



Preimplantation Genetic Diagnosis

A Discussion of Challenges, Concerns,
and Preliminary Policy Options Related to
the Genetic Testing of Human Embryos



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Today, there are some one million people for whom the journey toward personhood began when a fertility specialist peering through a microscope carefully added sperm to egg in a glass petri dish, a process known as in vitro fertilization.

Paralleling the rapid development and growing use of IVF have been dramatic advances in our scientific understanding of the human genome and the ability to test for genetic alterations associated with diseases and other inherited characteristics. Currently there are over 1000 genetic tests and the number is steadily growing.

By themselves, IVF and genetic testing each presents a host of issues that are technically, legally and ethically complicated. But now, the worlds of genetic testing and assisted reproduction have converged with the advent of preimplantation genetic diagnosis (PGD)—technology that allows parents to choose which embryos to implant in the mother's womb based on genetic test results. The arrival of PGD has engendered a host of new scientific, social, ethical and political quandaries, prompting many to consider not just the implications of this new genetic diagnostic tool but whether core concerns surrounding in vitro fertilization itself are really all that settled.

Adding genetic testing to the IVF process means that medical providers and scientists can now be deeply involved in the molecular mechanics of the most profound and mysterious of human activities: creating life. This unprecedented intercession of technology into human reproduction is, for some, a deeply offensive act in which science literally subsumes the role of God. For others, it is science mercifully intervening to lift the anguish of genetic disease and infertility.

PGD is a powerful tool that allows parents to identify and select the genetic characteristics of their children. The fundamental societal questions are whether and under what conditions PGD should be used. The basic tension involves concerns about the adverse consequences of proceeding too quickly versus fears that we have much to lose by applying too much restraint.

The challenge is to confront these questions by arming ourselves with knowledge about the technology, its limits and its implications and then considering the various policy decisions that could affect current and future applications. As with any new technology, the target is constantly moving as methods evolve. For example, a new technological advance may resolve particular medical or social concerns while simultaneously creating new ones. Similarly, as the science progresses, policies developed at one point in time may, in a relatively short period, be rendered inadequate.

The Genetics and Public Policy Center was established with a conviction that PGD in particular and new genetic technologies in general are so important that the public at large must be engaged in the discussion and formulation of policies to guide their use and development.

The Center's approach to the genetic testing of embryos is illustrative of how we hope to broaden and deepen the policy discussions surrounding all genetic technologies. The Center does not intend to advocate for or against a particular technology or policy. Instead, we are committed to providing objective information and analysis and encouraging an informed dialogue among a diverse array of interested individuals and groups. To help focus and facilitate the discussion of PGD, we are presenting a range of preliminary policy options, supported by expert analysis, that consider the potential effect, good and bad, of distinctly different choices. Our goal is not to advocate for a single position but to make sure that policy decisions, including the decision to maintain the status quo, are undertaken with a clear-eyed understanding of their potential impact.

In addition, the Center has undertaken an in-depth effort to assess public attitudes toward genetic technologies as a means of making the discussion of genetics and public policy more democratic (with a small 'd') and less the province of special interests. The goal is not to encourage decision-making by public referendum but to give stakeholders, policy makers and the public a better feel for the diversity of opinion that surround these issues.

The options presented in this report are being offered in preliminary form, and will then be refined based on the input we receive. The Center will use this document as an instrument to draw a wide array of individuals into the discussion of PGD. For example, the Center will be organizing meetings around the country to discuss our analysis of PGD and will actively solicit the participation of people whose voices typically are not heard when these issues are discussed. The Center also will convene meetings of stakeholders in order to gather their input on the options. Finally, the Center will establish and promote online, interactive forums designed to provide greater opportunity for a wide range of individuals to register their thoughts and opinions. The Center then will use input from all these sources to refine our PGD policy options.

Through a combination of expert scientific and policy analysis and robust research on public attitudes, the Center hopes to provide a productive framework for discussing PGD, one that allows people to simultaneously air their concerns and consider the potential risks, benefits and implications of a full range of policy options.



Kathy Hudson
Director, Genetics & Public Policy Center



What is PGD?

Preimplantation genetic diagnosis or PGD is a process in which embryos developed outside the womb are tested for particular genetic characteristics, usually genetic abnormalities that cause serious disease, before being transferred to a woman's uterus. PGD owes its existence to advances in the world of reproductive medicine and genetics that occurred in the late 20th century.

As understanding of the genetic basis of inherited disorders increased, so did the number of tests available to detect specific disorders. The use of these tests in prenatal diagnosis allowed the detection of genetic abnormalities in a human fetus in utero. As genetic medicine progressed, so did work on IVF. In 1978, scientists achieved the first viable human pregnancy from an egg fertilized outside the womb in a petri dish or in vitro. Eventually, scientists developed methods to perform genetic tests on a small amount of genetic material taken from an egg or embryo.

This new technique, PGD, permits doctors and prospective parents to select embryos for implantation that do not have a genetic abnormality associated with a specific disease, such as cystic fibrosis, or, alternatively, to select embryos that possess a genetic trait deemed desirable, such as a tissue type that matches that of an ailing sibling.

There are alternatives to PGD. Prospective parents at risk of passing a genetic condition to their offspring can choose to avoid pregnancy, conceive using donor egg or sperm from an individual who does not carry the mutation in question, proceed with a pregnancy but undergo a prenatal diagnostic test (and possibly terminate the pregnancy if it reveals a gene mutation) or accept the possibility that their child could be born with a genetic abnormality.

In the ten years since PGD was first made available to facilitate embryo selection, more than 1,000 babies have been born worldwide following a preimplantation genetic test.

Inherited chromosome abnormalities and single gene disorders including cystic fibrosis, Tay Sachs disease, muscular dystrophy and sickle cell anemia have been detected with PGD.

While originally used by families with a known genetic disease who were not infertile, more recently PGD has been used as an adjunct to standard IVF to detect chromosomal abnormalities, called aneuploidy, arising during egg or embryo development. Some providers recommend PGD for patients over 35 or those with repeated IVF failure. Given that many IVF patients are over 35, aneuploidy screening may soon account for the majority of PGD procedures.

Though initially developed as a means to detect serious genetic conditions, PGD can be used for other purposes. In fact, virtually any of the hundreds of genetic tests now commercially available, and the many more in development, could be used to test embryos.

The possible but controversial applications of PGD include its use to select an embryo that is an immunological match for a sick sibling, to select the sex of an embryo in the absence of a sex-linked disease risk, and to test embryos for gene mutations associated with diseases such as Alzheimer disease that do not appear until late in life, or mutations that indicate a heightened but uncertain risk of developing a particular disease such as hereditary breast cancer.

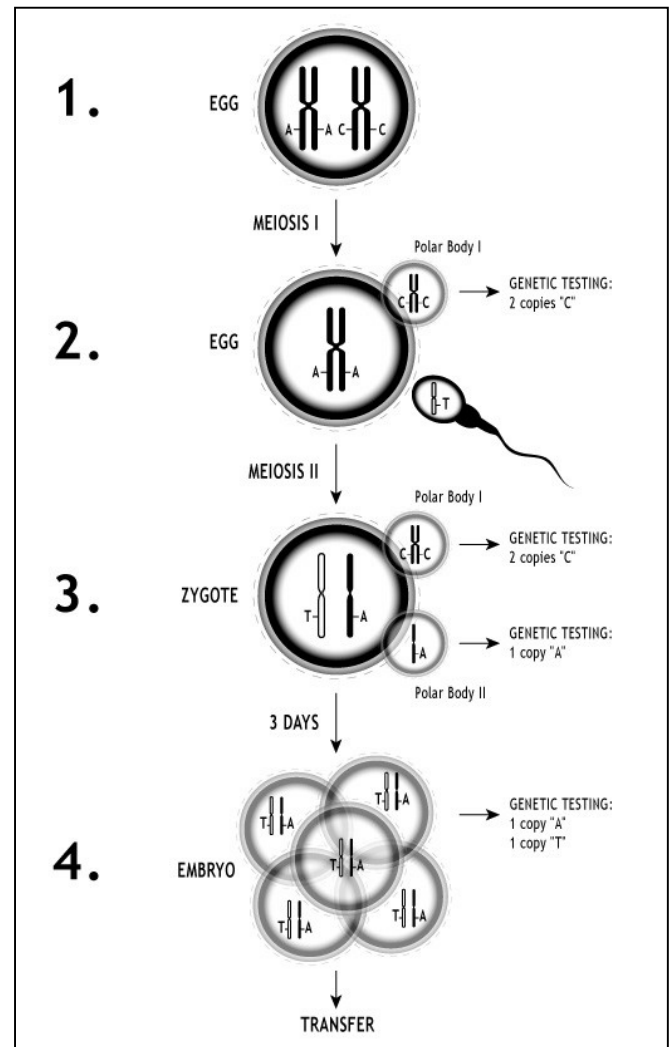
There are inherent limits to the use of PGD to avoid disease or seek out certain traits. For example, not all diseases have a clearly diagnosable genetic component. Many diseases, as well as traits, are the result of a complex interaction between genetic and environmental factors. Thus, a test of a single gene may not be particularly useful. And, of course, PGD cannot create new genetic characteristics that neither parent has. PGD can allow parents to select only among the genetic combinations present in the embryos they have produced.

The Mechanics of PGD

PGD is a multi-step process involving egg extraction, in vitro fertilization, cell biopsy, genetic analysis and embryo transfer. First, as in all in vitro fertilization processes, eggs removed from the mother after she has been given drugs to stimulate egg production are fertilized in the laboratory. The genetic material for testing can be obtained in two ways. The most common method is to use one or two cells taken from an embryo two to four days after fertilization. Alternatively, genetic tests can be performed on cells (called polar body cells) that are cast off by the egg as it matures and is fertilized. The results of the genetic tests on the polar bodies are used to infer the genetic makeup of the fertilized egg.

Two techniques are used to analyze the genetic material from single cells: chromosomal analysis to assess the number or structure of chromosomes present in the cells; and DNA analysis to detect specific gene mutations. For chromosomal analysis, fluorescently labeled, chromosome-specific probes are used to visualize spots representing each copy of that chromosome present in the cell. Too few or too many spots can indicate abnormalities. For direct DNA analysis, a technique known as a polymerase chain reaction (PCR) is used to make many copies of the targeted gene, which are then examined for evidence of a specific DNA sequence.

Regardless of the methods, the results of preimplantation genetic diagnosis are used to inform the selection of embryos for transfer to a woman's uterus.



Genetic Testing in PGD (figure legend)

Genetic testing in PGD can be done by testing one or both polar body cells (2 & 3) that are cast off from the egg as it matures and is fertilized or, by testing cells from the embryo (4).

1. Genetic testing in PGD starts with knowing the genetic makeup of one or both parents (only the egg is shown in 1).
2. Genetic testing of Polar Body I allows inference about the genetic composition of the egg. In this example, two copies of "C" are detected in the polar body inferring that the egg carries two copies of "A". If "A" was the desired copy of the gene, this egg could be used for fertilization. If not, it would be discarded.
3. Testing Polar Bodies I and II simultaneously after fertilization is another approach to polar body testing. In this example, two copies of "C" are detected in Polar Body I and one copy of "A" in Polar Body II, inferring that the fertilized egg contains one copy of "A".
4. More typically, PGD involves testing one or two cells of the embryo removed 2-3 days after fertilization when 5-8 cells are present. This permits direct analysis of the embryo's genes. In this example, "A" and "T" are detected in the cell.

What PGD is Not

PGD should not be confused with gene therapy or any other efforts to alter an embryo or a person's genetic make-up. PGD as currently practiced can reveal a considerable amount of information about an embryo's genetic make-up, but it is not possible today to correct or alter an embryo's genes.

Overview of Challenges and Concerns

PGD raises important concerns related to whether and when it should be used, its safety and effectiveness, costs and access and what it would mean to live in a society where one's genetics become more a matter of choice than chance. These are complicated dilemmas about which there has been little discussion or opportunity to form agreement.

The extent to which these issues command attention will likely be tied to how often and for what purpose PGD is used. Since PGD requires IVF, it is mainly used today by a relatively small number of parents who are willing to undergo IVF to avoid a known serious or fatal genetic condition or who are unable to get pregnant without IVF because of infertility problems. For the moment, one would expect very few people who otherwise have no problems achieving a healthy pregnancy to utilize PGD. Nonetheless, that could change as IVF techniques improve and the number of genetic tests that can be employed successfully in PGD increases.

If PGD becomes more widely used, there is likely to be growing public interest in developing policies that address the different ethical, technical and social concerns raised by the genetic testing of embryos. At a minimum, the public in general and policy makers in particular need to be aware of the implications of various policy choices, whether the choice is to ban PGD, create new forms of oversight or do nothing at all. It is important to consider a wide range of policy options that focus on particular aspects of PGD and consider arguments for and against their implementation.

Considering "Acceptable" Uses of PGD

For society as a whole it is the ethical and moral ramifications of PGD that have attracted significant attention. These mainly revolve around the issue of whether and under what circumstances the use of PGD is acceptable.

The fact that PGD and the underlying IVF process involve the creation and, frequently, the destruction of human embryos could present a major challenge to the development of policy that deals with moral and ethical concerns.

In vitro fertilization generally creates more embryos than will ultimately be transferred to a woman's uterus. PGD enables the selection of one or more embryos over others, with the likelihood that embryos deemed genetically undesirable will be destroyed.

There is the possibility that some of the extra embryos created as part of an IVF procedure could be donated to couples who would use them to try to achieve a pregnancy and have a child.

But the prevailing view is that, even if this were to occur, there would still be excess embryos. And embryos that have been found to carry genetic mutations linked to diseases or disabilities are less likely to be candidates for donation.

*"If you ask me if it should be allowed or legal, I would say yes it should be allowed and it should be legal. If you're going to say ethically, should I do it? Would I do it? Would I recommend it? I don't know. That would depend on a lot of different things. **

For some, the creation and potential destruction of embryos through PGD does not raise moral or ethical concerns. Others do view this as morally or ethically problematic but nevertheless think it may be defensible in some limited situations and that PGD should be strictly regulated and limited in order

to minimize the creation and destruction of embryos. Still others believe the creation and potential destruction of embryos is categorically unacceptable and thus are opposed to PGD and IVF under all circumstances.

For those who categorically oppose manipulation or destruction of human embryos, PGD is never appropriate because it necessarily involves one or both. But, even here, it is important to distinguish between personal preference and policy preference. The Center's public attitudes research has shown that some people who would never themselves consider PGD do not necessarily support policy prohibiting others from using it. Others may find PGD appropriate when used to detect certain serious medical conditions but have reservations about its use for other purposes.

Some question the ethics of using PGD to screen embryos for diseases, such as Huntington disease, that will not affect a person until adulthood, reasoning that children born today with those mutations would enjoy several decades of normal health before any symptoms began, during which time science may well find a treatment. And what about genetic mutations associated with a heightened risk, as opposed to a certainty, for developing a particular disease? For example, should embryos be tested for a genetic mutation linked to an elevated risk of developing hereditary breast cancer, even though some women who have this mutation never develop the disease? Should an embryo with that mutation be summarily discarded?

Safety, Accuracy and Effectiveness

For people who have decided to use PGD, the questions turn from the broad ethical and moral to more immediate concerns. Chiefly, is this procedure safe for the mother and the resulting child and can it be counted on to produce an accurate result? Exploring matters of safety, accuracy and effectiveness requires a consideration of the technical challenges and risks inherent in the genetic test itself and in the IVF procedure that it entails.

PGD involves technical pitfalls that can lead to a misdiagnosis of the embryo. Most notably, the small amount of DNA—from only one or two cells—available for testing and the need to get the results relatively quickly can present difficulties. If

* All quotations are from focus groups conducted by the Genetics & Public Policy Center in *April 2003*.

DNA analysis is done, both copies (alleles) of the gene may not be detected, which can result in a misdiagnosis. Performing chromosomal analysis of the embryo is also susceptible to mistakes. There are a limited number of fluorescent probes that can be used simultaneously so not all chromosome abnormalities can be detected.

Because an error can be made when testing the embryo, it is often recommended that the PGD result be confirmed by subsequent prenatal tests, such as amniocentesis or chorionic villus sampling (CVS).

There are many unanswered questions about the long-term health consequences of PGD and IVF for the mothers and the resulting children. In all IVF processes there are risks associated with the hormones used to stimulate ovulation, and there is the risk the procedure could result in an ectopic (outside the uterus) pregnancy. Because more than one embryo is usually transferred at once, there is a heightened risk the mother will carry multiple fetuses, which can make for a more complicated pregnancy, posing risks to both mother and fetus. In addition, there is no certainty that a pregnancy will occur after the embryo is transferred. PGD pregnancy rates are estimated to be about 20 percent. Also, it is not known whether and under what circumstances cell biopsy can harm an embryo or the development of the child.

Access to PGD Services

Because PGD is expensive, there are concerns that it will end up being accessible and affordable only to the wealthy. As with all new medical treatments and techniques, the availability of PGD will be influenced by a health care system in which cost-benefit considerations largely drive coverage. If there is to be widespread insurance reimbursement of PGD, those who underwrite coverage—mainly employers and insurance companies—must view it as cost effective. Otherwise, the cost of PGD will be paid out-of-pocket by patients.

Having access to PGD determined by financial status could lead to situations in which a poor mother is more likely to give birth to a child with a genetic disorder than a more affluent mother who can afford to have her embryos tested. Families who can least afford it will be more likely to suffer the financial burden of caring for a family member with a genetic disease.

In addition to the fact that the cost-benefit equation could inhibit coverage, there could be pressure on insurers not to pay for PGD services given the moral issues involved. And from a health policy standpoint, there could be an argument made that there are many other health care needs more important than PGD that should be covered first.

PGD and Its Future Implications for Society

Looking to the future, some observers view PGD, or any technology that allows parents the ability to choose the characteristics of their children, as having the potential to fundamentally alter the way we view human reproduction and our offspring as well. Rather than the currently prevailing view of reproduction as a mysterious process that results in the miraculous gift of a child, human reproduction could come to be seen more as the province of technology and children the end result of a series of meticulous, technology-driven choices.

Some argue that widespread use of PGD eventually could change the current framework of social equality in many areas. The most dramatic possibilities involve babies who are born with genes selected to increase their chances of having good looks, musical talent, athletic ability, high SAT scores or whatever a parent who can afford PGD may desire. Meanwhile, such advantages would be unavailable to the less affluent.

Such a scenario, while certainly not possible now given the current limits on the technology, is perhaps not totally implausible. Although PGD involves a diagnostic test, as opposed to the genetic manipulation or genetic “engineering” of the embryo, the information it reveals could conceivably allow a parent to select an embryo based on many factors other than the absence of a disease-causing gene mutation. Over time these factors could grow as science uncovers the links between individual genes and specific traits that play a role in intelligence, appearance and complex behaviors.

Another concern is that PGD eventually could change the way society views the disabled. PGD is capable of detecting conditions that are debilitating to various extents yet are not life-threatening. Some critics argue that some of the genetic conditions that PGD can now detect, such as those causing hereditary deafness, are merely human differences that do not limit an individual's ability to live a useful and satisfying life.

“I’m not sure if it’s better to be born with muscular dystrophy and live with that, or to not be born at all, so I can’t make that decision. It’s a personal one for each individual.”

“Eliminating diseases is certainly good for the society...but being able to choose the eye color of your child, or being able to choose their build or whatever it is, I think that’s starting to cross over a different line.”

Advocacy groups point out that children with these conditions can and routinely do grow into healthy, active and productive citizens with normal life spans. Using technology to prevent their birth, these groups argue, will lead to a society in which aesthetic concerns, convenience or mere prejudice supplant the inherent dignity due to every human being, regardless of how closely he or she conforms to some ideal of normality or perfection. They worry that societal norms will evolve such that parents who are at risk of having affected children will be pressured to use PGD, even if they find the procedure objectionable.

“I just think we’re putting so much power into people’s hands. I cannot look at any one of those [special needs] kids and say, ‘you just don’t deserve to be here.’ Who should be able to do that?”

Others have responded that for some time now parents have had the option of using amniocentesis and other types of prenatal diagnostic tests to probe for the same genetic abnormalities PGD can now detect. This information sometimes prompts parents to terminate a pregnancy to avoid having a child with a disability. Yet despite the tests’ widespread availability, many parents still choose to decline testing and to give birth to children with disabilities and society continues to support families who make these choices.

Specific concerns also have been raised about the societal impact of using PGD for sex selection, when the purpose is to satisfy parental preferences and not to avoid sex-linked disease. One issue is that, historically, in many societies females have been subjected to discrimination based purely on gender, and, in some parts of the world, there are cultures that still openly prefer male children to female. Given this history of discrimination and existing cultural preferences for boys, some observers see using PGD for sex selection as having the potential to devalue women.

However, others argue that in many countries, including the U.S., one sex is not currently preferred over the other and sex selection has been used to select boys and girls equally. Some providers of PGD services have refused to conduct tests that would allow for gender selection unless it is related to a genetic condition, while others actively advertise these services.

Additional societal concerns have been raised about the potential for PGD to alter childhood and family dynamics, particularly when it comes to parental expectations and sibling relationships. For example, parents could end up being more critical and demanding of a child they view as having been carefully selected to possess certain attributes. Also, there could be tension among siblings when one is the product of PGD and the other is not, or when one has been selected via PGD to serve as an immunological match for another.

Ultimately, the issues of appropriate use, safety and accuracy, access and societal impact are interrelated. Scientific advances

that make embryo testing more reliable may calm parental fears about accuracy, but those same advances may intensify moral and ethical concerns if they prompt an increase in both the frequency and variety of PGD applications. Similarly, advances that make the procedure safer and more precise could also make it more expensive, widening the gap between those who have access to PGD and those who do not.

Current Oversight

Federal Oversight of PGD

The federal government does not typically directly regulate the practice of medicine, leaving such oversight to the states. Nevertheless, there are a variety of mechanisms that governmental agencies use to regulate or to influence the safety and availability of health care services and medical products. These include requirements for safety and effectiveness testing, outcome reporting and oversight of clinical research. However, Congress has not explicitly authorized federal regulation of PGD.

PGD sits at the intersection of two technologies with a confusing regulatory status: assisted reproduction and genetic testing. To the degree that there is federal oversight of PGD or its component technologies, it is “derivative”—that is, it is derived from existing statutes having broader applicability. This section will briefly describe existing government oversight related to PGD. To the extent that there are gaps in oversight, new regulations or laws may be required.

Three federal agencies within the U.S. Department of Health and Human Services oversee areas related to PGD: the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) and the Center for Medicare and Medicaid Services (CMS, formerly known as the Health Care Financing Administration).

Centers for Disease Control and Prevention

CDC implements the 1992 Fertility Clinic Success Rate Reporting Act (FCSRA). This law requires clinics that provide IVF services to report pregnancy success rates annually to the federal government. The FCSRA requires clinics to report data concerning the type of assisted reproduction procedure used, the medical diagnosis leading to IVF treatment, the number of cycles of IVF attempted, whether fresh or frozen embryos were used, the number of embryos transferred in each cycle, the number of pregnancies achieved and the number of live births. The statute does not require clinics to report the health status of babies born as a result of the procedure or the use of diagnostic tests such as PGD.

CDC analyzes the data and makes its findings available to the public, including via the Internet. The data are collected from

clinics by the Society for Assisted Reproductive Technologies (SART), a professional society whose members comprise clinics engaged in reproductive medicine.

In 2001, the most recent year for which data are available, 384 clinics reported data to SART. The law requires CDC to list on its website the names of clinics that do not report at all or that fail to verify the accuracy of the data. Thirty-seven clinics are listed as non-reporters. Other than being listed by CDC, there are no penalties for failure to report.

Food and Drug Administration

FDA regulates drugs and devices, including those used as part of IVF treatments (such as drugs to induce ovulation and laboratory instruments used in IVF). Depending on the type of product, FDA may require submission of data from clinical studies (premarket review) and agency approval before the product may be sold.

Some of the products used by clinical laboratories to perform genetic tests are regulated as medical devices by FDA. However, most genetics laboratories develop their own tests, and FDA's jurisdiction over these so-called "home brew" tests has been a subject of debate. FDA does not currently regulate home brew tests, although it does regulate certain components that laboratories use to make them. Given the existing confusion about FDA's jurisdiction over genetic testing in general, there is uncertainty regarding its authority to regulate PGD tests.

FDA also regulates human tissues intended for transplantation. The agency's statutory authority is limited to preventing disease transmission. FDA regulations require facility registration, screening to detect infectious diseases, record keeping and the proper handling and storage of tissues. FDA can inspect tissue banks and order the recall or destruction of tissue found to be in violation of regulations. Recently, FDA has decided to extend this form of limited regulatory oversight to reproductive tissues under certain circumstances.

In addition, FDA regulates certain human tissue-based therapies as "biological products," such as tissues that are manipulated extensively or are used in a manner different from their original function in the body. However, FDA has not determined that reproductive tissues are "biological products" when used for IVF or PGD procedures and has not required premarket review for these tissues. Whether FDA has the legal authority under current statutes to take such a position, and whether it would choose to do so even if it did, is an open question.

Although FDA regulates claims a manufacturer may make about an approved product, it does not have authority to regulate the actual uses of approved products by physicians. Such decisions are considered part of medical practice. Thus,

even if FDA required premarket approval for the reproductive tissue or the genetic tests used as part of PGD and limited the claims that could be made about them, the agency could not restrict the actual use of these products by PGD providers.

Center for Medicaid and Medicare Services

CMS implements the Clinical Laboratory Improvement Amendments of 1988 (CLIA). CLIA was enacted in order to improve the quality of clinical laboratory services. Although it is administered by CMS, it applies to clinical laboratories regardless of whether or not they service Medicaid and Medicare beneficiaries. CLIA defines a "clinical laboratory" as a laboratory that examines materials "derived from the human body" in order to provide "information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings."

CLIA includes requirements addressing laboratory personnel qualifications, documentation and validation of tests and procedures, quality control standards and proficiency testing to monitor laboratory performance. CMS has not taken a position regarding whether laboratories engaged in IVF (sometimes called embryology or embryo laboratories) are "clinical laboratories" within the meaning of the statute. CMS has similarly not taken a position regarding whether laboratories that engage in the genetic analysis component of PGD are subject to regulation as clinical laboratories.

The outstanding question is whether the genetic tests performed in PGD laboratories provide information that will be used to diagnose, treat or prevent disease or to assess human health. Some within the agency worry that including PGD within the definition would require CMS to take the position that an embryo meets the legal definition of a human being, although it is unclear whether this concern is well-founded since neither the agency nor any court has had occasion to formally address it. In addition, IVF providers argue that their activities constitute the practice of medicine and are not within the scope of CLIA.

If CLIA were applied and enforced with respect to laboratories performing embryo biopsy, then the laboratories would need to comply with the rules applicable to all other clinical laboratories, including those relating to personnel, record keeping, documentation, specimen handling and other quality control and assurance measures. The federal government also would have the authority to inspect PGD laboratories and review their records, and to impose sanctions on those not complying with the regulations.

If CLIA were applied and enforced with respect to genetic analysis of preimplantation embryos, laboratories engaged in this activity would be required to do proficiency testing under CLIA's general proficiency testing requirements for high complexity laboratories. However, CMS has not yet established specific proficiency testing regulations for

molecular genetic testing, leaving the determination of how to comply up to the individual laboratory. In 2000, CDC announced its intention to develop a proficiency testing standard for molecular genetics, but no further formal action has been taken.

Federal Oversight of Research

Research carried out at institutions supported with federal funds is subject to federal requirements for protecting human research subjects. These requirements also are mandatory for research to support an application to FDA for product approval. However, they are not mandatory for privately funded research (which includes research supported by foundations) that is unrelated to a request for an FDA approval, though a company or research institution may have internal guidelines that offer protections for human subjects.

As it now stands, any research on PGD techniques involving human subjects would probably fall outside federal requirements for protecting human research subjects. First, there is a law against providing federal funding for research involving the creation or destruction of human embryos. Second, since FDA does not currently require premarket approval for PGD services, private research into PGD techniques that use human subjects also would fall outside the agency's purview.

State Regulation

No state has enacted laws that directly address PGD. In general, states have considerable authority to make laws and regulations that govern the practice of medicine. Some states have passed laws related to assisted reproductive technology (ART). They are mainly concerned with defining parentage, ensuring that the transfer or donation of embryos is done with informed consent or ensuring insurance coverage for fertility treatment. Some states prohibit the use of embryos for research purposes and one state, Louisiana, prohibits the intentional destruction of embryos created via IVF. For the most part, states have not assumed oversight responsibilities for fertility clinics.

For laboratories, states can create their own regulatory schemes that go beyond the federal mandates, but most states have not included laboratories that conduct IVF or PGD in their laboratory oversight duties. However, New York is in the process of developing standards for laboratories that will include oversight of the genetic tests associated with PGD.

Under the FCSRA, CDC developed a model state program for certifying laboratories that work with human embryos. It includes standards for procedures, record keeping and laboratory personnel and criteria for inspection and certification. According to CDC, no state has formally adopted the model program.

States also have jurisdiction over benefits included in insurance plans sold within their borders, and can thereby

influence access to PGD services by mandating insurance coverage. No state laws currently require insurance coverage for genetic testing of embryos, but 15 states have enacted laws mandating some degree of coverage for infertility treatments, including IVF services. However, there is a federal law (the Employee Retirement Income Security Act or ERISA) that provides an exemption from state coverage mandates to employers who assume the risk for their employees' health care costs. The practical effect is that nationwide about half of the 131 million Americans who get health insurance through their jobs may not be receiving the benefits required by state laws.

Oversight by Court Action

Courts have addressed a variety of cases relating to assisted reproduction, but only a few concerning PGD. In one case, the parents of a child born with cystic fibrosis (CF) following PGD, as well as the child, sued those involved with the embryo screening for failing to detect the condition. The parents made the claim of "loss of consortium," meaning the loss of the companionship they would otherwise have had with a healthy, non-CF-afflicted child. The court rejected this claim, finding that it was too speculative. Also, it ruled that the defendants could not be held legally responsible for causing the child to suffer from a genetic disease.

The court similarly rejected the child's claim of "wrongful life," which alleged that the defendants' negligent failure to detect CF denied his parents an opportunity not to give birth to him. Most courts have rejected wrongful life claims in other circumstances, such those arising from a flawed prenatal test, in part because doing so would require accepting the general argument that there can be instances in which an impaired life is worse than no life at all.

As more people take advantage of the new PGD technology, more legal questions may be brought before the courts, leading to the development of a body of "case law." Standards developed through case law frequently influence legislative action or become a de facto policy by themselves.

Self-Regulation by Professional Organizations

Medical and scientific professional organizations present another opportunity for oversight of PGD. These groups, which generally comprise members of a particular occupation or specialty, can serve a variety of functions. They can educate members about advances in the field, develop guidelines addressing appropriate conduct or practices and impose standards of adherence that are a prerequisite for membership.

For the most part, however, such standards are voluntary, in that an individual can choose not to belong to the organization and therefore avoid the obligation to follow the standards. Professional organizations also typically do not have authority to sanction members for noncompliance. Unless the organization is specifically authorized by the federal

government to act on the government's behalf in administering and enforcing government standards, actions of the professional organization do not have the force of law.

For PGD, a few different professional organizations have relevant expertise and either currently possess or could in the future develop PGD-specific guidelines or standards. For example, the American Society for Reproductive Medicine (ASRM) is a professional organization whose members are health professionals engaged in reproductive medicine. ASRM issues policy statements, guidelines and opinions regarding a variety of medical and ethical issues that reflect the thinking of the organization's various practice committees. These documents, while not binding on members, may be viewed as evidence of standards of practice in legal settings.

In 2001 ASRM issued a practice committee opinion addressing PGD stating that PGD "appears to be a viable alternative to post-conception diagnosis and pregnancy termination." It further states that while it is important for patients be aware of "potential diagnostic errors and the possibility of currently unknown long-term consequences on the fetus" from the biopsy procedure, "PGD should be regarded as an established technique with specific and expanding applications for standard clinical practice." ASRM has also issued an ethics committee opinion cautioning against the use of PGD for sex selection in the absence of a serious sex-linked disease.

Another example of professional oversight is the Society for Assisted Reproductive Technologies (SART). SART, an affiliate of the ASRM, is a professional society whose members comprise clinics engaged in reproductive medicine. As discussed above, SART, together with CDC, administers the legislatively mandated reporting requirements for fertility clinics. SART is responsible for collecting the data that is then analyzed and reported by CDC.

Compliance with the reporting and data validation requirements of the statute is a requirement of SART membership. SART provides voluntary consultation and guidelines to members in order to improve the quality of clinical practice. Its committees also develop practice, laboratory, advertising and other guidelines to which SART members must agree to adhere. The organization does not have any guidelines specifically addressing PGD. Overall, it views its role as a private "watchdog" whose activities will instill consumer confidence and preclude the need for governmental intervention. According to SART, its members represent 95 percent of all IVF establishments in the U.S.

One organization has recently formed to focus specifically on PGD. The PGD International Society (PGDIS), founded in 2003 in the United States, was created to promote PGD and to organize meetings and workshops on PGD research. PGDIS may take on additional functions in the future.

An international organization, the European Society for Human Reproduction and Embryology (ESHRE), tracks PGD outcomes on a voluntary basis, but captures primarily European data. ESHRE is an organization comprising individuals active in the field of reproductive medicine and science and is dedicated to facilitating the study and analysis of all aspects of human reproduction and embryology. ESHRE has over 4000 members, including some U.S. physicians and scientists engaged in PGD efforts.

A few professional organizations oversee the conduct of clinical laboratories and potentially could extend their oversight to the laboratory component of PGD. For example, the College of American Pathologists (CAP) has been empowered by the federal government to inspect laboratories seeking certification under the Clinical Laboratory Improvement Amendments. CAP also has developed a voluntary certification program for reproductive laboratories that perform embryology testing. However, this latter program does not currently include standards for PGD.

Similarly, the American College of Medical Genetics (ACMG) develops laboratory standards and clinical practice guidelines for genetic tests. However, these guidelines and standards do not currently address PGD.



Preliminary Policy Options

There are many alternatives, some complementary, some conflicting, for policies to guide the development and use of PGD. Some observers are content with the current level of oversight of PGD, while others have raised specific concerns about PGD's use, safety or implications for society.

These preliminary options are divided into five different sections. Within each section, more than one option may be presented, each exploring a different approach for addressing a specific issue.

Section I examines the possibility of a complete ban on PGD. Section II explores mechanisms to limit PGD's uses. Section III addresses ways to ensure the safety, accuracy and effectiveness of PGD. Section IV analyzes who has access to PGD and presents options to increase access. Section V explores options to address the impact of PGD on society. Finally, Section VI presents options to obtain data that may assist policy makers in making policy choices based on adequate evidence.

These preliminary policy options seek to explore the full measure of possible policy approaches, including federal, state and non-governmental strategies. Each option includes a brief overview of its purpose and potential implementation, and explains some of the arguments that could be made in support or opposition.

Ultimately, one's policy preferences are likely to be influenced by a range of factors, including perceptions of existing and likely future applications of PGD, core beliefs about the moral and ethical acceptability of PGD, assumptions about the expected costs and benefits and how they will be distributed and fundamental views about the proper balance between governmental involvement and individual liberty.

The Center neither supports nor opposes any of the options presented. Rather, the Center is presenting the options in preliminary form to stimulate public conversation about PGD and its implications and to encourage comments that will be used to revise and refine the policy alternatives.

**To Share your Thoughts
on the Preliminary Policy Options
Contact the Genetics and Public Policy Center**

- Visit our web site: www.dnapolicy.org and click on Policy Options.
- Send an email: inquiries@jhu.edu
- Write to:
PGD Comments
Genetics and Public Policy Center
1717 Massachusetts Ave, NW
Suite 530
Washington, DC 20036



Should PGD be Allowed at All?

A consideration of the genetic testing and subsequent selection of human embryos must begin with the first order question: Should PGD be permitted at all? Are there any circumstances that warrant this unprecedented exercise of human control over reproduction and the genetic characteristics of the next generation?

Some observers believe a unique human being is formed at the moment a sperm fertilizes an egg. PGD requires the creation and sometimes the destruction of embryos and thus, according to this view, is an act that destroys human life and should be banned. From this perspective, no use of PGD is truly “therapeutic.” The testing does not treat the condition it detects. Rather, it diagnoses a “patient” with the sole purpose of telling parents which “patient” to discard.

“Once it is conceived, it’s a child, and I just don’t like the idea of getting rid of any child, or picking out of a petri dish.”

There are others who do not hold such a firm position on the moral status of the early human embryo but who nonetheless oppose PGD because they view it as unnatural and as violating a deep respect for the ways of nature.

Also, some argue that PGD should be avoided even if it is not inherently wrong or offensive because it places society atop a slippery slope that will lead to genetic enhancement and human control of evolution.

Some who hold these various views want to see PGD banned permanently. Others would be willing to consider a temporary ban, to be revisited at some point in the future after society has an opportunity to consider more carefully the implications of this technology.

“I think we feel powerless to draw the line, but if I had the power to say where I would draw the line, I would say anytime that a life is being ended because of its assumed quality.”

Option: Federal or State Ban on PGD

Congress or state legislatures could decide that PGD is sufficiently problematic to justify banning the procedure entirely.

Arguments for:

- Any use of PGD, no matter how sympathetic the reason, is an unwarranted intrusion into the natural process of procreation.
- Any use of PGD is unacceptable because it results in human embryos being destroyed.
- A ban provides a bright-line rule and clarity for prospective parents, health care providers and society.
- New technologies should not be allowed without limits. PGD should be banned, at least until its implications are more clearly understood.

Arguments against:

- Banning PGD imposes a single moral or ethical perspective on those who may have different views.
- Like any governmental restriction on reproductive decision-making, a ban may raise Constitutional concerns.
- This approach is too blunt an instrument because it does not allow exceptions even under the most sympathetic circumstances.
- This approach is inconsistent from a policy perspective. There are no restrictions on the genetic tests that can be performed on a fetus or on the reasons for which a woman may terminate a pregnancy.
- Prospective parents may be forced to go to “underground” providers, or, for those who can afford it, to another country where PGD is legal.
- Bans on a medical procedure would be difficult to enact and enforce.
- Bans at the state level could lead to inconsistencies in access to PGD.



For What Purpose? Addressing Acceptable Uses of PGD

PGD is now used primarily to increase the chance of having a child free of a specific serious disease. But there are no legal limits on which of the many genetic tests can be used in PGD. Although some providers believe that certain uses of PGD are unethical and refuse to do PGD under certain circumstances (for example, to select an embryo of a particular sex for nonmedical reasons), others advertise these services and believe that parents should have the freedom to decide what is appropriate.

Some observers argue that parents always have tried to give their children every possible advantage, from vitamin supplements to private swimming lessons. PGD, they argue, should be viewed as a technology that simply extends the boundaries of this natural tendency.

Others are comfortable with using PGD to avoid serious genetic disease, but take issue with its use to detect mild conditions or superficial traits. For them, the use of PGD to avoid suffering outweighs the risks involved and the concerns they may have about the embryos. But, the balance tips when PGD is used for a mild or treatable condition or to select embryos based on genetic characteristics that do not cause suffering.

The discussion is made more complex because the lines often are not clear between what is a serious health problem, what

is a mild or treatable disease and what is purely a trait, a genetic characteristic unrelated to disease. For example, many in the medical community would say that a genetic predisposition to hearing loss represents a serious medical condition. Yet many in the Deaf community consider deafness to be a culture, not a disability. What about deaf parents who would like to select an embryo more likely to develop into a deaf child?

“[T]o me quality of life is the most important thing above religious beliefs, or playing God or whatever you want to call it. You want to provide, especially your own child, with the best life that they could possibly have, and if these procedures will help with that, then great.”

It seems unlikely that prospective parents who do not have a known serious genetic mutation in their family or do not need IVF techniques to get pregnant would choose to go

through the expense, discomfort, risk and uncertainty of IVF to use PGD. However, for people who already turn to IVF to treat infertility, PGD may become a more common tool to screen for genetic variants ranging from the serious to what some might consider trivial. And if IVF techniques become less expensive and invasive, it is possible that more prospective parents may consider using IVF so they can use PGD to “choose” their embryo.

“I agree to the point where, if you want to pick your sex, you want to pick the eyes and the color...that’s pushing it. But when you are talking about medical issues, I am a little bit more sensitive with that, and I think that I would want options for myself.”

Where is the line to be drawn between acceptable and unacceptable uses of PGD? Is it appropriate to test for a debilitating disease gene but not appropriate to screen for sex? What about traits that are

perceived to have social or aesthetic value? Perhaps more importantly, who should draw this line?

Federal Oversight

Option: Enact New Law Limiting PGD

Congress could enact a law clearly prohibiting PGD for uses it determines to be unacceptable (e.g. sex selection for non-health-related uses.) Congress would need to list and define prohibited uses. The legislation could contain civil and/or criminal sanctions for providers who violate the law, which a federal agency would enforce.

Arguments for:

- This approach would create clear and legally enforceable rules.
- The process of creating legislation would engage the public in the issue of appropriate limits on PGD applications. This kind of “public conversation” could provide a model for using a deliberative, democratic process to shape policy related to reproductive technology more broadly.
- By limiting the uses of PGD, fewer embryos would be created and destroyed.

Arguments against:

- This approach would constitute a significant intrusion into private medical practice.
- Any law that limits decision-making in human reproduction raises concerns about reproductive choice and could be subject to a Constitutional challenge.
- This approach would implicitly give government sanction to some uses of PGD, all of which may involve the destruction of embryos.
- This approach could negatively affect innovation in PGD medical practice and drive providers away from the field.
- It will be difficult for any entity, including a legislative body, to draw lines between acceptable and unacceptable uses.
- Limits on PGD would require that parents seeking to prevent the birth of a child with a genetic condition for which PGD testing is prohibited instead use prenatal diagnosis and possibly terminate a pregnancy.
- Limits on PGD testing would not prevent parents from using the same tests in prenatal testing and terminating a pregnancy for what some may view as inappropriate purposes.

Option: Authorize New or Existing Federal Agency

Congress could pass legislation delegating to a new or existing federal agency the authority to oversee PGD. The agency would be empowered to determine permissible uses of PGD. Such an entity could be charged with:

- Issuing regulations listing acceptable and unacceptable uses;
- Adjudicating specific requests for use of PGD tests;
- Approving new uses of PGD tests and techniques;
- Licensing and inspecting facilities that engage in PGD.

Arguments for:

- The agency would create clearly enforceable standards governing PGD use.
- A regulatory agency has more flexibility than Congress to respond to changing circumstances or scientific advances.
- The process of rulemaking would stimulate a productive public discussion about the rapidly developing world of human reproductive technology.
- The oversight would be tailored to PGD, avoiding the problems related to applying existing laws and regulations never intended to cover these new technologies.
- By limiting the uses of PGD, fewer embryos would be created and destroyed.
- An oversight body could also facilitate research into PGD’s impact on individuals, family and society.

Arguments against:

- This approach would constitute a significant, even unprecedented, intrusion into private medical practice.
- Any law that limits decision-making in human reproduction raises concerns about reproductive choice and could be subject to a Constitutional challenge.
- It is difficult to create a stable, effective and non-partisan oversight body. For example, if PGD tests cannot be performed without approval from a single government authority, lawmakers who disagree with the agency’s decisions about PGD use could effectively halt agency actions by denying the agency funding.
- Any new oversight will affect ease of access. In general, more scrutiny will mean restricted or delayed availability and increased costs.
- It would be extremely difficult to find a majority of lawmakers who could agree on the scope and powers of such an entity.

State Oversight***Option: Set Limits on PGD at the State Level***

States could, either through legislation or agency action, determine permissible uses of PGD. State legislatures or agencies would need to list and define prohibited uses. The legislation could contain civil and/or criminal sanctions for providers who violate the law, which a state agency would enforce.

Arguments for:

- States have historically played a primary role in health and safety issues.
- Developing public and political agreement on permissible and impermissible uses may be easier at the state level than at the federal level.
- This approach would create clear and legally enforceable rules.
- By limiting the uses of PGD, fewer embryos would be created and destroyed.
- The process of creating legislation would engage the public in the issue of appropriate limits on PGD applications. This kind of “public conversation” could provide a model for using a deliberative, democratic process to shape policy related to reproductive technology more broadly.

Arguments against:

- States may differ in the uses they permit, creating inconsistencies in available care.
- This approach could negatively affect innovation in PGD medical practice and drive providers away from the field or to move to more permissive states.
- Any law that limits decision-making in human reproduction raises concerns about reproductive choice and could be subject to a Constitutional challenge.
- This approach would implicitly give government sanction to some uses of PGD, all of which may involve the destruction of embryos.
- Limits on PGD testing would not prevent parents from using the same tests in prenatal testing and terminating a pregnancy for what some may view as inappropriate purposes.

Non-governmental Approaches***Option: Set Guidelines Through Professional Groups***

PGD providers could, through a new or existing professional society, create guidelines for acceptable uses of PGD. Guidelines are usually voluntary. To provide more incentive for providers to comply, the society could condition membership on adherence to guidelines. In addition, the society could encourage patients and those paying for PGD services (including employers and insurance companies) to use only the services of society members, creating market forces in favor of compliance.

Arguments for:

- Providers are the most natural group to monitor and oversee the use of PGD. They know the most about the use, limitations, risks and benefits of the technology and control access to it.
- This approach provides the most flexibility for the development of science and technology.
- This approach avoids government intrusion in medical practices.

Arguments against:

- PGD providers have many different views about appropriate use of PGD and it will be difficult to develop consensus.
- Professional guidelines are not effective at limiting misbehavior. There will always be a PGD provider willing to perform PGD for any reason the patient wishes.
- Decisions about a technology so profound that it could shape the future of humanity should not be left entirely to the discretion of providers. Broader societal consensus and input is needed.
- Providers may have a conflict of interest since they have a financial motivation to conduct PGD and a disincentive to limit their activities.
- Professional societies do not have sufficient resources to develop and enforce guidelines.

Non-governmental Approaches

Option: Establish Guidelines Through Patient Groups

Patient groups, which typically are organized around particular diseases or conditions, could develop their own recommendations for appropriate use of PGD.

Arguments for:

- Patient groups have special insight about particular conditions and can offer guidance to prospective parents who are considering PGD.
- Patient groups may have special insight into the impact of PGD on people living with genetic diseases and their families and can provide useful guidance to prospective parents about the impact of their decision.

Arguments against:

- Guidance from patient groups offers no enforceable limits on the use of PGD.
- Prospective parents seeking to use PGD for a particular purpose may have views that conflict with the guidelines of a patient group.
- Patient groups may be unable to develop guidelines because of conflicting opinions within the membership about the appropriate use of PGD and concern that PGD could affect the availability of treatments and support for people living with a particular condition.
- Patient groups may not see PGD guidelines as part of their mission and may have other priorities for their resources.
- Patient groups would focus on particular diseases and therefore would be unlikely to address the use of PGD for trait selection.

Option: Leave Decision to Parents and Providers

Currently it is prospective parents who decide whether to seek PGD to detect a particular condition or trait. PGD providers, in turn, make the decisions about what genetic tests they will offer. Some individual clinics and providers currently refuse to perform PGD for certain reasons, such as sex selection. This policy approach would continue to leave decisions about PGD use to parents and providers.

Arguments for:

- This approach avoids government interference in personal choices.
- This approach avoids government interference in the practice of medicine.
- This approach respects the different personal or professional reasons parents and providers may have for wanting or refusing to do PGD for various purposes.
- Beliefs about the appropriate use of PGD are rooted in moral and ethical concerns that are difficult to address through policy making.
- This approach permits scientific innovation to proceed unimpeded by government restraints.

Arguments against:

- Leaving the decision to parents and providers does not provide formal legal limits on the use of PGD.
- Decisions about a technology so profound that it could shape the future of humanity should not be left entirely to the discretion of parents and providers. Broader societal consensus and input is needed.
- Provider policies will be inconsistent, making it difficult for prospective parents to find services.
- Though difficult to craft, it is not unusual or inappropriate for policy to respond to moral or ethical concerns.
- PGD has consequences for the resulting children that are not adequately considered or protected with this approach.

Option: Provide Better Information to Prospective Parents about Genetic Conditions

This policy approach assumes that the demand for PGD would be lessened if prospective parents had more information about the condition for which testing is being sought and the reality of caring for a child with a disability. Although genetic counseling is generally provided to prospective PGD patients, it could be improved. Patient groups could educate genetic counselors and other health care professionals to include in their conversations with prospective parents the perspective of those living with the genetic disease or condition. Prospective parents could have the opportunity to meet with those living with the particular condition or disability and their families. Patient advocacy organizations working on behalf of people with the condition could facilitate such interactions.

Arguments for:

- This approach helps parents, without harming people already affected by genetic diseases, by providing balanced information about a particular condition.
- People with disabilities may have special insight for prospective parents about the reality of living with a genetic disease.
- More information could reduce the number of prospective parents seeking PGD.

Arguments against:

- This approach does not provide clear, enforceable limits on uses of PGD.
- This approach may have limited applicability for PGD uses for traits outside the purview of patient groups.
- Additional education of parents during genetic counseling requires additional coordination and resources that may not be available.
- Some prospective parents may perceive this approach as unwelcome pressure.



Is it Safe and Does it Work?

Addressing the Safety, Accuracy and Effectiveness of PGD

Prospective users of PGD want full information about its safety, accuracy and effectiveness. A number of questions exist about the underlying IVF procedure, the embryo biopsy and the genetic tests. Is the IVF procedure safe for the mother and the resulting fetus and child? Does the biopsy procedure destroy or harm the embryo and is it safe for the developing fetus and child? Are the genetic tests reliable and accurate? How do we know and who is best equipped to make these determinations?

There are incomplete and conflicting data concerning the risks IVF may present to mothers who undergo the procedure and the children conceived via this method, making it difficult to determine the extent to which adding PGD to the IVF process may introduce additional risks. One known risk related to PGD is that the biopsy to remove one or two cells from the embryo for genetic testing may harm or destroy the embryo.

As for the accuracy and effectiveness of genetic testing, currently there is no government review of the analytic or clinical validity of a genetic test before it is marketed. When done in the context of PGD, there have been a small number of cases in which PGD failed to detect the genetic abnormality it was intended to reveal. The targeted condition was later detected either during pregnancy or following the birth of the child.

Some recent data suggest that PGD may increase the success rate of IVF if it is used to test embryos for chromosomal aneuploidy but opinions vary on whether and under what circumstances this is useful.

“Maybe that piece of it [PGD biopsy] would add another element that we’re not aware of. It hasn’t been around long enough to know if it affects the growth of the fetus or something.”

“The one thing that would prevent me from going on with [PGD] is not knowing the long-term effects. There are no studies that have been done. We wouldn’t know what would happen long-term.”

“With this new PGD procedure, do they have data on rats or something because... when you start manipulating...nature, there is always a side effect.”

Federal Oversight***Option: Authorize New or Existing Federal Agency Oversight of PGD***

Congress could pass legislation giving a new or existing federal agency the authority to oversee PGD. The agency would be empowered to deal with matters of safety, accuracy and effectiveness. Such an entity could be charged with:

- Licensing and inspecting facilities that engage in PGD;
- Approving new PGD tests and techniques;
- Developing regulations concerning how PGD should be conducted, focusing on quality assurance and control;
- Collecting data on health outcomes of children born following PGD.

Arguments for:

- Such an entity would give the public a much greater level of confidence in PGD's safety, accuracy and effectiveness.
- The oversight would be tailored to PGD, avoiding the problems related to applying existing laws and regulations never intended to cover these new technologies.
- The process of developing legislation to create such an entity or extend the authority of an existing entity would stimulate a productive public discussion about how to ensure safety and effectiveness in the rapidly developing world of human reproductive genetic technology.
- An oversight body could facilitate research into PGD's long-term impact on individuals, family and society.

Arguments against:

- It is difficult to create a stable, effective and non-partisan oversight body. For example, if PGD tests cannot be performed without approval from a single government authority, lawmakers who disagree with the agency's decisions about safety, accuracy and effectiveness could effectively halt agency actions by denying the agency funding.
- Any new oversight will affect ease of access. In general, more scrutiny will mean restricted or delayed availability and increased costs.
- It would be extremely difficult to find a majority of lawmakers who could agree on the scope and powers of such an entity.
- Rules to improve safety, accuracy and effectiveness would not address uses of PGD tests that while safe and effective, may be viewed by some as unacceptable. Thus, the entity could be in the awkward situation of appearing to endorse uses that some find unacceptable, such as selecting for traits that involve appearance or selecting for what many would consider a disability, like deafness.
- It would be difficult to regulate safety and effectiveness of genetic tests that are used in PGD given that all genetic tests are now largely unregulated.
- It would be difficult to regulate IVF when used for PGD when IVF in general is not regulated.

Option: Expand Scope of CLIA

The Clinical Laboratory Improvement Amendments (CLIA) currently provide limited reassurance to patients about the safety and accuracy of genetic tests in general and PGD in particular. In addition, it is unclear whether CLIA applies to embryo laboratories.

CLIA could be applied and enforced with respect to genetic analysis of preimplantation embryos and proficiency testing for genetic testing as part of PGD could be developed. In addition, CLIA could be applied and enforced with respect to embryo laboratories.

Arguments for:

- CLIA oversight would ensure that PGD and embryo laboratories follow the same basic standards as other laboratories, e.g., document procedures, comply with personnel qualification requirements and undergo inspection, with penalties for noncompliance.
- Extending CLIA to PGD and embryo laboratories would be reassuring to those using and paying for these services.
- Proficiency testing for genetic tests done during PGD could serve as model for proficiency testing for all genetic tests.

Arguments against:

- This approach could just add more bureaucracy without necessarily improving the quality of clinical laboratory services.
- Given that some embryology laboratories consider their activities to be medical practice, CLIA's jurisdiction over these laboratories may need to be clarified through legislation. Such legislation may be controversial.
- It would be difficult to regulate the safety and effectiveness of genetic tests that are used in PGD given that all genetic tests are now largely unregulated.

Federal Oversight

Option: FDA Oversight

FDA could issue regulations requiring that, before PGD is offered to prospective parents, there must be evidence that both the genetic tests and the manipulation of reproductive tissue are safe and effective (premarket approval). As with other FDA regulated products, those seeking to offer PGD would be required to conduct controlled clinical trials and submit data from those trials to FDA. Pending FDA review of that data and agency approval of the tests and procedures, PGD could be provided only in the context of a research protocol.

Arguments for:

- Premarket approval would mean that there would be a much higher level of scrutiny of PGD. If FDA approved a test or procedure, the public could have a much greater level of confidence in its safety and effectiveness. In addition, FDA could require post-market reporting by those using the FDA-approved tests and procedures, leading to more information about their safety and effectiveness.

Arguments against:

- FDA’s involvement, particularly if premarket approval were required, would have the effect of significantly limiting access to PGD. Prospective parents would be able to use unapproved procedures only as part of a research study. Providers might choose to leave the field rather than comply with FDA requirements.
- It is not clear that FDA has the authority to regulate PGD or the IVF procedures required to perform it. FDA’s governing statutes don’t directly address PGD at all. Any extension of agency oversight in this area would require interpreting existing statutes as applicable to PGD.
- Given the charged political atmosphere surrounding what should and should not be done with preimplantation human embryos, it is not clear that FDA would want to get involved in this arena even if it has the authority. Without a specific directive from the Department of Health and Human Services or a new legislative mandate from Congress, the agency may be reluctant to get involved.

Does FDA Have the Authority to Regulate IVF and PGD?

Without new authority from Congress, it could be difficult for FDA to assert jurisdiction over IVF and PGD. The agency’s only option might be to argue that an embryo created by IVF meets its existing definition of a biological “product” and a laboratory test used to test the embryo’s DNA constitutes a “medical device,” since it will be used to treat or prevent a medical condition (e.g., infertility, genetic disease). Some are skeptical that FDA could lawfully extend existing authority to cover PGD and others are simply offended by the notion of calling an embryo a “product.”

State Oversight

States could use their agencies and authority to play a role in monitoring and improving the safety and accuracy of PGD.

Option: Involve public health agencies

The activities, authority and responsibilities of state public health agencies vary from state to state, but in general all endeavor to influence public health policy and practice. They promote health by tracking and monitoring disease, promoting disease prevention, screening newborns, regulating laboratories, licensing physicians and delivering basic health services.

It is difficult to create a uniform policy approach for state public health agencies because, statutorily and bureaucratically, they take so many different forms. Nonetheless, each agency could take its basic charge to protect the public health and apply it to improving the safety and accuracy of PGD. For example, New York State is developing standards for laboratories doing genetic testing for PGD.

States could also consider implementing the Centers for Disease Control and Prevention’s (CDC) Model Embryo Laboratories Certification Program. This certification program was developed by the CDC with public input and provides specific standards for laboratories that handle human embryos. States could adopt it as a first step toward expanding their oversight of PGD services.

Arguments for:

- State initiatives may be more politically feasible when a national approach proves too difficult.
- A state-by-state approach allows additional flexibility depending on the needs and resources of the state.
- State approaches are often testing grounds for systems that may later be adopted nationally.

Arguments against:

- A state-by-state approach means that safety, accuracy and effectiveness may vary depending solely on where the patient lives.
- State public health agencies already are stretched thin and would be hard pressed to find additional resources and develop new expertise to address new fields.

Non-governmental Approaches***Option: Establish Professional Certification Programs***

Professional organizations could provide significant oversight of PGD in ways that do not require the involvement of federal or state authorities. Certification of PGD personnel would ensure a minimum level of competency.

Because a number of different types of professionals are involved in providing PGD services (physicians, geneticists, embryologists, technicians), collaboration among several existing professional organizations could result in a comprehensive system to certify PGD providers in clinics and laboratories.

The American Board of Medical Genetics (ABMG) and the American Board of Obstetrics and Gynecology (ABOG) are the two boards whose certification work encompasses specialists who are most likely to be involved with PGD. Other programs certify laboratory personnel.

The American Association of Bioanalysts (AAB) maintains a Board of Registry, the primary purpose of which is to identify laboratory specialists who meet minimum standards. The American College of Medical Genetics (ACMG) has developed some standards and guidelines for clinical genetics laboratories but has not developed any guidelines or policies directly bearing on PGD.

The relevant medical specialty boards should collaborate with the other groups to develop a means for testing and certifying doctors and laboratory personnel as proficient in PGD. The combined expertise of these organizations could help create a valuable, uniform certification system.

Arguments for:

- Certification of personnel would improve the quality of services by establishing training criteria and demonstrating competency.
- Certification developed jointly by relevant organizations would have the benefit of combining multiple areas of expertise to set high standards for PGD clinical and laboratory services.
- Certification developed and implemented through professional organizations would be especially responsive to developments in science and technology.

Arguments against:

- Because there are several relevant organizations, as well as different kinds of providers and laboratory personnel, involved in PGD, developing a comprehensive testing and certification system would be challenging.
- Certification requirements have often functioned to limit competition, suppress innovation and increase costs.
- Private sector certification would be used as an argument to delay or eliminate federal oversight.
- Self-regulation would not be sufficiently rigorous, transparent or unbiased.

Option: Develop Practice Guidelines

PGD practitioners could create a self-governing professional society and develop comprehensive practice guidelines. This option differs from the previous one in that does not involve a formal certification process but, rather, a set of guidelines developed by a professional society.

Professional guidelines are traditionally voluntary, although they sometimes are viewed as the standard of care. Guidelines are more useful when some enforcement mechanism is contemplated. In this case, membership could be contingent upon adherence to the guidelines. The professional society could give this mechanism more authority through a campaign educating the public and payors about the benefits of using providers who are members.

Arguments for:

- Providers are the most natural group to monitor and oversee the uses of PGD. They know the most about the use, limitations, risks and benefits of the technology and control access to it.
- Guidelines are flexible and can change over time. They could include a review system to keep them current.
- Private systems do not create the same political problems that government oversight can. There is less fear of stifling innovation.

Arguments against:

- Private systems tend to be voluntary and less enforceable than government oversight rules. Patients may feel that without external enforcement, self-regulation provides little reassurance of the safety and accuracy of PGD.
- It would be difficult for PGD practitioners to reach a consensus on best practices for PGD. There are many different techniques and great debate over which are the safest and most accurate.



PGD for a Privileged Few? Addressing Access to Services

PGD is expensive. It requires IVF, which costs on average \$10,000-\$12,000. The addition of PGD can add \$2,500-\$4,000, bringing the total cost to approximately \$12,500-\$16,000.

Insurers may not cover PGD at all, or may pay only for the genetic testing, leaving prospective parents to pay for the IVF. Without coverage, PGD is available primarily to those who can pay significant out-of-pocket costs. Families who would face the greatest financial burden of caring for children born with conditions detectable via PGD may be the ones least able to afford it.

Many insurers do not cover IVF for infertility treatment or offer a limited benefit. Some fertility clinics offer ways to make IVF more affordable. Fifteen states have enacted some type of infertility insurance coverage law. There are no federal laws in this area.

There has been no systematic investigation of insurance coverage practices for PGD. Anecdotal evidence suggests that when families are using PGD to avoid serious genetic disorders, insurance companies are more willing to consider the PGD medically necessary and cover the cost. At least one insurance company covers the genetic testing component of PGD for detection of inherited genetic disorders but not for aneuploidy. However, that company will not cover IVF if used only to perform PGD.

For insurers, the question of whether to cover any medical procedure or test primarily comes down to an analysis of the potential costs and benefits of coverage. A cost-benefit analysis of PGD would have to take into account the cost of the underlying IVF, the embryo biopsy and the genetic testing. It is not clear whether any health insurer in this country has undertaken a formal cost-benefit analysis of PGD for inherited genetic disorders.

PGD is not unique in terms of its current level of relatively limited access. Most new medical technologies are first used by a small number of people who participate in research studies or who can afford to pay for them out-of-pocket. Broader use occurs when these techniques become the standard of care and health insurers agree to pay for them. The issue for PGD is whether and when this transition will occur.

“I just think it is inevitable that we come down to who can pay for it, or can get their health insurance to pay for it. So I can see it being regulated by the health insurance companies being willing to cover certain diseases.”

“I think that’s a real fear, that health insurance companies might say, ‘if you don’t have this test, or you don’t have this procedure, we are not going to pay to take care of that ill child that you have.’”

Federal and State Oversight

Option: Mandate Private Insurance Coverage

There is no federal or state law, either enacted or proposed, requiring health insurers to cover PGD. There are several possibilities for how such legislation could be structured.

Under federal law, employee health benefit packages in which the employer bears some or all of the risks of paying for the costs of care are completely exempt from any state insurance regulation including state mandates. Thus, even if a state law required coverage of PGD, people in these employer-sponsored plans would not be guaranteed this particular benefit. Approximately 61 million Americans are in employer-sponsored plans that are exempt from state mandates.

Employers who purchase coverage from an insurer who pays for the costs of care must comply with state mandates. The mandates also apply to plans purchased by self-employed people and individuals purchasing their own insurance.

This complicated regulatory scheme significantly affects how state and federal insurance laws can influence health care policy. To avoid this problem, Congress would have to pass legislation requiring employers to include PGD in their health benefits. Such intervention is rare but not without precedent. For example, Congress passed a law requiring all health insurers to provide coverage that allows new mothers a minimum 48-hour hospital stay following the birth of a child.

To require insurance coverage of all aspects of PGD, Congress and state legislatures would have to act to require coverage of IVF, embryo biopsy and genetic testing. Alternatively, legislators could cover just IVF or just the laboratory testing.

Arguments for:

- Any of these approaches would increase the number of prospective parents who have access to PGD.
- If insurers were required to cover PGD, they would be more actively involved in monitoring its use and outcomes.

Arguments against:

- Any of these approaches implies government endorsement of a procedure in which embryos may be destroyed.
- Requiring coverage of PGD and/or IVF would be costly, raising premiums significantly for all enrollees.
- Health care dollars should go to providing basic preventative and primary care, not to pay for relatively untested and expensive technologies like PGD.

Option: Mandate Coverage by the Federal Employee Health Benefit Plan

The federal government, the nation's largest employer, has significant direct regulatory control over the Federal Employee Health Benefit Plan (FEHBP), the system for providing health insurance to more than 8 million federal enrollees and their dependents, including approximately 1.2 million women of childbearing age. Currently, very few FEHBP plans cover IVF. There is, however, legislation pending that would require FEHBP (and military health plans) that cover obstetrics to cover assisted reproductive technology, including up to four attempts at IVF. It is unclear which plans, if any, do or would cover PGD.

Congress could pass a law requiring federal health plans to cover PGD and the IVF necessary for PGD. There are several ways to structure such a requirement. The requirement could apply to every plan, or just to those plans that cover prenatal genetic testing.

There is precedent for this approach. In 1998, Congress voted to require that all FEHBP health plans offer comprehensive coverage of contraceptives and this provision has been reenacted each year.

Arguments for:

- PGD services would provide an important benefit for federal employees and their families seeking to have children free of genetic disease.
- FEHBP covers more than 8 million people nationwide. It is a major purchaser of health care from health insurers, giving it tremendous influence over the benefits these insurers offer to smaller employers.

Arguments against:

- Requiring coverage of PGD and/or IVF would be costly, raising premiums significantly for all federal enrollees.
- PGD and IVF are controversial procedures that raise profound ethical and moral issues and the government should not tacitly endorse them.
- Federal health care dollars should go to providing basic preventive and primary care, not to pay for relatively untested and very expensive technologies like PGD.

Federal and State Oversight

Option: Mandate Coverage by Medicaid and Medicare

The federal government has significant control over Medicaid and Medicare benefits.

Medicaid is a program that pays for medical assistance for individuals and families with low incomes. It is jointly funded by the federal government and state governments and provides medical care for people who meet the eligibility requirements. Federal law determines the minimum standards that state Medicaid programs must meet in order to receive federal funds. Beyond that, each state determines the benefits included in its program. Medicaid is the largest source of funding for medical and health-related services for people with limited incomes.

The federal government could provide an incentive for states to include PGD in the state Medicaid benefit package by providing additional funding (an "enhanced match") for PGD tests and procedures. Alternatively, additional funds could be made available for one component of PGD, either the IVF or the genetic testing of the embryo.

Medicare is commonly known as the national health insurance program for people over 65 years of age, patients who have passed their reproductive years and have no need for PGD or IVF. However, Medicare also provides health insurance to some people under age 65 with disabilities.

The federal government could require Medicare to cover PGD for beneficiaries of reproductive age.

Significant obstetrical care is provided to patients in both programs, particularly those receiving care through Medicaid, who often are of reproductive age. The care provided includes prenatal diagnosis when indicated. Many patients may be interested in obtaining PGD, especially if there is a known genetic condition in the family and they would like to avoid prenatal testing and possible abortion.

Arguments for:

- PGD services would provide an important benefit for Medicaid and Medicare recipients by increasing the chance that they would have healthy children free of genetic disease.
- Low-income patients on Medicaid or disabled patients on Medicare may be interested in avoiding the burden of caring for a child with a disability.

Arguments against:

- Very few Medicaid and Medicare patients would pursue PGD, thus creating a mandate is a solution without a problem.
- Medicaid and Medicare reform should focus on providing basic preventive care, diagnosis and treatment to patients, not on providing every possible technology, especially when it is relatively untested and very expensive.

Non-Governmental Approaches

Option: Use Employer Purchasing Power

Employers could include PGD in their employee benefit plans.

Large employers spend significant money on purchasing health care for their employees. Smaller employers often work through purchasing coalitions, which are groups of employers who use their collective leverage in purchasing health care for their employees. Together, these employers determine the health benefits that will be made available to the millions of Americans who depend upon their employer for health insurance, and influence the benefits insurers offer more generally.

Employers make purchasing decisions based primarily on an analysis of what benefits they think will result in a more productive workforce (e.g., fewer sick days, greater efficiency at work). Employers may find that covering PGD improves workplace productivity. For example, an employee with a child affected by a serious genetic disease may frequently be absent from work to care for the child. This scenario could be avoided if the disease could be detected via PGD and the procedure were covered by the employee plan. Similarly, for an infertile woman, each cycle of IVF can result in days of work missed and decreased productivity. If chromosome screening using PGD could improve the IVF pregnancy success rate, the end result would be cost savings to employers.

Arguments for:

- This non-governmental solution avoids the challenge of passing new laws for insurance mandates.

Arguments against:

- Most employers do not have enough purchasing power to make tailored purchasing decisions. They make decisions based on what the market offers them, which may or may not conform to their notion of what benefits are best for their employees.

Option: Provide Financial Assistance Through Clinics

IVF clinics and PGD providers and laboratories could offer financial assistance directly to prospective parents seeking PGD.

Due to the high cost associated with assisted reproductive technologies, some IVF programs offer IVF on a “shared-risk,” “warranty,” “refund” or “outcome” basis. Shared-risk plans operate by refunding a portion of the fee paid for one or more IVF cycles in the event that they do not result in a pregnancy or live birth of a child. Typically, shared-risk patients pay a higher fee than other IVF patients and, in return, receive a refund of 70 to 100 percent of this fee if treatment fails. Accordingly, someone who succeeds in having a baby may pay more under the shared-risk plan than she would have under a traditional fee-for-service plan. However, this option helps ensure that unsuccessful couples will have the monetary resources to pursue other options for starting a family.

Critics of shared-risk plans have raised several concerns. They have argued that the plans are deceptive and exploitive because they induce patients who are desperate to have children into purchasing a more expensive IVF service, skew selection criteria in order to deny plan eligibility to high-risk patients, create conflicts of interest that are likely to sway clinical decision-making, and involve contingency fees that are considered unethical in the practice of medicine. Proponents, however, contend that the plans are a legitimate response to the lack of infertility insurance coverage.

In addition, many fertility clinics offer IVF at a reduced price to patients who provide their eggs to other patients, although some critics say this practice is coercive and creates psychological issues for some patients.

Clinics or laboratories could also offer discounts or payment plans for families who could not otherwise afford PGD. For example, a clinic could offer discounted IVF services if PGD is included.

Arguments for:

- Discounts and shared costs will give people access to PGD and IVF services that otherwise would be out of reach.

Arguments against:

- Because the market for PGD is significantly smaller than the IVF market, and will continue to be for some time, clinics may not want to offer discounts on PGD services.
- Critics find some financial assistance programs coercive because they create strong incentives for patients to donate eggs or embryos.



Where Will It Lead? PGD's Future Implications for Society

PGD raises a number of questions about its implications for family relationships, people with disabilities, societal mores, the sanctity of human life and the legal system. Answers to these questions may vary based on one's values, religious traditions, political views, life experiences and other factors, all of which may influence strongly one's choice of options.

Impact on Families

Will PGD change a child's sense of independence, self-worth or identity if the parents have "chosen" what type of child to have?

What message is sent to a child born after PGD about the parents' expectations for him or her?

For children living with a genetic disease or disorder, what is the psychological effect of having younger siblings who were selected specifically because they were unaffected? Conversely, what is the impact on a child chosen specifically not to have their sibling's disease?

In cases where parents use PGD to pursue an immunologically matched child whose blood can be used to treat a sibling's disorder, how might the sibling relationship be altered?

Are children at risk of being viewed as products of design rather than mysterious and wonderful gifts?

How will society treat children who do not have certain conditions or who do have certain traits because their parents used PGD? Will they be viewed as privileged or somehow different? How will these children view themselves in relationship to society, especially if they have siblings, family members or friends with genetic diseases?

Will parents feel pressure to screen embryos and will parents who decide not to use PGD be criticized?

What if some parents cannot afford to use PGD? Will this create a society in which those with the fewest resources are more likely to shoulder the burden of caring for children with debilitating diseases?

Impact on People With Disabilities

Will the availability of PGD lead to a decrease in resources and support for those living with disabilities? Will less money be directed to finding cures for diseases that can be avoided through PGD?

Will the availability of PGD to avoid some diseases lead to a more negative societal attitude towards people with disabilities generally?

Affect on Societal Mores and the Sanctity of Human Life

Is it harmful to allow one generation to choose the characteristics of the next generation?

Will the fact that PGD is used to select and reject embryos diminish respect for human life?

Does the use of PGD fundamentally change the act of human procreation?

What impact does PGD have on people's experience of both the joy and sadness of life? By attempting to remove suffering from people's lives, does PGD also diminish the richness of human experience?

What does the use of PGD say about parents, who, before pregnancy even has begun, would be willing to undergo potentially risky procedures that may harm the resulting children? Does this reveal a willingness to gamble with their children's well-being in other ways as well?

Does PGD foster a parental culture of conditional love for children, rather than one in which children are loved and valued for who they are, regardless of any genetic "flaws?"

Impact on the legal system

Will there be lawsuits against doctors for doing, or refusing to do, certain PGD procedures? For example, what if a deaf couple wants to use PGD in order to have a deaf child?

Will there be lawsuits against parents by their children for not using PGD and allowing a child with a particular genetic disease or trait to be born, or alternatively, for using PGD and thereby diminishing the child's autonomy?

Option: Provide Help for People with Disabilities and Their Families

There are several policy approaches that could improve the treatment and support for people with disabilities. Such improvements could limit the possible negative effects of PGD on this community. Also, by reducing fears associated with having a disabled child, these approaches could limit the overall demand for PGD.

Government actions could include support for research into new treatments and cures for people with disabilities, anti-discrimination laws to protect the rights of people with disabilities and more support for families caring for children with disabilities and for people living with disabilities.

Arguments for:

- This approach helps everyone, including people with disabilities.

Arguments against:

- This approach requires additional government spending at a time when most states and the federal government are complaining of revenue shortfalls. In the past, laws dealing with discrimination against people with disabilities that in the past have been viewed as costly and burdensome on small business.

Option: Provide Prospective Parents with Counseling Opportunities

Prospective parents considering PGD may not have had a chance to reflect on some of the larger issues such as how PGD could affect the resulting child and other family members. Counseling guidelines could be developed that help prompt prospective parents to give more attention to such matters so that they may make a more informed decision.

Arguments for:

- Counseling guidelines would be useful for clinicians and prospective parents and help ensure that all of the issues have been carefully considered.

Arguments against:

- Prospective parents already have a great deal to think about and cope with. They could view such counseling as an unwanted intrusion into private issues.



What Do We Need to Know? Research and Data Collection

While it is sometimes fashionable in science and policy to opine that “more research is needed,” in the case of PGD critical data are truly needed to develop effective, evidence-based policy. Information on the safety of PGD, its use and its impacts is vital to choosing the correct policy tools and approaches. A new statute, for example, may not be appropriate for a technology likely to affect only a small number of people. Similarly, constructing policy that is responsive to and reflective of the public’s mores and preferences requires a more detailed understanding of informed public attitudes toward this new technology.

This section presents key areas in which additional research and data collection activities are needed and proposes some specific options to obtain the necessary information. Options are presented that address laboratory and clinical research, monitoring, reporting and social science research.

Any proposal for research begs the question of who will fund it. For laboratory and clinical research on PGD, funding from the federal government is restricted by the Congressional ban enacted in 1996 that prohibits federal funding of research in which human embryos are created or destroyed. However, notwithstanding the ban, research to answer many questions concerning PGD would not involve the creation or destruction of embryos and thus would not be subject to the federal ban. In addition, the federal ban in no way restricts the private sector, including both industry and non-profit foundations and advocacy groups, from funding research involving human embryos that could help assess and improve PGD techniques.

Research sponsors, either individually or collaboratively, could establish a common set of research priorities, ethical standards for research, and data collection and distribution requirements.

Option: Investigate the Safety, Accuracy and Effectiveness of PGD

Many questions remain about the safety, accuracy and effectiveness of PGD. These include how often embryo biopsy damages or destroys embryos, how often PGD fails to detect a genetic mutation and whether and for whom aneuploidy screening improves IVF results. In addition, more research is needed on the genetic tests used in PGD in order to improve test validity and expand the number of genetic diseases that can be identified. Funding for such research could come from a variety of sources, including industry, private foundations and the federal government. Federal funding would, however, be limited to research not involving the creation or destruction of human embryos unless Congress lifted the current funding ban.

Arguments for:

- Such research would improve outcomes for women and children. For example, if research shows aneuploidy screening increases IVF effectiveness, fewer embryos could be transferred, decreasing risks to mothers and children from high-order multiple pregnancies.
- Such research would increase the number of genetic tests available for PGD.
- This research would provide prospective parents with more data for informed decision-making.

Arguments against:

- Absent federal funding for embryo research, there is not sufficient financial backing in the competitive, market-based IVF sector to do this research or incentives to make the results of such inquiries publicly available.
- Even if it involved only private funds, research on PGD would require experiments in which the price of knowledge may be the destruction of human embryos.

Option: Institute National Reporting Requirements for PGD

The Fertility Clinic Success Rate Reporting Act (FCSRA) administered by SART and CDC could be expanded to require IVF clinics to report when PGD is used as part of an IVF procedure. Information required to be reported could include the purpose for which PGD was used (e.g., aneuploidy, cystic fibrosis), whether pregnancy occurred and the outcome of such pregnancy. The CDC would add this information to its public reports on assisted reproductive technology.

Better enforcement of reporting requirements also may be needed. Currently, clinics that fail to report information on IVF procedures face no penalties. Officials could consider monetary or other penalties for failure to report.

Arguments for:

- These changes would provide better information on the prevalence and purposes of PGD use. This information would help policy makers choose the most appropriate regulatory approach
- Tracking PGD use could facilitate long-term follow-up of the children born as a result of PGD and their mothers as well.

Arguments against:

- These reporting requirements are administratively and financially burdensome and providers might pass along the costs to the patients, potentially affecting access.
- Once PGD results in a pregnancy, the woman's care is transferred to an obstetrician, and after the baby is born, a pediatrician cares for the baby. This may make it difficult for PGD providers to track pregnancy outcomes.

Option: Study Health Outcomes Following PGD

There are incomplete and conflicting data on the long-term health effects of IVF for women and children and no systematic studies on the health and developmental outcomes for children born following PGD. Thus, it is difficult to assess the baseline risk of IVF and any possible additional risk from the biopsy component of PGD.

Longitudinal studies of women who have undergone IVF and children born following IVF and PGD would provide valuable information about the safety and risks of IVF and embryo biopsy.

Arguments for:

- Research would allow people considering IVF and PGD to make more informed decisions about their treatment, would provide evidence to improve clinical practice and would allow oversight policies to be rooted in objective understanding of safety and effectiveness.
- Although reproductive genetic technologies like PGD are fraught with controversy, political consensus may be possible around collecting data on health outcomes of women and children.
- There is a dearth of data on the long-term health consequences of IVF and PGD. This is a major lapse in public health research.

Arguments against:

- This research would be expensive, and it is not clear whether funding would be available.
- Tracking patients raises privacy concerns, and patients may not want to participate in such studies.
- A decision to conduct research, particularly longitudinal studies that take years to produce informative data, could delay immediate governmental action to more rigorously oversee PGD's safety, accuracy and effectiveness or limit its uses.
- There could be difficulty in defining criteria for adequate long-term follow-up.
- Distinguishing the effect of PGD from the effect of IVF would be scientifically challenging.
- Although much of the research on use and outcomes would not involve work directly with human embryos—and probably would be eligible for federal funding—providing such funding risks sparking a major political controversy, with the funder viewed as either seeking to legitimize PGD and IVF or searching for information that would aid opponents.

Option: Assess Insurance Coverage and PGD's Costs and Benefits

Many questions exist about whether health insurers are paying for PGD—either to test for inherited genetic disorders or to test for aneuploidy. Further research is needed to clarify current coverage policies for PGD, the extent to which price is a barrier to patient access to PGD and the costs and benefits for third-party payors (insurance companies and employers) of covering PGD.

Arguments for:

- Research would facilitate policy decisions by providing better information to state and federal officials about the current status of insurance coverage for IVF and PGD.
- Insurers could obtain more data to conduct their analysis of the costs and benefits of PGD for inherited genetic disorders and for improving IVF outcomes.
- This type of research is not subject to restrictions on federal funding, which means public money could be available to perform the investigations.

Arguments against:

- This research would be expensive and insurers may lack motivation to do it.
- Cost-benefit analyses don't always capture moral, ethical and religious concerns adequately. For example, PGD is appealing to many people precisely because it avoids pregnancy termination, a value that may not be included in a cost-benefit analysis.
- A cost-benefit analysis could prompt some employers to stop providing a PGD benefit. For example, without PGD, other prenatal diagnostic techniques can be used to test a fetus for a genetic disease. At that point, the patient has the option to terminate the pregnancy. If termination were determined to be a more cost-effective option than PGD, an insurer could decide to cover only prenatal testing.

Option: Monitor Changes in Resources and Support for People With Disabilities and Study Psychological Outcomes of Families Using PGD

Many questions have been raised about the potential societal impact of PGD, but little information exists in this area. These issues could be better understood through additional theoretical and empirical research.

Disability advocates have raised questions about whether, in a society where genetic diseases can be avoided through PGD, fewer resources will be provided to those already living with disabilities, including both support services and funding for research to develop treatments. Some also question whether society's perception of people with disabilities will become more negative. To address these questions, researchers could track changes in resources available for the disabled and in societal perceptions over time.

Some observers believe that PGD will alter family dynamics, particularly relationships between siblings with and without genetic disorders. Longitudinal psychological studies of families who have used the procedure for a variety of reasons would provide data on the impact of PGD on families.

Arguments for:

- More research is needed to provide data to policy makers to make evidence-based policy.
- Research tends to be a less controversial policy approach, thus it may be possible to obtain political consensus, and perhaps federal funding, to study these issues.

Arguments against:

- The decision to seek more research is sometimes a political device intended to distract attention from an issue or neutralize it without addressing its core concerns.
- PGD is so new that it may not be possible to collect sufficient data on the impact on families and people living with disabilities.