

# Fact Sheet

## Preimplantation Genetic Diagnosis/Screening (PGD/PGS)



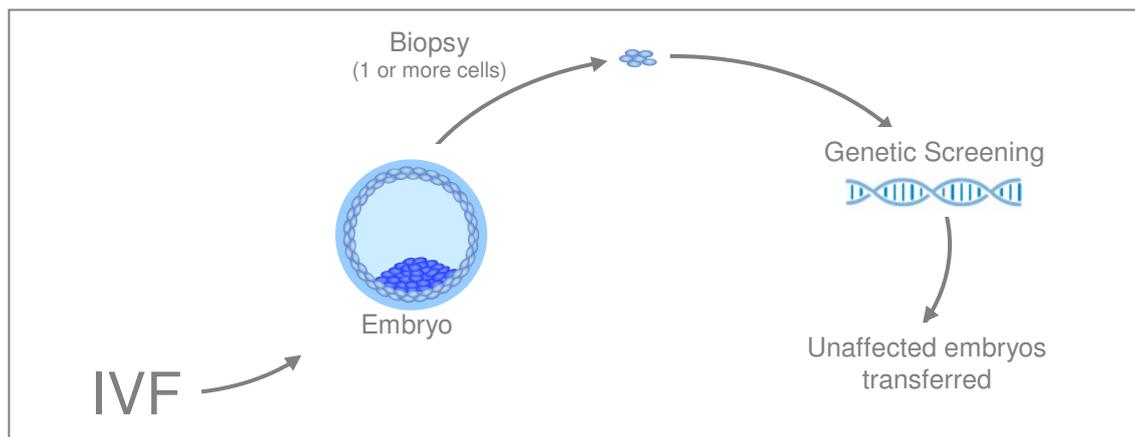
### Key points:

- PGD/PGS involves screening in vitro fertilization (IVF) generated embryos for genetic conditions prior to embryo transfer.
- PGD/PGS is available for single gene disorders, translocations, inversions, chromosomal aneuploidy or X-linked disorders.
- Only embryos that are unaffected will be considered suitable for transfer. Embryos that are affected or found to have a chromosome abnormality will not be considered suitable for transfer.
- PGD/PGS is NOT 100% accurate. Confirmatory prenatal diagnosis is highly recommended if a pregnancy is achieved following PGD/PGS.

### What is Preimplantation Genetic Diagnosis/Screening (PGD/PGS)?

PGD/PGS is a reproductive option for those at risk of passing a specific genetic disease or chromosome imbalance to their children. PGD/PGS involves screening IVF generated embryos for genetic conditions prior to embryo transfer, with only unaffected embryos transferred to the uterus. This provides the opportunity to screen embryos for genetic conditions before a pregnancy is established (Figure 1).

Figure 1: Preimplantation Genetic Diagnosis/Screening



Individuals choose PGD/PGS over prenatal diagnosis for many reasons including objection to termination of pregnancy, loss of a child from the genetic disease, recurrent implantation failure or recurrent miscarriage.

PGD/PGS testing may be appropriate for:

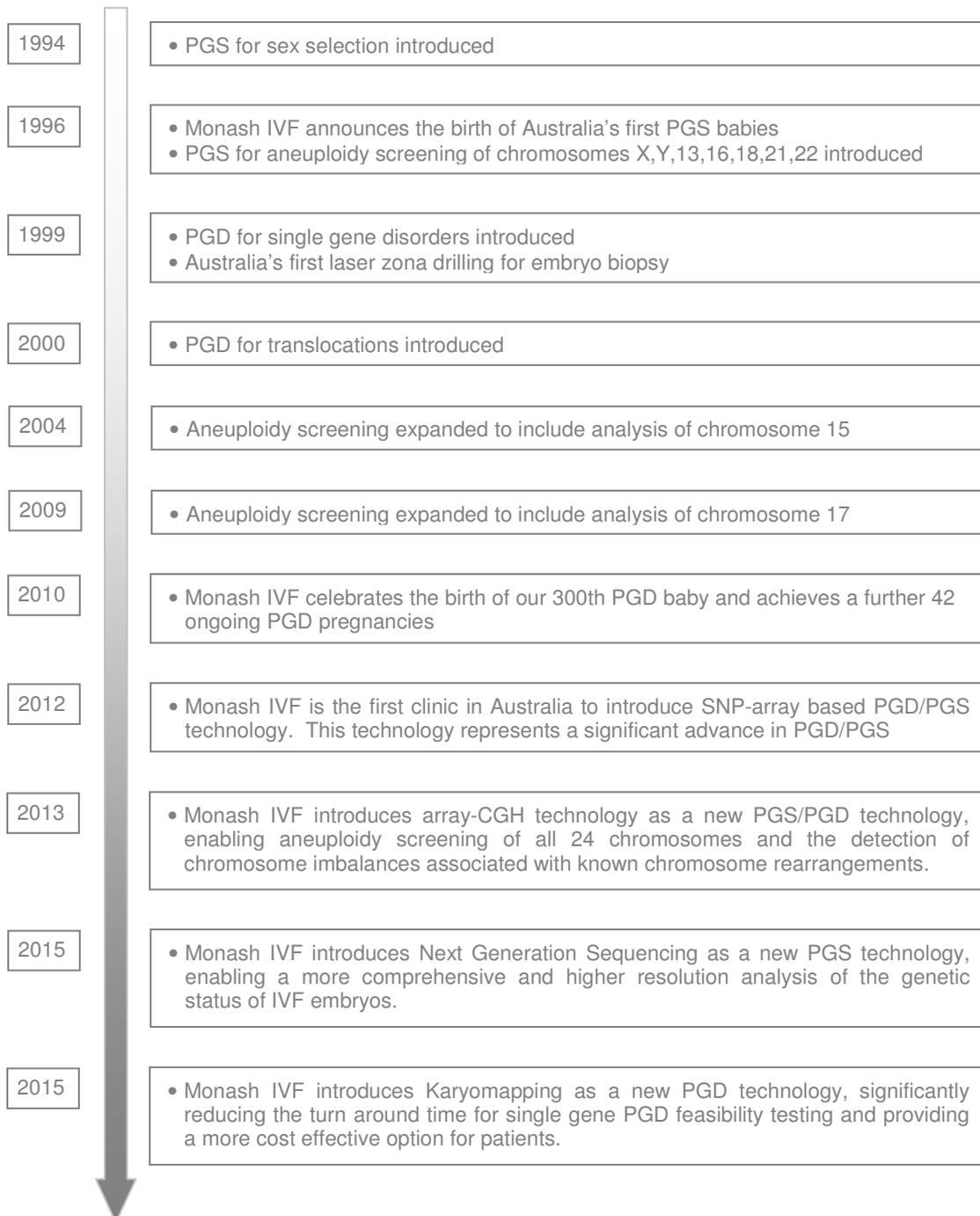
- Individuals at risk of passing a single gene disorder on to their children
- Individuals at risk of having children with a particular X-linked disorder
- Individuals who carry a balanced chromosome rearrangement
- Individuals with an altered sex chromosome complement (eg: XXY)
- Individuals with advanced maternal age (>36 years of age)
- Individuals who have experienced recurrent implantation failure
- Individuals who have experienced recurrent miscarriage
- Individuals who have previously had a pregnancy with a chromosome abnormality

Genetic counselling is an important step to ensure that PGD/PGS is the right way forward.

### PGD/PGS at Monash IVF

Monash IVF has offered PGD/PGS since 1994 and is one of the few centres in Australia that specialises in this area of reproductive medicine. Monash IVF Clayton (in Melbourne, Australia) has a highly specialised in-house genetics team, which helps ensure the highest quality of care to patients. The genetics team is responsible for providing a specialised PGD/PGS service not only to our own patients but also to patients undergoing IVF cycles at numerous IVF clinics throughout Australia and New Zealand. While the main PGD/PGS laboratory is located at Clayton, embryo biopsy can be performed away from the PGD/PGS laboratory and the embryonic cells sent by courier to Clayton. Centralising the PGD/PGS testing enables patients to access the highest levels of expertise without having to leave their home state. Monash IVF has consistently been at the forefront of PGD/PGS technology. Some of our milestones are listed in Figure 2.

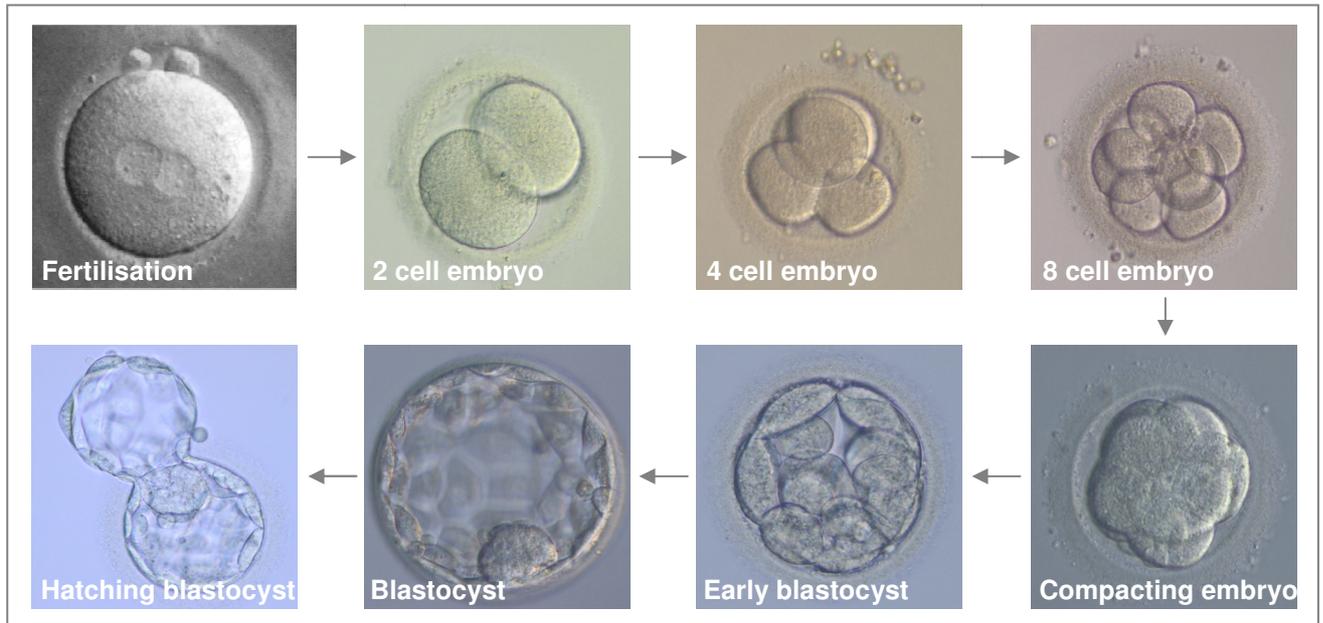
Figure 2: Key PGD/PGS milestones at Monash IVF



### What does PGD/PGS involve?

Individuals requesting PGD/PGS must first undertake an IVF cycle to stimulate the woman's ovaries to produce a number of eggs. These eggs are collected and fertilised using the male partner's sperm. The resulting embryos are cultured in the laboratory (See Figure 3).

Figure 3: Embryo culture



Embryo biopsy is typically performed on Day 5/6 after egg collection. By this time, the embryo should have developed to the blastocyst stage, and should consist of an inner cell mass (which will go on to form the fetus) and trophoctoderm cells (which will go on to form the placenta). Embryos need to have a clear inner cell mass and a suitable number of healthy trophoctoderm cells to be considered suitable for biopsy. A small hole is made in the outer shell of the embryo on Day 3 of development and the embryo is returned to the culture dish. By Day 5/6, some of the trophoctoderm cells should have herniated through the hole in the outer shell of the embryo and these cells can be collected for analysis. Approximately 5 trophoctoderm cells are removed for genetic analysis (Figure 4).

Figure 4: Day 5/6 embryo biopsy



The biopsied cells are transferred to a small tube for genetic testing. Due to the time taken to perform the genetic testing, the embryos must be frozen following biopsy. It is important that patients are aware that some embryos will not be considered suitable for biopsy, some embryos will not be considered suitable for freezing, and some embryos may not survive the freeze/thaw process. A Genetic scientist/Embryologist will discuss the PGD/PGS results with the patient at the completion of testing.

If an embryo is found to be unaffected and is genetically suitable for transfer, it can be thawed for use in a frozen embryo transfer cycle. The patient's IVF nurse will organize a pregnancy test to be performed on Day 16 of the frozen embryo transfer cycle. Surplus unaffected embryos will remain in storage. These embryos may be used in a subsequent cycle. Embryos that are found to be affected will be removed from storage and allowed to succumb.

### Accuracy of diagnosis

The results obtained from PGD/PGS are NOT 100% accurate. Test accuracies vary from 90% to 99%, depending on the PGD/PGS test used. Consequently, there may be up to a 10% error rate associated with PGD/PGS.

Many factors influence the accuracy of PGD/PGS testing including:

- The cell/s biopsied from the embryo. It is possible that the biopsied cell/s are NOT representative of the entire embryo. This may lead to a misdiagnosis.
- The clarity of results obtained. Some PGD/PGS results are more difficult to interpret than others. If the results are not clear a reduced accuracy may be reported.

Every effort is made to ensure that the PGD/PGS test offered has the highest possible accuracy using the currently available technology. However, given that PGD/PGS is not 100% accurate, **confirmatory prenatal diagnosis is highly recommended.**

### Other important information

- Embryo biopsy has been performed extensively throughout the world. Follow up studies at Monash IVF have shown that the procedure is safe and does not appear to have an adverse affect on the embryo's potential to implant and develop normally.
- Not all embryos will be considered suitable for biopsy. Day 5/6 biopsy will only be performed on embryos that have a clear inner cell mass and a suitable number of healthy trophectoderm cells.
- Due to the complexity of the genetic tests, an inconclusive result may be obtained for some or all embryos. In some situations it may be possible to re-biopsy these embryos to try to obtain a conclusive result. If this is possible and unaffected embryos are identified, these may be transferred in a frozen embryo transfer cycle.
- PGD/PGS tests are specifically designed to detect genetic abnormalities related to the clinical indication for referral (ie: single gene disorder, translocation, inversion, aneuploidy screening or sex selection). The test does not give any information relating to other genetic conditions or abnormalities.

### What are the costs?

Information relating to the cost of PGD/PGS is available from your IVF clinic.

### How to get started

Those interested in PGD/PGS should discuss this procedure with their IVF doctor or with a member of the Genetics team. Genetic counselling may help individuals decide whether PGD/PGS is the right option for them.

Individuals considering PGD/PGS are encouraged to meet with a clinical geneticist and/or genetic counsellor to discuss the PGD/PGS process. During this consultation the genetic specialists will:

- Thoroughly review the genetic history.
- Provide the couple with information regarding the PGD/PGS process.
- Answer any questions the couple has in relation to their specific genetic condition and the PGD/PGS process.
- Arrange for any further clinical and/or DNA testing to confirm genetic status.
- Arrange for collection of blood samples for test development (if appropriate).
- Offer guidance and support to alleviate any anxiety.

Following counselling, individuals should be aware of the relative risks of embryo screening and the possible outcomes. This will place them in a sound position to make an informed decision about PGD/PGS. For further information, please contact our genetic counsellor on +61 03 9590 8336.