



Second trimester trisomy screening with assays on KRYPTOR analyzers

Different screening strategies with high-quality biomarker assays



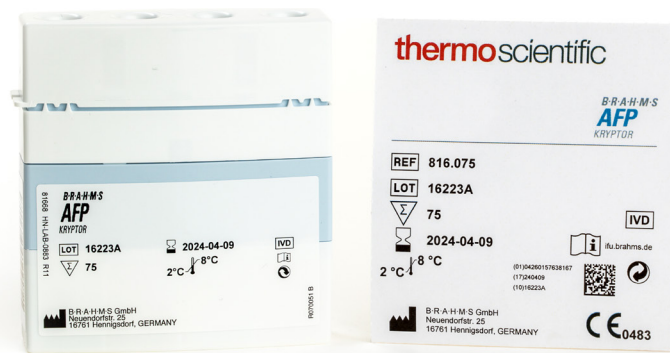
B·R·A·H·M·S KRYPTOR GOLD

Thermo Scientific™ B·R·A·H·M·S™ AFP KRYPTOR™,
Thermo Scientific™ B·R·A·H·M·S™ Free β hCG KRYPTOR™,
Thermo Scientific™ B·R·A·H·M·S™ hCG+ β KRYPTOR™,
Thermo Scientific™ B·R·A·H·M·S™ uE3 KRYPTOR™



B·R·A·H·M·S KRYPTOR compact PLUS

and Thermo Scientific™ B·R·A·H·M·S™ Inhibin A KRYPTOR™ assays are used in combination with B·R·A·H·M·S™ KRYPTOR™ analyzers



Ease of handling

	AFP*	hCG+β*	Free βhCG*	uE3*	Inhibin A**
Sample volume	14 µl	26 µl	26 µl	50 µl	70 µl
Incubation time	9 min	14 min	19 min	19 min	39 min (preincubation step 30 min, incubation step 9 min)
Linear direct measuring range	1.91-700 ng/mL	5.0-2000 IU/L	0.74-150 IU/L	0.52-17 nmol/L	53.3-5000 pg/mL
Limit of Detection	0.21 ng/mL	2.0 IU/L	0.09 IU/L	0.20 nmol/L	20.9 pg/mL
Limit of Quantitation	1.91 ng/mL	5.0 IU/L	0.74 IU/L	0.52 nmol/L	53.3 pg/mL
Kit stability on board	15 days	29 days	29 days	15 days	15 days
Calibrator	1 point	1 point	1 point	2 points	1 point
Calibration stability	15 days	15 days	15 days	7 days	7 days
Assay principle	Sandwich	Sandwich	Sandwich	Competitive	Sandwich

* AFP = Alpha-fetoprotein

hCG+β = total human Chorionic Gonadotropin Hormone

Free βhCG = Free beta subunit of human Chorionic Gonadotropin Hormone

uE3 = unconjugated estriol

** Inhibin A is available on B-R-A-H-M-S KRYPTOR GOLD only.

Specimen collection and storage

Analyte	Sample matrix	Room temperature	2-8°C	Freezing	Freeze-thaw cycles
AFP	Serum, plasma (heparin), amniotic fluid*	8h	24h	-20°C (up to 1 years)	Not recommended
hCG+β	Serum	8h	24h	-20°C (up to 1 years)	Not recommended
Free βhCG	Serum	8h	24h	-20°C (up to 6 years)	Not recommended
uE3	Serum	8h	24h	-20°C (up to 1 years)	Not recommended
Inhibin A	Serum	8h	24h	-20°C (up to 22 months)	Not recommended

*A fixed 1:50 or 1:100 dilution is recommended

Intended use

Risk assessment for	Trisomy 21	Trisomy 18	NTD* in serum and plasma (heparin)	NTD* diagnosis in amniotic fluid
AFP	√	√	√	√
hCG+β	√	√		
Free βhCG	√	√		
uE3	√			
Inhibin A	√			

*Neural tube Defects

Clinical performance

Trisomy risk assessment in second trimester of pregnancy	Sensitivity (%)	Specificity (%)	Reference
Screening for T21 (hCG+β or Free βhCG + AFP+ uE3 + Inhibin A)	75.8	95	Internal study (291 unaffected and 33 T21 pregnancies)
Screening for T18 (AFP+ Free βhCG)	64.5	99	Spencer K et al., Prenat Diagn 1999

Normal values in serum samples

Data from healthy individuals

Gestational age*	Analyte	ng/ml	n	5th percentile	median	95th percentile
	AFP	IU/L				
	hCG+β	IU/L				
	Free βhCG	IU/L				
	uE3	nmol/L				
	Inhibin A	pg/mL				
14	AFP		529	15.2	26.3	52.5
	hCG+β		429	16 850	40760	87060
	Free βhCG		528	7.4	20	59
	uE3		220	0.96	1.8	3.6
	Inhibin A		53	62	156	427
15	AFP		1908	16.2	29.4	53.4
	hCG+β		1 629	11 870	31550	77520
	Free βhCG		1906	5.6	15	46
	uE3		220	0.91	2.2	4.3
	Inhibin A		50	66	121	272
16	AFP		1090	18.8	34.0	62.5
	hCG+β		854	8 797	25 460	64 070
	Free βhCG		1088	4.2	12	35
	uE3		243	1.2	2.7	5.3
	Inhibin A		62	41	113	370
17	AFP		509	21.4	37.1	66.5
	hCG+β		514	7 491	18 830	51 240
	Free βhCG		507	3.4	9.1	26
	uE3		244	1.9	3.6	7.5
	Inhibin A		99	64	131	274
18	AFP		246	24.5	41.2	88.7
	hCG+β		115	5 489	17 480	47 730
	Free βhCG		246	2.9	8.4	27
	uE3		68	2.6	4.1	7.8
	Inhibin A		51	39	129	276
19	uE3		53	3.1	5.5	9.0
	Inhibin A		53	44	135	306
20	uE3		8	3.9	5.8	9.5
	Inhibin A		45	32	142	362

*completed week

Normal values for AFP in amniotic fluid

Gestational age (completed weeks)	n	Median (ng/mL)
13	129	14 600
14	382	15 580
15	512	14 870
16	495	12 980
17	280	10 630
18	131	8 835
19	61	7 350

Gestational age (completed weeks)	n	Median (ng/mL)
20	30	5 188
21	39	4 230
22	19	3 557
23	17	3 001
24	10	2 205
25	7	2 277
26	9	2 060

Precision

Precision/Repeatability and within-laboratory precision

Repeatability and within-laboratory precision % CV were calculated from the measurement of samples over 20 days, with 2 runs per day in 2 replicates using 2 (3 for uE3 and Inhibin A) reagent lots according to CLSI Guideline EP05-A3 (Evaluation of Precision of Quantitative Measurement Procedures).

Precision / Reproducibility

For reproducibility, samples were measured for 5 days, with 1 run per day on 3 instruments in 5 replicates and calculated according to CLSI Guideline EP05-A3 (Evaluation of Precision of Quantitative Measurement Procedures).

AFP

Precision	Conc (ng/mL)	Repeatability CV%	Within - lab precision CV%	Reproducibility CV%
Sample 1	2.85	2.9	-	-
Sample 5	5.29	-	8.3	-
Sample 9	5.35	-	-	4.7
Sample 2	11.1	1.2	-	3.6
Sample 6	11.2	-	3.8	-
Sample 7	68.6	-	2.7	-
Sample 3	511	1.2	-	-
Sample 8	1096	-	2.9	-
Sample 11	1149	-	-	3.0
Sample 4	335142	1.4	-	-

hCG+β

Precision	Conc (IU/L)	Repeatability CV%	Within - lab precision CV%	Reproducibility CV%
Sample 11	8.9	-	-	8.1
Sample 1	12	5.3	6.8	-
Sample 2	29	3.7	7.4	3.9
Sample 3	65	1.5	-	-
Sample 13	107	-	-	1.7
Sample 8	449	-	3.5	-
Sample 4	1287	0.9	2.8	-
Sample 14	1324	-	-	2.1
Sample 10	2882	-	2.1	-
Sample 5	2939	0.8	-	-
Sample 15	2998	-	-	1.6

Free β hCG

Precision	Conc (IU/L)	Repeatability CV%	Within - lab precision CV%	Reproducibility CV%
Sample 1	0.56	8	17.7	-
Sample 9	1	-	-	10.8
Sample 2	2.9	2.1	5.8	-
Sample 10	11	-	-	4.3
Sample 7	35	-	3.8	-
Sample 11	67	-	-	4.5
Sample 3	97	0.7	-	-
Sample 12	193	-	-	1.2
Sample 4	1000	1.9	3.6	-

uE3

Precision	Conc (nmol/L)	Repeatability CV%	Within - lab precision CV%	Reproducibility CV%
Sample 4	0.75	-	13.9	-
Sample 1	0.91	7.4	-	-
Sample 7	1.7	-	-	9.2
Sample 5	1.9	-	9.5	-
Sample 8	2.9	-	-	7.2
Sample 2	3.0	4.3	-	-
Sample 6	8.2	-	6.3	-
Sample 9	8.4	-	-	5.7
Sample 3	12	3.8	-	-

Inhibin A

Precision	Conc (pg/mL)	Repeatability CV%	Within - lab precision CV%	Reproducibility CV%
Sample 1	113	6.7	8.7	-
Sample 7	116	-	-	8.3
Sample 8	264	-	-	5.4
Sample 2	304	3.4	5.4	-
Sample 3	1165	2.3	-	-
Sample 9	2738	-	-	4.0
Sample 6	4247	-	4.0	-

Calibration

Analyte	Units	International Standard
AFP	ng/mL	1st NIBSC 72/225
hCG+β	IU/L	4th WHO 75/589
Free βhCG	IU/L	NIBSC 75/551
uE3	nmol/L	No international standard available
Inhibin A	pg/mL	WHO 91/624



Reagents overview

Kits

	Content	Shelf life* (2-8°C)	Stability after opening onboard the instrument (2-8°C)
B-R-A-H-M-S AFP KRYPTOR	75 tests Reconstituted on the instrument	12 months	15 days
B-R-A-H-M-S hCG+β KRYPTOR	50 tests Reconstituted on the instrument	12 months	29 days
B-R-A-H-M-S Free βhCG KRYPTOR	75 tests Ready for use	12 months	29 days
B-R-A-H-M-S uE3 KRYPTOR	75 tests Reconstituted on the instrument	12 months	15 days
B-R-A-H-M-S Inhibin A KRYPTOR	75 tests Reconstituted on the instrument	15 months	15 days

Calibrators

	Content	Target concentrations	Shelf life	Stability after opening at room temperature (18-25°C)
B-R-A-H-M-S AFP KRYPTOR	6 vials Ready for use	150 ng/mL	12 months	2h
B-R-A-H-M-S hCG+β KRYPTOR	6 vials Ready for use	250 IU/L	19 months	2h
B-R-A-H-M-S Free βhCG KRYPTOR	6 vials Ready for use	40 IU/L	12 months	2h
B-R-A-H-M-S uE3 KRYPTOR	2 x 6 vials Reconstituted manually with 0.75 mL of distilled water	Cal1: 2 nmol/L Cal2: 1000 nmol/L	24 months	5h
B-R-A-H-M-S Inhibin A KRYPTOR	6 vials Reconstituted manually with 0.85 mL of distilled water	1000 pg/mL	24 months	5h

Controls

	Content	Target concentrations	Shelf life* (2-8°C)	Stability after opening		
				Room temperature	2-8°C	Freezing
B·R·A·H·M·S GM KRYPTOR QC	6 vials (2 x 3 levels) Reconstituted manually with 3 ml of distilled water	AFP Level 1: 10 ng/mL Level 2: 35 ng/mL Level 3: 100 ng/mL Free βhCG Level 1: 80 IU/L Level 2: 20 IU/L Level 3: 8 IU/L	24 months	8h	24h	1 month at -20°C
B·R·A·H·M·S hCG+β KRYPTOR QC	6 vials (3 x 2 levels) Reconstituted manually with 2 ml of distilled water	Level 1: 20 IU/L Level 2: 200 IU/L	24 months	8h	24h	2 months at -20°C
B·R·A·H·M·S uE3 KRYPTOR	6 vials (2 x 3 levels) Reconstituted manually with 2 ml of distilled water	Level 1: 3.4 nmol/L Level 2: 6.8 nmol/L Level 3: 13.6 nmol/L	24 months	5h	24h	1 month at -20°C
B·R·A·H·M·S Inhibin A KRYPTOR	6 vials (2 x 3 levels) Reconstituted manually with 2 ml of distilled water	Level 1: 200 pg/mL Level 2: 400 pg/mL Level 3: 800 pg/mL	24 months	5h	24h	1 month at -20°C

* from date of production



References

1. IFU B·R·A·H·M·S AFP KRYPTOR
2. IFU B·R·A·H·M·S hCG+β KRYPTOR
3. IFU B·R·A·H·M·S Free βhCG KRYPTOR
4. IFU B·R·A·H·M·S uE3 KRYPTOR
5. IFU B·R·A·H·M·S Inhibin A KRYPTOR



Advantages/Benefits

Safe results

KRYPTOR assays are not impacted by biotin and other unknown interferences

High-quality and reliable tests

Lot-to-lot stability provides high quality for essential indications

Outstanding precision

Nobel Prize™ winning TRACE™ technology provides high precision for the entire measurement range

Optimized workflow

Self-determining dilution factor for out-of-range samples

Different screening Strategies

Double, triple and quadruple tests implementable screening strategies

AFP intended use in Neural Tube Defects (NTD)

Alpha-fetoprotein in serum for NTD screening and in amniotic fluid for NTD diagnosis

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