



Thermo Scientific
Early Prenatal Care

The gold standard

in prenatal screening

Combined 1st trimester screening • Free β hCG and PAPP-A:
The importance of precise measurement • Key elements of
calculating the risk of trisomy 21

Thermo
SCIENTIFIC

Precision is essential

Free β hCG and PAPP-A on KRYPTOR Systems

Determining the individual risk of carrying a baby with a chromosomal abnormality is a highly sensitive issue for an expectant couple. **Therefore, it is essential to provide them with a result that is as reliable and accurate as possible.**

This can only be achieved by using the best available methods with highly skilled and adequately trained personnel.

The calculation of the individual risk is based on numerous factors: measurement of the maternal serum markers Free β hCG and PAPP-A, several ultrasound parameters, and various correcting factors from the maternal history.

Every single factor itself has a certain imprecision. The more parameters included in the risk calculation, the higher the total imprecision of the final result – the individual risk.¹

An imprecision <8% for the individual risk needs to be obtained, especially for those couples with a high or high to intermediate risk. Otherwise, an imprecise result can lead to unnecessary invasive procedures.

Accordingly, the use of the most precise available methods in 1st trimester screening is of primary importance.²

The biochemical assays Thermo Scientific™ B-R-A-H-M-S™ Free β hCG KRYPTOR™ and Thermo Scientific B-R-A-H-M-S PAPP-A KRYPTOR provide highly precise measurements and a consistent and excellent long-term performance, therefore making the KRYPTOR platform the instrument of choice in 1st trimester screening.





Key elements of calculating the risk for chromosomal abnormalities

Accurate dating of gestation and precise measurement of fetal nuchal translucency (NT)

Besides the measurement of the biochemical markers Free β hCG and PAPP-A, the measurement of the fetal NT in week 11-13 is the most important factor. Again, accuracy in the determination of the nuchal translucency via ultrasound and the correct gestational age is essential for the risk calculation. A reliable result depends on the skills and experience of the ultrasound examiners and requires a high quality ultrasound device.³



The Fetal Medicine Foundation approval requires the commitment to the highest quality standard and an ongoing quality assurance. Thermo Scientific B·R·A·H·M·S serum markers and Thermo Scientific B·R·A·H·M·S KRYPTOR Systems fulfill these strict quality standards since 1999.

Excellent reproducibility and quality: Proven by a coefficient of variation (CV) <4%

Between-day variation of biochemical marker concentrations over a one year period on the same instrument (n=500 for each sample)²

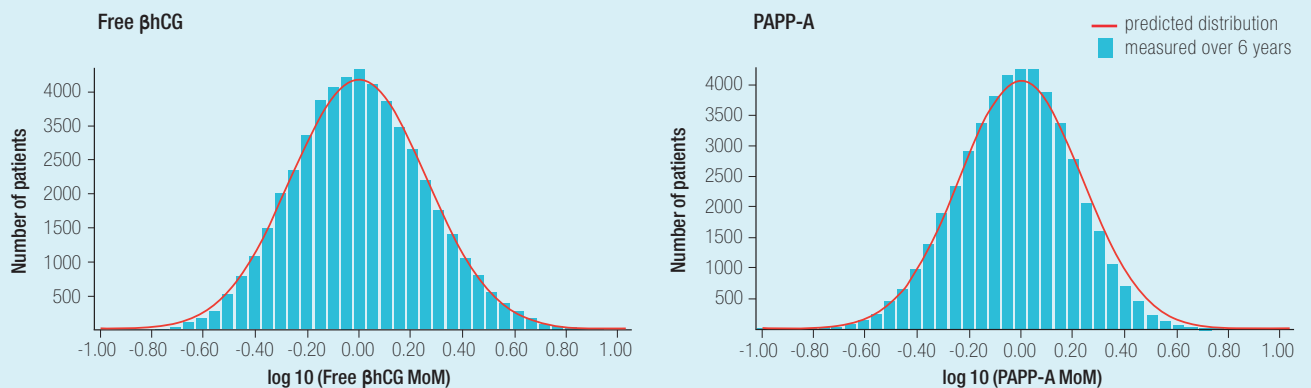
	Sample	Mean [IU/L]	CV (%)
Free β hCG	1	8.05	3.69
	2	20.88	2.72
	3	86.40	2.90
PAPP-A	1	0.286	2.21
	2	1.414	2.19
	3	3.994	2.30

Between-day/between-instrument variation of biochemical marker concentrations over a one year period (n=1000 for each sample)²

	Sample	Mean [IU/L]	CV (%)
Free β hCG	1	8.12	3.94
	2	21.22	2.78
	3	86.11	3.03
PAPP-A	1	0.296	3.00
	2	1.463	2.43
	3	3.957	2.78

The unique Thermo Scientific TRACE™ technology of B-R-A-H-M-S KRYPTOR Systems allows the determination of analytes with the highest precision through measurement without separation steps.

Excellent robustness: Security and stability of a population distribution of markers



Distribution of the cumulative measurement of Free β hCG and PAPP-A respectively over a period of 6 years (n \approx 55 000) vs. the predicted distribution, calculated by Spencer.⁴

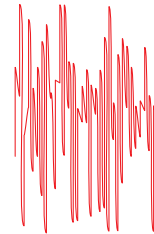
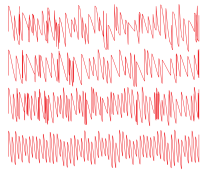
The medians of the B-R-A-H-M-S KRYPTOR biochemical markers Free β hCG and PAPP-A are extremely stable.

Therefore, a recalculation of medians and MoMs is not required.



Risk as a quality control parameter

The analytical error has a great impact on the calculation of the risk in 1st trimester screening.⁵



Input

Parameters for 1st trimester screening

- Biochemical marker values (Free β hCG, PAPP-A)
- Ultrasound marker values (NT, NB...)
- Correction factors (maternal age, weight, ethnicity...)

Risk calculation

Output

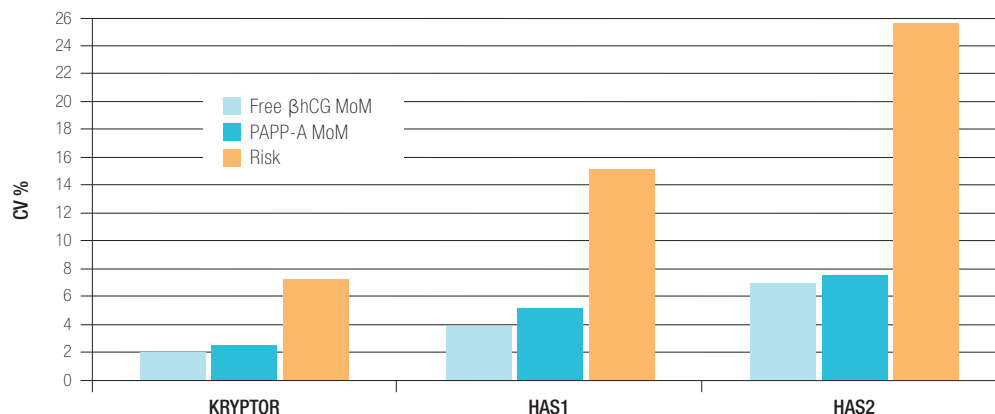
Individual risk

For the most precise and accurate determination of the individual risk the precision of the biochemical markers are of utmost importance!

Influence of reproducibility on risk quality

Simulation to demonstrate the impact of the analytical variability on risk estimates:²

- Between-day variation of 1st trimester risk using the standard deviation for Free β hCG and PAPP-A measured on KRYPTOR was set as the reference.
- Hypothetical analytical systems (HAS) with standard deviations twice (HAS1) or three times higher (HAS2) than the ones for KRYPTOR were calculated.



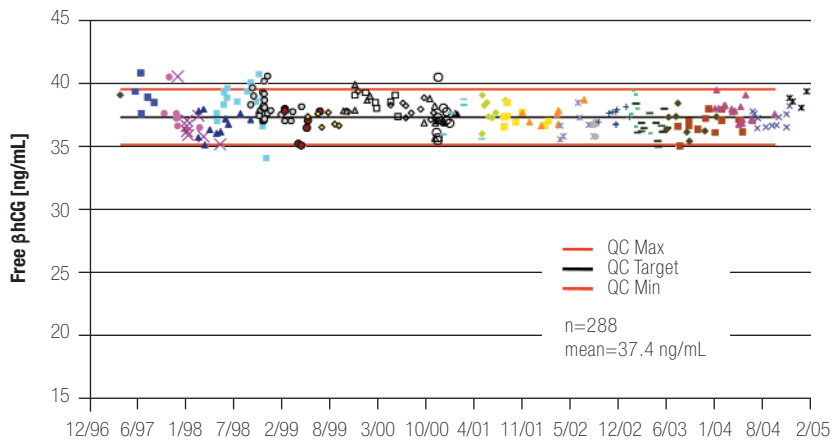
Even a modest increase of the CV to 4-5% for a single marker lead to a CV for the risk of over 15%!

Long-term precision data

Thermo Scientific B·R·A·H·M·S Free β hCG KRYPTOR

B·R·A·H·M·S QC Data

Total CV = 3.3%



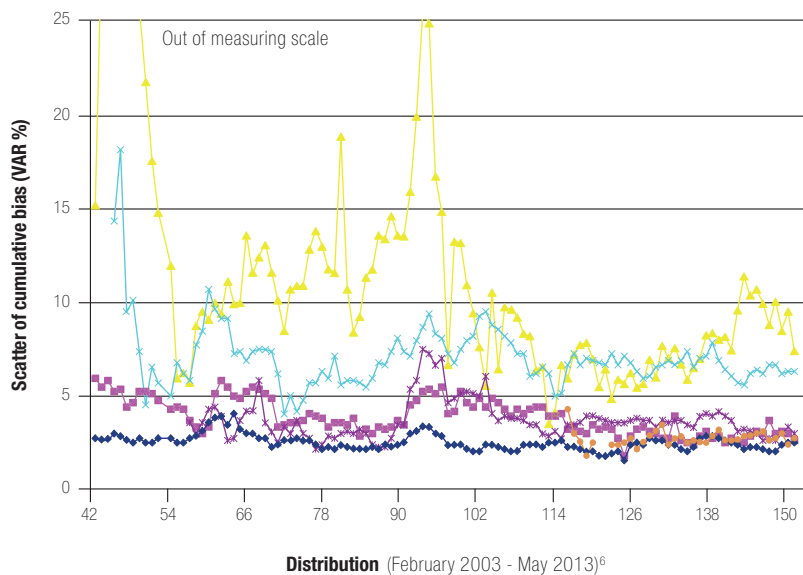
More than 10 years.

- Reagent lot 1-31, several lots of calibrators
- KRYPTOR models A, B, C, D, E, F and KRYPTOR compact

- UR01
- UR02
- UR03
- UR04
- UR05
- UR06
- UR07
- UR08
- UR09
- UR10
- UR11
- UR12
- UR13
- UR14
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- UR20
- UR21
- UR22
- UR23
- UR24
- UR25
- UR26
- UR27
- UR28
- UR29
- UR30
- UR31

External Quality Data

Mean CV = 3%



- KRYPTOR
- Competitor A, Instrument 1
- Competitor B, Instrument 1
- Competitor B, Instrument 2
- Competitor A, Instrument 2
- Competitor C

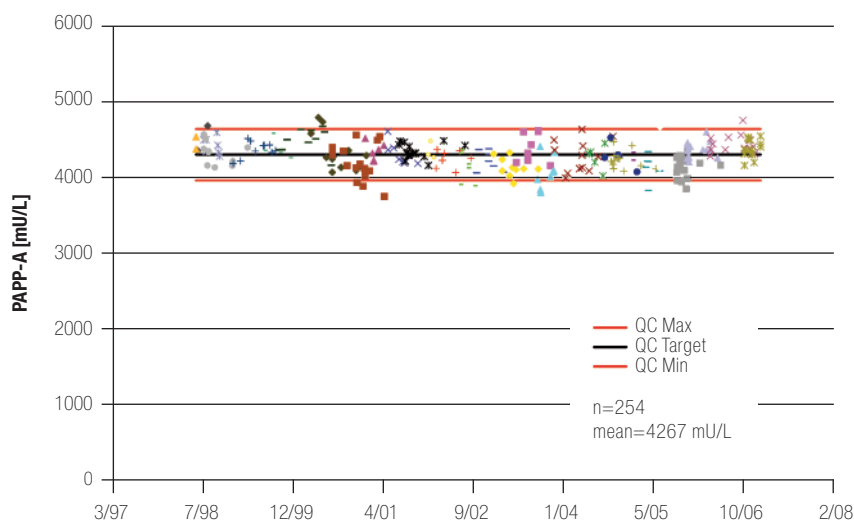


1% increase of CV in Free β hCG and PAPP-A MoMs results in an up to fourfold increase of CV in risk.²

The United Kingdom National External Quality Assessment Service (UK NEQAS) helps ensure that results of investigations are reliable and comparable. The independent UK NEQAS analysis proves the outstanding precision, reliability and stability of the B·R·A·H·M·S assays for more than 15 years.

Thermo Scientific B·R·A·H·M·S PAPP-A KRYPTOR

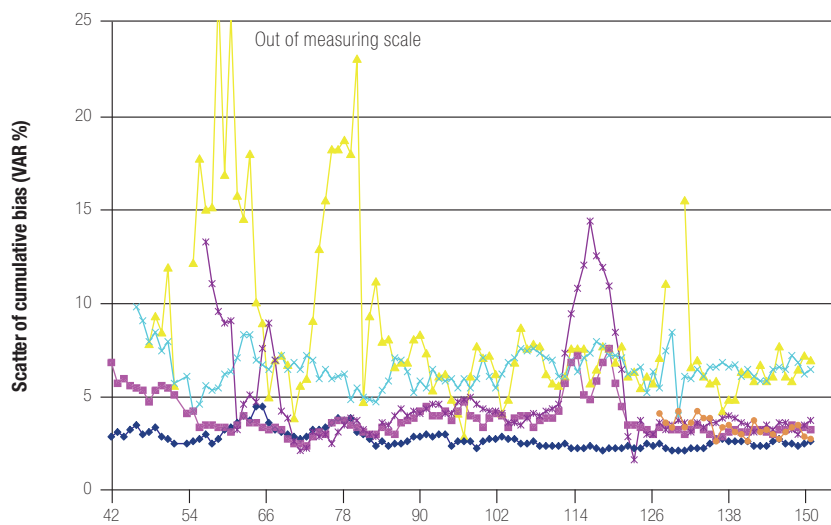
Total CV = 4.4%



More than 10 years.
 • Reagent lot 1-30, several lots of calibrators
 • KRYPTOR models A, B, C, D, E, F and KRYPTOR compact

- | | |
|--------|--------|
| ◆ UR01 | — UR16 |
| ▲ UR02 | ◆ UR17 |
| × UR03 | ■ UR18 |
| ● UR04 | ▲ UR19 |
| + UR05 | × UR20 |
| - UR06 | ★ UR21 |
| — UR07 | ● UR22 |
| ◆ UR08 | + UR23 |
| ■ UR09 | - UR24 |
| ▲ UR10 | — UR25 |
| × UR11 | ◆ UR26 |
| ★ UR12 | ■ UR27 |
| ● UR13 | ▲ UR28 |
| + UR14 | × UR29 |
| - UR15 | ★ UR30 |

Mean CV = 3.1%



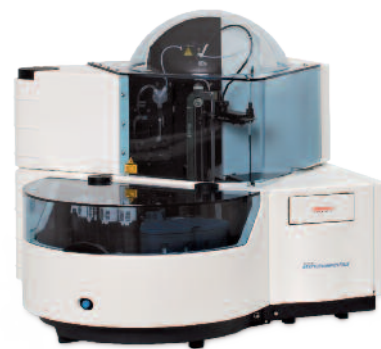
- | |
|------------------------------|
| ◆ KRYPTOR |
| ■ Competitor A, Instrument 1 |
| ▲ Competitor B, Instrument 1 |
| × Competitor B, Instrument 2 |
| ★ Competitor A, Instrument 2 |
| ● Competitor C |

Distribution (February 2003 - May 2013)⁶

15 Years Reliable Results

15 Years Confident Decisions

- All KRYPTOR platforms FMF approved
- In routine use by FMF since 1999
- Excellent precision and data stability
- Same set of medians on all platforms
- OSCAR compatible



B-R-A-H-M-S KRYPTOR compact PLUS
Article number: 106172



B-R-A-H-M-S KRYPTOR
Article number: KRYPTOR AUTOMAT

Thermo Scientific B-R-A-H-M-S Biomarkers Prenatal Screening Markers on KRYPTOR Systems

- | | |
|---|-------------------|
| • B-R-A-H-M-S Free βhCG KRYPTOR | Art. no.: 809.075 |
| • B-R-A-H-M-S hCG+β KRYPTOR | Art. no.: 841.050 |
| • B-R-A-H-M-S PAPP-A KRYPTOR | Art. no.: 866.075 |
| • B-R-A-H-M-S AFP KRYPTOR | Art. no.: 816.075 |
| • B-R-A-H-M-S PIGF KRYPTOR* | Art. no.: 844.075 |
| • B-R-A-H-M-S sFlt-1 KRYPTOR | (available soon) |
| • B-R-A-H-M-S Fast Screen pre I plus Software | Art. no.: 105750 |

* Available on KRYPTOR compact PLUS only

References

- 1 Cuckle H. Coefficient of variance. DSNEWS 2007,14(2):25
- 2 Spencer K. Risk, a QC parameter. DSNEWS 2003,10(1):30-31
- 3 <http://www.fetalmedicine.com/fmf/>
- 4 Spencer K et al. Presentation on B-R-A-H-M-S KRYPTOR User Meeting, Cambridge, March 2007
- 5 Wrigh, D. Presentation at FMF World congress; June 2010
- 6 Monthly UK NEQAS reports, February 2003 – May 2013

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