Information for physicians

PrenaTest®

Non-invasive prenatal testing (NIPT)
Analysis in Germany since 2012

Genome wide
RAA & CNV analysis

eurofins | LifeCodexx

Get Clarity.
Reliable. Rapid. Safe.

Focus on all chromosomes

Europe's first NIPT
Starting from the tenth week of pregnancy (9+0 weeks since LMP) the PrenaTest® determines fetal trisomies 21, 18 and 13, gonosomal aneuploidies (Turner, Triple X, Klinefelter, and XYY syndromes), the 22q11.2 microdeletion (associated with the DiGeorge syndrome) as well as rare autosomal aneuploidies (RAAs) and (Micro-)deletions and -duplications (Copy Number Variations, CNVs) from maternal blood. If desired, the gender of the fetus may also be determined. With the PrenaTest®, you can fully implement the recommendations of the professional societies in Germany, Austria and Switzerland1 as it provides the appropriate test spectrum.

The Plus for more knowledge: Genome wide screening for further autosomal findings
With the **PrenaTest® options 2 Plus** and **3 Plus**, you can additionally determine **rare autosomal aneuploidies** (RAAs) as well as autosomal (micro-)**deletions/-duplications** (Copy Number Variations, CNVs).

The **RAAs** include the **examination of the autosomal chromosomes** 1 – 12, 14 – 17, 19 – 20 and 22 for monosomy and trisomy as well as chromosomes 13, 18 and 21 for monosomy.

	Basic Screening			**Extended Screening**		
	Common Aneuploidies			SCAs	Genome wide screening	
	Trisomy 21	Trisomy 18	Trisomy 13	Sex chromosome aneuploidies	RAAs	CNVs (Micro-)deletions/ -duplications (≥ 7 Mb)
Clinical Manifestation	Down syndrome	Edward syndrome	Patau syndrome	E.g., Turner syndrome, Klinefelter syndrome	Early miscarriage, fetal anomalies, growth retardation UPD and stillbirth	E.g., fetal anomalies, developmental delays
Positive Rate (at Screening)	0.39%	0.13%	0.04%	0.39%	0.34%	0.1%
Combined Positive Rate		0.56%		0.39%	0.44%	

Source: 8, 9

The **CNVs** include detection of (Micro-)**deletions and -duplications** of parts of autosomal chromosomes (Chr. 1 – 22) at a size of ≥7 Mb.

qNIPT or NGS
Two technologies as needed

The smart qNIPT assay is based on a quantitative real-time PCR (qPCR). It assures a cost-efficient and rapid laboratory analysis and is used for PrenaTest® Option 1 for the determination of fetal trisomy 21. Next generation sequencing (NGS) is the most routinely employed NIPT method worldwide and is used to determine a broad range of fetal aneuploidies.

qNIPT – fast and cost-efficient
Due to different methylation patterns of specific gene regions of the maternal and fetal DNA, positive and negative samples will be distinguished. The amount of cffDNA is not decisive for the **qNIPT** assay. It is used to clarify whether the sample contains cffDNA at all.

NGS – proven and well-established
With the method of next generation sequencing (NGS) the cell-free DNA is decoded with the most modern analytical equipment. The objective is to determine whether the quantity of sequences for the respectively investigated chromosome exceeds the normal range found in the case of a euploid, i.e. normal, chromosome set. It is the most widely used NIPT technology worldwide to date and has been validated in numerous studies.

Our **NGS** method enables us to report a valid test result with a low level of cffDNA.[5]

The PrenaTest® has been analyzed in Germany since 2012.

Patient profile

54%
age 35 years and over

60%
week 11 + 0 up to week 14 + 0 p.m.

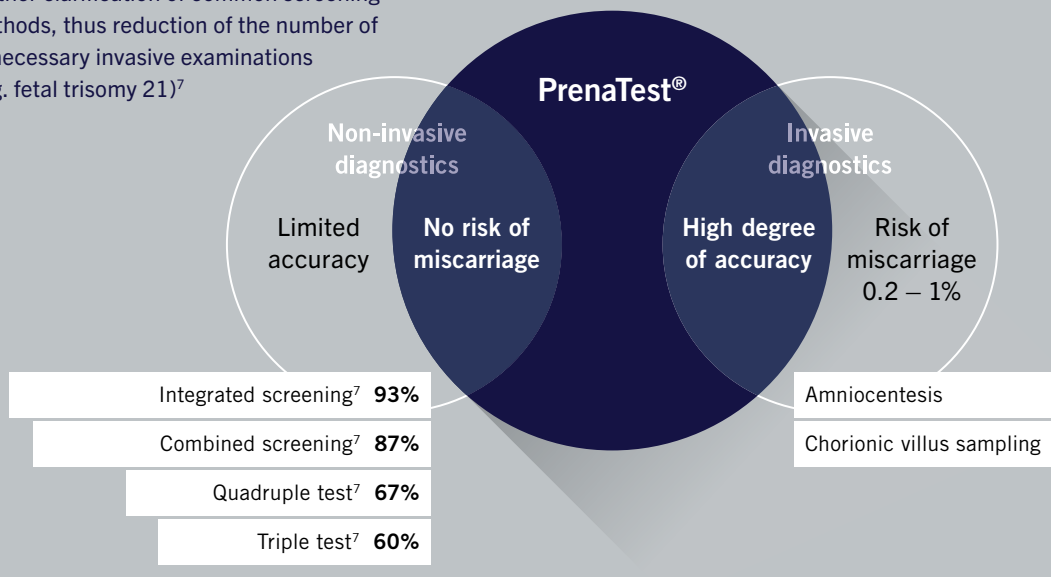
25%
after conspicuous FTS or ultrasound

PrenaTest®
Europe's first NIPT

Depending on the medical question, you can now choose between five test options. The PrenaTest® can be used without restriction after fertility treatment – also egg donation. The waiting time until the test result is only a few business days[6] after receipt of the blood sample in the laboratory and after successful quality control.

Option 1	Option 2	Option 2 *Plus*	Option 3	Option 3 *Plus*
for singleton pregnancy				
	for twin pregnancy			
Trisomy 21				
	Trisomies 18 and 13			
			Turner syndrome	
			Triple X syndrome	
			Klinefelter syndrome	
			XYY syndrome	
		RAAs		**RAAs**
		CNVs		**CNVs**
Optional:				
Gender determination				
	22q11.2 microdeletion (for singleton pregnancy) also as post analysis with data ≤ 3 months; a new blood sample is not required			

Reasons for PrenaTest®
Further clarification of common screening methods, thus reduction of the number of unnecessary invasive examinations (e.g. fetal trisomy 21)[7]



PrenaTest®
Analysis in Germany since 2012

Since its launch in August 2012 as Europe's first NIPT, we have been completely analyzing PrenaTest® in Germany. Below please find the clinical performance data for your genetic counseling.

PrenaTest® Option 1 *

	Trisomy 21
Sensitivity in %	99.21
Specificity in %	99.99
PPV in %	99.20
NPV in %	99.9

Professional societies recommend NIPT – in combination with a qualified ultrasound – as a primary screening for trisomy 21 in pregnant women of all ages and risks.[1] With the PrenaTest® Option 1, you can implement this recommendation cost-effectively for your patient.

175,000
PrenaTest® since market launch in August 2012
(as of 9/2019)

* Data from clinical routine (12/2016 to 05/2019) is based on successfully performed analyzes with valid test results as well as on responses from the physicians to discordant test results.

PrenaTest® Option 2 and 2 *Plus* as well as Option 3 and 3 *Plus*

Sensitivity and specificity for detecting trisomies 21, 18 and 13 for singleton pregnancies[5]

	Trisomy 21	Trisomy 18	Trisomy 13
Sensitivity	>99.9% (130/130)	>99.9% (41/41)	>99.9% (26/26)
2-sided 95% CI	97.1%, 100%	91.4%, 100%	87.1%, 100%
Spezifität	99.90% (1,982/1,984)	99.90% (1,995/1,997)	99.90% (2,000/2,002)
2-sided 95% CI	99.63%, 99.97%	99.64%, 99.97%	99.64%, 99.97%

Estimates for trisomy 21, 18 and 13 in simulated population of twin pregnancies[5]

	Trisomy 21	Trisomy 18	Trisomy 13	Presence of Y
Sensitivity	96.4%	95.7%	93.6%	>99.9%
2-sided 95% CI	(86.4%, 98.9%)	(68.3%, 99.4%)	(64.1%, 98.9%)	(99.9%, >99.9%)
Specificity	99.9 %	>99.9%	>99.9%	>99.9%
2-sided 95% CI	(99.8%, >99.9%)	(99.9%, >99.9%)	(99.9%, >99.9%)	(99.7%, >99.9%)

3,1%
of all PrenaTest® performed on twin pregnancies
(as of 9/2019)

Sensitivity and specificity for rare autosomal aneuploidy (RAAs); including known mosaics[5]

	Sensitivity	Specificity
Estimate % (n/N)	96.4% (27/28)	99.80% (2,001/2,005)
2-sided 95% CI	82.3%, 99.4%	99.49%, 99.92%

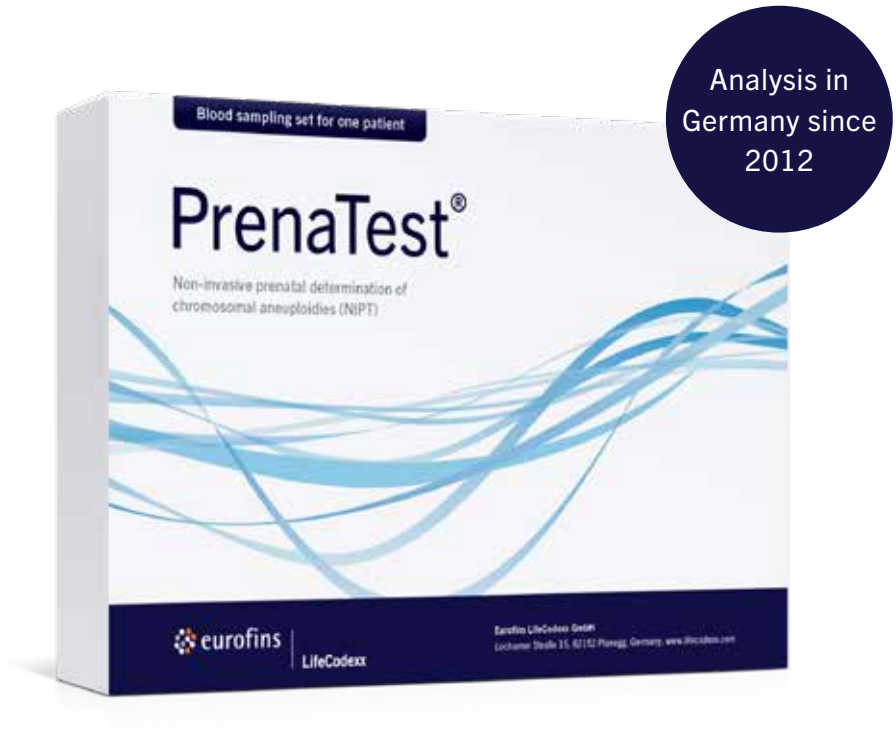
Sensitivity and specificity for Copy Number Variations (CNVs): (Micro-)deletions and -duplications ≥7 Mb size[5]

	Sensitivity	Specificity
	74.1% (20/27)	99.80% (2,000/2,004)

Percent concordance calculated for each sex chromosome within each clinical reference standard outcome[5]

	Phenotype from the newborn (physical exam)		Cytogenetic results				
	Female	Male	XO	XXX	XXY	XYY	Other**
Total	997/997	966/966	19/21	17/17	23/23	11/12	2/2
Percent Concordant	100%	100%	90.5%	100%	100%	91.7%	n.z.***

** Other cytogenetic results were XXXXX and XXYY. *** not applicable



1 Schmid M et al. Cell-Free DNA Testing for Fetal Chromosomal Anomalies in clinical practice: Austrian-German-Swiss Recommendations for non-invasive prenatal tests (NIPT). Ultraschall Med. 2015 Oct;36(5):507-10. doi: 10.1055/s-0035-1553804. Epub 2015 Oct 15.
2 Galjaard RJ et al. Implementing NIPT as part of a national prenatal screening program: The Dutch TRIDENT studies. Prenat Diagn 2018;38(S1):8
3 Scott et al. Rare autosomal trisomies: Important and not so rare. Prenat Diagn 2018;38:765-71
4 Pertile MD Genome-wide cell-free DNA-based prenatal testing for rare autosomal trisomies and subchromosomal abnormalities. In: Nonivasive Prenatal Testing, Academic Press 2018, Eds Page-Christiaens and Klein
5 Illumina VeriSeq NIPTSolution v2 Package Insert; Document#1000000078751v01; August 2019
6 Turnaround times are valid after sample receipt in the laboratory and following successful quality control. From Monday to Friday, except Saturday, Sunday and public holidays in Baden-Wuerttemberg, Germany. Turnaround times depend on the chosen test option.
7 Cuckle H, Benn P, Wright d (2005). Down syndrome screening in the first and / or second trimester: model predicted performance using meta-analysis parameters. Seminars in Perinatalogy 29,252-257
8 Pertile et al. Clin Chem, 2021;67:1210 – 1219
9 Liang et al. Gen Med, 2019;21:1998

Eurofins LifeCodexx
First NIPT provider in Europe

We have been developing clinically validated, non-invasive prenatal tests (NIPT) since 2010. In 2012, the PrenaTest® was launched on the market as Europe's first NIPT. It has now become firmly established in many gynecological practices in Europe, the Middle East, and Asia as a reliable, fast and safe test method. Since the start of 2018, LifeCodexx has belonged to Eurofins Scientific, a leading international laboratory group, and has strengthened the technology portfolio of the Clinical Diagnostics business unit.

www.lifecodexx.com

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