13 Implementation Issues

Consistent with the scheme developed in chapter 4, in this chapter we discuss implementation-related issues for each of the three areas of reproductive medicine (standard reproductive treatments, innovative reproductive procedures, and technologies of reproductive customization) and for biomedical research. We also discuss in some detail issues pertaining to compliance assurance, and we conclude by offering some considerations of cost.

13.1 Monitoring and Information Gathering

One of the first challenges the newly created regulatory agency would face is the design and implementation of a system of monitoring and information gathering. This system is indispensable to discharging the agency's statutory mandate and would serve several purposes. First, it would allow the agency to identify and evaluate health and safety risks associated with traditional ART procedures. As mentioned in chapter 4, this is possible today only in a very limited sense. Second, a tracking system would facilitate identifying and monitoring ART clinics performing innovative ART treatments, an area of reproductive medicine in need of closer scrutiny. Third, information gathered through a system of monitoring would make it possible for regulators to implement an effective mechanism of reciprocal learning within the ART industry – and in so doing, would contribute to improving the quality and reliability of ART treatments. Fourth, a comprehensive tracking system is crucial to ensuring compliance, not only in the ART sector, but also in the biotech industry and in the scientific community. Finally, a system of monitoring and information gathering would enable regulators to provide prospective parents with up-to-date information on a wide range of infertility-related questions, and would help improve our understanding of the causes of infertility.

A tracking system as proposed in this chapter would track the import, creation, manipulation, storage, trade, and export of human reproductive tissues. Reproductive tissues include human embryos, oocytes, and sperm. The term "creation" should be understood in the broadest possible sense: It includes not only traditional practices, such as the in vitro mixing of egg and sperm, but also laboratory practices that lead to the creation of viable oocytes and sperm by artificial means, such as experiments involving human embryonic stem cells, for example.[1]

Different reproductive tissues entail different record-keeping requirements. The import, export, creation, use, and trade of embryos would receive the greatest regulatory attention, followed by oocytes and by sperm. This ranking reflects the relative importance of ethical concerns. We discuss these differences in more detail in the following sections.

[1] Reporting requirements in this case are limited to fully functional reproductive tissues.

Among the parties subject to record-keeping requirements are ART programs, embryo laboratories, sperm banks, university hospitals, university labs, and research labs at biotech and pharmaceutical companies. This list is not meant to be exhaustive. Should the preservation of human oocytes become widely available, then oocytes banks would also be subject to regulatory oversight. In other words, any establishment that retrieves, produces, stores, and trades in human reproductive tissues would be subject to record-keeping and reporting requirements. The newly established registration requirements promulgated by the FDA for establishments involved in the trade, storage, and use of human tissues provide an excellent implementation basis.[2]

The tracking system proposed in this chapter could be implemented in various ways. The British HFEA, arguably the agency with most experience in this area, has adopted a fairly intrusive system of monitoring that consists of both a licensing and a reporting system. In the United States, it is the responsibility of the states to license the practice of medicine. For this reason, it is very unlikely that Congress would support a federal system of medical licensing, even a narrowly defined one. Furthermore, it is not entirely clear that additional licensing requirements at the federal level are necessary to meet the new agency's public mandate. On the other end, a mandatory establishment registration coupled with specific reporting requirements would satisfy most if not all regulatory demands.

A monitoring system that emphasizes the health and well-being of ART children and women would entail much more than just tracking the use of reproductive tissues. It would require gathering information concerning the ART children, their parents, the gamete donors (if the gametes were donated), and the type of ART procedure performed, among other things. These are not unreasonable requirements; Canadian regulators are in the process of implementing similar requirements. The British HFEA has been operating a comprehensive system of monitoring for years.

A statutory emphasis on the health and well-being of children could also mean that the personal identity of gamete and embryo donors must be preserved. Currently, ART clinics routinely destroy records that would allow ART children to identify gamete donors. It is a practice that protects the interests of prospective parents and donors, possibly to the detriment of ART children. Whether these children are ultimately better off knowing their biological parents is a question for others to ponder, but it can no longer be assumed that this information should simply be destroyed. That this requirement could significantly reduce the pool of available gamete donors is a risk that would have to be weighed against other benefits.

Record-keeping would be subject to inspection, and violations would trigger civil and/or criminal penalties, depending on the gravity of the violation. This is in marked contrast to current practice. The CDC has no authority to enforce the reporting requirements established by the Fertility Clinic Success Rate and Certification Act. Non-reporting, however, is rather modest, roughly 10 percent or less. This figure suggests that while actual sanctions for non-compliance are necessary, they would not have to be draconian. Furthermore, the implementation of a

[2] See chapter 5 for a discussion.

tracking and monitoring system would in part be delegated to third parties such as trade and professional societies. We discuss compliance assurance in more depth in section 13.6.

13.1.1 Embryos

Procedures involving human embryos raise the most serious ethical concerns and would be subject to the most stringent record-keeping requirements. The protracted controversy over the use of human embryos for stem cell research suggests that the import, creation, storage, use, manipulation, and export of human embryos should be carefully monitored. Developing and testing innovative reproductive procedures would be far less controversial activities if they were to be conducted with the blessing of the law. The view – shared by two-thirds of the American public – that embryos are not simply just another mass of cells but cannot be equated to actual human beings[3] underscores the importance of distinguishing between acceptable and unacceptable uses of human embryos.

Subject to record-keeping requirements would be all establishments involved in the import, storage, creation, use, trade, and export of human embryos, including ART programs, biotech firms, and university laboratories. These categories are not meant to exhaust the variety of establishments subject to record-keeping requirements. Any establishment more than marginally involved in these activities would be subject to the same requirements.[4]

The "creation" of embryos must be construed in the broadest possible way. Included in this definition are not only embryos created in vitro for ART purposes, but also embryos created through somatic cell nuclear transplantation or any other medical technology that may become available in the future.

Record-keeping requirements vary considerably depending on the enabling statute. Generally speaking, the more specific the statutory provisions, the more detailed the reporting requirements are likely to be. For example, should reproductive cloning be banned and research cloning legalized, regulators would have to adopt a record-keeping architecture that would discourage attempts to misuse cloned embryos. Regulators may consider limiting the maximum number of embryos that can be transferred to a woman's uterus to two or three, a limitation adopted by some European countries. They could grant researchers permission to conduct a controversial but particularly promising experiment involving the destruction of embryos, but require that only a small number of embryos be used. In all these cases, an architecture of record-keeping ensures that all parties operate in accordance with applicable rules and regulations. In short, record-keeping requirements for embryos greatly facilitate monitoring and compliance assurance efforts.

The nascent practice of "adopting" supernumerary embryos raises specific record-keeping issues. Among them is the question of just how much information should adopting parents be entitled to receive about a donated embryo. Many prospective parents are likely not only to

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[3] See chapter 8 for details.

[4] The transportation of human reproductive tissue would not be subject to reporting requirements.

demand in-depth health screening, a requirement that is now part of the new FDA human cellular and tissue-based products rules; they may also feel entitled to select an embryo based on extensive genetic testing information, and on detailed descriptions of the biological parents' physical characteristics and on their academic and personal achievements, among other things. "Informed choice" in this case would come dangerously close to private eugenics. Whether Congress is prepared to restrict the amount of information donor organizations are allowed to gather remains to be seen.

13.1.2 Oocytes

While the donation and manipulation of human oocytes do not raise ethical concerns as substantial as those surrounding the use of human embryos, they nevertheless must be taken seriously. The new FDA rules regulating human cellular and tissue-based products require that oocyte donors be screened for a wide range of communicable diseases. In this area, no additional requirements are necessary. Broadly speaking, oocytes are being donated for reproductive or research purposes. Each case raises a distinctive set of issues.

The for-profit trade of human oocytes for reproductive purposes is gaining popularity among affluent individuals. Oocytes from young, athletic, good-looking women with impeccable academic credentials are in high demand. In a few instances, these oocytes have been sold for as much as $200,000. The average price for oocytes is much lower, ranging roughly between $5,000 and $10,000.[5] High prices correlate strongly with parental desires. Prospective parents may wish to select oocytes based on a wide range of characteristics, ranging from good health and good looks to academic achievement. Accordingly, oocytes "donated" by students with high SAT scores or by super models fetch premium prices. This is more surprising, considering that this kind of eugenic selection is very unlikely to be effective. In any case, until oocyte cryopreservation is fully developed, oocyte donation will remain a fairly limited phenomenon.

Oocyte donation for reproductive purposes does not require extensive record-keeping. Preventing the spread of infectious diseases may entail preserving the identity of egg donors for an extended period of time. Donor identity may also have to be preserved if Congress decides that the well-being of ART children includes being able to meet their biological mothers.

Donating oocytes for research requires closer scrutiny. Should research cloning show promise, biomedical research would become a very important "buyer" of oocytes. That in this area abuses are indeed possible has recently been illustrated by Dr. Hwang Woo-Suk, the Korean researcher who in 2004 successfully cloned several human embryos. Dr. Hwang recently resigned amid allegation that he had pressured his female staffers to "donate" their oocytes, and

[5] The American Society for Reproductive Medicine has recognized the problematic nature of unregulated oocyte donation and has adopted guidelines that discourage the sale of oocytes but allow reimbursement for medical and other expenses up to approximately $4,200. Cf. Ethics Committee of the American Society for Reproductive Medicine, "Financial Incentives in Recruitment of Oocyte Donor," *Fertility and Sterility* 74, no. 2 (2000), p.219.

that he had falsified some of the data used for his seminal publications.[6] At a minimum, then, investigators would have to demonstrate compliance with rules of informed consent. Ensuring traceability may also be necessary, as research could produce results directly relevant to the donor's health. Finally, preventing abuses in the area of somatic cell nuclear transplantation would require keeping track of the number of donated eggs and their uses.

13.1.3 Sperm

Practices surrounding the trade, storage, and use of human sperm raise only modest ethical concerns. Unlike embryo and oocyte donation, sperm donation has a long history in the United States. The first recorded U.S. case dates back to nineteenth century. A full-blown market for sperm emerged only in the early 1960s. Nowadays, sperm banks have become a common and profitable industry across the country. The industry is represented by the American Association of Tissue Banks, which includes among its members many other types of tissue banks.

As for embryos and oocytes, the new FDA rules governing the production, trade, and use of cellular tissues (HCT/P rules) protect against the spread of communicable diseases. In this area, no additional action is necessary.[7] The FDA rules, however, do not address several important questions not directly related to preventing the spread of communicable diseases. For example, few sperm banks have policies to avoid the marriage between half-siblings, a substantial risk considering that sperm banks impose very few limitations on the maximum number of donations by an individual. Should Congress determine that this area is ripe for regulations, additional record-keeping requirements may be necessary.

Also in need of scrutiny is the long-standing industry practice to jealously protect donors' anonymity. This measure makes eminently good business sense, but it is far from clear that it is also in the best interest of children born through anonymous sperm donation. Requiring that sperm banks be able to identify sperm donors is likely to greatly reduce the pool of potential donors and to negatively impact this business sector. We are not arguing that Congress should eliminate donor anonymity, but it is worth pondering whether this practice can be justified.

Finally, the HCT/P rules are not designed to resolve whether eugenic practices should be tolerated. Sperm banks compete in part by encouraging prospective parents to select a sperm donor on the basis of physical, aesthetic, and academic stereotypes. Selecting a sperm donor in many cases is reduced to a shopping act: It is simply a matter of consulting a catalogue. That

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[6] David Cyranoski and Erika Check, "Clone Star Admits Lies over Eggs," *Nature* 438, no. 7068 (2005); David Cyranoski and Erika Check, "Korean Stem-Cell Crisis Deepens," *Nature* 438, no. 7067 (2005); Constance Holden, Gretchen Vogel, and Dennis Normile, "Korean Cloner Admits Lying About Oocyte Donations," *Science* 310, no. 5753 (2005).

[7] Despite its importance to the ART industry, no reliable information was available until recently about the number of existing sperm banks and their mode of operation. The HCT/P registration requirements will close this gap; as of February 28, 2005, 1,579 establishments had registered with the FDA. The actual number of sperm banks is significantly smaller, however, because this figure also includes IVF programs, embryo laboratories, and other kinds of human tissue establishments. See http://www.fda.gov/cber/tissue/hctregestabl.htm.

many prospective parents are attracted by physical appearance and academic performance is understandable, but the question remains as to whether Congress should unintentionally contribute to reinforcing all manner of stereotypes or whether it should limit the type of information prospective parents are entitled to request.

13.2 Standard Reproductive Procedures

To the extent that the enabling legislation emphasizes protection of the health and well-being of ART children, the tracking system would require regulators systematically to gather data and information about a wide range of ART-related defects and malformations. The British HFEA has been collecting ART-related health data since 1994. The kind of information the HFEA gathers on a regular basis is illustrated Table 11, gleaned from the 1999-2000 HFEA annual report.[8] This data has been collected every year since 1994, allowing the HFEA to identify both absolute and relative risks of various ART treatments and to detect possible long-term public health concerns.

Congenital abnormalities	Total	Fresh IVF	Frozen IVF	Donor Insemination	Micro-manipulation
Cleft lip with cleft palate	5	2			3
Anomalies of the alimentary system	5	1		1	3
Cardiac murmurs	6	3			3
Ventricular septal defect	5	2	1	2	
Other congenital cardiac anomalies	12	4	2	3	3
Other anomalies of the cardiac septa	1				1
Patent ductus	3	1			2
Anomalies of the cardiovascular system	4	1			3
Hypospadias, epispadias	2	1		1	
Renal anomalies	13	3	3	1	6
Reduction deformities of the limbs	1	1			
Talipes	9	2		2	5
Congenital dislocation of the hip	2	1			1
Other anomalies of the limbs or limb girdles	2	1			1
Anomalies of the nose, face, neck, and skull	2	1		1	
Ear anomalies	7		1		6
Exomphalos	5	1			4
Total number of children born	120	41	9	16	54

Table 11: Congenital abnormalities in ART children in 1999 (extract).

In an effort to improve its ability to detect new health risks, the HFEA has begun testing a new alert system designed to anonymously gather detailed information about new incidents. This

[8] Human Fertilisation and Embryology Authority (HFEA), "Ninth Annual Report and Accounts 2000," (London: 2000).

information is stored in a database and made available to all licensed facilities, thus contributing to improving the safety and efficacy of ART treatments. According to the HFEA, clinics have responded very positively to this initiative.

It should be mentioned that the British tracking system falls far short of a full-fledged longitudinal system of monitoring. While conducting a long-term longitudinal study of ART children in the United States as proposed by the President's Council on Bioethics would certainly be very useful, systematically monitoring the health of ART children up to one year of age would be considerably less costly and would provide a wealth of information currently not available. Putting the threshold at one year is not an arbitrary choice. ART specialists point out that some chromosomal and congenital abnormalities do not become immediately apparent, but that most of them have surfaced by one year of age.

It appears that as part of its collaboration with the Society for Assisted Reproductive Technology, the CDC has begun gathering data and information beyond success rates. Unfortunately, no details are available about these practices. Implementing a system of monitoring as outlined in this section would certainly be more costly than what is considered standard practice today, but far less costly than feared by the ART industry. Tracking the health of ART children up to one year of age does not pose insurmountable technical or legal problems. Technically, the system could be based on chip cards technology. This technology has been adopted by many transit systems around the country and by the credit card industry; it is considered mature and it is inexpensive. Chip card technology would allow select individuals, such as ART practitioners, pediatricians, parents, and regulators to verify, store, and retrieve personal health data while preventing unauthorized parties from accessing sensitive information. By affording adequate protection against the misuse of personal health data, this technology should be received favorably by prospective parents. Trust in this technical solution should also ensure high levels of participation and make a mandatory adoption superfluous.

13.3 Innovative Reproductive Treatments

The notion of innovative reproductive treatments was discussed in some detail in chapter 4. In a nutshell, innovative reproductive procedures, unlike standard reproductive treatments, may not only expose the future child to heightened health and safety risks, but may also be unacceptable from an ethical standpoint. Regulators have no systematic way to monitor these kinds of reproductive treatments. What so far has come to regulators' attention is sufficiently problematic as to justify adopting a robust system of monitoring and evaluation, including the possibility that regulators may impose a moratorium or ban on certain types of treatments.

Any suggestion that the practice of medicine should be regulated is bound to be controversial. Critics are likely to offer a broad range of arguments against direct regulatory interventions at the federal level, of a legal nature and of other varieties as well. While legal arguments against direct regulatory interventions are weak, some of the arguments offered by the profession to protect their autonomy are important and deserve to be taken seriously.

Traditionally, the practice of medicine has been regulated at the state level, and Congress has been very careful to avoid any suggestion that it intends to directly regulate the practice of medicine.[9] Perhaps for this reason, it is generally assumed that Congress does not have the authority to regulate this profession. We believe that this assumption is unfounded. Medical autonomy is certainly a jealously protected professional prerogative, but it is neither absolute nor uncontested. Congress indirectly regulates the practice of medicine in numerous ways. The FDA regulates drugs, biologics, and medical devices. The Medicare and Medicaid programs directly affect the selection of prescription drugs. The Department of Health and Human Services regulates clinical trials through informed consent regulations. Many of the measures aimed at containing the explosion of health care costs are predicated on limiting the discretion of the medical profession in choosing medical technologies and treatments.[10]

Some may argue that a direct regulatory intervention may run afoul of constitutional guarantees. A detailed examination of this question is well beyond the scope of the present discussion, but this argument seems implausible. If medical doctors had a constitutionally protected right to exercise their profession, then it is difficult to see why other professions shouldn't enjoy the same kind of constitutional protection. Shouldn't accountants, then, also be shielded from oversight by the Securities and Exchange Commission? Perhaps the medical profession does enjoy a modicum of constitutional protection. Washington v. Glucksberg, a case involving medically assisted suicide, does not lend much credibility to this hypothesis. A full discussion of this issue is beyond the scope of this chapter, but it is reasonable to assume that the Supreme Court is very unlikely to discover a broad new class of fundamental rights.

A more important argument against direct regulatory intervention is what may be described as asymmetrical information. Medicine remains both a science and an art. Dramatic advances in medical science and technology have not undermined the need for good professional judgment. Expert medical opinion remains indispensable to selecting the most appropriate therapy. Only the physician is in a position to select an appropriate treatment based on a set of unique clinical circumstances.[11] In its essence, this is an argument about the importance of decentralized, tacit knowledge. It is precisely because this kind of knowledge is both decentralized and tacit (i.e., not codified) that a regulatory authority should refrain from intervening in medical practice.

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[9] For example, the 1997 FDA Modernization Act (FDAMA) restates a doctor's right to prescribe drugs for off-label uses, an issue that was highly contentious at the time FDAMA was passed. Steven R. Salbu, "Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy," *Florida Law Review* 51 (1999).

[10] Barry R. Furrow, "Regulating the Managed Care Revolution: Private Accreditation and a New System Ethos," *Villanova Law Review* 43 (1998); Alycia C. Regan, "Regulating the Business of Medicine: Models for Integrating Ethics and Managed Care," *Columbia Journal of Law and Social Problems* 30 (1997).

[11] Not coincidentally, this is the same argument offered by advocates of the free market against excessive regulatory interventions.

Failure to acknowledge this fact, so the argument goes, often produces ineffective, wasteful, and quite possibly counterproductive rules and regulations.[12]

Generally speaking this argument has lost nothing of its relevance. In the case of the medical profession, however, it must be qualified in two important respects. Asymmetrical information should urge regulators to be cautious when considering intervening in *medical* decisions, but this argument is entirely irrelevant in examining the ethical aspects of these choices. As repeatedly argued in this report, bioethical dilemmas should not be decided by the medical profession and patients alone. Just as important is the observation that the health care sector has a very poor health and safety record. Consider the following bit of information: In 2000, the National Academy of Medicine estimated that every year in the United States, between 50,000 and 100,000 persons die from preventable medical errors.[13] No other sector in the United States has such a poor safety record. If the chemical or the airline industry caused 50,000 deaths per year, the federal government would immediately shut them down. Against this background, the argument that the federal government would do more harm than good in considering regulatory interventions in this sector loses much if not all plausibility.

It is instructive to explore some of the reasons for this situation. To date, the health care industry's main response to medical errors is the morbidity and mortality (M&M) conference. M&M conferences are convened on a regular basis at university hospitals around the country. Their primary purpose is to offer to doctors in residence an opportunity to discuss their mistakes with their colleagues without fear of incurring in legal liabilities.[14] M&M conferences have proven remarkably ineffective in reducing medical errors. Information about incidents and accidents is not gathered in a systematic way or widely shared. More importantly, perhaps, M&M conferences are informed by a very narrow view of safety, one that is focused exclusively on the actions taken by a medical practitioner. Broader organizational considerations that may negatively affect the performance of medical personnel are generally absent. Every incident is examined in isolation, and no effort is made to identify possible connections among similar incidents. Nor would it be possible to conduct a similar analysis, because, as mentioned earlier, no standardized system of data gathering exists in the health care sector. To make things worse, informal sanctions against poorly performing doctors, according to some insider reports, are largely ineffective.[15]

The situation in private medical practices is qualitatively different, but not much more encouraging. For example, it has been shown that randomized clinical trials often contradict

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[12] Perhaps the most forceful advocate of this perspective is Friedrich Hayek. Friedrich A. Hayek, *Individualism and Economic Order*. (London: Routledge & Kegan Paul, 1976); Friedrich A. Hayek, *The Fatal Conceit: The Errors of Socialism*, *The Collected Works of F.A. Hayek. Vol. 1* (London: Routledge & Kegan Paul, 1988).

[13] Institute of Medicine, *To Err Is Human: Building a Safer Health System* (Washington, D.C.: National Academy Press, 2000).

[14] Edgar Pierluissi et al., "Discussion of Medical Error in Morbidity and Mortality Conferences," *Journal of the American Medical Association* 290, no. 21 (2003).

[15] Gawande, *Complications: Decisions and Dilemmas of a Surgeon's Life*.

beliefs firmly held by medical practitioners about the efficacy of a given medical treatment. In some cases, these treatments do not even have a discernible therapeutic effect; in others, they are actually counterproductive.[16] Yet it appears that many physicians remain distinctively reluctant to accept recommendations based on randomized clinical trials. Conversely, physicians are more inclined to accept as validated knowledge recommendations from colleagues, even if these are based on a sample size of one. In sum, compared to other business sectors, the health care industry's approach to safety and quality assurance is wholly inadequate.

In the case of the ART industry in general, and of innovative reproductive treatments in particular, the situation is both better and worse. It is better because these treatments (and reproductive medicine more generally) clearly are not as dangerous for the patients as other medical fields. It is worse because in its 30-year history, reproductive medicine has never attempted to closely monitor the health and safety of the children born through ART.[17] Yet our discussion of innovative reproductive treatments in chapter 4 has shown that there have been several instances of ART practitioners performing potentially unsafe and quite possibly unethical procedures. The available evidence seems to indicate that ART physicians indeed are inclined to try wholly untested procedures on their patients but, absent a robust system of monitoring, it is impossible to determine whether these stories are isolated incidents or should be regarded merely as the tip of the proverbial iceberg. To use a now (in)famous formulation: In the area of reproductive medicine, regulators simply don't know what they don't know. What we do know is that we should learn a lot more about the nature and scope of innovative reproductive procedures.

In proposing a system of monitoring for innovative ART treatments, an important design consideration is minimizing intrusiveness. Practitioners should remain free to choose what they regard as the most promising course of action, even if this course of action may be regarded by some as an innovative but untested ART treatment. In this sense, our approach to monitoring preserves professional autonomy. However, the ART community and regulators should be able to examine the rationale for these procedures, analyze possible risks for the mother and the child, and evaluate the relevance of various ethical concerns. The concept of "information regulation" meets these requirements. This regulatory approach should not be confused with the well-established notion of informed consent, although the two concepts are related. By information regulation, we mean a system of mandatory information disclosure that would require ART practitioners to report to regulators every instance of an innovative ART treatment. Reporting requirements would include a statement explaining the reasons for the course of action taken, an

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[16] John F. Burnum, "Medical Practice a La Mode. How Medical Fashions Determine Medical Care," *New England Journal of Medicine* 317 (1987); David A. Grimes, "Technology Follies: The Uncritical Acceptance of Medical Innovation," *Journal of the American Medical Association* 269 (1993).

[17] This can be attributed in part to the fact that in this field of medicine, it is considerably more costly to conduct clinical trials and to follow the patients than in other fields of medicine, and in part to the fact that one party to the doctor-patient relationship, the child-to-be, cannot give his or her consent to performing an experimental reproductive procedure.

assessment of possible health and safety risks to the prospective mother and her child, and a discussion of possible ethical concerns. Regulators would use this information to build a record for various innovative ART procedures. The report would also form the basis for determining if the procedure poses unacceptable risks or serious ethical concerns. To this end, the regulators would solicit comments from the ART practitioners and from professional bioethicists. Note that this process would not have a suspensive effect on the proposed ART treatment unless the agency determines that it poses an obvious and immediate threat to the health and well-being of the child and/or the mother.

The rationale for mandating information disclosure is straightforward: Requiring that both the rationale for performing an innovative procedure be made available to the regulators and their peers will encourage ART physicians to more carefully examine the pros and cons of performing the procedure in the first place. It is not unreasonable to assume that mandatory disclosure requirements will discourage some ART practitioners from performing questionable procedures. They are also likely to induce the ART profession to evaluate much more carefully possible dangers associated with these procedures. Furthermore, mandatory disclosure requirements will set off a debate among ART professionals about the wisdom of the course of action taken, its benefits, and possible harms. An unintended but welcome consequence of these internal debates is the identification of alternative, less problematic, or less risky procedures. In sum, information regulation not only encourages accountability among ART practitioners; it is also an institutionalized mechanism of monitoring and learning.

Information regulation as proposed in this section has several precedents. It is at the core of many financial disclosure requirements mandated by the Securities and Exchange Commission; it has successfully been used to improve the safety of U.S. nuclear power plants,[18] and has found numerous applications in environmental policy.[19] Perhaps the single most successful example of information regulation is the Toxic Release Inventory (TRI) program established as part of the Emergency Planning and Community Right-to-Know Act of 1986 by the EPA. The TRI program requires industrial facilities to report to the EPA on a yearly basis the production of approximately 650 hazardous chemicals (as of 1999). It should be emphasized that the EPA does not directly regulate the production and disposal of the chemicals listed in the TRI; it only requires that chemical plants report hazardous waste production on an annual basis. According to

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[18] Rees, *Hostages of Each Other: The Transformation of Nuclear Safety since Three Mile Island*.

[19] Paul R. Kleindorfer and Eric W. Orts, "Information Regulation of Environmental Risks," *Risk Analysis* 18, no. 2 (1998). An illustration is provided by the Global Reporting Initiative, a program launched by the United Nations Environment Programme designed to improve environmental disclosure by large international corporations. See http://www.globalreporting.org/index.asp for more information. See also Thomas C. Beierle, "Environmental Information Disclosure: Three Cases of Policy and Politics," (Washington, D.C.: Resources for the Future, 2003). In developing countries, information disclosure has gained some popularity as a low-cost, effective regulatory tool. See for example Shakeb Afsah and Jeffrey R. Vincent, "Putting Pressure on Polluters: Indonesia's Proper Program " (Harvard Institute for International Development, 1997); Tom Tietenberg and David Wheeler, "Empowering the Community: Information Strategies for Pollution Control" (paper presented at the Frontiers of Environmental Economics Conference, Airlie House, VA, October 23-25, 1998).

some studies, the TRI program has been spectacularly successful in reducing the volume of hazardous wastes.[20]

There have been some instances of information regulation in medicine as well. The state of New York, for example, makes available to the public risk-adjusted mortality rates for cardiac artery bypass surgery on hospital-by-hospital basis and for individual physicians.[21] Whether this particular form of information regulation is an effective way to reduce medical errors is doubtful. Underlying this kind of mandatory system of disclosure is the assumption that patients will select a surgeon based on his or her safety record. This assumption may be seriously flawed. Every surgeon, even the best one, in his or her career will make at least one tragic error.[22] Prospective patients may be able to make an "informed decision," but one may wonder just how informed this decision really is.

Implementing a system of monitoring and information disclosure as envisaged in this section requires solving several problems. Among them is defining what constitutes an innovative treatment. Distinguishing between innovative and standard treatments is not as problematic as one might assume, however. The ART industry has settled on fairly straightforward definitions of standard treatments. Their number is small. A list of these procedures, complete with a brief description, fits comfortably on one page.[23] Reproductive endocrinologists routinely tweak and adapt these procedures to meet specific clinical requirements, but these modifications do not warrant introducing new categories. For example, some reproductive practitioners allow the embryo to develop in vitro for five instead of the more common three days. Tweaking the time of in vitro embryo development is just that, a marginal change that should not be construed as an innovative treatment.

Innovative procedures by definition have never been tested in animal models and depart significantly from standard ART treatments. Accurately defining "significant departure" may require some trial-and-error. Initial definitions are bound to be controversial, and in some instances, the courts may be called upon to resolve these controversies. It is quite possible that initially, regulators will cast the net too broadly. As a result, they may consider as innovative

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[20] Bradley C. Karkkainen, "Information as Environmental Regulation: TRI and Performance Benchmarking, Precursor to a New Paradigm?," *Georgetown Law Journal* 89 (2001); King and Lenox, "Industry Self-Regulation without Sanctions: The Chemical Industry's Responsible Care Program."

[21] See http://www.health.state.ny.us/press/releases/2004/cardiac_release_05-06-2004.htm. For a general discussion, see William M. Sage, "Regulating through Information: Disclosure Laws and American Healthcare," *Columbia Law Review* 99 (1999). It appears that information disclosure has little impact on actual consumer choices, but it does have a measure of impact on the quality of service. See Mark R. Chassin, E. L. Hannan, and B. A. DeBuono, "Benefits and Hazards of Reporting Medical Outcomes Publicly," *New England Journal of Medicine* 334 (1996); Edward L. Hannan et al., "Improving the Outcomes of Coronary Artery Bypass Surgery in New York State," *Journal of the American Medical Association* 271, no. 10 (1994); Eric C. Schneider and Arnold M. Epstein, "Influence of Cardiac-Surgery Performance Reports on Referral Practices and Access to Care," *New England Journal of Medicine* 335 (1996).

[22] Gawande, *Complications: Decisions and Dilemmas of a Surgeon's Life*.

[23] Centers for Disease Control and Prevention, "Survey of Assisted Reproductive Technology: Embryo Laboratory Procedures and Practices," (Chamblee, GA: Public Health Practice Program Office, Division of Laboratory Systems, Laboratory Practice Assessment Branch, 1999), Appendix G, p.2.

many procedures the industry regards merely as a form of tweaking. In time, however, a consensus between the regulators and the industry on what constitutes a "significant departure" is likely to emerge.

As a general principle, reporting requirements should ensure that other ART physicians could reproduce the procedure. The rationale provided by the performing practitioner should be specific enough as to allow other reproductive endocrinologists to debate the pros and cons of his or her decision. Finally, the performing ART practitioner should conduct a risk-benefit analysis that includes not only the prospective parents but the future child as well. We realize that risk-benefit analysis is an exercise fraught with unknowns and questionable assumptions. Implementing this requirement may represent a considerable hurdle for many ART practitioners. To overcome these difficulties, the regulators could provide extensive scientific and medical assistance, as well as detailed guidelines. More or less sophisticated approaches can be envisaged, but the principle that performing an innovative reproductive treatment requires assessing possible health and safety risks should be retained.

Performing innovative procedures will also trigger stricter standards of informed consent. A key aspect of these standards is informing the prospective parents that the reproductive procedure envisaged is indeed experimental. Whether stricter standards of informed consent will prompt prospective parents to reconsider questionable reproductive procedures is doubtful. As we have shown in chapter 4, the dividing line between parental desperation and reckless behavior is a thin one. Many parents are likely to expose future children to excessive risks even if they have received extensive and in-depth information about these risks. Nevertheless, we believe that the experimental nature of innovative reproductive procedures warrants a more rigorous approach to informed consent.

Having examined an innovative reproductive protocol, its rationale, its risks, and its benefits, and having heard the ART practitioners' views on the merits or demerits of the procedure in question, regulators can make one of several possible determinations. They may decide that the procedure in question does not raise significant concerns. Alternatively, given the uncertain nature of the risks involved, they may call for a moratorium while more research is conducted. They may also come to the conclusion that the risks outweigh the benefits and justify a ban. Finally, based on the feedback submitted by the ART industry, they may recommend taking a number of precautions and suggest tweaks that would mitigate the most important risks.

Reproductive specialists are likely to find these requirements problematic. There is no doubt that implementing a system of monitoring as discussed in this section would increase the cost of ART treatments and may prevent some prospective parents from realizing their dream. But the system of monitoring proposed here also has several important benefits. It provides a measure of legitimacy and legal protection to reproductive endocrinologists performing innovative reproductive procedures deemed acceptable by regulators; it protects the interests of ART children in a much more effective way; it improves the quality and safety of reproductive procedures; and it expands the number of reproductive treatments available to the ART industry. These benefits are well worth their costs.

13.4 Technologies of Reproductive Customization

Technologies of reproductive customization set themselves apart from standard reproductive techniques and innovative treatments for their purpose. These technologies are not used simply to increase the prospective parents' chances to have a family, but to meet specific parental requirements. A classic example is the use of pre-implantation genetic diagnosis for elective sex selection.

With regard to monitoring the use of technologies of customization or reproductive control, no additional action is needed. As for innovative reproductive treatments, ART practitioners would have to provide an assessment of possible health and safety risks and a discussion of possible ethical concerns, if the contemplated procedure is not already regulated. The notion of risk in this case should be construed broadly to include harm to the well-being of the child, and not simply health threats in the narrow sense of this term. Consistent with the view that technologies of reproductive customization should be more closely scrutinized, the review process would have a suspensive effect. The proposed procedure may not be performed until the agency has evaluated the documentation and has received feedback from the ART industry and the bioethics community.

Depending on the type of procedure and the concerns expressed, the agency could proceed as in the case of innovative reproductive treatments – i.e., offer a specific opinion on the pros and cons of the proposed treatment, or determine that the procedure at issue deserves broader public scrutiny. In the latter case, it would propose a new rule and initiate a process of public consultation.

Initially, the legal definition of a technology of reproductive customization could create some difficulties. It may not always be clear whether a certain treatment should be regarded as an instance of a traditional ART treatment, as an innovative technique, or rather as a technology of reproductive customization. Nor is determining what harm the child may experience a trivial matter. The debate over reproductive cloning has shown that it may be surprisingly difficult (but certainly not impossible) to demonstrate harm for the children involved. This is also the reason why we have suggested establishing an independent agency with quasi-judicial powers.

13.5 Biomedical Research

Of the four policy domains identified in this report, biomedical research poses perhaps the greatest challenge. Science and scientific institutions enjoy a special position in modern America. The public continues to regard science and technology as crucial to the future of our country. The libertarian ethos that is one of the constitutive elements of American exceptionalism is particularly strong among scientists.[24] Representatives of this profession often consider scientific freedom sacrosanct. Attempts by Congress to restrict freedom of research are

[24] See, for example, Lipset, *American Exceptionalism: A Double-Edged Sword*.

likely to meet with fierce resistance, more so perhaps than the suggestion that the practice of reproductive medicine should be regulated.

In select areas, the scientific community has recognized the importance of conducting research in a manner that is regarded by the public as ethical. The "Guidelines for Human Embryonic Stem Cells," a report published by the National Academy of Sciences (NAS) in early 2005, provides an illustration. Unlike most legislative proposals introduced in Congress over the last few years, the NAS report, in addition to recommending the usual procedural safeguards, proposes the creation of an infrastructure of evaluation and monitoring. The proposal is by far the most sophisticated and serious effort to establish a regulatory framework for a field of biomedical research. For this reason, we examine its main elements in some detail.

The NAS report establishes the principle that research proposals should be evaluated not merely on procedural but also on substantive grounds. Crucially, the report distinguishes between research that is "permissible" (i.e., that does not require additional review), research that is permissible only after additional review, and research that "should not be permitted at this time."

The derivation of new stem cell lines, either from donated embryos or created through somatic cell nuclear transfer, would trigger additional review. Additional scrutiny would also be necessary for introducing human embryonic stem cells into non-human animals at any stage of embryonic, fetal, or postnatal development.[25] Among the activities that should not be permitted are (a) the in vitro culture of human embryos for longer than 14 days or until the formation of the primitive streak, whichever occurs first; (b) research in which human embryonic stem cells are introduced into non-human primate blastocysts, or in which any embryonic stem cells are introduced into human blastocysts; and (c) the breeding of animals in which human embryonic stem cells have been introduced at any stage of development.[26]

Taken together, these provisions suggest that the scientific community is beginning to recognize the need to distinguish between research that is largely unproblematic, research that warrants additional scrutiny, and research that should not be conducted. In our view, this recognition is more important than where exactly the specific ethical lines should be drawn. The NAS recommendations are noteworthy for another reason as well: They implicitly acknowledge the need to create a regulatory institution that can operate in a contingent, quasi-adjudicative way rather than suggesting the creation of a system based on the seriously misleading assumption that ethical controversies can be resolved in an abstract, *a priori* fashion.

Chiefly responsible for the evaluation of research proposals would be an Embryonic Stem Cell Research Oversight (ESCRO) committee. ESCROs would be established at each research institution at which human embryonic stem cell research is being conducted, but they would not duplicate the functions of institutional review boards. The report recommends that

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[25] Committee on Guidelines for Human Embryonic Stem Cell Research, *Guidelines for Human Embryonic Stem Cell Research*, p.87.

[26] Ibid., p.87-88.

representatives of the general public as well as professional bioethicists and legal scholars be represented on each ESCRO.[27] It also recognizes the crucial importance of compliance assurance, and proposes what at first seems a practicable approach to compliance assurance – identifying in private institutions such as funding agencies, professional societies, publishers, and institutional review panels entities that can provide "valuable community pressure" and "impose appropriate sanctions to ensure compliance."[28] More specifically, the report recommends that compliance be ensured through three private institutions – review committees such as ESCROs and IRBs, funding agencies, and journals.[29]

Having emphasized several commendable aspects of the NAS report, three major shortcomings should mentioned. First, the role of the general public remains unspecified. Presumably, this requirement is inspired by the now fairly common practice to include a "community representative" on IRBs and ethics committees. This approach may be reasonable in the case of medical ethics committees, but it is hard to see how a few representatives of a local community may contribute to defuse anxieties, concerns, and opposition to controversial research proposals. Should a research protocol be prevented from moving forward if the local community is opposed to it? In which way are the community representatives accountable to the community? Should they be elected or simply selected by the research institution to participate? The credibility of ESCRO committees as moral authorities and independent bodies of evaluation and oversight depends crucially on how these issues are resolved.

One may also wonder why the report suggests implementing a decentralized system of oversight. Quite possibly, the preference for a decentralized over a federal system of oversight resides in a deep-seated distrust of the G.W. Bush administration, often regarded by the scientific community as being captured by religious interests inimical to medical science and to the scientific enterprise more generally. This argument ignores the simple fact that a decentralized system of oversight is not better protected against skeptical views than a federal system of oversight would be, and has some shortcomings of its own. As shown in chapter 10, citizen advisory boards can quickly become a platform for skeptical groups to voice their opposition. ESCRO committees, too, could become the focus of heated, protracted, and ultimately sterile political controversies between a research institution and the local community. A federal system

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[27] Ibid., p.44-46.

[28] Ibid., p.12. There is ample empirical evidence that private systems of reciprocal monitoring can produce surprisingly high levels of compliance with privately enacted rules and norms. See, for example, Lisa Bernstein, "Opting out of the Legal System: Extralegal Contractual Relations in the Diamond Industry," *Journal of Legal Studies* 21, no. 1 (1992); Lisa Bernstein, "Private Commercial Law in the Cotton Industry: Creating Cooperation through Rules, Norms and Institutions," *Michigan Law Review* 99 (2001); Robert D. Cooter, "Decentralized Law for a Complex Economy: The Structural Approach to Adjudicating the New Law Merchant," *University of Pennsylvania Law Review* 144, no. 5 (1996); Avery Katz, "Taking Private Ordering Seriously," *University of Pennsylvania Law Review* 144, no. 5 (1996); Mark D. West, "Private Ordering at the World's First Futures Exchange," *Michigan Law Review* 98 (2000).

[29] Committee on Guidelines for Human Embryonic Stem Cell Research, *Guidelines for Human Embryonic Stem Cell Research*, p.12.

of oversight as laid out in this report would provide both legal protection and legitimacy to the research community independently of idiosyncratic political landscapes at the local level.

The system of compliance assurance proposed by the NAS report has the merit of focusing on private organizations such as funding agencies and publishers that by virtue of their position could ensure high levels of compliance. These organizations could require sufficient and credible evidence of compliance with the NAS guidelines as a condition for funding or publication. In select areas, mainly with regard to compliance with procedures of informed consent, this approach could prove workable. In this case, the task of reviewing compliance records may be manageable, and the reviewing institutions could be expected to have the necessary administrative expertise to perform this task. Certainly, the leading funding institutions and highly reputable journals could perform this task. Smaller organizations, such as foundations and second-tier journals, may not have the necessary expertise and may be far less inclined to assume these responsibilities. Importantly, the system of compliance assurance proposed by the NAS guidelines does not explicitly contemplate a system of inspection, nor does it include any kind of sanctions for non-compliance. Finally, the report does not elaborate on how the integrity of a private system of compliance assurance could be protected.

Finally, as laid out in this report, the responsibility for determining the acceptability of new research protocols resides with the scientific community and with it alone. Local communities have an opportunity to be heard, but they certainly do not have the authority to prevent new research from moving forward. This is precisely the opposite of what we have proposed in this report: Scientists and the general public must be given ample opportunities to be heard, but the authority to decide what may or may not move forward must reside with an administrative entity created by Congress. It should be the responsibility of the regulatory advisory board (see chapter 11) to examine new research protocols and to make recommendations for the regulatory commission. For these reasons, we believe that the guidelines proposed by the National Academy of Sciences do not form the basis for a robust and trustworthy regulatory infrastructure.

13.6 Designing a System of Compliance Assurance

Implementing an efficient and effective system of compliance assurance is no easy task. In this regard, the British experience is only of limited help. As of August 31, 2004, the HFEA had exercised its oversight over 108 ART programs and ART laboratories.[30] Inspecting these facilities on a regular basis is a manageable task, considering the modest number of facilities and the limited travel distances involved. A U.S. regulatory agency would face a much more complex organizational landscape that includes more than 400 ART clinics, countless embryo labs, more than 900 biotech companies, several large pharmaceutical companies, and a potentially significant number of university laboratories. Furthermore, this very diverse

[30] Human Fertilisation and Embryology Authority (HFEA), "HFEA Annual Report 2003/04," p.8.

population of firms, clinics, laboratories, and universities is scattered over a very large territory, making it difficult for any administrative agency to implement a credible and effective system of compliance assurance.

Regulatory agencies facing a challenge of this magnitude routinely delegate some monitoring and enforcement authority to third parties, such as trade and professional organizations. Obvious candidates for surveying ART programs are the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technologies. The Biotechnology Industry Organization could monitor the biotech sector, and leading scientific societies such as the American Association for the Advancement of Science and the Federation of American Societies for Experimental Biology could audit academic laboratories.

Delegating monitoring and enforcement authority to third parties – referred to as intermediary organizations in the remainder of this section – has a crucial limitation: Trade and professional associations would have a very limited authority to ensure compliance; members could easily avoid compliance by simply leaving the association, while non-members would be exempt from oversight in the first place. This is not, however, an insurmountable problem. While limited, an intermediary organization's authority is not negligible; it varies depending on the nature of the benefits it provides to its members.[31] Intermediary organizations providing valuable, exclusive benefits to their members make it more difficult for a member to leave. The more valuable the exclusive benefits, the more difficult it is for a member to leave, and the more powerful an intermediary organization becomes.[32]

Regulators could bolster these embryonic systems of private governance either by making membership in intermediary organizations more attractive or by increasing the cost of leaving an intermediary group. For example, regulators could decide that the members of an intermediary organization would be inspected less frequently, and that the inspection process should be collaborative and should emphasize the correction of violations and the adoption of best practices over punishment, fines, and prosecution. The agency could also determine that serious violations by a member of an intermediary organization should be treated more leniently. By contrast, non-members would be inspected more frequently, their inspection process would be antagonistic, and violations would trigger severe penalties. Importantly, members of an intermediary organization would be inspected by their peers or by representatives of their intermediary organization, while non-members would be inspected by the regulators.

In this architecture of compliance, the regulator's main role shifts from compliance assurance to ensuring the integrity of a decentralized system of monitoring and inspection, i.e., to monitoring the monitors. Assuring the credibility and integrity of this system entails addressing several concerns. Chief among them are ensuring consistency of inspection and preventing

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[31] Typically, national trade associations advocate vigorously for their members, to avoid or mitigate regulations or to obtain specific benefits. They also offer a wide range of training and educational opportunities.

[32] Mancur Olson, *The Logic of Collective Action: Public Goods and the Theory of Groups* (Cambridge, MA: Harvard University Press, 1965); Posner, "The Regulation of Groups: The Influence of Legal and Nonlegal Sanctions on Collective Action."

collusion between inspectors and inspected parties. To achieve these goals, regulators would adopt a certification scheme. Only certified intermediary organizations would be delegated the authority to conduct inspections. Maintaining the certification would require intermediary organizations to periodically undergo extensive audits, for example, every three to five years. Serious irregularities could trigger monetary and other penalties for both the auditing and the audited organization. For the most egregious violations, the regulators could revoke the certification. The consequences of this measure would be severe, because in this case, both the intermediary organization and its members would be punished.[33]

Revoking certification is perhaps the most extreme illustration of a collective sanction. The threat of collective sanctions, if properly designed, could have several unintended but welcome consequences. It could trigger collaborative efforts to identify best practices and promote their adoption throughout the group. It could also encourage the members of an intermediary group to exercise pressure on violators to comply with all applicable laws and regulations. Failure to demonstrate improvement on the part of violators could prompt some members to file a report with the intermediary group. Finally, individual members would have an incentive to report cases of collusion between an audited organization and the auditor to the regulators.[34]

Collective sanctions are neither new nor unusual. In the early 1970s, the scientific community effectively faced a collective threat when its leaders at the Asilomar Conference proposed to establish a system of self-regulation. In this case, the threat originated not with regulators but with the general public. Scientific leaders recognized that even a single accident associated with recombinant DNA technology would have damaged the reputation of this nascent field of research beyond repair. This is by no means an exceptional pattern. Over the last 20 years, many industries that experienced a highly visible, catastrophic incident reacted by establishing elaborate systems of self-governance.[35]

This somewhat simplistic analysis of the impact of collective sanctions on intermediary organizations and their members masks a subtle but very important phenomenon: the gradual emergence among these organizations of civic norms and attitudes, i.e., the recognition of the crucial importance of obtaining a “public license” for conducting ethically controversial medical research. Key to initiating this learning process is a new professional role: a person charged by

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[33] The threat of revoking certification is credible only if the intermediary organization being audited is not too large compared to other intermediary organizations. Should a large intermediary organization loose its certification, it may be difficult for regulators to find a replacement. In turn, this would make the threat of decertification less credible.

[34] Note that whistle-blowing as outlined in this passage provides an additional incentive to intermediary organizations to properly audit their members.

[35] The classic example is the Responsible Care Program established by the American Chemistry Council (formerly the Chemical Manufacturers Association) in the aftermath of the Bhopal accident. Cf. Howard, Nash, and Ehrenfeld, "Standard or Smokescreen? Implementation of a Voluntary Environmental Code."; King and Lenox, "Industry Self-Regulation without Sanctions: The Chemical Industry's Responsible Care Program." Other chemical sub-sectors have followed suit, adopting their own programs of safety and environmental management. A similar approach has been taken by the nuclear power industry in the wake of Three Mile Island. Rees, *Hostages of Each Other: The Transformation of Nuclear Safety since Three Mile Island*.

an ART program, a biotech company, or a university to ensure compliance with applicable laws and regulations – a compliance assurance officer, so to speak. This person's job would be not only to make sure that researchers and ART practitioners follow procedures and maintain proper documentation, but also to determine whether a certain ART treatments should be considered traditional, innovative, or technologies of customization, and what ethical concerns they may raise. In the case of biomedical research, this person would help determine whether a given research proposal might raise special ethical concerns. Crucially, the compliance officer would cooperate with compliance officers at other ART programs or research institutions to resolve complex ethical problems created by new research protocols, and to identify possible harms involved in novel reproductive treatments. These patterns of collaboration eventually will morph into a horizontal network of personal and professional relations, and lead to the emergence of a professional culture that will find itself at the intersection of public virtues and private interests.

From a regulatory standpoint, the emergence of this network would have several important benefits: It would reduce the risks of collusion between member organizations and auditors. It would spur the ethical analysis of novel ART treatments and biomedical research protocols. It would contribute to developing new techniques of risk assessment. Importantly, it would also become an effective promoter of civic values among biomedical researchers and medical professionals.[36]

Admittedly, creating the position of compliance assurance officer, by itself, is unlikely to produce the kind of cultural change envisaged here. No one should be under the illusion that civic norms would quickly emerge. That compliance assurance could initiate a process of societal change is, however, both surprising and encouraging. This alone would justify its implementation costs, as discussed in the next section.

13.7 Operating Costs

In this section, we provide a rough estimate of the costs of operating a new regulatory entity as outlined in this report. This discussion is not meant to provide precise cost estimates. It is simply a back-of-the-envelope calculation that should demonstrate how modest the overall costs of operating a new regulatory agency would be. Our calculations are based on data derived from the British regulatory system, one of the most intrusive systems of ART regulation worldwide. The data is derived from the 2001, 2002, and 2003 annual HFEA reports, available on the HFEA Web site.[37] Each of them includes a financial statement and other operational data. They also describe in some detail the scope of the HFEA's regulatory activities.

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[36] An important precedent to this professional role is the environmental and safety (ES) manager common at large industrial firms. Several trade groups in the chemical sectors that in recent times have adopted extensive systems of self-regulation have learned that ES managers play a crucial role in resolving complex questions of implementation and in promoting high levels of compliance.

[37] See http://www.hfea.gov.uk.

Consider first the scope of the HFEA's regulatory activities. In 2003, the agency was responsible for overseeing 110 facilities. Most of them (80) offer both treatment and storage services; 15 had received all three kinds of license (treatment, storage, and research); the remaining ones are specialized in just one type of licensed activity. (See Table 12.)

Type of HFEA-licensed center	*Number of centers*
Treatment only	2
Storage only	8
Treatment and storage	80
Treatment with storage and research	15
Research only	5
Total	110

Table 12: The ART industry in Britain, 2002-2003, p.8.

Another measure of the size of the British ART industry is the number of licensed treatments granted by the HFEA on a clinic-by-clinic basis. As Table 13 shows, not every clinic is licensed to perform all ART treatments, but most perform donor insemination, in vitro fertilization, and intracytoplasmic sperm injection. They also offer the storage of embryos and sperm.

HFEA-licensed treatments	*Number of centers*
Storage of eggs (including ovarian tissue)	20
Storage of sperm (including testicular tissue)	103
Storage of embryos	76
Donor insemination	96
In vitro fertilization	75
Intracytoplasmic sperm injection	74
Pre-implantation genetic diagnosis	8
Pre-implantation genetic screening for aneuploidy	5

Table 13: Licensed treatments in Britain, 2002-2003, p.8.

Clinics are generally inspected on a yearly basis, although facilities in good standing are fully inspected only once every three years. Table 14 provides another indication of the tight control exercised by the HFEA over the ART industry, in the form of the total number of inspections conducted in 1999, 2000, 2002, and 2003.

Inspection	*1998-1999*	*1999-2000*	*2001-2002*	*2002-2003*
Number of inspection visits	106	109	115	121
Number of audits	28	25	106	93
Number of ICSI practitioners inspected	35	22	30	18
Number of PGD practitioners inspected	0	1		n/a

Table 14: Inspection visits and audits, 1999-2003.

By all accounts, the British regulatory system can only be described as comprehensive and fairly intrusive. And while the British ART industry is considerably smaller than its U.S. counterpart, it is large and complex enough to serve as a basis for assessing the operational costs of a domestic regulatory program.

Just how expensive is it to operate the HFEA licensing and inspecting scheme? Actual financial information about these two operational aspects is not available, but total operating expenses are a good substitute. Information about total expenditures is readily available and is reported in Table 15.

Year	*1998*	*1999*	*2000*	*2001*	*2002*	*2003*	*2004*
Total expenditures	1,552,909	1,706,657	1,772,910	2,743,558	1,716,845	5,629,560	7,444,580
Staff costs	848,288	932,093	969,503	1,363,038	1,263,038	2,523,912	3,665,204

Table 15: HFEA operating costs, 1998-2004 (in pounds).

Until 2000, total expenditures remained largely unchanged. In response to the rapid growth of the ART industry in 2001, the HFEA budget and its staff expanded considerably. Section 16 of the Human Fertilisation and Embryology Act requires the HFEA to recover 70 percent of its expenditures. The HFEA recoups its operating expenses through licensing fees (for first-time and for renewal applications) and through an annual fee based on the number of ART cycles performed. In 2000, the fee for performing an IVF cycle was reduced from £40 to £36, whereas fees for donor insemination were raised from £10 to £18. The HFEA has been quite good at achieving a 70 percent level of self-funding. In the fiscal year 2000-2001, its self-funding level was 67 percent. In 1999-2000, it reached 101 percent of its cash limit.

The U.S. ART industry is approximately four times larger than its British counterpart, not counting the sperm and embryo banks already regulated by the new FDA human cellular and tissue-based products rules.[38] The 2002 CDC report on ART success rates lists 391 ART programs, up from 384 a year before.[39] These programs generally do not conduct basic research on human embryos. On the other hand, according to news media reports, restrictions on federal funding for embryonic stem cell research have prompted private foundations to fill this gap, so it is quite possible that a fair number of universities are now receiving human embryos, though how many is anyone's guess.[40]

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[38] See chapter 5 for a discussion of these rules.

[39] These are the reporting programs. Appendix C of the report lists 37 non-reporting programs. Cf. Centers for Disease Control and Prevention, "2002 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports."

[40] Anne Harding, *Harvard Has Human Cloning Plans. Institute Seeks Nod to Create Embryos Using Genes from Patients with Diabetes, Parkinson's* (The Scientist, October 15, 2004 [cited September 20, 2005]); available from http://www.biomedcentral.com/news/20041015/03; Nancy Touchette, *New Stem Cells Created for Research: Harvard Scientist Will Make 17 New Lines Available* (Genome News Network, March 3, 2004 [cited September 20, 2005]); available from http://www.genomenewsnetwork.org/articles/2004/03/03/stem_cells.php.

There is some evidence that the biotech industry does conduct research in this area, but just how much research is unknown. A fairly recent survey conducted by the Department of Commerce in cooperation with BIO, the leading biotech industry trade association, shows that of 776 surveyed firms, 41 percent did perform "culturing/manipulation of cells, tissues,, embryos."[41] However, the survey does not provide any information on the relative importance of embryo research proper, or the significance of this research area in the industry research portfolio.

For the purpose of this discussion, we assume that the newly created regulatory agency would have to fund itself through user fees. (This is a worst-case scenario, as Congress is likely to fund this agency at least in part.) The regulators, then, would have to adopt a fee system similar to the one operated by the British HFEA. A simple way to assess the burden imposed on the ART industry and patients by this fee system is to compare fee levels to the cost of ART services to patients. Assessing the cost of ART services in the United Sates is no easy task. Prices vary considerably depending on the type of service rendered and the clinic's reputation and location. ASRM does not provide reliable cost information, nor does the CDC gather this kind of data. A rough estimate of the cost of various ART services can be gleaned from Web resources offering information to prospective parents and from fertility clinics' own published information. For example, www.babycenter.com provides the following price estimates per cycle:

- Artificial insemination: $300 to $700
- In vitro fertilization: $8,000 to $15,000
- Gamete intrafallopian transfer: $8,000 to $15,000
- Zygote intrafallopian transfer: $8,000 to $15,000
- Intracytoplasmic sperm injection: $10,000 to $17,000[42]

Note that these categories are not mutually exclusive. An individual cycle may require performing ICSI followed by traditional IVF. Other cycle-related services such as testing of reproductive tissues are charged separately. In the United States, by far the most common procedure remains IVF. According to the CDC, in 2001, 107,587 ART cycles were performed.[43] Assuming that the U.S. regulatory counterpart would charge the same fee as the British HFEA (i.e. £36, or $64),[44] and given the average price of $12,000 per cycle, a U.S. regulatory system

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[41] U.S. Department of Commerce, "A Survey of the Use of Biotechnology in the U.S. Industry," (Washington, D.C.: Technology Administration, Bureau of Industry and Security, 2003).

[42] See http://www.babycenter.com/refcap/preconception/fertilityproblems/1228997.html, page visited on July 20, 2005.

[43] Centers for Disease Control and Prevention, "2001 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports," (Atlanta, GA: National Center for Chronic Disease Prevention and Health Promotion, Division of Reproductive Health, 2003), p.6.

[44] Exchange rate as of April 26, 2006.

would add roughly 0.56 percent to the cost of this ART service. This figure must be regarded as a rough estimate; it does not include the one-time costs to ART programs to implement the new record-keeping and reporting requirements, and it does not include the additional operating expenses ART programs would incur in complying with reporting and other regulatory requirements. On the other end, it is quite possible that a U.S. regulatory agency would be less costly to operate and could charge lower user fees.

The new record-keeping requirements are likely to increase the operational costs of ART programs, though it is unclear by just how much. If we assume that ART programs depend on effective systems of record-keeping for their daily operations, and that in cooperation with SART and the CDC they have already adopted an IT-based reporting system, compliance with new reporting requirements is likely to cause only modest additional costs.

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