Barking, Havering and Redbridge University Hospitals NHS Trust

Evaluation of the Kryptor Gold analyser

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Please Rerun any PAPP A result <0.250IU/L FBHCG result >300IU/L
thermo scientific
KRYPTOR GOLD
TRACY

Overview

- FMF evaluation for first trimester combined screening for T21 and PLGF analysis:
- Inhibin-A assay evaluation – preliminary data

Imprecision

FMF targets:

Free Beta hCG	Within Day CV %	Between Day CV %
85iu/l	3.0	5.0
20iu/l	3.0	5.0
8iu/l	4.0	6.0
PAPP-A	Within Day CV %	Between Day CV %
0.30iu/l	4.0	6.0
1.50iu/l	4.0	6.0
4.00iu/l	3.0	5.0

Study results:
(Between day CV)

	Level 1	Level 2	Level 3
N	64	64	64
PAPP-A mean	0.32	1.648	4.164
PAPP-A CV%	**1.82**	**1.42**	**2.32**
N	58	58	58
Free Beta HCG mean	88.28	22.01	8.12
Free Beta HCG CV%	**1.85**	**1.69**	**2.12**
N	45	45	45
PLGF mean	30.11	103.1	430.5
PLGF CV%	**5.94**	**3.66**	**3.84**

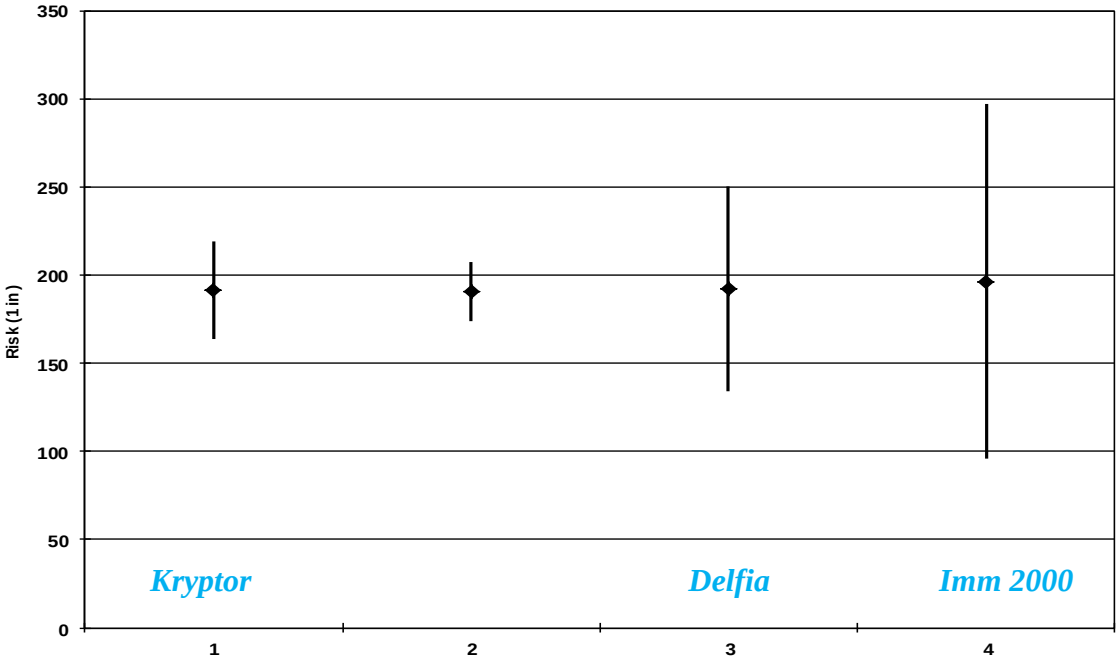
Imprecision

Real world performance (Jan-Feb 2019):

	GMC1	GMC2	GMC3
N	80	80	80
PAPP-A mean	0.33	1.62	4.33
PAPP-A CV%	**1.30**	**1.35**	**1.42**
N	78	78	79
Free Beta HCG mean	86.36	21.32	8.73
Free Beta HCG CV%	**1.28**	**1.35**	**1.29**

Influence of analytical precision on confidence interval of risk

Fβ-hCG=2.50MoM PAPP-A 0.55MoM NT 2.2mm CRL 55mm Age 24y

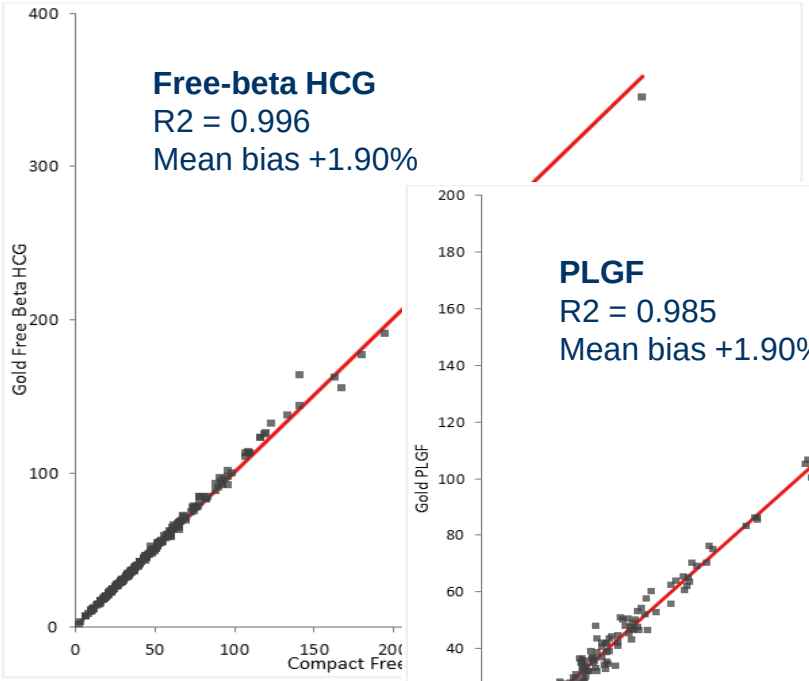


1=LR CV 7% Markers 2-2.5%
2=LR CV 4% Markers 1-1.5%
3=LR CV 15% Markers 4-5%
4=LR CV 25% Markers 6-7%

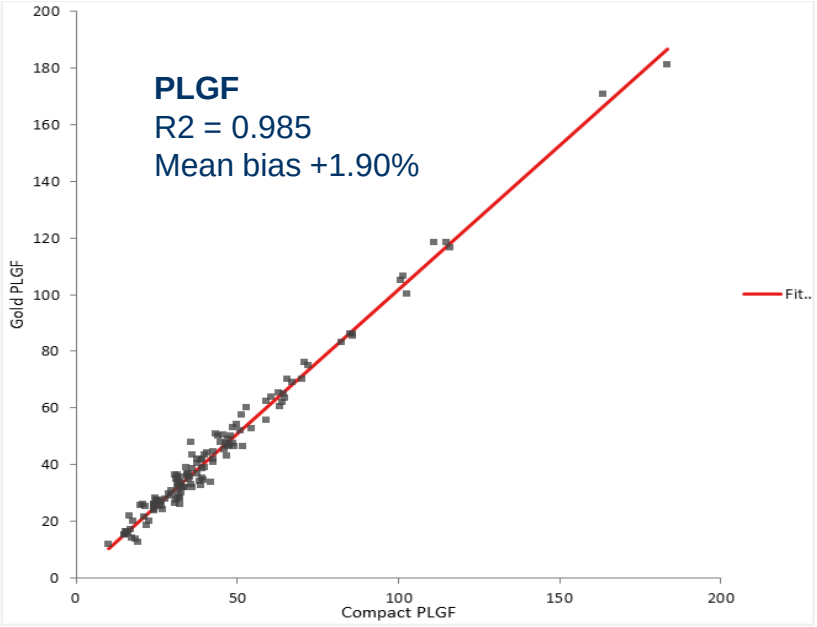
Spencer (2003) DS News
Spencer & Cowa ns 2013, PND

Correlation to Compact

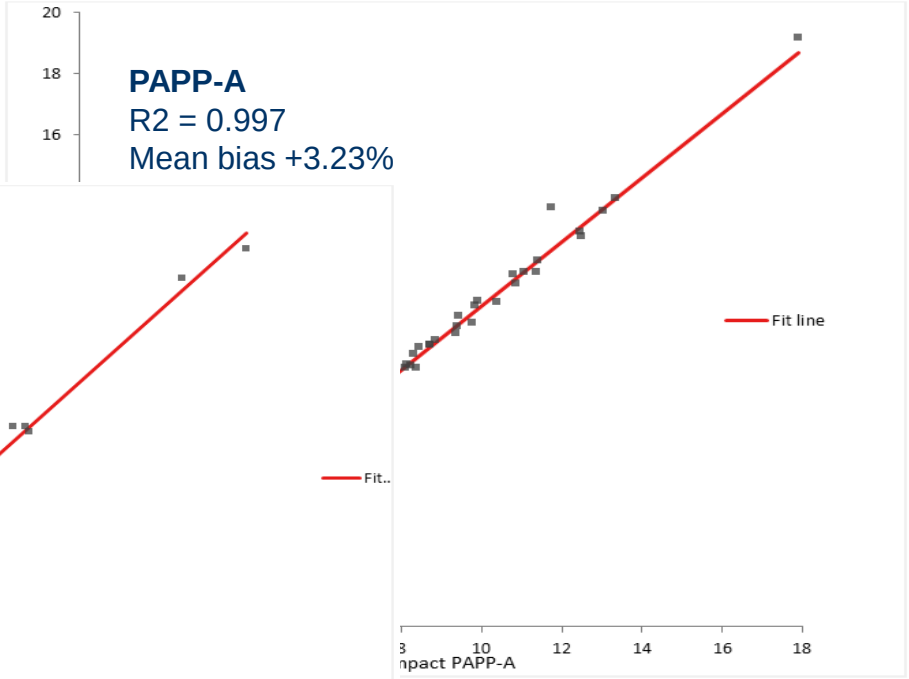
Free-beta HCG
R2 = 0.996
Mean bias +1.90%



PLGF
R2 = 0.985
Mean bias +1.90%



PAPP-A
R2 = 0.997
Mean bias +3.23%



External Quality Assessment

- UKNEQAS Peptide hormones EQA scheme
- 12 samples per marker
- Target = method group mean (Kryptor)

	Mean Z-Score*	Correlation (R^2)
PAPP-A	0.32	0.997
Free-beta HCG	0.21	0.999
PLGF	-1.09	0.938

*Z-Score is the number of standard deviations from method group mean

Linearity of dilution

- 5 samples per marker with high PAPP-A or Free-Beta HCG

PAPP-A Expected recovery (%)	PAPP-A Mean obtained (%)
80	79.5
60	59.9
40	39.3
20	19.4

Free-beta HCG Expected recovery (%)	Free-beta HCG Mean obtained %
80	80.8
60	60.8
40	40.5
20	20.2

Median study

Medians obtained from 474 samples from non-smoking, caucasian women:

Median GA week	N	Gold Free Beta hCG (IU/L)	Gold PAPP-A (IU/L)
10.57	110	44.81	1.316
11.43	120	40.01	2.030
12.57	116	36.50	3.109
13.28	128	30.89	4.811

Medians derived from established regression curve for Kryptor

GA week	Free Beta hCG (IU/L)	PAPP-A (IU/L)
10.57	46.11	1.286
11.43	41.89	1.908
12.57	35.78	3.218
13.28	31.99	4.455

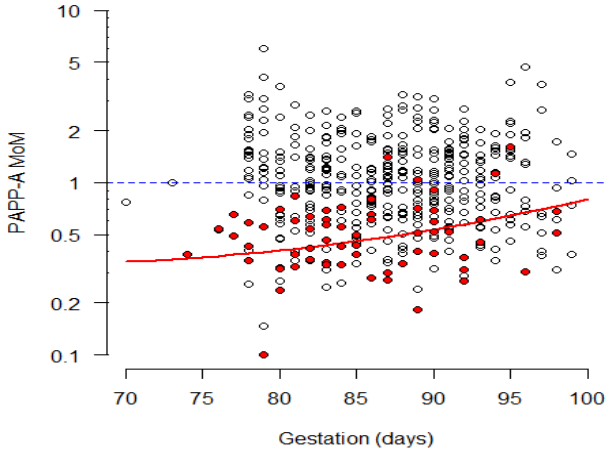
Clinical performance study

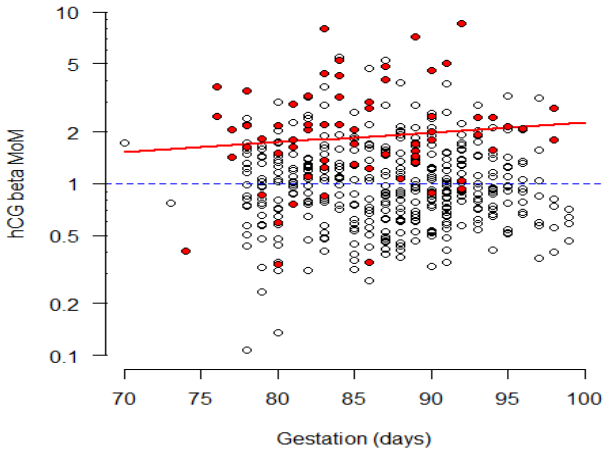
	T21 group	Control group
Number	65*	389
Median age (yrs)	37	32
Median CRL (mm)	63.3	63.9
Median GA (days)	89	88
Median weight (Kg)	68.3	67.3
Median storage (yrs)	5.92	5.91
Smokers (%)	7.4	7.8
Ethnicity Caucasian (%)	100	100
Median NT (mm)	3.20	1.5

* Includes 9 cases that were low risk on initial screening

Clinical performance study

MoM values calculated using existing FMF derived Kryptor medians:





Clinical performance study

	Target performance	Study performance
PAPP-A + FB	**FMF:** DR 60% FPR 5%	 DR 69.9% FPR 5.3%
PAPP-A + FB + NT	**FASP (cut-off 1:150)** DR 85% SPR 1.8-2.5%	 DR 86.3% FPR 2.1%

Throughput

	Compact	Gold
FT samples / hr	24	60

Inhibin-A on Kryptor Gold

ASSAY CHARACTERISTICS	
Sample Volume	70 µL
Incubation Time	39 minutes
Total Measuring Range	Up to 5000 pg/mL
Sample type	Serum
Kit stability on board	15 days
Calibration stability	7 days
Assay principle	sandwich
Traceability	WHO International standard 91/624

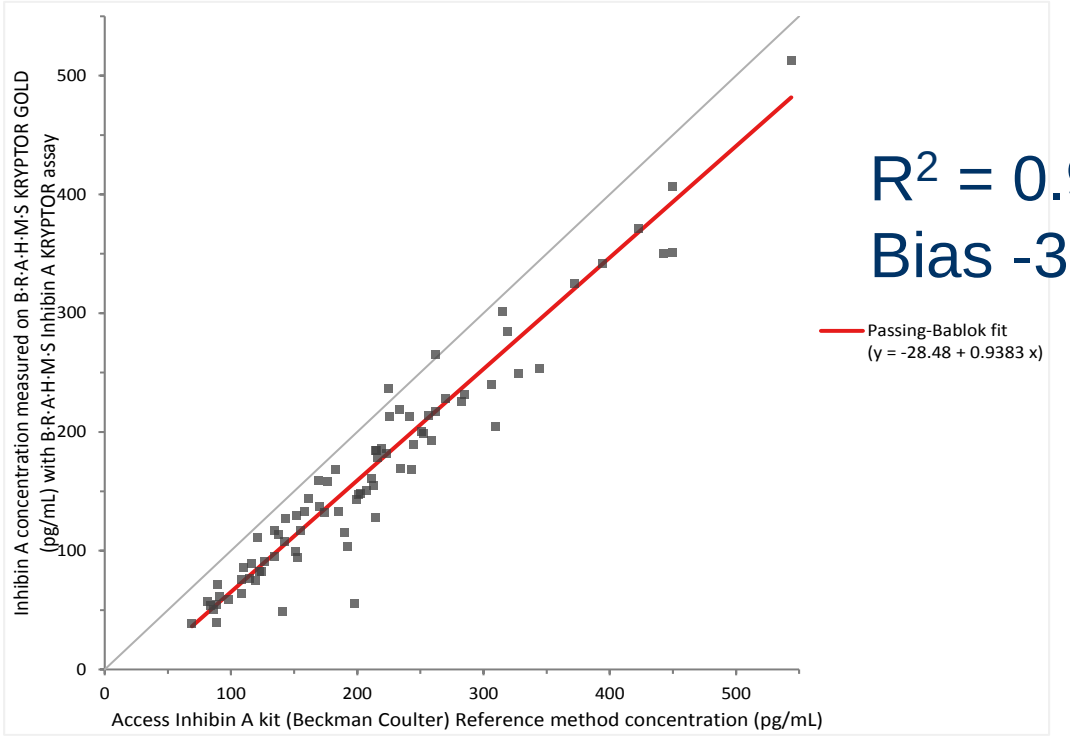
Inhibin-A – Imprecision

Concentration (pg/ml)	Within run (CV%)	Total imprecision (CV%)
161	3.1	5.1
302	3.4	3.5
664	2.3	2.3
1198	2.0	2.3
4336	1.6	2.0

Beckman Access precision:

Sample	Mean Dose (pg/mL)	Within Run (%CV)	Between Run (%CV)	Total Imprecision (%CV)
1	51.633	4.04	4.28	5.89
2	78.456	4.17	2.91	5.09
3	176.239	4.01	3.72	5.47
4	331.710	3.96	2.91	4.91
5	676.600	3.83	6.05	6.05
		Mean = 4.00%	**Mean = 3.97%**	**Mean = 5.48%**

Inhibin-A – Correlation to Beckman

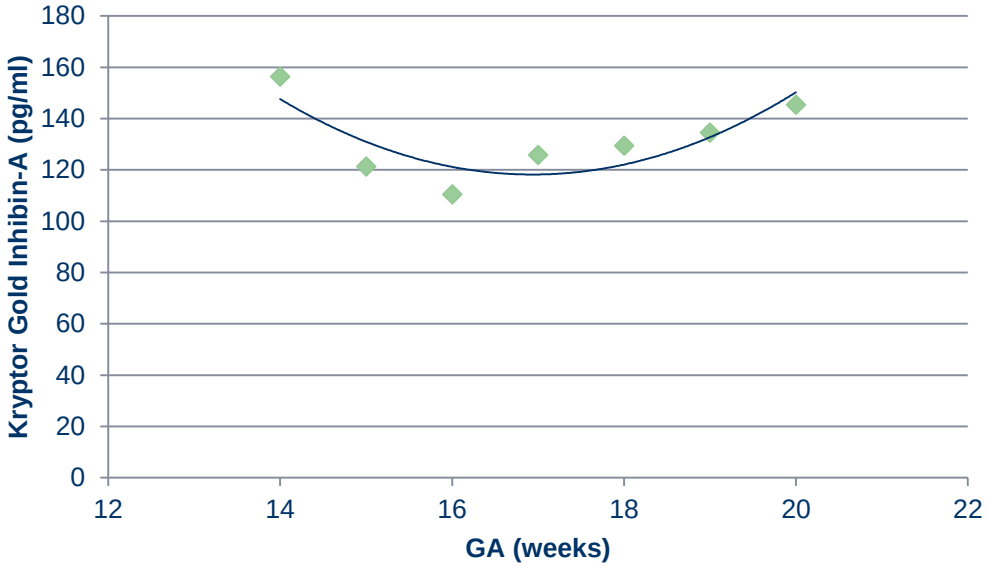


$R^2 = 0.95$

Bias -38.9%

Inhibin-A – Medians

Medians obtained from 346 samples (approx 50 per GA week):



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