

Mr. SOUDER. Thank you very much.  
Our next witness is Judy Norsigian.

#### STATEMENT OF JUDY NORSIGIAN

Ms. NORSIGIAN. Thank you, Chairman Souder, Mr. Cummings, and members of the committee for the opportunity to speak. Judy Norsigian, executive director of Our Bodies Ourselves, a women's health education and advocacy organization, best known for our landmark book about women's health and sexuality, "Our Bodies, Ourselves."

At the outset, let me make clear, as I did at similar hearings 4 and 5 years ago, that my organization supports most embryonic stem cell research. We fully support ESC research that utilizes otherwise discarded embryos from IVF clinics. Thus, we do not agree with President Bush, for example.

At the same time, we have serious concerns about a small subset of ESC research known as somatic cell nuclear transfer, more commonly referred to as research cloning, therapeutic cloning, or embryo cloning, as we have discussed today. My organization believes that our country should follow the prudent example already adopted by Canada and place a moratorium on all SCNT research until better safety data are available for some of the drugs used during multiple egg extraction procedures.

There are several reasons for this position, but I will focus my remarks primarily upon our concerns regarding the risks of multiple egg extraction. And although women who undergo these procedures experience similar risks whether doing this for reproductive purposes, as is the case in an IVF clinic, or for research purposes, there is a critical difference.

In the former instance, there is a 10 to 40 percent chance that someone, either the woman herself or another woman who is seeking to become pregnant at an IVF clinic, will be able to have a baby. That is a clear benefit. In the latter instance, when a woman undergoes these procedures solely for research purposes, the benefits to her or someone else are far more dubious at this time.

Although some stem cell researchers have discussed this matter and even share our concerns, few have been willing to write about these issues. It may be that one positive outcome of the scandal in South Korea will be greater recognition of just how risky multiple egg extraction can be, as well as how easily frenetic competition and unjustified hype can lead to a more ready dismissal of these risks.

In a recent issue of the American Journal of Bioethics, Stanford faculty David Magnus and Mildred Cho write the following: "In a previous paper, we argued that there were risks associated with being an oocyte donor that were not given adequate attention in the informed consent process. This claim was based upon the informed consent documents by the South Korean researchers, an accompanying written description of the consent process, and their responses to questions posed."

"We argued that it would be easy to give short shrift to the small but serious risks that typically arise in a clinical setting precisely because these risks are not associated with the research aspects of oocyte donation."

They go on to say that: “The language used to describe scientific experiments also makes a great deal of difference in how accurately we convey the nature of stem cell research.”

Finally, they say, “There is an important distinction between oocyte donation for research and live organ donation for transplantation. Live organ donation has a clearly established clinical value. Stem cell research does not. If that should change, we would agree that allowing women to donate oocytes for stem cell-based treatments would be permissible, if conducted properly. But allowing research donation to take place under these circumstances is an invitation for a new kind of therapeutic misconception, and should be avoided at this early stage of scientific development.”

The risks of multiple egg extraction are not well-enough studied, especially the risks associated with the drugs most often used to suppress a woman’s ovaries. Lupron, generally referred to as leuprolide acetate, the generic term, is the drug I would like to focus on now.

I have listed many of the adverse reactions in my testimony. These include: pituitary and liver function abnormalities; chronic joint, muscle, and bone pain; headaches and migraines; dizziness and blackouts; and serious memory disturbances and brain fog that persist well after the drug is discontinued.

And we have had this from numerous reports. The FDA has received numerous adverse drug reports, and one of the things we are hoping we will see in the near future is a data mining analysis by scientists at the FDA to give us better direction on what kind of research we need to conduct.

Lupron’s use in the IVF setting is off-label use, and as former Chief Medical Officer Suzanne Parisian pointed out in her memorandum of February 2005, there are serious safety concerns yet to be resolved. Only well-designed research will answer critical questions that would then allow true informed consent for women undergoing multiple egg extraction procedures for any purpose.

The drugs used to hyperstimulate the ovaries after ovarian suppression also have negative effects, most notably Ovarian Hyperstimulation Syndrome, a condition in which the ovaries continue to enlarge even after the eggs have been collected. Serious cases of this syndrome involve the development of many cysts and massive fluid buildup in the body. Rarely, death has resulted. The most recent one documented was in England in December.

And it is not only the women undergoing the procedures who may be at risk from ovarian hyperstimulation. A very important article published in the past month by a Dutch team including medical and basic scientists suggests that infants may also suffer adverse consequences.

This group has shown that female mice subjected to ovarian hyperstimulation had offspring with reduced birth weight as well as a high incident of congenital anomalies, including delayed formation of bones and an eightfold increase over background levels of cervical ribs, a condition which, when present in human infants, is associated with stillbirth and cancer.

Should SCNT research go forward despite the concerns mentioned here, it will be left to women’s health advocates to emphasize the inadvisability of women undergoing these procedures, espe-

cially younger women, whose risk of Ovarian Hyperstimulation Syndrome is actually greater than that for older women.

Also, if such research does go forward, certain regulations and oversight of the research with respect to egg procurement are essential. I have listed seven here: that eggs should be obtained without any hormonal stimulation, since there is still insufficient information to get true informed consent. No relatives or coworkers of those doing research on eggs should be allowed to provide eggs for research.

All medical expenses resulting from egg extraction for research should be covered; in cases where would be hormonally manipulated, longer-term healthcare coverage may be necessary to provide medical care for certain delayed health problems.

Those performing egg extraction for research purposes should function totally separate from IVF services. And no research should be allowed on eggs or stem cell lines developed from eggs procured by means other than those just mentioned. This would avoid use of stem cell lines created in other countries or regions where safeguards to women's health might not be in place.

We also believe that no patents should be allowed for products that might result from research on these eggs. Without such a policy, many therapies will likely never be accessible to the wider public. I can give you other such examples already. In addition, it would be extraordinarily difficult to avoid a problematic commercial market in women's eggs.

And, of course, no payment to egg providers beyond direct expenses. We think both the researchers and the women who provide eggs in this case may be going to be making a sacrifice.

So in conclusion, many scientists now acknowledge that individualized disease third parties will not research from embryo cloning research anyway, in part because of the need for massive numbers of eggs. The main benefit of embryo cloning would be the ability to develop research models for studying particular diseases and conditions, but some of this type of work can be done already with otherwise discarded embryos that result from PGD, pre-implantation genetic diagnosis, testing.

At this point in time, given both the known and unknown risks involved in multiple egg extraction procedures, these procedures should not be done solely for SCNT research. At the same time, we do support most embryo stem cell research.

Thank you.

[The prepared statement of Ms. Norsigian follows:]

**Statement of Judy Norsigian  
Executive Director, Our Bodies Ourselves**

**Subcommittee on Criminal Justice, Drug Policy and Human Resources  
Government Reform Committee  
U.S. House of Representatives**

**Hearing on Human Cloning and Embryonic Stem Cell Research after Seoul:  
Examining Exploitation, Fraud, and Ethical Problems in the Research  
March 7, 2006**

I am Judy Norsigian, the Executive Director of Our Bodies Ourselves, a women's health education and advocacy organization now in its 37<sup>th</sup> year. We are best known for our landmark book about women's health and sexuality - *Our Bodies, Ourselves* - which appeared in its 8<sup>th</sup> edition as a major revision last May. Thank you for this opportunity to speak.

At the outset, let me make clear, as I did at similar hearings four and five years ago, that my organization supports most embryonic stem cell (ESC) research. We fully support ESC research that utilizes otherwise-discarded embryos from IVF clinics. At the same time, we have serious concerns about a small subset of ESC research known as somatic cell nuclear transfer (SCNT) and more commonly referred to as "research cloning," "therapeutic cloning," or "embryo cloning." We believe that our country should follow the prudent example already adopted by Canada and place a moratorium on all SCNT research until better safety data are available for some of the drugs used during multiple egg extraction procedures.

There are several reasons for this position, but I will focus my remarks primarily upon our concerns regarding the risks of multiple egg extraction required for research cloning. Although women who undergo multiple egg extraction procedures experience similar risks whether doing this for reproductive purposes (as is the case in an IVF clinic) or for research purposes, there is a critical difference. In the former instance, there is a 10-40% chance that someone – either the woman herself or another woman who is seeking to become pregnant at an IVF clinic – will be able to have a baby. That is a clear benefit. In the latter instance, where a woman undergoes these procedures solely for research purposes, the benefits to her or someone else are far more dubious at this time.

Although some stem cell researchers have discussed this matter and even share our concerns, few have been willing to write about these issues. It may be that one positive outcome of the scandal in South Korea will be greater recognition of just how risky multiple egg extraction can be, as well as how easily frenetic competition and unjustified hype can lead to a more ready dismissal of these risks. In a recent issue of the *American Journal of Bioethics*<sup>1</sup>, Stanford researchers David Magnus and Mildred Cho write the following:

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<sup>1</sup> **A Commentary on Oocyte Donation for Stem Cell Research in South Korea**  
by David Magnus, Mildred K. Cho. 2006. *The American Journal of Bioethics* 6(1):W23

“In a previous paper (‘Issues in oocyte donation for stem cell research.’ *Science*, v.308: 1747-1748, 2005), we argued that there were risks associated with being an oocyte donor that were not given adequate attention in the informed consent process. This claim was based upon the informed consent documents by the South Korean researchers, an accompanying written description of the consent process, and their responses to questions posed. We argued that it would be easy to give short shrift to the small, but serious, risks that typically arise in a clinical setting precisely because these risks are not associated with the research aspects of oocyte donation. We therefore recommended recognition of a new category of research participants—research donors.”

They go on to say:

“The language used to describe scientific experiments also makes a great deal of difference in how accurately we convey the nature of stem cell research. We argued, for example, that referring to the process of deriving stem cells by somatic cell nuclear transfer as “therapeutic cloning” reinforces the mistaken impression that experiments are therapeutic in nature. In fact, there is no therapy currently associated with SCNT.”

Furthermore, they take a cautious position regarding egg procurement procedures for research cloning:

“...there is an important distinction between oocyte donation for research and live organ donation for transplantation. Live organ donation has a clearly established clinical value — stem cell research does not. If that should change, we would agree that allowing women to donate oocytes for stem cell-based treatments would be permissible, if conducted properly. But allowing research donation to take place under these circumstances is an invitation for a new kind of therapeutic misconception, and should be avoided at this early stage of scientific development.”

The risks of multiple egg extraction are still not well-enough studied, especially the risks associated with the drugs that first suppress the ovaries. (Afterwards, different drugs are used to create controlled ovarian hyperstimulation.) The drug most often used to suppress a woman’s ovaries is Lupron™ (leuprolide acetate), a GnRH agonist. Adverse reactions to this and similar drugs include the following: anemia; high blood pressure; formation of blood clots that could potentially cause damage to vital organs; fluid accumulation in the limbs; thyroid enlargement; liver function abnormality; joint, muscle and bone pain; chest pain; difficulty in swallowing; intestinal bleeding; headaches and migraines; dizziness and blackouts; memory disturbances; depression; anxiety; numbness; swelling of hands; constipation; nausea; vomiting; diarrhea; and vision abnormalities. Many people assume that this drug has been approved by the FDA for this particular indication, but that is not the case. All use of Lupron in the IVF setting is “off-label” use, and as former Chief Medical Officer Dr. Suzanne Parisian points out in the attached memorandum, there are serious safety concerns yet to be resolved. Only well-designed research will answer critical questions that would then allow true informed consent for women undergoing multiple egg extraction procedures for any purpose.

The drugs used to “hyperstimulate” the ovaries after ovarian suppression also have negative effects, most notably Ovarian Hyperstimulation Syndrome (OHSS), a condition in which the ovaries continue to enlarge even after the eggs have been collected. Serious cases of this syndrome involve the development of many cysts and enlargement of the ovaries, along with

massive fluid build-up in the body. As noted in an article about OHSS, “the reported prevalence of the severe form of OHSS is small, ranging from .5 to 5%. Nevertheless, as this is an iatrogenic complication of a non-vital treatment with a potentially fatal outcome, the syndrome remains a serious problem for specialists dealing with infertility.”<sup>2</sup> In her memo, Dr. Parisian also notes that ovarian stimulation in rare cases can lead to stroke and “arterial occlusion with loss of a limb and death.”

These risks were also noted in the informed consent document developed at the Bedford Stem Cell Institute several years ago (see “Consent to Participate in a Study Involving Egg Donation for Stem Cell Research”). Following is an excerpt from this document: “Complications associated with being an egg donor include unpredictable response to the hormones provided to you, surgical complications during the egg collection, and unknown long-term side effects from the hormones. If any of these complications arise the reproductive biologists involved in this research may choose, at their discretion, to terminate your continued participation in this research.” What is unclear, however, is whether or not the costs of medical treatments for problems resulting from these procedures would be covered.

And it is not only the women undergoing the procedure who may be at risk from ovarian hyperstimulation. An article published in the past month by a Dutch team including medical and basic scientists suggests that their infants may also suffer adverse consequences.<sup>3</sup> This group has shown that female mice subjected to ovarian hyperstimulation had offspring with reduced birth weight as well as a high incidence of congenital anomalies, including delayed formation of bones and an eight-fold increase over background levels of cervical ribs, a condition which, when present in human infants, is associated with stillbirth and cancer.

Should SCNT research go forward despite the concerns mentioned here, it will be left to women’s health advocates to emphasize the inadvisability of women undergoing these procedures (especially younger women, whose risk of Ovarian Hyperstimulation Syndrome is greater than that for older women).

Also, if such research goes forward, certain regulations and oversight of the research with respect to egg procurement are essential. The following policies should be adopted:

1. Eggs should be obtained without any hormonal stimulation, since there is still insufficient information to get true informed consent from would-be egg providers. Although Antagon, a GhRH antagonist, IS approved for such use, there are no long term safety data for this drug. Thus, only single cycling or extraction at the time of a sterilization or ovariectomy should be allowed for extracting eggs for SCNT research.

<sup>2</sup> Delvigne, Annick and Rozenberg, Serge. “Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review” *Human Reproduction Update*, vol. 8, no. 6, 2002, pp 559-577.

<sup>3</sup> Steigenga, Marc J., Helmerhorst, Hans M., De Koning, Jurien, Tijseen, Ans M.I., Ruinard, Sebastiaan, A.T. and Galis, Frietson. Evolutionary conserved structures as indicators of medical risks: increased incidence of cervical ribs after ovarian hyperstimulation in mice *Animal Biology*, vol. 56, no. 1, 2006, pp. 63-68.

2. No relatives or co-workers of those doing research on eggs should be allowed to provide eggs for research.
3. All medical expenses resulting from egg extraction for research should be covered. In cases where cycles would be hormonally manipulated, longer-term health care coverage may be necessary to provide medical care for certain delayed health problems.
4. Those performing egg extraction for research purposes should function totally separate from IVF services (an effective firewall is needed to avoid both financial and professional conflicts of interest).
5. No research should be allowed on eggs or stem cell lines developed from eggs procured by means other than those described in #1-4. This would avoid the use of stem cell lines created in other countries or regions, where safeguards to women's health might not be in place.
6. No patents should be allowed for products that might result from research on these eggs. Without such a policy, many therapies will likely never be accessible to the wider public. In addition, it would be extraordinarily difficult to avoid a problematic commercial market in women's eggs.
7. No payments to egg providers beyond direct expenses (eg, no payment for lost wages) should be allowed.

Many scientists now acknowledge that "individualized" disease therapies will not result from embryo cloning research anyway (see "Cloning: Mining the secrets of the egg," by Carina Dennis, *Nature*, February 9, 2006) The main benefit of embryo cloning would be the ability to develop research models for studying particular diseases and conditions, but some of this type of work can be done already with otherwise-discarded embryos that result from PGD (Preimplantation Genetic Diagnosis) testing. At this point in time, given both the known and unknown risks involved in multiple egg extraction procedures, these procedures should not be done solely for SCNT (embryo cloning) research.

Some researchers are already investigating alternatives such as nurturing immature eggs, growing artificial eggs in the lab, and using animal egg substitutes. Although each of these approaches has its own technical and ethical challenges, this trend does recognize how strikingly inefficient embryo cloning is, and that it will likely require – at least for a long time to come – that hundreds of eggs be extracted to obtain even one viable clonal embryo. Dr. Arnold Kriegstein, Director of the Institute of Stem Cell and Tissue Biology at the University of California, San Francisco, takes the approach that "We'll have to wait and see how difficult human eggs are to acquire" (see *Nature* article cited above), but I would hope researchers would follow the more cautious approach suggested by Drs. Magnus and Cho.