Bumrungrad International HOSPITAL
โรงพยาบาลบำรุงราษฎร์

Consent for Non-Invasive Prenatal Testing (NIPT)

Name: .....

HN: ..... **Date**: .....

Birth Date: ..... **Age**: .....

Room: ..... **Sex**: .....

Physician: .....

Allergies: .....

Consent for Non-Invasive Prenatal Testing (NIPT)

I (Mrs./Ms.)…….……..…Gestational age: ……..……..……..weeks consent to Dr.…….and Bumrungrad Hospital's personnel to draw my blood for the purpose of Non-Invasive Prenatal Testing (NIPT) that is planned for me;

☐ Plan 1 NIPT consist of**:**

1. Screening for Trisomy 13, Trisomy 18 and Trisomy 21
2. Screening for Other chromosome aneuploidy
3. Screening for Sex chromosome aneuploidy
4. Sex determination (optional)
5. Screening for DiGeorge syndrome : 22q11.2 deletion syndrome

☐ Plan 2 NIPT Plus consist of:

1. Screening for Trisomy 13, Trisomy 18 and Trisomy 21
2. Screening for Other chromosome aneuploidy
3. Screening for Sex chromosome aneuploidy
4. Sex determination (optional)
5. Screening for DiGeorge syndrome : 22q11.2 deletion syndrome
6. Screening for other 91 microdeletion/microduplication syndromes

☐ Plan 3 NIPT Twin consist of:

1. Screening for Trisomy 13, Trisomy 18 and Trisomy 21
2. Sex determination (optional)

I have already received information about the NIPT test including what the test is for, the test method, and the limitation of the NIPT test.

My signature below indicates I have read and understood the information of the test on this form, have been given the opportunity to ask any questions and receive appropriate counseling about this type of testing by a healthcare provider and give my consent for my sample to be analyzed NIPT test. I agree that the information provided will be held confidentially and may be used for auditing and quality control and that my data will be anonymized for such purposes.

Bumrungrad International HOSPITAL
โรงพยาบาลบำรุงราษฎร์

Consent for Non-Invasive Prenatal Testing (NIPT)

Name: .....

HN: ..... **Date**: .....

Birth Date: ..... **Age**: .....

Room: ..... **Sex**: .....

Physician: .....

Allergies: .....

Signature.....

(.....)

Physician's Signature.....

(.....)

(Physician provides explanation)

....

Date Time

Witness 1 .....

(.....)

Witness 2 .....

(.....)

(Fingerprint/consent over telephone)

Interpreter's Statement

I have given a translation of Consent for Non-Invasive Prenatal Testing (NIPT) including information that physician has explained to patient/patient's representative.

Translate to Language .....

Interpreter .....

(.....)

Status of Signer *(According to Thai Civil and Commercial Code)*

- ☐ Patient, who is 20 years old or above, and capable of giving consent
- ☐ Spouse in case that the patient is not capable of giving consent (unconscious)
- ☐ Holder of parental responsibility in case that the patient is minor (under 20 years old)
- ☐ Curator in case that the patient is quasi incompetent person (adjudged by the court)
- ☐ Guardian in case that the patient is incompetent person (adjudged by the court)

Please attach the following supporting documents:

1. *A copy of your national identification card/passport/driver's license, government official card, or any other ID card issued by the government in which your photo is attached, with a certified true copy (for the patient).*
2. *A copy of documents proving the relationship as a father, mother, spouse, child, adopted child, or sibling of the patient, such as a marriage certificate, house registration, birth certificate, custody certificate (in case the parents are not married), adoption registration certificate, or other government-issued documents, on which the information regarding religion and blood type appeared (if any) is redacted, with a certified true copy.*

Relationship with the patient .....

Identification number of the patient's representative .....

Telephone number.....

Email.....

Bumrungrad International HOSPITAL
โรงพยาบาลบำรุงราษฎร์

Consent for Non-Invasive Prenatal Testing (NIPT)

Name: .....

HN: ..... **Date**: .....

Birth Date: ..... **Age**: .....

Room: ..... **Sex**: .....

Physician: .....

Allergies: .....

Non-Invasive Prenatal Testing (NIPT) is a non-invasive test for pregnant women which estimates the risk of a fetus having chromosomal abnormalities. The non-invasive prenatal testing (NIPT) is an advanced screening test using next - generation sequencing technology that is carried out on a small maternal blood sample. During pregnancy, the placenta leaks cell-free DNA (deoxyribonucleic acid) which circulates in the maternal bloodstream. As a result, a maternal blood sample contains a mixture of fetal-placental and maternal circulating cell-free DNA. The non-invasive prenatal testing (NIPT) directly measures the amount of this cell-free DNA and can detect chromosomal abnormalities.

People usually have 23 pair of chromosomes or 46 chromosomes (23 from mother and 23 from father). There are many different types of chromosome abnormalities such as numerical abnormalities (trisomies, monosomies) structural abnormalities (microdeletions, translocations) and mosaicism.

Some fetal chromosome abnormalities may relate to advanced maternal age, but may occur as a result of errors in cell division, inheritance of abnormalities or by multiple factors.

Details of each test item as follows:

1. Screenign for Trisomy 13, trisomy18 and trisomy 21
   - Trisomy 13 (Patau syndrome): A chromosomal disorder that causes serious problems with the brain and heart as well as extra fingers and toes, cleft palate and lip, and other defects. Most infants with trisomy 13 die within the first year of life.
   - Trisomy 18 (Edwards syndrome): A chromosomal disorder that causes severe intellectual disability and serious physical problems such as a small head, heart defects, and deafness. Most of those affected with trisomy 18 die before birth or within the first month of life.
   - Trisomy 21 (Down syndrome): A chromosomal disorder that causes abnormal features of the face and body, medical problems such as heart defects, and intellectual disability. Many children with Down syndrome live to adulthood.
2. Screening for other chromosome aneuploidy includes chromosomes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 17, 19, 20 and 22.
3. Screenign for Sex chromosome aneuploidy
   - Monosomy X or XO (Turner syndrome): A chromosomal disorder that affects development in female, common feature is short stature, extra folds of skin on the neck, early loss of ovarian function, infertility. Developmental delay, learning disabilities and heart defects may present.
   - XXX (Triple X syndrome): Signs and symptoms can vary from no noticeable effect to delayed development of speech and language skill, learning disabilities and hypotonia. Normal sexual development and fertility are typical.
   - XXY (Klinefelter syndrome): Signs and symptoms often subtle, primary features are infertility and small testis. Intelligence is usually normal but reading difficulties and speech problems may present.
   - XYY (Jacob's syndrome): Signs and symptoms are few, may taller than average and increased risk of learning and speech problems, no problem with fertility.
4. Sex determination (optional)

5. Screenign for DiGeorge syndrome (22q11.2 deletion syndrome): A chromosomal disorder that causes heart defects, poor immune system function, cleft palate, and delayed development.
6. Screening for other 91 microdeletion/microduplication syndromes (in total 92 types, including DiGeorge syndromes, as shown in the table below)

Microdeletion and Microduplication Syndromes List (92 TYPES)

Chromosome 1p36 deletion syndrome	Chromosome 10q26 deletion syndrome
Chromosome 1q41-q42 deletion syndrome	Chromosome 10p12-p11 deletion syndrome
Chromosome 1p32-p31 deletion syndrome	Chromosome 10p duplication
Chromosome 2p16.1-p15 deletion syndrome	Chromosome 11p13 deletion syndrome
Chromosome 2q33.1 deletion syndrome	Chromosome 11p11.2 deletion syndrome
Chromosome 2q31.1 duplication syndrome	Jacobsen syndrome
Chromosome 2q37 deletion syndrome	Chromosome 11q23 deletion syndrome
Chromosome 2q31.1 microdeletion syndrome	Chromosome 12q14 microdeletion syndrome
Chromosome 2q duplication	Chromosome 12p12.1 microdeletion syndrome
Chromosome 3pter-p25 deletion syndrome	Chromosome 12p duplication
Dandy-Walker syndrome	Chromosome 13q14 deletion syndrome
Chromosome 3q13.31 deletion syndrome	Distal chromosome 13q deletion
Distal chromosome 3p duplication	Chromosome 14q11-q22 deletion syndrome
Chromosome 3q duplication	Chromosome 14q22 deletion syndrome
Chromosome 4p16.3 deletion syndrome	Proximal chromosome 14q deletion
Chromosome 4q21 deletion syndrome	Chromosome 14q duplication
Chromosome 4p duplication	Prader-Willi syndrome
Distal chromosome 4q duplication	Angelman syndrome
Distal chromosome 4q deletion	Chromosome 15q26-qter deletion syndrome
Cri-du-Chat syndrome	Levy-Shanske syndrome
Chromosome 5q14.3 deletion syndrome	Chromosome 15q14 deletion syndrome
Chromosome 5q12 deletion syndrome	Chromosome 15q24 microdeletion syndrome
Chromosome 5p13 duplication syndrome	Chromosome 15q26 overgrowth syndrome
Chromosome 5p duplication	Distal chromosome 15q deletion
Chromosome 6pter-p24 deletion syndrome	Chromosome 16p12.2-p11.2 deletion syndrome
Chromosome 6q24-q25 deletion syndrome	Chromosome 16p12.2-p11.2 duplication syndrome
Chromosome 6q11-q14 deletion syndrome	Chromosome 16p13.3 deletion syndrome
Chromosome 6p deletion	Chromosome 16p13.3 duplication syndrome
Chromosome 6q15-q23 deletion syndrome	Proximal chromosome 16q duplication
Chromosome 6q25-qter deletion syndrome	Smith-Magenis syndrome
Chromosome 6q26-q27 deletion syndrome	Chromosome 17p13.3 deletion syndrome
Chromosome 7q deletion	Potocki-Lupski syndrome
Chromosome 7q11.23 deletion syndrome	Chromosome 17p13.3 duplication syndrome
Chromosome 7q21-q32 deletion	Yuan-Harel-Lupski syndrome
Chromosome 7q31-q32 deletion	Chromosome 17p duplication
Chromosome 8p23.1 deletion syndrome	Chromosome 18p deletion syndrome
Chromosome 8p23.1 duplication syndrome	Distal chromosome 18q deletion syndrome
Langer-Giedion syndrome	Alagille syndrome 1
Chromosome 8q22.1 deletion syndrome	Chromosome 20p duplication
Chromosome 8q22.1 duplication syndrome	Chromosome 21q22 deletion
Chromosome 8p duplication	Chromosome 22q11.2 deletion syndrome
Chromosome 8q duplication	Chromosome Xp11.23-p11.22 duplication syndrome
Chromosome 9p deletion syndrome	Chromosome Xp21 deletion syndrome
Chromosome 9p duplication	Chromosome Xq27.3-q28 duplication syndrome
DiGeorge syndrome 2	Chromosome Xq21 deletion syndrome
Chromosome 10q22.3-q23.2 deletion syndrome	Chromosome Xq22.3 deletion syndrome

Examples of common disorders;

- DiGeorge syndrome (22q11.2 deletion syndrome): A chromosomal disorder that causes heart defects, poor immune system function, cleft palate and delayed development.
- 1p36 deletion syndrome: A chromosomal disorder that causes structural abnormalities of the brain, weak muscle tone, swallowing difficulties, seizures and severe intellectual disability.
- Prader-Willi syndrome/Angelman syndrome (15q deletion syndrome): A chromosomal disorder that causes neurological impairment, seizure, ataxia, behavioral and endocrine disorder.
- Cri-du-Chat syndrome (5p deletion syndrome): A chromosomal disorder that causes low birth weight and poor growth, small head, hypotonia, feeding difficulty, cognitive disabilities and heart defects.
- Wolf-Hirschhorn syndrome (4p deletion syndrome): A chromosomal disorder that causes distinct features of facial and head, growth restriction, heart defects, intellectual disorders, immunodeficiency and deafness may present.

Non-invasive prenatal testing (NIPT) results report

- **Low Risk :** This result suggests a low probability of the fetus having the chromosomal abnormalities included in the screening panel.
- **High Risk :** This result indicates a higher probability of the fetus having one or more of the chromosomal abnormalities being screened for. Further diagnostic testing, such as amniocentesis or chorionic villus sampling (CVS), is recommended to confirm or rule out these possibilities.
- **No Result :** In rare instances, insufficient fetal DNA may be detected in the maternal blood sample, resulting in an inconclusive test. In such cases, additional blood may be required for further analysis.
- **Sex Determination Failure :** This means that there was insufficient data to determine the sex of the fetus. However, this does not impact the accuracy of the screening results for other chromosomal abnormalities.

Information for non-invasive prenatal testing (NIPT)

Suitable for:

- Pregnant women with a gestational age of 10 weeks or greater
- Women with singleton or twin pregnancies
- Women who have conceived through in vitro fertilization (IVF) utilizing donor eggs or gestational surrogacy. In cases involving donor eggs, the age of the egg donor at the time of retrieval should be documented

Unsuitable if the mother has:

- Women with a history of cancer
- Women with known pre-existing chromosomal abnormalities
- Women who have recently undergone immunosuppressive therapy or stem cell transplantation
- Women who have received organ transplants
- Women who have received blood transfusion
- Women who have a vanishing twin pregnancy

Bumrungrad International HOSPITAL
โรงพยาบาลบำรุงราษฎร์

Consent for Non-Invasive Prenatal Testing (NIPT)

Name: .....
HN: ..... **Date**: .....
Birth Date: ..... **Age**: .....
Room: ..... **Sex**: .....
Physician: .....
Allergies: .....

Test limitations

- The non-invasive prenatal testing (NIPT) should be considered a screening test only. It is recommended that you discuss the results with your healthcare provider and that a positive result (i.e., a high chance of Down, Edwards or Patau syndrome being present) is considered along with other clinical screening results and may be followed up with an invasive procedure (i.e., amniocentesis or chorionic villus sampling (CVS)). Pregnant women with a Positive non-invasive prenatal testing (NIPT) screening result should be given an invasive prenatal diagnosis and referred for genetic counselling to confirm condition. On the other hand, a negative test result does not ensure an unaffected pregnancy.
- While non-invasive prenatal testing (NIPT) is a reliable screening tool, it may not detect all potential chromosomal abnormalities. Certain conditions, such as mosaicism, other microdeletion/duplication not indicated in the list, various chromosomal rearrangements (including balanced translocations or unbalanced translocation), copy number variation, inversions, unbalanced or balanced translocations, uniparental disomy may not be identified through NIPT. Furthermore, a negative NIPT result does not definitively exclude the possibility of chromosomal abnormalities
- Fetal fraction is required to be greater than or equal to 3.5% to generate reports for trisomy 13, 18, and 21, sex determination, sex chromosome aneuploidy, microdeletion/duplication, and other chromosome aneuploidy detection. In rare cases when a borderline screening result or no result can be provided, patient blood redraw is required to confirm conditions.
- Performance NIPT and NIPT Plus are indicated in the table below.

Performance only for reference

CONDITIONS		SENSITIVITY	SPECIFICITY	PPV	NPV	REFERENCES
T21		99.17%	99.95%	92.19%	99.99%	Ultrasound Obstet Gynecol. 2015 May;45(5):530-8.
T18		98.24%	99.95%	76.61%	100.00%	
T13		100.00%	99.96%	32.84%	100.00%	
Fetal Sex		99.53%	99.20%	N/A	N/A	J Matern Fetal Neonatal Med. 2014 Dec;27(18):1829-33.
XO		75.00% (1)	99.90% (1)	23.53% (2)	N/A	BMC medical genomics vol.5 57. 1 Dec. 2012 (1) Chinese medical journal vol.133,13 (2020): 1617-1619. (2)
XXX		N/A	N/A	70.00% (2)	N/A	
XXY		100.00% (1)	100.00% (1)	75.00% (2)	N/A	
XYY		100.00% (1)	100.00% (1)	80.00% (2)	N/A	
Del/Dup	>10Mb	88.89%	99.32%	N/A	N/A	Plos One.2016 Jul 14;11 (7) :e01569233
	<10Mb	72.73%	99.09%	N/A	N/A	

The data in the table is based on historical literature and internal data, and only reflects past detection, not the actual condition of the tested sample

- In dichorionic twins, scientific publications suggest that the performance of the assay in detection of trisomy 13, 18, and 21 and sex chromosome determination is slightly different compared with singletons, as shown in the table below. If there is abnormality detection, the test cannot identify which one of the twins has a high risk. If a high-risk result is detected, selective invasive confirmatory testing would be required.

- Performance NIPT Twin are indicated in the table below.

Performance only for reference

CONDITIONS	SENSITIVITY	SPECIFICITY	REFERENCES
Trisomy 21	100% (1,2)	100% (1,2)	• J Matern Fetal Neonatal Med. 2013 Mar;26(4):434-7(1) • Prenat Diagn. 2014 Apr;34(4):335-40(2)
Trisomy 18	N/A	N/A	
Trisomy 13	N/A	N/A	

The data in the table is based on historical literature and internal data, and only reflects past detection, not the actual condition of the tested sample

Financial reimbursement and compensation for trisomy 13, 18 and 21

- Financial reimbursement for "High Risk" result

The non-invasive prenatal testing (NIPT) should be considered a screening test only. If the result is "High Risk" for trisomy13, trisomy 18 or trisomy 21, you are eligible for financial reimbursement towards the cost of invasive, confirmatory prenatal diagnostic testing including but not limited to amniocentesis, chorionic villus sampling (CVS), karyotyping analysis, chromosome in situ hybridization and fluorescence in situ hybridization (FISH). The reimbursement will be up to maximum reimbursement amount of 12,500 baht.

- Compensation for "False Negative" result (except mosaic chromosomal abnormality and vanishing twin)

The non-invasive prenatal testing (NIPT) should be considered a screening test only. Although, the non-invasive prenatal testing (NIPT) has high accuracy rate, false negative result may happen. If the test result is false negative, non-invasive prenatal testing (NIPT) result shows "Low Risk" but that later your baby is diagnosed with either trisomy13, trisomy 18 or trisomy 21 (karyotyping result shows 47,+13 for trisomy 13, 47,+18 for trisomy 18 or 47+21 for trisomy 21) by a qualified healthcare professional within one year of baby's birth date or you have terminated the pregnancy, you are eligible for compensation up to a maximum of 1,000,000 baht