Blank space reserved for IGENOMIX only

Test Requisition Form POC (Products of Conception)

Fields marked with * are required to perform the test

CLINICIAN INFORMATION

*Clinic: _____

*Referring Clinician: _____

*E-mail:_____ Telephone: _____

Address: _____

City: _____ County/Province/State: _____ Postal Code: _____

PATIENT INFORMATION

*MRN/Unique patient ID: _____ If not available, please state NOT APPLICABLE

*Patient's full name: _____ *Date of birth: _____

Partner's full name: _____ Date of birth: _____

Karyotype(s): Patient: _____ Partner: _____

INDICATION FOR TEST

☐ Advanced maternal age ☐ Abnormal ultrasound ☐ Abnormal karyotype

☐ Previous miscarriages (no. of miscarriages: ____) ☐ Family or personal history of aneuploidy ☐ High-risk combined screening

☐ 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 ☐ 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

Maternal DNA sample collection date: _____ Type of sample:(2) ☐ Blood ☐ Saliva

(2) The maternal DNA sample (blood/saliva) is required to rule out maternal cell contamination (MCC)

Comments: _____

_____

Clinician authorisation

I certify that the patient and prescribing doctor's details given in this request form are accurate to the best of my knowledge and that I have requested the test indicated above based on my professional criteria. I have explained the limitations of this test and have answered any questions based on medical judgement. I understand that Igenomix may require further information and I agree to provide this information if necessary.

*Clincian's signature_____ Date: _____

Patient consent

By signing this application form, I voluntarily ask Igenomix to perform the test indicated above. I have read and received a copy of the informed consent included in these pages. I have also been adequately informed of the risks, benefits and limitations of this test.

*Patient's signature_____ Date: _____

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INFORMED CONSENT FOR ANALYSIS OF FOETAL REMAINS OF PRODUCTS OF CONCEPTION (POC)

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. The POC test provides comprehensive information, faster than the conventional cytogenetic karyotype. With a combination of NGS (Next Generation Sequencing) and STR (Short Tandem Repeat) analysis, the presence or absence of chromosomes is detected, as well as any loss or partial duplications. Maternal cell contamination (MCC) could also be detected or ruled out.

PROCEDURES, 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 spontaneous miscarriage or by curettage by the gynaecologist if the miscarriage is retained or incomplete) and sent to the laboratory using the sample collection kit provided by Igenomix. In order to rule out or detect maternal cell contamination (MCC), it is necessary to obtain a biological sample (blood in EDTA tube/saliva) from the patient, which should be sent along with the POC sample for STR analysis.

To process the sample, the test requisition form will need to be correctly completed and signed. If this is not the case, the analysis may be suspended until the information required has been provided 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 family and clinical data, within the general context of a medical practice run by healthcare professionals. The result reports are strictly confidential.

The results of the **POC** test will be provided to the referring clinician within a period of no more than 15 **working days** following sample reception by the laboratory. 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 using NGS for all 24 chromosomes. The STR protocol is used to detect or rule out maternal cell contamination, as well as certain forms of polyploidy.

While there are considerable benefits to the POC test, limitations exist that are described below:

a. Not all genetic conditions and/or all chromosomal abnormalities can be detected. The following cannot be detected:

- Multiple chromosomal abnormalities, including balanced translocations and inversions
- Low levels of chromosomal mosaicism.
- POC test does not analyse specific genes and cannot detect conditions caused by individual genetic mutations, such as Sickle Cell Anaemia, Cystic Fibrosis or Tay-Sachs Disease.
- Some forms of Tetraploidy, such as 92,XXXX or 92,XXYY, but POC can detect Triploidy 69XXY, 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.

b. Losses or duplications of chromosomal material less than 10 Mb in size cannot be reported.

c. 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.

d. Probability of maternal cell contamination. These results are inconclusive.

e. It is possible that unforeseeable circumstances may occur, meaning that results cannot be obtained in the timeframe established. It is possible that that the sample received in the laboratory may be unsuitable for analysis and, therefore, results cannot be obtained from the sample provided.

DATA PRIVACY, STORAGE AND SAMPLES USED FOR RESEARCH

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

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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.

Samples and all associated data will be retained in the laboratory in accordance with the Igenomix's specimen retention policy which is in accordance with all the legal requirements.

Pursuant to the laws on the Protection of Personal Data[1], 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, limitation, 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 test, as well as the financial cost of said test.

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 giving a blood/saliva sample and my foetal remains at the Centre/Clinic which I have attended. I also consent to the sample being sent to the Igenomix facilities for the purpose of carrying out the aforementioned test.

I also accept that the results of the test may be passed on to my clinician, so that he or she can advise me correspondingly on the suitable treatment to follow and 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.

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