Blank Space reserved for IGENOMIX use only

Request form for POC test (Products of Conception)

The fields marked with * are mandatory in order to perform the test

CLINICIAN INFORMATION

*Clinic:_____

*Referring doctor:_____

*Email for delivery of results:_____

Address: _____

City: _____ County/Province/State: _____ Postcode: _____

PATIENT INFORMATION

*MRN/Unique Patiend ID (1):_____ **(1):** If there is none, please state NOT APPLICABLE

*Patient's name:_____*Surname(s):_____*Date of birth:_____

Partner's name:_____Surname(s):_____Date of birth:_____

Karyotype(s): ☐ Patient_____ ☐ Partner _____

Address: _____

City: _____ County/Province/State: _____ Postcode: _____

Contact email address: _____ Telephone:_____

INDICATION OF TEST

☐ Advanced maternal age ☐ Abnormal ultrasound ☐ Family or personal history of aneuploidy

☐ High-risk combined screening ☐ Previous miscarriages (no. of miscarriages___) ☐ Abnormal karyotype

☐ Other:_____

INFORMATION ON THE PREGNANCY

*Date of miscarriage._____*Gestational age (weeks):_____*Date of sample collection:_____

*Type of pregnancy: ☐ Single foetus ☐ Multiple pregnancy. State number of foetuses _____

☐ Natural pregnancy

☐ Pregnancy with assisted reproduction treatment:

*Origin: ☐ Own eggs ☐ Donated eggs

Treatment([1]): ☐ HAI ☐ DAI ☐ IVF ☐ ICSI ☐ PGT-A (PGS) ☐ PGT-SR (PGD) ☐ PGT-M (PGD)

([1]) Select one or more options, as required.

SAMPLE INFORMATION

*Type of sample: ☐ Guided biopsy ☐ Conventional curettage ☐ Spontaneous miscarriage ☐ Other:_____

Quality of sample: Hematic YES ☐ ☐ NO

Has a sample of maternal blood been sent?([2]): ☐ YES ☐ NO

([2]) The blood sample is required to rule out maternal cell contamination (MCC)

Comments: _____

_____

Doctor authorization

I certify that the information on this requisition form is correct to the best of my knowledge and that I have requested the above test based on my professional judgement of clinical indication. I have explained the limitations of this test and I have answered any question with medical judgement. I understand that Igenomix may need additional information and I agree to provide this information if necessary.

*Clinician's signature_____ Date: _____/_____/_____

Patient consent

By signing this requisition form, I voluntarily request Igenomix to carry out the test indicated above. I have read and received a copy of the informed consent, included in the following pages. The risks, benefits and limitations of this test have been explained to me.

*Patient's signature_____ Date: _____/_____/_____

INFORMED CONSENT FOR ANALYSIS OF FOETAL REMAINS OR PRODUCTS OF CONCEPTION (POC) 24-Chromosome aneuploidy screening

DESCRIPTION, PURPOSE AND ADVANTAGES OF ANALYSIS

Chromosomal abnormalities can lead to foetuses with deformities, miscarriages, or even neonatal deaths. Estimates of the frequency of chromosomal abnormalities in miscarriages range from 15% to 60%.

In the case of early termination of pregnancy or miscarriage, the diagnosis of a chromosomal abnormality may be important for planning future pregnancies.

Chromosomal tests on foetal remains, otherwise known as Products of Conception (POC), provide useful information and help patients and doctors to determine the causes of miscarriages, the risk of recurrent miscarriages and the subsequent risk of having children with chromosomal abnormalities.

POC tests provide more information faster than the conventional cytogenetic karyotype. With a combination of the NGS (Next Generation Sequencing) technique and STR (Short Tandem Repeat) analysis, the presence of additional or absent chromosomes is detected, as well as any loss or partial duplication of the chromosomes, and the presence of maternal cell contamination (MCC) is either ruled out or detected.

PROCEDURE, RISKS AND LIMITATIONS

For this analysis, samples of foetal remains or products of conception (POC) need to be collected (either by the patient in the event of miscarriage or by curettage by the gynaecologist if the miscarriage is retained or incomplete) and sent using the sample collection kit provided by Igenomix. In order to rule out or detect maternal cell contamination (MCC), it will be necessary to obtain a biological sample (blood in EDTA tube) from the patient, which will be sent along with the POC sample.

To process the sample, the test requisition form will need to be correctly filled out. If this is not the case, the analysis may be put on hold until the information required has been given to the laboratory.

Given the complexity of the genetic tests and the significant implications of the test results, the results obtained must be interpreted in conjunction with other clinical data, within the general context of a medical practice run by healthcare professionals. The result reports are strictly confidential.

The results of the test will be available in 10-15 working days after the sample is received. A small percentage of samples may be delayed due to unforeseeable causes. Should this occur, the corresponding clinic in charge will be notified.

Wherever possible, foetal tissue is identified separately to maternal tissue in the POC sample received. The sample is cleaned, dissected, the DNA extracted and analysed NGS for 24 chromosomes. The STR protocol is used to detect or rule out maternal cell contamination, as well as certain forms of polyploidy.

There are no associated risks to the patient in this type of test. However, the main limitations of the POC test are as follows:

1. Not all genetic conditions and/or all chromosomal abnormalities can be detected. The following are conditions that cannot be detected:
    - There are multiple chromosomal abnormalities, including balanced translocations and inversions, which this test cannot screen for
    - Low levels of chromosomal mosaicism
    - POC tests do not analyse specific genes and cannot detect conditions caused by individual genetic mutations, such as sickle cell anaemia, cystic fibrosis or Tay-Sachs disease
    - POC tests cannot detect some forms of tetraploidy, such as 92,XXXX or 92,XXYY, but they can detect triploidy 69,XXY, 69,XXX, and tetraploidy 92,XXXY and 92,XYYY
    - Uniparental Disomy (UPD)
    - Complete trisomies of acrocentric chromosomes cannot be distinguished from trisomies caused by a Robertsonian translocation (affecting chromosomes 13, 14, 15, 21, or 22) or from an isochromosome in one parent
    - Other causes of miscarriage not yet identified
2. Losses or duplications of chromosomal material less than 10 Mb in size cannot be reported.
3. Risk of misdiagnosis due to incorrect identification of the sample, inaccurate information on the relationship, mosaicism or other unidentified genetic abnormalities. Diagnostic errors due to a test failure occur in <1% of cases.
4. Probability of maternal cell contamination. These results are inconclusive.
5. It is possible that unpredictable and uncontrollable transport problems may occur, such as those related to the weather and air transport, or other uncontrollable circumstances, which would mean results cannot be obtained in the timeframe established. It is possible that that the sample received in the laboratory may be unacceptable for analysis and, therefore, results cannot be obtained from the sample provided.

DATA PRIVACY, STORAGE AND RESEARCH USE OF SAMPLES

Your privacy is a priority for the Igenomix Group ("**Igenomix**"). Your identity and all data referring to your personal information will be confidential and only Igenomix personnel will be permitted access to this information, along with the relevant authorities when required by the laws of the applicable jurisdiction. You will find further information on the Igenomix Privacy Policy, along with all your rights at www.igenomix.com, or this information may be provided to you upon request by sending an email to privacy@igenomix.com.

We would like to inform you that your personal data will only be processed to: (1) Fulfil the obligations arising from the provision of the services contracted by you; (2) Check and guarantee the quality of the services provided (internal audits, quality controls, laboratory validation studies); (3) For educational purposes, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (4) For research purposes, scientific publications and presentations, provided that it remains anonymous throughout and you cannot be identified during the analysis of the data, which will be removed from any publication; (5) Personally address any doubts or suggestions made by the patient during the process and monitor the proper performance and resolution of the test, including the indefinite retention of your data, except where local laws of the applicable jurisdiction state

otherwise; and (6) Contact you in the future to request an evaluation of the services received, send commercial communications (including 'cross-selling' and 'upselling') from associated companies, and also to invite you to participate in market research and the development of new products.

You also declare that you understand and accept that you will not obtain, either now or in the future, any economic benefit for any research carried out, and that there is no intention to compensate you for the products developed from any research.

The sample will be analysed by Igenomix or an associated group selected by Igenomix on an international level. Igenomix reserves the right to carry out part or all of the analyses included in the test through Third Party Laboratories certified with recognised international quality standards, or failing this, they will be periodically assessed by Igenomix. Any results obtained in this way will be inspected by Igenomix and this circumstance will be indicated in the final report issued.

Pursuant to the laws on the Protection of Personal Data1, the requesting party must have the patient's consent to perform the diagnostic tests requested and to process their data. You may, at any time, exercise your rights regarding access, rectification, opposition, erasure, automated decisions, restriction, portability, by sending an email to privacy@igenomix.com, providing proof of the requesting party's identity.

HAVING READ AND UNDERSTOOD THE FOREGOING, I AM AWARE OF:

The indications, procedure, success rate, risks and complications of the proposed treatment, as well as the financial cost of said test(s).

The fact that medical staff are at my disposal to expand on any aspect of the information that is not sufficiently clear to me.

I have understood the explanations given to me in clear and simple language, and the clinician who saw me allowed me to make comments, clarifying any issues I raised and informing me that I may freely withdraw my consent at any time.

I am satisfied with the information received and I freely consent to the foetal remains collected being sent to the Igenomix facilities for the purpose of carrying out the POC test.

I also accept that the results of the test(s) may be passed on to my clinician, so that he or she can advise me correspondingly on planning any future pregnancies.

[1] **For non-US patients:** customers residing outside the United States under certain jurisdictions may at any time request to have their personal information deleted from our active databases, subject to the applicable laws and regulations in each jurisdiction. Although we can delete your personal information from our active databases, part or all of your personal information shall remain stored in back-up files for the purpose of complying with legal, regulatory or other requirements. Information that has already been coded and/or anonymised may not be recoverable or traceable for destruction, deletion or modification. If you wish to have your personal information removed from our active databases, please contact us at privacy@igenomix.com