From: Surekha Gangakhedkar <surekhag@theranos.com>
Sent: Monday, May 10, 2010 11:11 AM
To: Victoria Sung <VSung@celgene.com>
Cc: Gary Frenzel <gfrenzel@theranos.com>
Subject: RE: Thank you
Attach: CONFIDENTIAL - Theranos Celgene Assay Update May 7 2010.pdf

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Hi Vicki,

We believe that the Friday meeting was very productive. Here is a copy of the Presentation. Please note that all the information is Theranos Confidential. We are looking forward to hearing back from you on the items noted below.

Best regards,
Surekha

Surekha Gangakhedkar
Team Manager, Assay System
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Palo Alto, CA 94304
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From: Victoria Sung [mailto:VSung@celgene.com]
Sent: Friday, May 07, 2010 5:31 PM
To: Gary Frenzel; Surekha Gangakhedkar; Daniel Young
Cc: Elizabeth Holmes
Subject: Thank you

Thank you all for your time this morning; we felt that our meeting was very productive and informative! We will be following up on a number of items we discussed earlier today:

1) Finalize the complete list of analytes to be assayed (Parts 1 and 2)
- Testosterone vs. DHT vs. DHEA?
- Estrogen vs. estradiol (Theranos only developing estradiol assay)?
- FGF23: intact vs. cleaved?
- EPO: do we want to exclude recognition of recombinant EPO (only detect endogenous EPO)?
- IGF: current assay detects only IGF bound to IGF-BP3 (not 1/2)?

2) Part 1: planning to use Theranos technology to assay PK, ADA **plus** Hgb, Vitamin D, FSH, sex steroids, PTH (validate these PD markers by comparing vs. ACM-generated data)
- Can we amend protocol to reflect that PD markers may be measured in Part 1 (i.e. extra blood draw in a pediatric tube for Theranos assays)
- Will part 1 sites be ok with loading multiple machines to look at PD markers (in addition to PK and ADA)?

3) For Theranos: testosterone to develop the assays (they are still waiting for a license to purchase steroids), Epogen or

Procrit to test if their assay recognizes recombinant protein, ACE-011 plus mouse/goat serum for ADA assay development (if possible, serum from monkey treated with ACE-011), the opportunity to "validate" their PD assay controls at ACM (Sharianne to arrange for work order with ACM).

4) We will also find out who should be on the user list for access to the web portal (blinded or unblinded) and also a list of patient ID# to pre-program into the machines for Part 1.

5) Amend 3-way NDA (Celgene/Theranos/Ron Bowsher) to expand scope of discussion to validation of PD biomarkers and data.

If there are other questions not included above, please feel free to e-mail me. In the meantime, would you please send me your presentation from this morning and also let me know when I should expect the validation reports to start trickling in? Do you think that it would be valuable to set a teleconference for later this month to address the above issues and anything else that develops between now and then?

Have a good weekend!
Vicki

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Celgene panel: Assay development update

May 7th, 2010

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Targeted Celgene Panels

Panel for part 1

	Analyte
1	ACE-011 PK
2	anti-ACE-011 antibody
3	Hgb
4	EPO
5	PTH
6	Vit D
7	FSH
8	LH
9	Estradiol
10	DHT
11	Testosterone

Panel for part 2

	Analyte		Analyte
1	ACE-011 PK	12	Hepcidin
2	anti-ACE-011 antibody	13	BSAP
3	Hgb	14	CTX
4	EPO	15	NTX
5	PTH	16	Trap5b
6	Vit D	17	Osteocalcin
7	FSH	18	P1NP
8	LH	19	P1CP
9	Estradiol	20	FGF-23
10	DHT	21	IGF-1
11	Testosterone		

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Assay Development Process

	Experiment	Information desired
1	MTP screen	Summary information of antibody screens, 4 point curves
2	Conjugation Type: SH or NH2	Compare SH vs. NH2 conjugations (For assays with limited antibodies to screen)
3	Cross reactivity	For 4 best Ab. Pairs:Test cross reactivity with related analytes, 6 point standard curves
4	Interference	For 4 best Ab. Pairs:Test interference with related analytes, 6 point standard curves
5	Epitope map	For 4 best Ab. Pairs
6	Theranos screen	For 3 best Ab. Pairs: Summary information for 6 point curves in A.B, whole blood and plasma
7	Training set	For 1 Ab. Pair correlation of N=10 clinical samples spanning the assay range range
	Antibody Pair finalized	*Based on the best dose response and % recovery of above experiments*
8	Plasma Screen	Screen normal plasma to see ranges
9	Whole Blood Screen	Screen normal blood to see ranges.
10	Capture titration	Show table with selected level and higher/lower levels
11	Detection titration	Show table with selected level and higher/lower levels
12	Detection Stabilizer	Biostab vs. Stabilzyme
13	Effect of Buffer	Test various blocking buffers during coating, Assay buffer compositions
14	Effect of Incubation time	Compare different incubation times
15	Edison protocol optimization	Different diliution effects, impact of PSW
16	% CV	Mid range analyte on 24 instruments
17	Precision tests	3 lot inter and intra assay results with standard curve, 3 cartridges per lot
18	Calibrator comparison	Run our controls on reference kit and vice versa, calibrate with WHO standards
19	Dilution linearity	Serial dilution of high samples in buffer and sera
20	Whole blood spike recovery	Spike into blood with known (low) endogenous level at 8 point curve
21	Hematocrit effect	Plasma from spiked blood tested, plot W.B vs. plasma
22	Plasma spike recovery	Spike into plasma with known (low) endogenous level at 8 point curve
23	LLOQ/ULOQ	Use 2x above ULOQ and below LLOQ to define assay limits
24	Selectivity	Spike into W.B at 3 levels over endogenous to calculate recovery
25	Stability	CAB, DAB stability, Reference tips in some cases, with a 4-point standard curve
26	Matrix effects	Spike recovery in hemolysed or lipemic samples for 6 spike levels
27	Extended range	Test linearity and dose reposnse of standard curve at 4x of ULOQ
28	Clinical samples	N=20, spanning the range to show correlation with kit

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ACE-011 update

- Acceleron-QPS assay range: 8 – 400 ng/mL
- Competitive ELISA
- Theranos assay range: 40 – 4000 ng/mL
- Both Sandwich and Competitive ELISA formats were evaluated
- Competitive assay was selected for Theranos assay as well
- Assay reagents for Theranos assay similar to used by QPS except the label is Alkaline Phosphatase.

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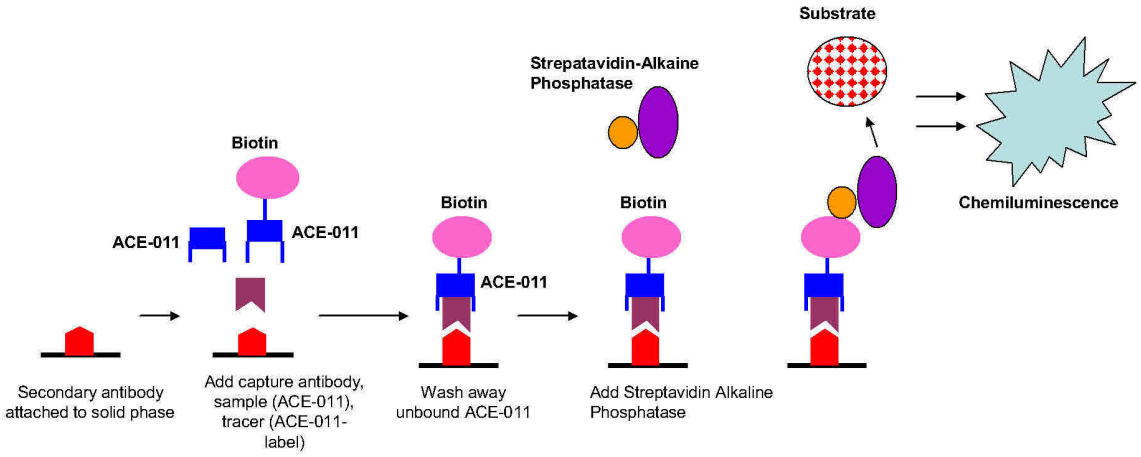
Representation of QPS ACE-011 assay



CEL-0007124

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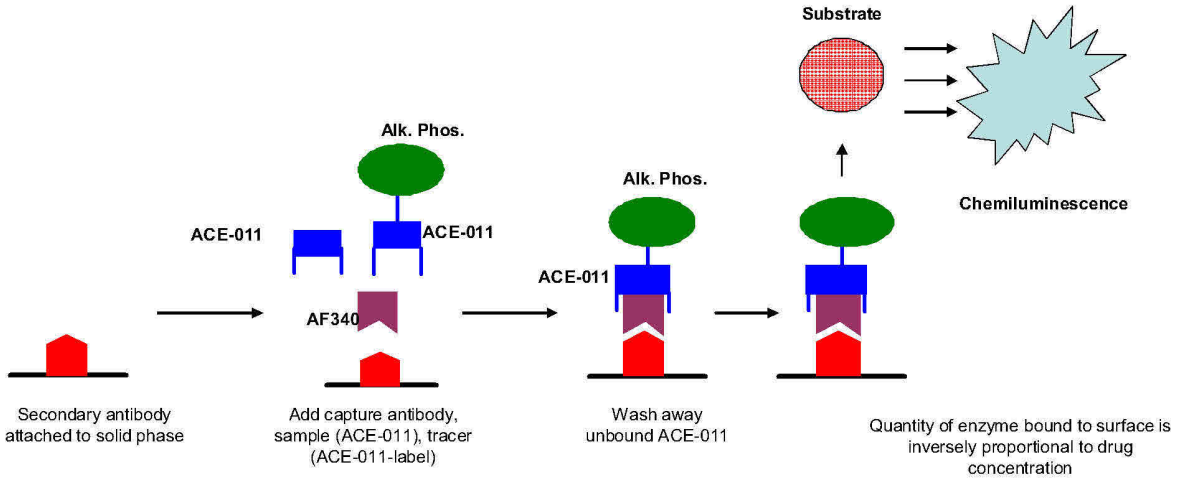
Representation of Theranos ACE-011 assay



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ACE-011: Precision test data

- Pooled serum 8- point standard curve
- 5 QC levels that were within the range of the assay
- QC levels generated by spiking ACE-011 into pooled serum
- 3 cartridges per day, duplicate data points for each cartridge. 2 days total.
- Back calculated concentrations of the QC levels obtained from standard curve.

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ACE-011 Precision test: Standard curve data

AVERAGE CONC. FOR EACH CARTRIDGE										
Conc.	Day 1			Day 2						
ng/mL	1	2	3	4	5	6	Average	Stdev	%CV	% Recovery
8000	8066	8484	8545	7551	7300	8171	8019	501	6	100
4000	3973	4059	4299	3754	3624	3833	3924	240	6	98
1200	1445	1391	1351	1258	1131	1054	1272	154	12	106
400	411	365	447	331	335	325	369	50	13	92
80	71	80	71	64	61	69	69	6	9	87
40	52	45	51	51	53	49	50	3	5	125
20	16	17	22	21	18	17	19	3	14	93
0										

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ACE-011 Precision test: QC levels data

	AVERAGE CONC. FOR EACH CARTRIDGE										
	Conc.	Day 1			Day 2						
	ng/mL	1	2	3	4	5	6	Average	Stdev	%CV	% Recovery
ULOQ	4000	4639	4637	4485	3668	3599	3598	4104	532	13	103
QCH	2000	2247	2383	2580	2498	2133	2265	2351	168	7	118
QCM	600	580	695	628	585	697	662	641	52	8	107
QCL	160	151	146	154	166	147	145	152	8	5	95
LLOQ	40	52	45	51	51	53	49	50	3	5	125

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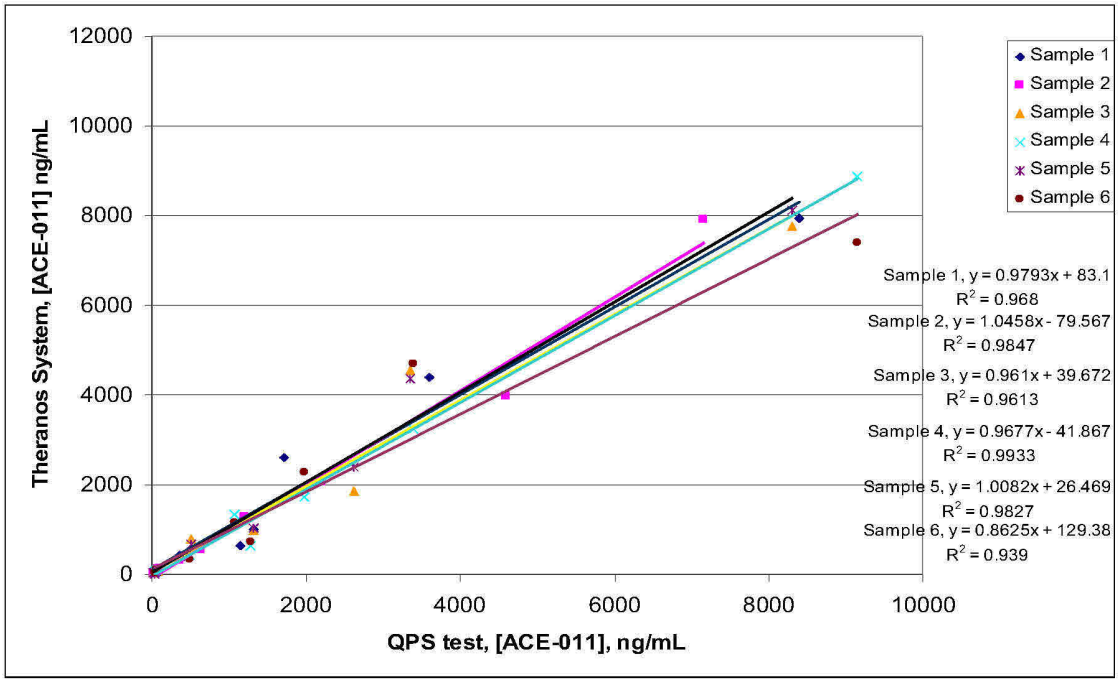
ACE-011
Comparison of whole blood spike of N=6 samples to QPS system



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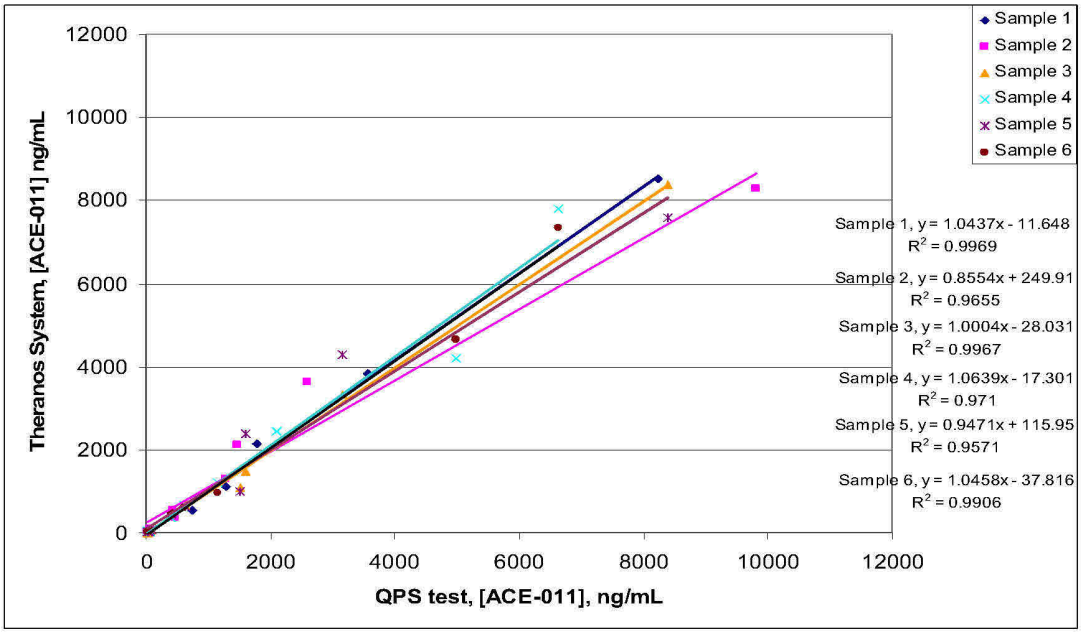
ACE-011
Comparison of plasma from spiked whole blood of N=6 samples to QPS system



CEL-0007130

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2. Bone specific Alkaline Phosphatase

• **Bone AP Clinical Range:**
Normal Female (≥25)=11.6 – 42.7 U/L
Normal Female (≥25)=15 – 41.3 U/L
Paget's Disease of Bone: Median 199.6 U/L
Osteomalacia: Mean 61.7 U/L
Osteoporosis (no anti-resorptives s): 6 – 25.9 U/L
Osteoporosis (On anti-resorptives): 4 – 17.9 U/L
• **Theranos Assay Range:** 200 – 3.125 U/L
• **Theranos Reference Assay 1 :** MicroVue BAP Kit. Vendor: Quidel, Range: 140 – 2U/L
• **Theranos Reference Assay 2:** Ostase BAP Kit. Vendor: IDS, Range: 90 – 7ug/L

Please note that the Theranos assay and the reference assays are direct assays that use capture only, no detection conjugate. All three assays use the activity of the analyte itself.

	Antibody	SH- Conj	NH2- Conj
Capture Ab	#1		
	#2		
	#3		
	#4		
	#5		
	#6		
	#7		
	#8		
	#9	N/A	
	#10	N/A	

Number of Capture antibodies tested: 10
Number of Detection antibodies tested: 0
Total Number of conjugates tested: 18

No Response
Poor response but potential
Modulation but background or other problem
Modulation, good candidate pair
Modulation, good candidate pair

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BSAP: Interference Testing

For interference testing, the stated level of secondary substances was spiked into a six point standard bone AP curve and the resulting solutions tested against a standard control curve.

Substance Tested	Level Tested	Avg %Recovery of BAP	Interference?
Alendronate	50ug/mL	85	No
Estradiol	100ug/mL	92	No
Acetaminophen	350ug/mL	88	No
TRAP 5b	31.8 U/L	94	No
Ace-011	24,000ng/mL	87	No
Liver Alkaline Phosphatase	400 U/L	93	Yes at BAP Levels 3.125 U/L and below
Intestinal Alkaline Phoshatase	1000 U/L	96	Yes at 12.5 U/L and below

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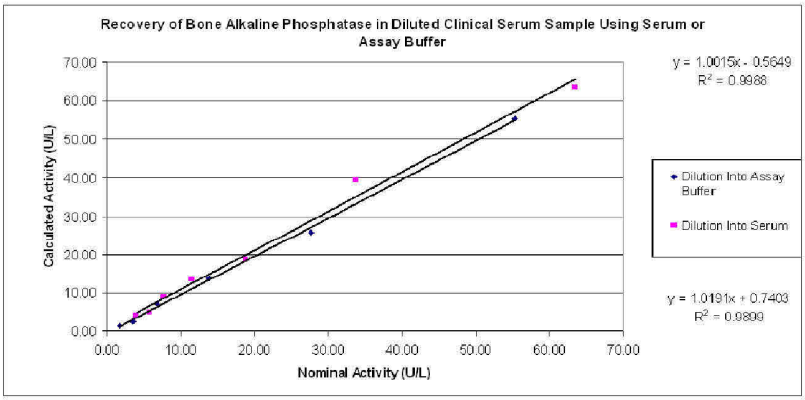
BSAP: Dilution Linearity: Serum and Buffer

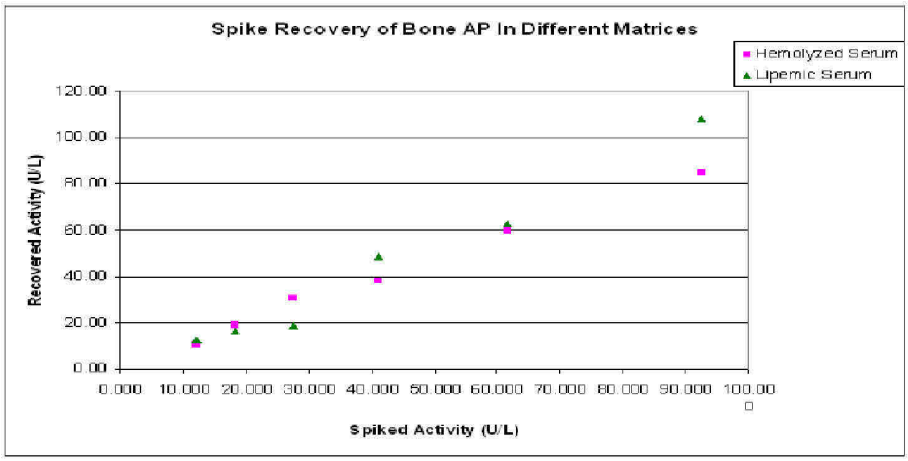


Summary of Results for Dilution Linearity Diluting Clinical Serum #26

Dilution Matrix	Dilution	Calculated [BAP] U/L	% Recovery
Assay Buffer	None	55.33	[100]
	2X	25.86	93
	4X	13.72	99
	8X	6.96	101
	16X	2.52	73
	32X	1.33	77
Serum	None	63.54	[100]
	2X	39.47	117
	4X	18.63	99
	8X	13.56	119
	16X	8.77	114
	32X	4.97	86

BSAP: Matrix Effects

Matrix=>	Hemolyzed Serum	Lipemic Serum
Activity (U/L) Spiked	%Recovery	%Recovery
92.500	92	117
61.667	96	101
41.111	92	118
27.407	111	67
18.272	103	90
12.181	88	102
Avg% Recovery	97	99



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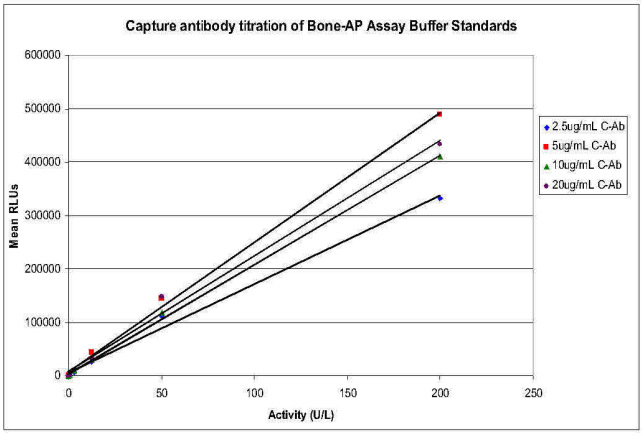
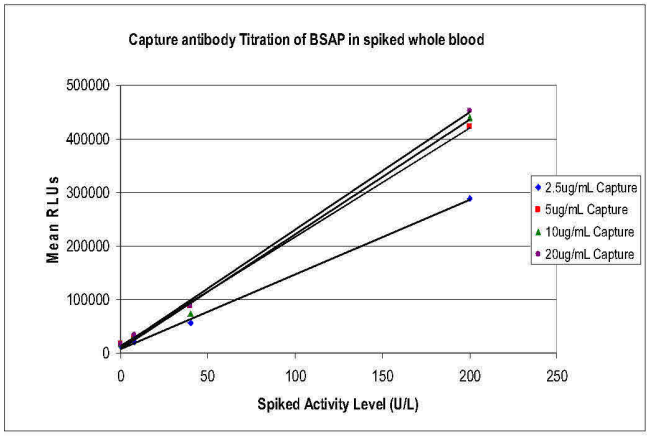
BSAP: Capture antibody Titration





Capture antibody Titration: Assay Buffer Standards

Capture Concentration (ug/mL)	2.5	5	10	20
Std 1/6	1703	2399	2006	2083
Std 5/6	10.18	14.27	11.20	11.16
Average Ratio	4.94	5.83	5.18	5.26
Avg % Signal CV	11.7	12.6	12.8	10.1
Avg % Conc CV	9.32	13.38	10.94	7.96
LOD in Sample (U/L)	0.53	0.49	0.35	0.30
Avg% Recovery	114	95	101	112

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3. EPO

- **Clinical sample ranges:**
- Normal subjects: EPO varies from 3 -16 mU/mL.
- Subjects with anemia: Aplastic anemia, hemolytic anemia and anemia due to iron deficiency all result in serum EPO elevation. The normal kidney's response to anemia is that when Hct levels fall <20% EPO levels increase normal, at times as high 50-500 mU/mL. There is an inverse relationship between the hematocrit level and EPO.
- RA, inflammation patients: 20-200 mU/mL
- Patients with CKD/ESRD: Anemia is a common side effect in these patients. In these patients the kidney does not have a normal response to anemia. Hence the levels are close or lower than normal.
- Leukemia patients: Anemia is a common condition in these patients as a result of chemotherapy. High levels of EPo are seen in patients after successive rounds of chemotherapy (~200 mU/mL).

- **Theranos assay range:**
- Spiked plasma/serum calibrators: 12 point curve: 250-1.25 mU/mL.
- Assay will be calibrated against NIBSC International standard 87/684 (recombinant hEPO).

- **Reference Commercial ELISA: R&D Quantikine IVD human EPO ELISA**

Reported sensitivity: 0.6 mU/mL , time: Benchtop protocol 4h 45' Sample volume per well 100 uL

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EPO: Antibody screen summary

Capture Ab	Detection Ab #1	#2	#3	#4	#5	#6	#7	# 8	# 9	#10	#11	#12	#13	#14	# 15	#16	# 17	# 18
#1																		
#2																		
#3																		
#4																		
#5																		
#6																		
#7																		
#8																		
#9																		
#10																		
#11																		
#12																		
#13																		
#14																		
#15																		
#16																		
#17																		
#18																		

EPO: Antibody pair cross reactivity

Ab pair 1

Cross reactivity Test analyte	1250-4.88 pg/mL		5000-5 pg/mL		1000-1 pg/mL		750-0.5 pg/ml		1000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL	
EPO Standard Curve(Control)	IL-4		IL-8		IL-6		IL1-beta		IFN-gamma		IGF-I		IGF-II		TNF-alpha	
Nominal mU/mL	Calc. (mU/mL)	%recovery	Calc.(mU/mL)	% Cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity
250	245	98	1.37	1	1.05	0	0.68	0	0.38	0	2.40	1	2.09	1	1.72	1	0.87	1
100	105	105	1.14	1	1.09	1	0.92	1	0.83	1	2.21	2	1.98	2	1.50	1	1.52	1
50	50	101	1.75	3	1.46	3	0.89	2	0.97	2	3.48	7	2.38	5	1.95	4	1.62	2
20	19	95	1.93	10	1.45	7	1.04	5	1.03	5	2.64	13	2.36	12	2.12	11	1.78	2
5	5	102	1.98	40	1.62	32	1.30	26	1.20	24	4.03	81	2.65	53	2.45	49	1.88	2

Ab pair 2

Cross reactivity Test analyte	1250-4.88 pg/mL		5000-5 pg/mL		1000-1 pg/mL		750-0.5 pg/ml		1000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL	
EPO Standard Curve(Control)	IL-4		IL-8		IL-6		IL1-beta		IFN-gamma		IGF-I		IGF-II		TNF-alpha	
Nominal mU/mL	Calc. (mU/mL)	%recovery	Calc.(mU/mL)	% Cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity
250	245	98	0.00	0.00	0.00	0.00	0.02	0.01	0.17	0.07	0.68	0.69	0.08	0.03	0.16	0.06	6.13	2.45
100	96	96	0.00	0.00	0.05	0.05	0.18	0.18	2.11	2.11	0.36	0.38	0.12	0.12	1.43	1.43	2.60	2.60
50	52	104	0.00	0.00	0.00	0.01	0.01	0.01	0.07	0.13	0.01	0.01	0.01	0.02	0.06	0.12	1.32	2.65
20	18	92	0.00	0.00	0.01	0.05	0.11	0.53	2.04	10.22	0.92	1.00	0.01	0.03	0.04	0.21	2.03	10.16
5	5	101	0.00	0.03	0.01	0.21	0.08	1.52	0.18	3.51	0.00	0.00	0.00	0.00	0.00	0.03	0.39	7.76

Ab pair 3

Cross reactivity Test analyte	1250-4.88 pg/mL		5000-5 pg/mL		1000-1 pg/mL		750-0.5 pg/ml		1000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL	
EPO Standard Curve(Control)	IL-4		IL-8		IL-6		IL1-beta		IFN-gamma		IGF-I		IGF-II		TNF-alpha	
Nominal mU/mL	Calc. (mU/mL)	%recovery	Calc.(mU/mL)	% Cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity
250	250	100	8	3	1	1	1	0	0	0	7	7	6	2	4	2	1	0
100	101	101	6	6	2	2	1	1	1	1	6	6	5	5	3	3	3	3
50	49	98	3	7	3	6	1	2	1	2	13	14	7	15	5	10	4	7
20	20	102	3	17	3	15	1	7	1	7	9	9	7	36	6	30	4	22
5	5	99	4	84	4	72	2	46	2	39	16	16	9	176	8	154	4	78

Ab pair 4

Cross reactivity Test analyte	1250-4.88 pg/mL		5000-5 pg/mL		1000-1 pg/mL		750-0.5 pg/ml		1000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL		6000-5 pg/mL	
EPO Standard Curve(Control)	IL-4		IL-8		IL-6		IL1-beta		IFN-gamma		IGF-I		IGF-II		TNF-alpha	
Nominal mU/mL	Calc. (mU/mL)	%recovery	Calc.(mU/mL)	% Cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-rea	Calc. (mU/mL)	%cross-reactivity	Calc. (mU/mL)	%cross-reactivity
250	245	98	1.84	1	1.74	1	1.97	1	2.19	1	1.47	1	1.67	1	1.68	1	2.42	2
100	97	97	1.60	2	1.93	2	2.80	3	2.21	2	1.70	2	1.53	2	1.64	2	1.88	2
50	58	116	1.94	4	2.43	5	1.92	4	1.90	4	1.60	3	1.74	3	1.54	3	1.56	1
20	17.1	85	1.54	8	1.44	7	2.41	12	2.25	11	1.77	9	1.52	8	1.83	9	1.69	2
5	5.3	106	1.43	29	1.86	37	2.28	46	2.01	40	1.45	29	1.51	30	1.97	39	1.90	2

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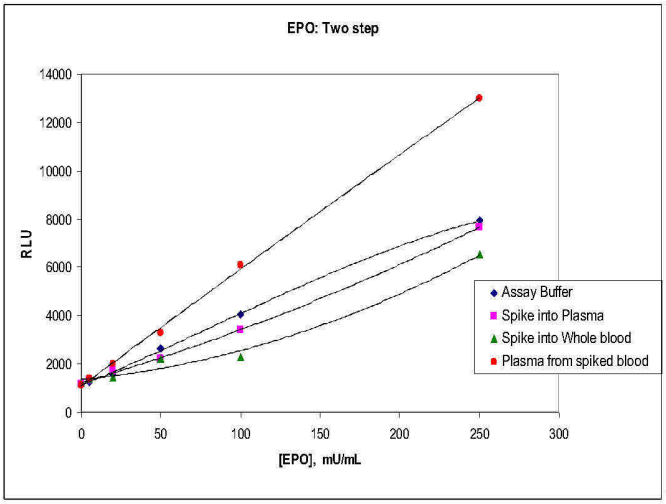
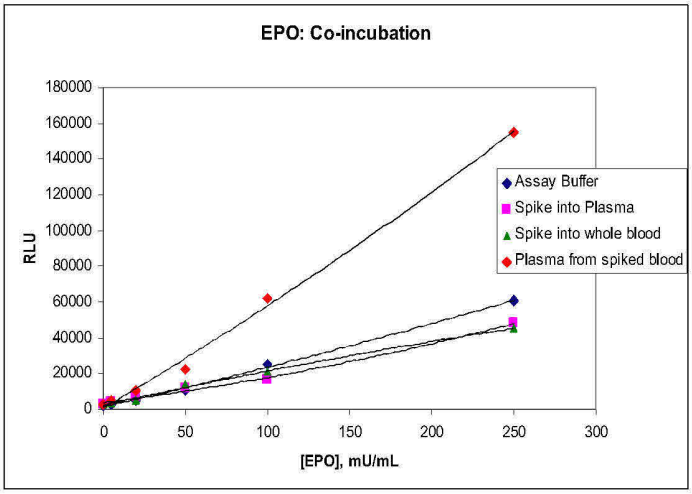
EPO: Assay Optimization





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4. Estradiol

- Males: 8 - 43 pg/ml
- Females:
  - Follicular Phase 13 - 166 pg/ml
  - Ovulation Phase 86 - 498 pg/ml
  - Luteal Phase 45 - 211 pg/ml
  - Postmenopause: <5.0 - 54 pg/ml
  - Pregnant 1st trimester 38 - 3175 pg/ml
  - Pregnant 2nd trimester: 678 - 16633 pg/ml
  - Pregnant 3rd trimester: 43 - 33781 pg/ml

- Up to 99% of estradiol in the blood is bound to either SHBG or human serum albumin (HSA).
- 2 approaches are generally used to measure estradiol in light of these challenges:
  1. Displacement of estradiol from binding proteins by displacement agents
  2. Utilization of an anti-estradiol antibody with a sufficiently high affinity and/or an epitope that allows the antibody to bind to SHBG-bound and HSA-bound estradiol

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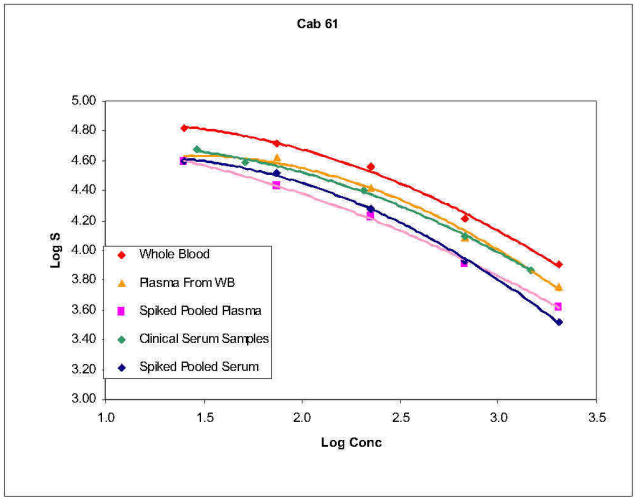
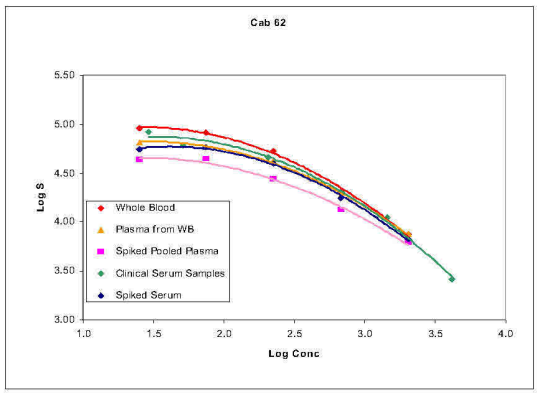
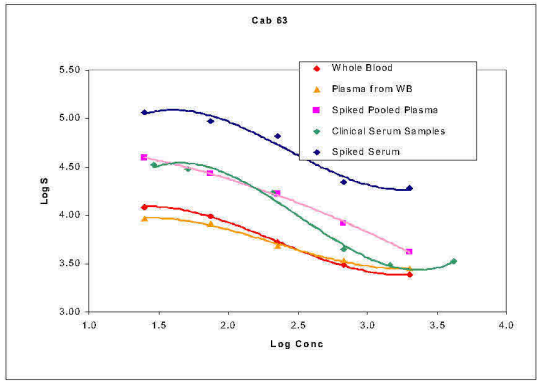
Estradiol

- 63 commercially available anti-estradiol antibodies were screened: 32 monoclonal and 2 goat polyclonal, 7 sheep polyclonal, and 22 rabbit polyclonal antibodies
- Spiked serum calibrators were used for screening
- Displacement agents including Danezol and a commercial buffer containing DHT failed to improve S/B for the low-response antibodies
- Only 3 of the antibodies yielded > 2 Signal/BG at 2000 pg/mL in a serum matrix
- The 3 final candidates were tested in the following matrixes to determine matrix effects:
  - Spiked whole blood
  - Plasma derived from spiked whole blood
  - Pooled plasma, directly spiked
  - Pooled serum, directly spiked
  - Clinical serum samples, concentration previously determined via 2 reference methods: Alpco and Invitrogen

Estradiol Matrix Screening Results







- Cab 61 showed the most parallel slopes for all matrixes tested
- Cab 63 was eliminated due to major matrix effects
- Cab 61 and Cab 62 were chosen for further testing

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Estradiol Clinical Correlation Screen

- Candidates Cab 61 and Cab 62 were tested for clinical correlation with a reference method
- 5 clinical samples from across the assay range were chosen
- Based on the low matrix effects, availability, and good clinical correlation, Capture Antibody #61 was chosen

Sample #	Sample Type	Alpco Result pg/mL	Theranos Results pg/mL	
			Cab 61	Cab 62
58	Pregnant Week 22	1455	956	1000
50	Pregnant Week 12	681	442	575
16	Menstrual Day 16	208	107	118
7	Menstrual Day 7	52	38	41
80	Post-Menopausal	29	22	4

Continued next slide

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Checkerboard Titration for Estradiol

- A checkerboard titration was performed with spiked serum calibrators to determine dilutions of CAb and Estradiol conjugate for initial tests
- Cab @ 1:25,000 and Estradiol-AP @ 1:50,000 was determined as optimal

CAb	Estradiol-AP	ɜtradiol] pg/r	Mean RLU	StDev	CV%	S/B
1:25,000	1:10,000	2031.0	15545	1467	9	9.4
		231.0	69654	9649	14	2.1
		31.0	128544	8766	7	1.1
		6.0	146240	10812	7	
1:50,000	1:10,000	2031.0	6352	1527	24	9.4
		231.0	31145	7145	23	1.9
		31.0	54489	7835	14	1.1
		6.0	59443	7832	13	
1:150,000	1:10,000	2031.0	2503	224	9	9.8
		231.0	10092	626	6	2.4
		31.0	20039	2833	14	1.2
		6.0	24545	1955	8	
1:25,000	1:25,000	2031.0	6017	557	9	13.8
		231.0	30413	3221	11	2.7
		31.0	63891	8434	13	1.3
		6.0	83247	5881	7	
1:50,000	1:25,000	2031.0	3599	76	2	12.5
		231.0	16067	705	4	2.8
		31.0	35674	136	0	1.3
		6.0	45160	1240	3	
1:150,000	1:25,000	2031.0	1331	29	2	12.2
		231.0	5328	296	6	3.1
		31.0	12597	106	1	1.3
		6.0	16308	623	4	
1:25,000	1:50,000	2031.0	4228	699	17	15.6
		231.0	21350	1727	8	3.1
		31.0	45574	4210	9	1.4
		6.0	65896	11094	17	
1:50,000	1:50,000	2031.0	2319	540	23	13.9
		231.0	11217	2707	24	2.9
		31.0	24905	4235	17	1.3
		6.0	32257	4268	13	
1:150,000	1:50,000	2031.0	1046	90	9	11.8
		231.0	3889	419	11	3.2
		31.0	9465	1261	13	1.3
		6.0	12372	919	7	
1:10,000	1:100,000	2031.0	5077	829	16	10.2
		231.0	20358	15574	77	2.5
		31.0	47242	706	1	1.1
		6.0	51762	800	2	
1:25,000	1:100,000	2031.0	1795	106	6	13.2
		231.0	8208	69	1	2.9
		31.0	20912	2263	11	1.1
		6.0	23694	1287	5	
1:50,000	1:100,000	2031.0	1093	155	14	15.0
		231.0	4607	313	7	3.6
		31.0	11922	881	7	1.4
		6.0	16431	254	2	

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5. FSH

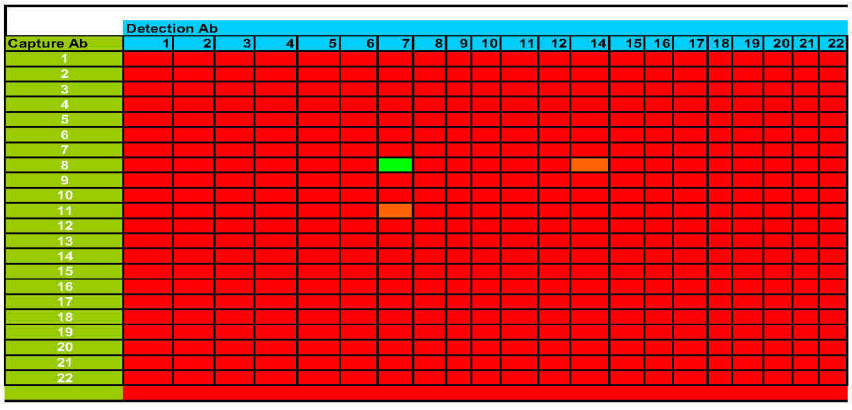
- **Normal ranges**

- **Females:**

Follicular phase	3.5 - 12.5 mIU/ml
Ovulation phase	4.7 - 21.5 mIU/ml
Luteal phase	1.7 - 7.7 mIU/ml
Postmenopause	25.8 - 134.8 mIU/ml

- **Males** 1.5 - 12.4 mIU/ml

- Theranos assay ranges: 200mIU/ml to 0.5mIU/ml
- Reference assay: Genway Biotech FSH Elisa Kit



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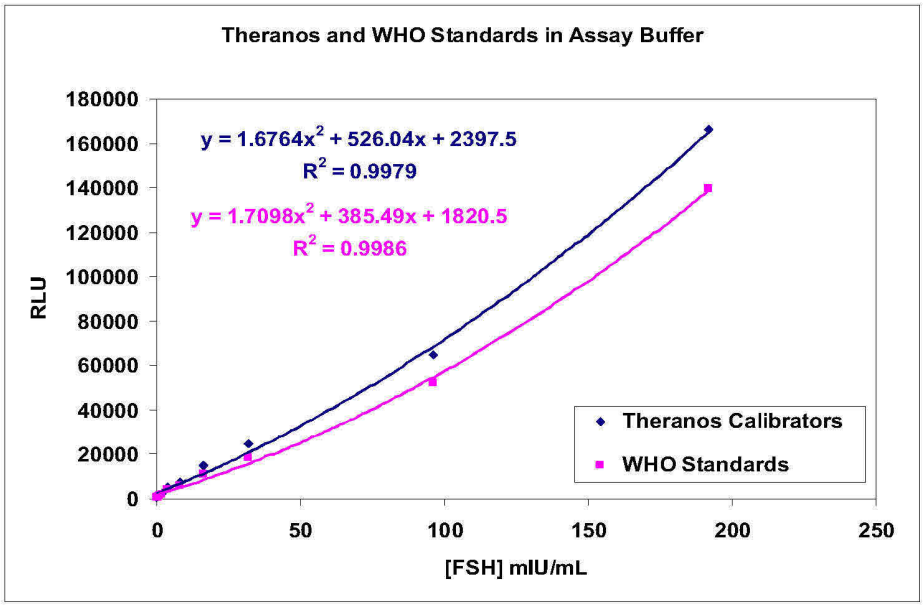
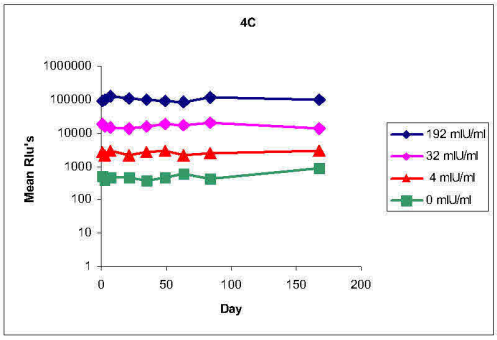
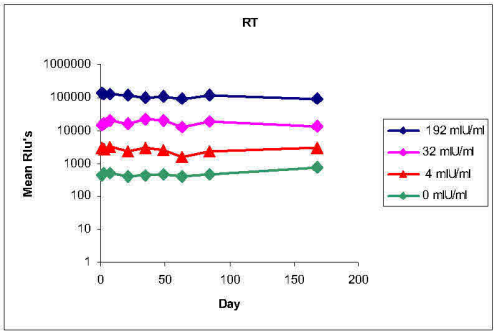
FSH: Analyte verification



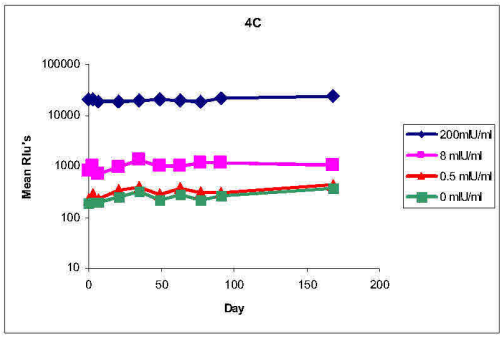
FSH: Stability

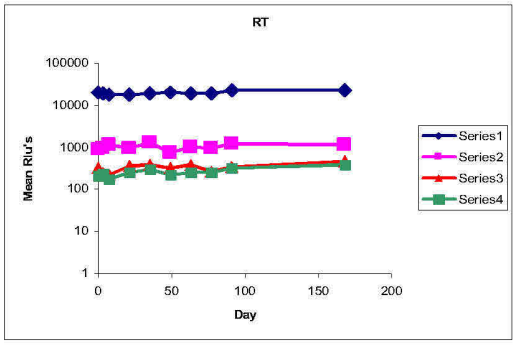
Capture Surface





Detection antibody Stability





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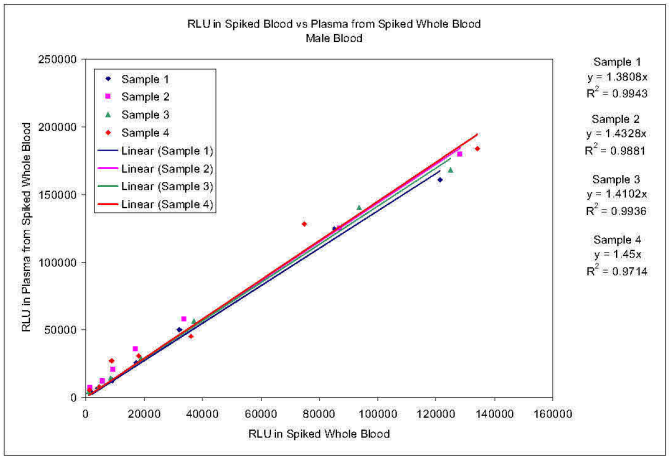
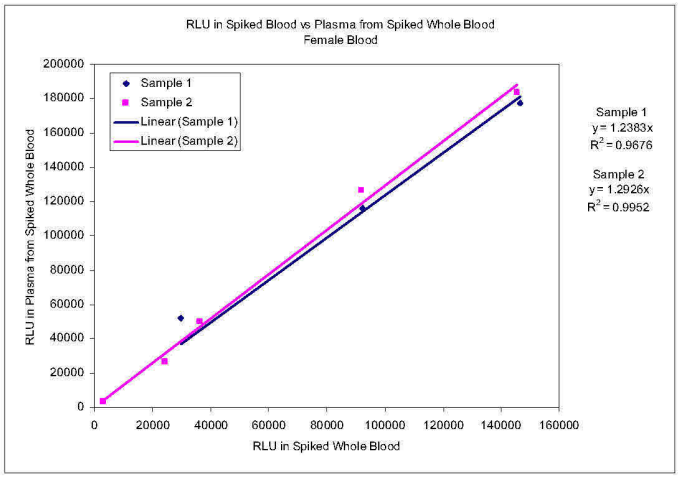
FSH: Hematocrit effect





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FSH: Precision for 3 reagent lots

Concentration		RLU						Calc. Concentration			Total Concentration CVs			
(mIU/ml	Cartridge	Lot 1	Lot 2	Lot 3	Mean	StDev	Intra %CV	Lot 1	Lot 2	Lot 3	Mean	StDev	CV %	% Recovery
200	1	303290	350590	369117	334859	33100	10	**198**	**201**	**200**	200	1	**0.6**	**100**
		314890	365651	316310										
	2	356880	300340	313569				**201**	**199**	**199**				
		346391	341572	344499										
	3	380078	278943	373281				**201**	**198**	**199**				
		356791	349508	265771										
40	1	38368	37484	33409	36169	3232	9	**44**	**43**	**37**	40	4	**9.7**	**101**
		39616	39126	34447										
	2	36379	37857	26766				**42**	**44**	**32**				
		38866	39458	33057										
	3	36100	37456	34489				**42**	**41**	**37**				
		39123	35530	33512										
8	1	10458	9826	9901	10227	957	9	**8**	**8**	**7**	8	1	**11.4**	**98**
		11078	10172	8604										
	2	11941	9717	9613				**9**	**7**	**7**				
		11241	9419	9223										
	3	10324	8842	10697				**9**	**7**	**8**				
		12001	10236	10791										
2	1	3892	3878	4018	3748	300	8	**2.1**	**1.9**	**2.2**	2	0	**7.8**	**102**
		3797	3257	3913										
	2	3093	3626	3847				**1.7**	**2.0**	**2.0**				
		3587	3776	3545										
	3	3642	3804	4458				**2.1**	**2.0**	**2.3**				
		4007	3539	3783										
0.5	1	1239	1088	1010	1114	85	8	**0.5**	**0.5**	**0.5**	0	0	**5.0**	**100**
		1022	1030	1142										
	2	1178	1098	1160				**0.5**	**0.5**	**0.5**				
		1197	941	1180										
	3	1067	1109	1098				**0.5**	**0.5**	**0.5**				
		1247	1051	1199										
0	1	516	583	543	551	36	6	**0**	**0**	**0**	0	0	**3.5**	**N/A**
		510	596	555										
	2	631	586	515				**0**	**0**	**0**				
		522	600	505										
	3	548	533	532				**0**	**0**	**0**				
		538	569	544										

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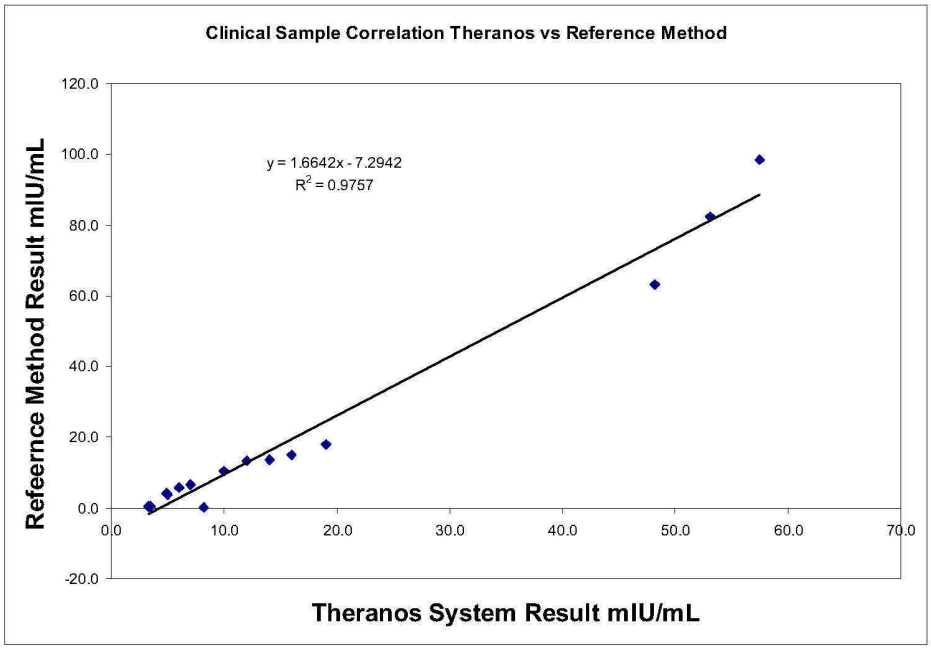
FSH: Training set of clinical samples



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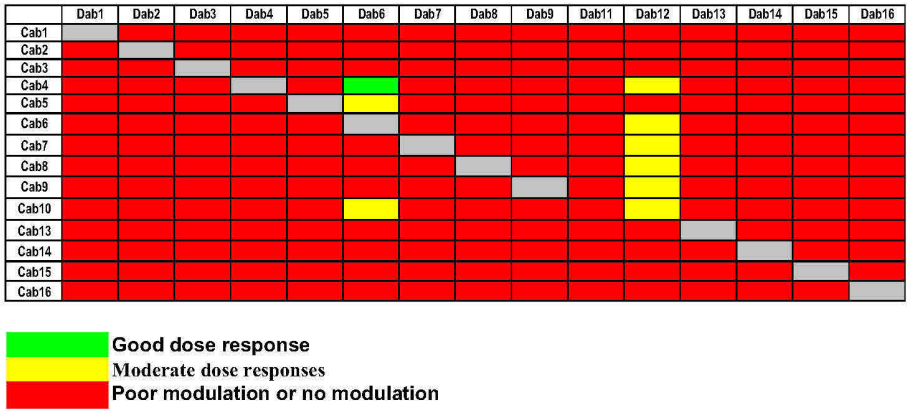
6. FGF-23

- Clinical range: 20 -1400 pg/mL
- Reference assays
  - ➢ Millipore ELISA, 10 - 2400 pg/mL, measures native FGF-23
  - ➢ Kainos ELISA, 10 - 800 pg/mL, Full length FGF-23
- Antibody screening data



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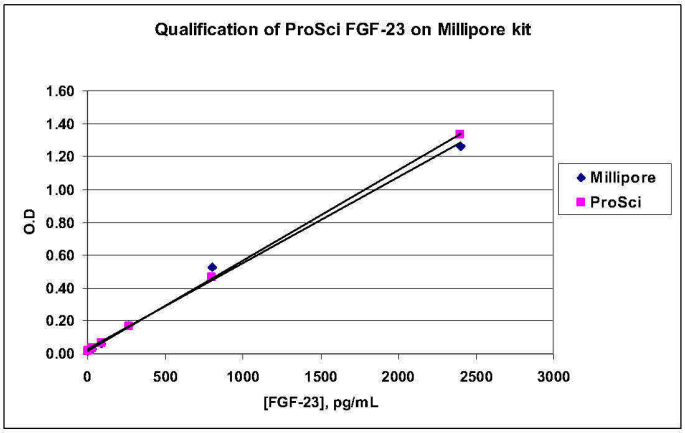
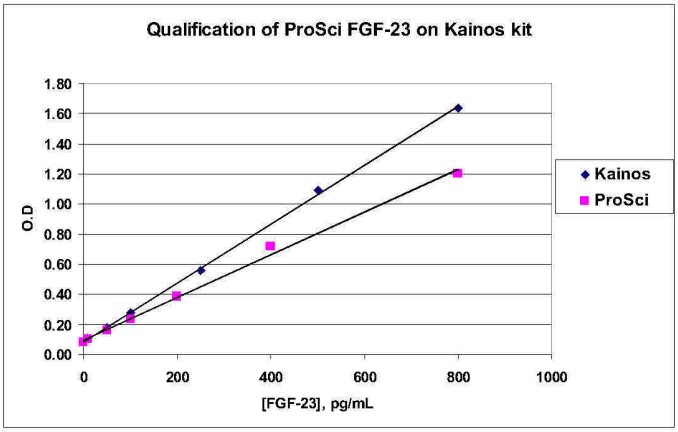
FGF-23: Calibrator Qualification

- Calibrators used for Theranos assay development are qualified against standards from Reference ELISA kit
- When available, analyte is qualified against WHO reference standards





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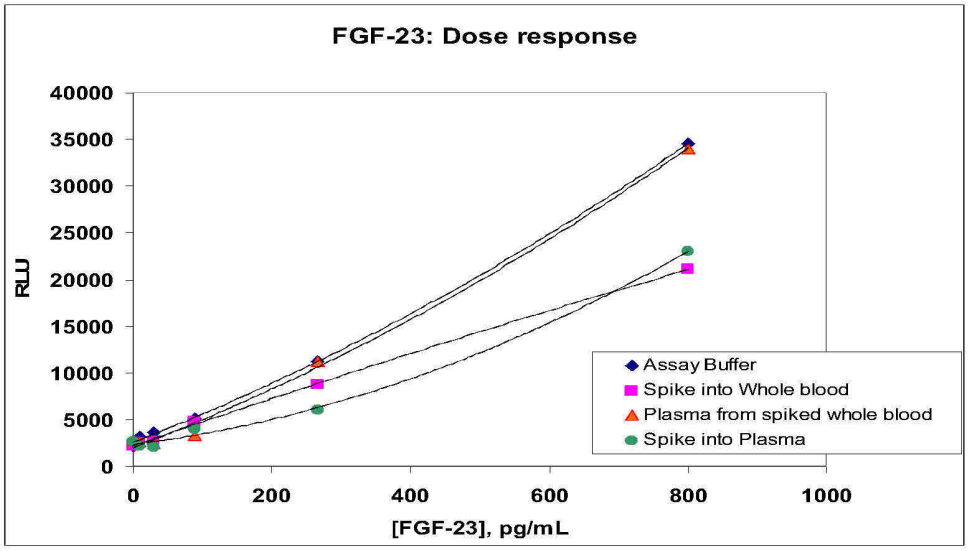
FGF-23: Effect of Matrix



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7. Hemoglobin

Normal & Clinical Ranges

Male – 140-150 mg/ml normal
130-175 mg/ml clinical

Female – 135-145 mg/ml normal
120-160 mg/ml clinical

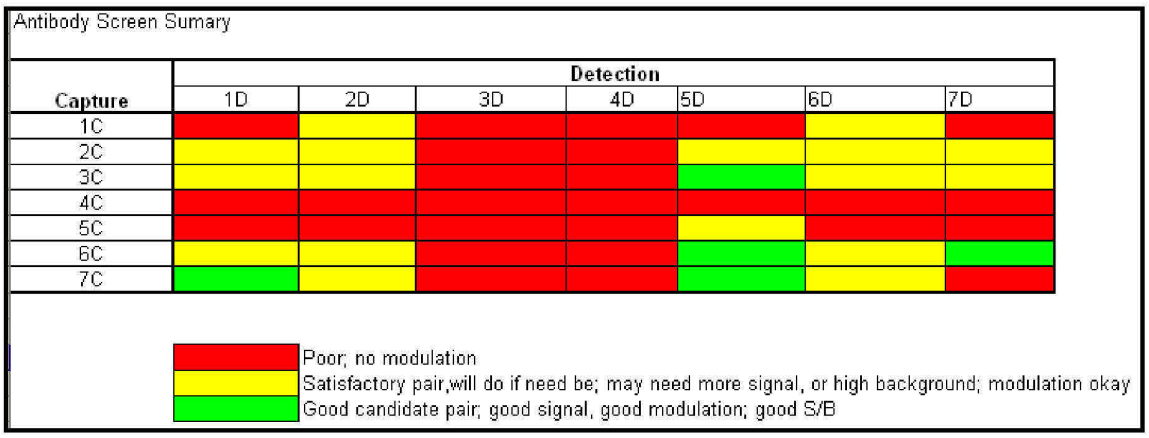
Theranos Assay Range

50 mg/ml – 250 mg/ml

Reference ELISA

Arbor Assays DetectX Hb Kit

Range: 0.25-16 g/dL (2.5-160 mg/ml)



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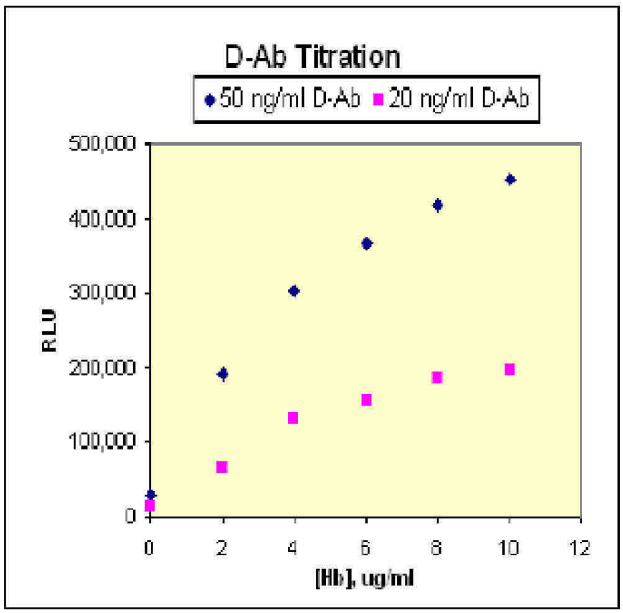
Hemoglobin Assay Data: D-Ab Titration

50 ng/ml D-Ab					
[Hb], ug/ml	Tip 1	Tip 2	MeanValue	StDev	CV
10	423,561	479,886	**451,723**	39,828	9%
8	396,188	437,695	**416,941**	29,350	7%
6	360,913	372,323	**366,618**	8,069	2%
4	274,037	333,798	**303,918**	42,258	14%
2	198,480	183,279	**190,880**	10,748	6%
0	30,862	28,934	**29,898**	1,363	5%

20 ng/ml D-Ab					
[Hb], ug/ml	Tip 1	Tip 2	MeanValue	StDev	CV
10	185,739	205,882	**195,811**	14,243	7%
8	178,181	192,013	**185,097**	9,780	5%
6	149,992	166,412	**158,202**	11,611	7%
4	124,511	134,000	**129,256**	6,710	5%
2	71,124	63,460	**67,292**	5,419	8%
0	12,127	12,750	**12,439**	440	4%



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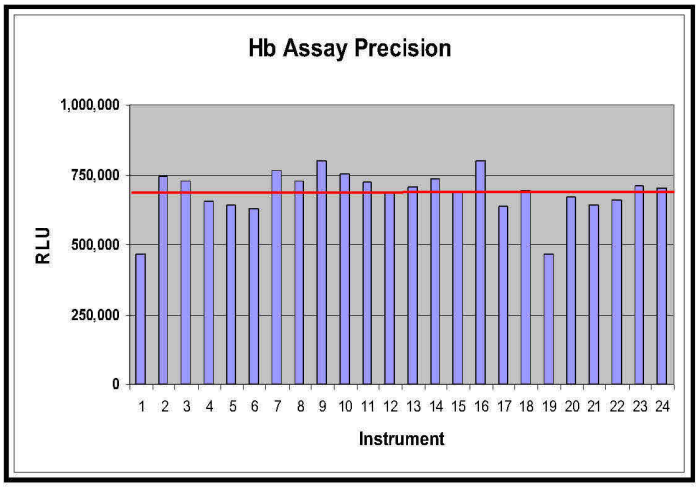
Hemoglobin Assay Data: Precision

Instrument	Tip 1	Tip 2	MeanValue	StDev	CV
1	459,592	468,692	**464,142**	6,435	1%
2	732,104	678,129	**743,045**	38,167	5%
3	700,275	753,520	**726,897**	37,650	5%
4	616,048	692,613	**655,331**	52,726	8%
5	619,372	665,056	**642,514**	31,879	5%
6	604,632	655,197	**629,915**	35,755	6%
7	765,795	761,147	**763,471**	3,286	0%
8	729,940	725,110	**727,525**	3,416	0%
9	748,514	853,418	**800,966**	74,179	9%
10	757,282	748,643	**752,963**	6,108	1%
11	735,558	706,053	**720,806**	20,863	3%
12	657,125	710,617	**683,871**	37,824	6%
13	785,322	623,868	**704,595**	114,165	16%
14	793,571	679,926	**736,248**	81,066	11%
15	676,690	699,957	**687,823**	15,745	2%
16	810,560	769,766	**000,163**	14,703	2%
17	732,005	540,400	**636,202**	135,485	21%
18	713,245	669,382	**691,314**	31,016	4%
19	519,450	411,689	**465,569**	76,199	16%
20	654,783	686,870	**670,827**	22,689	3%
21	704,591	574,090	**639,340**	92,278	14%
22	549,361	770,325	**659,843**	156,245	24%
23	702,559	716,568	**709,564**	9,906	1%
24	731,676	673,044	**702,360**	41,459	6%
	AVERAGES		683,970	47,469	7%



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8. Insulin like growth factor (IGF-1)

- Clinical range for normals ranges from 10 -1000 ng/mL
- Theranos range is 12 -1200 ng/mL
- Approximately 98% of IGF-1 is always bound to one of 6 binding proteins (IGF-BP). IGFBP-3, the most abundant protein, accounts for 80% of all IGF binding. IGF-1 binds to IGFBP-3 in a 1:1 molar ratio.
- Sandwich Elisa established with Capture Antibody specific to IGF-1 and the Detector antibody specific to the IGF Binding Protein 3 so that the complex can be accurately measured in sample.
  - Eliminates the need for a purification/separation step which all commercial Elisa Kits require.

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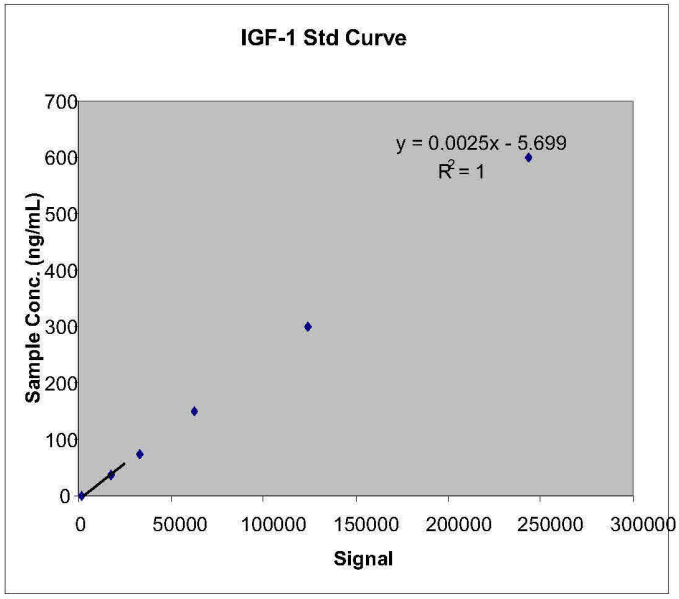
IGF-1: Whole Blood and Plasma Screens



Sample	Whole Blood	Plasma
#	ng/mL	ng/mL
1	216	214
2	161	152
3	152	224
4	108	162
5	72	102
6	106	176
7	211	69
8	147	181
9	116	236
10	60	117

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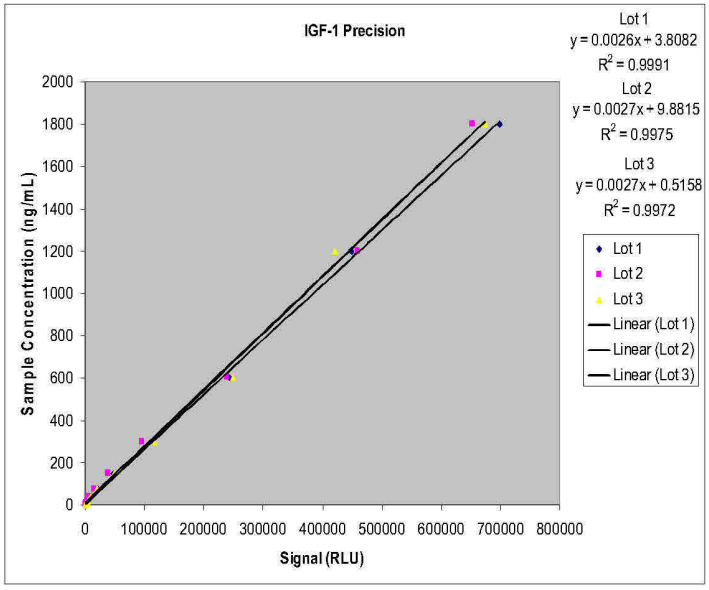
IGF-1: Precision for 3 reagent lots



Concentration CV's

Std	Conc. (ng/mL)	Lot 1	Lot 2	Lot 3	Avg
1	1800	6%	6%	20%	10%
2	1200	8%	17%	10%	12%
3	600	4%	12%	5%	7%
4	300	11%	8%	8%	9%
5	150	8%	13%	12%	11%
6	75	18%	19%	4%	14%
7	38	11%	7%	29%	16%
8	19	4%	5%	29%	13%
9	10	9%	7%	19%	12%
10	5	11%	5%	23%	13%
11	2.5	9%	2%	25%	12%
12	0	11%	2%	28%	14%

IGF-1: 24 Instrument CV's

	CV_24 Instruments							
		Signal	Signal	Signal	Conc.	Conc.	Conc.	Conc.
Tray #	Conc. (ng/mL)	MeanValue	Std.Dev.	CV%	Values	MeanValue	Std.Dev.	CV%
1	150	64356	1492	2%	203	199	5	3%
2		43484	2396	6%	134	128	8	6%
3		55193	2100	4%	173	168	7	4%
4		58476	3312	6%	171	179	11	6%
5		57275	6779	12%	159	175	23	13%
6		49718	1222	2%	152	149	4	3%
7		44512	2133	5%	127	132	7	6%
8		52312	2114	4%	163	158	7	5%
10		47881	8825	18%	122	143	30	21%
10		45165	4354	10%	124	134	15	11%
11		50414	1429	3%	148	152	5	3%
12		48907	3601	7%	138	147	12	8%
13		50168	3985	8%	161	151	14	9%
14		52205	203	0%	158	158	1	0%
15		50687	1481	3%	149	153	5	3%
16		52442	117	0%	158	159	0	0%
17		61306	659	1%	187	189	2	1%
18		55454	1082	2%	172	169	4	2%
19		58580	1598	3%	176	180	5	3%
20		59187	1147	2%	184	182	4	2%
21		59891	3077	5%	191	184	10	6%
22		60227	NA	NA	185	185	NA	NA
23		58181	4339	7%	168	178	15	8%
24		51319	432	1%	156	155	1	1%
		53639			Avg	163		
		5692			Stdev	19		
	Signal	**10.6**		Concentration	CV	**11.9**		

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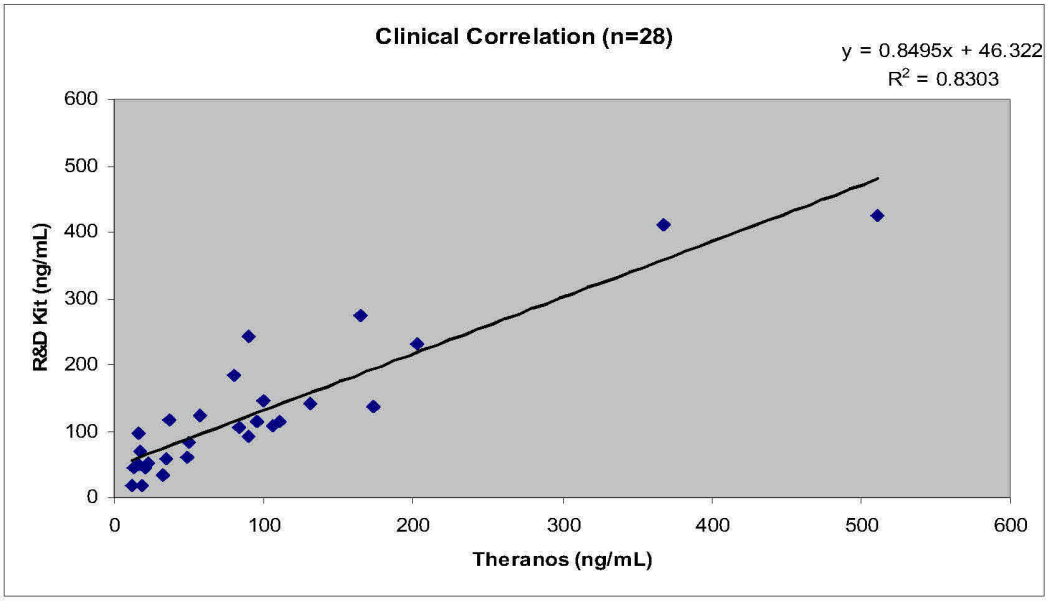
IGF-1 Clinical Correlation



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9. Luteinizing Hormone

- Clinical range:
- Females - menstruating: Follicular phase 2.4 - 12.6 mIU/ml Ovulation phase 14.0 - 95.6 mIU/ml Luteal phase 1.0 - 11.4 mIU/ml Postmenopause 7.7 - 58.5 mIU/ml
- Males: 1.7 - 8.6 mIU/ml
- Theranos assay range: 0.5 – 20 ng/mL (9 – 400 mIU/mL)
- Antibody screen: 22 antibodies
- Reference assay: BioQuant ELISA
- Precision: 3 reagent lots, 8-point standard curve: Average CV:11 %
- Precision: Assay midpoint (5 ng/mL) tested across 24 instruments: Average CV: 9 %

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Luteinizing Hormone: Dose response

Sample	Nominal [LH] ng/ml in sample	RLU 1	2	3	Mean	Std.Dev.	CV%	Cal [LH] ng/ml in sample	% Recovery of Cal. Conc.
1	80	1127802	844348	1075637	1017998	125119	12	80.01	100
		1105411	872988	1081802					
2	40	609976	542767	568565	562601	37058	7	39.91	100
		562180	503364	588756					
3	20	269374	321966	314255	302778	23426	8	20.30	102
		295266	330480	285331					
4	10	144002	131394	158923	147868	10385	7	9.60	96
		150877	143866	158147					
5	5	77399	78458	93617	80341	7322	9	5.14	103
		81546	71541	79487					
6	2	36556	28421	32448	31101	3286	11	1.96	98
		30965	27203	31014					
7	1	15392	16118	17644	15866	1276	8	1.00	100
		16424	15847	13773					
8	0.5	7578	8241	10573	8432	1128	13	0.52	105
		7431	8371	8401					
9	0.1	2445	2147	2127	2300	155	7	0.14	137
		2337	2444	520					
10	0	500	538	424	496	47	9	0.02	NA
		536	523	456					

Theranos LH assay: ULOQ – 20 ng/mL; LLOQ – 0.5 ng/mL

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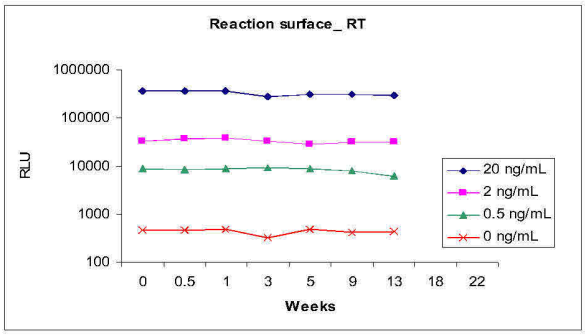
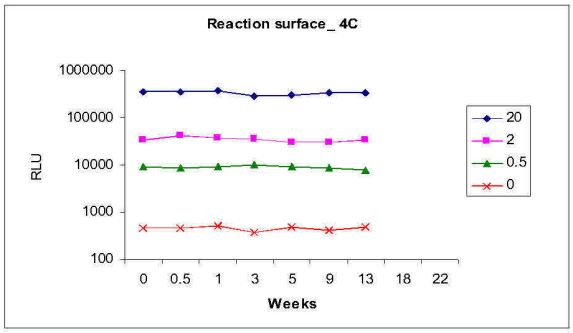
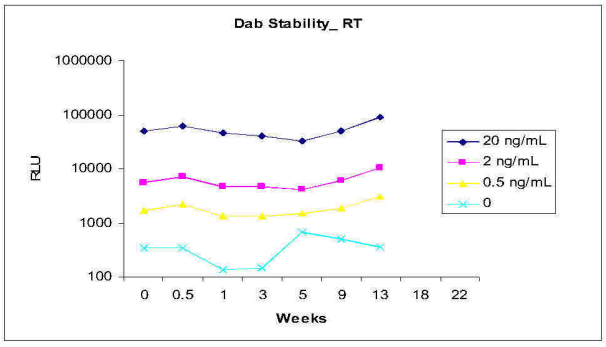
Luteinizing Hormone: Stability data

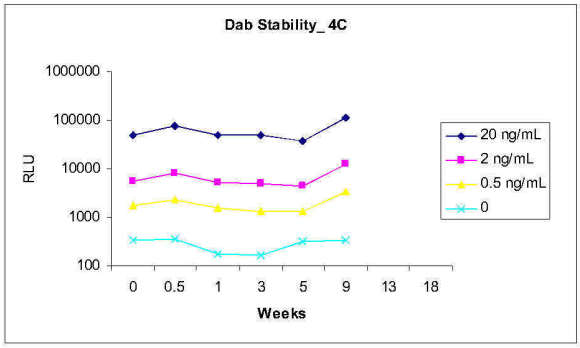
Reaction Surface





Detection Stability





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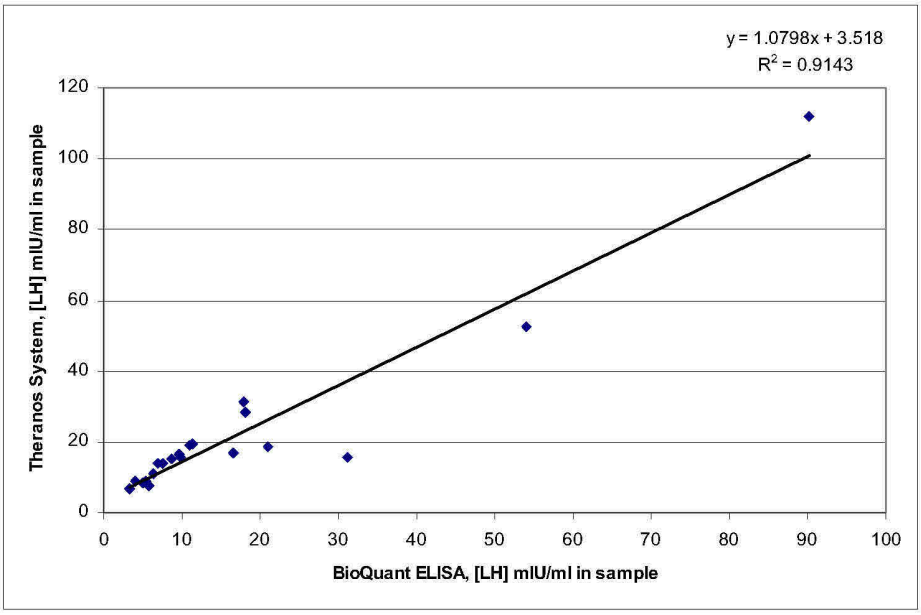
Luteinizing Hormone: Clinical sample correlation to Reference kit



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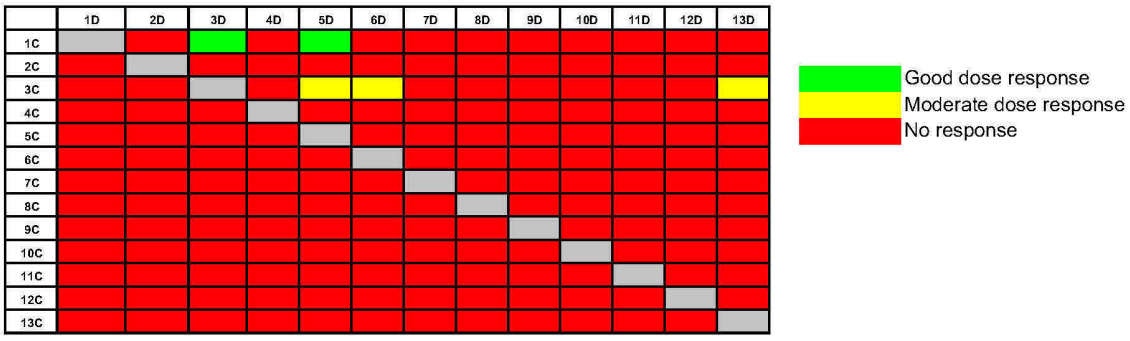
10. Osteocalcin

- Theranos assay: Intact human Osteocalcin 1 -49 is used to develop the assay
- Assay range: 1.2 – 75 ng/mL
- Antibody screen summary



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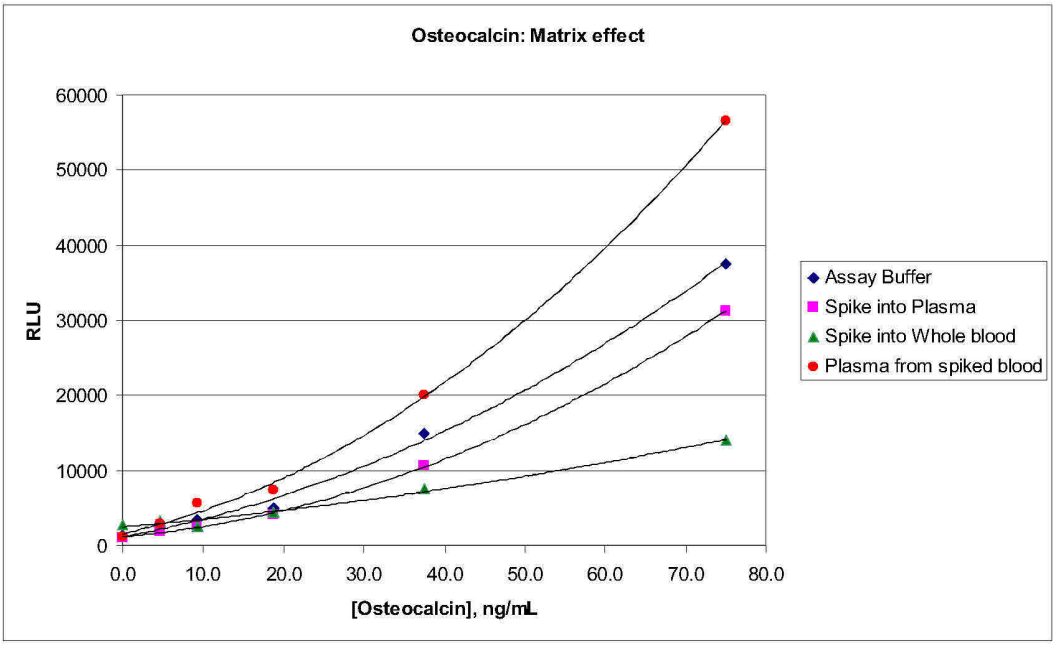
Osteocalcin: Impact of Matrix



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11. Progesterone

- **Progesterone Clinical Range:**

Female (pre-ovulation), Male and Postmenopausal Female: less than 1 ng/mL

Female (mid-cycle): 5 to 20 ng/mL

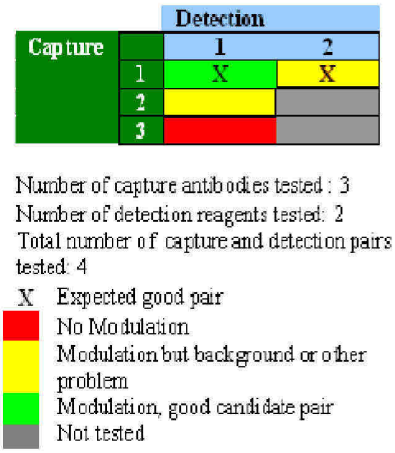
Pregnancy 1st trimester: 11.2-90.0 ng/mL

Pregnancy 2nd trimester: 25.6-89.4 ng/mL

Pregnancy 3rd trimester: 48.4-42.5 ng/mL

- **Theranos Assay Range:** 100 – 0.3ng/mL
- **Theranos Preferred Reference Assay :** Progesterone ELISA Kit. Vendor: IBL America, distributed by Fitzgerald. Range: 40 – 0.3ng/mL
- **Theranos Secondary Reference Assay :** Progesterone EIA Kit. Vendor: Alpco. Range: 60 – 0.3ng/mL

Antibody Screening Data



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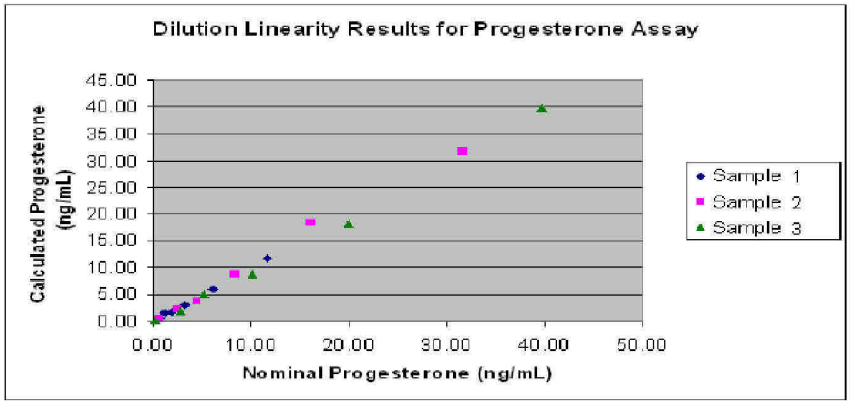
Progesterone Dilution Linearity



Summary of Results for Dilution Linearity for Progesterone Assay

Sample	Dilution	Calculated [Progesterone] ng/mL	% Recovery
1	None	11.71	[100]
	2X	5.86	96
	4X	2.97	89
	8X	1.85	95
	16X	1.49	119
2	None	31.67	[100]
	2X	18.29	113
	4X	8.68	103
	8X	3.66	81
	16X	2.21	86
3	None	39.77	[100]
	2X	18.06	90
	4X	8.71	86
	8X	5.13	98
	16X	2.06	75

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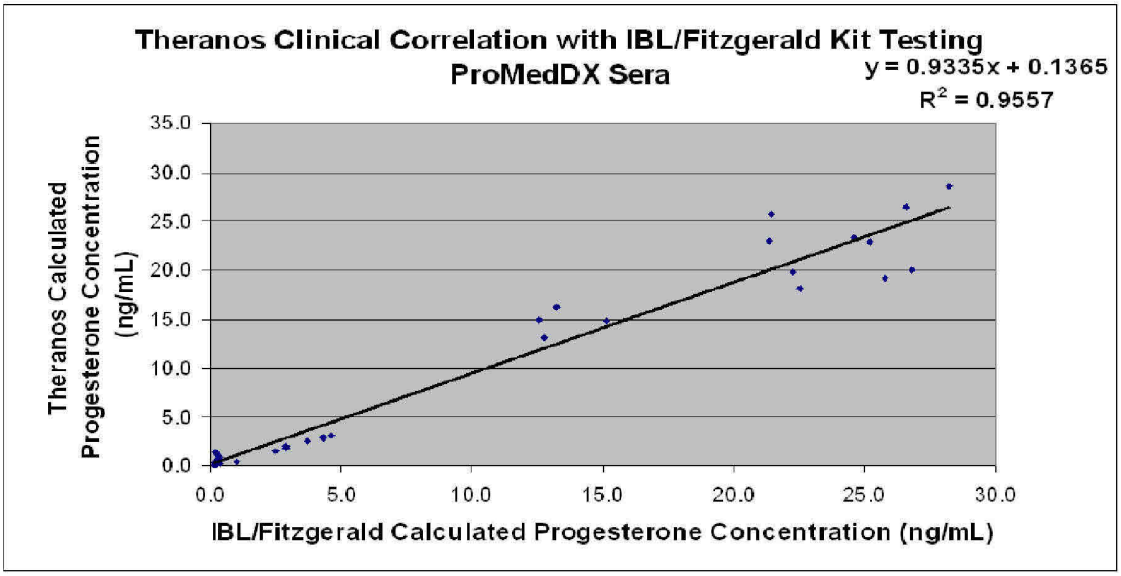
Progesterone: Clinical Correlation with IBL America Kit

For a set of 32 samples, the average Theranos system concentration % CV was 11.3. Please note that samples at or below 0.3ng/mL are at the edge of the limit of detection for both the Theranos and IBL assays. R^2 = 0.96, slope = 0.93.



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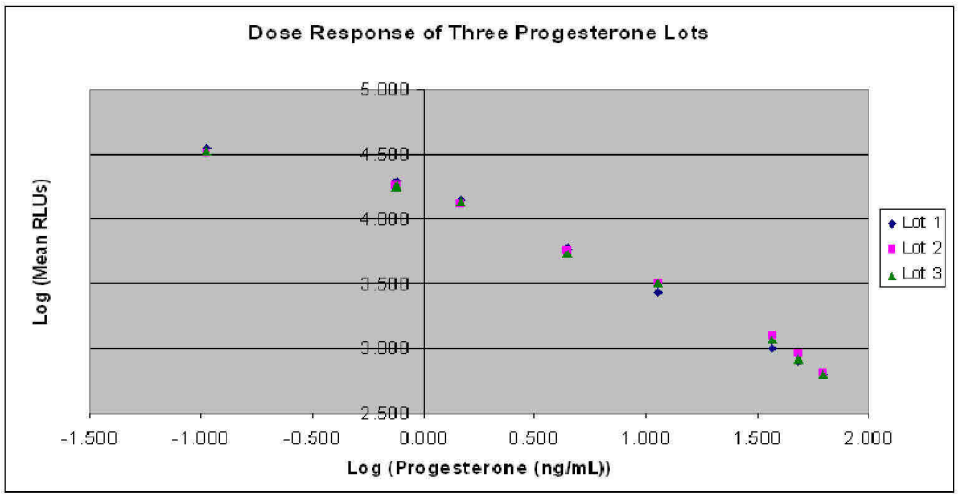
Progesterone: Precision for 8 Point Serum Curve in Duplicate Across Three Assay Lots

Avg Total Signal CV %	8.9%
Avg Total Concentration CV %	13.8%
Overall Average Intra Conc CV	11.4%
Overall Average Intra Signal CV	7.4%



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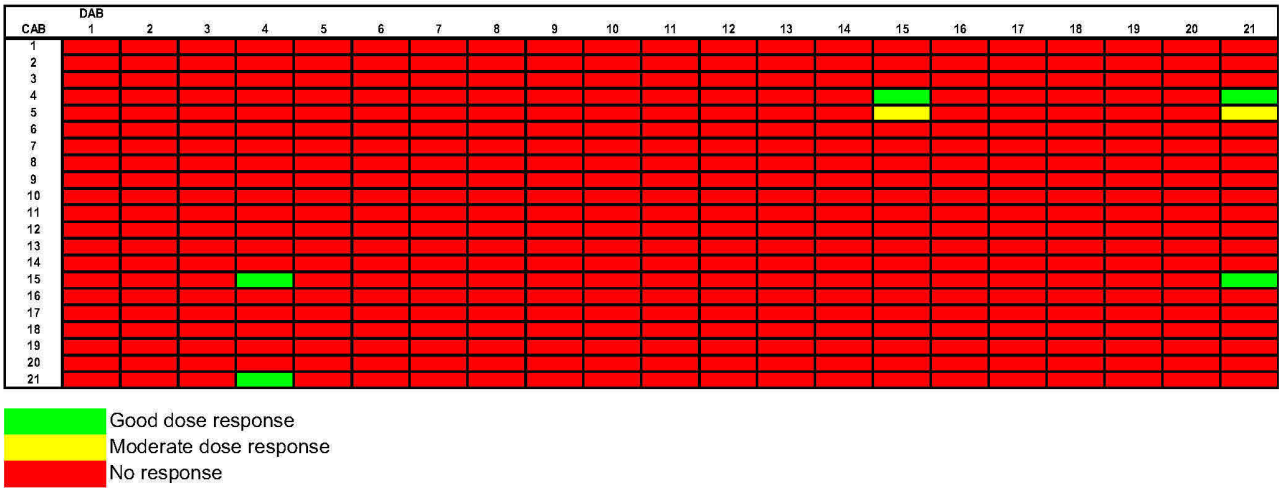
12. Parathyroid Hormone

- Clinical range: normal: 8 – 65 pg/mL,
- Theranos assay range: 10 – 2000 pg/mL
- Antibody Screening summary



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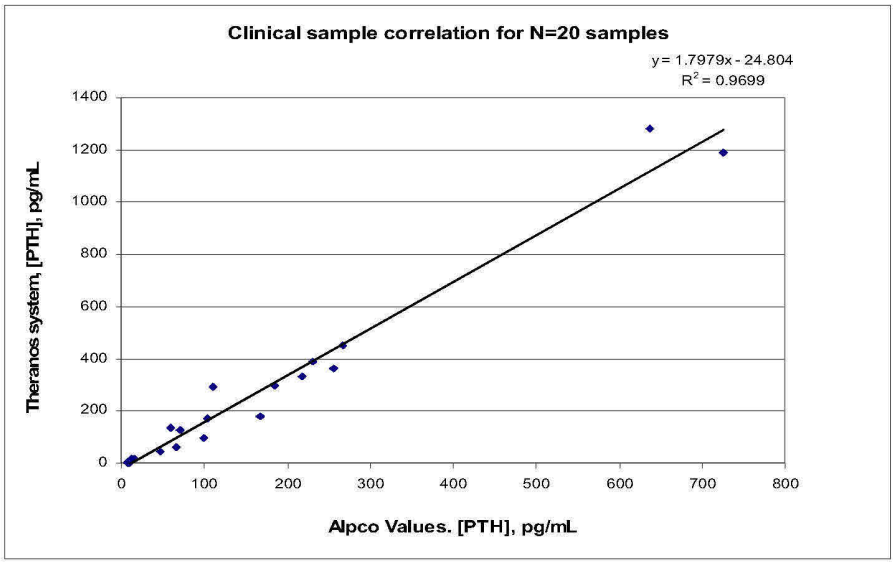
Parathyroid hormone: Training set data



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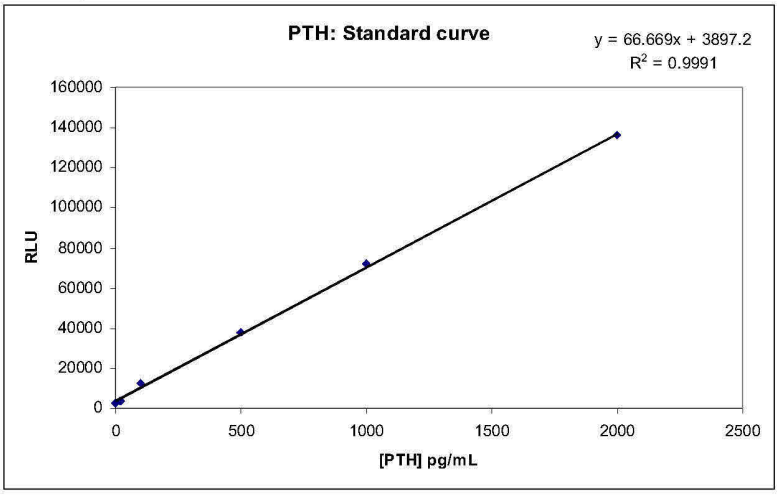
PTH: Whole blood and Plasma screen

Assay Buffer Standard curve					
PTH pg/mL	Average RLU	Stdev	%CV	Calculated pg/mL	%Recovery
2000	136063	10022	7	2223	111
1000	72512	14236	20	991	99
500	37780	4058	11	429	86
100	12142	1582	13	100	100
20	3618	595	16	21	106
0	2611	300	11		

	[PTH] pg/mL	
Sample #	W. blood	Plasma
1	19	25
2	23	55
3	19	21
4	15	18
5	15	24
6	20	21
7	17	32
8	18	19
9	29	37
10	23	32



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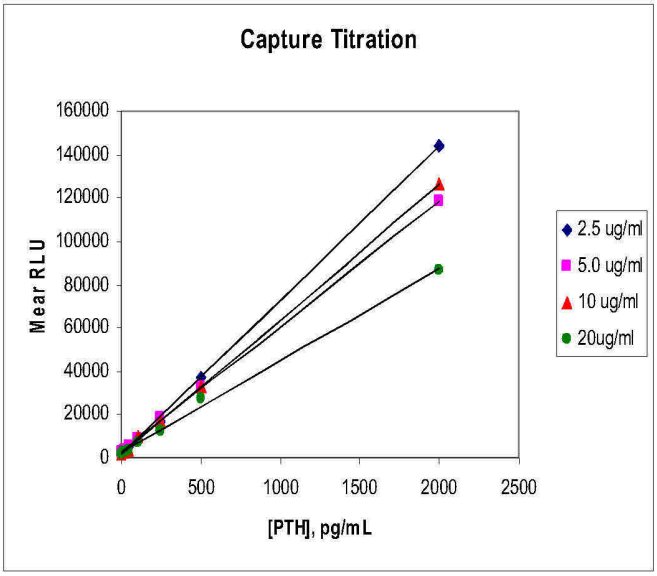
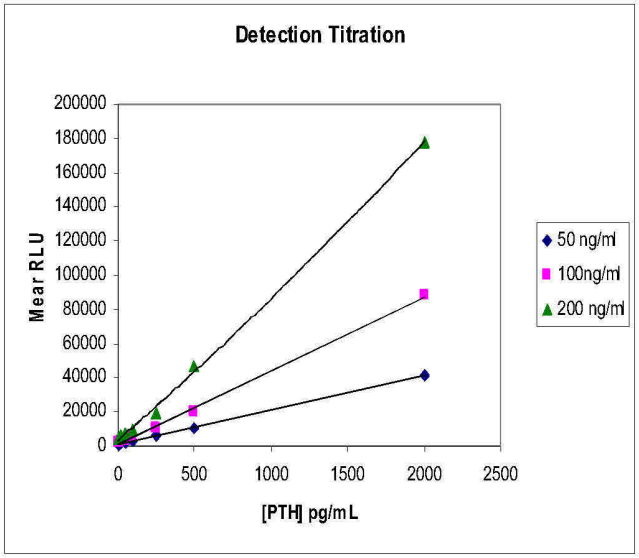
PTH: Assay Optimization





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13. TRACP 5b

- **Normal ranges (U/L)**

Healthy men - 2.1-11

Healthy premenopasusal women- 1.8-10.3

Healthy postmenopausal women- 4.2-12.9

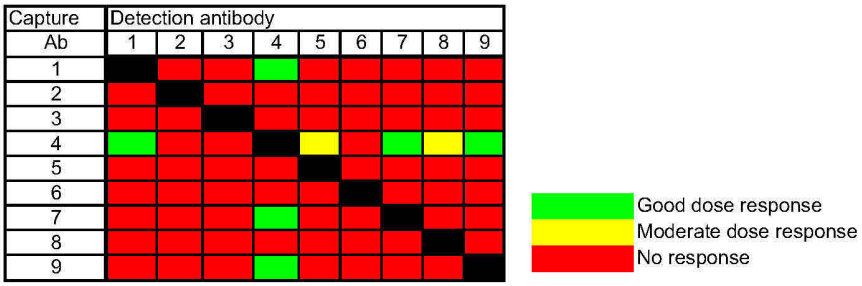
Hyperparathyroid premenopasusal women- 8.1-26.3

Hyperparathyroid postmenopausal women- 11.7-21.8

Hyperthyroid premenopasusal women- 5.5-17.2

Hyperthyroid postmenopausal women- 20.9-26.3

Chronic renal failure- 5.8-20.1



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TRACP5b: Antibody selection, cross reactivity

Analyte	Range	Units
TRACP5b	1.06 - 7	U/L
Bone Alk. Phos	0.78 - 200	U/L
Liver Alk. Phos	1.9 - 2000	U/L
Placental Alk. Phos.	3.2 - 10,000	U/L
Intestinal Alk. Phos	4.8 - 5000	U/L