Civic Scientist
précis

JAMES A. BAKER III INSTITUTE FOR PUBLIC POLICY
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U.K. Stem Cell Policy – A Civic Scientist's Journey through Regulation

Stephen Minger, Ph.D., previously a senior lecturer at King's College London and now director of research and development for cell technologies at GE Healthcare in the United Kingdom, never set out to change public policy in 2007 when he applied for a license to create a new cell line. But this was the consequence of his actions. Minger, an American stem cell biologist and now a British citizen, and his colleagues Susan Pickering and Peter Braude applied for a license from the Human Fertilisation and Embryology Authority (HFEA), the United Kingdom's regulatory agency for embryonic research, to create a new human embryonic stem cell (hESC) line using animal eggs and human DNA.

As a result of Minger's application, as well as those from two other institutions applying to do research on animal–human hybrid eggs, HFEA did an internal review of its hESC policies. And the U.K. Parliament, which was due to update the act that had created HFEA, held hearings debating the research. By actively engaging parliament officials, Minger and his scientific colleagues successfully lobbied so that support for hybrid embryonic research was included in the HFE Act of 2008.

Minger described the debate, scientists' reactions, and the ultimate passage of the HFE Act of 2008 during a lecture at the James A. Baker III Institute for Public Policy on February 6, 2009. The talk, titled "The New Consensus: How Scientists and Government Created Embryo Legislation in the United Kingdom," demonstrated the impact a scientist can have on policy decision making and highlighted Minger's role as a "civic scientist."

Background

In 1978, Louise Brown became the world's first baby to be born using in vitro fertilization (IVF). Although IVF today is a well-established and accepted procedure, at the time it was incredibly controversial because of the ethics and potential ramifications of this new technology. Some of these issues, such as the morality of picking embryos with desirable traits (i.e., specific eye or hair colors) to make "designer babies," still have yet to be resolved in the United States. In the wake of the public debate, British lawmakers created the HFEA in 1991 to be an independent statutory agency that strictly regulated all reproductive medical practices and research. Unlike United States, where regulation of embryonic research is found in multiple agencies and sometimes does not exist, in the United Kingdom, "everything related to reproductive medicine is very, very tightly regulated and controlled," Minger noted in his talk. HFEA places a tight, simple leash on research by mandating that a scientist or doctor desiring to perform experiments using human embryos or any other reproductive material obtain a license for a specific proposed procedure, even IVF. The United States does not regulate such research in industry. By contrast, U.K. regulation applies to all research organizations, government or private.

To obtain such a license, HFEA requires that the scientific research in question concern either: the treatment of infertility, causes of congenital disease, causes of miscarriage, the development of more effective IVF, or improvements in preimplantation genetic diagnosis (PGD). The agency also stipulates that the proposed research be "necessary or desirable." In 2001, Parliament passed legislation that

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gave British scientists the ability to conduct hESC research, which was already taking place in other parts of the world following the 1998 creation of the first hESC lines. This research would be permitted as long as it: increased knowledge about the development of embryos, improved understanding of serious diseases, or applied existing knowledge to the development of treatments for serious diseases. In addition, the United Kingdom developed a stem cell bank, and "every research group that has a license to derive human embryonic stem cells has to deposit their cells in the bank," stated Minger in his presentation.

Stem Cells

hESC research quickly became an important field of study following the discovery that the cells could become almost any tissue found within the human body. Although several types of adult stem cells exist, many believe that hESCs are more powerful. They are pluripotent, which means that they can differentiate into nearly every type of human tissue, as opposed to stem cells harvested from a child or adult, which can only develop into a handful of tissue types.

The creation of hESCs is controversial because they are harvested from the inner cellular mass of a human egg 5–6 days following fertilization. The majority of the embryos used to harvest hESCs in the United Kingdom are obtained from couples who have chosen to donate their unused embryos that were originally intended for IVF. After the maximum five-year storage period in the United Kingdom, couples can decide to have their leftover embryos destroyed or donated, without compensation, to science.

An alternative to hESC might be somatic cell nuclear transfer (SCNT), or therapeutic cloning. Specifically, an embryo is created by implanting the nucleus of a somatic (or normal) cell from a patient afflicted with, for example, Alzheimer's disease into an unfertilized egg cell that has had its nucleus removed. A researcher should be able then to grow the brain cells from an embryo with the genetic predisposition to Alzheimer's to trace the disease's progression.

Unfortunately, as Minger noted in his talk, there is one problem—obtaining human eggs. "Where do you get eggs? How many eggs do you need to create a cloned human embryonic stem cell line?" While this has not been achieved with human embryos, the process has been performed on animals, including Dolly, the first cloned mammal. Indeed, SCNT has yet to successfully produce any hESCs, making it an inefficient and, so far, an unviable option. Minger estimated that it would require over 10,000 eggs for him to successfully perform the procedure, a potentially unethical use of human eggs.

Minger believes a more practical option is hybrid embryo research, also referred to as interspecies cloning, which utilizes animal, rather than human, egg cells. The cloning process remains the same: Once the nucleus is removed from the animal egg, the egg loses all genetic or species identity, with the exception of a small amount of DNA residing in the mitochondria. Thus, upon insertion of a human somatic cell nucleus, the created embryo would become a human embryo. This technique would allow researchers access to a large supply of eggs, which would be needed to perfect human SCNT.

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— Stephen Minger

Hybrids and HFEA

Although HFEA presides over issues of hESC and SCNT (U.K. legislation has banned reproductive cloning—i.e., the cloning of a human being), there were questions in 2006 about the legality and regulation of the hybrid technique. That year, Minger and his colleagues Pickering and Braude applied for a license from HFEA to perform interspecies cloning for research. During the three-month license consideration period, the British government began working on the updated HFE Act of 2008; the original legislation was set to expire. Under the proposed legislation, the United Kingdom would have banned all hybrid embryo research, suggesting it was ethically wrong and medically useless.

The report sparked an outcry from the majority of the U.K. scientific community, including Minger—HFEA was intended to be independent of government and political influence. The British Parliament's interference not only violated that principle but set a bad precedent for policymakers deciding scientific questions. Minger and several prominent stem cell researchers—Sir Ian Wilmut, Ph.D., from Edinburgh University and creator of Dolly, the cloned sheep; Lyle Armstrong, Ph.D., from Newcastle University; Chris Shaw, M.D., from King's College London; and Dame Anne McLaren, D. Phil., from the University of Cambridge—quickly reacted to the report and participated in a press conference, saying, "We want to do this research," and encouraging the government to support hybrid embryo research. In January 2007, Minger joined 45 scientists, academics, and politicians in sending a letter to The Times newspaper in London urging HFEA to support the research.

In response to the British Parliament's efforts, HFEA placed the license application on hold while it decided whether the hybrid embryos were in fact human embryos—and therefore under the purview of HFEA regulation—and held a consultation period to ask various experts for advice. During this period, the British Parliament decided to have a committee conduct hearings on the topic, calling in a number of scientists and ethicists to testify. The hearings lasted three months. Hundreds of scientists, ethicists, lawyers, people of religious faiths, heads of the funding council (U.K. funding agencies), and Minger himself came to explain the research and its scientific value. In addition, more than 200 medical research charities and patient groups signed a letter to then-Prime Minister Tony Blair supporting the research.

Simultaneously, HFEA on its own consulted scientists and community leaders to determine public opinion on the topic. Because of the efforts of Minger and other scientists in the United Kingdom, the Parliament committee eventually "unanimously" concluded that these "hybrids" were in fact human embryos and therefore needed to be regulated by HFEA. In late 2007, HFEA agreed with their conclusion, and again undertook the process of considering Minger's license application.

Before HFEA could render a decision on the application, a new scientific breakthrough, the creation of the first line of human induced pluripotent stem (iPS) cells in Japan and the United States, revived the hybrid debate once more. iPS cells are normal adult cells (like a skin cell) which are activated to regain their pluripotency and behave like hESCs. This new technology led many Parliament members to believe that hybrid cells were no longer necessary and should be banned. Nonetheless, HFEA granted the license for Minger, clearing the way for hybrid research on the basis that it was still a new area of research that needed to be investigated.

"You've convinced us that the science is worth doing."

— member of British Parliament to Minger

In early 2008, the Parliament forged ahead with the HFE Act update, seeking to include legislation regulating hybrid embryo research. The support for hybrid embryos outraged a number of religious groups, who accused the government of stifling the opinions of religious members of Parliament. The British minister of health contacted Minger and other outspoken scientists, suggesting that support for the research would have to be won through communication between the scientific and political communities. As a result, Minger said, from March to October 2008 some 30 scientists spent "hundreds of hours briefing members of Parliament." As a result, the HFE Act of 2008 included regulation not only of the hybrid cloning technique Minger was working on, but a variety of other human–animal cloning methods as well. The British Parliament, recognizing that science is continuously progressing, placed guidelines and safeguards to regulate research they found appropriate. At the same time, the regulations inhibited inappropriate research, such as creating embryos by mixing human and animal gametes (sperm or egg cells). Minger believes that this was a wise decision because "if these are in the HFE Act, they are then legislated and you cannot create any of these without a license." Thus, if a scientist desired to attempt this type of ethically ambiguous research they would have to show that it is "necessary or desirable" and apply for a license through HFEA.

At the end of the debate, it was the votes from the conservative members of Parliament whose minds had been changed that saved the research from being banned. One member in particular sought Minger out to tell him that, although he initially found the concept of hybrid embryos strange and unsettling and favored a ban, the scientists' efforts in coming to Parliament to explain why they should be allowed to conduct the research had changed his mind. Minger said the member told him, "You've convinced us that the science is worth doing." Indeed, it was impressive how Minger and his colleagues managed to convince Parliament that hybrid research should be allowed for the sake of investigating a new field, despite being deemed "weird" by some members and having been supplanted by newer techniques.

Equally important was that he helped secure the passage of regulations for techniques that have not yet been developed. According to Minger, "As scientists, we fight very hard for research not to be banned." Rather than having research stymied through a ban or letting potentially unethical experiments proceed unchecked, he preferred to petition regulatory agencies, as well as governmental authorities, to expand their focus to include more prospective areas of research.

Civic Scientist

Minger's tireless efforts supporting stem cell research exemplify the goal of a civic scientist. As often stated by Neal Lane, Baker Institute senior fellow for science and technology policy and former science adviser for President Bill Clinton, a civic scientist "is someone who uses his or her knowledge, accomplishments and skills to help bridge the gap between science and society."

Minger used his scientific knowledge and accomplishments to educate and persuade policymakers to create new and better guidelines for hESC research. His initiation of dialogue and engagement of public officials and private citizens brought about an informed debate on the issue, culminating in a shift in opinion regarding hybrid cloning. The new legislation, rather than banning the research, allowed it to

proceed in a regulated manner. Minger's example also highlights the impact a scientist can have on the policy—hopefully encouraging more scientists to engage in the process.

Minger is only one of many examples of a civic scientist. The Baker Institute Science and Technology Policy Program hosts an annual lecture by a civic scientists and encourages local scientists and engineers to engage in public policy and outreach through its Rice Civic Scientist Outreach initiative. For more information on the Baker Institute Civic Scientist program, see the Web site: http://www.bakerinstitute.org/programs/civic-scientist-program. To view the webcast of Minger's talk at the Baker Institute, "The New Consensus: How Scientists and Government Created New Embryo Legislation in the United Kingdom," go to: http://www.bakerinstitute.org/events/minger.

Biosketch – Stephen Minger

Stephen Minger is the director of research and development for cell technologies at GE Healthcare in the United Kingdom. Previously, he was the director of the Stem Cell Biology Laboratory and a senior lecturer in the Wolfson Centre for Age Related Diseases at King's College London. Minger received his Ph.D. in pathology (neurosciences) in 1992 from the Albert Einstein College of Medicine. From 1992 to 1994, he was a postdoctoral fellow at the University of California, San Diego, where he first began to pursue research in neural stem cell biology. In 1995, Minger was appointed an assistant professor in neurology at the University of Kentucky College of Medicine. He moved his stem cell research program to Guy's Hospital, London, in 1996 and was appointed a lecturer in biomolecular sciences at King's College London in 1998.

Over the past 15 years, his research group has worked with a wide range of somatic stem cell populations, as well as mouse and human embryonic stem cells. In 2002, together with Susan Pickering and Peter Braude, Minger was awarded one of the first two licenses granted by HFEA for the derivation of hESCs. His group subsequently generated the first hESC line in the United Kingdom and was one of the first groups to deposit this line into the U.K. Stem Cell Bank. They have gone on to generate five new hESC lines, including one that encodes the most common genetic mutation resulting in cystic fibrosis and another one that contains the Huntington's disease mutation.

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