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EILEEN AGAR • AUTOBIOGRAPHY OF AN EMBRYO



REPROGENETICS

AND PUBLIC POLICY

REFLECTIONS AND RECOMMENDATIONS

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Reproductive Genetics

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REPROGENETICS AND PUBLIC POLICY

► REFLECTIONS AND RECOMMENDATIONS ◀

by ERIK PARENS AND LORI P. KNOWLES

At the first of the discussions that led eventually to this report, a respected researcher-clinician in the world of reprobogenic medicine referred to his field as “one big embryo experiment.” The phrase nicely captures what this report is about. It is about the ethical issues and policy challenges that arise in the context of researchers and clinicians doing new things with embryos. The range of such activities is wide and growing: from studying embryos for the sake of basic knowledge about developmental biology; to using them as sources of embryonic stem cells that can be coaxed to cure disease; to creating, selecting, and altering them for the sake of producing children. This report focuses on that last set of aims and emphasizes the need for improved public oversight—a need that grows more urgent as reproductive and genetic medicine converge to produce the new field of “reprobogenics.”¹

For a variety of reasons, research involving the use, creation, alteration, and storage of gametes and embryos is subject to little regulation in the United States. This situation is potentially dangerous. Unlike older *in vitro* fertilization (IVF) techniques, many new reprobogenic techniques make structural changes to cells,² and with structural changes arise concerns about the safety of the children produced by the technology. Further, both older and newer techniques raise concerns about the safety of the women who donate the eggs and the women in whom the fertilized eggs are implanted—the egg donors and the gestating mothers.

But concerns about reprobogenics are not only about safety. Just as important are concerns about the *well-being* of children produced by these techniques—and about the well-being of the families and society that will welcome those children. Are we in danger of allowing the market mentality to colonize childbearing, as it has already colonized so much of our lives? Could the proliferation of techniques that increasingly enable us not just to have children, but to choose characteristics unrelated to their health, exacerbate our tendency to think of children as the objects of our making? Could these techniques lead us to think of ourselves as mechanisms that are valued for our individual parts or traits rather than as individuals who are valued for being unique wholes? Could it aggravate some

forms of unfairness, or complicity with unjust norms?³ Put positively, what can we do to increase the chances that these techniques are used in ways that further the happiness of children, families—and ultimately the well-being of our society as a whole?

The answers to these questions will rest on fundamental beliefs and commitments to such values as liberty, equality, solidarity, and justice. They will likely be complex and will sometimes reveal deep disagreements. But such disagreement should not stand in the way of trying to talk together about matters of such great importance.

We, the authors of this document, cannot help but have views of our own about some of these contested questions. But our primary purpose is not to defend those views. Rather, we wish chiefly to establish that our society needs to find better ways to grapple with—and regulate—reprobogenic activities. The future of reprobogenic practice is too important to be decided solely by the market. We call for the creation of an oversight structure that will make possible a thorough and transparent policy discussion of reprobogenics and effective regulation of those facilities involved in reprobogenic research and services.

The report is divided into five parts: In the first, we delineate what we mean by *reprobogenics*. In the second, we identify some of the ethical concerns that commentators have broached about reprobogenics and argue that questions about well-being must be part of the policy conversation. Part three describes the historical roots of our current oversight situation. Reproductive medicine and genetics have long been overseen separately—and with very different degrees of care. The politics of abortion have largely prevented any effective oversight of reproductive medicine. But as reproductive medicine and genetics converge, the current state of affairs does not allow us as a society to anticipate and contemplate the emerging reprobogenic picture in all of its complexity.

To shed light on what a better approach to reprobogenics policy in this country might look like, part four briefly explores the weaknesses and strengths of the regulatory approaches adopted by the United Kingdom and Canada. The final part sketches a proposal for an oversight body that can respond to the technological and ethical realities of reprobogenics in this country.

What Is “Reprogenetics”?

This report defines *reprogenetics* broadly, as the field of research and application that involves the creation, use, manipulation, or storage of gametes or embryos. The report also defines *embryo* broadly. It adopts the definition that Congress uses in its ban on funding for embryo research: “any organism . . . that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.”⁴ Of course, there are alternative definitions that reflect the choices a society makes.⁵

The techniques used to create, use, and manipulate embryos for *reproductive* purposes can also be put to *non-reproductive* purposes. For example, the somatic cell nuclear transfer (SCNT) or cloning technique can be used, in principle, for the reproductive purpose of creating a child or for the nonreproductive purpose of creating a source of embryonic stem (ES) cells (and ultimately transplantable tissue). Because the reproductive and nonreproductive uses of embryos are inextricably entwined, we must consider them together if we want to understand and anticipate the implications of our “big embryo experiment.”

This broad understanding of reprogenetics—all interventions involved in the creation, use, manipulation, or storage of gametes and embryos—delimits a fairly distinct class of interventions. Reprogenetic research and practice include interventions aimed at creating embryos, whether for reproductive or therapeutic purposes, and whether by “traditional” means such as IVF or by newer means such as SCNT or intracytoplasmic sperm injection (ICSI). Also included are interventions aimed at altering gametes or embryos, whether by the “traditional” techniques of recombinant DNA or by the newer techniques involving cellular surgery or the use of artificial chromosomes. (Interventions aimed at transferring genes to *somatic* cells to cure individuals of disease are plainly excluded.)

The scope of reprogenetics, and correspondingly of this report, could have been broadened still further to include surrogacy arrangements and prenatal testing. Ultimately, following the example set by the mandate of the United Kingdom’s Human Fertilisation and Embryology Authority, it *excludes* all interventions on embryos and fetuses *inside* a woman’s body.⁶ Research on and treatment of embryos and fetuses that are in a woman’s body are regulated to differing extents by regulations for human subjects’ research and by statutory and common law.⁷ Also, a conception of reprogenetics broad enough to encompass these other domains would threaten to grow unwieldy.

Alternatively, the scope of the reprogenetics could have been limited to those techniques that involve emerging technologies. This narrower conception of reprogenetics, however, would make it impossible to contemplate the bigger reprogenetic picture—the ways in which reproductive and genetic technologies are converging. Of course, future discussions may identify different ways of delimiting the scope of reprogenetics. Such discussions should be encouraged.

Reprogenetics in Action

The past few years have provided several opportunities to notice the very different purposes to which we can put our growing capacity to do things with gametes and embryos—to notice the very different ways in which reproductive research and practice converge with genetic research and practice.

■ In September 1998, news broke about a technology that can sort sperm according to the weight of the chromosomes they carry with an accuracy rate of approximately 85 percent.⁸ The company that developed this technology markets it to couples that desire to select the sex of their children. Today approximately 430 children have been born using this technique.⁹

■ Molly Nash was afflicted with Fanconi’s anemia. Her parents wanted to have a second child who would not be afflicted with Fanconi’s, and who also could be a histocompatible donor to Molly—a source of compatible cord blood. To help the Nashes have such a child, researcher-clinicians used preimplantation genetic diagnosis—genetic diagnosis of embryos created in a laboratory to identify suitable embryos for transfer to Molly’s mother’s uterus. A child who was both free of disease and histocompatible with Molly was born in August 2000.¹⁰

■ In March of 2001, researchers at the Institute for Reproductive Medicine and Science at Saint Barnabas announced that an experimental technique had helped approximately twenty women become pregnant. These women had previously been unable to conceive as the result of defects in their eggs’ cytoplasm—the “ooplasm.” The researchers performed “ooplasm transplantation” by injecting healthy ooplasm from donor eggs into defective ones. Because the ooplasm contains tiny organelles called mitochondria, and because each mitochondrion contains a small loop of DNA, ooplasm transplantation entails the



Dreaming of Offspring,
Paul Klee

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Bonn; Photo: Erich Lessing /
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transfer of genetic material from one egg to the other. Indeed, the researchers announced that they had achieved the first successful “germ-line modification” and that it had resulted in apparently healthy babies.¹¹

■ To date, much of the public and policy conversation about research on embryonic stem cells (ES cells) has focused rather narrowly on the moral status of embryos and the potential of ES cells to be put to the therapeutic purpose of creating transplantable tissue. If the ES cells were created through SCNT techniques, they could be used to generate transplantable tissue that was fully histocompatible with the person who received it. Largely missing from this discussion has been a recognition that, in theory, ES cell research could be combined with both SCNT and gene transfer techniques for the reproductive purpose of creating either healthy or “enhanced” embryos—and children.¹²

These four examples suggest some of the ways in which reproductive and genetic technologies are coming together to increase our capacity to prevent or cure disease—and to create children with traits we desire, some of which are related to health, others of which may not be. IVF can help prospective parents have a child—whatever child they get

in the genetic lottery. The newer techniques go one step further: they promise to help prospective parents choose what kind of child they get—or at least to increase the *chances* that their children will have some traits rather than others. Some of those traits will be related to the health of someone other than the child—like Molly Nash’s brother, Adam. Other traits, someday, may be related not to anyone’s health, but to some perceived advantage.¹³

It is altogether too early in our understanding of the genetics of complex traits to know how far the project of “enhancing” children can go, in good part because complex traits appear to involve extremely complex interactions among many genes and environmental factors.¹⁴ But even if adding genetic material (whether genes or artificial chromosomes) to embryos to enhance human traits does not prove feasible, we are likely to learn enough about genotype-phenotype relationships that some entrepreneurial individuals will promise that they can at least increase the chances of having a child with some desired trait, even if the child is created merely through IVF and preimplantation genetic diagnosis rather than through SCNT and gene transfer. We are just beginning to explore what that new power may mean for the well-being of children, parents, and society as a whole.¹⁵

What's at Stake?

The convergence of reproductive and genetic technologies raises complex and sometimes profound ethical questions that call out for informed policy, publicly and transparently developed. Some of these questions are about tangible harms; others, however, are about non-tangible harms. Into the first category fall concerns about the safety of the women who provide oocytes as well as the safety of the gestating mothers and of the children produced. The second includes broader concerns about human well-being. Although some of the reproductives technologies are increasingly thought to be within the purview of the Food and Drug Administration, the FDA is not mandated to consider well-being concerns.

Well-being concerns are not all equally persuasive for all commentators. It is not the goal of this report to defend them all, however—nor to defend exactly our way of articulating or organizing them. Delineating a representative range of these concerns is enough to establish the need for a transparent policy discussion of reproductives. That discussion will allow us to accept or reject the various concerns that commentators have broached. Yet given the concerns, we should not forego that discussion and leave regulation to the market alone.

Safety

In reproductive medicine, more than in most other areas of medical practice, the line between clinical innovation and human experimentation is fuzzy: “patients” in reproductive medicine sometimes can be subjected to the high levels of uncertainty and risk commonly associated with being a research subject.¹⁶ Consequently, reproductives raises concerns about the safety of the women, children, and tissue providers who are involved in reproductive medicine. As in all scientific experimentation, it is important to be realistic about the nature of scientific uncertainty. Although researchers and clinicians are often confident that they can predict what the outcomes of a particular technique may be, in fact we often cannot reliably predict the outcomes. We must expect the unexpected. At the very least we need adequate testing and record keeping to approach the standard of scientific research mandated in other areas of research.

The newer reproductives techniques raise a number of unresolved safety concerns.¹⁷ The potential health risks to children who might be created by means of cloning technologies have been widely publicized.¹⁸ In addition, it remains unknown how safe and effective ooplasm trans-

plantation is. There is some evidence to suggest that ooplasm transplantation may involve an increased risk of aneuploidy (that is, having an atypical number of chromosomes), although the clinical data are too incomplete to support any clear conclusions.¹⁹ But safety concerns are of course not limited to the newer reproductives technologies. Insofar as traditional IVF often produces multiple births, babies born by such methods are at increased risk of “prematurity, low birth weight, infant death, and life-long disability.”²⁰ Recent studies have suggested that children produced by means of intracytoplasmic sperm injection may be at an increased risk of aneuploidy.²¹

Reproductives technologies often require a supply of eggs from either the patient or from “donors” (who actually often sell their eggs or provide them in exchange for fertility services). New technologies like ooplasm transplantation and ES cell research will only increase the demand for oocytes. The risks to women who provide eggs are associated primarily with the drugs used to induce superovulation. Severe ovarian hyperstimulation syndrome is a rare but life-threatening event. A potential increase in the risk of ovarian cancer is also thought to be associated with superovulation. In addition to the drug-related risks, there are also some surgical risks, including possible “puncture of the fallopian tubes, infection or bleeding.”²² Traditional assisted-reproductive techniques also put gestating women at increased risk of preeclampsia, diabetes mellitus, bleeding, and anemia.²³ In addition to risks associated with the drugs and surgical techniques, women and children are also at increased risk of the infections that accompany tissue (including egg or sperm) transplantation.

In discussing safety-related risks, it is important to remember that the couples seeking to have children with these techniques are often more than willing to bear them. There is, however, an ethical consensus that parents have a *prima facie* obligation to shield their prospective children from preventable impairments.²⁴ Needless to say, an obligation to shield children from preventable, reproductively induced impairments must be balanced against the parental right to try to create a child. In other words, parents must balance their desire to create a child with their desire to shield the child from preventable harms.

How best to balance those competing values and desires is open to debate, and oversimplified generalizations about what individuals want and what they owe each other are not adequate to help us understand the complex relationships and motivations that are inherent in good family life. Everyone can agree, however, that there is a

need for good data about the real risks inherent in these technologies.

Unfortunately, experimental reprogenetic techniques have been rapidly introduced on the market “without sufficient prior animal experimentation, randomized clinical trials, or the rigorous data collection that would occur in federally funded studies.”²⁵ In fact, ooplasm transplantation was advertised on the Internet before the Food and Drug Administration intervened to collect information and conduct hearings on the technique’s safety and efficacy.²⁶ Without good data, no one can give meaningful informed consent to engage in such activities, no matter how important the aim of having a child.

Well-Being

Public policy in the field of reprogenetics is more challenging than in some other domains because, even if all the safety concerns were addressed, other vital concerns would remain. Given the depth and complexity of the desire to have a biologically related child, the techniques used to gratify that desire can raise equally deep and complex questions about human *well-being*.

Arguably, many well-being concerns are facets of the same fundamental worry that, in a consumer culture such as ours, using technology to produce “better” children will drive us toward making the fundamental mistake of treating children—and the rest of us—as commodities rather than as persons.²⁷ Whereas we think it appropriate to give a price to commodities, we think it is a category mistake to give a price to children; to do so is to miss that the sort of being we’re dealing with is “priceless.”²⁸ Insofar as reprogenetic practices will promote the view that the value of gametes, embryos, or children depends on their particular traits, those practices will raise similar concerns.

Skeptics sometimes claim that such concerns conceal nothing more than fear of the new.²⁹ Very likely they can be a sign of fear, but they can also reflect a desire to affirm the intrinsic value of the diversity of human forms. Well-being concerns are, in part, about the fact that reprogenetic technologies are being used, not by persons who aim to shape themselves, but rather by parents who aim to shape their *children*. Using reprogenetic means for this goal may exacerbate parents’ tendencies to think of children as the objects of their making and to have unrealistic expectations of their children. Well-being concerns are also, in part, about the belief that in using reprogenetic means to shape children, we are expressing a problematic conception of what it is to be a human being.³⁰ The worry is that in using these means we will lose sight of the fact that children are wholes who cannot be reduced to the sum of their traits if we are to adequately understand what they are.

Another source of concern is the prospect that we might someday use reprogenetic means to *enhance* children’s traits. If we presume that access to such “enhance-

ments” is unequal, then there is reason to worry that parents who already purchase social advantages will be able, in effect, to purchase genetic capacities to use those advantages—thereby potentially increasing the gap between the haves and have-nots.³¹ Imagine that the teenager already blessed with social advantages like Stanley Kaplan prep courses has already been outfitted at birth with a reprogenetic form of Ritalin—with the capacity to be especially good at exploiting social advantages like the prep courses. That children with advantages are already using psychopharmacological agents in just that way is hardly an argument for permitting reprogenetic means to achieve more of the same. Nor can we regard the decision to use reprogenetic means as a “private choice,” for such choices would generate pressures on others to follow suit. Some parents will no doubt fervently want to acquire such advantages for their prospective children, yet if they obtain them, other parents will likely feel pressured, perhaps even obligated, to purchase the same services for their children.³²

If we assume instead that all parents have equal access to new enhancements for their children, concerns about justice still do not disappear. Some commentators argue that if we approved general use of reprogenetic enhancements, we might then begin to use reprogenetic means to solve complex social problems, and in so doing undermine our commitments to equality and diversity; prospective parents might use the technology to increase the chances that their children will better live up to dominant ideals, which at least in some cases will be unjust.³³ Imagine an intervention that increases the chances that a child will have the pale pigmentation currently valorized in the West; although we might readily imagine why parents would want to insulate their children from the norm that values pale pigmentation, we might nonetheless worry that using reprogenetics to deal with discrimination leaves the unjust norms in place.

Still other concerns center on the well-being of the women who will provide the eggs, whether for research or for reproduction. As has been articulated in a parallel fashion in the debate over the ethics of commercial surrogate pregnancy,³⁴ these women seem to be candidates for coercion and exploitation. The potential for exploitation is aggravated when the phenotype of the woman providing the eggs is irrelevant. In those cases, the woman may be especially vulnerable to economic coercion. Although high prices are reportedly sometimes offered for college women’s eggs, researchers will likely seek a cheaper source of oocytes for techniques such as therapeutic ES cell research and ooplasm transplantation. Many of the women who undergo hyperstimulation and surgical removal of oocytes for research purposes would likely do so because they need the money, yet they would likely not be as well placed to protect themselves. Just as we do not encourage the buying and selling of organs because such a market



The Newborn, Constantin Brancusi

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could exploit the poor, we should be wary of a market in human reproductive materials.³⁵

There are other long-standing questions about the effects such commercialization of reproduction will have on us as a society.³⁶ One reason many argue that commercialization of human reproduction should be avoided is that they object to putting a price on something priceless, to rendering it open to comparison and to bargaining.³⁷ Some also argue that we lose something important by replacing gift relationships with market exchanges.³⁸ Although markets already exist in a number of human “goods” intimately tied to our personhood, such as human labor and human beauty, there need not be markets in all such “goods.” We need these issues to be part of the discussion that informs reprobogenetics policymaking, rather than fatalistically accepting the colonization of children- and family-making by the market.

The Controversy over Well-being

In the U.S. public policy debate, concerns such as the ones mentioned above have often been viewed by some commentators with skepticism, if not derision. They are sometimes referred to as “symbolic,” “speculative,” “vague,” and sometimes “religious.”³⁹ Yet even ardent critics of these concerns still accord them weight. For example, John Robertson, one of the strongest proponents of procreative liberty, acknowledges that “[a]t a certain point

... a practice such as cloning, enhancement, or intentional diminishment of offspring may be so far removed from even pluralistic notions of reproductive meaning that they leave the realm of protected reproductive choice.”⁴⁰ Robertson understands that if we are to place limits on procreative liberty, then there is no way around the difficult work of taking well-being concerns seriously.

Similarly, Dr. Charles Strom, who used preimplantation genetic diagnosis to help Molly Nash’s family produce a histocompatible sibling without Fanconi’s anemia, recognizes that PGD could also be used to test for non-health related traits, and he appears to have concerns about some of those uses. He told a *New York Times Magazine* reporter that reprobogenetics research of the sort he himself conducts has “all been forced into the private sector . . . where there are no controls.” He added, “There should be limits. It is up to us, as a society, to decide what they are.”⁴¹ It is important to note that Strom’s call for controls and limits is not based on concerns about safety alone.

It will not be easy to fully articulate the limits that should be placed on these technologies. But if we are to have any limits, then we as a society will have to find a language in which to articulate them.

Though making public policy based on well-being concerns will be difficult, it will not be without precedent. We already allow questions about the well-being of individual children to guide some reproductive decisions. For example, the state considers the well-being of children in adoption decisions.⁴² Before prospective parents are permitted to adopt a child, they are required to provide evidence that they would be good parents. What constitutes a good parent is far from obvious, and making such judgments is difficult, but that does not prevent us from making such determinations.

Indeed, the New York State Task Force on Life and the Law has suggested that physicians are “entitled to consider the welfare of any child who might be born” as a result of reproductive and genetic procedures.⁴³ Although the task force staunchly supports procreative liberty, it does, in the name of child welfare, identify circumstances that may warrant refusing prospective parents access to assisted-reproductive services.⁴⁴ Consequently, despite a general reluctance to address well-being issues in reproductive policy, there are precedents for defining limits to procreative liberty in the name of child welfare in public policy.⁴⁵ Similar judgments could be made to define limits to the circumstances in which reprogenetic technologies are used.

There’s no denying that we hold dear different and sometimes competing fundamental values, including liberty, equality, solidarity, and justice. When those values come into conflict, we in the United States generally prefer to allow individuals to resolve the conflict themselves—to exercise their individual liberty and choose for themselves. But we do not always leave it to individuals alone to resolve conflicts between values. For example, we have decided as a matter of public policy that people cannot buy and sell other people. In this case, equality trumps freedom. Similarly, we prohibit a market in organs because such a market would undermine some values that we esteem even more than we esteem an individual’s liberty to buy and sell what she wants. We have decided, instead, to rely on the altruism of donors, even though donors do not meet the demand for organs, because doing so furthers the ethical commitments of our society.⁴⁶

Absent systematic regulation, reprogenetic technologies are limited mainly by the constraints of the market and the piecemeal constraints of professional self-regulation. The extent to which reproductive decisions, materials, and techniques should be left to the market should be part of our public policy discussion. Though no one would dare place an ad for a kidney, much less a child, in a college newspaper, ads are placed in university papers to induce young women with particular traits to sell their eggs for use in IVF.⁴⁷ And, as mentioned earlier, it is now possible in this country to purchase an increased chance that you will get a baby with the sex you prefer.⁴⁸ Most countries with similar cultures have prohibited sex selection that is unrelated to disease prevention.⁴⁹ Indeed, many countries

hold that markets in human reproductive tissues, technologies, and services are simply “blocked exchanges,”⁵⁰ or “hors du commerce.”⁵¹ The United Nations’ Universal Declaration on the Human Genome and Human Rights asserts that civilized societies must avoid putting a price on human reproduction.

Embryo Research

Most western industrialized countries share a view that embryos in petri dishes are neither persons nor mere property.⁵² Insofar as embryos could become persons if they were transferred from petri dishes into wombs, they deserve our respect; *how much* respect the entity deserves depends in part on how far along the developmental path it is. The farther along the path it is, the more respect it deserves. We express that respect with prohibitions and limits that restrict the uses and conditions under which embryos may be used in research.⁵³ But many think that some research is acceptable. Long before reproductive specialists were creating and manipulating embryos to produce children, they had to conduct experiments on embryos, which no one would have dreamed of implanting in a woman. IVF would never have gotten off the ground without embryo experimentation.

Yet even if many people agree that at least some embryo research is ethically permissible, many questions remain about what it means for us to use embryos to serve our purposes. Will a given technique or manner or purpose of embryo research express appropriate respect for these entities? Or will it incline us to think of embryos as “mere stuff” to put to whatever purposes we see fit? Will our activities involving embryos incline us to treat these entities as mere instruments for pursuing other goals—and will doing so affect how we understand our relationships to each other and, ultimately, our relationships to the rest of the natural world? All of those questions are ultimately about the well-being of individuals and our society as a whole.

Other countries have struggled to think about these issues at a policy level and make clear the ethical commitments that underlie their embryo research policies. We must do the same. The overall task, therefore, is to design an oversight system that allows debate about both safety and well-being to inform responsible reprogenetics policy.

Public Policy, Regulation, and Reprogenetics

The current public policy stance regarding reproductively genetic technologies is a compromise and a patchwork, derived from deep divides in American politics and the accidents of scientific progress. It is riddled with redundancies, inconsistencies, gaps, and inefficiencies. The political division that has hampered public policy on reproductively genetic is rooted in the vitriolic U.S. debate over abortion. Given the polarizing dynamics of this debate, much of the public policy conversation about embryo research and reproductive policy has consisted of pro-choice and anti-abortion activists shouting past each other. Unsurprisingly, many policymakers have chosen to avoid entering that fray, and they have therefore not been able to agree that some embryo research is acceptable for some purposes, but not for others. As a result, almost all embryo research has been driven into the private sector. The natural secrecy of the private sector can have two results: it can impede the progression of the science given the need for confidentiality,⁵⁴ and it can reduce the public's role in deliberating about the direction of the science. For the bulk of such work to go on in the "shadowlands" of the private sector⁵⁵ can be both dangerous for participants and incompatible with the ideal of conducting such work in the light of forthright public deliberation.

The second reason we lack a productive public conversation about reproductively genetic has to do with the historical fact that until very recently, reproductive medicine and genetic medicine have been separate lines of inquiry, pursued by professionals with training in quite independent scientific and medical fields. Even if genetic and reproductive technologies were not in the midst of converging, the redundancies, inconsistencies, gaps, and inefficiencies in the current systems of oversight for genetic and, especially, for reproductive medicine would call out for reform. But genetic and reproductive technologies are converging. A new system to oversee reproductively genetic research and services is needed, therefore, for functional reasons, since the old categories of "genetics" and "reproductive" research do not reflect the new technological realities. The ooplasm transplantation protocol (see page S4) is a prime example of an intervention that does not fit cleanly into either of the old categories: the purpose is reproductive, but achieving it entails a genetic change.

Converging Lines of Research

In the mid-1970s, when research into reproduction and genetics was getting off the ground in earnest, the two fields appeared largely unrelated. Reproductive medicine had begun to promise that IVF could help infertile couples have children. There really was no genetic medicine, just genetic researchers dreaming of curing terrible diseases. The possibility of genetically modifying gametes and embryos was quickly dismissed, citing a consensus that our society would never embark upon making such changes. The ethical and technical barriers, it was regularly asserted, were simply too high.⁵⁶

At that time, the two fields were overseen in quite different ways. Gene transfer research underwent intense regulatory oversight and became the subject of a well-developed policy conversation about its purposes; reproductive medicine has received much less careful attention.

GENETICS. The National Institute of Health's Recombinant DNA Advisory Committee (the RAC) was created in 1974 in part to be a forum for better public conversation about genetics research. In the beginning, RAC was a forum to discuss concerns about the safety of splicing foreign genes into microorganisms. In 1982, the report *Splicing Life*, produced by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, argued that RAC's purview should be expanded to include gene transfer protocols in humans and that its membership should be expanded to include, among others, lay public participants, and ethicists.⁵⁷ In 1985, when RAC adopted guidelines for researchers proposing to embark upon gene transfer experiments in humans, it was responsible for making recommendations to the NIH director about protocol approval and for promoting a public conversation about the purposes of such research. It became, therefore, a place to discuss questions about both safety and well-being. Even though researchers in the private sector were not required by law to put their protocols before RAC, they did so voluntarily—at least until 1996.

In 1996, NIH director Harold Varmus announced that he would eliminate RAC. He argued that because the basic issues surrounding gene transfer research had been resolved, RAC oversight was redundant.⁵⁸ When observers responded that RAC was needed more than ever because of the prospect of germ-line modification and genetic enhancement, Varmus revised his recommendation to elimi-

nate RAC. He left it standing, but took away its power to approve protocols, opting instead to rely on a system of IRB and FDA oversight.

While there are redundancies and even some inconsistencies between RAC and FDA oversight of genetics research,⁵⁹ together at least they provide mechanisms for broaching both safety and well-being issues. Further, most genetics research carried out in the private sector is overseen by the FDA, and private sector genetics research is often voluntarily taken before RAC if researchers or their sponsors think they are broaching a “novel issue.”

Unfortunately, however, RAC’s guidelines describe its mandate in terms of the technology that was around in the 1980s; it considers only those interventions that involve recombinant DNA.⁶⁰ Thus the ooplasm transplantation protocol technically fell outside of RAC’s purview, even though it involved inheritable genetic modifications, because the protocol employed cellular surgery rather than recombinant DNA. It was only that technological detail that kept the protocol, which the researchers themselves called the first successful “human germline genetic modification,” from being subject to RAC scrutiny.⁶¹ And thus that research was conducted without public conversation, under the supervision only of the researchers and of their institution’s IRB.

The lack of a comprehensive, informed oversight system means that researchers in reprogenetics risk violating two critical moral obligations, one to individuals and one to society. The first is the researcher’s obligation to avoid harming individuals. Researcher-clinicians are obliged to refrain from offering techniques to produce children until the techniques have been shown to pose minimal risks to such children. But many reprogenetic techniques have not yet been shown to pose such minimal risks. In the ooplasm transplantation protocol, the researchers acknowledged that the long-term effects of the intervention are simply not known.⁶² Indeed, two of the fourteen fetuses they produced had Turner’s syndrome.⁶³ (One spontaneously aborted and the other was selectively aborted.) Turner’s is not an uncommon genetic disorder, and the Turner’s births may not have been caused by the procedure; or, they may have. Researchers and clinicians here and abroad expressed concern that such risks were taken with little understanding of the long-term health consequences.⁶⁴ Similar safety concerns have surrounded the use of ICSI.⁶⁵ The potential danger of such procedures calls out for a public system of oversight that relies on more than the discretion of individual researchers and their institutions.

Second, since scientists are members of a democratic community who share resources (and all researchers in this country benefit directly or indirectly from our extraordinary scientific infrastructure), they are obliged to subject their research to public scrutiny, especially if the research promises to affect future children and thus the future of our society. That obligation is embodied in the RAC. But

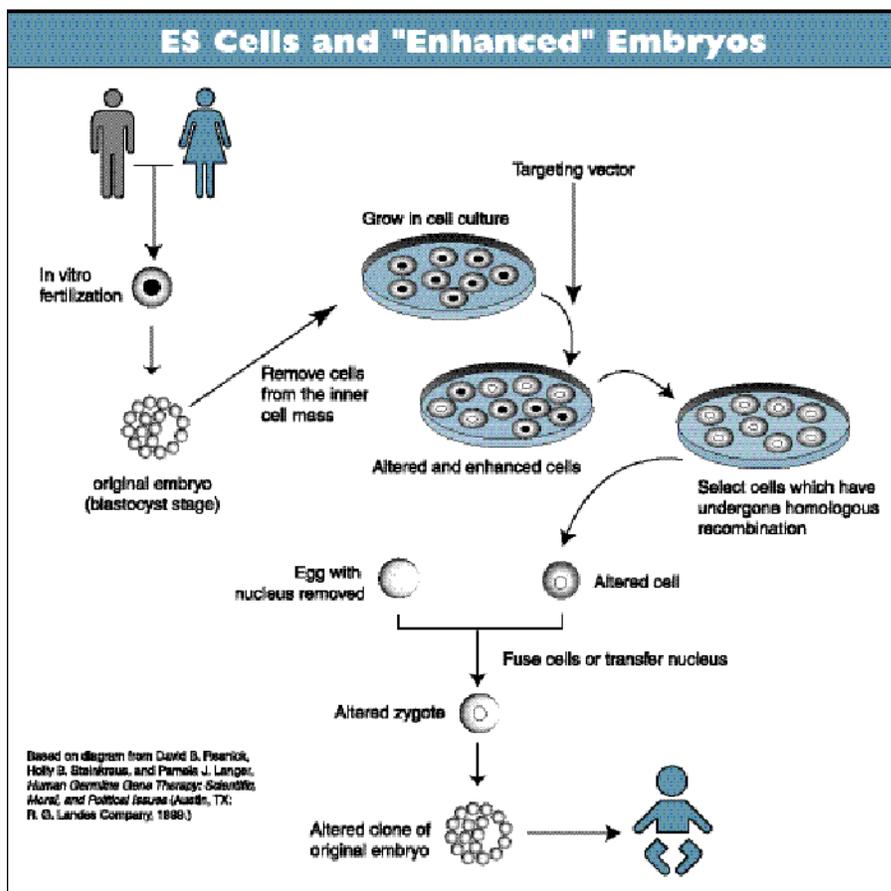
the ooplasm transplantation protocol ran afoul of the spirit of this obligation. The decision to make inheritable genetic modifications in the human genome should not be left to individuals. It should be made at a policy level after public discussion about both safety and well-being concerns.⁶⁶

REPRODUCTIVE MEDICINE. In contrast to genetic research, reproductive research in the United States goes on with relatively little public scrutiny. The National Conference of State Legislatures recently summed up the current system of regulation in this country when it wrote: “[A] substantial proportion of research and innovative therapy in reproductive medicine need not be subject to peer review, may not conform to current standards for informed consent, and may be offering services that have never been fully evaluated for safety and efficiency.”⁶⁷ This minimalist approach is in stark contrast to that taken in much of the rest of the democratic world.⁶⁸

The history of the oversight of reproductive medicine is heavily influenced by the dynamics of the abortion debate. Those dynamics make policymakers reluctant to engage in a discussion about embryo research. In the late 1970s, the Ethics Advisory Board (EAB), which was appointed by the Carter administration, endorsed the idea of federal support for embryo research. According to the EAB guidelines, federally funded embryo research had to be reviewed by the EAB. Thus, when under Carter, Reagan, and Bush Sr., funding for the EAB was denied, the result was a de facto ban on federally funded embryo research. The Health Research Extension Act of 1985 precluded embryo research not intended to benefit the particular embryo.⁶⁹ In 1993, however, with the arrival of the Clinton administration, Congress nullified the EAB-approval requirement and temporarily ended the ban.⁷⁰

Also in 1993, NIH director Harold Varmus created the Human Embryo Research Panel (HERP) to give him advice regarding what kinds of embryo research NIH ought to fund. In 1994, HERP endorsed funding for embryo research, including funds for some creation of embryos. Presciently, HERP argued that if ES cells were ever isolated in humans, ES cell research would be one form of embryo research that should be eligible for federal funding. Although Clinton rejected HERP’s recommendation with respect to funding the creation of embryos for research, he otherwise endorsed the HERP report. In 1995, in reaction to HERP and Clinton, Congress passed the Dickey-Wicker amendment, which precludes federal funding of embryo research through annual NIH Appropriation Acts.⁷¹ Consequently, where embryo research goes on, it does so without public money or scrutiny—in the private sector.⁷²

Another part of the explanation for the current lack of oversight of reproductive medicine is that many new interventions in the field are considered “innovative application”—not research—by those who offer them. And since they are presented as innovative clinical practice rather



created guidelines for gamete and embryo donation in 1998, and revised them in 2002.⁷⁸ Members of ASRM's Society for Assisted Reproductive Technologies (SART), who account for as many as 90 percent of the providers of reproductive services, comply with FCSRCA, allow inspections, run accredited embryology laboratories, and follow the ethical guidelines of ASRM.

Finally, the FDA has asserted its jurisdiction over cloning and ooplasm transplantation on grounds that such interventions create "products" analogous to the biologic products already within its mandate (gene-therapy products, for example).⁷⁹ Given that the FDA's mandate is limited to the con-

sideration of issues related to safety and efficacy, therefore leaving out concerns about well-being, it would be best if technologies like cloning and ooplasm transplantation did not fall exclusively within FDA's mandate.

than as research, oversight of them is left to the discretion of the individuals or institutions offering them.

Moreover, because most insurance companies still do not pay for infertility services, they have not insisted on scrutinizing the results of reproductive research in the way they scrutinize other forms of medical research. And because patients often accept that the failure rate of reproductive interventions is high, malpractice litigation has not effectively brought legal scrutiny to the field.⁷³

Presidential bioethics advisory commissions have taken up both the safety and well-being issues raised by certain technologies involving embryos—cloning and stem cell research—but only on an ad hoc basis. The modus operandi of President Clinton's National Bioethics Advisory Commission (NBAC) was to respond to the president's specific requests, which made it difficult to consider the full reproductic picture. President Bush's President's Council on Bioethics (PCB) recently issued an advisory report on the use of cloning technology,⁸⁰ but like NBAC, its resources and mandate are limited, it will likely be replaced by a change in presidents, and its role is purely advisory. Consequently, the NBAC and PCB reports will likely join the thoughtful, articulate advisory reports that form part of this country's academic bioethics work, but not part of its public policy.

None of this is to say that reproductive research and services go on without any oversight or regulation. Virginia and New Hampshire have comprehensive legislation regarding assisted reproduction,⁷⁴ and many states have laws regulating some aspects of, or techniques used in, embryo research.⁷⁵ At the federal level, the 1992 Congressional Fertility Clinic Success Rate and Certification Act (FCSRCA) requires clinics offering assisted reproduction technologies to disclose pregnancy success rates to the Centers for Disease Control. And laboratories that perform the diagnostic tests related to assisted reproduction, such as semen or hormonal analysis, must be certified under the federal Clinical Laboratories Improvement Act (CLIA).⁷⁶

In sum, many groups, commissions, and federal agencies have commented on or asserted authority over various aspects of reproductive services and research, yet there is, at best, a patchwork system of oversight. There is no standing body to promote public conversation about both the safety and well-being issues that arise in the context of new reproductive technologies.

Professional organizations in reproductive medicine have also set practice standards. The American Society for Reproductive Medicine (ASRM) set practice standards for IVF, GIFT, and related procedures in 1998.⁷⁷ ASRM also

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EMBRYONIC STEM CELLS: A CRITICAL MOMENT.

We are at a critical and perhaps a propitious juncture in the development of reprognetics and in the history of the debates over embryo research. Research on embryonic stem cells (ES cells) occurs at the convergence of reproductive and genetics technologies. That convergence brings promise and peril, which may prove vivid enough to make both sides of the abortion debate contemplate a compromise regarding embryo research.

It is widely known both that research on embryonic stem cells (ES cells) holds the promise of producing transplantable tissue for people in desperate need and that isolating ES cells entails the destruction of embryos. It is less widely known that ES cells also could be crucially involved in the *creation* of embryos; ES cells could ultimately be used to create healthy children, and—at least in principle—to create genetically “enhanced” children.

ES cells have three remarkable properties. The first is their pluripotentiality—their capacity to be coaxed to develop into many tissue types. The second is their “immortality”—their capacity to proliferate indefinitely in an undifferentiated form. Because of their immortality, if a researcher wanted to insert genes into cells, ES cell lines provide an unlimited supply of “targets.”⁸¹ Finally, ES cells are extraordinarily “malleable”; that is, it is easier to insert genes where you want them in ES cells than in other kinds of cells.⁸² The combination of their immortality and malleability not only makes ES cells superb targets for gene insertions but also makes them excellent vehicles for producing inheritable genetic modifications.⁸³

If researchers were to perform gene transfer on ES cells and then employed cloning to transfer an ES cell’s nucleus into an egg, they could move from creating transplantable tissue to creating altered embryos (see figure 1). Those alterations could be aimed at producing healthy embryos—or “enhanced” embryos. In this respect, then, ES cell research is part of the bigger reprognetic picture.

In 1998, when James Thomson and his colleagues isolated human ES cells, President Clinton asked the National Bioethics Advisory Commission to provide advice regarding ES cell research. NBAC delivered a report in late summer of 1999. Given the medical promise of the research, NBAC argued, an exception should be made to the statutory ban on federal funding of embryo research to permit federal agencies to fund research involving the derivation of human ES cells.⁸⁴ Thus a second high-level government panel followed HERP in arguing that some embryo research ought to be publicly funded.

Clinton rejected his own ethics advisory commission’s advice, however, opting instead to accept the legal opinion of the Department of Health and Human Services’ general counsel, Harriet Rabb, that the Dickey-Wicker amendment applies to research on *embryos* and that ES cells are not embryos.⁸⁵ Dickey-Wicker also states that federal funds may not be used for research “in which a human embryo or embryos are destroyed,” and ES cell research

entails the destruction of embryos. But Rabb opined that the letter of the law permitted federally-funded researchers to *use* ES cells as long as they did not *derive* them. Derivation could be left to researchers in the private sector. In August of 2001 George W. Bush employed the same use-derivation distinction but stipulated that federally funded researchers could use only ES cells that had been derived with private money before 9 August 2001.⁸⁶

By relying on the use-derivation distinction, the Clinton and Bush administrations squandered an opportunity to make a distinction instead between acceptable and unacceptable purposes for embryo research. Everyone who has used IVF has been the beneficiary of one sort of embryo research. And if anyone ever benefits from the ES cell research that the federal government now funds, that person will be the beneficiary of another form of embryo research.

If we want to enjoy such benefits, we should forthrightly support continued embryo research. In giving our support we must recognize that the embryo research enterprise, which requires a destruction of human embryos, does entail a moral cost—as do many things we desire. Many would allow, for example, that slaughtering animals for food and allowing medical students to dissect cadavers have their costs, even though they are justifiable. In thinking about embryo research, we must work out how we can both respect embryos and, under some circumstances and for some purposes, benefit from the things we can do with them. We need to figure out the difference between the purposes of the embryo research we want to endorse and the purposes of that we reject. Hiding behind distinctions like the one between use and derivation makes no sense for those who wish to face the bigger reprognetic picture in all of its complexity.

The basic point here is that ES cells in particular, and embryos in general, can be put to many different purposes. Adequate responses to those purposes will require more than the blanket yes of the advocates or the blanket no of the critics. To their credit, some people in the anti-abortion camp have already, in light of the therapeutic possibilities opened up by ES cell research, begun to modulate their blanket no to embryo research. Senator Hatch, who is opposed to abortion, has stated that ES cell research is a form of embryo research he can support, and he supports a bill that would permit the use of embryos in therapeutic cloning research. As anti-abortion advocate Tony Blankley wrote in the *Washington Times*, “The imminent private sector exploitation of [ES cell research] will force intellectually honest right-to-lifers to abandon our cherished illusion of moral clarity on this issue.”⁸⁷ Similarly, pro-choice supporters like George Annas and Lori Andrews have suggested that there ought to be limits on what we can do with embryos.⁸⁸

These are perhaps but preliminary calls for compromise, and they might prove ephemeral. If they are to lead to any genuine accord, with substantive consequences for

promoting some forms of research and constraining others, they must receive some institutional support. We must create a governmental body that will, among other things, facilitate systematic and nuanced policy deliberation about the wide variety of health and non-health-related things we can do with embryos.

The Role of Government in Reprogenetics

There will be little disagreement about the claim that safety concerns warrant government oversight. Many people from within infertility medicine believe that we need improved government oversight to protect participants/consumers.⁸⁹ Many of those same people would probably also agree that there ought to be some form of public discussion about how this new research and practice will affect the well-being of us all.

Two objections, however, can be raised against attempting to promote broad-based public deliberation about questions of well-being and against attempting, through political and moral deliberation, to develop a common framework of values within which public policy on reprogenetics could be formulated.⁹⁰ First, questions about possible future consequences are necessarily based on claims that are more tentative than the scientific knowledge and empirical data that policymakers often wish to have on hand before making decisions. But in fact, making public policy decisions under conditions of uncertainty and incomplete knowledge is a familiar problem, and the remedy is not policy inaction. What are required are open and reasonable deliberation, a sense of humility in the face of very complex questions, a willingness to listen and learn, and the flexibility and honesty to make corrections to policy when initial assumptions or beliefs turn out to be mistaken.

Second, some have argued that public deliberation and public policy should be limited to procedural and technical questions. This is primarily because, they believe, opening the public sphere up to issues as difficult and controversial as what constitutes human well-being would be dangerous in a pluralistic democracy.⁹¹ It would be dangerous partly because it would be a source of conflict, and partly because policies or laws informed by a particular conception of human well-being could threaten the liberty of those who hold different beliefs about human well-being.

This second viewpoint is important as a caution against the possible misuse of public deliberation, but it does not provide a compelling reason to forgo the process of deliberation altogether. Even in so contentious and sensitive an area as human reproduction and family life, public policy cannot and should not be limited to procedural issues alone. Doing so suggests that all human relationships are characterized only by rational, voluntary contract and self-interested exchange. In this realm, public policy cannot and should not be limited to the negative, protective func-

tions of providing for individual security and the prevention of harm, as important as these are. The function of public policy even in a democratic, pluralistic society is also positive; it is to promote the enjoyment of liberty and rights, to promote social justice, and to promote the well-being of its citizens.

Liberty itself is an aspect of human well-being. Liberty and autonomy cannot flourish in a society in which the individual is merely protected from harm; they can flourish only where the individual also is supported in her human dignity and worth—where she is educated and is provided with equal opportunities to develop personal talents and abilities. It would be supremely ironic if, out of concern for the protection of individual liberty and diversity of opinion, we hobbled the primary democratic vehicle we have that creates a context within which liberty itself can prosper and be most meaningful. That vehicle is the process of fair and open public deliberation about the conditions of justice and liberty in our polity, and the conditions of human well-being in our society. Contrasting visions of human well-being are the lifeblood of politics and are always at work, even though sometimes they are so “self-evident” to so many that we do not notice them at all. We should not fear this aspect of political discourse and deliberation, we should embrace it and put it to good use.

One of the government’s responsibilities is to promote the public welfare, and how reprogenetic technologies are developed and disseminated will affect the public welfare. Some of those effects will be relatively narrow: among these more contained consequences might be legal dilemmas regarding the identities of children and responsibilities of parents; questions regarding the care and support of children, and issues surrounding the medical treatment decisions of children produced by these new techniques.⁹² Other effects will be broader: reprogenetics might transform the meaning of having a child, being a member of a family, and being a member of a community.

Our government has an interest in influencing the development and dissemination of technologies with this kind of power. Given that the current system of reprogenetics oversight is potentially dangerous, out of step with the reality of the convergence of reproductive and genetic medicine, and sometimes subverts genuine public conversation, it is time to contemplate new reprogenetic policy mechanisms. It is, of course, ambitious to try to describe mechanisms that are less dangerous, that reflect current technological developments, and are capable of facilitating a conversation about the bigger picture. Such a task could not possibly be accomplished in one fell swoop by any single group. We are at the beginning of a long process, and this report merely points in one direction we might go to create safer and better-informed oversight of reprogenetic research and practice.

International Regulation of Reproductive Genetics

There are several possible regulatory vehicles that might allow for better oversight of rerogenetics, and each strategy has strengths and weaknesses. The overarching recommendation of this report is for comprehensive regulation of rerogenetic techniques in both the private and public sphere. That recommendation is guided, in part, by an analysis of the regulatory strategies of other countries, in particular those of the United Kingdom and Canada. In spite of the close cultural ties between those countries and our own, differences in culture and political tradition make wholesale importation of either of their regulatory schemes both impossible and inappropriate. Nonetheless, it is informative to consider what in these countries has worked and what has failed.

The United Kingdom

In 1984, the Committee of Inquiry into Human Fertilisation and Embryology headed by Dame Mary Warnock (the “Warnock Committee”) issued a detailed report outlining the results of a two-year consultation process on embryo research and assisted human reproduction.⁹³ The Warnock Report reviewed the ethical issues associated with new reproductive techniques and stated the committee’s opinions (both majority and minority opinions, in some cases) about what policymakers ought to adopt in designing oversight.

The Warnock Report covered many issues, including some controversial topics that generated significant disagreement, such as the moral status of the human embryo and the acceptability of human embryo research. Ultimately, the report articulated a number of opinions about the acceptability of human embryo research, the need for limits and restrictions to certain practices, and the need for a centralized oversight body that could create and implement public policy and adapt to technological developments.

The government adopted the recommendations of the Warnock Report and drafted legislation aimed at regulating the storage and use of gametes and embryos in treatment and research. The legislation, the Human Fertilisation and Embryology Act 1990 established a national oversight body called the Human Fertilisation and Embryology Authority (HFEA).⁹⁴ The HFEA has the status of a “quango”—a body in an arms-length relationship to the government that is housed outside the Department of Health yet is accountable to the Secretary of State. To en-

sure that it is not “overloaded” by scientist and clinician voices, the act stipulates that membership is interdisciplinary.

The HFEA is responsible, through various committees, for licensing and monitoring clinics and laboratories involved in gamete or embryo storage, creation, or use, and the act sets out the purposes for which licenses will be required (falling under the rubric of licenses for treatment, storage, or research).⁹⁵ In addition, the HFEA functions as an information resource for patients, clinics, and clinicians alike. It achieves this, in part, by establishing and publishing a code of practice “giving guidance about the proper conduct of activities carried on in pursuance of a license under the Act.” Through the setting of standards and the provision of licenses, the HFEA provides both quality control and assurances that ethical conduct in embryo research is maintained.

The act also details the situations in which consents must be obtained.⁹⁶ Through a series of detailed and mandatory consent procedures, it attempts to ensure that patients consider some later contingencies and how they would respond to them. Should the couple divorce, for example, to whom do stored IVF embryos resolve? Consequently, in the face of disagreements and unforeseen circumstances, the parties involved will have already articulated their wishes with respect to dispositional authority, discard, or storage of their gametes or embryos, and unnecessary litigation can be avoided. Not all contingencies can be foreseen, of course, but the system has proven quite effective.

Since research, storage, and treatment involving gametes and embryos are to be monitored, committees of the HFEA have been formed to approve protocols that use gametes and embryos in research and medicine. Consequently, the HFEA has responsibility for licensing novel applications with embryos and gametes and, therefore, fulfills a policymaking function. When a novel application that raises questions of well-being comes before a committee, the protocol is sent to the full HFEA for discussion and approval. Thus the smaller licensing committee does not make policy decisions that should be subject to broader discussion and approval. Finally, in addition to its licensing and monitoring functions, the HFEA maintains an information registry on the gametes, embryos, patients, and children that have been involved in licensed activities.⁹⁷

The authority of the HFEA to grant licenses is limited by the purposes described in the act.⁹⁸ The decision to articulate the purposes of embryo usage rather than specific

techniques has ensured that the act can incorporate novel techniques that were not envisaged when the act was drafted. In addition, if new techniques and applications emerge that fall outside the HFEA's statutory authority, the act allows parliament to expand the range of purposes that are placed under the HFEA's authority, thereby ensuring that new purposes do not call for new oversight agencies and preserving the integrity of the system. The act has been drafted in sufficiently general terms, however, that it remains almost unchanged more than a decade after its inception.

One reprogenetic development that the act could not incorporate, as initially written, was the isolation of ES cells. The response was a good, if not painless, example of well-informed democratic policymaking in the face of rapid scientific advance.⁹⁹ The government spearheaded a public and policy debate about whether and when ES cell research and cloning techniques are valuable enough to be permitted for some purposes, and about what those purposes might be.¹⁰⁰ Both the HFEA (together with the Human Genetics Advisory Commission) and an independent expert group formulated policy recommendations.¹⁰¹

The independent expert group recommended that ES cell research be allowed for specific therapeutic purposes and that cloning techniques be permitted for the creation of research embryos that might lead ultimately to autologous transplantation techniques.¹⁰² In addition, the group's report (known as the Donaldson Report) recommended that future review of approved ES cell protocols be conducted to determine whether the research has proven fruitful and merits continued use of human embryos. The Donaldson report was accepted in its entirety by the government, which drafted additional purposes to add to the Act by way of regulation. These amendments were accepted in a free (non-partisan) vote by parliamentarians.¹⁰³ Consequently, these new reprogenetic techniques now fall under the oversight of the HFEA, maintaining a comprehensive, coherent oversight of reproductive genetics.

The HFEA has been a model law for many countries attempting to craft regulation in this area, including Canada, Australia, and France. It is important to note, however, that the United Kingdom is not mired in a divisive abortion debate, and that fact probably helps explain the public acceptance (for the most part¹⁰⁴) of the oversight system's decisions.

The support in the United Kingdom for the HFEA extends to the scientific and regulatory communities, which appear to have worked out a nonadversarial relationship. When a clinic cannot be licensed due to insufficiencies in its standards or its protocols, the HFEA works with that clinic to ensure that it understands what is required for it to successfully apply for a license. Despite the comprehensive and highly centralized regulation, the United Kingdom remains committed to scientific freedom, and ar-

guably has one of the most liberal embryo research policies in the world.

There are a number of lessons to be gleaned from the experience in the United Kingdom. First, recommendations for Congress should be framed in general terms outlining suggested restrictions, conditions, and limits on the use, storage, and creation of embryos and gametes. Second, acceptable and unacceptable purposes of embryo research should be articulated rather than specific techniques. Third, a mechanism for adding to or adapting the enabling legislation in the face of new developments or information should be incorporated into the legislation. Fourth, a detailed informed consent procedure should be considered as a way of preventing unnecessary litigation and respecting patient autonomy. Fifth, the oversight authority should be responsible for developing a code of practice as a means of educating researchers, clinicians, and patients. And, finally, the respect the HFEA enjoys is partly the result of its ability to make scientifically informed and coherent decisions. This ability derives from its members' considerable expertise and the wide discretion accorded them. Similarly, any U.S. oversight authority will possess an expertise not likely shared by the members of Congress and should be granted significant discretion in making its decisions.

Canada

The Canadian policy experience in overseeing human reprogenetic technologies has followed a slightly more tortured path than the British. Its different experience is partly the result of Canada's diversity of opinions about reprogenetics, the depth and effort put into the public consultation process, and the constitutional and political division of powers between the federal and provincial governments.

In 1989, a Royal Commission on New Reproductive Technologies was established by the Federal Government to consult the public on issues related to "new reproductive technologies." The commission was charged with developing a substantive analysis of the technologies' implications for Canadian citizens and society, and with making recommendations to the government for public oversight. Over 40,000 Canadians were directly involved in the commission's public consultation process.¹⁰⁵

In 1993, the commission released its findings in a two-volume report, with fifteen volumes of supporting material and discussion.¹⁰⁶ The report articulated an "ethic of care" that should govern this area of research and practice and eight detailed principles that informed its recommendations. The commission made specific recommendations with respect to prohibitions and restrictions that should apply to embryo research. In addition, it recommended the establishment of a national regulatory body responsible for mandatory licensing of treatment and research involving gametes and embryos. Like the HFEA, the com-

mission recommended that the regulatory body be at arms length from the government. In addition, the body was to be constituted with a membership of at least 50 percent women.

These recommendations were followed three years later by a voluntary moratorium on nine unacceptable practices,¹⁰⁷ which was widely regarded as unsuccessful. In 1997, a first legislative bill was introduced into parliament as an attempt to act on the commission's recommendations. That bill, Bill C-47 (the Reproductive and Genetic Technologies Act) sought to criminalize a number of activities already subject to the voluntary moratorium and came under intense criticism for its failure to establish a licensing scheme or national regulatory body.¹⁰⁸ The bill died when an election was called in 1997. In May 2002, after extensive consultations with the provinces, a second bill—this time entitled the Assisted Human Reproduction Act (the AHRA)—was introduced to parliament.¹⁰⁹ That bill has now had received its second reading and is working through the various governmental stages of legislative passage. Like its predecessor bill, it has been the subject of criticism for its heavy reliance on prohibitions and criminal sanctions.

Like the counterpart British act, the AHRA purports to govern the creation, use, and storage of embryos and gametes in both treatment and research. However, unlike the British act, it also bans commercial transactions in human reproductive tissues (sperm and eggs) and commercial surrogacy. One of the guiding principles of the AHRA is the prohibition of commercial exploitation of human reproduction. Interestingly, the AHRA enshrines the guiding principles of the act within the act itself rather than in a preamble, as is more common.¹¹⁰ Placing the principles within the preamble means that they are not strictly enforceable as part of the act and can be used primarily to clarify or interpret the meaning of the act. But if the principles are affirmed in the AHRA itself, they *must* be taken

into account when interpreting or implementing a section of the act or its supplementing regulations.

Also like the British act, the AHRA outlines the restrictions, conditions, and prohibitions on uses of gametes and embryos. Both Canada and the United Kingdom have prohibited modifying the human germline, sex selection for other than medical reasons, and creating human-non-human chimeras. It is worth noting that all these activities have taken place or been attempted in the United States in the absence of legal prohibitions and comprehensive oversight.

The AHRA follows the British lead in establishing a national oversight body that has an arms length relationship to the government. The Assisted Human Reproduction Agency is responsible for licensing and monitoring facilities and for maintaining an information registry.¹¹¹ In addition, it must communicate and consult with the public and set conditions to maintain a license under the act. The Canadian act, again like the British act, explicitly requires the oversight body to carry out a public consultation and information function, aimed not only at the lay public, but also at stakeholders such as clinicians and patients. Clearly, the blueprint for the Canadian Assisted Human Reproduction Act was the Human Fertilisation and Embryology Act 1990.

There are lessons to be learned from both the British and Canadian experiences, not the least of which is that the road toward coherent oversight is long and often tortuous. But the public conversation that forms the bedrock of that process is rich, informative, and important for individuals and society alike. The ability to oversee reproductive research and practice from a national perspective provides both scientific quality control and greater certainty that ethically unacceptable activities are not being conducted with gametes and embryos behind a veil of secrecy in the private sector.

A Policy Proposal

There are many obstacles to any serious political initiative to regulate reprobogenetics research—and human embryo research in general. Surely one of the greatest obstacles is the fear each side in the abortion war will have of losing any ground. Many people would prefer the status quo to any risk of a setback.

But some people have begun to take such risks. And if our society is to submit reprobogenetic innovations to public oversight, others must take such risks as well. Developments in, for example, preimplantation genetic diagnosis, ooplasm transfer, cloning, and ES cell research invite us to step back and contemplate the bigger reprobogenetic picture. Thoughtful people should accept that invitation and begin to think broadly and boldly: they should design a system that can foster the discussion of safety and well-being concerns—and can ensure that new reprobogenetic techniques that raise those concerns do not slip through the regulatory cracks.

First Steps toward Public Discussion

We make three recommendations.

■ First, to bring embryo research into the light of public deliberation, Congress should lift the current ban on federally funded embryo research. We cannot have responsible oversight of reprobogenetics research and practice, nor of embryo research generally, if we do not first acknowledge that we already support those activities in a wide variety of ways. Our country has already embarked upon “one big embryo experiment.” If we do not forthrightly accept that fact by allowing the federal government to oversee research and practice involving embryos, then the market will be the only mechanism that will distinguish between the acceptable and unacceptable purposes of those activities.

■ Second, to take action toward regulatory oversight in the United States, a commission must consolidate and translate the many documents that have already been written on this topic, solicit views from the diverse U.S. constituencies that are or should be engaged with this topic, and synthesize this material to make legislative recommendations about statutory authority for an oversight body. The work of the commission, referred to in this report as the Reprogenetics Technologies Advisory Commission (RTAC), would be similar in some respects to that of the Royal Commission in Canada, although the audience for this body would be Congress. The advisory commission

would, in part, engage the public, stakeholder, and expert constituencies in consultation; articulate the ethical commitments that must guide such a regulatory effort; and draft the terms of reference for embryo research, including the limits, restrictions, and prohibitions to be written into legislation. That commission would then report its findings in the form of recommendations to Congress for a legislative initiative.

■ Third, in formulating its recommendations, the commission should carefully consider the possibility of creating a standing federal entity, a Reprogenetics Technologies Board (RTB), to facilitate reasoned and systematic public and policy deliberation about the purposes of reprobogenetic research and practice. The board’s authority would extend to the public and private sectors, and it would factor concerns about safety and well-being into policy-making and license-granting decisions. The board would, in important respects, resemble the United Kingdom’s Human Fertilisation and Embryology Authority (HFEA).

Drawing from the lessons learned in the United Kingdom and Canadian experience, it will be important, first, that the Reprogenetics Technologies Advisory Commission’s recommendations for Congress be framed in general terms; it should only outline its suggested restrictions, conditions, and limits on the use, storage, and creation of embryos and gametes. Second, in defining the Reprogenetics Technologies Board’s purview, the recommendations (and the eventual legislation) should articulate acceptable and unacceptable *purposes* of embryo research rather than specific techniques. Third, recognizing that it is impossible to keep pace with scientific and technological developments, the legislative initiative should incorporate a mechanism for adding to or adapting the enabling legislation in the face of new developments or information. Fourth, the RTB should be granted significant discretion, since its members will need to develop an expertise not likely shared by the members of Congress. Fifth, a detailed informed consent procedure should be considered to enable patients to contemplate what they want done with their embryos and gametes in unexpected circumstances like death and divorce; such procedures would be aimed both at preventing unnecessary litigation and respecting patient autonomy. And, finally, the RTB should be responsible for developing a code of practice as a means of educating researchers, clinicians, and patients.

There are many possible obstacles to the creation of a new federal oversight board for reprobogenetics. First, there

is an open question about the constitutionality of any federal regulation of scientific research that occurs in the private sector. To date, there is no clear indication that Congress cannot implement such regulation; indeed, that it can has already been assumed in the bill recently passed by the House to ban all cloning. Yet the possibility remains that the federal oversight board envisioned here would face a constitutional challenge.

Second, the recommendations will likely face opposition from the entrenched participants in the abortion debate. The recommendation to lift the embryo research ban will raise deep concerns among anti-abortion advocates, who are likely to argue, starting from the premise that embryos are persons, that all embryo research is immoral and that none should be publicly funded. And at least initially, the prospect of any mechanism to oversee reproductives research and practice will raise deep concerns among pro-choice advocates, who may argue that accepting limits on the things researchers and clinicians can do with embryos is the first step down a slippery slope to limiting a woman's right to choose. Yet some people committed to the anti-abortion position now acknowledge that embryos in petri dishes are not persons, and agree that there are some things researchers ought to be permitted to do with embryos. Similarly, some committed to the pro-choice position now acknowledge that procreative liberty is not absolute, and agree that there are some things researchers and practitioners ought not to be permitted to do with embryos.

If any of these recommendations are to be taken seriously, then certainly, both sides of the abortion battle will have to believe that their concerns will be taken seriously. Thus if the advisory commission were to be appointed (much less if it were to recommend the creation of a standing board along the lines of the HFEA), then moderate representatives from all sides would have to be involved. Members of the commission would have to be appointed by a bipartisan committee, with representation from both the House, the Senate, and a variety of stakeholders. Possibly the former chair of the National Bioethics Advisory Commission and the current chair of the President's Commission on Bioethics could jointly help to nominate members.

Ongoing Discussion and Oversight

Even though the notion of creating an HFEA-like body in the United States will encounter resistance,¹¹² the time may be right. Others before us have called for regulatory action on some of the topics touched on in this report. These proposals have often focused on reproductive medicine, however, missing some of the larger concerns of reproductives, and they have typically sought mechanisms to ensure the safety of participants, neglecting well-being concerns.

For example, in 1996 the now-defunct National Advisory Board on Ethics in Reproduction (NABER) recommended that “serious and timely consideration be given in the United States to the establishment of a standing federal regulatory body to license infertility centers. This body would have responsibility and sufficient support for surveillance of infertility centers around the country for the purpose of regulating and accrediting the provision of services of assisted reproduction.”¹¹³ In a 1996 editorial in *Fertility and Sterility*, Howard Jones, founder of the Jones Institute of Reproductive Medicine (in Norfolk, Virginia), endorsed NABER's recommendation and claimed that it was also supported by the American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART).¹¹⁴ Jones cited a November 1995 news release issued jointly by ASRM and SART, which states that “[s]uch an independent licensing authority might oversee and validate the clinical and laboratory practice of ART, and function independent of and be funded separately from The American Society for Reproductive Medicine and The Society for Assisted Reproductive Technology.”¹¹⁵ The consumer advocacy group RESOLVE also endorsed the idea.¹¹⁶

Thus there appears to be some support in the provider-consumer community for the idea of a licensing authority to improve safety, efficiency, and accountability in reproductive medicine. A number of groups have also called for better oversight in reproductives. A working group convened by the American Association for the Advancement of Science¹¹⁷ called for a body to consider not only the safety but also the well-being issues raised by attempts to produce “inheritable genetic modifications.” The National Conference of State Legislatures, which is concerned about consumer safety, has called for improved oversight of reproductive services.¹¹⁸ The California Department of Health Services created a statewide advisory committee on human cloning that has called for oversight,¹¹⁹ and the National Research Council report on cloning technology specifically suggested that a HFEA-like body be created to govern reproductive genetics. Most recently, the President's Council on Bioethics called for a moratorium on “research cloning” in large part to allow Congress to develop regulatory oversight in this area.¹²⁰

What follows are some preliminary thoughts on how an HFEA-like oversight board might look in the United States. In accordance with our own advice, we frame our proposal in general terms. A different view of the board might of course emerge from the advisory commission we have recommended.

SCOPE. The RTB's scope of authority would be articulated in the legislation that creates it, as called for by the advisory commission. The legislation should indicate that the RTB would grant licenses, monitor and inspect facilities, create a code of practice, consult with the public, and keep an information registry. The legislation would articu-

late those purposes, related to both treatment and research, involving the creation, use, manipulation, and storage of gametes and embryos for which licenses may be granted by the RTB. The RTB would be empowered to make licensing decisions in light of concerns about both safety and well-being.

In addition, an important function of the legislation is to articulate those practices that are unacceptable and therefore may not be the subject of a license. Both the British and Canadian acts forbid, for example, reproductive cloning and use of an embryo past fourteen days of development. Which practices should be identified as unacceptable would be part of the deliberations of the advisory commission.

The RTB's authority would extend to both the public and private sectors. At least with respect to safety concerns, a system of regulatory separation is arbitrary. It defies commonsense to protect participants in federally funded research from bodily harm, but not to protect those in privately funded research from the same. Respect for the safety and dignity of persons does not change with their location. In accordance with this line of reasoning, NBAC recently recommended the creation of a new federal-level body to oversee *all* human subjects research.¹²¹

MEMBERSHIP. The RTB should be composed of persons from inside and outside the scientific community. The United Kingdom's HFEA has seventeen members and a staff of approximately forty-five. The proposed Canadian Agency would seat thirteen members, at least half of which must be women. Given the volume of work required to oversee rerogenetics in the United States, the RTB should have approximately seventeen members, and be well staffed and funded. According to the act establishing the HFEA, at least half of the HFEA's members must *not* be involved in medicine or science; neither the chair nor deputy chair is allowed to be a physician or scientist; the chair represents the "lay non-scientific opinion on these matters."¹²² This seems an appropriate balance of expertise for the RTB as well. In addition, a minimum of 50 percent of the RTB members should be women.

Such a body should be as independent and insulated as possible from the undue influence of election politics, consumer or business advocates, and pro- or anti-abortion activists. For it to have moral authority, it must represent a wide range of perspectives and interests. Its membership would need to draw upon researchers, clinicians, consumers, lawyers, ethicists, and others. Yet every effort must be made to enable members to speak as individuals, with particular views, rather than as defenders of a given group's agenda. Striking this balance will be crucial and very difficult, but not impossible.

FUNCTIONS. A body such as the RTB can be thought of as fulfilling three intimately related functions. The first would be to *make policy* regarding the things people do

with gametes and embryos, from basic embryo research to rerogenetics services, by applying and interpreting the purposes, principles, and strictures of the enabling legislation. This policymaking function would be accomplished by granting (or denying) licenses for laboratories and clinics to carry out the research and clinical activities described in the legislation. The enabling legislation will probably flatly prohibit some activities, but other activities will likely be left partly to the RTB's discretion. Thus the licensing might, for example, make it possible to sell pre-implantation genetic diagnosis to prospective parents seeking to test for disease-related traits but not to test for traits unrelated to disease (such as height, if testing for such traits became technically feasible). The licensing would be analogous to that performed by the HFEA in the United Kingdom.¹²³ Also like the HFEA, the RTB would monitor and inspect premises and activities carried out under a license and maintain a register of information about donors, treatments, and children born from those treatments.

The second function of the RTB is to *set standards* for those activities by creating a Code of Practice. Such a code might detail informed consent procedures, for example, or delineate the proper handling of embryos that are to be transferred to a woman's uterus in the course of IVF. The code would necessarily change over time, of course, but at any given time it would establish a uniform standard for everyone offering reproductive services covered under the legislation. The code would also articulate the general guiding principles, which might build on the established U.S. principles of justice, beneficence, and autonomy.

A third and fundamentally important function of the RTB would be to *engage in public consultation and promote public conversation* about emerging issues in embryo research generally and rerogenetics more particularly. This responsibility to promote public conversation—indeed to create new constituencies committed to exploring this fascinating and important new arena of endeavor—is essential. In effect, we are calling not merely for the creation of a regulatory body, but for richer and more nuanced democratic deliberation about these vital issues. But one note of caution must be sounded here. Public consultation and transparency of political process are both important, and public consultation must not stand in the way of action. Public consultation should be immediate and ongoing, but so too must be the creation of policy.

The Bigger Picture

The convergence of reproductive and genetic medicine will lead to a vast increase in our capacity to relieve suffering and distress. It may also eventually increase our capacity to shape our children. Thus that convergence raises questions not only about the safety of children, but also about the well-being of those children and of the society they will join. Asking questions about the well-being of the participants in this endeavor is as important as ask-

ing questions about their safety. As Harold Shapiro, chair of President Clinton's National Bioethics Advisory Commission, has stated: "[O]ne of our greatest responsibilities is to consider the full implications of our new knowledge not only for relieving human suffering and distress but for the social and cultural institutions that are as critical as DNA to supporting our individual and collective lives."¹²⁴

To deal with the emerging field of rerogenetics, to address those questions and implications, and to fulfill that responsibility, we need a new structure for oversight and regulation and transparent public policy discussion. The preliminary suggestions offered in this report about the shape that structure might take are not as important as the underlying recommendation that we begin quickly and formally to grasp and respond to the bigger rerogenetic picture.

It is easy to view rerogenetics as a train that has left the station. The speed of the science and the passion of the pro-market and anti-regulatory advocates can convince one that calls for thoughtful oversight and regulation in this area are futile. But while this train certainly is not going to return to the station, it would be a terrible mistake to act as if its destination were foreordained.

Ruth Deech, formerly the chair of the Human Fertilization and Embryology Authority, recently recounted hearing a lecture by the great British infertility specialist Robert Edwards in the early days of IVF. According to Deech, Edwards asserted that to have an authority like the HFEA to make policy and to regulate research involving embryos was to bring "Nazism and Stalinism into the bedroom."¹²⁵ But as Deech replies, civilized societies have always exerted some control over reproduction, whether by crafting rules to govern incest, or the appropriate age of marriage, or abortion, or contraception, or adoption.

The situation today is significantly more complex than in the early days of IVF. Assisted reproduction now encompasses a multifaceted arena of scientific research, some of which is not even devoted primarily to reproduction. We should be relieved to learn that the fundamental ethical questions regarding the ethics of producing children are not new, even as we acknowledge that the technological possibilities render ever greater the need for careful oversight and regulation. To respond to that need, we should ask ourselves what we can do to increase the chances that we are creating a society into which good parents will want to bring children.

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110. "An Act Respecting Assisted Human Reproductive Technologies and Related Research," Section 2.
111. *Ibid.*, Section 24.
112. J.G. Palmer and R. Cook-Deegan, "National Policies to Oversee Inheritable Genetic Modifications Research," in *Designing Our Descendants: The Promises and Perils of Genetic Modifications*, ed. A.R. Chapman and M.S. Frankel (Baltimore, Md.: Johns Hopkins University Press, 2003), 275-95.
113. "Report and Recommendations on Oocyte Donation by the National Advisory Board on Ethics in Reproduction (NABER)," in *New Ways of Making Babies: The Case of Egg Donation*, ed. C. Cohen (Bloomington: Indiana University Press, 1996), at 301.
114. Jones, Jr., "The Time Has Come," at 1092.
115. *Ibid.*
116. D.D. Aronson and K.M. Zieselman, "A Consensus for Regulation?" *Fertility and Sterility* 66, no. 5 (November 1996): 862-63, at 863.
117. Frankel and Chapman, *Human Inheritable Genetic Modifications*. The scope of the AAAS recommendations is narrower than ours, however, since it speaks only to the alteration of gametes and embryos, whereas we seek to address the creation, use, and storage of gametes and embryos. Our recommendations are also more expansive in that they suggest the creation of a federal-level body that both makes policy and grants licenses. Whereas the AAAS report looks primarily to the RAC as a model body, our report looks first to HFEA.
118. New York State Task Force on Life and the Law, *Assisted Reproductive Technologies*, p. 31.
119. Statewide Advisory Committee. <http://www.applications.dhs.ca.gov/pressreleases/store/pressreleases/51-00.html>.
120. President's Council on Bioethics, "Human Cloning and Human Dignity: An Ethical Inquiry" (July 2002). <http://www.bioethics.gov/cloningreport/>. See A. Bonnicksen, *Crafting a Cloning Policy: From Dolly to Stem Cells* (Washington, D.C.: Georgetown University Press, 2002).
121. National Bioethics Advisory Commission, *Ethical and Policy Issues in Research Involving Human Participants*, vol.1 (Bethesda, Md.: National Bioethics Advisory Commission, 2001).
122. R. Deech, "Assisted Reproductive Techniques and the Law," *Medico-Legal Journal* 69, part 1 (2000): 13-24, at 17.
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124. H. Shapiro, "Reflections on the Interface of Bioethics, Public Policy, and Science," *Kennedy Institute of Ethics Journal* 9, no. 3 (1999): 209-24, at 223.
125. Deech, "Assisted Reproductive Techniques and the Law," 14.

