

**Genetics and Public Policy Center
Reproductive Genetics Policy: Framing the Issues
Meeting Report
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INTRODUCTION

The Genetics and Public Policy Center was established in April 2002 with the generous support of the Pew Charitable Trusts. Its first initiative addresses reproductive genetics. Chief among the goals of this initiative is to produce a range of policy options that could guide the development and use of reproductive genetics. In January, the Center held , “Reproductive Genetics Policy: Framing the Issues,” a meeting that brought together experts from diverse fields and perspectives to help the Center identify the key issues on which the Center could most usefully focus its attention in developing policy options. The input and insight from the meeting have been invaluable in helping the Center map out its work on policy options for the coming months.

Participants were experts from the fields of science, medicine, law, policy, ethics, philosophy, theology, and consumer advocacy. Each field tended to frame reproductive genetics issues through their unique lens. Scientists often frame the issues in terms of the technology, legal experts in terms of the rights of individuals in a society, ethicists in terms of societal and family relationships, consumers in terms of who gets cutting-edge health care. It is clear to us that no single perspective is adequate; none is “better” or “worse” than another. Therefore, in order to develop useful policy options, the Center will frame the issues from multiple perspectives.

The following is a categorized record of thoughts and ideas that surfaced during group discussions and working group sessions. In many cases, areas in need of more information and study were identified. These are captured under the subsections, “For Further Analysis.”

WHAT IS REPRODUCTIVE GENETICS?

Reproductive genetics is the use of genetic information to inform when, whether, and how to have children, and the use of genetic technologies to select or modify the genetic characteristics of children. Reproductive genetics includes genetic testing, genetic modification, and reproductive cloning.

Genetic testing in the reproductive context can inform parental decisionmaking about the timing, means, and circumstances of procreation and parenting. Hundreds of genetic tests are now available that can be used

- to test couples prior to initiating a pregnancy (“carrier testing”),
- to test embryos produced in vitro to allow selection of those embryos with the desired genetic characteristics for implantation (pre-implantation genetic diagnosis or “PGD”), or
- to test a fetus during pregnancy to inform decisions about abortion or prepare for the birth of a child with genetic disease. (“prenatal testing”)

Genetic modification, also known as gene transfer, is a relatively new possibility for the treatment of genetic diseases. Typically gene transfer involves using a vector such as a virus to deliver a therapeutic gene to the appropriate target cells. The technique, often called gene therapy, is still in its infancy and is not yet available outside clinical trials. Gene transfer can be targeted to somatic (body) or germ (egg and sperm) cells. In somatic gene transfer, germline cells are not targeted and hence, the change is not intended to be passed on to the next generation. In germline gene transfer, the recipient's egg or sperm cells are changed and the change can be passed on to their offspring.

Reproductive cloning means reproduction using the somatic nuclear genetic material of one or more currently or previously existing person(s).

MAKING THE CASE: THE IMPORTANCE OF REPRODUCTIVE GENETICS

Some participants recommended that the Center clearly articulate the rationale for focusing specifically on reproductive genetics and explain why reproductive genetics is an area of inquiry appropriately separable from other aspects of genetic testing, other kinds of health care, and other issues relating to reproduction.

Several participants stated their belief that the average person cares more about having a healthy baby than about the process of testing or the molecular mechanisms underlying human heredity. In addition, people do not understand the difference between genotype and phenotype and may not understand that genotype does not always predict phenotype. Thus members of the public may not feel that the science or ethics of reproductive genetics affects them unless they understand how it will affect their family. But, as one participant said, the Center must embrace “the importance of knowing or defining the technology before making claims about possible outcomes.”

For Further Analysis:

Need more information about what the public thinks are the most important issues relating to reproductive genetics and its effect on families and children.

THE FUTURE DEMAND FOR REPRODUCTIVE GENETICS. WHAT IS KNOWN?

Several participants argued that in the next 15-25 years, there will be an increased demand for reproductive genetic testing, including carrier testing, prenatal genetic testing, and PGD. One speaker stated that primary factors contributing to this increased demand include:

- Individuals will have more information about their own genetic make-up, increasing their interest in avoiding potential diseases in offspring.
- The trend towards having children later in life will continue, increasing the statistical risk for chromosomal disorders; and people will continue to have smaller families, increasing their desire to “get it right” the first time.
- Genetic testing will become cheaper, more accurate, and more widely accepted as time goes on.

Some participants mentioned other factors, both consumer-driven and provider-driven, that can affect demand. Some testing increases will come from increases in routine or universal testing. Others will come from specific demands from families concerned about particular genetic conditions. In addition, genetic testing will increasingly become an “add-on” for people already going through IVF because of infertility, which will increase demand.

Attendees noted that new recommendations by professional societies for offering universal carrier testing, (example: cystic fibrosis testing) will dramatically increase the number of individuals that are tested. Participants noted that such recommendations also affect liability issues, because once a test is recommended providers feel they must offer it or risk liability.

On the other hand, some participants believe that there will be, and should be, less use of reproductive technology in the future.

- Several participants questioned the impact of these technologies on society and expressed the hope that before such technologies become widespread, policies are developed to limit their use in ways society deems acceptable.
- One speaker stated that he hoped PGD and other technologies requiring the invasive and costly nature of IVF, resulting in discarded embryos, would become obsolete as better therapies for disease are developed, including perhaps genetic modification. However, it was acknowledged by most participants that the clinical use of germline gene transfer is far off in the future.
- Several participants questioned whether there will ever be widespread use of PGD/IVF by families who are neither infertile nor trying to avoid a known genetic disease in their family. They pointed out that IVF is invasive, painful and expensive – so that people are unlikely to choose to go through it lightly.

There was some discussion of whether an increase in use of reproductive genetic testing would increase or decrease overall health care costs. For example, carrier testing or even PGD could save money that insurance companies would otherwise spend on prenatal care, abortion, or illness. If insurers recognized the cost savings, they might increase their coverage of these new tests and help drive up use. But, given the frequency with which individuals change insurance companies, an individual insurer is unlikely to reap the benefits of coverage for reproductive genetics testing and preventive care in general.

For Further Analysis:

Need models to project future usage of reproductive genetic technologies in the future and the economic consequences thereof. Such analysis would need to consider which tests would be used for what purposes and whether there will be improved access to reproductive genetics technology in the future. This information would inform the design of appropriate oversight mechanisms and enhance our ability to project various consequences.

Economic analysis must considering costs and benefits: are preconception testing methods, such as universal carrier testing or PGD, cost effective compared to prenatal testing and abortion? Compared to the cost of serious genetic illnesses? If these technologies are cost-effective, insurance will be more likely to cover them and usage will increase.

Some participants thought more information was needed about who profits from new genetic technologies and how this influences demand.

SAFETY

Participants noted the lack of data on long-term safety of assisted reproductive technologies (ART) generally. Several participants mentioned the federal ban on funding for embryo research as part of the reason new ART techniques are, in practice, often introduced into clinical practice without controlled studies in humans. Several participants asked whether private clinics are describing research as therapeutic or clinical in order to avoid IRB review and regulation. A few participants mentioned that even IRB review does not necessarily adequately protect patients and suggested the need for more rigorous IRB standards.

Several participants noted that animal data is often not helpful in determining whether a new technology will be safe in humans, for a number of reasons: For example, there are some techniques that have not been at all successful (i.e., have not led to reproduction) in animals but have in humans. Thus, for some techniques, appropriate animal models may not exist. Even when such models do exist, techniques may work differently in animals than in humans, so that it may not be possible to determine whether the animal data are relevant until we actually have human data.

One participant noted that research with primates, perhaps the best animal model for studying new human reproductive technologies, is even more heavily regulated than in humans. Some participants asked whether, in the absence of good animal models, there would ever be enough safety evidence. Other participants added that even with good animal models, it is difficult to determine how much data are enough to begin clinical use in humans. Also, people who are considering a new ART technique have limited time

frames in which they can hope for success – requiring long-term clinical studies would mean they would be precluded from access to new procedures.

Although the discussion of the safety of gene transfer was brief, several participants cited this as an area where it is difficult to know how to translate research into clinical applications, given the shortage of funding, paucity of good animal models, and heavily regulated environment.

For Further Analysis:

Need more data about the safety of ART, and specifically IVF and PGD, including the long-term safety and outcomes for mothers and children, and the accuracy of PGD testing. This information could come from a registry or long-range studies of these procedures. Some participants noted that there are registries in existence that do track information about these procedures and outcomes; however, the data collection is a time consuming and onerous task. Some participants questioned the fairness of asking IVF clinics to collect this information without providing additional funds.

Need more information about how new genetic tests or techniques are developed, marketed, and adopted into clinical use.

THE IMPACT OF LIABILITY

Many participants felt that liability issues needed additional analysis.

For Further Analysis:

Need more information about how the potential to incur legal liability influences the adoption or diffusion of new technologies.

Need to consider arguments in favor of implementing no-liability rules for prenatal diagnosis – would this promote better care?

THE NEED FOR MORE EDUCATION OF THE PUBLIC

Participants overwhelmingly felt that the public understands very little about reproductive genetics. Many participants cited the need for the public to understand the difference between media hype (which may raise fears or expectations unnecessarily) and what is actually happening or scientifically possible. Many participants thought parents or other consumers would want to get facts about their options, receive guidance on how to think through their choices, and learn how to navigate the system should they choose to pursue

new technologies. Some participants felt that for parents considering using new technologies, it would be helpful to formalize access both to families with experience with those technologies, and to families who had decided not to use those technologies.

Several participants thought the public, as well as policymakers and professionals and providers, would want specific, nuanced information about how to differentiate between the use of reproductive genetics to avoid serious disease as opposed to the use for reasons that seem less critical, such as trying to give an extra skill or attribute to a child. However, at least one participant cautioned that what society, or an individual views as morally acceptable may not neatly track what treats a disease versus what enhances a normal child.

Some participants suggested the need for innovative educational models, especially for young people and school settings.

For Further Analysis:

Need more information about what the general public knows and understands about reproductive genetics and how individuals make decisions about using these technologies.. The public needs more information to draw its own lines between “acceptable” and “unacceptable.” Families considering using these technologies may need specialized information.

Need standardized, accurate terminology in an effort to reduce the confusion surrounding reproductive genetics.

PUBLIC PARTICIPATION IN POLICY DEVELOPMENT

Many participants felt that once the public knows more about reproductive genetics, it will be critical to find ways to increase opportunities for open public discussion about these technologies. Several participants stated that public policy needs to come from the public. However, participants were not able to give examples of successful fora for public discussion or deliberative democracy. Many participants felt that Congress, although in theory representative of the public, was not in fact a useful model or forum.

Some participants stressed the importance of including new voices in public discussions: young people starting families, people affected by genetic disorders, children conceived through ART. Several participants noted the need to engage the “real” public, not interest groups. Some participants were concerned that the real public is overwhelmed by information and disenfranchised. Some participants noted the limited ability of federally appointed commissions like the former National Bioethics Advisory Commission (NBAC) or the current President’s Council on Bioethics (PCB) to fully engage the “real” public.

INTERNATIONAL POLICY

Most participants were quite skeptical about the usefulness of international laws or treaties in this area. One participant stated that although moral analyses may differ little from country to country, political systems and philosophies vary greatly and would make international laws difficult to harmonize. In addition, many participants felt that enforcing international laws against violators was impractical and might constitute an overreaction to a relatively minor problem.

FEDERAL POLICY

Several participants alluded to the fact that certain “hot button” issues, such as abortion politics, family law issues, or views of the appropriate role of government, influence which policies might or might not work in the “real world.”

Several participants saw a need for a systematic assessment of existing regulatory mechanisms for reproductive genetics and an evaluation of whether those mechanisms are working, although it was acknowledged that the answer to the latter question depends on what one believes the goals are of regulation. There was discussion among some participants as to whether reproductive genetic technologies are underregulated or poorly coordinated. For example, several participants noted there is currently an absence of a mechanism for reviewing germline gene transfer protocols, since the Recombinant DNA Advisory Committee (RAC) of the National Institutes of Health (NIH) will not review such protocols.

Participants discussed the phenomenon of old statutes, written long before policymakers knew about reproductive genetics, being reinterpreted and stretched to cover modern issues. This avoids the problem of trying to get Congress to pass a new law on a complicated and controversial subject, but also precludes important and necessary public debate and Congressional consideration.

Some participants thought it was better to consider regulating technologies not yet in widespread use (such as gene transfer) rather than try to stop already popular techniques (such as IVF). However, other participants noted the difficulty of getting Congress or other policymakers to focus prospectively on issues not of immediate concern.

For Further Analysis:

Need to assess regulatory agencies and their roles in regulating reproductive genetics. The Federal Food and Drug Administration (FDA) is perhaps the most visible in the context of gene transfer, and several participants thought that the regulatory role of the

FDA needed particular analysis: What is the basis for FDA regulation? Is there an adequate mechanism for public input into the FDA?

STATE POLICY

Several participants raised the issue of whether, given the difficulty of creating new federal policies, state legislatures should be given the opportunity to decide how to regulate these technologies. The benefit of such a system is that the 50 states have traditionally been viewed as the “laboratories of democracy,” and permitting a diversity of approaches might also yield new approaches. Others noted that permitting a diversity of regulatory approaches in the context of such politically charged issues could create difficulties for researchers and industries, who would need to choose their location based on the particular state policies. Such “forum shopping” might also lead states to pass industry-friendly laws to attract new businesses.

For Further Analysis:

Need to consider examples of other policy areas where state laws have served as models for federal law and policy, and/or have affected technology development and access.

RENEGADES

Even if uniform regulation of reproductive genetics were achieved within the United States, what should we do about the possibility of “renegades” who pursue techniques overseas that we view as morally objectionable? Many participants agreed that we should keep the danger of such activity in perspective. Such activities do not pose the same level of threat to our society as, for example, an offshore renegade building an atom bomb. Much of the harm, said one participant, will be to the individuals affected, not to society in any meaningful sense.

Some participants questioned whether it makes sense to try to develop any policy aimed at renegades – these participants felt Congress and other policymaking bodies are blunt and imprecise instruments, and overreaction would have unintended negative consequences.

Participants asked whether it would be ethical for “legitimate” researchers to base protocols on information gleaned from renegade research. Most, but not all participants, thought that the answer was yes, as long as the goal of the new research would be to help those thought to be hurt by renegades.

EFFECT ON FAMILY RELATIONSHIPS

Many participants viewed questions concerning the effect of new reproductive genetics on families to pose compelling moral issues.

Several participants thought that public discussion needed to focus on the overall well-being of children, including changes to the parent-child relationship, and not just their physical health.

Many participants acknowledge that techniques such as IVF, PGD, and selecting an HLA-matched sibling will change the way families discuss childbearing and a child's own "beginning." One participant who had used HLA matching told the story of her child wanting to know what his sister looked like when she was "an egg."

Other participants expressed concern that if parents are given a wide range of choices, children will hold their parents responsible for what they are or are not – both their health and other characteristics. In response, some participants pointed out that we put few limits on the choices parents can make on behalf of their children in other contexts, such as what medical care, education, or music lessons a child will receive. Some participants argued very strongly that parents are in the best position to decide what is appropriate for their family, and that we do a disservice to families by not trusting that judgment or assuming that parents will make frivolous decisions. However, several participants questioned whether we should allow parents total control over choices about reproductive genetic testing, particularly once there are tests for what can best be called "traits" such as hair color, sexual orientation or intelligence. Several participants were particularly concerned that decisions made resulting in gene transfer, especially germline gene transfer, would affect future generations and potentially have unintended consequences.

Participants who favored limitations on parental decisionmaking in the reproductive genetics context proposed that this be accomplished through governmental regulations (state or federal), while others recommended voluntary health professional standards. Others felt equally as strongly that it is inappropriate for outside agencies to be making family decisions. Some thought additional education of individual families regarding the implications of various choices would be useful.

For Further Analysis:

Need to know more about the attitudes and experiences of parents who have used and refused reproductive genetics.

Need to learn more about the attitudes and experiences of children and young adults whose parents used and refused reproductive genetics.

CIVIL RIGHTS

Many participants were concerned that the increased availability of reproductive genetic technology not disadvantage people with disabilities. One speaker stated that one goal of public policy in the area of reproductive genetics should be to enable everybody to fully participate in all aspects of society regardless of ability or disability. Participants cited the need to consider parents who might choose not to (or not be able to afford to) avail themselves of all technology, be it pre-conception, PGD, or prenatal testing. In addition, participants agreed that the ability to avoid or treat certain disabilities must not result in worse treatment of people living with those conditions.

Several participants noted that prospective parents' fear of disability and fear of the cost of caring for children with disability is what drives the need to try to have a genetically "perfect" child. One speaker suggested that to prevent increased discrimination from increased reproductive genetic testing, society should provide better services and supports for parents with children with disabilities and consider how the genetic counseling process could include or promote access to people living with disabilities.

Several participants raised the question of whether it would be moral for parents with a disability such as deafness or dwarfism to use reproductive genetics technology to have a child who has the same disability. One participant asked whether this would be morally any different from those same parents opting out of using reproductive genetics technology to avoid having a child with the disability.

For Further Analysis:

Need more information about how families decide to use or refuse reproductive genetics.

ACCESS ISSUES

There was near-universal agreement that for the foreseeable future, only a select few will have access to many aspects of reproductive genetics, particularly Assisted Reproductive Technology (ART) and PGD. The cost of ART precludes widespread access. Some participants noted that these disparities are true in all areas of health care – new techniques or products (pharmaceuticals, experimental procedures) are expensive and often not covered by insurance at first. Thus for some participants, access issues are impossible to solve; they exist in so many other areas we should not pay special attention to them in this context. One participant suggested we should be most concerned about who gets first access to new techniques and how potentially life-saving new treatments are first tested.

Participants briefly discussed ways that access to ART and related techniques could theoretically be improved including universal health care that covered reproductive genetics. For carrier testing, participants pointed out the critical role of professional

societies: once the American College of Obstetrician-Gynecologists (ACOG) recommended universal carrier testing for cystic fibrosis, it became the standard of care and insurance companies became more willing to pay for it, in part because of liability concerns if doctors didn't offer it.

ROLE OF INSURERS

One speaker pointed out that insured individuals always want to have everything covered, at the cheapest possible cost to themselves. He also pointed out the key role that employers play in determining and purchasing the package of benefits that will be offered to their employees through employer-sponsored health care. He cited the example of one insurance company that covered IVF but found that families choose their coverage only while undergoing the procedures, then went elsewhere, leaving the insurance company unable to evaluate whether by covering the procedure they saved money or reaped other benefits over time.

One participant noted that the cost/benefit analysis of techniques such as PGD is unknown, and might be useful to insurers considering covering the technique to avoid known genetic diseases or for HLA matching.

For Further Analysis:

Need more information about the costs and benefits of reproductive genetic technologies. This information could help insurers make decisions about coverage.

CONCLUSION:

This meeting produced a wealth of ideas that will be extremely helpful to the Center as we develop policy options. As this report attempts to show, the diverse backgrounds and perspectives present at the meeting illuminated those areas where there is disagreement about how to proceed policy-wise -- even if there is, at least sometimes, general agreement that new policies are needed.

As a first step, we are choosing several projects from among the many areas participants identified as needing further analysis. With this additional information in hand, we will strive over the coming months to develop options for policymakers that reflect the many viewpoints present at our meeting.

The Center is extremely grateful to all of the participants who gave their time and energy to this meeting.