

1 **CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS**

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3
4 NBAC was charged with the task of considering the ethical implications of human pluripotent
5 stem cell research, specifically research which uses cells derived from *ex utero*,
6 preimplantation embryos (embryonic stem cells) or from aborted fetuses (embryonic germ
7 cells), and recommending the appropriateness of federal regulation, if any, of this area of
8 study. The central controversy in this type of research arises from sharply differing moral
9 views regarding elective abortion or of using embryos for research. Indeed there has been a
10 continuing and earnest national debate on the ethical, legal, and medical issues that arise in this
11 arena. Thus, there are a number of important ethical concerns that have been identified and
12 that must be carefully weighed in deciding whether such research is appropriate and, in
13 particular, whether to use federal funds to support research that includes the use and/or
14 derivation of human embryonic stem cells. Although NBAC is aware of the existing statutory
15 and regulatory environment surrounding the use of federal funds for this area of research,
16 bioethical considerations were the primary focus of NBAC's deliberations.

17
18 The public debate surrounding the moral status of embryo research has tended to be
19 polarizing. On one side are those that would prohibit embryo research holding that it is a form
20 of homicide, because a living human embryo at this stage of development is, from a moral
21 perspective, a person. For those that hold this view, research activities that result in the
22 destruction of that embryo are morally unacceptable regardless of the potential benefits of
23 such research. On the other side of the debate are those who feel that given the prospective
24 benefits of preimplantation embryo research to cure disease, the practice raises no
25 overwhelming ethical questions. For those who hold this position, the human embryo—
26 without implantation and gestation to fetal viability—is not, from a moral perspective, a
27 person with interests to protect. These opposing positions make incommensurate the
28 alternative evaluations of the moral status of human embryos. Neither science, society, nor a
29 public bioethics body can fully reconcile the differences between opposing evaluations of the
30 moral status of the embryo.

1

2 NBAC recognizes the important moral commitments reflected within each opposing
3 position and realizes that, while society may not be able to find consensus on the foundations
4 of moral norms to guide embryo research, it is critical to explore the areas of disagreement and
5 seek compromise where possible and mutual understanding where compromise is not
6 possible. In the arena of human embryonic stem cell research society may also seek consensus
7 on certain mid-level principles (e.g., respect for embryos) and safeguards that should be in
8 place that reflect these principles before such research can go forward.

9

10 As a public bioethics body, NBAC in its deliberations and development of conclusions
11 and recommendations relied on the history of the on-going debate in the United States,
12 international experience, public input, and the best moral judgements of the commissioners.
13 The conclusions and recommendations of NBAC represent its best effort to understand these
14 various moral concerns and to incorporate these, in part, into its own consensus regarding the
15 moral status of the fetus and the embryo. From considerations of the moral status of the
16 human embryo flow some of the keys to the appropriate public policy approach to research
17 using human embryonic stem cells (whether in the public or private sector) and to questions
18 on the permissibility of and the restrictions and prohibitions on this type of research. NBAC's
19 approach seeks to balance the ethical, scientific, and medical costs of not pursuing such
20 research with the ethical, medical, and scientific benefits to proceeding with such research.
21 NBAC also recognizes that in a democracy, States often choose to embody in their laws and
22 regulations varying views of the moral status of embryos.

23

24 The question of whether federal policy ought to permit or even sponsor pluripotent
25 stem cell research is characterized by a tension between the desire for great therapeutic
26 benefits that may be derived from that research and the need to recognize that human
27 embryonic material be treated with some respect. NBAC considered it crucial in deciding the
28 ethical acceptability of human embryonic stem cell research to evaluate the clinical promise of
29 such research; specifically the possibility of cell-replacement therapy for disorders caused by
30 early cell death or injury and for expanded knowledge of normal human development. In its

1 deliberations, NBAC heard testimony from several scientists conducting work in this area as
2 well as from patient advocates and carefully considered the validity and probability of their
3 claims in terms of scientific merit and utility.

4
5 NBAC also considered the current legal and regulatory status of research using aborted
6 fetal material or *ex utero* embryos. Current federal law permits the research and therapeutic
7 use of fetal tissue under carefully regulated conditions. In the private sector current federal law
8 not only does not prohibit embryo research, but also leaves it completely unregulated.
9 Although existing federal law that prohibits the use of human embryos in federally sponsored
10 research can be interpreted to permit the use of existing human embryonic stem cells (cite
11 Rabb opinion, January 15, 1999), that legal interpretation does not address the ethical issues
12 that surround such research. For example, this interpretation does not address one way or the
13 other the issue of whether federally sponsored research, which involves the derivation of new
14 human embryonic stem cell lines, would also be legal. It is NBAC's view that there is no
15 compelling ethical justification for distinguishing between the derivation and use of human
16 stem cells.

17
18 Although law does not always fully reflect the moral beliefs and values that need to be
19 considered, the law can, in some cases, rightly be seen as reflecting society's views of what
20 might be morally permissible acts. For example, the law does not prohibit many activities and
21 choices that to some are open to serious moral challenge, such as sex selection by prenatal
22 diagnosis. For this reason there is a need for a fuller moral defense of access to donated
23 embryos for research than one afforded by either the presence or absence of a particular law.

24
25 As noted in Chapter 3, many other national commissions and advisory bodies have
26 addressed some of the questions NBAC takes up in this report. Indeed, in 1989 the Canadian
27 Royal Commission on New Reproductive Technologies identified several guiding principles
28 and values that NBAC also found useful in developing its conclusions, as well as its
29 framework for its own recommendations. They include:

30

- 1 • respect for human life and dignity
- 2 • the quality, including safety, of medical treatment
- 3 • respect for free and informed consent
- 4 • minimizing harm and maximizing benefit
- 5 • the relief of human suffering
- 6 • freedom of research
- 7 • non-commercialization of reproduction-

8

9 **Sources of Stem Cells**

10

11 NBAC believes it is useful to focus its ethical analysis on the various sources of human
12 embryonic stem cells because it is the origins of the cells, not their use, that is at the center of
13 controversy about the ethical acceptability of proceeding with such research. Despite the
14 enormous scientific and clinical potential offered by research use of human pluripotent stem
15 cells derived from various sources, many find certain sources more ethically problematic than
16 do others. In this sense, NBAC's recommendations reflect to some extent a respect for the
17 differing views of society in that even among commissioners there were not uniform views on
18 the relative ethical acceptability of the derivation and use of such cells from various sources.

19 These sources include:

- 20 1. those derived from human fetal tissue following elective abortion;
- 21 2. those derived from human embryos available in excess of clinical needs to treat infertility
22 by *in vitro* fertilization (IVF);
- 23 3. those derived from human (or hybrid) embryos generated asexually by somatic cell
24 nuclear transfer (SCNT) or similar cloning techniques (using enucleated human or animal
25 ova); and
- 26 4. those derived from human embryos made from donated gametes for the sole purpose of
27 research.

28

29 Although each source of stem cells poses its own scientific, ethical, and legal
30 challenges, much of the ethical analyses are dependent on the scientific necessity of using a

1 specific source. NBAC recognizes that it is possible that each source could eventually be
2 important to research and clinical application because of, for example, their differing
3 proliferation potential, their differing availability and accessibility, their differing ability to be
4 manipulated, and possibly significant differences in cell biology. However, because of some of
5 the unresolved ethical difficulties, NBAC believes that the scientific and clinical import of
6 these differences needs fuller exploration before justifying federally funded research access to
7 all sources of these cells. Until more research is conducted, determinations of clinical and/or
8 research need for each source should be based on future results using non-human animal
9 models. Scientists agree, for example, that the most immediate scientific uses of human
10 pluripotent stem cells can be satisfied by the derivation and use of cell lines derived from fetal
11 tissues (which is already legal in both the public and private sectors) and from embryos
12 remaining after infertility treatments.

13

14 It is possible that eventually pluripotent stem cells isolated from SCNT-generated
15 human embryos will be needed to study differences, if any, between cell lines grown from
16 cells derived from fetal material and donated embryos. Moreover, it is possible that embryos
17 produced by cloning technology, using the somatic cells of patients, will be needed to study
18 the feasibility of autologous cell replacement therapy and to avoid the graft vs. host reaction.
19 NBAC also recognizes that embryos made via *in vitro* fertilization specifically as a source of
20 pluripotent stem cells might be needed to create banks of multiple cell lines representing a
21 spectrum of alleles for the major histocompatibility complex. This goal might require that ova
22 and sperm of persons with specific genotypes be selected to make embryos from which to
23 derive particular stem cells.

24

25 Finally, although much promising research is currently being conducted with stem
26 cells obtained from adult organisms, studies in animals suggest that this approach will be
27 scientifically and technically limited, and in some cases, the anatomic source of the cells might
28 preclude easy or safe access.

29

1 In NBAC’s view, the most immediate uses of pluripotent stem cells in research are
2 consequent to derivation from fetal material and embryos remaining after IVF treatment.
3 Future uses of such cells derived from embryos produced via SCNT or IVF for research
4 purposes only are related to the pace of scientific advances. NBAC notes that a responsible
5 federal science policy does not necessarily require public funding for access to all sources of
6 pluripotent stem cells at this time.

7

8 ***Fetal Tissue***

9

10 ***Conclusion: Research involving the derivation and use of human stem cells obtained***
11 ***from fetal tissue should continue to be eligible for federal funding.***

12

13 ***Recommendations:***

14

15 ***Such research should be conducted only under appropriate oversight and institutional***
16 ***review, a comprehensive framework for which is already in place in this country.***

17

18 ***Clarification of current laws—{Note: please see attached memorandum from J.Kyle***
19 ***Kinner that follows this chapter}***

20

21 Research that uses tissue from aborted fetuses is analogous to the use of fetal tissue in
22 transplantation. Although abortion remains a highly contentious issue in our society, NBAC
23 concludes that the use of fetal tissue to obtain stem cells for research is less problematic than
24 the similar use of human embryos for four reasons. First, the removal of the fetal germ cells
25 does not occasion the destruction of a live fetus. fetus. Second, fetal tissue is not intentionally
26 or purposefully created for research. Third, the use of fetal tissue to develop therapies for
27 people unrelated to reproduction has been raised before in the context of fetal tissue
28 transplantation, and therefore a number of laws and policies exist regarding this use. Fourth,
29 there is considerable, although not uniform agreement in the United States and in the

1 international research community that the use of fetal tissue in therapy for people with
2 diseases, such as Parkinson’s disease, is acceptable.

3

4 Prior moral opposition to fetal tissue transplant research, because of its association
5 with abortion, helped shape a system of safeguards to prevent widening or encouraging the
6 social practice of abortion. These rules require that the consent process about abortion
7 decisions must precede and be conducted separately from the consent process to donation of
8 fetal tissue for transplant research. Although some contest it, there is a sufficient moral
9 consensus that society ought to respect the autonomous choices to donate fetal tissue for
10 research of women who have made legal abortion decisions. If women have a liberty right to
11 make abortion choices, it follows that the self-determination or autonomy expressed in that
12 right extends to the choice to donate fetal tissue for research.

13

14 Other existing rules prohibit designated donation, monetary inducements to women
15 undergoing abortion, and buying or selling fetal tissue. Existing policies state that there be no
16 for-profit trade be permitted in fetal tissue and some recommend that the “prohibition on
17 commercial exchange of fetuses and fetal tissue extend to tissues imported from other
18 countries.”¹ This prohibition is in place to prevent the exploitation of poor women, especially
19 in developing countries, who might be persuaded to begin and end pregnancies for money.² :
20 In NBAC’s view, there is an important distinction to be made between the possible
21 exploitation (or commodification) of persons that occurs when individuals are coerced or
22 inappropriately induced to give over parts of themselves for money, and the exchanges that
23 occur when companies, research institutions, or other groups provide reasonable
24 compensation. This issue is a familiar one in discussions about remuneration for participation
25 in research, and about which Federal regulations rightly defer to IRBs for their judgment [cite
26 regs]. The difference, of course, is the potential for exploitation may be greater given the
27 commercial value of the tissue and stem cells derived therefrom.

28

¹ *Proceed with Care*, at 1003.

² *Proceed with Care*, at 1001.

1 Due to the contentious and polarizing nature of the abortion debate in the United
2 States, over a decade ago legal restrictions were enacted which blocked the use of fetal tissue
3 in research on transplantation therapy. Until 1993, the only permissible source of tissue for
4 such research was tissue from spontaneously aborted fetuses or ectopic pregnancies—sources
5 that were largely unsuitable for research. In 1993, President Clinton lifted the ban on the use of
6 fetal tissue from elective abortions for fetal tissue transplantation research. Consequently,
7 there are no legal prohibitions that would inhibit the use of that tissue for pluripotent stem cell
8 research.³

9
10 In NBAC’s view, society ought not to forgo the biomedical knowledge or therapeutic
11 benefits to persons of uses of transplants with fetal tissue obtained after legal elective
12 abortions. The consequences of forgoing benefits from using fetal tissue are harmful, and the
13 consequences of using it are almost always worthy for science and patients. Also, unless the
14 tissue is used in research, it will otherwise be discarded. In view of this risk of lost
15 opportunity, and since elective abortions that open access to fetal tissue are legal, no
16 overriding reason compels society to forgo this opportunity to benefit science and suffering
17 persons.

18
19 NBAC concurs with the intent of these safeguards and believes they should apply to
20 research in which stem cells are obtained from aborted fetuses. *[need for additional*
21 *protections?]*

22

23 ***Embryos Remaining After Infertility Treatments***

24

³ Use of fetal tissue in research is also permitted in Canada, the United Kingdom, Australia, and in most countries in the European Union. Germany for example does not permit embryo research but does permit the use of fetal tissue for the derivation of germ cells. The DFG [SPELL OUT] statement concerning human embryonic stem cells upholds the ban on destructive embryo research effectively banning the derivation of hES cells because the option of deriving hEG cells exists in that country. See DFG Statement concerning question of human embryonic stem cells, March 1999 at 8-10.

1 ***Conclusion: Research involving the derivation and use of stem cells derived from***
2 ***embryos remaining after infertility treatments is ethically acceptable for federal***
3 ***funding, given an appropriate framework for oversight and review.***

4
5 ***Recommendations:***

6
7 ***Congress should rescind in part its ban on the use of Federal funds to conduct***
8 ***research using embryonic stem cells.***

9
10 ***Congress should rescind in part its ban on the use of Federal funds to support***
11 ***research involving the derivation and use of embryonic stem cells.***

12
13 ***Federal agencies supporting research in this area should develop and maintain a***
14 ***system of national and local review of such protocols.***

15
16 The current congressional ban on embryo research prohibits federal support of any
17 research “in which a human embryo...[is] destroyed, discarded, or knowingly subjected to
18 risk of injury greater than that allowed for research on fetuses in utero..”⁴ The term “human
19 embryo” in the statute is defined as “any organism. . .that is derived by fertilization,
20 parthenogenesis, cloning, or any other means from one or more human gametes or human
21 diploid cells.” The ban is transitory in the sense that it is revisited each year when the language
22 of the NIH appropriations bill is considered.

23
24 The ban, which only concerns federally sponsored research, reflects a moral point of
25 view that either embryos deserve absolute protection from society because of their moral
26 status as persons, or that there is sufficient public controversy that federal funds should not be
27 used for this type of research. However, some effects of the embryo research ban raise serious

⁴ Pub. L. No. 105-78, 513(a) (1997).

1 moral and public policy concerns for those who hold opposing views of the ethics of embryo
2 research. In NBAC's view, the ban conflicts with several of the ethical goals of medicine,
3 especially healing, prevention, and research—goals which are rightly characterized by the
4 principles of beneficence and nonmaleficence, jointly encouraging the pursuit of each social
5 benefit and avoiding or ameliorating potential harm.

6

7 While it is sometimes the practice in the United States to resolve some moral
8 disputes—especially about human reproduction—by denying federal funding (e.g., elective
9 abortion, embryo research) yet not interfering with the activity in the private sector, the ban
10 has discouraged the development of a coherent public policy not only on embryo research but
11 on health research more generally. There is a widespread practice of unregulated investigative
12 embryo research on the fringes of public life. At best, these activities are guided by traditions
13 of self-regulation in science and medicine. The ban may also have larger effects on the other
14 areas of research currently supported by the federal government, and in so doing raises
15 concerns about the distribution and allocation of federal research resources. For example, by
16 limiting the Federal government's ability to fund promising areas of basic research, a ban on
17 embryo research could prevent promising, collaborative studies in other areas, such as
18 infertility, cancer, and genetics. NBAC recognizes that many factors affect how federal
19 research priorities are set in this country. However, in NBAC's view, the intentional
20 withholding of federal funds for research that may lead to promising treatments may be
21 considered unjust or unfair. *[This idea needs discussion. In addition, here would be the*
22 *opportunity to say more about the public/private issues]*

23

24 Although there is no consensus about the moral status of the embryo, there is
25 agreement that if research is permissible, some limitations and/or regulations are necessary
26 and appropriate. As such, this regulation of research reflects an appreciation of the disparate
27 views about the acceptability and unacceptability of embryo research and are a means of
28 providing accountability, allaying public anxiety, promoting beneficial research, and
29 respecting the connection between human embryos and the rest of the human community. As
30 one commentator has noted, these limits represent both acknowledgments that public fears are

1 respected and are a “sign of respect for the special status of the embryo without the ethical
2 and medical costs of an outright ban.”⁵

3

4 ***Need for Informed Consent***

5 To allow the use of donated embryos in research, informed consent is required. First, it
6 reflects the importance placed on respecting the autonomous choices of individuals. This
7 choice includes not donating embryos for research, donating the embryos to another couple
8 for implantation, discarding the embryos, or having them stored for a period until a decision
9 can be made. Second, it reflects a desire to protect vulnerable people, including patients
10 undergoing infertility treatment who may be subject to emotional stress. Informed consent
11 functions in this way by giving individuals and couples the opportunity to weigh their present
12 situation and needs against any future desires or preferences. Not only is the consent form a
13 method of providing information, but so too is the consent process (including when couples
14 are presented with this option, and how much time they have to think about it).

15

16 Respect for the autonomous choices of donors of embryos also favor allowing access
17 to these materials. Parents who donate embryos may want to contribute to knowledge about
18 infertility, cancer, and genetic disorders. These altruistic motives deserve recognition as do the
19 procreative intentions that caused the original creation of the embryos. Moreover, IVF
20 embryos are generated by decisions of couples who care about their embryos and would want
21 the right to make decisions about options for disposition. These embryos, therefore, exist
22 within a web of caring relationships and are not isolated “research material.” ***[Other specific***
23 ***recommendations to be added]***

24

25 ***Recommendation: Individuals (or couples) receiving infertility treatments should be given***
26 ***the opportunity to consent to the research use of embryos remaining only after the***
27 ***infertility treatments have ceased.***

28

⁵Lori B. Andrews and Nanette Elster, *Cross Cultural Analysis of Policies Regarding Human Embryo Research*,

1 *Embryos Made for Research Purposes*

2

3 *Conclusion: At this time, there are no compelling reasons to provide federal funds*
4 *for the purpose of making embryos specifically for the generation of stem cells.*

5 *More research should be done on pluripotent stem cells derived from aborted*
6 *fetuses and embryos remaining after infertility treatment to determine the extent of*
7 *the need of these additional sources of embryos for research.*

8

9 Stem cells can be derived from human (or hybrid) embryos generated asexually by
10 somatic cell nuclear transfer (SCNT), using enucleated human and perhaps animal ova for
11 fusion, or through traditional IVF. The primary objection to creating embryos specifically for
12 the purposes of research is that there is a qualitative difference between creating an embryo,
13 which may have a chance of implantation, and creating embryos without even that chance of
14 implantation. Objections about creating embryos for research often appeal to arguments about
15 respecting human dignity by avoiding instrumental use of human embryos: using embryos
16 merely as a means to some other goal treats them without respect or concern. For example,
17 creation of embryos without the intention of implanting them is argued by some to be
18 disrespectful.

19

20 *Use of Somatic Cell Nuclear Transfer to Obtain Stem Cells*

21 The product of SCNT cloning (using an enucleated human egg) is clearly a human
22 embryo. To date, however, little is known scientifically about cloning as a source of human
23 stem cells although there is reason to believe there is therapeutic potential to their use. The use
24 of SCNT to make an embryo is arguably different from all the other cases considered by
25 NBAC due to the asexual origin of the source of the stem cells, although a form of donation is
26 involved. Producing embryos by SCNT for the purposes of obtaining stem cells would be
27 done to promote clinically promising research to help human beings, which is a very different

at 11 quoting John Robertson.

1 case from the original intent with which embryos are made, for the purposes of treating
2 infertility.

3

4 *Use of IVF to Make Embryos to Obtain Stem Cells*

5 Stem cells can be derived from human “research” embryos created from donor
6 gametes for the sole purpose of deriving such cells for research. Although the result is the
7 same—research involving human embryos—this source has an important and morally
8 relevant difference from aborted fetuses and excess embryos, i.e., the deliberate creation of
9 embryos for research from donated gametes. The donors may be individuals or couples,
10 depending upon the circumstances.

11

12 In 1994, the NIH Human Embryo Research Panel argued in support of Federal funding
13 of this option in exceptional cases, such as the need to create banks of cell lines from different
14 genotypes that encoded different transplantation antigens, the better to respond, for example,
15 to the transplant needs of groups with different genetic profiles. This would require
16 recruitment of embryos from genetically diverse donors.

17

18 When deciding how to deal with this issue, there are a number of points to keep in
19 mind. First, it is possible that the creation of such embryos provides the only way to conduct
20 certain research, such as research on the process of human fertilization. Second, as techniques
21 for IVF improve it is possible that the need to create surplus embryos will be eliminated; one
22 of the frequently approved uses of embryo research is the improvement of IVF techniques.⁶
23 As this happens, and if embryo research is dependent on the existence of embryos remaining
24 following infertility treatments that are donated with informed consent, it is possible that the
25 supply of embryos for research will dwindle.

26

⁶ The *Warnock Report* echoes this thought “A further argument for the generation of embryos for research is that as the techniques of freezing become more successful there would be fewer spare embryos available for research.” at 68.

1 *The Need for National Oversight and Review*

2 Several countries have recommended the establishment of a regulatory board or
3 national commission to license and regulate assisted reproductive treatments and embryo
4 research. The United Kingdom uses such a method. Although national oversight of this kind
5 has certain advantages, the use of law to regulate (rather than set limits) in this area would be
6 inappropriately burdensome given the rapid development in uses of technologies. A national
7 commission or authority would provide flexibility and adaptability and relieve the need to
8 campaign for removal of legislative bans and prohibitions as technologies and attitudes
9 change.⁷ In addition, national regulation ensures more consistent application of safeguards
10 and can ensure greater public accountability and transparency.⁸ One of the principal benefits
11 of federal funding of biomedical and behavioral research is the reliance on a system of public
12 oversight and review.

13

14 The need for national as well as local oversight of stem cell research is crucial. No
15 such system currently exists in the United States with reliance placed on a system of review by
16 local institutional review boards (IRBs). The ability of IRBs to adequately assess the scientific
17 merit and ethical acceptability of stem cell protocols given their time and resources is surely
18 limited. A national review mechanism, which reviewed not only stem cell research but also of
19 the research protocols using human embryos would ensure strict adherence to guidelines and
20 standards across the country. Thus, federal oversight can provide the public with the assurance
21 that research involving stem cells is being undertaken appropriately. Other mechanisms are
22 provided for by individual agencies supporting or conducting research and through the
23 activities of OPRR and the FDA.

24

25 In 1994 the NIH Human Embryo Research Panel considered and then explicitly
26 rejected reconstituting the Ethics Advisory Board for the purpose of reviewing proposals
27 involving embryos or fertilized eggs:

⁷This is the recommendation of the Canadian Royal Commission and the system used by the United Kingdom Human Fertilisation and Embryology Authority.

⁸*EGE Opinion* at Art. 2.11. See also the Australian *NHMRC Guidelines* advocating complementary national ART standards or legislation be adopted in the Australian States.

1
2 Although revisiting the EAB experience offers the potential for public consensus
3 development and a consistent application of the new guidelines, it nonetheless has
4 significant disadvantages. These include the creation of an additional standing government
5 board, the likelihood of significant delay before embryo research could be funded in order
6 to meet legal requirements for new rulemaking prior to the official creation of the
7 government body, and possible further delay if all proposals for embryo research were
8 required to be considered individually by an EAB-type board, despite appearing to be
9 consistent with a developed consensus at NIH about acceptability for funding” (HERP, p.
10 72).

11
12 Instead, the NIH panel recommended that “national review of all protocols by a
13 diverse group of experts is warranted for a time. It is the hope of the Panel that this ad hoc
14 group will develop additional guidance gained from experience with actual protocols that can
15 be communicated to IRBs through existing mechanisms at NIH” (HERP, p. 73).

16
17 These recommendations envisioned a time when, following sufficient experience by
18 the ad hoc panel, guidelines for embryo research review could be decentralized to the local
19 IRB. (The ad hoc panel was recommended to function for at least three years). NBAC used
20 similar reasoning in a previous report when recommending that the Secretary of Health and
21 Human Services convene a Special Standing Panel to review certain categories of research
22 involving persons with mental disorders (NBAC, 1998, Recommendation 2). Like the NIH
23 panel, NBAC did not specify when such guidelines could be decentralized; but unlike the NIH
24 panel, NBAC recommended that the panel be standing, not an ad hoc body.

25
26 The NIH panel’s recommendations need to be viewed in the context of its reporting
27 relationship: its charge was to advise the NIH Director about research that could be sponsored
28 or conducted by NIH. NBAC notes, however, that NIH is not the only agency in the Federal
29 Government that might be interested in sponsoring or conducting research involving human

1 stem cells, thus there must be some accommodation for review of proposals not funded by
2 NIH.

3

4 Other elements of the NIH panel's recommendation, however, require more
5 assessment. For example, it recommended that

6

7 "once the ad hoc panel completed its tasks, research involving pre-implantation embryos
8 and fertilized ova will be subject to all the ordinary and routine forms of review necessary
9 for NIH-sponsored research. These include review by a local IRB, an NIH study section
10 committee, and the council for each of the institutes...The Panel recommends that all
11 such research proposals continue to be specially monitored by the councils and the NIH
12 Office for Protection from Research Risks." (HERP, p. 74).

13

14 NBAC is less sanguine than the NIH panel about the ability of OPRR to provide the
15 needed oversight and monitoring for stem cell research at this time. Given the moral issues
16 involved in stem cell research—where heightened sensitivity about the very research itself led
17 the President to request that NBAC study the issue—the public and the Congress must be
18 assured that oversight can be accomplished efficiently, constructively, and in a timely fashion.
19 Moreover, since OPRR only has jurisdiction over those agencies and departments with whom
20 an Assurance of Compliance has been negotiated, and since only 17 Federal Agencies have
21 agreed to be bound by the Common Rule, it is unlikely that OPRR and the FDA can exercise
22 thorough, consistent and timely oversight and monitoring. While OPRR's role in the oversight
23 of human subjects research, like that of the FDA remains a central pillar in the structure of
24 human subjects protections in this country, NBAC believes that an additional mechanism is
25 necessary for review and oversight of research involving human stem cells.

26

27 NBAC shares the concern of the NIH panel, investigators, and IRBs that the process of
28 protocol review should not be seen simply as a bureaucratic hurdle that researchers must
29 successfully navigate solely to satisfy a procedural or regulatory requirement. Done well,

1 protocol review often improves the quality of studies by pointing to concerns in the design,
2 selection of subjects, recruitment, informed consent, and dissemination of results.

3
4 NBAC has developed a set of *Points to Consider* that might be used to review basic
5 research involving human stem cells. [See Box XX]. These *Points to Consider* are not
6 presented not to prejudge the question of whether human stem cell research should be
7 performed. Rather, this document describes the ethical, clinical, scientific, and legal
8 considerations that could be considered when designing studies that involve access to and use
9 of human stem cells. These *Points to Consider* would only be used for considering studies
10 where the role of the individual who provides gametes, fetuses or embryos is limited to that of
11 provision or donation of the sources of materials for such research intending to develop
12 generalizable, new knowledge. These *Points to Consider* do not apply to situations in which
13 an individual would be the recipient of a stem cell-based therapy, nor do they apply to studies
14 involving human/animal hybrids.

15
16 *Recommendations Regarding Oversight and Review*

17
18 *Recommendation: Review of research protocols using federal funds involving the use and/or*
19 *derivation of human pluripotent stem cells must should by conducted by an Institutional*
20 *Review Board, with the sufficient expertise to assess the scientific merit and ethical*
21 *acceptability of the protocol. Approval of such protocols should be contingent on the*
22 *following:*

- 23 a) *The IRB must apply to the Ethics Advisory Board (see recommendation xx), and be*
24 *granted approval to review protocols involving human pluripotent stem cells. Approval*
25 *will be granted once the EAB has been assured that the institution will adopt as policy*
26 *the following procedures:*
- 27 • *the IRB will make publicly available brief descriptions of the policies and procedures*
28 *that characterize its ongoing work*
 - 29 • *the IRB shall publish and use a set of criteria, or “Points to Consider” that it will use to*
30 *assist its deliberations about research protocols involving human pluripotent stem cells.*

- 1 • *the IRB shall provide, on an annual basis appropriate summary statistics regarding the*
 2 *nature and scope of the protocols it has approved*

3
 4 *Recommendation: Each institution receiving federal funds for research involving human*
 5 *pluripotent stem cells shall adopt appropriate internal and external audit procedures to*
 6 *assure itself that its IRB (or IRBs) are in compliance with the Federal Policy for the*
 7 *Protection of Human Subjects*

8
 9 *Recommendation: The Ethics Advisory Board shall be reconstituted in statute to provide*
 10 *advice and make recommendations regarding the following activities:*

- 11 *a) to review applications by Institutional Review Boards [or Institutions] who wish to*
 12 *review protocols involving human pluripotent stem cells, and to determine whether the*
 13 *conditions for an IRB have been met (See recommendation xx)*
 14 *b) to evaluate, after a suitable period of time, not to exceed five years, the impact,*
 15 *importance, and value of human pluripotent stem cell research*
 16 *c) to provide oversight and monitoring of those IRBs that review protocols involving*
 17 *human pluripotent stem cells. [Need to decide how EAB would work with OPRR/FDA etc.*
 18 *who have regulatory authority]*

19 BOX

20 Points To Consider

21 In Evaluating Basic Research Involving Human Stem Cells

22
 23 The following *Points to Consider* are presented not to prejudge the question whether human
 24 stem cell research should be conducted using federal funds. Rather, this document describes
 25 some of the ethical, clinical, scientific, and legal issues that could be considered when
 26 designing and/or reviewing studies that involve access to and use of human stem cells. These
 27 *Points to Consider* are only relevant for designing and evaluating studies where the role of the
 28 individual(s) who provide gametes, fetal tissue or embryos is limited to providing these
 29 materials for research that is intended to develop generalizable new knowledge. *These Points*
 30 *to Consider do not apply to situations in which an individual would be the recipient of a*
 31 *stem cell-based therapy, nor do they apply to studies involving human/animal hybrids.*
 32
 33

1 I. Scientific and Research Design Considerations

2
3 Several issues arise when designing research involving human stem cells, consideration of
4 which would help ensure that research is well-designed, important, feasible, and timely. These
5 issues are of particular significance given the nature of the materials.

6
7 A. The Source From Which The Human Stem Cells Will Be Obtained

- 8 1. From existing cell lines (such as neuronal or hematopoietic stem cells)
9 2. From aborted fetal tissue (following spontaneous or induced abortion or surgical
10 termination of ectopic pregnancy)
11 3. From stored/spare embryos obtained from infertility treatment
12 4. From embryos produced for research purposes (including somatic cell nuclear
13 transfer)

14
15 B. Previous Research Involving Animals

16
17 C. Alternatives To Using Human Stem Cells

18
19 D. Future Plans And Conservation Of Gametes, Fetal Tissue, and Embryos

- 20 1. Will stem cells be produced and stored for later use?
21 2. If a particular protocol is being proposed using stored embryos, does it use only
22 the number of embryos necessary?
23 3. What plans exist in the event that additional stem cells are needed?
24

25 E. The Research Setting

- 26 1. Are the investigators scientifically qualified to carry out the proposed research?
27 2. Is the research environment (including facilities) appropriate for the conduct of
28 research involving stem cells?
29
30

31 **II. Identification of Providers and Donors, Recruitment Practices, and**

32 **Compensation**

33
34 Several issues in identifying individuals (or couples) who may be asked to consider
35 providing gametes, fetal tissue, or embryos for research involving human stem cells,
36 consideration of these issues could help to ensure that no inappropriate burden,
37 inducement or exploitation would occur.
38

39 A. Identification And Recruitment Practices

- 40 1. Are potential donors or providers identified through advertisements to the general
41 public? Are they identified through direct solicitation? Do they self-select?
42 2. Is the selection of such individuals equitable and fair?

- 1 3. Are these individuals vulnerable to undue influence, coercion or exploitation? Does
- 2 the recruitment method raise concerns about undue influence or coercion of the
- 3 prospective donors? embryos?
- 4 4. Are the potential donors capable of giving an informed consent?
- 5 5. In which circumstances is it appropriate to identify and recruit an individual as well
- 6 as his or her partner?

7

8 B. Compensation And Reimbursement

- 9
- 10 1. Will any financial compensation be paid to individuals (or couples) who provide
- 11 source material ?
- 12 2. Does the compensation exceed the costs already being incurred (for example,
- 13 the cost of embryo storage)? Will this fact be disclosed?
- 14 3. Does the compensation reimburse the individual (or couple) for specific services
- 15 (e.g., gametes, infertility services)?
- 16 4. When is the offer of compensation made relative to individual's (or couple's)
- 17 decision to make available the materials from which stem cells will be derived?
- 18

19 III. Informed Consent

20

21 Several issues arise in the process of informed consent (including the content of consent

22 forms); considering these issues would help to ensure that ensure prospective donors or

23 providers of source materials would receive timely, relevant and appropriate information to

24 make informed and voluntary choices

25

26 A. General Considerations For Individuals (or Couples) Who Provide Gametes, Fetal

27 Tissues or Embryos

- 28
- 29 1. Who will obtain informed consent? Will a clinician and researcher be available to
- 30 answer questions?
- 31 2. Is it appropriate for others to participate in the consent process (e.g., partner or
- 32 family member)?
- 33 3. Will psychological support mechanisms be in place when needed?
- 34 4. Are the purposes of stem cell research (in general) fully described?
- 35 5. If a specific research protocol is being contemplated with stem cells obtained, is
- 36 the protocol fully described?
- 37 6. What are the possible risks to the woman (or partner) from the procedure to
- 38 obtain stem cells, and how will these be minimized?
- 39 7. Will the consent form clearly disclose that stem cell research is not intended to
- 40 benefit them directly?
- 41 8. Is it clear that decisions to consent to or refuse the procedures to obtain stem
- 42 cells will not enhance the quality of care they will receive?

- 1 9. Will individuals be informed that no medical or genetic information about the
- 2 gametes, fetal tissue, embryos, or stem cells derived from these sources will be
- 3 provided?
- 4 10. What measures will be taken to protect the privacy and confidentiality of
- 5 individuals who provide gametes, fetal tissue or embryos?
- 6 11. Is the source of funding for research (public, private, public/private,
- 7 philanthropic) disclosed?
- 8 12. What known commercial benefits, if any, are expected to arise for the
- 9 investigators seeking to obtain human stem cells?

10
11 B. Issues Specific To Consenting To The Use of Fetal Tissue

- 12
- 13 1. Is there a description of what is usually done with fetal tissue at the institution at
- 14 which individuals are undergoing termination of pregnancy? Is this information
- 15 available in written form and provided to the individuals?
- 16 2. Is there a description that the decision to permit research will entail that research
- 17 may begin immediately.

18
19 C. Issues Specific To Consenting To The Use of Embryos Obtained From Infertility

20 Treatments

- 21
- 22 1. Is there a description of what is usually done with spare embryos at the institution
- 23 at which individuals are undergoing infertility treatment? Is this information
- 24 available in written form and provided to the individuals?
- 25 2. Will information be made available about whether the spare embryo was viable
- 26 and normal or non-viable and abnormal?
- 27 3. Is there a description of options available (e.g., permit material to be used in
- 28 research, cryopreserve, discard, donate to another couple for infertility treatment)?
- 29 4. Is it clear that the embryos used in research will not, under any circumstances, be
- 30 transferred to any woman's uterus?
- 31 5. Is it clear that the research will result in the destruction of the embryo? Is the
- 32 method described?

33
34 D. Issues Specific To Consenting To The Use of Gametes⁹

- 35
- 36 1. Will individuals be informed whether embryos will be produced with the
- 37 gametes (e.g., using *in vitro* fertilization, or somatic cell nuclear transfer?)
- 38 2. Is there a description of what is usually done at this institution with gametes not
- 39 used for research?

⁹ Note: For persons who provide sperm anonymously, the details of the consent form and the specificity of the informed consent process may vary—EMM 2/15/99

- 1 3. Is there a description of options available (e.g., permit materials to be used in
2 research, cryopreserve, discard, donate to another couple for fertilization and
3 transfer)?
- 4 4. Is it clear that the embryos produced for research purposes (whether by IVF or
5 somatic cell nuclear transfer) will not, under any circumstances, be transferred to
6 any woman's uterus?
7

8 IV. Review Issues

9 Several issues arise in the review and oversight of research involving human stem cells;
10 consideration of these issues will provide assurance that, regardless of the source of funding,
11 appropriate compliance with applicable regulations, guidelines and other standards will occur.
12 These considerations would supplement, not replace, applicable federal and state regulations.

13 A. Applicability of Relevant Regulations

- 14 1. What current guidelines, regulations, rule, or policies apply to the conduct of this
15 research?
- 16 2. What mechanisms are in place to assure compliance with these regulations?
17
- 18 3. **Relevant international regulations**
- 19

20 B. Applicability of Professional Practice Standards

21 C. IRB Review

22 D. Submission of Research Findings for Publication

23 E. Other Responsibilities of Investigators and Collaborating Clinicians

24
25
26
27