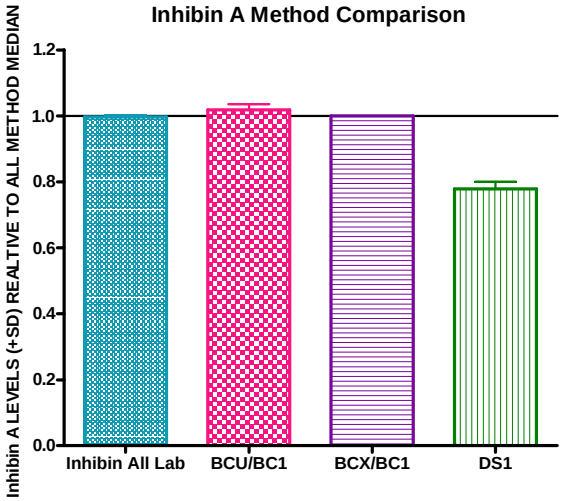

Figure 9B

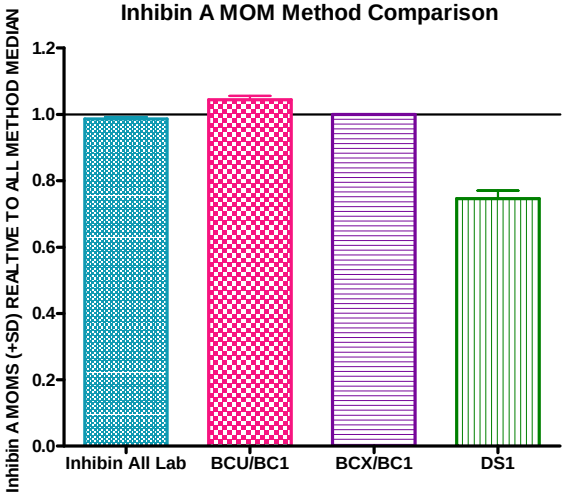

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Figure 10

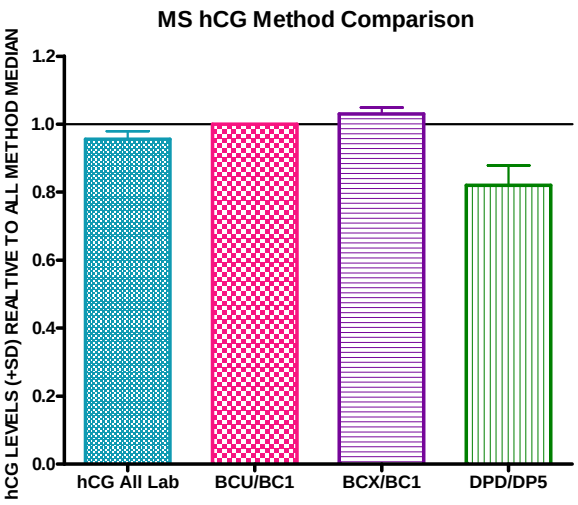


Figure 11

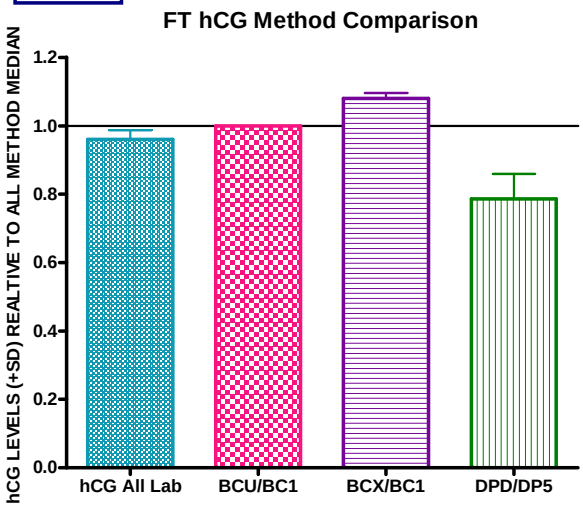


Figure 12A

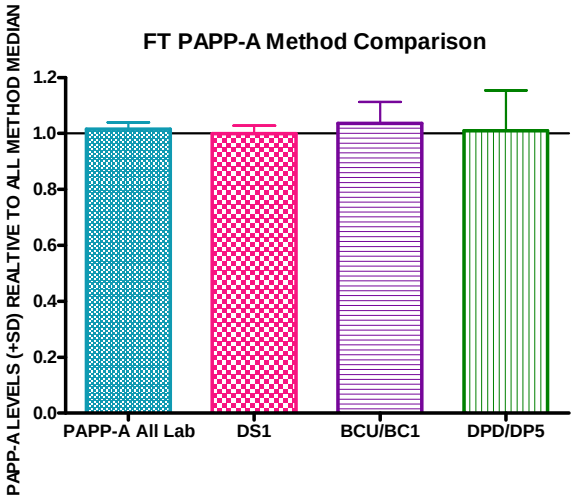
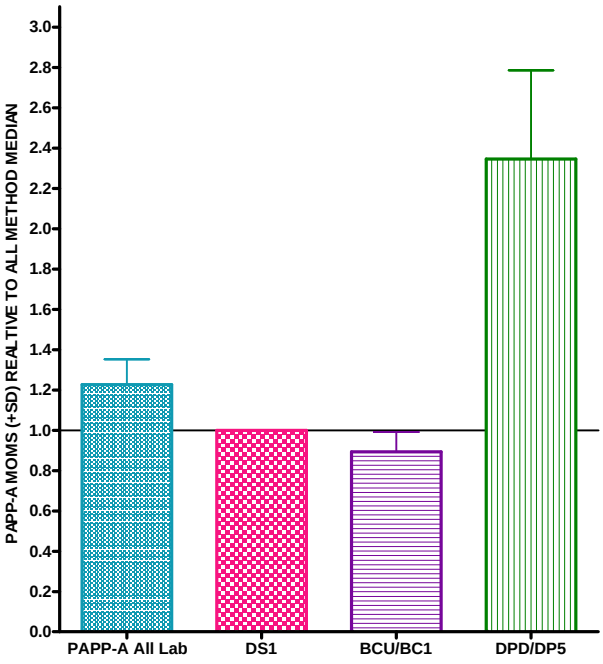


Figure 12B



ABB/AB1 = Abbott Asxym
BCX/BC1 = Beckman Access/2
BCU/BC1 = Beckman Unicel
DPD/DP5 = Siemens Immulite 2000
DS1 = Diagnostic Systems Labs

Figure 13

Graphic Distribution of First Trimester
Trisomy 21 Risk Estimates

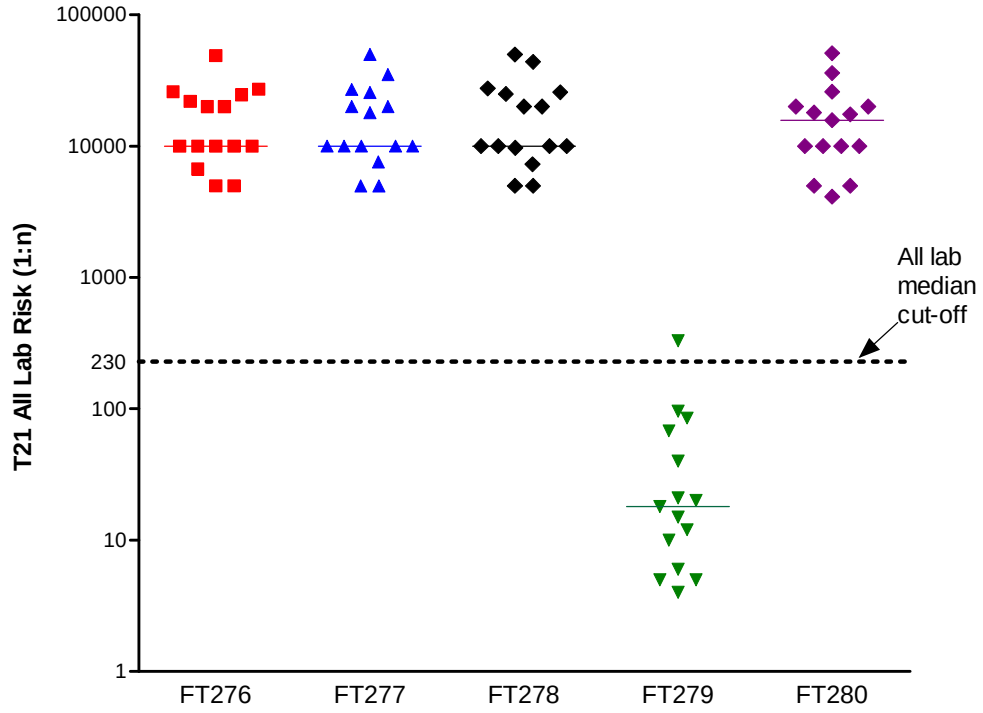


Figure 14

Graphic Distribution of First Trimester
Trisomy 18 Risk Estimates

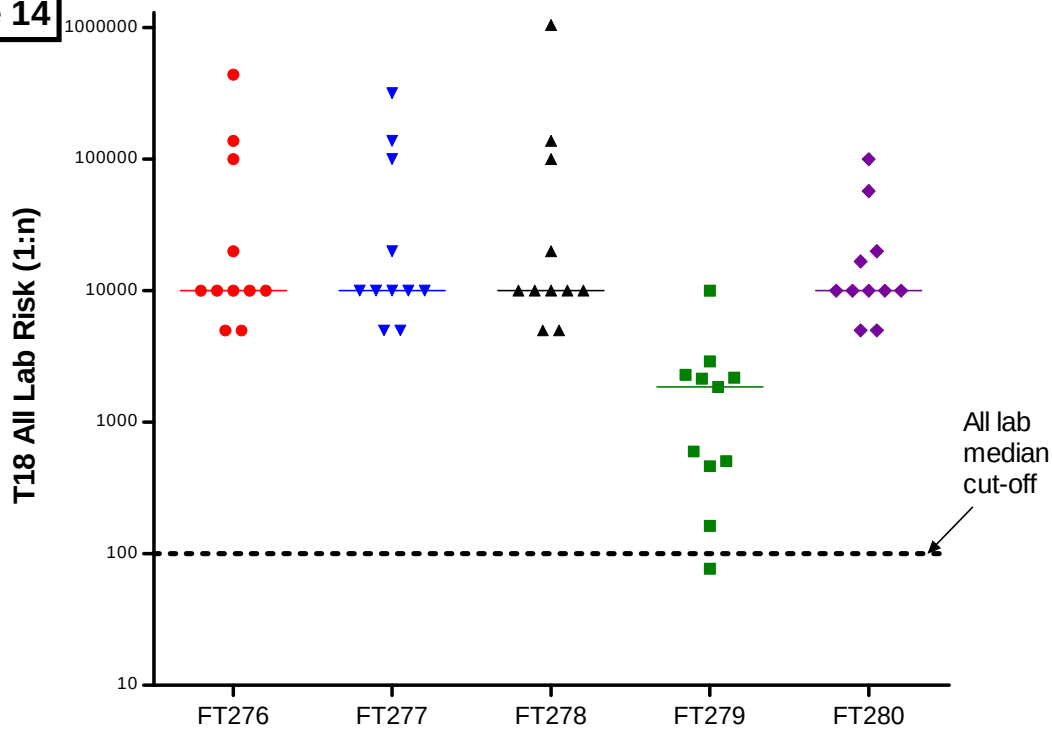


Fig. 15A

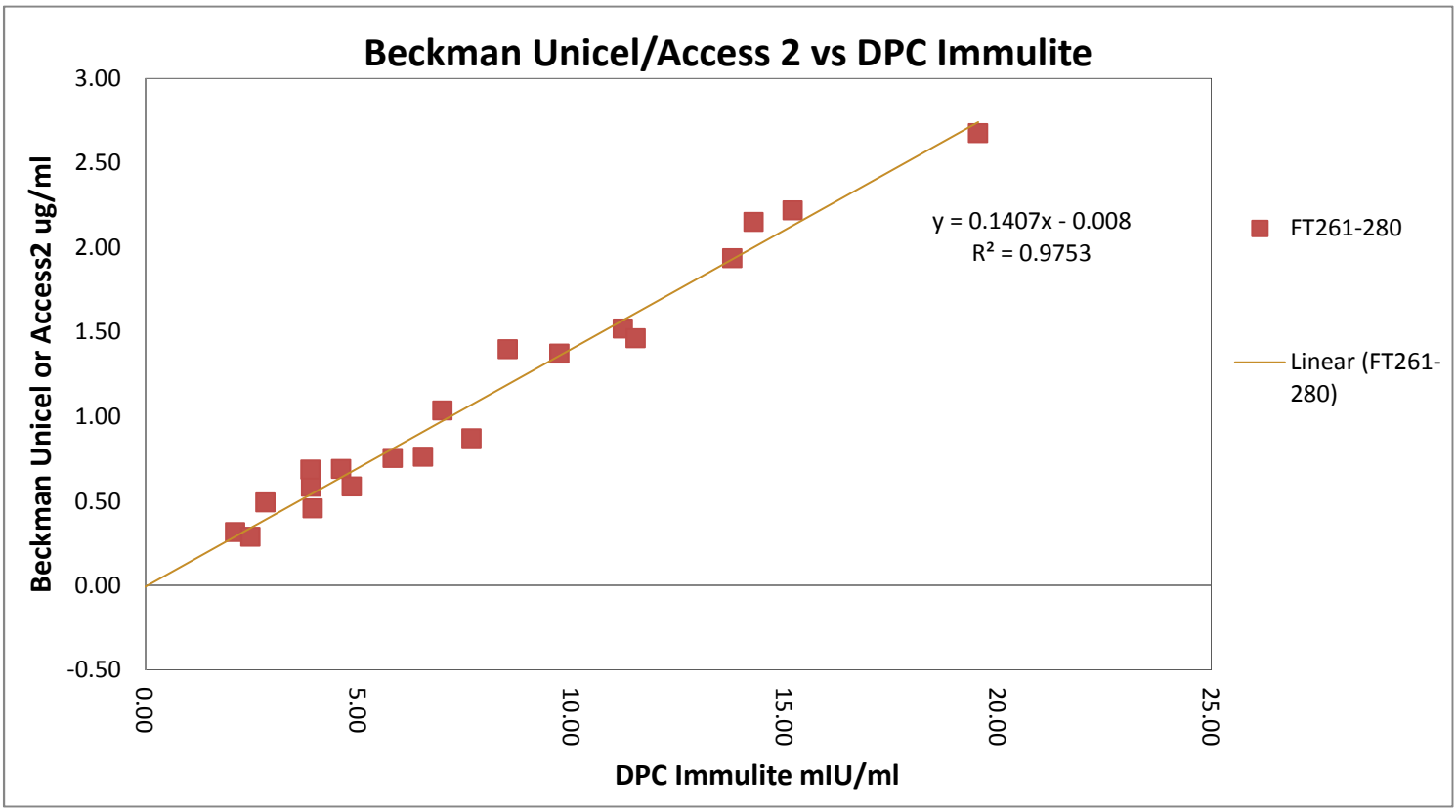
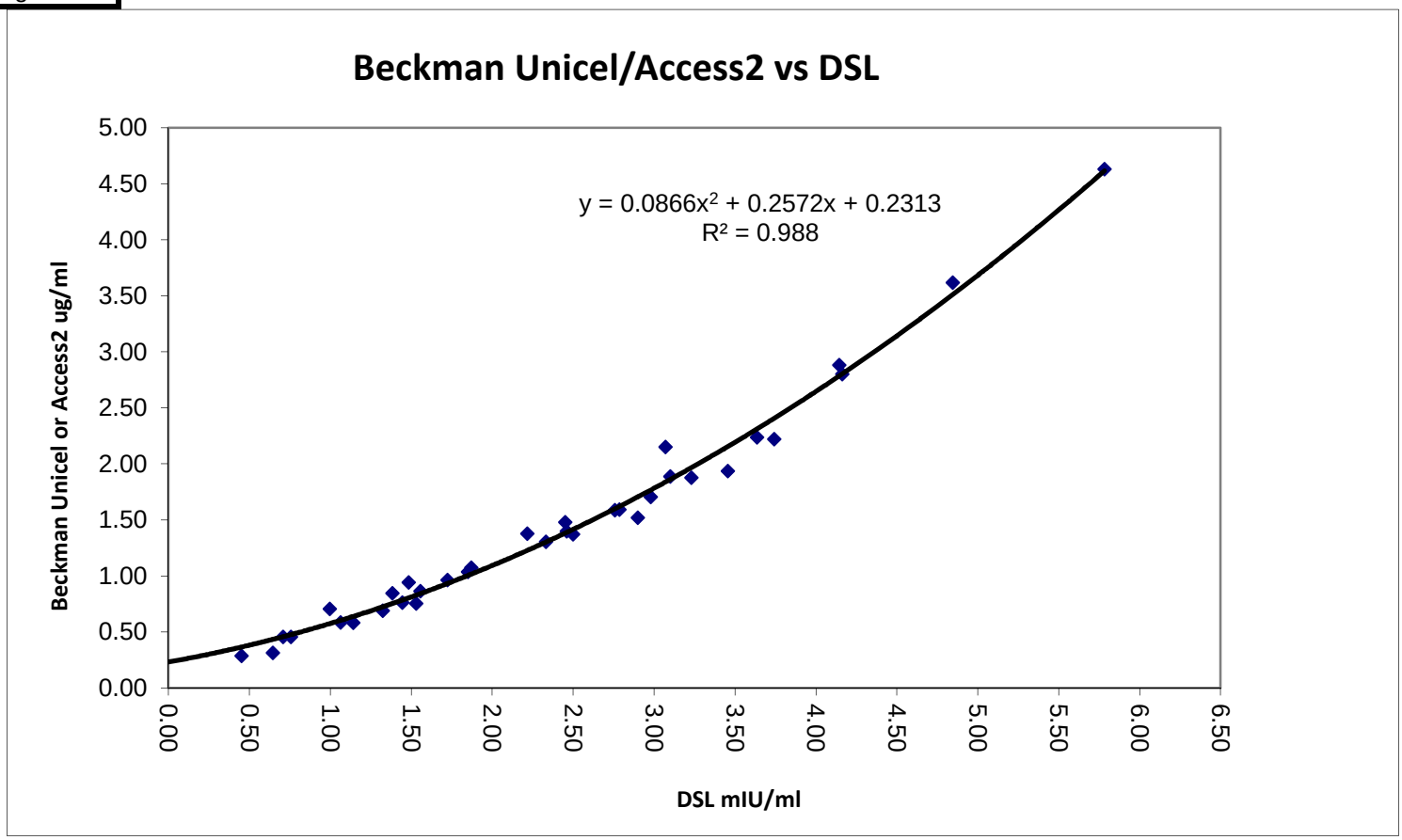


Fig. 15B



New York State Fetal Defect Markers Proficiency Test, FEDM PT, January 2012

PFI __ __ __ __ (1) **Lab Name and address** _____

Date samples obtained __ __ /__ __ /__ __ **Analyzed** __ __ / __ __ / __ __ (2) _____

Due Date: **February 8, 2012** _____

_____

Analyte	**Analytical results**					Instrument code*	Reagent code*
Second Trimester Maternal Serum	Vial **MS276**	Vial **MS277**	Vial **MS278**	Vial **MS279**	Vial **MS280**		
Gestational Age (weeks)	__ __.__ (3)	__ __.__ (4)	__ __.__ (5)	__ __.__ (6)	__ __.__ (7)		
MS AFP (ng/ml)	__ __ __.__ (8)	__ __ __.__ (9)	__ __ __.__ (10)	__ __ __.__ (11)	__ __ __.__ (12)	__ __ __ (13)	__ __ __ (14)
MS AFP MoM	__ __.__ __ (15)	__ __.__ __ (16)	__ __.__ __ (17)	__ __.__ __ (18)	__ __.__ __ (19)		
MS uE3 (ng/ml)	__ __.__ __ (20)	__ __.__ __ (21)	__ __.__ __ (22)	__ __.__ __ (23)	__ __.__ __ (24)	__ __ __ (25)	__ __ __ (26)
MS uE3 MoM	__ __.__ __ (27)	__ __.__ __ (28)	__ __.__ __ (29)	__ __.__ __ (30)	__ __.__ __ (31)		
MS hCG Please Check: _Total(IU/ml)/ _freeβ (mIU/ml)	__ __ __.__ (32)	__ __ __.__ (33)	__ __ __.__ (34)	__ __ __.__ (35)	__ __ __.__ (36)	__ __ __ (37)	__ __ __ (38)
MS hCG Total or Freeβ MoM	__ __.__ __ (39)	__ __.__ __ (40)	__ __.__ __ (41)	__ __.__ __ (42)	__ __.__ __ (43)		
MS Dimeric Inhibin A (pg/ml)	__ __ __.__ (44)	__ __ __.__ (45)	__ __ __.__ (46)	__ __ __.__ (47)	__ __ __.__ (48)	__ __ __ (49)	__ __ __ (50)
MS Dimeric Inhibin A MoM	__ __.__ __ (51)	__ __.__ __ (52)	__ __.__ __ (53)	__ __.__ __ (54)	__ __.__ __ (55)		
Neural Tube Screen 1 = positive, 0 = negative	__ (56)	__ (57)	__ (58)	__ (59)	__ (60)	NTD Based on: ❑ MoM cut-off ❑ Risk cut-off	←
Trisomy 21 Screen 1 = positive, 0 = negative	__ (61)	__ (62)	__ (63)	__ (64)	__ (65)	Based on: ❑ Quad ❑ Triple	←
Trisomy 18 Screen 1 = positive, 0 = negative	__ (66)	__ (67)	__ (68)	__ (69)	__ (70)		

New York State Fetal Defect Markers Proficiency Test, FEDM PT, January 2012

Amniotic Fluid	Vial **AF276**	Vial **AF277**	Vial **AF278**	Vial **AF279**	Vial **AF280**	Instrument code*	Reagent code*
AF AFP (μg/ml)	__ __.__ 71	__ __.__ 72	__ __.__ 73	__ __.__ 74	__ __.__ 75	__ __ __ 76	__ __ __ 77
AF AFP MoM	__.__ 78	__.__ 79	__.__ 80	__.__ 81	__.__ 82		
Interpretation **1 = elevated w/ Ache indicated 0 =Normal**	83	84	85	86	87	Please indicate the Cut-off → MoM value used for interpretation	_____

***codes are on P. 4**

Risk Assessment Ratio (1:n) and Further Action	**MS276**	**MS277**	**MS278**	**MS279**	**MS280**	**Risk (MoM) Cut-off (white, Black, IDDM)**
NTD Risk (or MoM)						**White**_____ **Black**_____
R=Repeat, U=Ultrasound, A=Amnio NFA=NoFurtherAction, G=Genetic Counseling						**IDDM white**_____ **IDDM black**_____
Trisomy 21 Risk by Quad						**White**_____
R=Repeat, U=Ultrasound, A=Amnio NFA=NoFurtherAction, G=Genetic Counseling						**Black**_____ **IDDM**_____
Trisomy 21 Risk by Triple						**White**_____
R=Repeat, U=Ultrasound, A=Amnio NFA=NoFurtherAction, G=Genetic Counseling						**Black**_____ **IDDM**_____
Trisomy 18 Risk						**White**_____
R=Repeat, U=Ultrasound, A=Amnio NFA=NoFurtherAction, G=Genetic Counseling						**Black**_____ **IDDM**_____
Indicate software company used to calculate risk	_ αlpha	_ Benetech PRA		_ RMA	_other_____	

We, the undersigned, attest that the findings provided were produced in this laboratory from the analysis of proficiency test samples which were introduced into the routine workflow of the laboratory and analyzed using protocols and procedures which are (or which will be) routinely applied to **clinical** specimens. We further attest that the laboratory did not engage in any form of communication with individuals outside of our laboratory regarding the proficiency test and/or results obtained therefrom. **The laboratory director or the authorized assistant director who holds a CQ in Fetal Defect Markers must sign this form (stamps are not acceptable). If the director does not hold a CQ in this category, then the assistant director holding the appropriate CQ must sign. Do not forget to add your CQ codes; these are required for proper tracking of your results. Forms without all the required information will be returned. Failure to submit the required signatures will result in a score of zero.**

Analyst _____ **Laboratory director** _____ **CQ code**__ __ __ __ __ __

Analyst _____ **Assistant director** _____ **CQ code**__ __ __ __ __ __

(Please print and sign your names)

New York State Fetal Defect Markers Proficiency Test, FEDM PT, January 2012

Demographic Data:

Sample	Date of Birth	Race (B,W,H)	NT[1] (mm)	M. Wt (lbs)	LMP[3]	**CRL[4] (mm)**	US[2]/ Draw Date
FT 276	1/1/1984	H	1.10	140	11/8/2011	**45**	1/24/2012
FT 277	1/1/1982	A	1.24	120	11/1/2011	**53**	1/24/2012
FT 278	1/1/1983	B	1.60	160	10/25/2011	**67**	1/24/2012
FT 279	1/1/1987	W	2.90	150	11/1/2011	**53**	1/24/2012
FT 280	1/1/1991	W	1.09	125	11/4/2011	**47**	1/24/2012

[1]NT = Nuchal Translucency [2]US = Ultrasound [3]LMP = Last Menstrual Period [4]CRL = Crown Rump Length

First Trimester Maternal Serum	Vial **FT 276**	Vial **FT 277**	Vial **FT 278**	Vial **FT 279**	Vial **FT 280**	Instrument code*	Reagent code*
FT Gestational Age (weeks)	__ __.__ 88	__ __.__ 89	__ __.__ 90	__ __.__ 91	__ __.__ 92		
FT NT MoM	__.__ __ 93	__.__ __ 94	__.__ __ 95	__.__ __ 96	__.__ __ 97		
FT hCG Please Check: _Total(IU/ml)/ _freeβ (mIU/ml)	__ __ __.__ 98	__ __ __.__ 99	__ __ __.__ 100	__ __ __.__ 101	__ __ __.__ 102	__ __ __ 103	__ __ __ 104
FT hCG Total or Freeβ MoM	__ __.__ __ 105	__ __.__ __ 106	__ __.__ __ 107	__ __.__ __ 108	__ __.__ __ 109		
FT PAPP-A Please Check: _ mIU/ml _ng/ml	__ __.__ __ 110	__ __.__ __ 111	__ __.__ __ 112	__ __.__ __ 113	__ __.__ __ 114	__ __ __ 115	__ __ __ 116
FT PAPP-A MoM	__ __.__ __ 117	__ __.__ __ 118	__ __.__ __ 119	__ __.__ __ 120	__ __.__ __ 121		
FT Trisomy 21 Screen 1 = positive, 0 = negative	__ 122	__ 123	__ 124	__ 125	__ 126		
FT Trisomy 18 Screen 1 = positive, 0 = negative	__ 127	__ 128	__ 129	__ 130	__ 131		

Results will *not* be graded. Information will be used for future possible implementation.

Risk Assessment Ratio (1:n)and Further Action	**FT276**	**FT277**	**FT278**	**FT279**	**FT280**	**Risk Cut-off (white, Black, IDDM)**
Trisomy 21 Risk by First Trimester						**White**_____ **Black**_____ **IDDM**_____
R=Repeat, U=Ultrasound, A=Amnio, G=Genetic Counseling, C=CVS NFA=NoFurtherAction						
Trisomy 18 Risk by First Trimester						**White**_____ **Black**_____ **IDDM**_____
R=Repeat, U=Ultrasound, A=Amnio, G=Genetic Counseling NFA=NoFurtherAction						
Indicate software company used to calculate risk	_ αlpha	_ Benetech PRA		_ RMA	_other_____	

Instrument codes:

Abbott AxSym	ABB
Abbott Architect	ABH
Automatic (Robotic) Pipetting Station with or and Microplate Reader	APM
Bayer/Siemens Technicon Immuno-1	TNM
Siemens (Chiron) ACS-180	COS
Siemens ADVIA-Centaur	COB
Beckman Access/2	BCX
Beckman Unicel Dxl	BCU
Beckman Array	BCA
Siemens Diagnostic Dimension Rxl	DUD
Siemens Diagnostic MARK V with or and Microplate Reader	DPC
Qiagen Plato 3000 with or and Microplate Reader	QPM
Siemens Diagnostic Products Immulite	DPB
Siemens Diagnostic Products Immulite 2000	DPD
Siemens Diagnostic Products Immulite 2500	DPF
Trinity Biotech Nexgen	TBN
(DSL ELISA) with Microplate Reader	MPR
DSL Ario	DSA
DSL DSX with or and Microplate Reader	DSX
DSL Plato	DSP
UV/Vis Spectrophotometer	UVA
Gamma Counter	GAA
Rocket Immuno-Electrophoresis	RCE
P E Wallac Delfia	WAD
Analyzer/Instrument not shown, **specify on form**	ZZZ

Reagent/kit codes:

Abbott AFP Mono/Poly	AB1
Abbott AFP Mono/Mono	AB2
Abbott hCG	AB3
Abbott βhCG	AB4
Siemens (formerly Bayer)	BA1
Siemens (formerly Chiron)	CO1
Beckman Coulter	BC1
Siemens Diagnostic (Dade Behring)	DA1
Beckman Coulter, DSL ELISA (formerly Diagnostic Systems Lab EIA)	DS1
Diagnostic Systems Lab liquid RIA	DS2
Diagnostic Systems Lab solid RIA	DS3
DiaSorin-Clinical Assays	DC1
Siemens Diagnostic (DPC) Coat-A-Count	DP1
Siemens DPC Immulite, Immulite 2000 or Immulite 2500	DP5
New **Siemens DPC Immulite, Immulite 2000 or Immulite 2500 for uE3 only**	**DP6**
In-House	IH1
P E Wallac Delfia kit	PE1
Reagent/Kit not listed, **specify on form**	ZZZ

If an instrument and/or reagent you are using are not listed please provide us with the information, so that we can include it in the future. If you do not perform an assay leave the fields empty. No special codes are needed to indicate that an assay is not performed.

New York State Fetal Defect Markers Proficiency Test,
January 2012
Summary of Results

	MS 276	MS 277	MS 278	MS 279	MS 280
Gestational Age All Lab Mean:					
Mean	19.0	18.0	15.0	17.0	20.0
SD	0.00	0.00	0.00	0.00	0.00
%CV	0.0%	0.0%	0.0%	0.0%	0.0%
X+3*SD	19.0	18.0	15.0	17.0	20.0
X-3*SD	19.0	18.0	15.0	17.0	20.0
N	27	27	27	27	27

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP All Lab Mean:					
mean	57.7	157.8	16.3	39.3	159.0
SD	4.3	13.7	1.6	3.3	10.9
%CV	7.5%	8.7%	9.6%	8.3%	6.9%
mean+3SD	70.7	198.9	21.0	49.1	191.7
mean-3SD	44.7	116.7	11.6	29.5	126.3
N	27	27	27	27	26
median	56.9	155.0	16.1	39.6	157.15
mean/all kit median	1.00	0.97	0.98	0.98	0.99

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP Beckman Access (BCX/BC1) mean:					
mean	59.7	162.1	16.7	40.6	167.4
SD	4.9	18.9	2.0	3.9	16.8
%CV	8.1%	11.6%	12.0%	9.6%	10.1%
mean+3SD	74.3	218.7	22.7	52.3	217.9
mean-3SD	45.1	105.4	10.7	28.8	116.8
N	9	9	9	9	9
median	58.1	160.6	17.0	40.6	161.0
mean/all kit median	1.04	1.00	1.00	1.01	1.05

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP Beckman Unicel (BCU/BC1) mean:					
Mean	57.6	164.5	17.0	40.2	160.0
SD	4.4	7.4	1.4	2.9	11.5
%CV	7.6%	4.5%	8.3%	7.2%	7.2%
mean + 3SD	70.7	186.8	21.2	48.8	194.4
mean - 3SD	44.5	142.3	12.8	31.5	125.5
N	8	8	8	8	8
Median	57.2	166.1	17.0	40.6	161.1
mean/All kit median	1.00	1.02	1.02	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP DPC Immulite 2000 (DPD/DP5) mean:					
mean	55.7	147.4	15.3	36.7	151.8
SD	3.4	5.3	0.8	1.6	7.3
%CV	6.1%	3.6%	5.1%	4.3%	4.8%
mean+3SD	65.9	163.4	17.6	41.5	173.7
mean-3SD	45.6	131.3	12.9	31.9	129.8
N	8	8	8	8	8
median	55.6	147.0	15.1	36.5	151.5
mean/all kit median	0.97	0.91	0.92	0.91	0.95

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP MoMs All Lab Mean:					
mean	1.13	3.41	0.54	1.00	2.79
SD	0.11	0.39	0.06	0.12	0.27
%CV	9.9%	11.5%	11.9%	11.8%	9.6%
mean+3SD	1.47	4.59	0.73	1.35	3.60
mean-3SD	0.80	2.23	0.35	0.64	1.98
N	27	27	27	27	27

	MS 276	MS 277	MS 278	MS 279	MS 280
MS AFP kit average:					
mean	57.7	158.0	16.3	39.1	159.7
SD	2.0	9.3	0.9	2.1	7.8
all kit median	57.6	162.1	16.7	40.2	160.0

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 All Lab Mean:					
mean	1.36	1.19	0.36	0.71	1.39
SD	0.09	0.09	0.03	0.06	0.09
%CV	6.9%	7.5%	9.5%	8.5%	6.7%
mean+3SD	1.65	1.46	0.46	0.89	1.67
mean-3SD	1.08	0.92	0.25	0.53	1.11
N	25	26	25	25	26
mean/all kit median	1.00	0.99	1.00	1.00	0.99

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 Beckman Unicel (BCU/BC1) mean:					
Mean	1.32	1.12	0.33	0.66	1.30
SD	0.05	0.03	0.03	0.02	0.05
%CV	3.7%	3.0%	7.6%	3.0%	4.0%
mean+3SD	1.46	1.22	0.41	0.72	1.46
mean-3SD	1.17	1.02	0.26	0.60	1.14
N	8	8	8	8	8
Median	1.32	1.12	0.34	0.66	1.32
mean/all kit median	0.96	0.92	0.93	0.93	0.92

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 BeckmanAccess (BCX/BC1) mean:					
mean	1.37	1.21	0.36	0.71	1.41
SD	0.11	0.07	0.04	0.05	0.06
%CV	7.7%	5.7%	9.9%	7.4%	4.4%
mean+3SD	1.68	1.41	0.46	0.87	1.60
mean-3SD	1.05	1.00	0.25	0.55	1.22
N	9	9	9	9	9
median	1.33	1.21	0.36	0.70	1.39
mean/all kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 DPC Immulite 2000 (DPD/DP6) mean:					
Mean	1.44	1.24	0.40	0.79	1.46
SD	0.15	0.10	0.05	0.11	0.08
%CV	10.3%	8.2%	13.2%	14.6%	5.3%
mean+3SD	1.89	1.55	0.56	1.13	1.70
mean-3SD	1.00	0.94	0.24	0.44	1.23
N	9	9	9	9	9
Median	1.45	1.25	0.38	0.77	1.48
mean/All Kit Median	1.06	1.03	1.12	1.11	1.04

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 kit average:					
mean	1.38	1.19	0.36	0.72	1.39
SD	0.06	0.07	0.03	0.06	0.08
all kit median	1.37	1.21	0.36	0.71	1.41

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoMs All Lab Mean:					
Mean	0.98	1.03	0.64	0.86	0.84
SD	0.21	0.23	0.22	0.26	0.23
%CV	21.4%	22.0%	34.7%	30.3%	27.4%
X+3SD	1.61	1.71	1.31	1.64	1.54
X-3SD	0.35	0.35	-0.03	0.08	0.15
N	26	26	27	27	27
mean/All Kit Median	1.13	1.11	1.26	1.22	1.16

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoMs (BCU/BC1) Mean:					
Mean	0.85	0.86	0.50	0.68	0.68
SD	0.05	0.06	0.04	0.04	0.03
%CV	5.4%	6.6%	8.4%	6.5%	4.7%
X+3SD	0.98	1.03	0.63	0.81	0.77
X-3SD	0.71	0.69	0.37	0.55	0.58
N	8	8	8	8	8
mean/All Kit Median	0.98	0.93	0.98	0.97	0.93

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoMs (BCX/BC1) Mean:					
Mean	0.87	0.93	0.51	0.70	0.73
SD	0.09	0.09	0.07	0.07	0.06
%CV	10.5%	9.8%	12.8%	10.3%	7.6%
X+3SD	1.14	1.20	0.71	0.92	0.89
X-3SD	0.59	0.65	0.31	0.49	0.56
N	9	9	9	9	9
mean/All Kit Median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoM (DPD/DP6) Mean:					
Mean	1.21	1.29	0.84	1.11	1.05
SD	0.19	0.18	0.19	0.21	0.20
%CV	15.7%	13.9%	22.8%	18.7%	18.8%
X+3SD	1.78	1.83	1.41	1.73	1.64
X-3SD	0.64	0.75	0.26	0.49	0.46
N	9	9	9	9	9
mean/All Kit Median	1.39	1.39	1.64	1.57	1.44

	MS 276	MS 277	MS 278	MS 279	MS 280
MS uE3 MoM kit average:					
mean	0.97	1.03	0.62	0.83	0.82
SD	0.20	0.23	0.19	0.24	0.20
all kit median	0.87	0.93	0.51	0.70	0.73

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG All Lab Mean:					
mean	16.04	55.17	63.98	18.03	18.76
SD	1.77	7.39	10.55	2.04	2.15
%CV	11.0%	13.4%	16.5%	11.3%	11.4%
mean+3SD	21.4	77.3	95.6	24.1	25.2
mean-3SD	10.7	33.0	32.3	11.9	12.3
N	26	26	26	26	26
mean/all kit median	0.98	0.94	0.93	0.95	0.98

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG Beckman Access (BCX/BC1) mean:					
mean	17.0	59.7	70.9	19.2	20.3
SD	1.5	5.5	5.9	1.3	0.8
%CV	9.0%	9.3%	8.4%	6.8%	4.0%
mean+3SD	21.6	76.3	88.7	23.1	22.8
mean-3SD	12.4	43.1	53.1	15.2	17.8
N	9	9	9	9	9
median	16.9	60.4	71.1	19.1	20.4
mean/all kit median	1.03	1.02	1.03	1.01	1.06

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG Beckman Unicel (BCU/BC1) mean:					
mean	16.44	58.63	68.74	19.00	19.21
SD	1.76	4.35	7.65	1.05	2.09
%CV	10.7%	7.4%	11.1%	5.5%	10.9%
mean+3SD	21.56	76.31	88.66	23.08	22.76
mean-3SD	12.35	43.07	53.09	15.25	17.84
N	8	8	8	8	8
median	16.35	58.20	66.65	19.45	19.45
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG DPC Immulite 2000 (DPD/DP5) mean:					
mean	14.6	46.6	51.1	15.7	16.4
SD	1.3	4.0	4.7	1.6	1.3
%CV	8.7%	8.6%	9.2%	10.1%	8.0%
mean+3SD	18.3	58.6	65.2	20.4	20.4
mean-3SD	10.8	34.5	37.1	10.9	12.5
N	8	8	8	8	8
median	14.3	44.6	51.0	15.9	16.2
mean/all kit median	0.89	0.79	0.74	0.82	0.86

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG MoMs All Lab Mean:					
mean	0.87	2.59	1.60	0.77	1.12
SD	0.10	0.31	0.26	0.10	0.10
%CV	11.3%	11.8%	16.0%	12.5%	9.3%
mean+3SD	1.16	3.51	2.37	1.06	1.44
mean-3SD	0.57	1.68	0.83	0.48	0.81
N	26	26	26	26	26

	MS 276	MS 277	MS 278	MS 279	MS 280
MS hCG kit average:					
mean	16.0	55.0	63.6	17.9	18.7
SD	1.3	7.3	10.8	2.0	2.0
all kit median	16.4	58.6	68.7	19.0	19.2

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A all lab mean:					
Mean	193.43	405.28	356.34	212.24	411.84
SD	13.64	33.07	29.93	16.02	30.26
%CV	7.1%	8.2%	8.4%	7.5%	7.3%
mean + 3SD	234.4	504.5	446.1	260.3	502.6
mean- 3SD	152.5	306.1	266.5	164.2	321.1
N	25	25	25	25	25
All Lab Median	195.1	411.3	365.6	213.6	416.5
mean/all kit median	0.99	1.00	1.00	0.99	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A Beckman Access (BCX/BC1) mean:					
Mean	195.8	405.8	356.0	214.2	413.7
SD	9.8	20.7	22.1	14.9	29.9
%CV	5.0%	5.1%	6.2%	7.0%	7.2%
mean + 3SD	225.1	467.9	422.4	259.0	503.3
mean- 3SD	166.5	343.7	289.5	169.4	324.1
N	13	13	13	13	13
median	197.1	418.4	365.6	214.3	419.0
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A Beckman Unicel (BCU/BC1) mean:					
Mean	195.5	418.1	369.3	215.1	420.6
SD	14.1	33.7	25.0	14.1	20.9
%CV	7.2%	8.1%	6.8%	6.5%	5.0%
mean + 3SD	237.9	519.3	444.2	257.3	483.3
mean- 3SD	153.2	316.9	294.4	172.9	357.9
N	10	10	10	10	10
median	194.6	417.7	366.1	214.3	417.0
mean/all kit median	1.00	1.03	1.04	1.00	1.02

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A Diagnostic System Labs (DS1) Mean:					
Mean	151.5	309.4	271.3	172.6	328.4
SD	28.9	49.2	42.7	23.5	49.4
%CV	19.1%	15.9%	15.7%	13.6%	15.1%
mean + 3SD	238.0	456.9	399.3	243.2	476.7
mean- 3SD	64.9	161.9	143.3	102.0	180.0
N	3	3	3	3	3
median	161.2	332.0	277.3	177.5	344.0
mean/all kit median	0.77	0.76	0.76	0.81	0.79

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A kit average:					
mean	180.9	377.8	332.2	200.6	387.6
SD	25.5	59.5	53.1	24.3	51.4
all kit median	195.5	405.8	356.0	214.2	413.7

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	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM All Lab Mean:					
mean	1.08	2.27	1.80	1.32	2.13
SD	0.16	0.32	0.28	0.17	0.28
%CV	14.5%	13.9%	15.7%	12.8%	13.3%
mean+3SD	1.56	3.21	2.65	1.83	2.99
mean-3SD	0.61	1.32	0.95	0.82	1.28
N	26	26	26	26	26
mean/All kit median	0.98	0.99	0.98	0.99	0.99

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM Beckman Unicel (BCU/BC1) mean:					
Mean	1.14	2.40	1.90	1.41	2.26
SD	0.14	0.24	0.23	0.14	0.20
%CV	12.6%	9.9%	12.0%	10.2%	9.0%
X + 3SD	1.58	3.10	2.58	1.84	2.87
X - 3SD	0.71	1.69	1.21	0.98	1.65
N	10	10	10	10	10
Kit Median	1.08	2.28	1.81	1.34	2.18
mean/All kit median	1.04	1.04	1.03	1.06	1.05

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM Beckman Access (BCX/BC1) mean:					
Mean	1.10	2.30	1.84	1.33	2.15
SD	0.09	0.18	0.21	0.09	0.17
%CV	8.0%	8.0%	11.3%	6.5%	8.1%
X + 3SD	1.37	2.85	2.47	1.59	2.67
X - 3SD	0.84	1.75	1.22	1.07	1.63
N	13	13	13	13	13
Kit Median	1.09	2.30	1.84	1.35	2.18
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM Diagnostic System Labs (DS1) Mean:					
Mean	0.81	1.70	1.32	1.01	1.67
SD	0.19	0.47	0.33	0.20	0.48
%CV	23.0%	27.4%	24.8%	19.8%	29.1%
X + 3SD	1.36	3.10	2.30	1.61	3.12
X - 3SD	0.25	0.30	0.34	0.41	0.21
N	3	3	3	3	3
Kit Median	0.72	1.56	1.27	1.00	1.51
mean/All kit median	0.73	0.74	0.72	0.76	0.78

	MS 276	MS 277	MS 278	MS 279	MS 280
MS Inhibin A MoM kit average:					
mean	1.0	2.1	1.7	1.3	2.0
SD	0.2	0.4	0.3	0.2	0.3
all kit median	1.1	2.3	1.8	1.3	2.1

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	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP All Lab Mean :					
mean	8.71	8.13	8.99	5.66	18.50
SD	1.28	1.24	1.13	0.98	2.28
%CV	14.7%	15.2%	12.6%	17.2%	12.3%
mean+3SD	12.6	11.8	12.4	8.6	25.3
mean-3SD	4.9	4.4	5.6	2.7	11.7
N	22	22	22	22	22
All kit median	9.2	8.4	9.3	5.8	19.1
mean/All kit mean	0.95	0.97	0.97	0.97	0.97

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP Beckman Unicel (BCU/BC1) mean:					
Mean	7.5	7.1	8.2	4.8	16.9
SD	0.6	0.5	0.7	0.5	1.2
%CV	7.6%	7.6%	9.0%	10.0%	6.8%
X+3SD	13.1	11.9	13.6	8.3	28.4
X-3SD	4.4	4.2	4.4	2.9	9.8
N	7	7	7	7	7
median	7.6	7.2	8.0	4.9	17.3
mean/All kit median	0.82	0.84	0.89	0.83	0.89

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP MoMs All Lab Mean:					
mean	0.76	0.87	0.54	0.74	2.90
SD	0.10	0.12	0.08	0.12	0.33
%CV	13.3%	14.4%	14.5%	15.9%	11.3%
mean+3SD	1.06	1.24	0.77	1.09	3.89
mean-3SD	0.46	0.49	0.30	0.39	1.91
N	22	22	22	22	21

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP Beckman Access (BCX/BC1) mean:					
mean	8.8	8.0	9.0	5.6	19.1
SD	1.5	1.3	1.5	0.9	3.1
%CV	16.7%	16.0%	16.9%	16.2%	16.2%
mean+3SD	13.1	11.9	13.6	8.3	28.4
mean-3SD	4.4	4.2	4.4	2.9	9.8
N	7	7	7	7	7
median	8.5	8	9.3	5.7	19
mean/all kit median	0.95	0.95	0.97	0.96	1.00

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP DPC Immulite 2000 (DPD/DP5) mean:					
mean	9.7	8.8	9.5	6.1	19.0
SD	0.7	0.7	0.6	0.4	1.8
%CV	7.3%	7.5%	6.1%	7.3%	9.7%
mean+3SD	11.8	10.8	11.2	7.4	24.5
mean-3SD	7.5	6.8	7.8	4.7	13.5
N	5	5	5	5	5
median	9.4	8.7	9.5	5.9	18.4
mean/all kit median	1.05	1.05	1.03	1.04	1.00

	AF 276	AF 277	AF 278	AF 279	AF 280
AF AFP Abbott Axsym (ABB/AB2) mear:					
mean	10.1	10.1	10.2	7.6	20.3
N	2	2	2	2	2
mean/all kit median	1.09	1.20	1.10	1.29	1.07
AF AFP kit average:					
mean	9.0	8.5	9.2	6.0	18.8
SD	1.1	1.3	0.8	1.1	1.4
all kit median	9.2	8.4	9.3	5.8	19.1

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	FT276	FT277	FT278	FT279	FT280
FT Gestational Age All Lab Mean:					
Mean	11.2	11.9	13.0	11.9	11.4
SD	0.13	0.11	0.05	0.11	0.10
%CV	1.2%	0.9%	0.4%	0.9%	0.8%
mean+3*SD	11.6	12.2	13.1	12.2	11.7
mean-3*SD	10.8	11.6	12.8	11.6	11.1
N	17	17	17	17	17

	FT276	FT277	FT278	FT279	FT280
FT NT MoMs All Lab Mean:					
Mean	0.96	0.93	0.98	2.20	0.91
SD	0.07	0.07	0.06	0.17	0.06
%CV	7.0%	7.6%	5.8%	7.7%	6.8%
X+3SD	1.16	1.14	1.15	2.71	1.10
X- 3SD	0.76	0.72	0.81	1.69	0.73
N	16	16	16	16	16
All Median	0.97	0.92	0.98	2.14	0.90

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	FT276	FT277	FT278	FT279	FT280
FT hCG All Lab Mean:					
mean	55.10	51.91	48.09	121.63	41.11
SD	7.78	10.64	6.36	25.76	6.19
%CV	14.1%	20.5%	13.2%	21.2%	15.1%
X+3SD	78.4	83.8	67.2	198.9	59.7
X-3SD	31.8	20.0	29.0	44.3	22.5
N	16	16	16	16	16
mean/All kit median	0.99	0.95	0.98	0.92	0.96

	FT276	FT277	FT278	FT279	FT280
FT hCG Beckman Unicel (BCU/BC1) mean:					
mean	55.53	54.57	49.15	131.63	42.85
SD	2.73	2.05	2.01	4.89	1.41
%CV	4.9%	3.8%	4.1%	3.7%	3.3%
X+3SD	78.06	74.10	62.22	171.64	58.63
X-3SD	43.52	45.87	43.58	109.13	31.89
N	4	3	4	4	4
median	55.00	54.60	48.95	129.65	42.70
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	FT276	FT277	FT278	FT279	FT280
FT hCG DPC Immulite 2000(DPD/DP5) mean:					
mean	46.8	44.5	40.5	87.4	33.9
SD	5.4	3.6	4.6	11.2	3.8
%CV	11.5%	8.2%	11.3%	12.8%	11.3%
X+3SD	62.9	55.4	54.2	120.8	45.5
X-3SD	30.7	33.6	26.8	53.9	22.4
N	5	5	5	5	5
median	44.6	43.1	40.0	84.1	33.3
mean/All kit median	0.84	0.82	0.82	0.66	0.79

	FT276	FT277	FT278	FT279	FT280
FT hCG Beckman Access (BCX/BC1) mean:					
mean	60.8	60.0	52.9	140.4	45.3
SD	5.8	4.7	3.1	10.4	4.5
%CV	9.5%	7.8%	5.9%	7.4%	9.8%
X+3SD	78.1	74.1	62.2	171.6	58.6
X-3SD	43.5	45.9	43.6	109.1	31.9
N	7	7	7	7	7
median	61.8	60.8	52.7	141.0	45.3
mean/All kit median	1.09	1.10	1.08	1.07	1.06

	FT276	FT277	FT278	FT279	FT280
FT hCG MoMs All Lab Mean:					
Mean	0.67	0.62	0.75	1.63	0.48
SD	0.09	0.11	0.07	0.25	0.07
%CV	12.9%	17.5%	9.5%	15.0%	14.6%
mean+3*SD	0.94	0.95	0.96	2.37	0.69
mean - 3*SD	0.41	0.30	0.54	0.90	0.27
N	15	15	15	15	15
All Median	0.69	0.63	0.77	1.62	0.47

	FT276	FT277	FT278	FT279	FT280
FT hCG kit average:					
mean	54.4	53.0	47.5	119.8	40.7
SD	7.1	7.9	6.3	28.4	6.0
all kit median	55.5	54.6	49.2	131.6	42.9

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	FT276	FT277	FT278	FT279	FT280
FT PAPP-A All Lab Mean:					
Mean	920.45	1471.23	2749.12	458.71	620.11
SD	115.21	142.85	298.12	51.61	75.65
%CV	12.5%	9.7%	10.8%	11.3%	12.2%
mean + 3SD	1266.08	1899.78	3643.47	613.53	847.07
mean- 3SD	574.82	1042.67	1854.77	303.89	393.15
N	14	14	14	14	14
All Lab Median	895.60	1476.20	2760.00	476.64	646.03
mean/All kit median	1.03	1.01	1.00	0.99	1.05

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A DPC Immullite 2000 (DPD/DP5) Mean:					
Mean	1069.29	1610.05	2740.34	388.77	537.45
SD	101.91	73.11	296.58	36.80	22.61
%CV	9.5%	4.5%	10.8%	9.5%	4.2%
X + 3SD	1375.03	1829.38	3630.09	499.17	605.29
X - 3SD	763.56	1390.72	1850.59	278.38	469.60
N	3	3	3	3	3
Kit Median	1111.97	1652.26	2904.49	405.66	528.07
mean/All kit median	1.20	1.10	1.00	0.84	0.91

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A Beckman Unicel(BCU/BC1) Mean:					
Mean	870.43	1461.58	2674.82	490.73	685.10
SD	58.84	96.31	156.60	27.67	25.73
%CV	6.8%	6.6%	5.9%	5.6%	3.8%
X + 3SD	1046.96	1750.53	3144.61	573.75	762.29
X - 3SD	693.91	1172.64	2205.03	407.72	607.91
N	6	6	6	6	6
Kit Median	892.6	1470.2	2723.4	496.5	677.3
mean/All kit median	0.98	1.00	0.98	1.06	1.16

	FT276	FT277	FT278	FT279	FT280
***FT PAPP-A Diagnostic Systems Lab (DS1) Mean:**					
Mean	891.16	1399.50	2843.55	462.25	591.71
SD	110.35	176.15	441.27	42.42	71.06
%CV	12.4%	12.6%	15.5%	9.2%	12.0%
X + 3SD	2.26	3.24	5.55	1.06	1.53
X - 3SD	1.02	1.70	2.83	0.38	0.54
N	5	5	5	5	5
Kit Median	891.45	1394.92	3059.98	480.69	601.24
mean/All kit median	1.00	0.96	1.04	1.00	1.00

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A kit average:					
mean	943.63	1490.38	2752.90	447.25	604.75
SD	109.32	108.19	85.07	52.61	74.69
all kit median	891.16	1461.58	2740.34	462.25	591.71

***Note: The above 2 tables contain converted values (mIU/ml->ng/ml) from equations obtained based on in house correlation data.**
(see critique)

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	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM All Lab Mean:					
Mean	1.93	2.10	2.79	0.74	1.00
SD	1.09	1.29	1.61	0.32	0.43
%CV	56.6%	61.3%	57.8%	44.0%	42.5%
mean + 3SD	5.19	5.97	7.62	1.70	2.28
mean- 3SD	-1.34	-1.77	-2.05	-0.23	-0.28
N	14	14	14	14	14
All Lab Median	1.49	1.64	2.34	0.67	0.90
mean/ All kit median	1.35	1.34	1.25	1.10	1.09

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM DPC Immulite 2000 (DPD/DP5) Mean:					
Mean	3.88	4.40	5.40	1.28	1.71
SD	0.37	0.65	1.37	0.12	0.10
%CV	9.7%	14.7%	25.4%	9.0%	5.6%
X + 3SD	5.00	6.34	9.52	1.63	2.00
X - 3SD	2.75	2.45	1.28	0.94	1.42
N	3	3	3	3	3
mean/All kit median	2.72	2.80	2.43	1.92	1.86

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM Beckman Unicel(BCU/BC1) Mean:					
Mean	1.43	1.57	2.22	0.67	0.92
SD	0.21	0.17	0.50	0.06	0.14
%CV	14.4%	10.7%	22.7%	8.5%	14.9%
X + 3SD	2.04	2.08	3.73	0.84	1.33
X - 3SD	0.81	1.07	0.71	0.50	0.51
N	6	6	6	6	6
Kit Median	1.39	1.56	2.16	0.67	0.91
mean/All kit median	1.00	1.00	1.00	1.00	1.00

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM Diagnostic System Labs (DS1) Mean:					
Mean	1.42	1.46	2.15	0.53	0.73
SD	0.31	0.29	0.57	0.12	0.17
%CV	22.0%	19.7%	26.7%	23.6%	23.5%
X + 3SD	2.35	2.33	3.87	0.90	1.25
X - 3SD	0.48	0.60	0.43	0.15	0.21
N	4	4	4	4	4
Kit Median	1.39	1.51	2.25	0.51	0.72
mean/ All kit median	0.99	0.93	0.97	0.79	0.79

	FT276	FT277	FT278	FT279	FT280
FT PAPP-A MoM kit average:					
mean	2.24	2.48	3.26	0.83	1.12
SD	1.42	1.66	1.86	0.40	0.52
all kit median	1.43	1.57	2.22	0.67	0.92