Choices & boundaries

Should people be able to select embryos free from an inherited susceptibility to cancer?

HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

Choices and boundaries – Chair's foreword

The Human Fertilisation and Embryology Authority (HFEA) is responsible for licensing Preimplantation Genetic Diagnosis (PGD) under *the Human Fertilisation and Embryology Act 1990*. Decisions about PGD are made using the guidance in our *Code of Practice*, which was informed by previous consultative work. This enables effective decisions to be made about PGD licensing for a wide range of conditions.

PGD is a technique that has been used in the UK for a number of years. Since the introduction of PGD thousands of children world wide have been born free from life-threatening conditions, such as cystic fibrosis or haemophilia, which otherwise would have severely threatened their quality of life.

Another potential use for this technology in the UK is PGD to avoid passing on a susceptibility to later onset cancer conditions such as inherited breast cancer. Such conditions affect a small proportion of the population but can be devastating to families that carry the faulty gene. They are different from conditions that the HFEA has previously licensed for PGD in that only a proportion of people with the affected gene will develop cancer and those who do so will develop it as adults.

We expect that the HFEA will be asked to consider applications for using PGD for inherited breast cancer and other inherited susceptibility conditions in the near future. Before we do so, we want to hear the views of patients, carers and representatives of affected families, staff in treatment centres, disability groups, parliamentarians, academics and the wider public about the use of PGD for these types of conditions. The views of respondents will be used to inform an Authority statement on the use of PGD for these late onset cancer susceptibility conditions. If an application is received by the HFEA to carry out PGD for these conditions the guidance in the *Code of Practice* and the Authority statement will guide our decision making.

In order to make a decision based on as many views as possible, please let us know your thoughts on this important issue by responding to the questions at the end of *Choices and boundaries*.

Suzi Leather
Chair, Human Fertilisation and Embryology Authority
November 2005

Choices and boundaries

Should people be able to select embryos free from an inherited susceptibility to cancer?

This is the decision that is going to have to be taken by the Human Fertilisation and Embryology Authority in the near future. *Choices and boundaries* aims to find out the views of the public on this issue.

Overview

Choices and boundaries is about the use of genetic testing in embryos to avoid passing on a predisposition to a specific cancer.

The law gives the Human Fertilisation and Embryology Authority (HFEA) discretion to licence genetic testing in embryos to avoid a wide range of medical conditions. The technique used is known as Preimplantation Genetic Diagnosis (PGD).

The HFEA has licensed PGD for many years now and through previous consultative work has developed effective guidance. This is used when considering licensing of new PGD conditions. So far, around fifty genetic conditions have been tested for in embryos under licences issued by the HFEA.

An emerging issue is the use of PGD to test embryos for the presence of a gene that will result in a predisposition to an inherited cancer. Such conditions include inherited forms of ovarian and breast cancer susceptibility and a type of inherited bowel cancer susceptibility.

The cancer predisposition conditions that we are discussing here are different to those that have previously been licensed by the HFEA for PGD. This is because not everyone who carries the faulty gene that predisposes them to cancer will develop cancer. Those who do develop the cancer are likely to do so as adults and have access to screening and treatment. Although the law gives the HFEA discretion to licence the testing of embryos for these conditions, we welcome the views of the public and interested groups on this issue.

The purpose of *Choices and boundaries* is to gather the views of the public to inform licensing decisions and help the Authority decide if PGD should be used to avoid passing on a faulty gene that causes a susceptibility to a type of cancer.

Choices and boundaries asks a number of questions on which we would welcome your views. You can submit your response in writing or online. More details on how to respond can be found on back cover. The Authority expects to make an announcement about its findings in the spring of 2006.

05

01 Inherited cancer susceptibility

1.1 What is the difference between sporadic cancer and inherited cancer susceptibility?

Everyone in the population is at risk of developing cancer at some point in their lives. Not everyone who has cancer will necessarily have inherited a faulty copy of a susceptibility gene. In the general population (where there is not an inherited faulty susceptibility gene that causes a predisposition to cancer), cancer develops as a result of a cascade of genetic changes to a single cell and its descendants leading to uncontrolled growth in a subset of cells in the body. Because the genetic mistakes are accumulated over time, the risk of developing cancer increases with age.

In an individual who has a faulty cancer susceptibility gene present, the faulty gene is usually present in every cell in the individual (including the embryo). This means that fewer genetic mistakes are needed to accumulate in an individual cell of that person for cancer to develop, since the cell already contains one mistake. Because less time is needed to accumulate the mistakes, cancer often develops earlier in people who inherit a faulty susceptibility gene than in people with the sporadic cancer. For example, women that have an inherited fault in the gene that causes breast cancer are more likely to develop it in their late thirties and forties, whereas women that develop the cancer sporadically are more likely to get it in their sixties and seventies.

These inherited cancer susceptibility conditions are responsible for only a small proportion of cancers in the population. About 5 per cent of individuals with common cancers have an inherited cancer susceptibility condition.

The risk of developing cancer that is associated with a susceptibility gene condition can vary depending on the specific condition. Some genetic faults can cause a very high susceptibility to specific cancers, such that almost all people who have the faulty gene will develop the condition. These conditions are called highly penetrant conditions. For other conditions, having an inherited copy of the faulty susceptibility gene only results in the cancer developing in a proportion of individuals that carry the susceptibility gene. These conditions will be referred to as lower penetrance susceptibility conditions.

1.2 Lower penetrance susceptibility conditions

Genetic tests are now available to detect the presence of a number of lower penetrance inherited cancer susceptibility genes:

- inherited breast cancer susceptibility
- inherited ovarian cancer susceptibility
- a type of inherited bowel cancer susceptibility — Hereditary non-polyposis colorectal cancer (HNPCC)

In the future, it may become possible to test embryos for other inherited forms of cancer susceptibility such as prostate cancer, brain cancers or more complicated conditions.

Box 1: Examples of inherited cancer conditions

Familial Adenomatous Polyposis (FAP) – highly penetrant
FAP is a condition which causes hundreds of polyps to develop in the colon, and they begin to appear at an average age of 16 years. The risk of colorectal cancer developing from a polyp is virtually 100 per cent unless prophylactic (before symptoms) removal of the colon is carried out. Polyps also develop in the upper gastrointestinal tract and cancer may occur in other sites including the brain and the thyroid (although not as frequently). The penetrance of FAP is 95-100 per cent meaning that most people who carry a faulty gene for this condition will develop the cancer unless they have prophylactic surgery.

Retinoblastoma – highly penetrant
Retinoblastoma is a cancer which develops in the cells of the retina, the light sensitive lining of the eye. In cases of inherited retinoblastoma, the penetrance is about 90 per cent. The tumour usually develops before the age of 5 years and some children are born with retinoblastoma. Children with bilateral (both eyes) disease tend to present during the first year of life whilst the peak age of diagnosis for children with unilateral disease (one eye) is between 24 and 30 months.

Multiple Endocrine Neoplasia 2 (MEN 2) – highly penetrant
MEN2 is a complex inherited condition that causes a predisposition to various cancers, often with different risks. For example, medullary thyroid cancer, parathyroid adenomas and an adrenal tumour called a phaeochromocytoma. Because of the difficulty of screening for the thyroid cancer it is recommended that children diagnosed with MEN2 have the thyroid gland removed in early childhood to prevent them from developing this cancer. If they do not, the risk of medullary thyroid cancer is very high. If the thyroid gland is removed, it is still necessary to screen for adrenal tumours, which may develop in adulthood. The penetrance for the thyroid cancer is 95 per cent in most families (although the other cancers develop less frequently), with an age at diagnosis between 20-40 years for thyroid cancer, and later for the adrenal tumours. Affected people often develop parathyroid tumours but these are not usually malignant. The risk of specific tumours varies with different faults in the same gene.

Breast cancer and ovarian cancer – lower penetrance
Inherited forms of breast and ovarian cancer can both be caused by faults in the BRCA1 and BRCA2 genes (BReast CAncer). Around 5-10 per cent of all breast and ovarian cancer are caused by an inherited fault in one of these predisposition genes. The age at diagnosis for breast cancer in women with such an inherited fault is about 10 to 20 years earlier than for sporadic breast cancer.

Women who carry a fault in the BRCA1 gene have a lifetime risk of breast cancer of about 80 per cent, and 40 per cent of ovarian cancer — women carrying a fault in the BRCA2 gene have a similar risk of breast cancer but a smaller risk of ovarian cancer. Men carrying these mutations have some increase of prostate cancer risk, and men who carry an alteration in the BRCA2 gene have a 5-7 per cent risk of developing breast cancer in their lifetime. Screening measures are not sufficiently sensitive and specific at present and so prophylactic options to reduce the risks of breast and ovarian cancer (mastectomy and oophorectomy) are often considered, although management of these risks is likely to improve with time.

Bowel cancer (Hereditary non-polyposis colorectal cancer (HNPCC)) – lower penetrance
Individuals with HNPCC have up to an 80 per cent lifetime risk of colorectal cancer and increased risks of uterine cancer (up to 60 per cent) and other mostly gastrointestinal cancers. Screening is available by colonoscopies annually from 25 years, and ultrasound scans may be offered to women with HNPCC. The age at diagnosis of colorectal cancer in the condition is usually in the forties but can be earlier.

1.3 Why are we asking you about these conditions?

Inherited cancer susceptibility conditions are different from other conditions licensed by the HFEA for PGD. This is because of a combination of several factors:

- they are **lower-penetrance** (i.e. not everyone with the faulty gene will develop the cancer)
- the occurrence of cancers have a **later age of onset** — in adult life in many cases
- there is a possibility for preventative surgery, early detection and effective **treatment** for these cancers in susceptible individuals.

The HFEA has licensed PGD for conditions that may have one or two of the features listed above. For example, late onset conditions like Huntington's have been licensed. However, lower penetrance conditions have all three features and it is the combination of these features that makes these conditions different to those that have been licensed before.

Penetrance: The penetrance of a condition determines the proportion of people who carry a copy of a faulty gene that will be affected by a condition. If a condition is 100 per cent (or fully) penetrant, every person who carries a faulty gene will develop the condition. If a condition is 50 per cent penetrant, half of the people that carry a faulty gene will go on to develop the condition.

The penetrance for cancer development of the conditions we are considering here varies from around 30 per cent to 80 per cent depending on the condition or the fault within the gene. Carriers of these genes therefore have a strong likelihood, or predisposition, to developing cancer but not a certainty. In the past the HFEA has only licensed PGD for conditions that are fully penetrant or almost fully penetrant. For example, conditions with more than 90 per cent penetrance.

Age of onset: This refers to the age at which symptoms of the genetic condition are seen. The majority of conditions that have been licensed by the HFEA for PGD to date cause illness in the baby when it is born or in childhood. If a person inherits a faulty gene that causes a predisposition to cancer, the person is not likely to be affected by this condition until they are in their late thirties, forties or fifties. The HFEA has licensed PGD for other late (adult) onset conditions such as Huntington's disease but only where the conditions are fully penetrant.

The potential for preventative surgery, early detection and effective treatment: Although there are treatment options for many of the conditions already licensed by the HFEA, for example cystic fibrosis, these are usually for the relief of symptoms rather than providing a cure. For people who develop cancer it is possible to be treated with drugs and/or surgery. Many people are successfully treated for cancer and this number is increasing as better treatments are developed. It is also possible for people who know that they are at risk to have regular checks and/or preventative – prophylactic – surgery to remove tissue that is likely to be affected by cancer such as the breasts (mastectomy) or bowel (colectomy). These are difficult decisions to make because there is a chance that the cancer may not develop, and if it does, it could be treated.

02 What are the options for affected families?

Families that are affected by an inherited condition may decide that they want to avoid passing on the condition to their children. These reproductive decisions are faced by many families who have often had experience of family members being affected by an inherited condition. The options that are available to people that want to avoid passing on a genetic condition are:

- not having children
- adopting
- using donor sperm or eggs instead of using the affected person's own gametes
- natural conception and hoping that the child is unaffected.

People are increasingly taking advantage of genetic testing to avoid passing on an inherited condition to their children. For people that choose to take advantage of these techniques there are two further options:

- natural conception and genetic testing of the fetus with an option of termination if the child is affected (prenatal diagnosis)
- in vitro fertilisation and preimplantation genetic diagnosis (PGD), replacing only unaffected embryos.

Preimplantation genetic diagnosis (PGD)
There are about 200 PGD treatments per year in the UK. PGD involves genetically testing an embryo in a laboratory. In order to achieve this, couples have *in vitro* fertilisation (IVF) treatment followed by an additional genetic testing stage. The embryo is grown in the laboratory for a couple of days until the cells have divided and the embryo consists of eight cells.

At this time a specially trained embryologist will remove one or two of the cells. The cells can then be tested to see if the embryo from which they were removed contains the faulty gene that causes the condition in the family. One or two of the embryos without a copy of the faulty gene can be placed into the woman in the hope that they will develop. Any remaining unaffected embryos can be stored for later use as required. Those embryos that had a copy of the faulty gene are allowed to perish.

Box 2: What happens when you have PGD?

Steps	Actions
1	A couple find out that they are at risk of passing on a genetic condition to a child at a clinical genetics centre. The options available are discussed with the couple.
2	If they decide to opt for PGD the couple approach a licensed PGD clinic.
3	The genetic test will be perfected so that it is possible to tell if an embryo is carrying the faulty gene from the one cell that is removed.
4	If the centre had not carried out the specific test before, it will apply to the HFEA for a licence to carry out PGD for the given condition. The application will include information about the condition and the genetic test.
5	A Licence Committee –a subgroup of the Authority, will consider the application and make a decision about whether to issue a licence
6	If a licence is granted, the centre will be informed and treatment can begin
7	The woman will be treated with drugs to stimulate egg development. Eggs will be collected and fertilised with her partner's sperm.
8	The embryos are allowed to develop until they're at the 8-cell stage. At this stage 1 or 2 cells are removed and tested for the presence of the faulty gene.
9	Any embryos that do not have a copy of the faulty gene can be replaced into the woman in the hope that they will develop.

2.3 Why do people choose to have PGD and what are the disadvantages?

People choose to have PGD for several reasons:

- it ensures that the child will not develop the inherited condition that is present in the family
- it avoids having to have a termination of an established pregnancy (many people choose to have PGD after already having several terminations of affected pregnancies)
- for some people who have a moral objection to terminations, having PGD is a suitable alternative.

However because of the problems associated generally with IVF treatments, PGD has some disadvantages.

- IVF associated risks:
  - invasiveness of treatment
  - cost of treatment – this is sometimes covered by the National Health Service (NHS)
  - risk of not getting pregnant
  - increased risk of a multiple birth
  - risks of ovarian hyper-stimulation syndrome (OHSS) caused by the drugs taken to stimulate egg production.
- PGD specific risks:
  - chance of inconclusive or incorrect test result
  - theoretical long-term risk to the person born following PGD.

More information about IVF and PGD can be found in the *HFEA guide to infertility* available at www.hfea.gov.uk

03 What does the law say?

3.1 Current legal framework

The legal framework, within which decisions about PGD are made, consists of the *Human Fertilisation and Embryology Act 1990* (the Act), *the HFEA Code of Practice* (the guidance) and case law (interpretations of the law made for specific cases). The HFEA is able to effectively make decisions about the use of PGD for lower-penetrance conditions using this legal framework.

The Department of Health has recently announced that it will be reviewing the Human Fertilisation and Embryology Act and have published a consultation. The consultation raises a question about who should make decisions about PGD in the future.

3.2 PGD and the law

Although PGD is not mentioned specifically in the Act, it is licensed

'as a practice designed to secure that embryos are in a suitable condition to be placed in a woman or to determine whether embryos are suitable for that purpose'.

Before a licence is granted for PGD the HFEA needs to be satisfied that carrying out PGD is

'necessary or desirable for the purposes of providing treatment services'.

The discretion of the HFEA to licence PGD was clarified by the House of Lords ruling in a recent case. They agreed that PGD is justified to determine if an embryo is suitable for the purpose of being placed in the woman. The woman makes a decision about suitability based on information about the genetic status of the embryo.

The House of Lords also confirmed that the Authority has a wide discretion to make difficult ethical decisions about the use of PGD and a duty to develop its policy as required to keep up with technical developments in the field.

The 6th edition of the *Code of Practice* contains guidance on the use of PGD and it states that PGD should be made available

'only where there is a significant risk of a serious genetic condition being present in the embryo'.

The *Code of Practice* also lays out other factors that should be taken into account when clinics are determining the appropriateness of PGD such as the views of the people who are seeking treatment (see box 3).

A Licence Committee refers to the guidance in the *Code of Practice* to determine whether the correct process was used when the clinician and the patient reached a decision to apply for a PGD licence to the HFEA.

Box 3: Guidance for the use of PGD in the HFEA *Code of Practice*

Indications for the use of PGD are expected to be consistent with current practice in the use of (post-implantation) prenatal diagnosis (PND).

It is expected that PGD will be available only where there is a significant risk of a serious genetic condition being present in the embryo. The perception of the level of risk by those seeking treatment is an important factor in the decision making process. The seriousness of the condition is expected to be a matter for discussion between the people seeking treatment and the clinical team.

In any particular situation the following factors are expected to be considered when deciding the appropriateness of PGD:

- The view of the people seeking treatment of the condition to be avoided
- Their previous reproductive experience
- The likely degree of suffering associated with the condition
- The availability of effective therapy, now and in the future
- The speed of degeneration in progressive disorders
- The extent of any intellectual impairment
- The extent of social support available and
- The family circumstances of the people seeking treatment

The complete PGD guidance can be found in chapter 14 of the *Code of Practice* can be found on the HFEA website under the guidance section www.hfea.gov.uk

04 Lower penetrance conditions and the guidance

4.1 PGD Guidance — The Code of Practice

Following its 1999 public consultation on preimplantation genetic diagnosis, the HFEA developed a number of ethical principles which guide its policy-making and licensing in this area. Those principles are:

- PGD should be available only where there is significant risk of a serious genetic condition being present in the embryo
- the perception of the seriousness of the condition by those seeking treatment is an important factor in the decision making process
- the indications for the use of PGD should be consistent with (not necessarily the same as) current practice in the use of prenatal diagnosis.

The principles have worked well since being implemented and have given the HFEA a clear framework within which to consider new applications of PGD technology. The HFEA does not intend to revisit these principles or to amend its guidance to centres on PGD. Therefore the HFEA are not seeking views on the merits of these principles. Instead, we want to hear views about the specific issue of PGD for lower penetrance cancer susceptibility, considered by reference to these principles. These views will help the Authority to decide if PGD should be used to detect lower penetrance cancer susceptibility condition in embryos.

The HFEA is sensitive to the views of some members of the public who feel that PGD (and IVF) itself is unethical because it involves discarding embryos, which they regard as having the same moral status as babies. The HFEA are considering the use of PGD for particular types of conditions and not its use in general and are therefore not seeking views on fully penetrant conditions. However, it would be useful to know how you feel about the use of PGD in general in order to put your views about the use of PGD for lower penetrance conditions into context.

We are interested to find out how you feel about using PGD to test for lower penetrance conditions such as inherited breast cancer. To help put your views about this in context, it is important to understand how you feel about PGD for fully penetrant conditions such as cystic fibrosis or haemophilia. Do you agree with the use of PGD in general? For example, for fully penetrant conditions that are present in the child?

4.2 PGD and lower penetrance cancer susceptibility

As outlined above, the Authority has three main ethical principles which guide its policy-making and licensing in PGD. What we are trying to address with the discussion and questions below is how should the HFEA regard the issue of using PGD to detect lower penetrance cancer susceptibility in embryos using these three principles?

4.3 PGD should be available only where there is significant risk of a serious genetic condition being present in the embryo

Serious genetic condition

How serious a condition is depends on how having the condition affects, threatens or limits the life of the individual, although these factors may be difficult to predict before the affected person is born. If the condition did not cause someone to suffer or detrimentally affect their life, the condition is unlikely to be regarded as serious. If, on the other hand, the condition required regular invasive treatment, or was life-limiting or life-threatening, it would be considered serious.

There are treatments available for inherited cancer susceptibility conditions however, survival rates are variable and there is still a risk that treatment will fail. Although the treatments and drugs available to treat cancer are continually improving, there is no single cure for cancer. As the lower penetrance inherited susceptibility conditions that we are discussing here, for example, inherited breast cancer susceptibility are unlikely to affect people until they are 30 years old, new drugs and treatments could be developed before the children of the people considering PGD now would require cancer treatment.

The HFEA guidance to PGD centres states that PGD should only be available where there is significant risk of a *serious genetic condition*. Given the lower penetrance, later age of onset and potential treatability of inherited cancer conditions, do you consider them to be serious genetic conditions?

Significant risks

Lower penetrance cancer susceptibility conditions cause an increased risk of developing a specific type of cancer above the risk in the general population. The risk depends on the penetrance of the condition. Fully penetrant conditions undoubtedly fall into the category of 'significant risk' because if the faulty gene is present, the condition will inevitably develop in the person with that faulty gene. For lower penetrance conditions, the risk is less certain — having a faulty copy of a gene for a predisposition to an inherited cancer results in anything between a 30 to 80 per cent chance (or risk) of developing the condition. For these conditions the risk is significantly above that of the general population but whether this would be considered to be a 'significant risk' is an issue for consideration.

The HFEA Guidance to PGD centres states that PGD should only be available where there is *significant risk* of a serious genetic condition. Does the penetrance of the condition affect whether or not you consider it to confer a significant risk? In your opinion what would be the lowest penetrance – in percentage terms – that would confer significant risk?

4.4 The perception of the condition by those seeking treatment is an important factor in the decision making process

When a person at high risk of having a child with a genetic condition comes to think about having a child, they may have a very different attitude from other at-risk people towards the chance that their child might be affected. For example, how negatively or positively a person views the possibility of having a child with a genetic susceptibility to breast cancer may depend upon a number of different factors, such as their experience of the condition, their attitude towards their own risk or that of their partner and how optimistic they are about treatment options in the future.

In the case of inherited cancer conditions, the people seeking PGD are likely to have witnessed several members of their family developing cancer and they will have first-hand experience of the impact this has on the affected person and the rest of the family. At least one of the people seeking PGD will also have a faulty copy of the gene — meaning that they are likely to develop cancer themselves. They will therefore have experience of how being at risk of the condition affects a person.

Because of these factors, people seeking treatment are in many ways best placed to judge the seriousness of the condition. However, many would argue that there should there be limits to the types of conditions for which PGD is offered, stopping short of what some might consider to be a trivial use of the technology. The HFEA needs to find the correct balance between respecting the views of those seeking PGD whilst preventing the use of the technology for purposes which are widely considered to be unacceptable.

The HFEA guidance to PGD centres states that the views of the people seeking treatment should be taken into account when considering whether to offer PGD. There needs to be a balance between the views of those people who would seek to use PGD to avoid passing on a condition and the views of wider society that may have ethical concerns about them doing so. In your opinion, how much emphasis should be placed on the views of those people seeking treatment?

Box 4: We spoke to people who are at risk of developing breast cancer through an inherited predisposition to ask them their views on the use of PGD for these conditions.

Louise is from a family where all the women have been affected by breast cancer. Because none of her family who were affected are still alive, it is not possible for her to be tested to see if she carries the family faulty gene but she is at high risk of being a carrier herself.

"If you offer PGD now, [for inherited breast cancer] then I worry where this screening will lead in the future. I and many members of my immediate family are short sighted and so this is likely to be genetic. Being short sighted is a disadvantage so would people want to test for this in embryos? I think that because you won't necessarily develop breast cancer and if you do, you may not die from it, I would not choose to have PGD to avoid passing on a BRCA mutation although I might consider it for conditions that would definitely affect the child, such as cystic fibrosis."

Sue is a carrier of the fault in the BRCA2 gene that is present in her family. She was the first person in her family who decided to have the genetic test. Finding out that she was a carrier had implications for the rest of her family and she had to decide how and when to discuss it with her family.

"Luckily for me, we have a very close family and we were able talk about it quite easily but I have known families where it has caused relationships to breakdown".

After being tested for the fault in the BRCA gene, Sue had to make a decision about whether to have a prophylactic double mastectomy.

"The cancer was very aggressive in my family members that had the mutation [faulty gene] so when I discovered that I was carrying the mutation [faulty gene], I knew that I had to have surgery to reduce my risk of developing the condition.

If I was starting a family now and I could have PGD to avoid passing on the BRCA mutation [faulty gene] to my children, I would choose to do so because I would not want them to go through what I have seen members of family go through or have to make the decisions that I have had to make."

4.5 The indications for the use of PGD should be consistent with (though not necessarily the same as) current practice in the use of prenatal diagnosis

Prenatal diagnosis is an alternative to using PGD to avoid passing on a genetic condition to a child. However, because the different stages of development at which PGD and prenatal diagnosis are carried out and the different practical implications surrounding the two techniques, there are sometimes situations in which their ethical implications diverge. For example, many people would argue that it is ethically acceptable to select an embryo according to its tissue type — in order to create a child who could donate tissue to a sick sibling, but they would not approve of the use of prenatal diagnosis followed by termination of pregnancy to achieve the same result. Avoiding the transfer of an embryo with the wrong tissue type is usually regarded as being ethically preferable to terminating a pregnancy (ending the life of a fetus) with the wrong tissue type.

In the context of using PGD to detect lower penetrance susceptibilities to cancer, the HFEA is interested in views about the extent to which practice in prenatal diagnosis should determine that in PGD. Although centralised records are not kept, it is understood that prenatal diagnosis has not yet been used to detect conditions like inherited breast or colon cancer (HNPCC). However, because there is no regulatory framework in prenatal diagnosis beyond that set by the *Abortion Act 1967*, it is not known whether tests for these conditions will be provided prenatally in the future.

The HFEA guidance to PGD centres states that the use of PGD should be consistent with current practice in prenatal diagnosis. Do you agree, with respect to lower-penetrance conditions, that the availability of PGD should be determined by current practice in prenatal diagnosis?

Finally, as the name of this document suggests, we would like to understand where people feel the limits – or boundaries – of this technology should lie. This is not an easy question as it involves some speculation about techniques that might be available in the future, for example PGD for Alzheimer's disease. However, if people have views on this issue, the HFEA would like to hear them. One way to approach the question is to take the factors already discussed in this document – the combination of age of onset, penetrance and treatability – and to think about different scenarios. For example, should very late onset conditions — where the condition will not develop until the person is in their seventies or eighties, or very low penetrance conditions — that only raise the risk of developing the condition slightly above that of the general population, be tested for using PGD?

The HFEA wants to know where you feel the boundaries for the use of PGD lie. Considering penetrance, age of onset and treatability, what type of condition do you think should never be tested for in embryos using PGD?

05 Questions

Below are questions for you to answer after reading through Choices and Boundaries. Please feel free to answer in full and give reasons for any views stated.

Question 1: We are interested to find out how you feel about using PGD to test for lower penetrance conditions such as inherited breast cancer. To help put your views about this in context, it is important to understand how you feel about PGD for fully penetrant conditions such as cystic fibrosis or Haemophilia. Do you agree with the use of PGD in general. For example, for fully penetrant conditions that are present in the child? Please give reasons for your answer.

Question 2: The HFEA guidance to PGD centres states that PGD should only be available where there is significant risk of a **serious genetic condition**. Given the lower penetrance, later age of onset and potential treatability of inherited cancer conditions, do you consider them to be *serious* genetic conditions? Please give reasons for your answer.

Question 3: The HFEA guidance to PGD centres states that PGD should only be available where there is **significant risk** of a serious genetic condition. Does the penetrance of the condition affect whether or not you consider it to confer a significant risk? In your opinion what would be the lowest penetrance – in percentage terms – that would confer significant risk? Please give reasons for your answer.

Question 4: The HFEA guidance to PGD centres states that the **views of the people seeking treatment** should be taken into account when considering whether to offer PGD. There needs to be a balance between the views of those people who would seek to use PGD to avoid passing on a condition and the views of wider society that may have ethical concerns about them doing so. In your opinion, how much emphasis should be placed on the views of those people seeking treatment? Please give reasons for your answer.

Question 5: The HFEA guidance to PGD centres states that the use of PGD should be **consistent with current practice in prenatal diagnosis**. Do you agree, with respect to lower-penetrance conditions, that the availability of PGD should be determined by current practice in prenatal diagnosis? Please give reasons for your answer.

Question 6: The HFEA wants to know where you feel the **boundaries** for the use of PGD lie. Considering penetrance, age of onset and treatability, what type of condition do you think should never be tested for in embryos using PGD? Please give reasons for your answer.

Where we refer to the penetrance of a condition we mean the proportion of people who have the faulty gene that will develop the condition. If a condition is fully penetrant (100 per cent penetrant) everyone who carries the faulty gene will develop the condition. As the penetrance of the condition decreases, so too does the proportion of people with the faulty gene that will develop the condition. If a condition is 50 per cent penetrant only half of the people carrying the faulty gene will develop the condition.

How to respond

This discussion is open for any organisation or member of the public to share their views. We will continue to receive responses until 16 January 2006.

Internet
If possible, please respond by answering the questions online at www.hfea.gov.uk/consultations

By email
Please follow the format of the inserted answer sheet provided in this document. Answer the questions in as much detail as is required and give reasons for your views. The responses can be emailed to pgd@hfea.gov.uk

By post
If preferred, please answer the questions and send to the following address:

Choices and Boundaries
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WC1B 3HF

Public meeting
We are holding a public meeting to discuss the issues raised in this paper; to request a place at the meeting on 12 December 2005 in London, please contact us by email pgd@hfea.gov.uk or please call 020 7291 8235.

For further information
If you would like any further information on this please go to our website www.hfea.gov.uk or contact us at pgd@hfea.gov.uk

If you have any questions about choices and boundaries please contact Katy Berry, Policy Manager, on pgd@hfea.gov.uk

HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

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