Accountability in Research, 13:207–224, 2006

ISSN: 0898-9621 print / 1545-5815 online
DOI: 10.1080/03605300600848136

HUMAN EMBRYONIC STEM CELL RESEARCH: AN ARGUMENT FOR NATIONAL RESEARCH REVIEW

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The US National Academy of Sciences (NAS) recently published voluntary guidelines for human embryonic stem (hES) cell research. The NAS guidelines propose two levels of oversight. At the local level, research institutions are to create Embryonic Stem Cell Research Oversight (ESCRO) committees with a mandate to assess the scientific merit and ethical acceptability of hES cell research. At the national level, a new committee is to be created, not to review specific research proposals, but rather to periodically assess, and as needed revise, the NAS guidelines. In this article, we critically assess this proposal. In particular, we review the benefits and limitations of local research review. On this basis, we argue that local review is insufficient for hES cell research and that while there are obvious pragmatic and political reasons for the NAS to favor local research review, there are more compelling reasons for the NAS to have recommended national review of hES cell research proposals.

Keywords: *research ethics, research ethics committees, stem cells, IRB, public policy*

Introduction

The United Kingdom (1990) and Canada, (2004; Canadian Institutes of Health Research, 2006) among other jurisdictions, have determined that human embryonic stem (hES) cell research is sufficiently complicated and ethically controversial so as to

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warrant national oversight and special research licenses (Kimmelman et al., 2006; Johnston, 2005). In the UK, for example, national oversight and research licenses are provided by the Human Fertilisation and Embryology Authority, while in Canada this is the responsibility of the Assisted Human Reproduction Agency.

Against this international backdrop, and in the absence of a federal regulatory system for hES cell research in the United States,[1] the U.S. National Academy of Sciences (NAS) recently published voluntary guidelines for hES cell research (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005). The NAS guidelines propose two levels of oversight. At the local level, research institutions are to create Embryonic Stem Cell Research Oversight (ESCRO) committees. These committees are to provide project specific scientific and ethics review of hES cell research, as well as general oversight of research involving the derivation and use of hES cells. This review is in addition to (and should not duplicate or interfere with) research review currently provided by local Institutional Review Boards (IRBs) and, where appropriate, Institutional Animal Care and Use Committees (IACUCs) (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005, p. 53). In addition to research review, ESCRO committees are to ensure compliance with all relevant regulations as well as the NAS guidelines, to monitor ongoing research, and to educate researchers involved in hES cell research (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005, p. 53).

At the national level, a new committee is to be created "to assess periodically the adequacy of the guidelines proposed in this [NAS] document and to provide a forum for a continuing discussion of issues involved in hES cell research" (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005, p. 59). Importantly, the proposed national oversight mechanism explicitly excludes scientific and ethics review of research proposals:

[1]In the U.S., ethics and science review of federally funded research is the responsibility of IRBs, as specified in federal regulations (45 CFR 46.103, 21 CFR 56.103). Research to derive hES cells is not federally funded, however, and thus not subject to IRB review. In 2001, President Bush prohibited the use of federal funds to derive hES cell lines (Bush, 2001). Further, IRB review of research involving existing hES cell lines is not required because this is not human subjects research as specified in the regulations (Office for Human Research Protections, 2002).

" . . . some [national] entity needs to be established to review the policies and guidelines covering appropriate practices in this field but not to review and approve specific research protocols, an activity that will best occur at the local institutional level" (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005, pp. 58–59).

The proposed division of labor between local research review of protocols and national review of research policies and guidelines marks a significant and noteworthy departure from international policy and practice regarding hES cell research — in several jurisdictions around the world, national committees are responsible for the research review of specific protocols. The NAS explains its preference for local research review with reference to perceived differences in policy contexts between the US and other jurisdictions. The NAS guidelines state:

> . . . national bodies [to review and approve specific research protocols] have been established in most other countries where hES cell research has been debated and approved — such as Australia, Canada, Israel, Singapore, and the United Kingdom . . . — usually under government auspices. Some of those bodies also have responsibility for reviewing individual research proposals, and such centralized review entities may serve well in smaller jurisdictions where public funds are being used in the research. (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005, p. 59)

The suggestion here is that in comparably smaller jurisdictions where publicly funded hES cell research is underway, government-authorized national research review may be possible and appropriate, but not so in the US.

Significantly, the proposed division of labor is not only a departure from international policy and practice, it is also a departure from prior US recommendations for national research review. In 1994, the National Institutes of Health (NIH) Human Embryo Research Panel recognized certain limitations with local IRB review and recommended "an additional review at the national level by an ad hoc body created with the discretionary authority of the Director of the NIH . . . " (NIH, 1994, p. xvi). Similarly, in 1999 the National Bioethics Advisory Commission (NBAC) called for a National Stem Cell Oversight and Review Panel "to review protocols for the derivation of embryonic stem (ES) and embryonic germ (EG) cells and approve those that meet the requirements

described in this report" (1999, 76). The NAS guidelines (perhaps unwittingly) mask the departure from these and other recommendations in suggesting that the guidelines are consistent with longstanding practice in human subjects research in the U.S.:

> . . . in line with the longstanding practice in the United States of using local review boards for human subjects research, . . . the committee believes that local review of individual research proposals by ESCRO committees . . . will be the best mechanism of oversight of hES cell research. (Committee on Guidelines for Human Embryonic Stem Cell Research, 2005, p. 59)

In this statement, the NAS also neglects equally longstanding (though admittedly limited) practice involving national review of complex, novel, and ethically contentious research, (e.g., Recombinant DNA Advisory Committee). In so doing, the NAS erroneously invokes current practice to promote the view that what is the case should be the case.

While it is undeniably true that the current research review system in the U.S. relies on local, institutional review and oversight the NAS could have concluded, consistent with the recommendations of other national committees, that national research review of embryo research and hES cell research is necessary. Indeed, the NAS could have taken more seriously the emerging interest in developing a more centralized review system for human subjects research, the impetus for which comes as a direct response to the many known deficiencies with local research review (Federman et al, 2002; Emanuel et al, 2004; National Bioethics Advisory Commission, 1999).

It is often said (and presumably the NAS believes) that local research review is important because community views, values, and knowledge may be duly reflected in the review process (Wainwright and Saunders, 2004). Indeed, this perspective is shared by the U.S. Office for Protection from Research Risks (now the Office of Human Research Protections) according to which one benefit of local review is that reviewers may be uniquely positioned "to weigh critical considerations like state and local laws, professional and community standards, institutional policies and the needs of differing patient or subject populations" (Lin and Miller, 1992). Another claimed benefit with local review is that it

may be easier to accurately assess whether there is local capacity (e.g., suitable facilities and research environment, adequate resources) and local competence (e.g., qualified local investigators and supporting staff) to successfully conduct and complete the proposed research (Wainwright and Saunders, 2004, p. 313–314). And finally, there may be an important role for local review in promoting public assurance, particularly as the local review committee may be more accountable to the community than a national review committee (Wainwright and Saunders, 2004, p. 315). For these reasons, one might applaud the NAS recommendation to create ESCRO committees to specifically review the science and ethics of hES cell research. But one could take a more critical stance as well: The NAS guidelines appear to ignore the many deficiencies with the current research review system which other jurisdictions have sought to address by requiring national research review in lieu of, or in addition to, local review.

A problem with arguments in support of local review is that frequently they rest on mistaken assumptions. There are, for example, those who argue in error: that there are local, as distinct from central, ethical issues in research; that an understanding of local laws and institutional policies is available only at the local level; and similarly that knowledge of local research capacities and competence is available only to local reviewers (Wainwright and Saunders, 2004; Wood et al, 2004; Emanuel et al, 2004). The fact is that issues of informed choice, truthtelling, confidentiality, the right to withdraw from research participation, and so on — which are among the more salient ethical issues addressed in the research ethics review process — are not local issues to be decided in accordance with local (possibly idiosyncratic) norms. There are national — even international — norms that ought to be followed. Secondly, while knowledge of local laws and institutional policies, as well as knowledge of local capacity and local competence is undeniably important, this is not privileged information available only to local research review committees. As well, where novel and complex research, such as hES cell research, is concerned there are few qualified researchers and research institutions which suggests that it would not be difficult for a national research review committee to ascertain the relevant information. Thirdly, as regards the issue of local accountability, it is not clear that accountability would not be the same at the national level given that hES

cell research is a national agenda item and has even been a campaign issue for presidential candidates.

Another problem with local research review is conflict of interest. Just as researchers may be personally invested in the success of their research — for financial, academic or professional reasons — local reviewers may have a comparable investment because of organizational, professional or personal relationships with the researchers whose protocols are under review. As others have duly noted with respect to local IRB review:

> . . . institutional conflicts of interest are inherent in the current system of review. Each IRB is funded by and operated under the auspices of the very institutions conducting the research the IRB reviews. Moreover, researchers submitting proposals for review often have IRB members as colleagues. (Emanuel et al, 2004, p. 283)

More general problems with the current system of local review include: the lack of resources and administrative support; inadequate education of IRB members; lack of accountability; and the absence of central coordination, data collection, standard setting and performance evaluation (Wood et al, 2004; Emanuel et al, 2004).

In our view, local review of hES cell research by ESCRO committees may be necessary, but is certainly not sufficient, especially considering both the limitations of local research review (summarized above) and the benefits of national review (summarized below).

Legitimacy, Authority, and Legitimate Authority

In our view, pragmatic and political considerations partly explain why the NAS elected to support local research review. The leading pragmatic consideration concerns the issue of *authority*. The NAS is not a national regulatory body with any kind of federal power. It is an honorific society of scientists and engineers "dedicated to the furtherance of science and technology and to their use for the general welfare" (NAS, 2005). In casual parlance, therefore, the NAS yields no "big stick" — there can be no direct consequences associated with failure to adopt NAS guidelines. As such, in the interest of ensuring widespread voluntary adoption of its guidelines,

the NAS must develop and promote recommendations that will be perceived as reasonable from the perspective of the public interest while still being attractive from the perspective of interested scientists. It follows that if the scientific community has no interest in (or tolerance for) an additional layer of review at the national level, then it makes no sense for the NAS to recommend such review. To be absolutely clear on this point: as the NAS's recommendations are voluntary, their adoption requires the buy-in of scientists. The NAS's ability to govern, so to speak, is thus limited to moral suasion and pragmatic self-interest. For obvious reasons, these operate best at the local level.

In addition to the pragmatic issue of authority, there is the political issue of *legitimacy*. Had the NAS recommended national research review of hES cell protocols, the challenge would have been to identify a legitimate national body to assume this responsibility. This would have been no simple feat, given the absence of a federal regulatory system for hES cell research.

To function effectively, the voluntary national review committee would have to be (and be seen to be) legitimate, both from the perspective of the general public and from the perspective of the scientific community. On this reasoning, an independent, non-partisan national science organization might have the required legitimacy. If we assume a preference for national review over local review, then one option might have been for the NAS to volunteer to set up a national review committee. This would seem appropriate given its role as an independent advisor to the nation and its role in issuing the stem cell research guidelines. Another option might have been for the NAS to recommend that the American Association for the Advancement of Science (AAAS) assume this responsibility. The AAAS has as its motto "[a]dvancing science, serving society," and one of its missions is to "[p]romote the responsible conduct and use of science and technology" (American Association for the Advancement of Science, 2005). The AAAS might be seen as more objective than the NAS as it would have no particular vested interest in the NAS guidelines, though the AAAS is also an advocacy group. A third option might have been to nominate a particular society of biologists for this job — or better still, a federation of such societies, such as the Federation of American Societies for Experimental Biology (FASEB), (Federation of American Societies for

Experimental Biology, 2006) though the NAS and AAAS are more widely known amongst non-scientists. Of course, whether the NAS, AAAS, FASEB, or another socially and scientifically legitimate organization would be willing to conduct national review and oversight of hES cell research is a separate issue. From an organizational perspective, accepting this responsibility would be onerous and might also be counterproductive relative to the mission of the respective organization. From a public interest perspective, nominating any one of these science organizations as responsible for national review might only serve to entrench the hegemony of science — as evident in the early regulation of recombinant DNA research (Powledge, 1977) — insofar as scientists would be the ones who not only control the science information (pro and con), but also set the guidelines and interpret their applicability. From yet another perspective, none of these organizations might have the requisite societal legitimacy except among their own members.

Finally, concerns about authority and legitimacy collude to raise additional concerns about *legitimate authority*. If there were to be a voluntary national review committee, how would it function? How would compliance with the NAS guidelines be monitored and, perhaps more importantly, how would noncompliance be judged and penalties assessed? What kind of reporting structure would be appropriate? Who would provide sustainable funding for the work of the committee? If institutions were to adopt the voluntary NAS guidelines, could committee decisions be binding, given specific individual state policies on hES cell research? Presumably, states that have relevant legislation would have to explicitly incorporate or otherwise endorse the NAS guidelines for committee decisions to have any relevance in those jurisdictions.

These contentious logistical aspects of the problem of *legitimate authority* are both pragmatic and political. They could be straightforwardly resolved if the national oversight and review body could be embedded within the NIH or the Food and Drug Administration (FDA), as would be the case if federal funding for hES cell research were generally permitted. Currently, however, such funding is limited to the research use of certain hES cell lines created prior to August 9, 2001 as decreed by President Bush (Bush, 2001). More specifically, federal funding for the derivation of hES cell lines is not permitted and, notwithstanding recent

efforts to pass the Stem Cell Research Enhancement Act (109th Congress, 2005), there is no evidence that it will be permitted in the foreseeable future. But, perhaps, federal oversight and review could nonetheless be achieved in line with current U.S. federal policy. Even though federal tax dollars are not to be spent on morally controversial hES cell research, there may be a governmental obligation to ensure, through legislative requirements, that if the research is happening with private funds — or, somewhat more problematically from a constitutional point of view, with state funds — that it be subject to proper national review with appropriate resources, administrative support, and so on.

National Review of hES Cell Research

The political plausibility of this last option depends strongly on the positive arguments in support of national review of ethically sensitive research. These arguments are neither advanced nor even mentioned in the NAS report, however. Instead, as noted above, the NAS sidesteps this issue, claiming that its recommendations are consistent with longstanding practice in the U.S. to require only local review of research protocols involving humans. Notably, however, there are exceptions to this practice — none of which are mentioned in the NAS report. For example, the section on "Additional Protections for Children Involved as Subjects in Research" of the Common Rule anticipates the need for ad hoc national review of pediatric research that is "not otherwise approvable" by local IRBs.[2] Also, until 1996, at which time the NIH Recombinant DNA Advisory Committee's (RAC) reviewing powers were limited, the RAC conducted case-by-case national review of every gene transfer protocol in the United States (*Ad hoc* Review Committee, 1995; Krimsky, 2003; Beach, 1999). And according to at least one member, RAC continues to function as a combination central IRB and scientific review panel, but now only for a very limited number of protocols in novel areas of gene transfer research (King, 2002). As a final example, there is the recent National Cancer Institute and Office for Human Research

[2]45 CFR Part 46, Subpart D §407 (2005). The "panel of experts" refers to an *ad-hoc* national committee of experts organized by the DHHS (Lahl, Personal Communication).

Protections pilot project involving central IRB review of multisite phase III oncology trials (Christian et al, 2002).

To be sure, there are differences between these areas of research and hES cell research involving the derivation or use of newly derived cell lines—most importantly having to do with eligibility for federal funding—but the point remains that, on occasion, national review is required in the U.S. In our view, while there may be pragmatic and political reasons for the NAS to support local review, we maintain that such reasons are insufficient and do not outweigh the arguments in support of national review. As we now show, national review can be established as desirable, both generally and for hES cell research in particular.

There are many sound, closely interwoven reasons for national review of ethically and socially contentious research at the cutting edge of science and medicine. Most important among these reasons are the need for public and scientific transparency, the need for appropriate independent scientific and clinical expertise, and the need to minimize the potential for conflicts of interest. To be sure, these needs are not unique to research review for hES cell research; they are undeniably important for the review of all research involving human subjects. These requirements are of added importance, however, when the science is new, complex, and ethically controversial, as is the case with hES cell research.

An obvious and undeniable advantage of national review is that it not only allows for but can effectively promote greater public transparency. With such transparency comes the possibility of increased public scrutiny (i.e., external review and assessment), based on better public understanding of science and science practice. In turn, this entrenches the hope that both the research review process and the research itself will be conducted in an ethically responsible and accountable manner. From another perspective, it is also reasonable to think that national research review is advantageous because of scientific transparency. Central review can maximize the scientific value and validity of proposed research in bringing to the review process disparate research talent and perspectives. As well, it is reasonable to anticipate that a national research review process would contribute to a flattening of the learning curve for reviewers (and possibly researchers)

from several institutions working together and learning from each other.

A second benefit of centralized review is that it makes possible independent expert review by one's peers in a way that is impossible at the local level in the case of frontier science. Researchers working at the cutting edge in a particular domain are typically few in number and frequently they are conducting their research in different geographical locations. In these circumstances, it is highly unlikely that the researchers with the requisite expertise to critically review the science will be members of the local research review committee. This is of significant concern for those who are worried about the quality of the review.

Compounding this problem is the problem of worrisome conflict of interest. If, contrary to the assumption above, people with the requisite scientific expertise are not geographically dispersed and as such they could be members of the local review committee, the problem of conflict of interest arises — the reviewers may be colleagues or competitors, neither of which bodes well for independent review. To be clear, insofar as this kind of conflict of interest is a problem, it is likely to be acute at the local level. At the national level, this type of conflict of interest could be diluted (if not completely eliminated) as there would be a more sizeable pool of qualified researchers to draw upon as potential reviewers, and so a greater likelihood that the reviewers would be at arm's-length from the proposed research and researcher(s). Reducing conflicts of interest is critically important in research contexts where there is an obvious need for increased transparency and public scrutiny to help foster public confidence in both research and the research review process.

A third potential benefit of national research review is that it may lessen problems that can arise as a result of institutional financial conflicts of interest. Such conflicts are particularly serious for local review in research areas that attract large sums of money from investors with commercial interests (whether public or private investors). The problem is hardly any less serious when the research is funded by an endowment to the institution that the local review committee is institutionally affiliated with. Again, the same problem arises at the local level when there is internal funding from an affiliated private foundation, or when the financial health of the institution is dependent

on the research dollars that attach to a project under review. While it may be impossible for the research review process to be completely independent of financial interests, national review at least mitigates this problem as there is no national entity to which financial benefits might accrue (leaving aside assumptions about the ways in which research might contribute to the national economy).

National review affords an additional advantage in that channeling protocols to a single review body will enable a pooling or collectivization of learning. In this way, expertise in reviewing both the science and ethics of hES cell research can be developed more quickly and efficiently than would otherwise be possible. It is exceedingly difficult to develop expertise without experience. If one presumes that the goal is to ensure high quality review that is rigorous, fair, and efficient, then the benefits of having one committee review ten protocols, as contrasted with ten committees each reviewing one protocol, or five committees each reviewing two protocols, are self-evident. It is also often true that "new" cases are the hardest to adjudicate. With a larger pool of research protocols to review, chances are protocols that might present as "new" at a local level would not present themselves as "new" at the national level.

A final advantage of national review is that it necessarily eliminates the possibility of variance in decision-making regarding the science or ethics of any particular protocol, and greatly diminishes the likelihood of variance in decision-making regarding distinct but very similar protocols. Variance of the first sort — about the science or ethics — could be deeply problematic. Consider, for example, the possibility that an hES cell research project that is part of a multicentre research initiative is submitted to two or more local ESCRO committees. If there are different verdicts reached by different ESCRO committees on the very same protocol, then the authority and relevance of the NAS voluntary guidelines might well be diminished should the researchers come to see the application of these guidelines as both arbitrary and an unwarranted infringement on their research and academic freedom. Variance of the second sort — regarding distinct but very similar protocols — would be similarly problematic, as when two similar protocols are submitted to two or more local ESCRO committees who reach different

decisions. Imagine an hES cell research project that involves the use of fresh embryos made specifically for research purposes using In Vitro Fertilisation (IVF) technology. One ESCRO committee approves the research, another states that it will authorize the research use of only those embryos initially made for reproductive purposes, frozen for later therapeutic use, and later obtained for research. Both practices are endorsed by the NAS voluntary guidelines, but the second ESCRO committee deems one of these practices unacceptable and has chosen to apply its own, more restricted, standards. With the proposed local research review system, there is nothing to preclude one ESCRO committee adopting more exacting (or lenient) standards than another. Consistency in the interpretation of the NAS guidelines, however, is of critical importance to the project of building trust within the research community as well as public trust in science. As a general rule, compromised trust in the fairness of the review process risks increasing the likelihood of infractions of the guidelines/rules and abusive interpretations. This plainly argues for national research review. Finally, national review would prevent researchers from "forum shopping" at least within their own country—i.e., seeking research review from local ESCRO committees that appear to have less onerous standards.

Thus far, the particular benefits of national research review can be summarized as follows. National review effectively promotes public transparency and accountability, maximizes the likelihood of independent expert peer review, minimizes different types of conflicts of interest, promotes the collectivization of learning, and reduces *ad hoc* decision-making about specific research projects. Together these benefits of national research review serve a larger purpose—increasing public trust in science, scientists, and the research review process. In addition to the above, there are a few likely pragmatic benefits with national research review insofar as it should be possible to ensure that members of the national research review committee are properly trained and that the committee is adequately resourced. These are serious problems with local review in general, but they are particularly important in the context of research review for novel and ethically contentious research such as hES cell research.

National Review in Practice

The advantages of an additional national layer of research review for hES cell research have been recognized in several jurisdictions where there is government support for such research. In the U.K., for example, the report of the Committee of Inquiry into Human Fertilisation and Embryology (the "Warnock" report) recommended long ago the establishment of a statutory licensing authority "independent of Government, health authorities, or research institutions . . . to regulate and monitor practice in relation to those sensitive areas [including embryo research] which raise fundamental ethical questions" (Committee on Human Fertilisation and Embryology, 1984). This recommendation became a legal requirement in 1990 with the introduction of the Human Fertilisation and Embryology Act (United Kingdom, 1990). A national review and licensing system was introduced to protect the public interest by placing the relevant activities of scientists in a well-organized ethical and legal framework.

More recently, in Canada, the Canadian Institutes of Health Research (CIHR) *Ad hoc* Working Group on Stem Cell Research concluded that "because of the complex ethical issues and the public concern in this area, it is essential that there be a mechanism to provide a nationally consistent review process for all proposals involving human pluripotent stem cell research." The *Ad hoc* Working Group (of which Françoise Baylis was a member) insisted that national ethics review of stem cell research would:

(a) Provide a greater degree of accountability than currently exists with the local research ethics review system and thereby foster public confidence;
(b) Ensure greater access to appropriate experts with the background and knowledge to review the research;
(c) Minimize the potential for conflict of interest, as the reviewers can be completely at arm's-length from the research proposals; and
(d) Set the stage for a truly national review system that can be implemented as part of the AHR [Assisted Human Reproduction] legislation and apply to both private and public sector research. (Ad hoc Working Group on Stem Cell Research, 2002)

The Final Report of the *Ad hoc* Working Group was approved by the Governing Council, (CIHR, 2002a) and in March 2002 the official CIHR guidelines were released (CIHR, 2002b) mandating national research review by a Stem Cell Oversight Committee (Françoise Baylis was a member of GC at this time). And, as foreshadowed in (d), national legislation was introduced in Canada in May 2004. Under the Assisted Human Reproduction Act hES cell research can only proceed with a license from the Assisted Human Reproduction Agency following national research review (Canada, 2004).

National review of all hES cell research (in lieu of, or in addition to, local review) is not a panacea, however. For example, while unifying research review at the national level would likely promote the rapid development of research review expertise, there is also the risk of developing a "moral monoculture." From this perspective, one might argue that there are benefits to allowing (possibly even encouraging) diversity in the interpretation and application of the research guidelines at the local level. In this way, no single, potentially dogmatic, interpretation of the NAS guidelines would become prematurely entrenched as the sole authoritative interpretation. Another, particularly thorny challenge with national research review of hES cell research concerns the potential for organizational conflict of interest on the part of science organizations (such as the NAS, AAAS, and FASEB) that might be responsible for the national research review if the NIH or another federal agency (existing or newly appointed) is unable or unwilling to assume the review of protocols on a case-by-case basis. Further, this worry brings to the fore an additional cluster of problems, mostly to do with the pragmatics of implementing a national review process. U.S. and international experience with national research review, however, may be instructive in this regard, presuming there is a willingness to embrace the many virtues of national review.

In conclusion then, we submit that the many and varied advantages of national research review are as relevant in the U.S. as in other jurisdictions where they have been deemed sufficiently important as to warrant national review. These advantages do not apply only to "smaller jurisdictions where public funds are being used in the research" as the NAS guidelines would have us believe. Arguably, they are particularly relevant in the U.S. context, where

the public/private divide permeates the science of hES cell research. Accordingly, we believe the NAS should have clearly stated the benefits of national research review. Then, as a next and separate step, the NAS might have insisted on the propriety of local review, but at least it would have done so having reviewed and presumably discounted the benefits of national review. Alternatively, the NAS might have concluded on principled grounds that national review was appropriate and desirable, and that legislative changes were needed. Then again, the NAS might have frankly admitted that for political and pragmatic reasons it could not plausibly advance a principled recommendation for national research review, given the absence of political will to change the relevant federal regulations.

Taking a principled stance but backing down for political and pragmatic reasons is, admittedly, not an obvious policy-making strategy. But the NAS is not a policy-making body per se, and the NAS's otherwise impressive report, on this count, is sorely lacking. The lack of transparency and, indeed, rigor regarding the arguments in support of national review may prove ultimately counterproductive insofar as this risks undermining trust both in the scientific enterprise and in and amongst scientists themselves. The recent scandal in South Korean stem cell research should give us all pause (Cyranoski, 2006), and force us to think creatively about whether and how to advance hES cell research responsibly, transparently, and with appropriate local and national oversight.

Acknowledgment

Thanks to members of the Novel Tech Ethics research team (especially Jocelyn Downie, Michael Hadsksis and Tim Krahn) <www.noveltechethics.ca> as well as Lee Zwanziger for discussion of previous versions of this article. We also thank an anonymous reviewer for helpful comments.

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