thermoscientific

The gold standard in prenatal screening

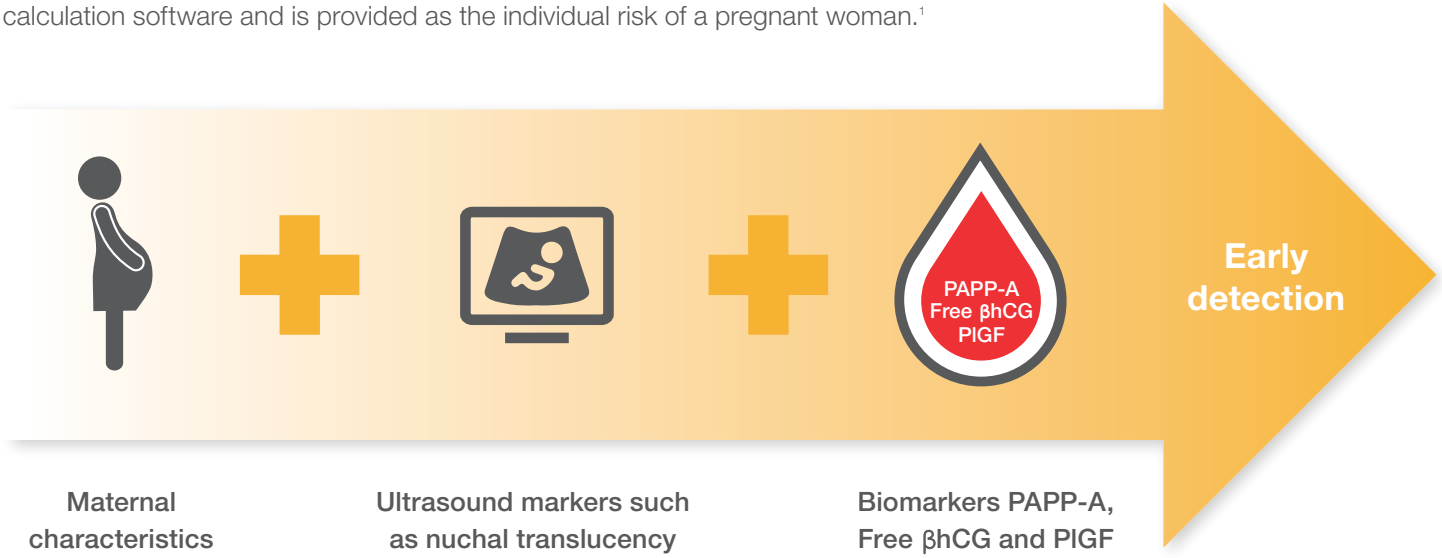
Combined 1st trimester screening with PAPP-A, Free βhCG and PlGF

ThermoFisher SCIENTIFIC

First trimester combined screening

Identification of multiple pregnancy complications

The main advantage of the first trimester combined screening approach is the possibility to predict many major fetal and maternal complications early in pregnancy by combining maternal characteristics and history with findings of biochemical and biophysical tests. The result of the screening is calculated via an appropriate risk calculation software and is provided as the individual risk of a pregnant woman.[1]



Maternal characteristics and history

Ultrasound markers such as nuchal translucency (NT) and nasal bone (NB)

Biomarkers PAPP-A, Free βhCG and PlGF in maternal blood

Because quality matters

It is essential that the result of a risk calculation provided to the pregnant woman is as reliable and accurate as possible. This can only be achieved by using the best available methods.

Biomarkers improve screening performance

With the combined screening approach, a detection rate for trisomy 21 and trisomy 18/13 of 90% and 95% respectively can be achived at a false positive rate of 3.1%.[2] In addition to the risk assessment for fetal aneuploidies, biomarkers can also be used to screen for other conditions. Measurement of serum **PIGF** and **AFP** can be performed in the same sample on the same platform and can significantly improve screening performance for

- **pre-eclampsia**
- **fetal growth restriction**
- **preterm birth**[3,4,5]

B·R·A·H·M·S biomarkers

- Outstanding long-term lot-to-lot stability[6]
- Highest precision for reliable results[6]
- CE marked and FMF approved for all indications

Highly precise biomarker determination

B·R·A·H·M·S Fast Screen pre I plus

- CE marked software for risk calculation of trisomies, pre-eclampsia and neural tube defects
- High quality algorithms based on FMF data and database with over 220 000 pregnancies[7]
- Stable KRYPTOR™ medians[8]

Reliable and effective risk calculation

B·R·A·H·M·S KRYPTOR instruments

- Fully automated random access immunoanalyzer
- Unique and Nobel Prize® winning TRACE™ technology

Fast, efficient and precise measurements

Key elements of calculating the risk

Accurate determination of biochemical and ultrasound markers

PAPP-A and Free βhCG on KRYPTOR Systems

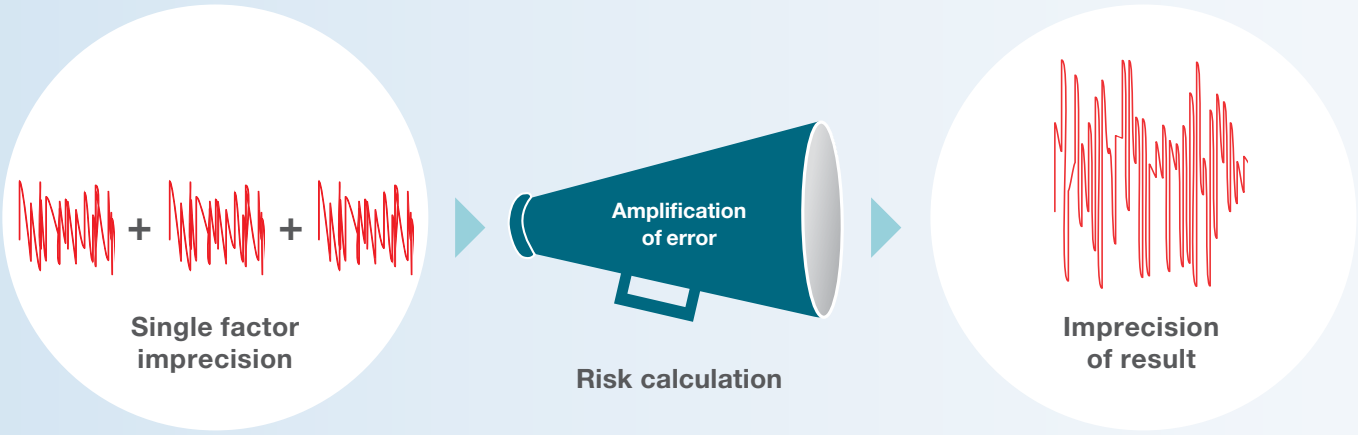
The calculation of the individual risk is based on numerous input factors: measurement of the maternal serum markers PAPP-A and Free βhCG, several ultrasound parameters, and various correction factors from maternal history.

Every single factor has a certain imprecision which influences the risk calculation. The more parameters included in the risk calculation, the higher the total imprecision of the final result – the individual risk.[9]

Therefore, the use of the most precise available methods in 1st trimester screening is of utmost importance.[10]

The biochemical assays Thermo Scientific™ B·R·A·H·M·S™ PAPP-A KRYPTOR™ and Thermo Scientific B·R·A·H·M·S Free βhCG KRYPTOR provide highly precise measurements and a consistent and excellent long-term performance.[6]

The analytical error has a great impact on the calculation of the risk in 1st trimester screening[11]



Input

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

Output

Individual risk

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

Besides the measurement of the biochemical markers, the determination of ultrasound markers such as nuchal translucency (NT) and nasal bone (NB) at weeks 11-13 is the most important factor in first trimester aneuploidy screening. Again, accuracy in the measurement as well as the correct determination of the gestational age is essential for a correct risk calculation. A reliable result depends on the skills and experience of the ultrasound examiners and requires a high quality ultrasound device.[12]

It is recommended that a sonographer holds a certification of the Fetal Medicine Foundation (FMF)[13] or a corresponding local organization.

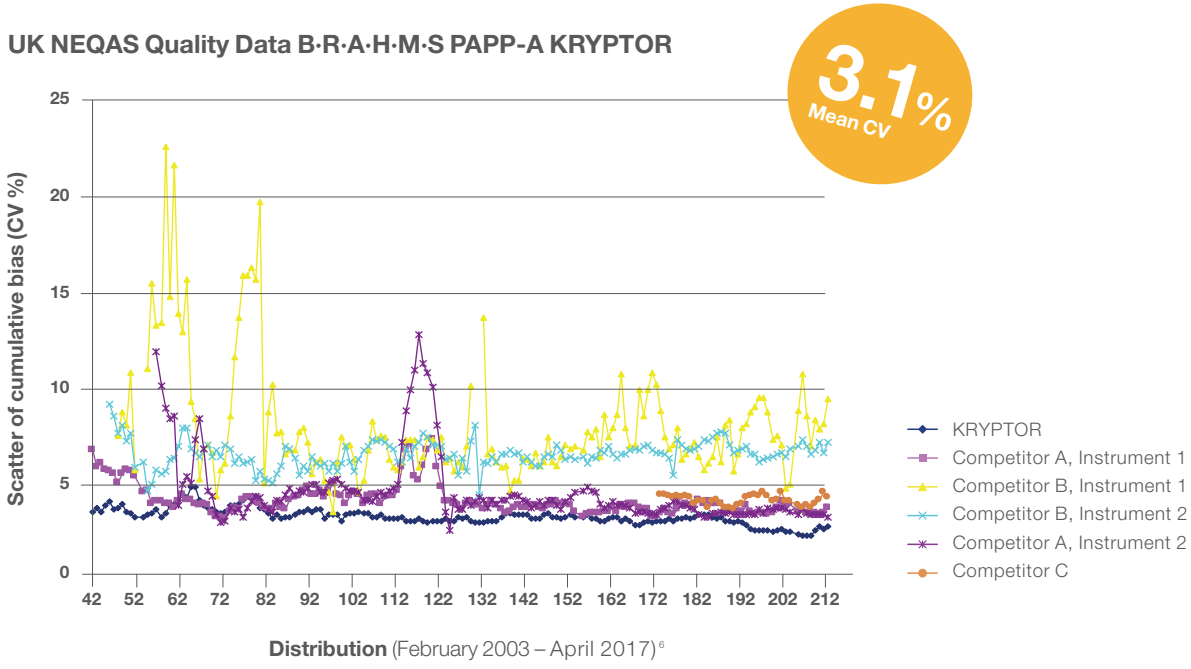
The Fetal Medicine Foundation approval requires the commitment to the highest quality standard and an ongoing quality assurance. Thermo Scientific B·R·A·H·M·S serum markers and Thermo Scientific B·R·A·H·M·S KRYPTOR Systems fulfill these strict quality standards since 1999.

Proof of quality: Long-term precision data

The coefficient of variation (CV) is a measure for precision showing the extent of variability in relation to the mean. The lower the CV the higher the precision of the biomarker measurement.

PAPP-A and Free βhCG measured on KRYPTOR instruments provide the lowest mean CV and therefore the highest precision as shown by the external UK NEQAS data.[6]

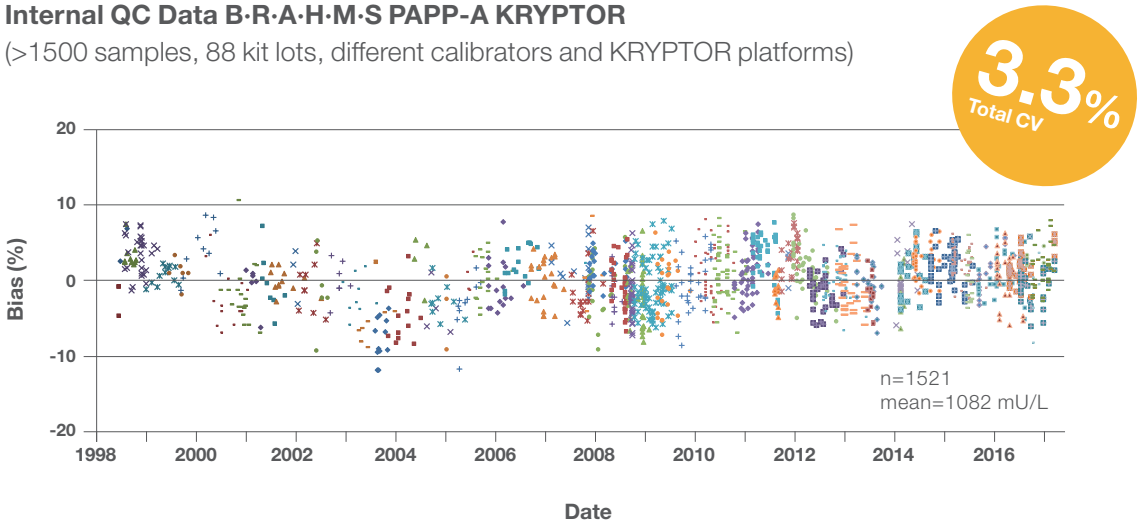
UK NEQAS Quality Data B·R·A·H·M·S PAPP-A KRYPTOR



Distribution (February 2003 – April 2017)[6]

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

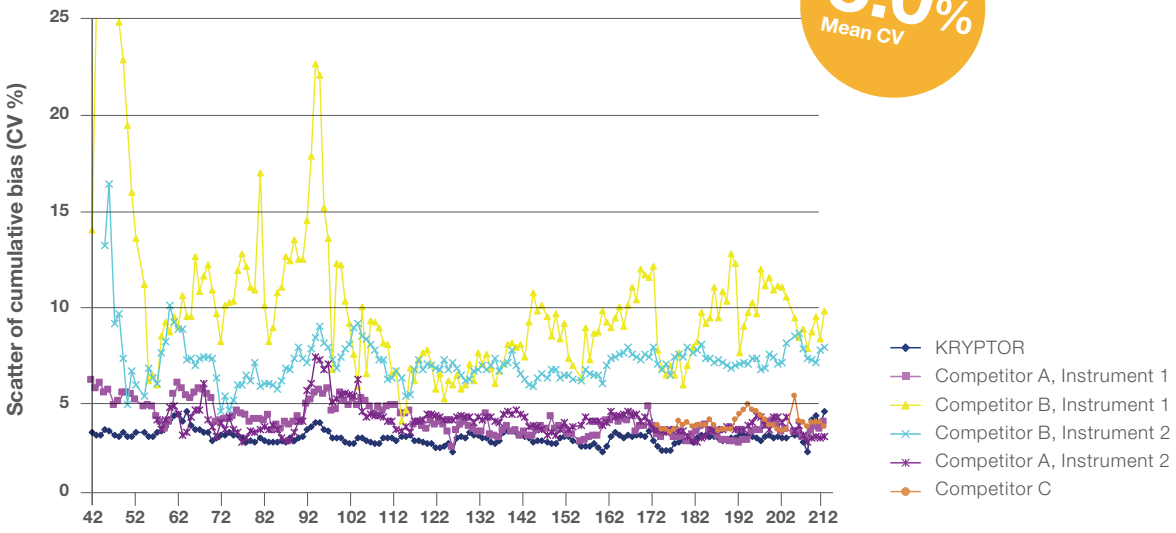
(>1500 samples, 88 kit lots, different calibrators and KRYPTOR platforms)



The outstanding precision and stability of the B·R·A·H·M·S prenatal screening assays is proved by the independent United Kingdom National External Quality Assessment Service (UK NEQAS)[14] analysis since 2003.

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

3.0% Mean CV

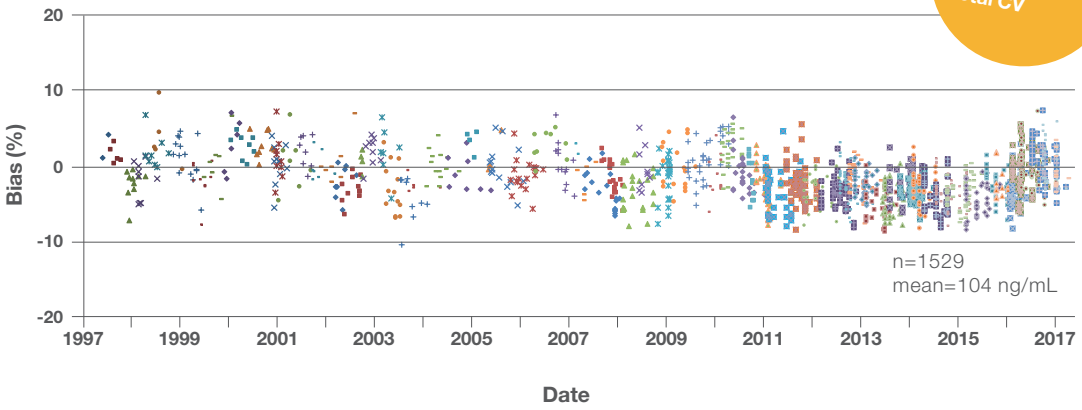


Distribution (February 2003 – April 2017)[6]

Internal QC Data B·R·A·H·M·S Free βhCG KRYPTOR

(>1500 samples, 84 kit lots, different calibrators and KRYPTOR platforms)

3.1% Total CV



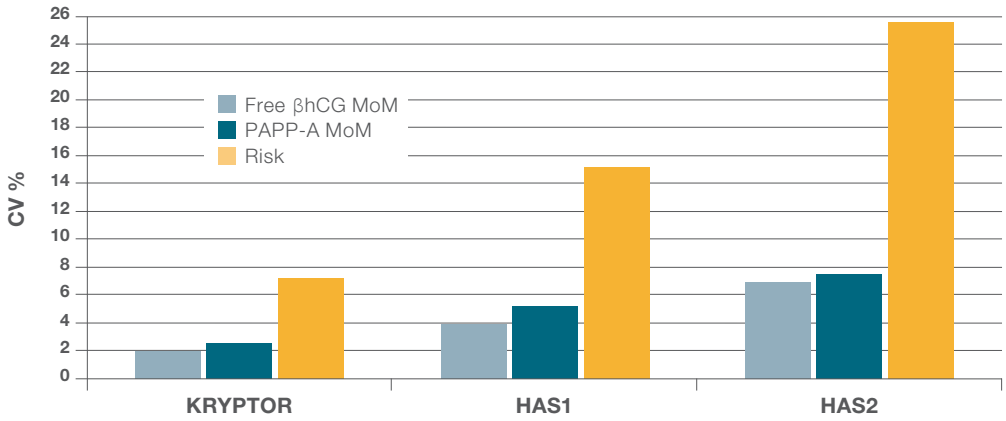
Reproducibility: A measure for quality

Influence of reproducibility on risk quality

Simulation to demonstrate the impact of the analytical variability on risk estimates: [10]

- Between-day variation of 1st trimester risk using the standard deviation for PAPP-A and Free βhCG 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%!



Adding PlGF to T21 screening strategies

Besides the proven benefits of Placental Growth Factor (PlGF) in first trimester pre-eclampsia screening [15-18] this biomarker can also be intergrated into first trimester screening strategies for fetal aneuploidies. In the first trimester, **PlGF levels are significantly decreased** in pregnancies with a fetus affected by trisomy 21 compared to healthy controls.[19]

Implementation of PlGF in different screening strategies for trisomy 21 can either **increase the detection rate** or **decrease the false-positive rate**. In consequence, an improved false-positive rate results in a reduced number of women who will require an invasive test.[19]

Median placental growth factor multiples of the median in trisomy 21 and impact on performance of combined first-trimester screening in selected studies [19]

First-trimester studies on PlGF	Trisomy 21			Combined screening			
				Without PlGF		With PlGF	
	n	GA (weeks)	Median PlGF-MoM	FPR (%)	DR (%)	FPR (%)	DR (%)
Prospective							
Pandya et al.[20]	44	11–13	0.61	2.7	85	2.6	88
Retrospective							
Zaragoza et al.[21]	90	11–13	0.71	3.0	60	3.0	67
Cowans et al.[22]	70	11–13	0.76	3.0	91	3.0	92
Koster et al.[23]	91	11–13	0.78	3.0	71	3.0	73
Kagan et al.[19]	100	11–13	0.73	2.7	85	2.6	87
Koster et al.[23]	60	8–10	0.84	3.0	79	3.0	80

This improved screening performance can also be considered as an added benefit when screening for pre-eclampsia, where PlGF is used as a routine biomarker.

Thermo Scientific B·R·A·H·M·S prenatal screening biomarkers

High sensitivity and exceptional precision

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

Automated immunofluorescent assay for the determination of pregnancy associated plasma protein-A (PAPP-A) in human serum and heparin plasma.

- **CE mark for trisomy and pre-eclampsia first trimester screening**
- **75 determinations per kit**
- **19 min incubation time**
- **Single-point calibration**
- **Wide measuring range: 0.004–90 IU/L**

B·R·A·H·M·S PAPP-A KRYPTOR provides an **outstanding precision** with a mean CV of only 3.1%, proven by UK NEQAS data 2003–2017.[6]

Thermo Scientific
B·R·A·H·M·S Free βhCG KRYPTOR

Automated immunofluorescent assay for the determination of free beta subunit of human chorionic gonadotropin hormone (hCG) in human serum.

- **CE mark for trisomy screening in first and second trimester**
- **75 determinations per kit**
- **19 minutes incubation time**
- **Single-point calibration**
- **Wide measuring range: 0.16–50 000 IU/L**

B·R·A·H·M·S Free βhCG KRYPTOR provides an **outstanding precision** with a mean CV of only 3.0%, proved by UK NEQAS data 2003–2017.[6]

Thermo Scientific
B·R·A·H·M·S PIGF plus KRYPTOR

Automated immunofluorescent assay for the determination of placental growth factor (PlGF) in human serum. The assay is specific for the measurement of human free PlGF-1.

- **CE mark for trisomy and pre-eclampsia first trimester screening**
- **75 determinations per kit**
- **29 min incubation time**
- **Single-point calibration**
- **Wide measuring range: 3.6–7000 pg/mL**

With the lowest FAS and lowest cross-reactivity to other PlGF isoforms B·R·A·H·M·S PlGF plus KRYPTOR provides the **highest sensitivity** needed for reliably measuring low PlGF levels in the first trimester of pregnancy.[24]

Thermo Scientific
B·R·A·H·M·S KRYPTOR compact PLUS

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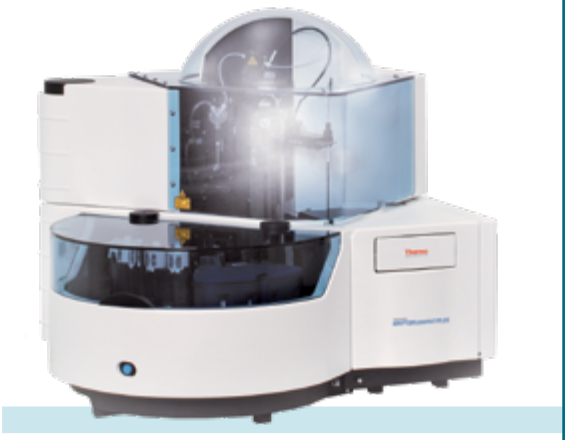
Exceptionally precise, fast and easy

Thermo Scientific B·R·A·H·M·S KRYPTOR compact PLUS



18 Years Reliable Results
18 Years Confident Decisions

The Fetal Medicine Foundation

- All KRYPTOR platforms FMF approved
- In routine use by FMF since 1999
- Excellent precision and proven median stability
- OSCAR compatible

Thermo Scientific B·R·A·H·M·S Biomarkers Prenatal Screening Portfolio 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***	Art. no.: 850.075
B·R·A·H·M·S **PAPP-A** KRYPTOR	Art. no.: 866.075
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**	Art. no.: 803.075
B·R·A·H·M·S **Fast Screen pre I plus Software**	Art. no.: 105750

* Available on KRYPTOR compact PLUS and KRYPTOR GOLD
** Available on KRYPTOR, KRYPTOR compact PLUS and KRYPTOR GOLD
*** Available on KRYPTOR GOLD

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Clinical Diagnostics

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