1 Introduction

This report presents a proposal for a new approach to regulating human biomedicine in the United States. It is the product of more than three years of research, and of a study group convened in Washington, D.C., dedicated to this subject. The members of the study group (listed in Appendix A) were chosen to be representative of the different stakeholders in human biomedicine; while they have intensively discussed various issues raised in this report, they have not been asked to endorse the report or its final conclusions. Those remain the responsibility of the report's primary authors.

It is our belief that the existing system for regulating human biomedicine in the United States, while unrivaled in many respects by that of any other country, contains certain gaps or omissions that will render it increasingly inadequate to meet the challenges posed by new biotechnologies and medical procedures in the coming years. Other developed countries have put new regulatory institutions in place already or are in the process of doing so in anticipation of new developments, and the United States needs to follow suit.

In putting forth this proposal, the authors of this report fully understand the downsides of regulation. If you regulate something, you get less of it, and many people fear that excessive regulation of biomedicine will stifle innovation and progress in many areas critical to human health and well-being.

While this fear is often well-founded, we believe that properly designed regulation can have the exact opposite effect: It can promote research and scientific advance by establishing a clear framework under which innovation can take place, a framework that reassures the broader society that the research is being conducted safely and ethically. Clinical trials for new drugs are facilitated, for example, by having clear rules established for human subject research by the National Institutes of Health (NIH) and the Food and Drug Administration (FDA). As we will demonstrate below, the benefits of a properly designed regulatory environment would be felt in one particular area of acute concern – embryonic stem cell research.

1.1 The Challenge of New Biotechnologies

It has been clear for more than a generation that advances in biomedical technology pose ethical challenges deeper and more abiding than those raised in other areas of scientific research. Biotechnology from the start spawned a whole new field of bioethics; information technology, by contrast, has not led universities to train professionals in "information ethics." Recombinant DNA (or rDNA), cloning, psychotropic drugs, and behavioral genetics have generated moral and political controversies due to the ways that they could potentially affect human well-being, both for good and ill.

When societal concerns about biotechnology first appeared in the 1970s, the scientific research community and the biomedical industry reacted responsibly, putting in place new institutions to reassure the public that biotechnological advance was not coming at the expense of human safety or dignity. The scientific community, for example, organized the Recombinant DNA Advisory Committee (RAC) under NIH auspices to vet new research projects in this area and guard against the emergence of "superbugs." There was also a major push to fund advisory committees on bioethics at major research and medical institutions, and a whole series of governmental boards, commissions, and councils were established to provide ethical guidance to the U.S. government. The Human Genome Project has regularly devoted 3 percent of its research budget to studying the ethical, legal, and social implications of genetic research.

The various communities involved in human biomedical research in the United States have thus developed a model of self-policing in which bioethics plays a role, but only in an advisory capacity. This model has by and large worked over the past generation. However, as John Evans has pointed out,[4] this model was also put in place deliberately as a means of fending off more overt regulation. All of the different bioethics advisory boards around the country have effectively served as a cover for the scientific community, allowing it to argue that it was paying attention to ethical issues while not giving those bodies any real authority to limit or sanction research. The professional bioethics community, moreover, has tended to adopt a rather "thin" view of ethical concerns centered on principles like autonomy, fairness, beneficence, and justice, as opposed to the "thicker" moral views held by many Americans.

Bioethical discussion and debate remains critical; there are many ethical concerns that do not have black-and-white answers and cannot be addressed through laws or regulation. But it is our view that the time has come to move beyond bioethics and to begin considering a different kind of regulatory system for human biomedicine that goes beyond current considerations of safety and efficacy and takes ethical and normative concerns into account. How to institutionalize a system that is representative of the interests of the different stakeholders and of the general public, one capable of fostering rational deliberation and likely to promote necessary and beneficial research and innovation, is the subject of this report.

1.2 To Regulate or Not to Regulate

Having just argued that the scientific community has held off overt regulation of many forms of research and of biotechnology, it may seem contradictory to assert in the same breath that human biomedicine is and has for a long time been one of the most heavily regulated areas of endeavor in the United States. But both statements are true: The regulatory scene is a contradictory patchwork of both under- and over-regulation. The FDA's "gold standard" of costly double-blind clinical trials for pharmaceuticals is unmatched in any other country in the world. On the other hand, the FDA regulates only drugs and medical products, and can regulate

[4] John H. Evans, *Playing God? Human Genetic Engineering and the Rationalization of Public Bioethical Debate* (Chicago, IL: University of Chicago Press, 2002).

them only on the basis of safety and efficacy. It does not regulate the practice of medicine, which means that the large area of medicine involving assisted reproductive technologies (ARTs) receives virtually no government oversight. In Europe, things are typically rather different: Drugs are given less careful scrutiny, while ARTs are closely monitored by governments. While the FDA strictly enforces testing rules for new drugs, it does not control their off-label uses, meaning that doctors are free to innovate, and in effect experiment on their patients in such cases.

The other major regulatory institution in the United States is the National Institutes of Health, which through its control over federal funding exerts enormous influence over the nature, scope, and direction of scientific research in biomedicine.[5] It is the NIH that now oversees bodies like the RAC, and establishes requirements for institutional review boards (IRBs) to monitor research involving human subjects. The NIH is not limited to considerations of safety and efficacy like the FDA; it can and has introduced moral and ethical concerns into its decision-making. President George W. Bush's August 2001 decision limiting federally funded stem cell research to existing stem cell lines reflected his concerns over protecting embryos, and was implemented by the NIH. Here, the limits of regulatory authority are different than in the FDA's case. The NIH can influence science only through its control of funding; it cannot prohibit privately funded research and has no say over what happens in the private biotech industry.

No one designed this overall regulatory system. It was put together piecemeal in response to scandals like those over sulfanilamide elixir and thalidomide, or those in response to the Tuskegee or Willowbrook abuses. The fact that the United States regulates some things very strictly and other things not at all is largely a path-dependent and contingent product of its history. The question that confronts us is whether this system is adequate to meet the challenges of twenty-first century biomedicine.

What some of those challenges are and why the present system may not be adequate to cope with them is the subject of the growth hormone case study given in chapter 2. In light of these challenges, we face a problem of institutional design: Do we stick with the existing regulatory framework, or do we seek to introduce new regulatory powers or different kinds of institutions?

Most Americans rightly regard regulation as a necessary evil; with the growth of state sectors in the twentieth century, it became clear to many people by the 1970s that many sectors of the American economy were over-regulated. Much of the thrust of policy in the United States since then has been to cut back on regulation in areas ranging from airlines to trucking to electricity to telecommunications. In some cases, this has been met with great success; in others, less so. The dangers of over-regulation remain, however, and the burden of proof should lie with anyone who argues that new regulatory bodies are necessary. A useful prudential rule in public administration is not to multiply regulatory agencies unnecessarily when the new functions required can be performed just as easily by existing bodies.

---

[5] There are, of course, any number of other agencies that have regulatory authority over various aspects of human biomedicine, including the Centers for Disease Control and Prevention (CDC), the U.S. Patent Office, the Drug Enforcement Agency, and state licensing boards.

On the other hand, certain historical precedents suggest that it is at times wiser to create a new institution to deal with a new problem. Take the case of transportation, for example. The Interstate Commerce Commission (ICC) was created in 1887 to regulate the new railroad industry.[6] The Interstate Commerce Act that established it was a milestone in American administrative law, extending for the first time the writ of the federal government into areas that had previously been reserved for states.

At the beginning of the twentieth century, the rise of interstate trucking posed the question of who should regulate this new industry. The Hepburn Act of 1906 gave regulatory authority to the ICC on the grounds that trucking and railroads were similar, both being means of moving goods across state borders. Most experts in administrative law believe now, in retrospect, that this was a mistake: The economics of the rail and trucking industries were very different, the interest groups involved differed substantially, and the technical expertise require to regulate rail service did not spill over into trucking.

When commercial aviation emerged in the 1920s, the ICC could have been charged with regulating this sector on the grounds that airplanes are simply another means of interstate commerce. Instead, the Air Commerce Act of 1926 created a new, independent Aeronautics Branch within the Commerce Department to promote and ensure the safety of civil aviation. With the advent of commercial jet aircraft after World War II, this branch eventually evolved into two independent agencies – the Federal Aviation Administration and the Civil Aeronautics Board. It is doubtful that anyone today regrets this choice to create new agencies to regulate aviation rather than building on the authority of the ICC.

The question to consider here, then, is not the broad one of whether or not to regulate human biomedicine and biotechnology, as a positive choice was made in that area long ago. The question, rather, is whether we are currently at a juncture similar to the mid-1920s, when civil aviation first emerged as a new and highly promising industry. Do we regard the issues raised by new biotechnologies as problems we are already familiar with, or are they sufficiently different as to merit new regulatory powers? Surely, no one in a liberal society wants to multiply regulatory agencies or add more layers of bureaucracy unnecessarily. On the other hand, it is sometimes more efficient to begin afresh rather than trying to change bureaucratic cultures to handle problems they were never designed to handle. The idea that a democracy may want to create a new statutory authority to deal with new technologies cannot be totally outlandish, as a number of other developed countries have decided to do precisely that.

1.3 The Domain of Inquiry of this Report

Human biomedicine is a huge field, and it is necessary at the outset to define the realm of technologies and practices that we believe need to be regulated. There are many existing and potential targets of regulation, including drugs and medical devices, various types of scientific

[6] The ICC was disbanded in 1995 and its powers were given to the National Surface Transportation Board.

research, and clinical and medical practices. Many critics of the FDA have argued that the agency over-regulates many drugs, preventing patients from having timely access to important pharmaceuticals. This could well be true; a complete overhaul of the American regulatory system may require deregulation of some areas as well as new regulation of others at the same time.

In this report, we intend to focus more narrowly – on the one end on technologies and medical practices related to human reproduction, and on the other on biomedical research involving embryos and other reproductive tissues. Our reason for choosing these areas is that they encompass most of those technologies – existing, on the horizon, and possible in the more distant future – that bioethicists have pointed to as raising significant moral and ethical issues. Within this domain lie not only traditional ARTs, the most important of which remains in vitro fertilization (IVF), but also novel forms of reproduction (the creation of embryos from genetic material from one, three, four, or more parents, for example) and new reproductive services like pre-implantation genetic diagnosis (PGD) and sex-selection technologies and, possibly, germ-line genetic modifications (see chapter 3). This domain also includes laboratory research involving embryos. Embryonic stem cell research is a well-known example; less familiar but just as relevant is the creation of human-animal chimeras and hybrids.

It should be emphasized at the outset that to say that these technologies are related to human reproduction does not necessarily mean that they are *intended* to produce children. This is particularly true of embryonic stem cell research, whose end is of course the development of treatments for diseases affecting already-living human beings. Nonetheless, the fact that such stem cells are derived from embryos and may in the future be capable of producing embryos means that it is impossible to regulate the broader field of human reproduction without regulating them. Indeed, the manipulation of stem cells may become one of the means through which other reproductive technologies become possible.

To say that these practices should be regulated is not to say that they should be banned or unduly restricted. As we explain at greater length below, it is our view that stem cell research would benefit greatly from being placed within a regulatory framework. But precisely because embryonic stem cell research today requires the use of embryos and may at some point in the future lead to the creation of embryos, it is not possible to separate this kind of work from research and medical practices that aim directly at the creation of children.

In defining the domain of inquiry in this fashion, we are excluding a great many other issues that may deserve greater or lesser degrees of regulation. Psychopharmacology is an area of pharmaceutical development that is exploding, one that is regulated already and may deserve a fresh look in light of new drugs coming on the market in the near future. These are issues, however, that lie beyond the scope of the current report.

1.4 Science, Politics, and Democracy: Some General Considerations

Many people, including some members of our own study group, are strongly opposed to any regulation of scientific research, and believe that science is a self-contained, self-justifying

enterprise that should be shielded from politics. To many people, the idea of Congress intervening in this area evokes images of Galileo being prosecuted by the medieval Catholic Church. As Congressman Ted Strickland of Ohio said during the House debate on cloning legislation in 2001, "We should not allow theology, philosophy, or politics to interfere with the decision we make on this issue." It is therefore worth stepping back and raising the more general question of who, legitimately, gets to make rules in this area.

This issue was settled in principle long ago: All scientific research is *ultimately* subject to rules set not by scientists, but by the broader political community. In a liberal democracy, that community consists of the sovereign people speaking through their elected representatives – that is, Congress (and, in the case of presidential systems like that of the United States, the president). Indeed, in a democracy, the people are sovereign not only over science, but over every other field of activity.[7]

The reasons for this are straightforward. Scientists *qua* scientists have no special authority to make ethical or political judgments about the ends of their scientific research. Data is data: Even if obtained by deliberately infecting experimental subjects with deadly disease agents in double-blind clinical trials, as was done by Nazi scientists, the results are still scientifically meaningful. The fact that we do not allow this kind of research to be carried out in the United States reflects an ethical judgment that it is wrong, based in part on the crimes of the Nazis. Virtually all American scientists strongly support existing rules protecting human subjects of research. They do so, however, not in their capacity as scientists, but as citizens, moral agents, religious believers, or simply as human beings. It is precisely "theology, philosophy, and politics" that provides guidance on this kind of issue.

While it is clear in principle that Congress and the president ultimately have legitimate authority to set rules and boundaries for science and scientists, in practice science operates in a much more autonomous fashion. There is a general political consensus that science and scientific progress are good things that should be encouraged, and also a recognition on the part of elected officials that they do not have the knowledge to intervene in most scientific issues. This has led to a certain degree of self-restraint on the part of political authorities when it comes to scientific rule-making, and a willingness to delegate considerable rule-making power to the epistemic communities directly involved in scientific research and technology research and development. Congressman Strickland's comments about theology, philosophy, and politics interfering in science reflect a default condition in which scientists regulate themselves, subject to broad political guidelines set by Congress. While most Americans would accept the right of politicians to regulate science, most also hope – rightly – that this does not happen too often.

---

[7] Strictly speaking, in a liberal democracy like the United States, popular sovereignty is limited by a pre-existing set of individual rights, which in the American case are said to come from nature rather than the people's will. Practically speaking, the definition of what constitutes these "natural" rights is a matter of popular choice (i.e., through ratification of the Bill of Rights and its subsequent interpretation through the courts), but one based on supermajorities rather than simple majorities.

Congress' powers over scientific research and technology research and development come in many different forms. In some cases, the government has statutory powers to set rules, like the FDA's power to regulate drugs and medical devices. In other cases, political influence is exercised through funding decisions made by agencies like the NIH or the National Institute of Mental Health (NIMH). The fact that the United States chooses to wage a "war on cancer" rather than sponsor research on tropical diseases like malaria reflects political judgments about U.S. national priorities. Activities like embryonic stem cell research that are not banned but also not federally funded reflect either political compromises or complex judgments as to their moral acceptability. In light of these decisions, no one should pretend that the types and levels of research carried out in the United States do not embed a host of normative judgments made by the broader political community.

The issue we seek to address in this report is the proper modality of political intervention. In doing so, we hope to avoid several pitfalls. The first is routine intervention by Congress to ban or limit certain practices, technologies, or medical procedures. In 2001, legislation was introduced into Congress to ban, in one version, reproductive cloning, and in another, both reproductive and research cloning. While the latter bill passed the House of Representatives, neither made it through the Senate due to a failure to agree on the legitimacy of research cloning. While one of the present authors is on record in support of the broad cloning ban, neither of us believes that this bill represents a good general model for future Congressional intervention in biomedicine. While human cloning constitutes an important symbolic threshold meriting Congressional action,[8] many future innovations emerging over the coming decades will not. We do not believe that Congress has the time, energy, or expertise necessary to pass specific new laws in response to the many future innovations that will emerge.

On the other hand, we also do not believe that the current model under which authority is de-facto delegated to the epistemic communities and their stakeholders is adequate to meet future challenges. The regulatory authority of the FDA and NIH is not only limited by statute in the ways described above; it is administered almost exclusively by the epistemic communities involved, with little opportunity for participation by other societal actors with an interest in biomedicine. (Institutional review boards, with their statutory requirement that they include members drawn from outside the scientific community, are the one exception). On the adequacy of this arrangement, see chapter 5 below.) In designing new regulatory institutions, the issue then is not only whether they should be given statutory authority to go beyond safety and efficacy as criteria for regulatory decisions, but also whether those making the decisions on an agency level should include people from outside the scientific research communities and the biotech and reproductive industries.

We do not by any means mean to suggest that existing epistemic communities should be deprived of their traditional self-regulatory powers. Rather, the question is whether participants

[8] The recent report of the President's Council on Bioethics *Reproduction and Responsibility: The Regulation of New Biotechnologies* outlines a possible legislative agenda that would in effect ban reproductive cloning as well as a number of other procedures, like the production of human-animal hybrids.

in the standard-setting process can be broadened to include other stakeholders more representative of the broader society. There are a number of reasons for wanting to do this. While the scientific community, ART professionals and the biotech and pharmaceutical industries are the primary sources of knowledge about human reproductive medicine and biomedical research, they are also self-interested actors whose goals and ethical orientations do not necessarily coincide with those of the larger society. And even though scientists generally aspire to the disinterested search for truth as an ideal, many also have financial relationships with biotech or pharmaceutical companies that affect their personal incentives. These communities will continue to play an important role in this field, if for no other reason than their possession of critical scientific and medical information. The purpose of broadening participation in the resolution of contemporary moral and ethical dilemmas is not to dilute this expertise, but to make the regulatory body more representative of the society around it.

The final pitfall to avoid is the under- or over-delegation of authority to a new regulatory authority. Regulatory agencies exist in the first place because Congress lacks the time or knowledge to make the myriad complex decisions required by the statutes it enacts. Legislators do not want to have to decide how many parts per million constitutes a dangerous level of contamination for a particular chemical, or whether the results of a clinical trial are statistically significant. On the other hand, there are certain issues that are much too large and controversial to be delegated to a regulatory agency, and that ultimately must be debated and decided by the broader political community. The key issue for the design of a new regulatory authority, therefore, is what authority Congress should delegate and what issues it has responsibility for deciding directly. Nowhere is this more true than in the area of stem cell and cloning research.

1.5 Abortion Politics and the Moral Status of the Embryo

It is safe to say that in the United States, all legislation in the general area of reproductive medicine and embryo research is made vastly more complicated by the underlying societal controversy over the moral status of the embryo. Other developed countries that have passed legislation in this area have reached consensus either to permit (as in the case of Britain) or to prohibit (as in the cases of Germany and Canada) certain forms of cloning research. In the United States, there are passionate proponents of both the pro-life and pro-choice positions. One reason that cloning legislation has remained stalled in the Senate since 2001 is that neither side can muster more than about 40 votes for its preferred version of a cloning ban.

For what it is worth, we do not begin from a pro-life position. We believe that human embryos have an intermediate moral status.[9] They are, on the one hand, not the moral equivalents

[9] Some people have argued that human moral status is an "on" or "off" condition, and that the concept of an intermediate moral status is incoherent. There are, however, other entities that have such intermediate status. Dead human bodies are one example: We permit them to be used instrumentally for research and training purposes, on the one hand, but we do not allow them to be used for less dignified ends, or to be disposed of casually.

of newborns; destruction of an embryo for us is not tantamount to murder. On the other hand, we do not believe that embryos are just clumps of cells like any other tissue specimen; because they are potential human lives, they deserve some degree of respect. We believe that a regulatory system that keeps track of such embryos, permitting their use for select scientific purposes of scientific research but prohibiting their casual creation or destruction, is an appropriate way of recognizing this intermediate status. Our ethical concerns in this area relate not to embryo destruction per se as much as to other technological possibilities that are either emerging now or will appear in the coming years (see chapter 4 below).

We raise this issue not to persuade others of our case, but rather to point out that there are several deeply held alternative views on this issue, among which there is unlikely to be consensus any time in the near future. This kind of large moral question cannot possibly be delegated to a regulatory agency. They must rather be adjudicated at higher levels of the political system, in Congress and the state legislatures or, less optimally, through the court system (as has happened in the case of the legalization of abortion). Indeed, if any kind of regulatory system involving human embryos is to succeed, it is critical to fence off the realm of delegated authority from the issues of abortion and the moral status of embryos.

It is important to understand that a system to monitor and regulate biomedical research, artificial reproductive technologies, and related areas does not necessarily presuppose a particular position on the moral status of embryos. That is, such a system can be used to monitor and enforce a ban on research cloning, stem cell research, and the like, or it can be used to promote some or all of these activities.[10] The Germans and Canadians have constructed systems to do the former, while the British have constructed a system to do the latter. The institutional design of the regulatory system is in some sense independent of one's stand on the underlying moral question.

If we are to proceed with the construction of a new regulatory system, then, the political system has to make a decision on the underlying legitimacy of embryo research and the broad realms of what will be permitted and restricted in this area. These are not regulatory issues but political ones. Only when the society has made a decision on the prior question will it be possible to proceed to construct an institution capable of enforcing the agreed-upon rules.

As noted at the outset, we believe that embryonic stem cell research should proceed with federal funding, and that a new regulatory system will actually promote that end. To those opposed to any form of embryo research, we would point out that achieving their goals would require a similar type of regulatory system. The current system, in which federally funded research is restricted but private research is virtually unregulated, serves the interests of neither camp.

If at a future point the American political system decides to drop existing limits on federal funding of stem cell research, a solid regulatory system will become all the more necessary.

[10] Indeed, a regulatory system with good enforcement powers is particularly essential if the government seeks to permit some activities and restrict others.

Many people (ourselves included) are not concerned with the destruction of embryos per se, but rather with potential slippery-slope consequences of using embryos in this fashion (for example, setting a precedent for the harvesting of tissues and organs from cloned fetuses). Such concerns could be largely put to rest if embryonic stem cell research were conducted under a comprehensive regulatory framework that among other things kept track of cloned embryos to prevent them from being implanted or grown into fetuses. The minority position taken by supporters of stem cell research on the President's Council on Bioethics argued in favor of precisely such a regulatory environment.[11] While most stem cell research proponents make at least a nod to the need for a regulatory framework for embryo research, relatively few have thought seriously about the institutional design that would make this possible. It is noteworthy that Britain, with its Human Fertilisation and Embryology Authority (HFEA), has one of the world's strictest regulatory environments in this area, and yet is a leader in stem cell research.

We do not have any illusions that the American political system will produce a clear consensus one way or another on the issue of the legitimacy of embryo research, and we therefore anticipate that the kinds of regulatory changes we propose in this report will face an uphill struggle to be enacted. As in the case of other regulatory initiatives, it may take a major scandal or controversy on the order of Thalidomide or the Enron collapse to persuade the American people and Congress to act. We do believe, however, that we need to initiate a debate over the adequacy of the current regulatory system, and to begin a broad discussion of the types of institutions that will be sufficient to carry us into the twenty-first century.

[11] See President's Council on Bioethics, *Reproduction and Responsibility: The Regulation of New Biotechnologies* (Washington, D.C.: 2004).

1.6 Bibliography

Evans, John H. *Playing God? Human Genetic Engineering and the Rationalization of Public Bioethical Debate*. Chicago, IL: University of Chicago Press, 2002.

President's Council on Bioethics. *Reproduction and Responsibility: The Regulation of New Biotechnologies*. Washington, D.C., 2004.