Analysis of Non Invasive Prenatal Genetic Testing In Europe Market

Project report submitted in fulfillment of the requirements for the degree of

Masters of Technology

(INTEGRATED 5 YEARS)

In

Biotechnology and Bioinformatics Engineering

By

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May, 2019

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CERTIFICATE

This is to certify that the work which is being presented in the title of **"Analysis of Non Invasive Prenatal Genetic Testing In Europe Market"** for the end semester of Integrated M.Tech in Biotechnology and submitted in the department of Biotechnology and Bioinformatics, **Jaypee University of Information Technology, Waknaghat** is an authentic record of work carried out by Shivangi Kapoor (141843) during the period of February 2019 to May 2019 under the supervision of Mrs.**Shivani Hanjura**, Senior Manager, HealthCare Team, Unimrkt Research.

The above statement made is correct to the best of my knowledge.

Date: May 2018

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ACKNOWLEDGEMENT

The work carried out in this thesis is an outcome of continual work over a period of time and intellectual support from various sources. It is therefore almost impossible to express adequately the debts owed to many persons who have been instrumental in imparting this work a successful status.

I take this opportunity to thank our esteemed mentor and supervisor **Ms. Shivani Hanjura**, Senior Manager, Healthcare Department, Unimrkt Research and **Ms. Dipika Maheshwari,** Team Leader, Healthcare Department for lending us stimulating suggestions, innovative quality guidance and creative thinking. Their practicality, constructive criticism, constant encouragement and advice helped me in all stages of the project. Their scientific views and scientific approach will always be the source of motivation for me. We are grateful to them for the support, they provided me in doing things at my pace and for being patient with my mistakes.

I can never forget my guide in the University, **Dr. Jitendraa vashitt**, Head of the department, Biotechnology and Bioinformatics and **Ms Monika Chaudhary** who have always been a constant source of inspiration and helped me in numerous ways.

I would also express my gratitude towards my family and my friends for their support throughout the execution of this study.

Shivangi Kapoor

Date:

DECLARATION

I hereby declare that the present work on **Analysis of Non Invasive Prenatal Genetic Testing in Europe Market** is a record of original work done by me under the guidance of **Shivani Hanjura at Unimrkt Research** (Gurgaon), from February 2019 to May 2019.

I also declare that no part of this report has previously been submitted to any University for acquiring any degree.

SUMMARY

Non-invasive prenatal testing is a next generation prenatal genetic testing. It is majorly used to screen Down 's syndrome in the fetus. Many NIPT tests in the market also offer screening for other chromosomal abnormalities such as Edwards syndrome, Pataus syndrome and sex chromosomal abnormalities such as Turners syndrome, Klienfilters syndrome, Jacobs syndrome and Triple X syndrome. Today, some tests may also additionally screen for selected microdeletion. This report focuses on the use of NIPT tests globally and in Europe. It includes the procedure of NIPT general workflow. It also includes competitive analysis of three major companies in the global NIPT industry, which are Natera, Lab Corp (Sequenome), and Illumina. It provides with a comparative study of the three commercial NIPT solutions offered by these companies.

CHAPTER 1: INTRODUCTION

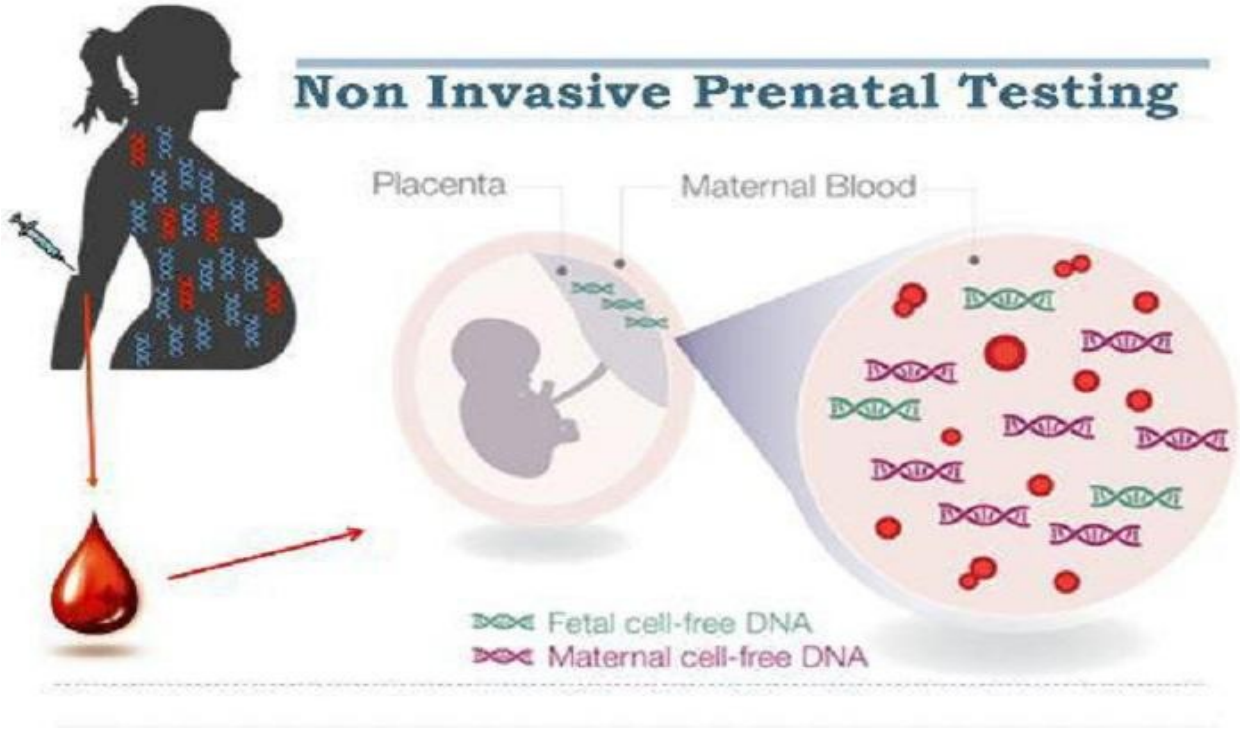
Prenatal genetic screening is done to know whether the fetus might have any genetic abnormality. Prenatal genetic tests include both screening and diagnosis test. Screening test lets us know the risk of the fetus having any genetic abnormality. If the results for screening tests conclude positive, it is important to take a diagnostic test for the particular genetic abnormality.

These tests are of invasive as well as non-invasive methods. This report focuses on the non-invasive technology. Non- invasive genetic screening tests includephysical fetal examination using medical imaging technology as well as Non-invasive prenatal test (NIPT). NIPT requires analysis of fetal cfDNA found in the mother's blood.

The fetal genetic disorders include chromosomal aneuploidies such as trisomy (presence of extra chromosome and monosomy (missing chromosome). The most common genetic abnormality is trisomy of chromosome number 21 which results in Downs's syndrome. Other genetic disorders may include mutation in a single gene which may be heredity or caused by environmental factors.

NIPT was initially used to screen Down's syndrome. It is also used to screen trisomy of chromosome 18, Edward's Syndrome and chromosome 13, Patau Syndrome. This technology has now advanced to screen for sex chromosome aneuploidies and selected microdeletions. The NIPT test today is now used to screen for the following chromosomal abnormalities.

- Trisomy:
  - Down's Syndrome (21)
  - Edward's Syndrome (18)
  - Patau Syndrome (13)
- Sex Aneuploidies:
  - Turners Syndrome (XO)
  - Klinefelters Syndrome (XXY)
  - TripleX Syndrome (XXX)
  - Jacobs Syndrome (XYY)
- Microdeletions:
  - DiGeorgeSyndrome
  - PraderWilli/Angelman Syndrome,
  - Criduchat Syndrome,
  - 1p36microdeletion Syndrome,
  - Jacobsen Syndrome,
  - Langer Giedion Syndrome
  - Wolf-Hirschhorn Syndrome



Source: Melbourne IVF resources

CHAPTER 2: LITERATURE REVIEW

2.1 Prenatal Genetic Screening Test

There are various genetic disorders that can affect the fetus of pregnant women. Varioustypes of screening and diagnostic tests are available which can be provided to thepregnant women to help

them take decisions and plan ahead. Predisposition to these genetic disorders can be due to various factors such as:

- Family history of genetic disorders
- Either of the parent having chromosomal abnormality
- A previous child with any genetic defect
- Superior motherly age (>35 years) or fatherly age (>40 years)
- Previous case of multiple miscarriages or stillbirth

There are three broad types of genetic disorders of the fetus in pregnant women.

These are:

- ❖ Singlegene disorders: These are rooted by a single gene change in the fetus. This solitary gene alteration can be caused by mutation in a nucleotide base pair which may then code for a faulty protein. Examples of these disorders comprise cystic fibrosis, sicklecell anemia, TaySachs disease, hemophilia, and Marfan syn drome.
- ❖ Chromosomal Abnormalities: These are caused by changes in the fetus's chromosomes. Aneuploidy is a condition in which the fetus may have an extra chromosome also known as trisomy or a missing chromosome also known as monosomy. Down's syndrome is the most common trisomy due to additional chromosom numeral 21, which can be inherited from a blood relation or caused by possibility.
- ❖ Multifactorial or compound genetic disorders: These can be founded by various factors like heritable predisposition or ecological factors. Examples of such diseases include heart defects, cleft palate or spinal bifida.

Prenatal screening and diagnosis of congenital malformations and genetic disorders is inclusive of non-invasive and invasive techniques.

Invasive techniques of prenatal screening and diagnosis include:

- Amniocentesis: An ultrasound guided needle is inserted into the uterus through the abdomen to collect the amniotic fluid which collects the fetal cells. These are then analyzed to confirm if the fetus has any genetic abnormality. This test has a risk of miscarriage around 0.5-1%.
- Chorionic Villus Sampling: A tiny piece of placental tissue is removed from the placenta through the cervix or the abdomen and is tested for genetic abnormalities. It can be performed between 10-13 weeks. It has a risk of miscarriage around1-2%.
- Nucal Translucency: This procedure is collection of fluid from under the baby's neck. It measures the thickness of the fluid. It is not a diagnostic test but it gives a measure of risk for genetic abnormality.

The non-invasive techniques can include fetalvisualization using medical imaging techniques, maternal serum testing or blood testing. These tests are used for screening congenital malformation in the fetus and genetic disorders.

Prenatal genetic screening includes fetal visualization imaging techniques such as:

- Ultrasound
- Fetal echocardiography
- Magnetic Resonance Imaging
- Radiography

❖ Non-Invasive prenatal test (NIPT) or cell free DNA is a highly advanced next generation screening technology which screens for genetic aneuploidies from sequencing the cfDNA of the fetus from the mothers blood.

2.2 Fetal Chromosomal Aneuploidies

2.2.1 Down's syndrome

Down syndrome occur while a person has a complete or fractional additional duplicate of chromosome 21.This second inherited material cause the characteristics of downs syndrome. These characteristics may consist of low muscle size, in the air slant in the eyes, a crease across through the center of the palm, some may have intellectual disability. Each someone ma showcases these different exceptional characteristic with changeable degrees or some not at all.

2.2.2 Epidemiology

Center for Disease Control and Prevention reports that on an average one in every 700 babies in the United States are born with Downs's syndrome. In Europe, EUROCAT states that down's syndrome constitutes of 8% of total congenital abnormalities. It is the most prevalent chromosomal condition globally.

2.2.3 Trisomy 21 Non Disjunction

During the time of conception, chromosome 21 from either the sperm or egg fails to separate and this causes the embryo to develop with trisomy of chromosome 21. These type of non-disjunction downs syndrome accounts for 95% of all the scenarios.

2.2.4Mosaicism

This rare type of downs syndrome is diagnosed when some of the fetal cells consist of normal set of chromosome i.e. 46 set while some cells consists of 47 chromosomes, with an extra chromosome 21. This accounts for 1% of total cases.

2.2.5Translocation

This is characterized by the presence of an extra set of chromosome number 21 either full or partial on another chromosome. The other chromosome usually being chromosome 14. This type of cases accounts for 4% of cases.

2.3 Cause and risk of reoccurrence

All the types of downs syndrome case are genetic condition but only the translocation type is said to be heredity.Thisis only 1% of the case. The age of the mother is also not linked with downs syndrome, however the most number of downs cases are found to be in mothers of age more than 35 years.

If the mother has given birth to a baby with downs syndrome the chances of second baby having downs syndrome is seen. If the mother is the carrier in case of translocations then the risk is comparatively higher (10-15%) as compared to the father being a carrier (chance of 3-5%)

Genetic counseling cam help figure out the cause of translocation.

2.4 Edwards Syndrome

Edwards condition is the top mainly frequent inherent fetal abnormality following Downs syndrome. It is cause by the attendance of extra gene number 18 in all or some cells in the fetus. It affects one in 5,000 live births. The chances of a baby surviving the non-disjoint type of Edwards syndrome are rare. The fetus usually dies before birth. It is mostly seen in female fetus as compared to male fetus.

The genetic conditions of Edwards syndrome are as follows:

2.4.1 Non-Disjoint type: During the meiotic division of the gamete cells either the egg or the sperm, there can arise an error during the separation of chromosomes. This can cause an extra set of chromosome to be incorporated in the zygote. The presence of extra chromosome number 18 results in Edwards syndrome.

2.4.2 Translocation: In this phenomenon a part or the extra chromosome 18 gets translocated and attaches to a different chromosome. The fetus is present with a pair of chromosome and the extra chromosome may be attached to another pair of chromosome.

2.4.3 Mosaicism: In this rare phenomenon the trisomy of chromo-some 18 is there in several cells of the fetus and not every cell. The symptoms in this type of trisomy are comparatively less and depend on the amount of extra chromosome present.

Physical signs of Edwards' syndrome include:

- low weight during birth
- microcephaly (small head)
- abnormally narrow jaw
- Webbed toes and hands
- Clen-ched fist
- low-set ears
- downy foot with round sole
- a fissure lip and palate
- exomphalos- (in this the entrails are placed in a sac exterior the stomach)

Children with Edwards' syndrom e also characteristically have:

- deformities of heart and kidny
- feed difficulties
- breathing difficulty
- hernias in the tolerance (where domestic tissues push during a weak point in the muscle wall)
- bone-deformity – for example a curved spine
- recurrent infection of the lungs and urinary system
- academic disability
- Ultrasounds and NIPT tests are used to screen and calculate the risk of this condition. Although final diagnosis is required to confirm the presence of Edwardssyndrome, which include amniocentesis.

2.5 Patau's syndrome

Patau's syndrome is a rare genetic disorder of trisomy 13. It affects all the cells of the body in case of non-disjunction type and affects some cells of the body in mosaism and chromosomal translocation.

This syndrome severely disrupted the normal developmental pattern of the fetus and 95% of the case results in death of the fetus either due to miscarriage or stillbirth of the baby or death of the baby shortly after death. Amongst the babies which live, 9 out of 10 babies die within a year. The

once who survive more than a year have the partial or mosaic form of trisomy.

2.5.1 Symptoms and features

- They have restricted growth which causes them to develop underweight and also with heart defects.
- The brain does not divide into the two halves and cause facial abnormalities such as small eyes or absence of an eye, muchreduced distance between the eyes and problem with the formation of nasal passage.
- The fetus may have microcephaly i.e. small head size, ear malformation causing deafness, and raised birthmarks.
- The intestines may be formed outside of the body cover onlyby a membrane
- Abnormal formation of cyst in the kidneys
- Cause abnormally small penis in the males
- Or may have enlarged clitoris in the female
- They may also have abnormal formation of feet and hands.

2.6 EU 5 (Europe Market)

Blood diagnosis of Down syndrome has turn out to be a significant part of routine prenatal checkup in most of the European Union (EU) countries, especially UK, Germany and France. The preference is accredited to multiple advantages like high accuracy, high sensitivity, increased precision, efficiency. The incidence rate for Down syndrome in EU is in the ratio 1:900. In Europe, Denmark was the first country that introduced a prenatal screening for Down syndrome in 2006 as a public health care program. This was followed by other EU countries. European market for non-invasive prenatal genetic testing (NIPT) was fixed at around $400 million in 2018 and is predicted to reach $650 million by 2023 at the CAGR of 11%, with UK projected to drive the overall growth in the market owing to the NHS support.

Few of the most reliable NIPT tests in EU include Panorama (Natera), PrenaTest™ (LifeCodexx Germany), Verifi (Illumina US), MaterniT21 Plus (LabCorp US/Sequenom US).

2.6.1 Market size

EU market size (Volume) is estimated to be ~ 600000 NIPT tests in 2018 and UK was leading at the market share of 40%, followed by Germany at 30% and France at 15%.
It is analyzed that Panorama test which is proposed by Natera had the largest volume share in EU in 2018 as compared to the other commercialized tests. It's expected to capture 35% in the US volume market.
The first NIPT test was launched by Life Codexx AG in 2012 under the name PrenaTest, to screen the common abnormalities in the fetus.

2.6.2 Trends

There has been an increased acceptance of non-invasive prenatal testing and the number of laboratories and distributors are also increased which improves easy access.Growing Pharmacogenomics testing in EU-5 with firms like Natera and Illumina collecting and recording all the data from down's syndrome and other genetic testing in electronic health record (EHR) forms.There are constant considerations regarding the need/applications of data analytics explanations for prenatal. The increased adoption of next-generation sequencing techniques (NGS) can help to decrease the rates of test failures. The volume of NIPT tests is snowballing in UK and Germany owing to enhanced involvement of health agency and technology assessment organizations.

2.6.3 Drivers

As there is an increased incidence of Down's syndrome in newborns in EU, patients are choosing NIPT. This has chances of low risks of miscarriage of termination of pregnancy associated with the screening procedures.
UK – NIPT is fast, accurate and safe; Increased focus from NHS on NIPT coverage.
Germany – NIPT test is more cost-effective, it cuts down the overall high cost associated with the screening; G-BA to launch Down syndrome blood test through public payers.
France – Higher risks of genetic abnormalities with increasing maternal age (>35 years) in past few years; coverage by HAS
Spain – Substantially increased rate of women with miscarriages with invasive methods
Italy – Increase in education and awareness regarding genetic testing and earliest testing for down's syndrome

2.6.4 Challenges

There are non stop variations in the controlling framework in EU countries. There is some principled concern allied with the blood diagnosis of Down's syndrome. In UK there is misuse of these tests by few of the private institutes especially clinics, like for sex identification. In Germany, most of the patients tend to pay out of their own pocket and there are less accurate results in case of twin pregnancy. In France there are high rates of false alarms that eventually lead to invasive approaches. While in Spain there are limited certified vendors and distributors. And in Italy the blood testing is not considered conclusive and is only perceived as preliminary diagnosis.

2.6.5 Regulatory Framework

Prenatal screening of Down's syndrome is a routine procedure in Europe, though the internal policies and uptake is varied across different countries. In November 2016, the UK government accepted the use of NIPT tests for detecting Down's Syndrome, Patau's syndrome and Edward's as part of the prenatal testing/screening program. NIPT was moved out over a three-year period, along with staff training, and the department expected the test to be offered within the UK's National Health Service in 2018 or 2019. G-BA is presently estimating/evaluating the indications available for NIPT to determine fetal trisomy's 13, 18 and 21 for risk-pregnancies. A decision pertaining to NIPT is expected in August 2019.In France, NIPT has been recommended by HAS, as per which NIPT test for Down syndrome is included in the French testing policy. HAS has enabled the access of NIPD (non-invasive prenatal diagnosis) to all pregnant women. While there are no strongrules in Spain that express the positioning of NIPT tests in prenatal care of pregnant women, however Spanish National Health Service/HTA are evaluating the role of NIPT.Ministry of Health in Italy has issued strategies in 2015 as per which NIPT is mentioned as the first line test and preceded by accurate Ultrasound after week 11.

2.6.6 Reimbursement scenario

Major payers offering NIPT in Europe are private insurance players (Bupa UK, Techniker Krankenkasse Germany, etc.), while in some EU countries, it is funded by national public payers.The NIPT test in UK, costs in the range of £400–£1500, while in other EU-5

countries, the price is between €300–€900. In UK NHS implemented NIPT test to choose the program at the country level as a second stage NHS screening test, based on the results from RAPID trial in 2018.NIPT is wholly compensated on reliant with threatbigger than 1: 150 with first-trimester combined testing.In GermanyNIPT is shielded by private payers but G-BA is scheduling to deliver it through public payers by August 2019 under statutory health insurance. NIPT has been approved by the HAS in France in the year 2017. French National Health System reimburses around € 400 to all pregnant women for screening and prenatal diagnosis. While Spain and Italy lacks a public reimbursement policy for NIPT and but the countries currently covered by few private insurers. Multiple national, regional and local working groups are assessing the inclusion of NIPT.

2.7 Company Profile

2.7.1 NATERA: It is a world leading company for diagnosis and genetic testing. It focuses on analyzing DNA for analysis of reproductive health and prenatal genetic screening for pregnant women. In 2013 it launched Panorama which is the company's NIPT solution.

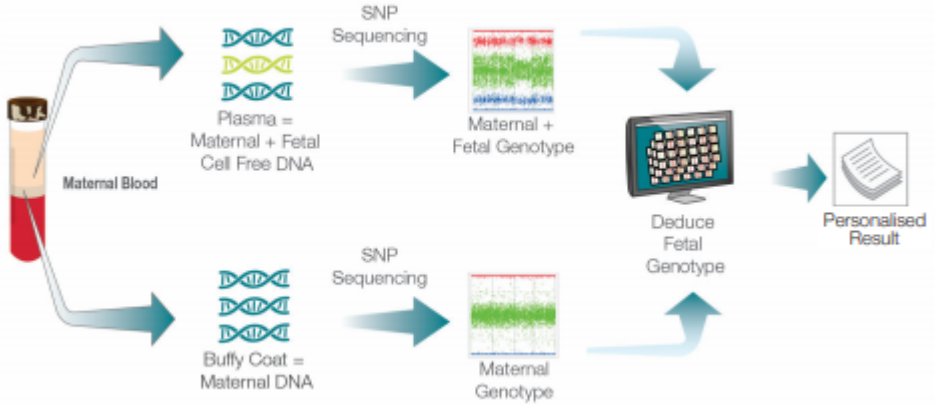
NIPT Test: PANORAMA

It is a market leader in NIPT test which detects the fetus's risk of genetic abnormalities. It analyses the baby's DNA (derived from placenta) from the mother's blood. It analyses as early as nine weeks into gestation. It provides screening for twin pregnancies, egg donor pregnanciesandsurrogatepregnancies.

It screens for trisomy21, trisomy18 and trisomy13. It also screens for sex chromosomal abnormalities of Turners, Klienfilters, Jacob's and triple X Syndrome. It additionally screens for 5 micro deletions namely, (22q11.2) removal syndrome, prader- (willi syndrome), (angelman syndrome), 1p36-deletion syndrome, cridu-chat syndrome.

It is the only NIPT test which can differentiate between maternal and fetal DNA.

Sequencing technology: SNPs (Single nucleotide polymorphism) technology of sequencing maternal/placental and fetal DNA.



Source: Melbourne IVF resources

2.7.2 LAB CORP (SEQUENOME): It is an American company which provides molecular technologies and highly sensitive genetic testing for NIPT. It was acquired by the diagnostic giant Lab Corp in 2016.

NIPT Test: MATERNIT21

It was the first NIPT test launched in the market to screen for fetal genetic chromosomal abnormalities. It screens the fetus in the 10^{th} week into gestation period for singleton as well as multiple pregnancies. It screens for trisomy-21, trisomy-18 and trisomy-13. It also screens for sex chromosomal abnormalities of Turners, Klienfilters, Jacob's and triple X Syndrome. It additionally screens for selected microdeletions namely, 22 q 11.2 deletion syndrome, prader- willi-syndrome, angelman-syndrome, 1 p36 deletion syndrome, criduchat syndrome, di-geroge-syndrome, jacobsen-syndrome, Langer-Giedion syndrome and WolfHirschhorn syndrome.

Sequencing Technology: Whole genome sequencing for sequencing cfDNA found in the mother's blood.

2.7.3 ILLUMINA (VERINATA): It is an American company headquartered in San Diego. It provides with products related to sequencing, genotyping, and to genomics and proteomics market. It is a leader in the sequencing industry. It acquired Verinata Health for its genetic tests in reproductive health specifically for it NIPT test solution.

NIPT Test: VERIFI

It is a safe prenatal screening test for prenatal genetic screening for singleton and twin pregnancies as early as 10 weeks into gestation period. It screens for prevalenttrisomy and sex chromosomal abnormalities namely, trisomy 21, 18 and 13 and Turners, Klienfilters, Jacob's and triple X Syndrome. The verifi plus tests for all chromosomal trisomy. It also screens additionally for selected micro-deletions namely, 1p36 deletions, 4p- (WolfHirschhorn syndrome), 5p(cridu-chat-syndrome), 15 q11 (Prader Willi syndrome/Angelmans syndrome) and 22 q11 deletion (Di Geo-rge). It is the NIPT test with the fastest turnaround time.

Sequencing technology: It provides with paired- end sequencing technology for whole genome sequencing. It is a fully automated, PCR free technology with only 2 hours hands on time and 26 hours from start to finish, thus effectively decreasing the turnaround time.

CHAPTER 3 METHODOLOGY

Market Research: It is a systematic way of gathering information about any product, service or company and to draw analysis for future trends or business development. Market research is used to analyses the market and draw conclusions which are then used to make business strategy and further developments by the companies.

Market research can be done by two ways namely, primary and secondary research.

Primary Research:

It includes direct communication with people to gather their opinions. This can be done by face to face interviews, telephonic interviews, online surveys or panel interviews. We use CATI (Computer aided telephonic Interview) and IDI (In-Depth Interviews) to gather information and opinions from people. It is also known as field research.

Unimrkt research primarily uses CATI form of primary research to gather information from people. We curate database according to our target audience, in this case doctors (gynecologists and obstretians) and contact them to conduct surveys and interviews to gather data. The data gathered from the doctors are kept strictly confidential.

We conducted IDI with doctors in different countries of Europe to gather knowledge about the use of NIPT tests in their daily clinical practice.

Secondary Research:

It is gathering information from secondary sources such as market reports, guidelines, research papers, case studies etc. It is also known as desk research. It also includes competitive intelligence studies to understand the major companies competing in manufacturing of a product or its services. The CI analysis helps understand the current market and analyses the major leaders in the industry and upcoming new ventures in the industry.

We gathered secondary data points from the website of major companies providing NIPT test. We also researched case studies, clinical validation studies of the products, sequencing

technology. We analyzed the different NIPT product offered by them compared and contrasted for analysis.

Competitive Intelligence:

It is comparative analysis of different companies in a particular industry. We compare three leading competitors of NIPT test globally. The three leading companies are Natera with its NIPT test Panorama, Lab Corp (Sequenome) and its NIPT test MateriT21 plus and Illumina with its NIPT test Verifi. We do comparative analysis of these three products by the above companies.

CHAPTER 4: RESULTS AND DISCUSSION

Europe market size in terms of the test volume is estimated to be around ~6000000 NIPT in the year 2018. This is estimated to grow up to 8000,000 by the year 2023. The country leading the market will be UK.

Panorama test by Natera had the largest test volume share in all Europe. It is also predicted that it will capture 33% of the market in the US NIPT industry.

Europe Union (EU5)

The market volume share covered by each country as in the year 2010 is

UK: 40%

Germany: 30%

France: 16%

Italy: 2%

Spain: 4%

Rest of Europe: 8%

The regulatory scenarios in each of the countries can be highlighted in brief.

The worldwide Society of Ultrasound in Obstetric and Gynecology of UK has compiled prenatal ultrasoundpractice guidelines that are followed in Europe. The European Society of Human Genetics recommends using NIPT as a next trial after mutual first trimester screening or as a substitute for shared first trimester viewing.

UK

- The NHS Fetal Anomaly screening programed undertakes Prenatal Testing and Downs syndrome screening in accordance with the NICE guidelines screening of Trisomy 21, 18, 13 syndromes.
- The UK government approved use of NIPT test for detecting Downs, Patau's, Edwards as part of the prenatal testing screening. All screening laboratories need to be accredited with UK accreditation Service.

Germany

- Federal Joint Committee of Germany (G-BA) is currently evaluating or assessing the evidences available for NIPT to determine fetal trisomy 13, 18, and 21 for risk pregnancies.

- Germans Society of Ultrasound in Medicines and Fetal Medicine Foundation recommends NIPT after an ultrasound with appropriate counseling of the test as a primary screening test to pregnant women of any age and especially the high risk groups.

France

- NIPT has been endorsed by the French High Authority Health (HAS), that has recommended the NIPT for down to be included in the French testing policy.
- The Inter national society of Ultrasounds in Obstetricsand Gynecology of UK has compiled prenatal ultrasound practice guidelines that are followed in Europe.
- As per guidelines, NIPT is offered as first line screening test.

Spain

- No clear policies in place regarding NIPT caps though discussions are under way.
- Spanish society of gynecology and obstetrics is undertaking an evaluation of use of NIPT in pregnant women.
- The adaptation of NIPT assessment and the development of national screening policy for prenatal screening, voice included in the 2018 work plan of the Spanish network of HTA agencies.

Italy

- Italian Ministry of Health issued guidelines in 2015 as per which NIPT is received as first line test and preceded by accurate after week 11.
- Italian Medicines Agency (AIFA) recommends that NIPT should proceed with the invasive test like amniocentesis as the existing NIPT tests are not conclusive.
- It is mandatory to undergo genetic counseling to understand the characteristics and limits and to sign the informed consent document before the test.
- In Europe, parents are opting for the prenatal testing because of the lower risk of miscarriage and reduction in the termination of pregnancy.

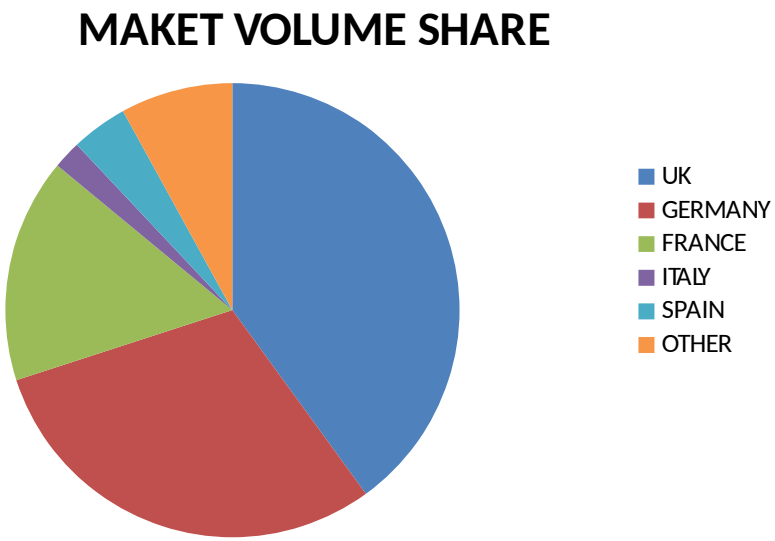


Fig: Pie chart depicts the Market volume share in EU 5

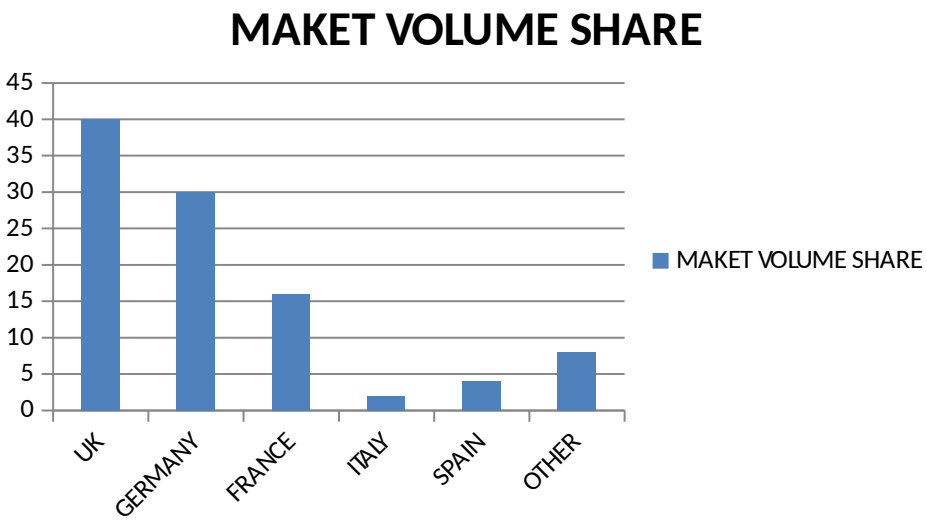
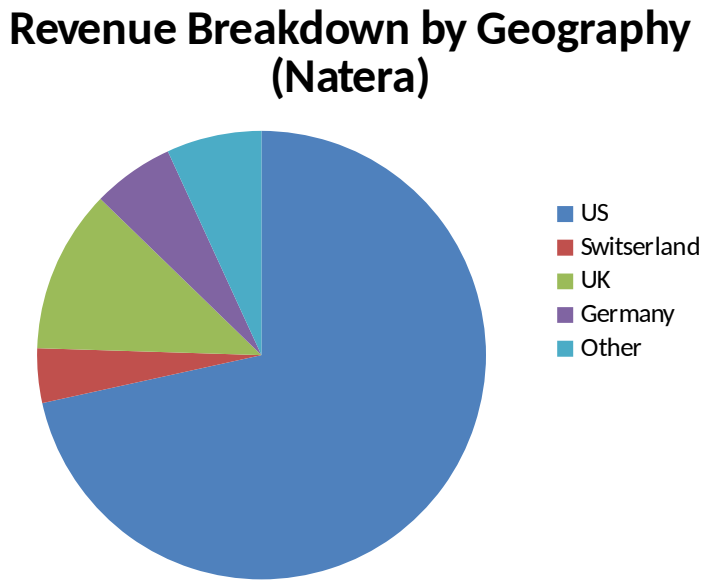


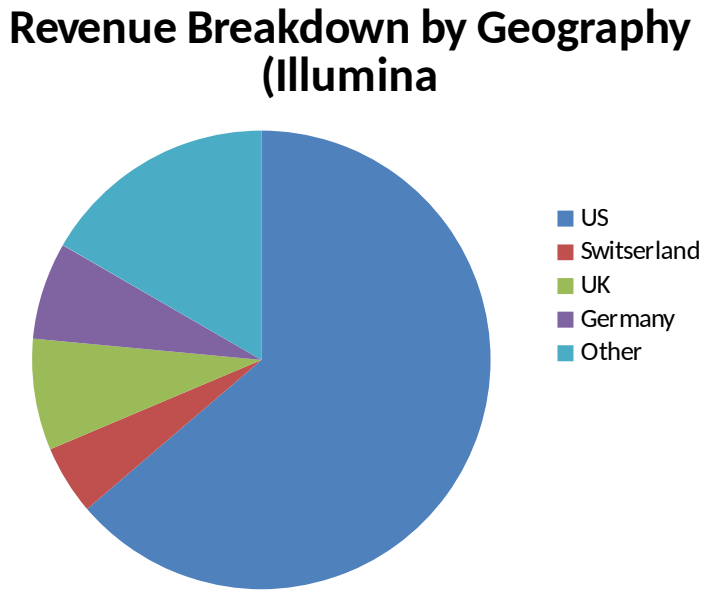
Fig: Graph representing the market volume share in EU 5

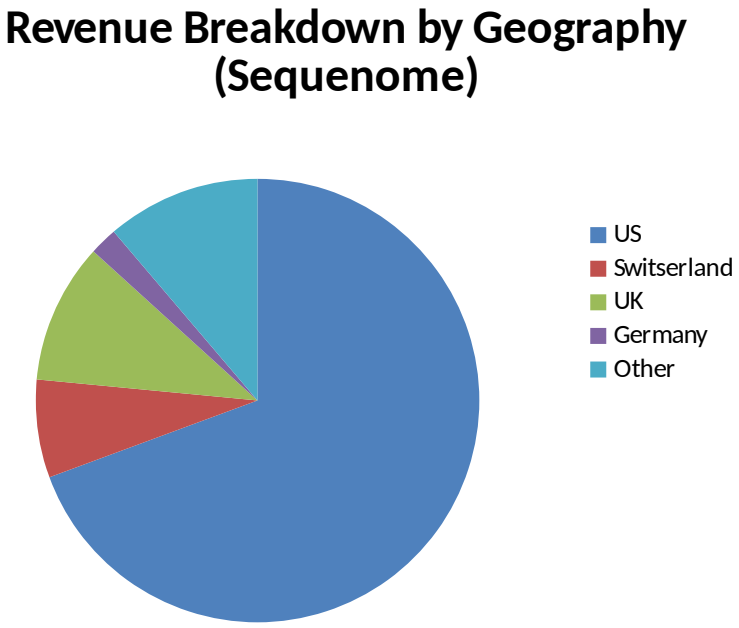
Comparative Analysis:

Performences / Players	Natera's Panorama	Sequenom's MaterniT21 PLUS	Illumina's Verifi
Trisomy tested	21,18,13	21,18,13,16,22	21,13,18
Monosomy tested	Turner's syndrome	NA	Turner's syndrome
Genetic testing method	Panorama, Horizon	MaterniT 21 PLUS, MaterniT	Verifi, VerifiPlus
Triploidy	Panorama	NA	NA
Sensitivity	>99%	99.1%	>99%
Acurracy	1	1	1
False Positive Rate	>0%	1%	0.7%
Price	$1495	$2700	$1500
Gestation age	9 weeks	10 weeks	10 weeks

Revenue Breakdown By Geography:







- Unment needs in the NIPT area are resolved by these major plonfidentialayers.
- Swot analysis results are to be kept c

CHAPTER 5: Conclusions

Information collected through primary and secondary research has helped us understand the NIPT scenario globally and in Europe.

There are various NIPT tests available in the market in Europe. The first NIPT test was launched in Europe in 2012 which was known as Prena Test. The three most popular tests in Europe were compared in the above report. The three tests namely, Panorama by Natera, MaterniT21 by Sequenome and Verifi by Illumina; all the three tests for downs syndrome with a specificity of more than 99%. All the tests screen for trisomy21, trisomy18 and trisomy13. It also provides screening for selected micro-deletions by some tests. Panorama test has the advantage of differentiating between maternal and fetal cfDNA. MaterniT21 is the first commercially available test and is validated by maximum number of clinical studies. Verifi uses Illumina's sequencing technology which now provides advanced next generation sequencing technology and screens for all autosomal trisomy.

CHAPTER 6: REFERENCES

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