Mr. Chairman, and Honored Members of the Committee.

Thank you for the opportunity to testify on this important legislation.
I am testifying in SUPPORT of HB 308

I am a cell biologist, currently working for a policy think tank in Washington, D.C. and as an adjunct professor at a local university. For the previous 20 years, I was Professor of Life Sciences at Indiana State University and Adjunct Professor of Medical & Molecular Genetics at Indiana University School of Medicine. Prior to that I was a faculty member in the Department of Obstetrics, Gynecology and Reproductive Sciences, University of Texas Medical School at Houston, and I have done federally-funded laboratory research, lectured, and advised on these subjects extensively, in the U.S. and internationally. I was selected by the Bush President’s Council on Bioethics to write the comprehensive review of adult stem cell research for the Council’s 2004 publication “Monitoring Stem Cell Research”. I’ve taught embryology, developmental biology, molecular biology and biochemistry for over 30 years to undergraduate and graduate students, as well as medical and nursing students.

This bill seeks specifically to prohibit various laboratory procedures that artificially create human embryos, or animal-human hybrid embryos, for experimental purposes.

Let’s first deal with the biology and the terminology related to embryos.

“Zygote. This cell results from the union of an oocyte and a sperm during fertilization. A zygote is the beginning of a new human being (i.e., an embryo).”

“The development of a human begins with fertilization, a process by which the spermatozoon from the male and the oocyte from the female unite to give rise to a new organism, the zygote.”

“Almost all higher animals start their lives from a single cell, the fertilized ovum (zygote)... The time of fertilization represents the starting point in the life history, or ontogeny, of the individual.”

So the normal method for production of a human embryo is fertilization, the union of a human egg with a human sperm. Whether fertilization takes place within a woman’s body, or in a laboratory via “in vitro fertilization” (IVF, sometimes termed Assisted Reproductive Technology or ART), this is the normal method by which a new human being comes into existence and begins development.

This bill does not address IVF or any production of a human embryo by fertilization, the union of a human egg with a human sperm. IVF and similar reproductive techniques are unaffected by this legislation.

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HB 308 only addresses artificial techniques of embryo production—cloning and animal-human hybrids.

**Human cloning is human asexual reproduction,** termed “asexual” because it does not involve the combining of egg and sperm to form an embryo. The most notable technique to accomplish this is “somatic cell nuclear transfer” (SCNT)—placing the nuclear genetic material from one or more human somatic (body) cells into a fertilized or unfertilized egg cell whose nuclear genetic material has been removed or inactivated, producing a human embryo who is virtually genetically identical to an existing or previously existing human being. Other artificial methods of embryo production include manipulation of eggs to begin development, as well as artificial twinning or cloning by embryo splitting or by separation of blastomeres, the cells of the very early embryo.

Proponents of human cloning hold out two hopes for its use: (1) creating live born children, for infertile couples, for those grieving over the loss of a loved one, or genetically-treated children designed to be without disease, so-called “reproductive cloning” (live birth cloning), and (2) promises of medical miracles to cure diseases by harvesting embryonic stem cells from cloned embryos created from patients, euphemistically termed “therapeutic cloning” (more properly termed research cloning.)

Biologically, this most common process of cloning (somatic cell nuclear transfer; SCNT) produces a zygote, a one-celled embryo, at the starting point for development. As the Bush President’s Council on Bioethics noted, “The first product of SCNT is, on good biological grounds, quite properly regarded as the equivalent of a zygote, and its subsequent stages as embryonic stages in development.”

Likewise, the National Institutes of Health has affirmed that SCNT cloning produces an embryo.

The National Academy of Sciences noted the following:

“**The method used to initiate the reproductive cloning procedure is called nuclear transplantation, or somatic cell nuclear transfer (SCNT).** It involves replacing the chromosomes of a human egg with the nucleus of a body (somatic) cell from a developed human. In reproductive cloning, the egg is then stimulated to undergo the first few divisions to become an aggregate of 64 to 200 cells called a blastocyst. The blastocyst is a preimplantation embryo that contains some cells with the potential to give rise to a fetus and other cells that help to make the placenta. If the blastocyst is placed in a uterus, it can implant and form a fetus. If the blastocyst is instead maintained in the laboratory, cells can be extracted from it and grown on their own.”

The equivalence of the embryo, as zygote and blastocyst, has also been noted by the National Academy of Sciences, which has noted that the embryos produced by fertilization and the embryos produced by SCNT cloning are indistinguishable.

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4 “Human Cloning and Human Dignity: An Ethical Inquiry”, Report of the President’s Council on Bioethics, July 2002; p.50
6 Scientific and Medical Aspects of Human Reproductive Cloning, Report of the National Academy of Sciences and the Institute of Medicine, National Academy Press, Washington, DC, Jan 2002; Preface page xii
8 National Academy of Sciences, Guidelines for Human Embryonic Stem Cell Research (2005), p. 29
Another technique, “parthenogenesis”, has also been used to create embryos. In this technique, a human egg is chemically treated in such a way to make it retain a complete set of chromosomes, all derived from the egg alone (again, without use of sperm.) Activation allows this parthenogenetic embryo to begin cell division and development, though because all the chromosomes are derived only from an egg (maternal chromosomes), the resulting embryo only proceeds part way through development unless there is some genetic manipulation to activate placental genes. Born parthenogenetic mice have been produced using this technique.9

Fertilization compared to Cloning (Somatic Cell Nuclear Transfer, SCNT)

9 Kono T et al., Birth of parthenogenetic mice that can develop to adulthood, Nature 428, 860-864, 2004
Other techniques have been used in the laboratory to create embryos at later stages of development. For example, “embryo splitting” has been used to cut embryos in half to double the number of embryos available for experiments. In some cases, embryo cells are dissociated, separating them from one another; if done early in development, each cell can begin development of a new, complete embryo, creating multiple copies of the same organism at the embryonic stage. These methods of embryo splitting are common for domestic animals, but have also been shown to be possible even for human embryos, splitting or even dissociating human embryos to create multiple copies.\textsuperscript{10,11,12} This raises serious concerns about creating and manipulating human embryos in the lab, even potentially as an assembly-line procedure.

Another technique that has been used to create embryos at later stages of development is called “tetraploid complementation”.\textsuperscript{13} The technique combines normal cells with embryonic stem cells fused together that contain twice the normal amount of chromosomes (“diploid” being the normal amount, these doubled-up embryos are called “tetraploid”). The tetraploid cells form the outer layer of an early embryo, while the normal cells are held inside and go on through embryonic development. Born mice and cattle have been produced using this technique.

\begin{itemize}
  \item \textsuperscript{10} “Human embryo cloning reported”, Science 262, 652-653; 29 Oct 1993
  \item \textsuperscript{11} Illmensee K et al., Human embryo twinning with applications in reproductive medicine, Fertil. Steril. 93, 423, 2010
  \item \textsuperscript{12} Van de Velde H et al., The four blastomeres of a 4-cell stage human embryo are able to develop individually into blastocysts with inner cell mass and trophectoderm, Hum. Reprod. 23, 1742, 2008
\end{itemize}
Both sexual reproduction (fertilization, egg+sperm) and asexual reproduction (cloning, i.e., somatic cell nuclear transfer) produce a human embryo, a living human organism, species *Homo sapiens*.

**Cloning by this SCNT procedure creates an embryo, not stem cells, not organs, not tissues.** If the cloned embryo continues to develop, the developing human will form stem cells, tissues and organs, just as any normal embryo produced by fertilization will form stem cells, tissues and organs.

Among the various cloning techniques, **somatic cell nuclear transfer (SCNT)**, was the process used to create the cloned sheep Dolly.

Both “reproductive” and “therapeutic” cloning use exactly the same techniques to create the clone, and the cloned embryos are indistinguishable. The process, as well as the product, is identical. The only distinction is the end purpose for use of the embryo—either transfer to a uterus in the hopes of a live birth, or destruction in the hopes of a medical miracle.

The technique of cloning is finished once that first cell, the one-celled embryo (zygote) is formed. Anything beyond that step is simply growth and development. And despite attempts to employ various euphemisms, scientifically, genetically, what is created is a human being; its species is *Homo sapiens*, it is neither fish nor fowl, monkey nor cow—it is human. The use of disingenuous euphemisms to describe the embryo as something other than an embryo likewise is not scientific, and diverges from the accepted objective definitions as put forth by the National Academy of Sciences, the National Institutes of Health, and others, including well-known proponents of human cloning.

This fact is also made clear by leading proponents of embryo research:
“Moreover, because therapeutic cloning requires the creation and disaggregation ex utero of blastocyst stage embryos, this technique raises complex ethical questions.”

"[Therapeutic cloning] requires the deliberate creation and disaggregation of a human embryo." 

Q: The people who use nuclear transfer generally say that the technique is optimized for producing the stem cells rather than making babies. They would not want to equate this with the process that produces embryos that were fit for implantation, and they’d argue that they’re using the reproductive process differently …

A: (James Thomson) “See, you’re trying to define it away, and it doesn’t work. If you create an embryo by nuclear transfer, and you give it to somebody who didn’t know where it came from, there would be no test you could do on that embryo to say where it came from. It is what it is. It’s true that they have a much lower probability of giving rise to a child. … But by any reasonable definition, at least at some frequency, you’re creating an embryo. If you try to define it away, you’re being disingenuous.”

The assumption that cloning (SCNT) will produce matching tissues for transplant that will not be rejected is still theoretical. When tested in mice in 2002, the ES cells from the cloned mouse embryo were rejected by the genetically-identical host:

“Jaenisch addressed the possibility that ES clones derived by nuclear transfer technique could be used to correct genetic defects… However, the donor cells, although derived from the animals with the same genetic background, are rejected by the hosts.”

In 2008, another lab attempted to treat Parkinson’s in mice, first cloning the mice, then harvesting stem cells from the cloned embryos. When placed back into the mice, there was some improvement in their condition, but 1 out of 6 mice showed “graft overgrowth” in their brains, most of the cells produced showed chromosomal abnormalities, and the authors noted that it was “technically complex” and required a huge number of eggs to get a single dish of cells. It is unknown whether tumors might have developed later in other animals as the experiment was terminated early. Moreover, the data are equivocal in terms of transplant matching, due to the fact that the brain is an immuno-privileged site (very little immune reaction).

In fact, the best results to date (even though equivocal) in animal studies actually come from gestating cloned animals to the fetal stage and then harvesting tissue stem cells.


15 Stem-cell pioneer does a reality check. James Thomson reflects on science and morality, By Alan Boyle  Science editor  MSNBC  Updated: 4:13 p.m. ET June 22, 2005


18 Tabar et al., Nature Medicine 14, 379, April 2008


The idea of therapeutic cloning—cloning an individual to create embryos, from whom stem cells are harvested—is outdated and the science superseded by better, easier scientific methods for matching stem cell production.

Moreover, the assertion that cloning is the only method for preventing immune rejection of transplanted embryonic stem cells is completely false, and this has been known for some time. In an article published March 18, 2002 (Abate, San Francisco Chronicle), researchers with Geron Corp. and with Advanced Cell Technologies admitted that there are ways to prevent rejection of transplanted cells without therapeutic cloning, but that “that message has not gotten out,” and that “the need for cloning to overcome immune system rejection has been overstated.” The report goes on to note “the scientific community has put out the message that a ban on therapeutic cloning will prevent researchers from solving the immune-system problem—an argument that seems at best a stretch, and at worst, a deception.”

Other scientists have admitted in testimony that therapeutic cloning will not prevent transplant rejection of cloned tissues:

“There is no question in my mind that the possibility exists that if you are doing an egg donor, and nuclear transfer into an egg, that there possibly exists that that cell -- that the embryonic stem cells derived from that could be rejected. Absolutely.” Dr. John Gearhart, Johns Hopkins

“I should say that when you put the nucleus in from a somatic cell, the mitochondria still come from the host.” He concluded, “And in mouse studies it is clear that those genetic differences can lead to a mild but certainly effective transplant rejection and so immunosuppression, mild though it is, will be required for that.” Dr. Irving Weissman, Stanford

Dr. James Thomson, who originally isolated human embryonic stem cells, has stated in one of his published papers that cloning is unlikely to be clinically significant.

“[T]he poor availability of human oocytes, the low efficiency of the nuclear transfer procedure, and the long population-doubling time of human ES cells make it difficult to envision this [therapeutic cloning by SCNT] becoming a routine clinical procedure…”24

Evidence from animal studies indicates that it will indeed require a tremendous number of human oocytes (eggs) to produce cells from cloned embryos. Dr. Peter Mombaerts, who was one of the first mouse cloners, estimated that it will require a minimum of 100 eggs.25 The reports from South Korea of human

[Footnote continued from previous page]


22 Dr. John Gearhart; transcript of the April 25, 2002 meeting of the President’s Council on Bioethics; p.47; http://www.bioethics.gov/meetings/200204/0425.doc

23 Dr. Irving Weissman, Stanford, before the President's Council on Bioethics on February 13, 2002


26 Hwang WS et al., Patient-specific embryonic stem cells derived from human SCNT blastocysts, Science published online 19 May 2005
embryo cloning were shown to be a fraud, but even so the news stories reveal that the researchers obtained over 2,200 human eggs for use in their unsuccessful experiments, through paying women to go through the risky procedures of egg harvesting, as well as through coercion of students. Even at an optimistic rate of 10 eggs per patient, to treat the 25 million diabetics in the U.S. by this technique would require at least a quarter of a billion human eggs.

In 2008 the report of the first documented success at cloning human embryos by the California company Stemagen (in which one of the scientists, Wood, admitted that he cloned himself) did not result in any cells obtained from the clones; they attributed their cloning success to use of fresh, high-quality human eggs from a nearby fertility clinic with which they were associated. The only reported case of obtaining embryonic stem cells from cloned monkey embryos was in 2007. It took over 100 eggs each to produce only 2 ESC lines (one of which had chromosomal problems.) The group had worked for almost 10 years, using around 15,000 monkey eggs.

Dr. Rudolph Jaenisch, a cloning scientist at Massachusetts Institute of Technology, noted:

“The procedure is very complicated, he said, and has ethical implications because the embryos have to be destroyed to obtain the stem cells.  “Nobody in their right mind would think this is useful for therapies,” Dr. Jaenisch said.”

In a recent profile of Dr. Jaenisch, he discussed the uselessness of so-called “therapeutic cloning” and how the technique is of no practical relevance:

“Ten years ago, we talked about the potential of nuclear transfer for therapy. But it turns out the technique was of no practical relevance. You would never do it in humans for a number of reasons.  First, it’s very inefficient. With mice, that doesn’t matter because we can do hundreds of transfers to get a few mice. But human cloning is another order of magnitude more difficult than in mice. And people can’t even get the eggs to practice [on]. My former student Kevin Eggan, along with his colleagues at Harvard, spent years putting in place a protocol to get volunteer egg donors. They spent a couple hundred thousand dollars just in advertising. And I think they got one or two donors.  Kevin’s postdoc, Dieter Egli, who went to Columbia, told me that he got a couple [of] human nuclear transfers going, but they all arrested at the 6- or 8-cell stage.”

Only two labs in the world have been able to isolate stem cells from cloned human embryos, after years of attempts. One lab in 2011 obtained only chromosomally-abnormal cells, with triploid chromosome numbers (50% more chromosomes than normal), which renders them useless in the lab or in the clinic. In May 2013 a lab in Oregon was able to produce a few dishes of stem cells from cloned human embryos, but had to find a woman with a specific genetic composition as an egg donor for the experiments, in order

27 French AJ et al., “Development of human cloned blastocysts following somatic cell nuclear transfer (SCNT) from adult fibroblasts”, *Stem Cells* published online Jan 17, 2008; DOI: 10.1634/stemcells.2007-0252
31 Hopkin K, "Ready, Reset, Go" The Scientist 25, 52, 2011
to get any of the experiments to work or cells to survive.\textsuperscript{33} That same Oregon lab has also been developing similar techniques of egg and embryo manipulation to construct 3-parent embryos.\textsuperscript{34}

Moreover, allowing “therapeutic” cloning while trying to ban reproductive cloning is unfeasible, and will simply hasten development of the process supposedly to be banned, reproductive cloning. Again, honest proponents of cloning have noted this themselves:

“It is true that the techniques developed in CRNT [cell replacement through nuclear transfer, aka therapeutic cloning] research can prepare the way scientifically and technically for efforts at reproductive cloning.”\textsuperscript{35}

The American Society for Reproductive Medicine (ASRM), the largest professional organization with expertise in reproductive technologies, says that SCNT is simply the procedure that clones embryos for whatever purpose (whether for starting a pregnancy or destroying for research). And ASRM concedes that if cloning for research is allowed, that research will be used to refine the process and will make it easier to perform “reproductive” cloning:

“If undertaken, the development of SCNT for such therapeutic purposes, in which embryos are not transferred for pregnancy, is likely to produce knowledge that could be used to achieve reproductive SCNT.”\textsuperscript{36}

In terms of the egg issue and numbers involved, one proposal has been to use animal eggs instead, to produce a animal-human hybrid or “chimera”. Some have claimed that this is improbable science, yet in 2003 a Chinese lab reported success using rabbit eggs to produce cloned animal-human hybrids,\textsuperscript{37} and the U.K. in fact issued three licenses to begin such research, and in 2008 one lab reported success at creating human-animal hybrid embryos using this technique with cow eggs, though they did not obtain any cells from the cloned embryos.\textsuperscript{38} Some laboratories, such as Advanced Cell Technology, have failed to produce cells from human-animal hybrid embryos and concluded that the technique is implausible.\textsuperscript{39} It should be noted that the same lab also failed to produce cells from fully-human clones. Such experiments, while ethically questionable and unlikely to produce useable results, are still not impossible, as noted above.

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\textsuperscript{33} Tachibana M, et al., Human Embryonic Stem Cells Derived by Somatic Cell Nuclear Transfer, Cell 153, 1228, 6 June 2013 (published online 15 May 2013)
\textsuperscript{34} Tachibana M et al., Mitochondrial gene replacement in primate offspring and embryonic stem cells, Nature 461, 367, 2009; Tachibana M et al., Towards germline gene therapy of inherited mitochondrial diseases, Nature 493, 627, 2013; Bredenoord AL et al., Nuclear transfer to prevent mitochondrial DNA disorders: revisiting the debate on reproductive cloning, Reproductive BioMedicine Online 22, 200, 2011
\textsuperscript{36} The Ethics Committee of the American Society for Reproductive Medicine; “Human somatic cell nuclear transfer (cloning)”; Fertility and Sterility 74, 873-876; November 2000.
\textsuperscript{37} Chen Y et al., Cell Research 13, 251, 2003
\textsuperscript{39} Chung Y et al., Cloning and Stem Cells 11, 1, 2009;
\end{flushleft}
In fact, advances in stem cell research have passed by the efforts at cloning. There is now an easier, less expensive and more direct method to produce embryonic-type stem cells from a patient’s own tissue, with a real potential for a tissue match and with no need for embryos. These cells, termed iPS (induced Pluripotent Stem) cells were first developed in 2006 from mice by the Japanese scientist Shinya Yamanaka. In November 2007 Yamanaka’s lab and Thomson’s lab in the U.S. showed this same technique worked with human cells as well, easily producing human iPS cells directly from human tissue. Yamanaka won the 2012 Nobel Prize in Physiology or Medicine for this technique, which has many advantages over cloning human embryos for their cells, and has already shown its usefulness for lab models of disease and for drug testing.

Some have claimed that cloning is needed to replace stocks of human embryonic stem cells originally obtained from IVF embryos, but this is not true. In March 2009, President Obama issued an executive order, and NIH issued guidelines, that allow many more human embryonic stem cell lines to be produced and federal taxpayer dollars to fund embryonic stem cell research. It is worth noting, however, that scientists were most concerned that the oldest, best characterized and reliable stem cell lines, previously funded, be approved; the stocks of those cells obviously did not need to be replaced. The NIH has at this date approved 234 embryonic stem cell lines for federal funding, including the oldest and best characterized lines.

Stem cell science has moved beyond the outdated cloning technique and the only remaining reason at this point to practice embryo cloning would be if the researcher wished to produce cloned embryos for gestation and birth.

Stem cell science has also moved well beyond cloning and hybrids in terms of real treatments for patients, by using adult stem cells. A wealth of published scientific papers document the successes of adult stem cells, which are already being used clinically to treat many conditions in human patients. A 2010 *Journal of the American Medical Association* article provided a global perspective on adult stem cell transplants, noting that adult stem cell transplants have become “the standard of care for many patients” with blood disorders and malignancies, are starting to be used for other conditions including autoimmune disorders and heart disease, and that their study “demonstrates that it is an accepted therapy worldwide”.

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40 Takahashi K and Yamanaka S, Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors, *Cell* 126, 663-676, 25 August 2006
41 Takahashi K et al., Induction of pluripotent stem cells from adult human fibroblasts by defined factors, *Cell* 131, 861-872, 30 November 2007; published online 20 November 2007; Yu J et al., Induced pluripotent stem cell lines derived from human somatic cells, *Science* 318, 1917-1920, 21 December 2007, published online 20 November 2007
45 Gratwohl A et al., Hematopoietic stem cell transplantation, *JAMA* 303, 1617-1624, 2010
Thus, while some misleadingly claim that cloning or animal-human hybrids are necessary to manufacture embryos for stem cell research, nothing could be further from the truth. These techniques are also not needed for commonly used animal tests for pluripotent stem cells. The technique used involves injection of stem cells into immune-compromised mice, where the pluripotent stem cells form a tumor (called a teratoma) within the mouse, providing potential data on their ability to form different tissue types. This test is done by injecting the cells into born mice, not by creating embryos.

There have also been fraudulent claims that patients who might theoretically receive injections of stem cells from their clones, created and destroyed outside of the state of Ohio, would be at risk of arrest upon entering the state of Ohio if HB 308 passes. This interpretation is based on a naïve or willful misreading of the bill. Cells incorporated into a patient’s body would not be covered by the bill, just as any person who eats a hamburger would not be arrested at the state line for transporting hazardous meat that might contain mad cow disease.

In the U.S., the federal government prohibits any federal taxpayer funding for creation of human embryos for research (including cloned embryos) or for destruction of human embryos. In addition, 8 states ban human cloning for any purpose (AR, AZ, IN, MI, ND, OK, SD, VA), with other states considering similar legislation. Internationally, many countries have moved to ban all human cloning, including countries such as France (7 years in jail), Germany (5 years in jail), Canada (5 years in jail), and in March 2005 even the United Nations passed a declaration against all human cloning.

HB 308 only bans production of cloned human embryos and production of animal-human hybrids. It does not address nor does it affect stem cell research, or human embryos produced by fertilization. HB 308 does not restrict any vital or viable medical research. Cloning and nuclear transfer techniques for production of DNA, other molecules, cells other than human embryos, tissues, organs, plants, and animals are all allowed.

There are no valid or compelling grounds—ethical, scientific, or medical—to allow cloning of human embryos for any purpose, nor for production of animal-human hybrids. HB 308 provides common sense restrictions on human cloning and animal-human hybrids in Ohio and would prohibit these abuses, without limiting any valid medical research. I encourage you to pass this bill.

Thank you for the opportunity to contribute to the information on this important issue.