Thermo Scientific
Early Prenatal Care

The gold standard

in prenatal screening

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

Thermo SCIENTIFIC

Precision is essential

Free βhCG 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.

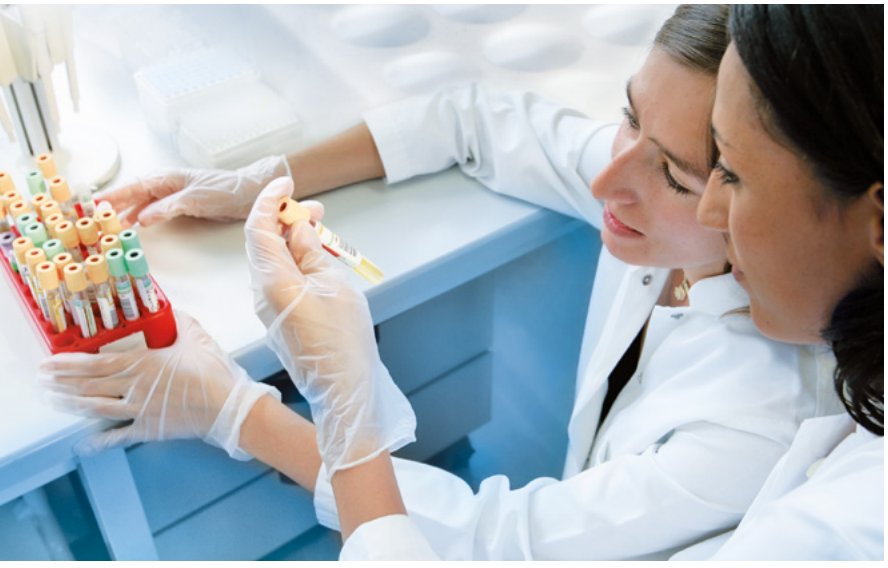
The calculation of the individual risk is based on numerous factors: measurement of the maternal serum markers Free βhCG and PAPP-A, several ultrasound parameters, and various correcting factors from the maternal history.

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 βhCG 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 βhCG 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]

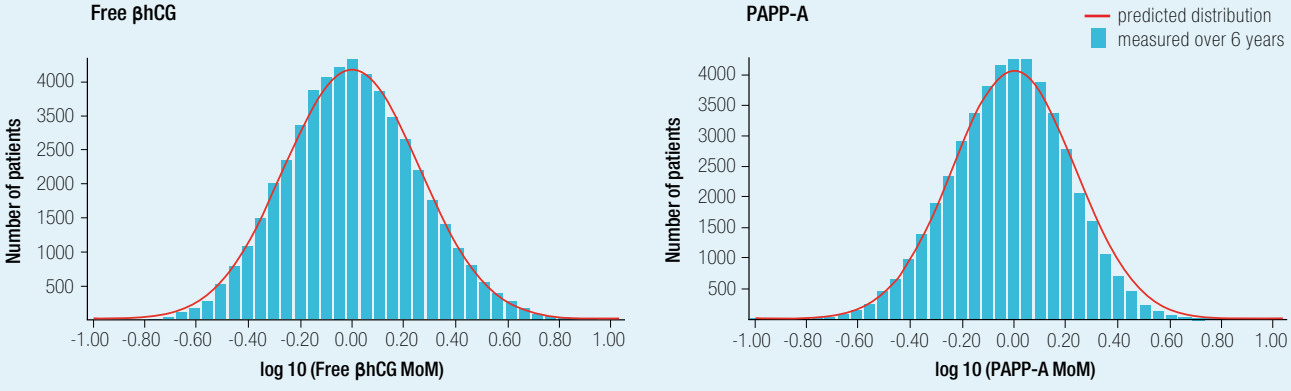
	Sample	Mean [IU/L]	CV (%)
Free βhCG	1	8.05	3.69
	2	20.88	2.72
	3	86.40	2.90
PAPP-A	1	0.286	2.21
	2	1.414	2.19
	3	3.994	2.30

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 βhCG	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



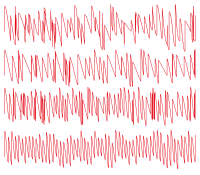
Distribution of the cumulative measurement of Free βhCG and PAPP-A respectively over a period of 6 years (n≈ 55 000) vs. the predicted distribution, calculated by Spencer.[4]

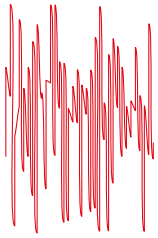
The medians of the B·R·A·H·M·S KRYPTOR biochemical markers Free βhCG and PAPP-A are extremely stable.

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 βhCG, PAPP-A)
- Ultrasound marker values (NT, NB…)
- Correction factors (maternal age, weight, ethnicity…)

Risk calculation

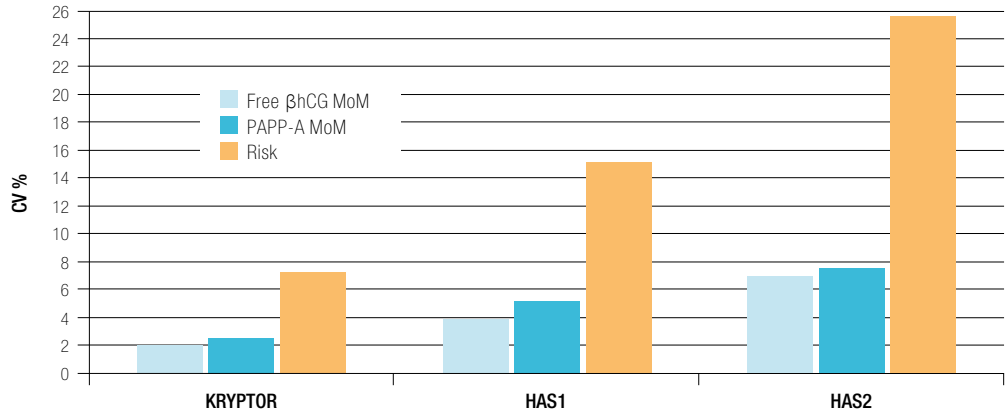
Output
Individual risk

For the most precise and accurate determination of the individual risk the precision of the biochemical markers are of outmost 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 βhCG 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.

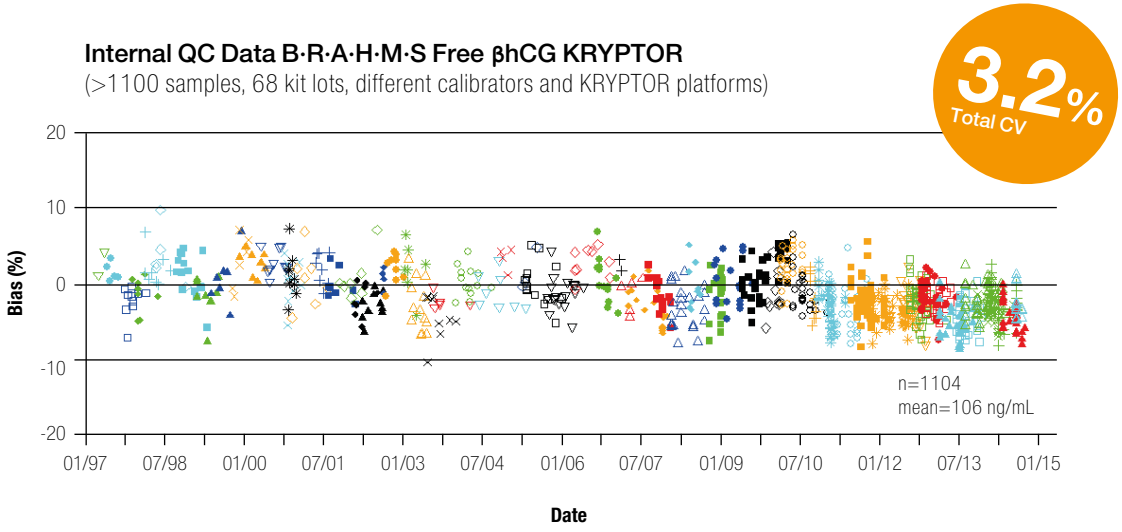


Even a modest increase of the CV to 4-5% for a single marker lead to a CV for the risk of over 15%!

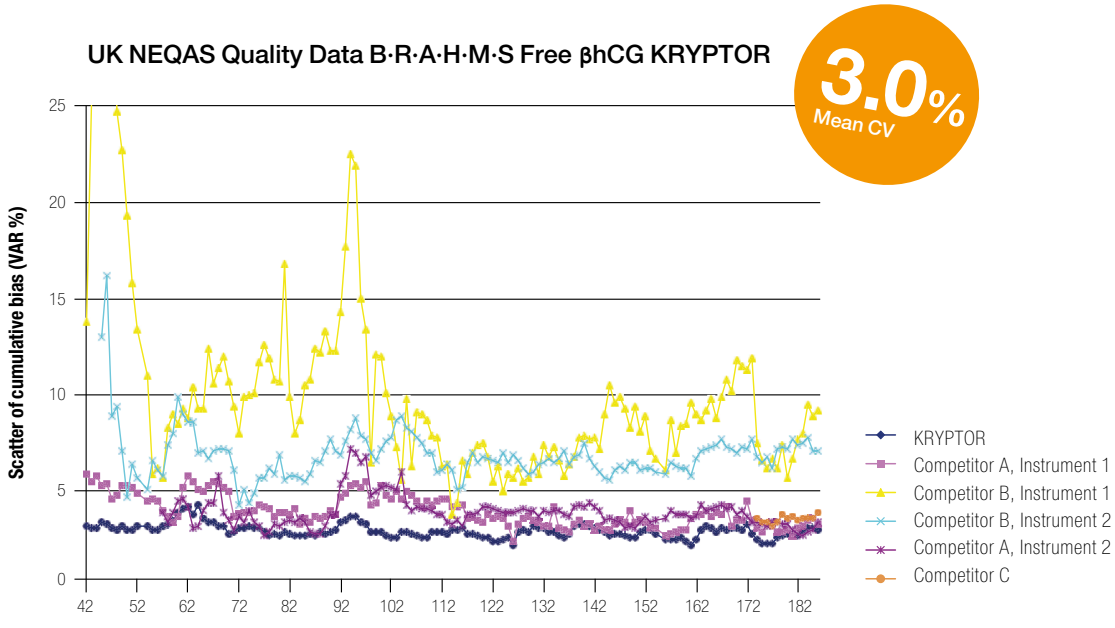
Long-term precision data

Free βhCG

Internal QC Data B·R·A·H·M·S Free βhCG KRYPTOR
(>1100 samples, 68 kit lots, different calibrators and KRYPTOR platforms)



UK NEQAS Quality Data B·R·A·H·M·S Free βhCG KRYPTOR

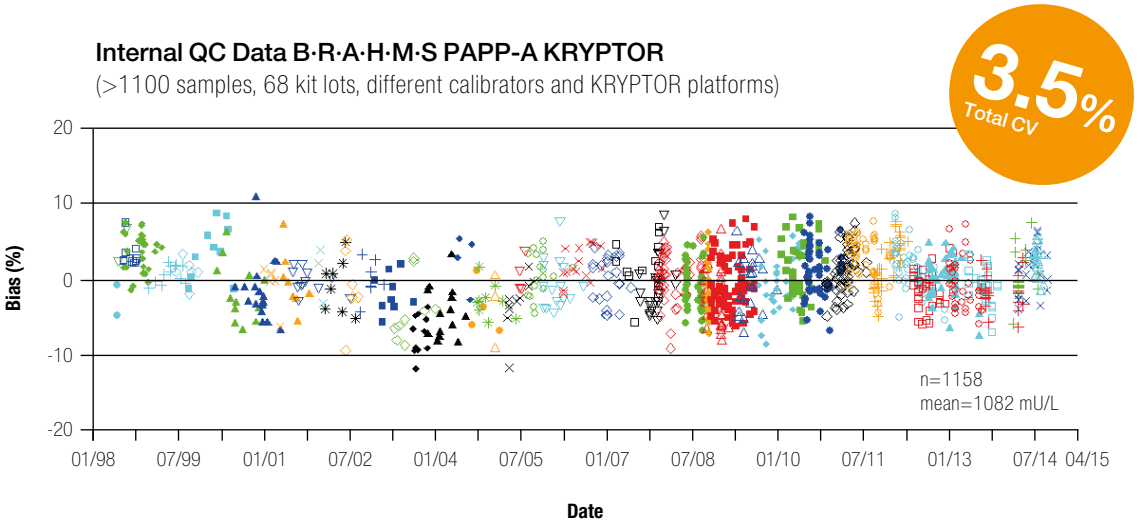


Distribution (February 2003 - February 2015)[6]

1% increase of CV in Free βhCG and PAPP-A MoMs results in an up to fourfold increase of CV in risk.[2] The outstanding precision and stability of the B·R·A·H·M·S assays is proved by the independent United Kingdom National External Quality Assessment Service (UK NEQAS)[7] analysis since 2003. B·R·A·H·M·S provides 16 years of continuous QC data proving an outstanding lot-to-lot stability.

Internal QC Data B·R·A·H·M·S PAPP-A KRYPTOR

(>1100 samples, 68 kit lots, different calibrators and KRYPTOR platforms)

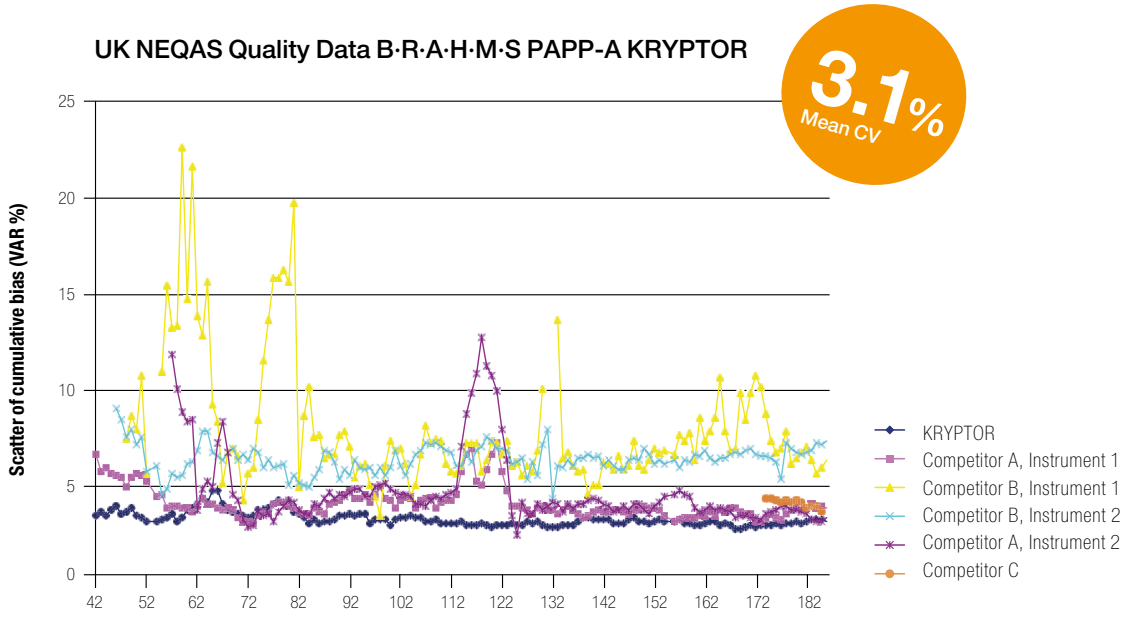


CV = coefficient of variation, shows the extent of variability in relation to the mean.

Bias = percentage of deviation from the average

PAPP-A

UK NEQAS Quality Data B·R·A·H·M·S PAPP-A KRYPTOR



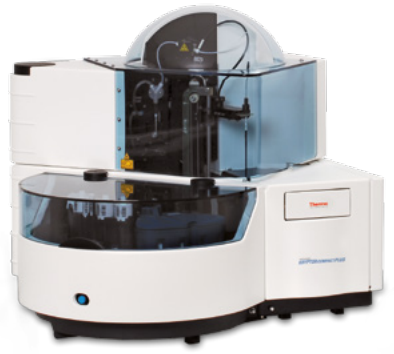
Distribution (February 2003 - February 2015)[6]

16 Years Reliable Results

16 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

The Fetal Medicine Foundation



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 **AFP** KRYPTOR	Art. no.: 816.075
• 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 **Inhibin A** KRYPTOR	(under development)
• B·R·A·H·M·S **PAPP-A** KRYPTOR	Art. no.: 866.075
• B·R·A·H·M·S **PIGF** KRYPTOR*	Art. no.: 844.075
• B·R·A·H·M·S **PIGF plus** KRYPTOR*	Art. no.: 859.075
• B·R·A·H·M·S **sFlt-1** KRYPTOR*	Art. no.: 845.075
• B·R·A·H·M·S **uE3** KRYPTOR	(under development)
• B·R·A·H·M·S **Fast Screen pre I plus Software**	Art. no.: 105750

* Available on KRYPTOR compact PLUS only

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2 Spencer K. Risk, a QC parameter. DSNEWS 2003,10(1):30-31
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4 Spencer K et al. Presentation on B·R·A·H·M·S KRYPTOR User Meeting, Cambridge, March 2007
5 Wright, D. Presentation at FMF World congress; June 2010
6 Monthly UK NEQAS reports, February 2003 – February 2015
7 http://www.ukneqas.org.uk

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