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CLONING: A RISK TO WOMEN?

HEARING

BEFORE THE

SUBCOMMITTEE ON SCIENCE, TECHNOLOGY AND SPACE

OF THE

COMMITTEE ON COMMERCE, SCIENCE, AND TRANSPORTATION UNITED STATES SENATE

ONE HUNDRED EIGHTH CONGRESS

FIRST SESSION

MARCH 27, 2003

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SENATE COMMITTEE ON COMMERCE, SCIENCE, AND TRANSPORTATION

ONE HUNDRED EIGHTH CONGRESS

FIRST SESSION

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CLONING: A RISK TO WOMEN?

THURSDAY, MARCH 27, 2003

U.S. SENATE,
SUBCOMMITTEE ON SCIENCE, TECHNOLOGY, AND SPACE,
COMMITTEE ON COMMERCE, SCIENCE, AND TRANSPORTATION,
Washington, DC.

The Subcommittee met, pursuant to notice, at 9:35 a.m. in room SR–253, Russell Senate Office Building, Hon. Sam Brownback, Chairman of the Subcommittee, presiding.

OPENING STATEMENT OF HON. SAM BROWNBACK, U.S. SENATOR FROM KANSAS

Senator BROWNBACK. Good morning. The hearing will come to order. Today, we will conduct our second hearing in this Subcommittee on the issue of human cloning. We particularly want to try and better understand whether or not human cloning for so-called "therapeutic purposes" poses a risk to women's health. That will be the question we will examine today.

Many of the proponents of human cloning claim that a cure to many of the diseases that plague humanity lies just around the corner. In this hearing, we will examine some of these claims and also what would have to happen in order for these claims to be realized.

First, we should start with a few definitions. The bipartisan Human Cloning Prohibition Act of 2003, S. 245, sponsored by myself and Senator Landrieu, defines "human cloning" as human asexual reproduction that is accomplished by introducing nuclear material from one or more human somatic cells into a fertilized or unfertilized oocyte, or human egg, whose nuclear material has been removed or inactivated so as to produce a living organism at any stage of development that is genetically virtually identical to an existing or previously existing human organism.

The definition is very important. The fusion of the somatic cell and the oocyte creates a human embryo that is genetically identical to the somatic cell donor. This genetic match is what proponents of human cloning claim will solve the immune-response rejection problem and will provide treatment to millions of people.

This hearing will examine what would be necessary in order to realize the promise held out to those suffering by those who are advocating human cloning as a means to cure the diseases that plague humanity. And clearly, we all want to see a cure for these horrible diseases.

However, it is clear that in order to be effective, "therapeutic" cloning must rely on the collection of a vast number of human eggs.

In order to conduct so-called "therapeutic cloning" on the scale that would yield just a portion of the benefit that the advocates promise, one would need to harvest a vast number of human eggs from women of childbearing age. Dr. David Stevens estimates that—and this is a quote from him—"To get enough eggs to seek clone cures for these four diseases"—just four diseases—"ALS, Parkinson's, Alzheimer's, and diabetes, every woman in the U.S. aged 18 to 44—that is approximately 55 million—would have to endure two cycles of ovarian hormone hyperstimulation and then undergo surgery."

The "egg dearth" is a mathematical certainty. It is one reason why some researchers say that therapeutic cloning will not be generally available as a medical treatment.

Recently, biotech researchers, John Odorico, Dan Kaufman, and James Thompson, admitted the following in the research journal, Stem Cells, and stated this, "The poor availability of human oocytes, or eggs, the low efficiency of the nuclear cell procedure, and the long population doubling time of human ES cells make it difficult to envision this—therapeutic cloning—becoming a routine clinical procedure, even if ethical considerations were not a significant point of contention."

Perhaps this is what led Dr. Thomas Okarma, Chief Executive of Geron Corporation, to state that it would take, quote, "thousands of human eggs on an assembly line" to produce a custom therapy for a single person. He then goes on, "This process is a nonstarter, commercially."

Concerns such as these, as well as others, have led a group of progressive activists, many of whom support abortion rights, to state in their letter of support for a ban on all human cloning that, "Although we may differ in our views regarding reproductive issues, we agree that a human embryo should not be cloned for the specific intention of using it as a resource for medical experimentation or for producing a baby. Moreover, we believe that the market for eggs, women's eggs, that would be created by this research will provide unethical incentives for women to undergo health-threatening hormone treatment and surgery. We are also concerned about the increasing bio-industrialization of life by the scientific community and life science companies, and shocked and dismayed that clonal human embryos have been patented and declared to be human, 'inventions.'"

As I am sure many of our witnesses are already aware, and as many in this audience already know, the typical in vitro fertilization procedure involves the collection of eggs from women who seek to become pregnant in this manner. The market for these eggs is already developing. In fact, it is now known that Advanced Cell Technology of Massachusetts, the pioneers in human cloning, paid women up to $4,000 per egg donation. Such a market for women's eggs will clearly be a threat to the health of many women. That women undergo the health risks associated with egg donation for the purpose of having children is one thing; but that they would be induced by some to undergo this health risk for money is another matter.

I am hopeful that we can use this hearing to better understand the threats posed to women and whether or not this is a route we should even consider. But more importantly, I am growing increas-

ingly concerned that some of the proponents of human cloning are holding out the hope for a cure as a tool to build support for a morally dubious enterprise.

In the past, we have heard that fetal tissue research held the cure to the whole host of dread diseases that plague humanity. To date, we have met only with failure upon failure from fetal tissue research. Almost five years ago, we heard that human embryonic stem cell research held the cure. In fact, at one hearing Senator Specter asked Dr. James Thompson, "Illustrative for Parkinson's now, for Parkinson's, how long for a cure?" And Dr. Thompson's response, "Parkinson's? I am going to say five to ten years more. It will be one of the first ones." This December marks five years since he made that statement, and, to date, there is no cure for Parkinson's from human embryonic stem cells in sight.

I want to fight for a cure to Parkinson's disease. I want to see cures. I want to see us going routes and ways that we can get there. I want to get to the bottom of this, but we cannot continue to play with people's hopes.

Finally, I would like to note, with some satisfaction, that we are making some clear progress on the issue of human cloning. The Governor of Arkansas signed a bill very similar to S. 245, the bipartisan Human Cloning Prohibition Act of 2003, into law earlier this week. The State Senate of North Dakota voted, 46 to zero, yesterday to approve similar legislation, the State House in North Dakota having already voted, 90 to one, to approve the same legislation. There is a movement taking place across the board in a number of states.

We want to examine this, in particular, regarding women's health. And with that, I want to call up the first panel to testify here today. And if you would come forward. I think Senator Landrieu may be coming up later on. But the first panel of Dr. John Bruchalski, from Fairfax, Virginia, Dr. Maria del Carmen Bustillo, from Miami, Florida, and I think Lynne Millican called in earlier, sick, so I do not know if she has been able to arrive yet or not, apparently not. So we'll proceed with the two of you as the first panel.

I very much appreciate your attendance and your presentations. I will be happy to take your full written statement into the record and allow you to summarize, if you would like to; or if you would like to present that full statement, that would be fine, as well.

Dr. Bruchalski, I am sure I butchered your name. Would you give me the correct pronunciation?

Dr. BRUCHALSKI. Bruchalski.

Senator BROWNBACK. Bruchalski. I was making too much of it. I apologize for that.

Dr. Bruchalski, the floor is yours. Thank you very much for joining us here today.

STATEMENT OF DR. JOHN T. BRUCHALSKI, OBSTETRICIAN AND GYNECOLOGIST, FAIRFAX, VIRGINIA

Dr. BRUCHALSKI. Thank you, Senator, and good morning.

The tragic human backdrop to this Senate hearing is the very real and painful reality that one in six women of reproductive age

will seek professional help during their lifetimes because of infertility.

I come before you today because of my personal experience as an obstetrical and gynecologic resident from 1987 to 1991 at the Norfolk Medical Program, the home of the Jones Institute for Reproductive Medicine. It is the American infertility center that not only successfully produced America's first in vitro child, but was also the center that coined the term "pre-embryo" while I was there.

And because of what I have learned in the last dozen years as a practicing obstetrician and gynecologist, I want to focus my remarks to the very real issues of egg donation in the cloning process, otherwise termed "human somatic cell nuclear transfer," and their detrimental impact on women.

To appreciate this deleterious effect and the massive scope of this risk to women, I would just like to briefly review the cloning process. An egg is surgically, usually transvaginally, taken from the hormonally treated woman's ovary. The nucleus is removed from that egg, and a somatic nucleus from the individual to be cloned is transferred into an empty egg and fused with electric current. Then development occurs through the morula stage when the preembryo is screened for gene expression and imprinting defects. This is done until the blastocyst stage, when it is implanted into the woman's uterus.

However, this process is quite fragile, that despite having cloned five animal species, we hypothesize the need for hundreds, if not thousands, of eggs to be obtained for each clone to be used to treat the mentioned diseases of Parkinson's, Alzheimer's, and diabetes, to name a few.

Where and how and from whom are these eggs to be obtained? We need look no further than our present IVF data. If IVF donors average 10 to 15 eggs retrieved per hyper-stimulated cycle and each patient with Parkinson's disease needs 50 to a hundred eggs to clone to obtain stem cells, for the 1 million people with Parkinson's disease, 50 million eggs would be required to be retrieved from possibly 5 million egg donors. For the 17 million people with diabetes, 850 million eggs would be required, and, subsequently, 85 million egg donors needed.

To obtain these eggs, we must turn to drugs and/or to donors. But remember, the success of cloning in the IVF process used rests literally on the bodies of the women experimented on. IVF was successful in humans before it was successful in animals. ICSI, intracytoplasmic sperm injection, an assisted reproductive technology used in up to 40 percent of all cycles now was successful in humans before it was successful in animals. There appears to be a fuzzy boundary between research and treatment when it comes to those women undergoing these processes.

Our reproductive industry is not enveloped by a coherent, whole, regulatory framework. The drugs are regulated by the FDA without long-term data, and the process of mixing sperm and egg together in any way in combination is not regulated at all. The natural progression of research is to do experiments in cell cultures in animal models to look at safety issues first and whether these experiments are effective. Then, after you have this data, you move on to humans, specifically women in the case of this reproductive tech-

nology. This has not happened with the reproductive technologies up until now, and this is my concern.

Institution review boards that are found in hospitals are only required for research in federally backed institutions or for FDA-regulated products. And ART has been largely privately funded.

The Genetics and Public Policy Center at Johns Hopkins Hospital University is beginning to look into this travesty. Women have borne the positive and negative effects of being experimented on through the years of IVF, and now it appears the same with cloning.

Kathy Hudson, who is the director of the above-mentioned institute at Hopkins said, "Scientifically, there are some unanswered questions about the long-term consequences those drugs might have on women. There are questions about whether they lead to the production of unhealthy eggs and whether they pose a cancer risk to the mother. That is an area that we, at the center, hope to examine."

Drugs such as Fertinex, Gonal-F, Pergonal, Cetrotide, and Lupron are all to be under review. Significant headaches, abdominal swelling, abdominal pain are some of the more common side effects. And since we have now had a plateau in the success of IVF procedures, we are now beginning to look into other user-friendly protocols that have fewer side effects.

In 2002, alone, at least 12 studies in articles in peer-review journals suggest a potential link between these reproductive technologies and birth defects, like heart defects and genetic diseases, childhood cancers, decreased cognition, and others. We truly do not know whether it is due to the nature of the problems of infertility or due to the drugs and the procedures of assisted reproduction.

The fertility drug-cancer link refers to ovarian stimulation in ovarian cancer. The initial Whittemore study, a meta-analysis of 12 case-controlled studies on ovulation induction seemed to show a 27-fold increased odds ratio for developing ovarian cancer, even though some of the analysis was determined to be flawed. Later, the Rossing study reported a similar association between the drugs of ovulation and ovarian cancer.

This alleged increased risk of ovarian cancer in patients using ovulation-inducing agents is very disturbing, and a consensus among our American Fertility Society recommends that women who are considering the use of fertility drugs should be told that there is a possibility of increased risk and should be given alternatives. But at this point, there is no data overall to support discontinuing or changing these ovulation-induction procedures. Two small numbers, detection bias and recall bias, were all used to statistically support their conclusions.

These drugs also have spurred the profound rise in multiple births—twins, triplets, and above. In the year 2000, 35 percent of ART births were multiples, and their higher risks for birth defects and low birth weight and added healthcare costs are a significant psychological burden for women, not to mention the process of selection reduction where the infertile woman is faced with the decision to terminate one of her fetuses to improve outcome.

Now, the other approach to obtain eggs is to seek a donor, a woman who is willing to donate her eggs for the cloning process.

Again, we can look to in vitro experience for what to expect in the cloning scenario. Last month, experts in the United Kingdom publicly questioned whether such selfless acts are justified given the health risks they may face in later life. These women are paid between 1,500 to 3,500 American dollars, or 4,000 to 5,000 British pounds, oftentimes going to the highest bidder over the Internet.

A prominent physician at a London IVF clinic, citing the unknown long-term effects and the possible cancer risks, says that they cannot duck this issue any longer for their donor egg patients. However, the British Human Fertilization and Embryology Authority says it has no plans to review the system for egg donation.

On this side of the Atlantic, it is illegal to buy or sell human body parts, except eggs. In 1999, we transferred more than 8,000 embryos produced from fresh or frozen donated eggs into the uteri of women, according to the American Society for Reproductive Medicine. Ads placed in campus newspapers dangling tens of thousands of dollars before women with the right pedigree of looks, talent, and SAT scores is the method for attracting these precise donors. For a month, the woman turns over her body to the process of superovulation with the above-mentioned agents and the harvesting procedure of transvaginal aspiration. One out of a hundred will develop the hyperstimulation syndrome, which includes ascites, pulmonary overload, and sometimes hospitalization. One Stanford woman recently even had a stroke while being treated for egg donation.

The psychological component of this process is being questioned. "Are we leading them to make a decision that later in life they may regret? The money will be spent, and, in the end, she will have given up her genetic child forever. We have to really care about these women."

So, in conclusion, I agree that the problem of infertility is quite enormous and that we have made great strides since the late 1970s and early 1980s. However, my profession has recently seen the data on the benefits of menopausal hormonal therapy crumble in less than a year while listening to all the angst and betrayal spoken of by my older patients who have taken these hormonal therapies.

After considerable pressure, my alma mater, despite private funding, decided to stop creating human embryos specifically for stem cell research this past January. That is the Jones Institute. They were the first institute in the world to make human embryos for research and then to destroy them after harvesting the stem cells. We perfected ART in humans before we did it in animals, using women as research subjects and treatment end points. There was no animal data before IVF and ICSI were done in humans.

In 1993, the award-winning prized paper at the conjoined meeting of the American and Canadian Fertility Societies came out of George Washington University and Dr. Hall. Seventeen abnormal human embryos were taken and multiplied to obtain 48 embryos. Two embryo clones developed to the 32-cell stage before the procedure was stopped. This was done in 1993 and presented at that conference and received the top prize.

I come before this Committee, and I urge this Subcommittee to see cloning as another risk to women.

Thank you very much.
[The prepared statement of Dr. Bruchalski follows:]

PREPARED STATEMENT OF DR. JOHN T. BRUCHALSKI, OBSTETRICIAN AND GYNECOLOGIST, FAIRFAX, VIRGINIA

Introduction

Good morning. The tragic human backdrop to this Senate hearing is the very real and painful reality that one in six women of reproductive age will seek professional help during their lifetimes because of infertility. [1] I come before you today because of my personal experiences as an obstetrical and gynecologic resident from 1987 to 1991 at the Norfolk medical program that houses the Jones Institute for Reproductive Medicine, the preeminent, American infertility Center that not only successfully produced America's first in vitro child, but also the Center that coined the term "pre-embryo" while I was there; and because of what I have learned in the last dozen years as a practicing obstetrician and gynecologist I want to focus my remarks to the very real issues of egg donation in the cloning process, (human somatic cell nuclear transfer), and their detrimental impact on women.

Cloning's Abuse of Women: Issues With Egg Donation

To appreciate the deleterious effects and the massive scope of this risk to women, let's briefly review the cloning process. An egg is surgically, usually transvaginally, taken from the hormonally treated woman's ovary. The nucleus is removed from the egg, and a somatic nucleus from the individual to be cloned is transferred into the empty egg and fused with electric current. Then development occurs through the morula stage when the pre-embryo is screened for gene expression and imprinting defects, until the blastocyst stage (64 to 200 cell stage) when it is implanted into the woman's uterus. [2]

However, this process is so fragile that despite having already cloned five animal species, we hypothesize the need for hundreds, if not thousands of eggs to be obtained for each clone to be used to treat the mentioned diseases of ALS, Parkinson's, Alzheimer's and diabetes. Where and how and from whom are these eggs to be obtained? We need look no further than our present IVF data. If IVF donors average 10 to 15 eggs retrieved per hyper-stimulated cycle presently, and each patient with Parkinson's Disease need 50 to 100 eggs to clone, to obtain stem cells; for the one million Parkinson patients, 50 million eggs would be required to be retrieved, from possibly 5 million egg donors. For the 17 million with diabetes, 850 million eggs would be required, and subsequently, 85 million egg donors needed. [3]

To obtain these eggs we must turn to drugs and/or to donors, but remember, the success of cloning and the IVF processes used rests literally on the bodies of the women experimented on. IVF was successful in humans before it was successful in animals. ICSI, an assisted reproductive technology, used in up to 40 percent of all cycles, was successful in humans before it was successful in animals. There is a fuzzy boundary between research and treatment when it comes to those women undergoing these processes. [4] Our reproductive industry is not enveloped by a coherent, whole regulatory framework. The drugs are regulated by the Food and Drug Administration without long term data, and the process of mixing sperm and egg together in any way and combination is not regulated at all. The natural progression of research is to do experiments in cell culture or animal models, to look at safety issues first, and whether these experiments are effective. Then after you have a lot of animal data, you move into humans, specifically women in the case of reproduction. This hasn't happened with ART and this is my concern. Institutional Review Boards are only required for research if federally backed institutions, or for FDA regulated products, and ART has been largely privately funded. The Genetics and Public Policy Center at Johns Hopkins University is beginning to look into this travesty. Women have born the positive and negative effects of being experimented on through the years of IVF and now it appears the same with cloning.

Drugs

Kathy Hudson, the director of the above mentioned new institute at Hopkins said, "Scientifically, there are some unanswered questions about the long term consequences those drugs might have on women. There are questions about whether they lead to the production of unhealthy eggs, and whether they pose a cancer risk to the mother. That's an area that we at the Center hope to examine". [5] Fertinex, purified FSH from urine; Gonal F, FSH engineered from recombinant DNA; Pergonal, a mixture of FSH and LH collected from postmenopausal women; Cetrotide, a GnRH antagonist; and Lupron, the initial GnRH agonist mainstay are

all to be under review. Significant headaches, abdominal bloating changing clothes size, and abdominal pain are some of the more common side effects. [6]

In 2002 alone, at least 12 studies and articles in peer-reviewed journals suggest a potential link between ART and birth defects like heart defects and genetic diseases; childhood cancer; decreased cognition and more. We do not know whether it is due to the nature of the problems of infertility or due to the drugs and the procedures of assisted reproduction. [7, 8]

The fertility drug/cancer link refers to ovarian stimulation and ovarian cancer. The initial Whittemore study, a metaanalysis of 12 case controlled studies on ovulation induction seemed to show a 27 fold increased odds ratio for developing ovarian cancer even though some of the analysis was determined to be flawed. [9] Later, the Rossing study reported a similar association between the drugs of ovulation and ovarian cancer. [10] This alleged increased risk of ovarian cancer in patients using ovulation inducing drugs is very disturbing, and a consensus among our American Fertility Society recommends that women who are considering the use of fertility drugs should be told that there is a possibility of increased risk and should be given alternatives, but there is no data to support discontinuing or changing ovulation induction, follicular stimulation, or in-vitro fertilization. [11] Too small numbers, detection bias, and recall bias were used to support their conclusion.

These drugs also have spurred the profound rise in multiple births; twins, triplets, and above. In 2000, 35 percent of all ART births were multiples, and their higher risk for birth defects and low birth weight and added health care costs are a significant psychological burden for women, not to mention the process of selective reduction where the infertile woman is faced with the decision to terminate one of her fetuses to improve outcome. [12]

Egg Donors

The other approach to obtain eggs is to seek a donor, a woman who is willing to donate her eggs for the cloning process. Again, we can look to the in-vitro experience for what to expect in the cloning cases.

Last month, experts in the United Kingdom publicly questioned whether such selfless acts are justified given the health risks they may face in later life. These women are paid from $1,500 to $3,500 in America to 4,000 to 5,000 pounds in the UK, oftentimes going to the highest bidder over the internet. [13] A prominent physician at a London IVF clinic citing the unknown long term effects, and the possible cancer risks says they can not duck this issue any longer for their donor egg patients. However, the British Human Fertilization and Embryology Authority says it has no plans to review the system for egg donation. [13]

On this side of the Atlantic it is illegal to buy or sell human body parts, except for eggs. In 1999, we transferred more than 8,000 embryos produced from fresh or frozen donated eggs into the wombs of women according to the American Society for Reproductive Medicine. [14] Ads placed in campus newspapers, dangling tens of thousands of dollars before women with the right pedigree of looks, talent and SAT scores is the method for attracting the precise donor. [15] For a month, the woman turns over her body to the process of superovulation with the above mentioned drugs and the harvesting procedure of transvaginal aspiration. One out of hundred will develop the "hyperstimulation" condition that includes: fluid shifts, ascites, pulmonary overload and sometimes hospitalization. One Stanford woman even had a stroke while being treated for egg donation. The American Society for Reproductive Medicine developed guidelines that place a $5,000 limit on donor compensation, and calling for independent medical and psychological evaluations of the donors. The guidelines seem to be on target but not all centers adhere to them. [15]

The psychological component of this process is being questioned, "Are we leading them to make a decision that later in life they may regret? The money will be spent and, in the end, she has given up her genetic child forever. We have to really care about these women." [16]

Conclusion

We have to really care about these women. My profession has seen the data on the benefits of menopausal hormonal therapy crumble in less than a year, while listening to all the angst and betrayal spoken by my elder patients.

After considerable pressure, my alma mater, despite private funding, decided to stop creating human embryos specifically for stem cell research this past January. They were the first institute in the world to make human embryos for research and then to destroy them after harvesting the stem cells. [17]

We perfected ART in humans before we did it in animals, using women as research subjects and treatment endpoints. There was no animal data before IVF and

ICSI were done in humans. With this as background and fact, I urge this Subcommittee to see cloning as another risk to women.

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Senator BROWNBACK. Thank you, Dr. Bruchalski. I appreciate that.

Dr. Bustillo, thank you very much for joining us here today. We look forward to your testimony.

STATEMENT OF DR. MARIA BUSTILLO, DIRECTOR, ASSISTED REPRODUCTIVE TECHNOLOGIES, SOUTH FLORIDA INSTITUTE FOR REPRODUCTIVE MEDICINE

Dr. BUSTILLO. Thank you very much. Good morning, Mr. Chairman.

I am Dr. Maria Bustillo. I am the director of Assisted Reproductive Technologies, or ART, at the South Florida Institute for Reproductive Medicine in Miami, Florida. However, today I am representing the Coalition for the Advancement of Medical Research. It is a group of more than 75 patient advocacy, scientific, and research organizations dedicated to stem cell research.

Since 1981, I have been involved in ART working to assist women and their families to bring children into this world. I have worked in human reproduction since the earliest days of in vitro fertilization and its related technologies. The field, which, like embryonic stem cell research and somatic cell nuclear transfer today, was filled with controversy.

Over the last 20 years, the science and clinical practice of ART has improved dramatically. To date, more than 150,000 children have been born in the United States thanks to these treatments.

Over the past two decades, I have advocated for the adequate inclusion of women in clinical trials. Early on in this debate, some individuals were concerned about the exploitation of women, but the Institute of Medicine of the National Academy of Sciences, in its landmark 1994 report, concluded that both justice and science

were best served by the adequate inclusion of women in well designed scientific research.

Similarly, today, as we view this new area of science, regenerative medicine, individuals again have expressed concerns about the exploitation of women. I believe that this relatively new area of science, properly regulated, potentially holds more hope for treatments and cures for diseases for which women and men suffer than it poses risks to their health. In this belief about therapeutic cloning I am in agreement with 40 Nobel Prize winners and the former First Lady, Nancy Reagan.

Today's discussion relates to research to improve the health of millions of patients, many of whom are women, while preventing the specter of human reproductive cloning in an area which I believe is unethical and unsafe. Categorically, I am against the cloning of a new human being, and I believe that most Americans, including scientists and physicians, would agree.

Opponents of therapeutic cloning protest that women will become egg-producing factories endangering themselves and deepening the divide between socioeconomic classes, because poor women will be more willing to sell their eggs. Donating eggs is far more complicated than contributing sperm, but women are smart enough to make informed choices about their bodies, including what they want to do with their eggs.

It is important that we deal with facts, not speculation and not rhetoric. We have a great deal of experience with egg donation. It is a vital therapeutic option which has been used to help more than 15,000 American families to have children.

I was a member of the American team that performed the first egg donation in 1983, and I have personally treated many egg donors over the last 20 years. I can assure you that I would not do that if it were not safe. All potential egg donors first undergo extensive medical and psychological screening. Ordinarily, a woman matures and releases only one egg in a menstrual cycle. In our techniques, including egg donation, medications are given to achieve the development of multiple eggs. Over that time period, the woman is monitored. And after the development is deemed appropriate, the eggs are retrieved transvaginally using ultrasound guidance.

The American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology have guidelines which they have promulgated extensively that are both clinical and ethical guidelines for gamete donation. And all its member clinics, 370 member clinics of SART, are required to adhere to these guidelines.

I would like to ask that these reports and statement be entered into the record.

Senator BROWNBACK. Without objection, they will be in the record. *

Dr. BUSTILLO. Many of the standards the profession has had in place for a number of years will now be enforced by the FDA as they make final the regulations of reproductive tissues within the next year.

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*The information referred to has been retained in Committee files.

In sum, there is a long history of egg donations for reproductive uses. Protections and safeguards for both the donor and the recipient are in place and, I think, could be easily modified to accommodate egg donation for research or clinical applications of embryonic stem cells.

As a scientist and long-time women's health advocate, I also find a complete ban on research troubling. About 25 years ago, because of similar religious and ethical considerations, there was a call for a ban on research involving recombinant DNA. Today, hundreds of thousands of people are healthier or alive because of the use of recombinant DNA to produce insulin, interferons, and other therapeutic recombinant molecules.

This leads me to discuss why I believe women, as well as men, have tremendous potential to benefit from therapeutic cloning. Regenerative medicine, including using cloning techniques to create new cells more like a patient's own cells holds the promise to treat and cure numerous debilitating and deadly diseases like cancer, autoimmune diseases like lupus, multiple sclerosis, and early-onset diabetes, cardiovascular disease, and neurological diseases like Alzheimer's and Parkinson's. Annually, these diseases strike more than a hundred million individuals, a large proportion of whom are women. This field of research holds the potential to restore normal, healthy functions to cells and replace those that no longer function.

Therapeutic cloning using somatic cell nuclear transfer holds great promise to develop new and innovative treatments for numerous diseases. For instance, let us discuss breast cancer. Using somatic cell nuclear transfer, scientists could take a cell from a patient with breast cancer and reprogram the cell to its earliest stage of development. Then they can compare the diseased cell's development to the healthy cell's development. In so doing, scientists could learn about the trigger mechanisms that lead to that disease. These fundamental insights offer tremendous potential for the development of interventions to treat or prevent disease. This is an example of why extracting stem cells from in vitro fertilized embryos is inadequate in tackling certain research.

Women are affected not only by the diseases that attack them, but also by the diseases contracted by other family members, as they, women, are routinely their families' predominant caretakers. Women's, wives', mothers', daughters' lives quickly become subsumed by the illnesses within their families.

I realize that embryonic stem cell research is in its infancy and an enormous amount of research must be performed before it can be translated into medical treatments, but we must carefully weigh the implications of any roadblocks that might halt this research. As with any technology, procedures become more efficient in time, so fewer eggs will be required. Researchers in therapeutic cloning also are hopeful that in the future they will know how to generate stem cells without needing eggs.

Senate bill 303, the Hatch-Feinstein bill, strictly punishes unlawful conduct by providing criminal and civil penalties for violating the law while at the same time allowing physician and patient access to potential life-saving therapies without the fear of reprisal.

I thank you for your time.

[The prepared statement of Dr. Bustillo follows:]

PREPARED STATEMENT OF DR. MARIA BUSTILLO, DIRECTOR, ASSISTED REPRODUCTIVE TECHNOLOGIES, SOUTH FLORIDA INSTITUTE FOR REPRODUCTIVE MEDICINE

Good morning, Mr. Chairman and Members of the Subcommittee. I am Dr. Maria Bustillo, Director of the ART at the South Florida Institute for Reproductive Medicine in Miami, Florida. I also am a founding member and former board member and vice president of the Society for Women's Health Research; past President of the Society for Assisted Reproductive Technology and former board member of the American Society of Reproductive Medicine. Today I am representing the Coalition for the Advancement of Medical Research, a group of more than 75 patient advocacy, scientific and research organizations dedicated to stem cell research.

Since 1981, 1 have been involved in assisted reproductive technology, working to assist women and their families to bring children into this world. I have worked since the earliest days of In-Vitro Fertilization and related Assisted Reproductive Technologies, a field which like embryonic stem cell research and somatic cell nuclear transfer today, was filled with controversy. Over the last twenty years, the science and clinical practice of ART has improved dramatically. To date, more than 150,000 children have been born in the United States thanks to these treatments.

Throughout my career I also have worked to advance research on women's health and supported work to alleviate their suffering and improve the quality and longevity of their lives. With the Society, over the past decade, I have advocated for the adequate inclusion of women in clinical trials and the subsequent analysis of resultant data so that scientific conclusions take into account any differences between women and men. Early on, in this debate, some individuals were concerned about the exploitation of women. But, the Institute of Medicine (of the National Academy of Sciences) in its landmark 1994 report concluded that both justice and science were best served by the adequate inclusion of women in well-designed scientific research.

Similarly, today as we view this new area of science, regenerative medicine, individuals again have expressed concerns about the exploitation of women. Once again, I am in agreement with the National Academy of Sciences. Two of its recently published reports support the exploration of the potential of regenerative medicine and therapeutic cloning. I believe that this relatively new area of science, properly regulated, potentially holds more hope for treatments and cures for diseases from which women and men suffer than it poses risks to their health.

Today's discussion relates to research to improve the health of millions of patients, many of whom are women, while preventing the specter of human reproductive cloning—an area which I believe is unethical and unsafe. Categorically, I am against the cloning of a new human being, and I believe that most Americans, including scientists and physicians, would agree. Just this month, in a poll commissioned by the Coalition for the Advancement of Medical Research, more than two thirds of Americans support therapeutic cloning research to produce stem cells for treating life-threatening diseases and conditions and want the government to allow it to proceed. I agree with them and the National Academy of Sciences, 40 Nobel Prize winners, and former First Lady Nancy Reagan in my support for therapeutic cloning.

Initially, I would like to counter opposition to therapeutic cloning as it relates to women. First, opponents of cloning protest that women will become egg-producing factories, endangering themselves and deepening the divide between socioeconomic classes because poor women will be more willing to sell their eggs.

It is true that donating eggs is far more complicated than contributing sperm. But women are smart enough to make informed choices about their bodies, including what they want to do with their eggs. Women who believe that they can help an ailing family member or even help women like themselves who have a history of, say, Alzheimer's disease, should be allowed to make these choices.

It is important that we deal with facts, not speculation and not rhetoric. We have a great deal of experience with egg donation. It is a vital therapeutic option which has been used to help more than 15,000 American families have children. Twenty years ago, I was on the team that performed the first egg donation and I have personally treated many egg donors over the past 20 years. I can assure you I would not do that if it were not safe.

All potential egg donors first undergo extensive medical and psychological screening. Women who are deemed as suitable donors enter a pool of potential donors who are then matched with recipient couples. The donor undergoes what is known as controlled superovulation. Ordinarily a woman matures and releases only one egg in each menstrual cycle. In ART techniques, including egg donating, the physician administers a combination of hormonal medications for about two to three weeks to trigger the development of many eggs. Over that time period, the patient is mon-

itored using ultra sound technology and diagnostic blood tests. Finally the eggs are retrieved using transvaginal aspiration, using an ultrasound guided needle and intravenous sedation.

As with any medical procedure, there are some potential risks to the patient/donor. There is a slight risk (less than 1 percent) of ovarian hyper stimulation, though even this risk is thought to be lower in donors than in normal ART patients. There have also been some studies reporting a link between some of the medicines used in ART procedures and ovarian cancer, which caused some initial concern. However further research has led us to conclude that there may well be an underlying medical problem which may be associated with both infertility and ovarian cancer. That is, it is not the medicines which lead to a higher cancer rate.

The American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology have promulgated extensive clinical and ethical guidelines on gamete donation, and all 370 member clinics of SART are required to adhere to these standards. I would like to ask that these reports and statement be entered into the record.

These standards include the extensive screening I described early, a limitation on the number of times any one woman can donate, and a cap on compensation to the donor. The ASRM ethics committee has determined that sperm and egg donors can be compensated for the time and trouble associated with the donation, but that compensation should not vary according to the traits of the donor.

Many of the standards the profession has had in place for a number of years will now be enforced by the FDA as they make final their regulations of reproductive tissues next year.

In sum, there is a long history of egg donation for reproductive uses. Protections and safeguards for both donor and recipient are in place and could easily be modified to accommodate egg donation for research or clinical applications of embryonic stem cells.

As a scientist and longtime women's health advocate, I also find a complete ban on research troubling. I am aware that the word "moratorium" is used in Senator Brownback's legislation, but I view a "moratorium" the same as a ban because after a hiatus in an area of scientific research, trained scientists are no longer available, the field diminishes, and the United States would have to play catch-up with other nation's research achievements. About 25 years ago, because of similar religious and ethical considerations, there was a call for a ban on research involving recombinant DNA. Today hundreds of thousands of people are healthier or alive because of the use of recombinant DNA to produce insulin, interferons, and other therapeutic recombinant molecules.

This leads me to discuss why I believe women, as well as men, have tremendous potential to benefit from therapeutic cloning. Regenerative medicine, including using cloning techniques to create new cells more like a patient's own cells, holds the promise to treat and cure numerous debilitating and deadly diseases, like cancer, autoimmune diseases like lupus erythematosus (lupus), multiple sclerosis, and early onset diabetes, cardiovascular disease and neurological diseases like Alzheimer's and Parkinson's disease. Annually, these diseases strike more than 100 million individuals, a large proportion of whom are women. This field of research holds the potential to restore normal healthy functions to cells and replace those that no longer function.

Therapeutic cloning, using Somatic Cell Nuclear Transplantation (SCNT) holds great promise to develop new and innovative treatments for numerous diseases. For instance, let us discuss breast cancer. Using SCNT, scientists can take the cell of a patient with breast cancer and reprogram the cell to its earliest stage of development. Then, they can compare the diseased cell's development to the healthy cell's development. In so doing, scientists can learn about the trigger mechanisms that lead to disease. These fundamental insights offer tremendous potential for the development of interventions to treat or prevent disease. This is an example of why extracting stem cells from In-Vitro Fertilization (IVF) embryos is inadequate for tackling certain research.

Cardiovascular disease, including heart attacks and congestive heart failure, is the nation's number one killer of both women and men. Annually, approximately one-half million more women than men die of this dreaded disease. Restoring the function of damaged heart cells is a daunting challenge. The National Institutes of Health reports that recent research provides early evidence that adult and embryonic stem cells may be able to replace damaged heart muscle cells and establish new blood vessels to supply them. Scientists believe that embryonic stem cells in contrast to adult stem cells hold greater potential because they have the ability to be come any type of cell in the human body and hold virtually unlimited ability to replicate.

Many autoimmune diseases like lupus, multiple sclerosis, rheumatoid arthritis, and Sjogren's disease, strike women disproportionately. Lupus and Sjogren's are nine times more frequent in women; rheumatoid arthritis is four times more frequent in women; and multiple sclerosis strikes women twice as frequently as men. (Other autoimmune diseases like early onset diabetes are more evenly distributed among the population.) For all autoimmune diseases, complex biological questions remain unanswered about why the body's immune system fails to protect the body against disease and allows it to turn against itself. Research on stem cells is providing new ways to remove errant immune cells and restore normal immune cells to the body. However, obstacles to some type of adult stem cells are the limited number that can be harvested and the difficulties in propagating them in the laboratories.

Women also are affected not only by the diseases that attack them but also by the diseases contracted by other members of their family, as they routinely are their family's predominant caretakers. Wives', mothers', and daughters' lives quickly become subsumed by the illnesses within their families.

I realize that embryonic stem cell research is in its infancy, and an enormous amount of research must he performed before it can be translated into medical treatments. But we must carefully weigh the implications of any roadblocks that might halt this scientific research.

S. 245, the Human Cloning Prohibition Act, legislation introduced by Senator Brownback, to my knowledge, for the first time in U.S. history, dead ends a promising new avenue of research, perhaps sending it underground, or at the least, sending it overseas along with our most promising scientists. It outlaws research that scientists believe could play a critical role in curing and alleviating the suffering of millions of patients, including women. This bill also makes criminals of anyone who would bring into this country the potential products of this research.

The Coalition for the Advancement for Medical Research believes that S. 303, the Human Cloning Ban and Stem Cell Research Protection Act, the legislation introduced by Senators Hatch, Feinstein, Specter, Kennedy, Harkin, and Miller strikes the appropriate balance between preventing unsafe and unethical research on human reproductive cloning and permitting scientific research endorsed by the National Academy of Sciences, 40 Nobel laureates, former First Lady Nancy Reagan, and former Presidents Gerald Ford and Jimmy Carter.

S. 303 applies the Common Rule, the law governing federal ethical standards, to SCNT research so that institutional review boards already in place at universities and hospitals would ensure that women participating in research are fully informed about the procedures and risks involved in donating eggs. As in all areas of research, stringent safeguards must be in place to protect people against coersion. Otherwise informed consent is not truly informed consent. As I already discussed, egg donation in all circumstances must be conducted with rigorous informed-consent procedures. (As with any technology, procedures become more efficient in time, so fewer eggs will be required. Researchers in therapeutic cloning also are hopeful that in the future they will know how to generate stem cells without needing eggs.) S. 303 also strictly penalizes unlawful conduct by providing for criminal and civil penalties for violating the law while allowing physician and patient access to potentially life-saving therapies without fear of reprisal.

Thank you.

Senator BROWNBACK. Thank you. Thank you for your testimony. Dr. Bustillo? Am I——

Dr. BUSTILLO. Bustillo, uh-huh.

Senator BROWNBACK. Bustillo. There a number of diabetes cases in the country, how many people suffer from diabetes in the U.S.?

Dr. BUSTILLO. Well, there are two different kinds of diabetes, but the majority of patients with diabetes have adult-onset diabetes. But juvenile-onset diabetes affects millions of young people, as well.

Senator BROWNBACK. Just walk me through the numbers of what it would take if human cloning were allowed for treatment just in diabetes, of how many——

Dr. BUSTILLO. I think what we——

Senator BROWNBACK.—eggs it would take to provide this as a broad-scale treatment across the country.

Dr. BUSTILLO. I think what we need to remember is that those numbers seem huge, but the issue is that I think we need to do some very basic research that would allow us to generate, for instance, stem cell lines that would divide themselves and that would need, as the technology gets more efficient, fewer and fewer eggs to treat the patients. But we are at the stage where we really are just beginning to learn about this.

So, yes, it will take hundreds and thousands of eggs to do this.

Senator BROWNBACK. Where will we come up with those eggs?

Dr. BUSTILLO. Well, I think there are a number of ways to come up with those eggs. The one is what the folks at Norfolk did, which is actually to recruit women, under review, institutional review board, screened, paid to do this as they would otherwise do it, as most women who do egg donation do get paid in the United States and are often anonymous to the recipient couple, and would provide these eggs for the purpose of research either because they have a family member that might in the future benefit from this research or because they are interested in helping humanity.

Senator BROWNBACK. Should we be paying women for eggs?

Dr. BUSTILLO. I think the position of the Fertility Society or the Society of Reproductive Medicine is that we should pay women for their time and trouble. This is a procedure not as easy as just giving a sperm sample. And as my colleague here stated, it does take several weeks, several medications, so we are really paying them for time off, babysitting, the things that they need. So we have determined what a reasonable cost is to them.

Senator BROWNBACK. So you would put a cap on how much we could pay women for eggs?

Dr. BUSTILLO. Yes.

Senator BROWNBACK. Have you come up with a——

Dr. BUSTILLO. I think——

Senator BROWNBACK.—position of what that——

Dr. BUSTILLO.—as he mentioned it——

Senator BROWNBACK.—price——

Dr. BUSTILLO.—in the United States, it is somewhere between 1,500, and in states like New Jersey and New York it is a lot higher. So it varies, depending on the part of the country that you are with. But I think, no, not more than 5,000, 6,000 would be a very reasonable amount.

Senator BROWNBACK. To put a national upper price tag on women's eggs?

Dr. BUSTILLO. I think it would be dangerous to do that, because—again, hopefully, as we get more efficient with new medications, new protocols, it may involve less trouble, less time, et cetera, so to put a national cap which may actually be higher than you might need in the future would not be wise.

Senator BROWNBACK. But you agree that now some women are being recruited and paid very high prices based upon their mental capacity, their physical nature, is that correct?

Dr. BUSTILLO. Well, they are being recruited. I do not know how widespread that is. And again, the American Society for Reproductive Medicine, the Fertility Society, is definitely opposed to that and encourages its members not to proceed in that fashion.

Senator BROWNBACK. But you would encourage women to be recruited for egg donation for human cloning.

Dr. BUSTILLO. For therapeutic cloning, yes.

Senator BROWNBACK. And you would——

Dr. BUSTILLO. For the generation of stem cells, yes, sir.

Senator BROWNBACK. Okay, so you would. And you do agree that that—if we were to go with this on a broad-scale effort to try to cure a number of these diseases, we are talking of, you said, hundreds of thousands of eggs.

Dr. BUSTILLO. Yes, sir.

Senator BROWNBACK. And that is going to involve at least hundreds of thousands of women, is that correct, or millions?

Dr. BUSTILLO. Well, also another source of eggs would be infertility patients. We cannot forget them. And especially as infertility patients, if we get the younger infertility patient—if we should provide insurance coverage, for instance, for in vitro and make it amenable to the younger patient, they generally would produce more eggs than they require to generate their own, to solve their own fertility problem.

Senator BROWNBACK. But how many women are you envisioning? Let us say we just said therapeutic cloning is fabulous, we are going to go full scale with therapeutic cloning, start recruiting women. We have got a hundred million people, in your testimony, that suffer from these debilitating diseases. Are we not talking about millions of women donating——

Dr. BUSTILLO. No, because——

Senator BROWNBACK.—their eggs?

Dr. BUSTILLO.—again, I think as the research gets better, hopefully we will not even need eggs at some point once—I mean, we will still need some eggs for some of the cell-development studies that I mentioned, with breast cancer and other diseases, but as we get more efficient and we learn how to replicate and keep stem cell lines going, et cetera, I think we are going to need fewer and fewer fresh donated eggs.

Senator BROWNBACK. Well, let us say we really get good at this and you only need five eggs per patient. I mean, that is a fabulous number relative to—I think Dolly was 300 tries, something like that, to get——

Dr. BUSTILLO. Two hundred and almost forty experiments, yes.

Senator BROWNBACK. So let us say we get it to a five to one ratio, that you only need five eggs for the try, which would be a—that would be a great technological move forward.

Dr. BUSTILLO. Uh-huh.

Senator BROWNBACK. Are you not truly still talking about millions of women who are going to have to sell their eggs for this process——

Dr. BUSTILLO. Again——

Senator BROWNBACK.—to really be engaged?

Dr. BUSTILLO. Again, it would be—you know, there are probably close to 50,000 women undergoing in vitro for therapeutic reasons for their own infertility, so that would also add to the pool of the donation.

Senator BROWNBACK. Okay. All right, 50,000, and we get five—let us say—how many eggs do we get per those——

Dr. BUSTILLO. It is——

Senator BROWNBACK.—50,000?

Dr. BUSTILLO.—age related, and you can—in donors, in general, we get 15 to 20, 25 eggs. In——

Senator BROWNBACK. Say we get 20.

Dr. BUSTILLO.—patients, we get fewer.

Senator BROWNBACK. What if we—can we get 20 eggs from those 50,000 women? Twenty eggs——

Dr. BUSTILLO. We could——

Senator BROWNBACK.—each?

Dr. BUSTILLO.—we could get 15 eggs from each, right. But I think what we have to do to make it much more efficient is not each time get the egg, but obtain stem cells from the initial few women who would donate eggs for research purposes, obtain these stem cells, do the research, do the work, keep them going, and then this would be much more effective than having to do the therapeutic cloning each time you want to treat a patient.

Senator BROWNBACK. Okay, so you are saying you just do not think we are going to be needing therapeutic cloning in the future. You think we need it now, but we are not going to need it in the future. Is that——

Dr. BUSTILLO. That's very——

Senator BROWNBACK.—correct?

Dr. BUSTILLO.—possible.

Senator BROWNBACK. But, now, you base that on——

Dr. BUSTILLO. Just——

Senator BROWNBACK.—nothing but hope at this point——

Dr. BUSTILLO. No, I think——

Senator BROWNBACK.—in time.

Dr. BUSTILLO.—I base that on some of the things we are learning about what to do, how to treat these cells to make them go in certain tissues, like, you know, pancreatic tissue, et cetera; and if we can learn the mechanisms of how these cells go from undifferentiated cells to these specific cells, then I think we will be able to reproduce those and need them less and less.

Senator BROWNBACK. Okay, then why do we not do that in animals first and than take that to humans? Why do we not perfect what you are saying first in animals before we go to——

Dr. BUSTILLO. Well——

Senator BROWNBACK.—humans?

Dr. BUSTILLO.—always, animals are wonderful, but they are not necessarily humans.

Senator BROWNBACK. But do we not normally, in this country, start with animal——

Dr. BUSTILLO. And we——

Senator BROWNBACK.—models and——

Dr. BUSTILLO.—do, and we have, and there are some wonderful animal models and some recent data on the model for Parkinson's disease in the mouse. And work has been done in that area which shows very promising results in the mouse now being mobile after transferring of cells generated from stem cells from mouse embryos.

Senator BROWNBACK. No, I understand, but why would you not perfect your technique that you are hoping we get to so we do not

need the millions of women's eggs? Why do we not perfect that first in animals and then take it to humans?

Dr. BUSTILLO. No, I think we have been doing that. However, the animal is never a perfect model for the human.

Senator BROWNBACK. Well, have we developed what you have said in animals yet and perfected it and the technique so we do not have to do the cloning, which you are saying we——

Dr. BUSTILLO. I think——

Senator BROWNBACK.—should need to in the future?

Dr. BUSTILLO. I think we are in the process of doing that, yes, sir.

Senator BROWNBACK. But it has not been done yet.

Dr. BUSTILLO. Not perfected for every cell type.

Senator BROWNBACK. It is not even close, is it?

Dr. BUSTILLO. I do not think so.

Senator BROWNBACK. So you are basing this, that we are going to do this in humans, off of what you hope will take place but what we have not produced in animal models even yet, is that correct?

Dr. BUSTILLO. I think so. You have to remember that the isolation of stem cells in animals has only been around for about 10, 15 years, so the work is just beginning. Things in science often take a long time. So we are at a very early stage of this kind of research.

Senator BROWNBACK. Do we normally, then, in early stages of research, do that on humans?

Dr. BUSTILLO. In this country, we have done that—for instance, as my colleague mentioned, in vitro fertilization—because often there is absolutely no financing for this kind of work, particularly from the Federal Government. So, oftentimes, this research is advocated and driven by the patients affected by the disease, such as——

Senator BROWNBACK. But is it not normally true we develop our animal models first; and then, when we perfect it, we take it to humans?

Dr. BUSTILLO. Again, that was not done in in vitro fertilization.

Senator BROWNBACK. I understand, but do we not normally——

Dr. BUSTILLO. Yes, and I——

Senator BROWNBACK. We are talking about therapeutic cloning here, correct?

Dr. BUSTILLO. Right.

Senator BROWNBACK. Okay.

Senator Landrieu has arrived and is limited on her time. Would you mind if we have her testify now, and you can stay seated there, and we will receive her testimony?

Senator Landrieu, thank you very much for joining us. I appreciate you being here, a cosponsor of the bill, and I am happy to receive your testimony.

STATEMENT OF HON. MARY L. LANDRIEU,
U.S. SENATOR FROM LOUISIANA

Senator LANDRIEU. Thank you, Mr. Chairman. I am going to submit a more detailed statement for the record.* I would like to

*The information referred to was not available at the time this hearing went to press.

thank our witnesses for being a part of this very important hearing. I also wanted to thank you, Mr. Chairman, and to show my support for your efforts to try to help the public better understand that the alternative to a ban on human cloning is actually the licensing of a brand-new industry. I think this hearing is very important in trying to communicate to the public what that industry would look like.

What the witnesses have just described, I think, would be very upsetting to many, many people in this country. The level of experimentation that would have to go on, the numbers of women that would be needed for these types of experiments, and the lack of fine-tuning of the procedures is concerning. I think that your point about the normal course of scientific work in this country is to perfect some of these techniques on animals before we move to the human population is a good one.

I applaud your efforts this morning to help focus on the shortcomings of this Feinstein-Kennedy proposal, and force us to consider how licensing a brand-new industry, crosses the ethical line, as well as the line of common sense.

I also want to note for the record that as the weeks and months go on with many legislatures in session around the country, two legislatures have recently passed a ban in North Dakota and Arkansas. Many people in my State of Louisiana, are very concerned about this issue, not because they are against research, or because they oppose science or finding cures for the terrible diseases that our children and our grandchildren suffer from, but because we have grave concerns about opening up an industry where the marketplace dictates or moves women to donate hundreds and thousands of the—what is to prevent the situation arising where the smarter you are, "prettier" you are, the "more attractive" you are, you get paid more for your egg than someone else, who is "less attractive" or "less smart," to have an industry that virtually is, in many ways, unregulated. Even if it were regulated with our best attempts here, I am not sure that we could eliminate some of the more gruesome aspects of what is being discussed here today.

I thank the scientists here for their work and their efforts. I appreciate we have different views. But again, it is important to be clear what Congress is debating. The issue is whether to license a new industry that would use women as manufacturers and eggs as commodities. Do we want to be setting prices on eggs and injecting hormones into women to produce eggs for the benefit of experimentation? I think this is too far for where the American people want to go at this time.

Thank you, Mr. Chairman.

Senator BROWNBACK. Thank you for submitting the statement for the record, and thank you for coming by, Senator Landrieu.

Dr. Bruchalski, what would happen if you took just a hundred thousand women and collected their eggs for therapeutic cloning? What is the likely impact on that hundred-thousand women? Do we have any notion of studies of how many would be impacted negatively, physically, by just that many going through? Not a million, but just a hundred thousand.

Dr. BRUCHALSKI. At a hundred thousand people undergoing this process——

Senator BROWNBACK. Pull that microphone a little closer.

Dr. BRUCHALSKI. For a hundred thousand women undergoing this process, there would be the effects of hyperstimulation on all these women, including abdominal bloating, tenderness so significant that we are now trying to perform or have newer protocols to decrease these side effects that are so pervasive. We believe that it is close to 1 percent of these women would undergo the hyperstimulation syndrome, so whatever 1 percent of a hundred thousand—it is in this small subset where you have a fluid overload situation, where the abdomen is filled with fluid, and it is called ascites. You can develop pulmonary edema, and you have to hospitalize this group of patients to prevent further decompensation. And so that occurs in 1 percent of the present—almost 1 percent of the present-day cycles. So you are looking at a sizeable number of women who would undergo serious side effects in order to obtain the outcomes desired. And at a hundred thousand, that is, relatively, a very, very, very conservative estimate for any of the diseases mentioned.

Senator BROWNBACK. Well, what if we extend that to a million women? I would gather we are going to get a broader cross-section of women to donate—or sell eggs, rather—at that point in time, a broader cross-section of health potential difficulties if you are going at a million women. What potential health side-effects could we have with that large of a pool?

Dr. BRUCHALSKI. Well, you would still be looking at the numbers that I suggested, but it would be, you know, multiplied by a factor of ten. You would have still that 1 percent of a million having to be hospitalized, and the vast majority of those other women having to often take time off through that month's therapy to deal with not only the procedures itself, but many of the side effects, which I just mentioned, which include headache, abdominal tenderness, abdominal pain, pelvic pain.

Senator BROWNBACK. Do we have any idea of the price we would have to pay to get women to do this, where it is not for a child for themselves, which I would think—you know, a number of women, if this is for a child, their child, they are willing to go through a lot of things to do that, and I am so grateful, but if this is to sell eggs, do we have any notion of price that you are going to have to bid to to be able to get a million women to donate eggs and go through this process?

Dr. BRUCHALSKI. No, we do not know exactly the amount. The guidelines that are given are—how can I say? They are encouraged. They are not really required; they are encouraged for the various centers to follow. And I appreciate my colleague's hopeful optimism in regard to this, how possibly we can try to decrease that number over time so we do not have this impact.

But I still keep coming back to the reality that in in-vitro fertilization cycles today, we still are able to get 10 to 15 eggs per cycle. We have not improved on our efficiency in 20-plus years of in vitro fertilization work in this country. We have made incredible strides. We have helped many centers, instead of placing six, seven, eight, nine, ten embryos back into uteri, we are now recommending only three to four, in many cases, because of the horrors and the difficulties with multiple births. We have made many strides.

But I do not know the exact top-dollar amount that would have to be placed, because right now, as you mentioned, that number is quite high, in some cases.

Senator BROWNBACK. Dr. Bustillo, do we have any idea of how many women now sell their eggs, not for their own childbearing for themselves, but for somebody else? Do we have any notion of what that market is now?

Dr. BUSTILLO. Well, we have——

Senator BROWNBACK. The total number?

Dr. BUSTILLO. Right. We have data, the American Society of Reproductive Medicine, actually under the—the CDC collects that data from these member clinics of the American Society for Reproductive Medicine, and the last—we collect the data after birth, so we have numbers, and I believe the 2000 data, which he mentioned was the last data, and I believe it was around 8-, 9,000 cycles of egg donation. Now, those women do not necessarily all sell their eggs, because some women who donate their eggs are actually relatives—i.e., sisters, friends—of the women who need the eggs.

Senator BROWNBACK. Okay.

Dr. BUSTILLO. So we do not have a hard number on how many are actually paid. But I would suspect that the majority of egg donation is done with paying the donors. And again, just for the——

Senator BROWNBACK. Somewhere 8- to 9,000?

Dr. BUSTILLO. No, sir.

Senator BROWNBACK. 8- to 9,000 that——

Dr. BUSTILLO. Yes.

Senator BROWNBACK.—did not——

Dr. BUSTILLO. That——

Senator BROWNBACK.—this is not for their own child.

Dr. BUSTILLO. Right, that is correct.

Senator BROWNBACK. Okay. So let us say we have got to increase that number up to a hundred thousand, which I think is dreadfully low. I mean, for what we have of current technology, you are really looking at the millions to make this broadly available for people. But let us say it is just a hundred thousand women that we want to pay to give eggs so that we could go on some scale of therapeutic cloning across the United States, just a hundred thousand women. So these are not going to be for a baby for themselves; this is going to be for research purposes, this is going to be for trying to develop health cures. How much of a market bid-up are we going to have to do to get a hundred thousand women to donate eggs?

Dr. BUSTILLO. Again, you are assuming that those eggs will only come from women who are volunteering for the research, because I still think that some women who are going through in vitro fertilization for their own benefit, again, as we—and I disagree with my colleague; we have made great strides in the success rate of IVF.

Senator BROWNBACK. How much would we have to pay to get a hundred thousand women to donate eggs?

Dr. BUSTILLO. How much do we have to pay them? Again, it depends on what they have to go through, and——

Senator BROWNBACK. Well, you know what they have to go through.

Dr. BUSTILLO. Well, I know what they have to go through today. I know what they had to go through 20 years ago, which is much more than they have to go——

Senator BROWNBACK. Well, how much——

Dr. BUSTILLO.—through today.

Senator BROWNBACK.—what they'll have to go through next year.

Dr. BUSTILLO. Next year? They——

Senator BROWNBACK. Are we just going to open it up——

Dr. BUSTILLO. Yes.

Senator BROWNBACK. So the technology is basically——

Dr. BUSTILLO. I would say——

Senator BROWNBACK.—what you have today.

Dr. BUSTILLO.—you'd have to pay about $3,000.

Senator BROWNBACK. You think we can get a hundred thousand women for $3,000 each to donate eggs, go through the process that we're involved in.

Dr. BUSTILLO. I mean, it's not going to be easy. They need to be motivated, you know, for the betterment of humanity, for the relative with diabetes.

Senator BROWNBACK. Well——

Dr. BUSTILLO. It's going to be——

Senator BROWNBACK.—if you were asked to do this, could do this, or had a daughter that wanted to do this, would you do this for $3,000?

Dr. BUSTILLO. Yes, sir.

Senator BROWNBACK. And you would recommend your daughter to do it for——

Dr. BUSTILLO. I would——

Senator BROWNBACK.—3,000.

Dr. BUSTILLO.—if she was comfortable with it. She would have to be screened medically, psychologically, all the implications of that, yes.

Senator BROWNBACK. What all is the screening that's going to need to take place?

Dr. BUSTILLO. Well, we have been doing this for a number of years, but you would have to screen them for—and the screening may be different, because the screening we do now is because they're going to hopefully produce babies, so we screen them genetically, a number of tests, routine tests, that we do for cystic fibrosis, et cetera. We screen them to make sure they have no other medical illnesses. We screen them for their family history. They meet with psychologists. They have a number of visits to make sure they understand the implication of their eggs going either to someone else or to research, so they have to be very comfortable with it.

Senator BROWNBACK. So——

Dr. BUSTILLO. I would say, in my practice, we screen ten women to have one accepted, just—and this is for——

Senator BROWNBACK. So we're talking about a million women needing to come forward to get a hundred thousand to——

Dr. BUSTILLO. It's very possible.

Senator BROWNBACK. Wow.

Dr. BUSTILLO. But, again, you are assuming that you're going to need this sort of generation of fresh eggs on a continuing basis.

Senator BROWNBACK. Well, if we start this right now, we obviously are going to need that.

Dr. BUSTILLO. No, because you're talking about treating everyone at once. All research, you know, doesn't start by application to a hundred million people that are affected by these diseases. We're talking about beginning slowly and hopefully perfecting it so we need fewer eggs, you know, because we're going to create stem cell lines, et cetera.

Senator BROWNBACK. We are going to perfect it amongst people as we go along.

Dr. BUSTILLO. Because, again, animal models are being worked on, but I think they are not perfect. And eventually you will have to jump from animals to people.

Senator BROWNBACK. It would be nice if we knew it worked in animals first before we tried it in people, do you not think?

Dr. BUSTILLO. I think it would, and I think we have some very encouraging new data coming out that it does for certain diseases, like Parkinson's.

Senator BROWNBACK. With therapeutic cloning, we are—talking about therapeutic cloning at this point. Do you think we are——

Dr. BUSTILLO. We are talking——

Senator BROWNBACK.—perfected enough on the——

Dr. BUSTILLO. We are talking——

Senator BROWNBACK.—cloning process to take that from animals to humans and move this on forward?

Dr. BUSTILLO. I am talking about the generation of stem cells that then can be directed to make tissues that would treat diseases like Parkinson's, diabetes, et cetera.

Senator BROWNBACK. Now, have you studied the cloning research in animals and whether or not we have any health problems in those animals. If we have——

Dr. BUSTILLO. Not——

Senator BROWNBACK.—perfected the cloning process in animals.

Dr. BUSTILLO. You are now talking, sir, about reproductive cloning, and I am adamantly opposed to that.

Senator BROWNBACK. But would you agree that there are health problems in reproductive clones?

Dr. BUSTILLO. In reproductive cloning, yes, sir.

Senator BROWNBACK. Where would they carry those health problems from? Do they get them from the very first genetic pool that they are in or not?

Dr. BUSTILLO. We do not know what the problems are—I mean, how the problems start. And as you said, there were over 200 experiments to generate Dolly. But——

Senator BROWNBACK. Dolly——

Dr. BUSTILLO.—we are confusing the issue a little bit that——

Senator BROWNBACK. Well——

Dr. BUSTILLO.—we are talking now about——

Senator BROWNBACK.—but let me ask you——

Dr. BUSTILLO.—reproductive cloning.

Senator BROWNBACK. Then correct me as I go through this. Dolly was just put to sleep.

Dr. BUSTILLO. Yes.

Senator BROWNBACK. Aged prematurely, I believe. Did she have lung and liver problems?

Dr. BUSTILLO. Yes.

Senator BROWNBACK. Okay.

Dr. BUSTILLO. Lung problems, I believe.

Senator BROWNBACK. Do we think any of these, or do we know, if these were genetic problems that she had?

Dr. BUSTILLO. We do not know for sure.

Senator BROWNBACK. Is it a good chance they were——

Dr. BUSTILLO. But again, sir——

Senator BROWNBACK.—genetic problems?

Dr. BUSTILLO.—we are talking about reproductive cloning. I am not in——

Senator BROWNBACK. I understand.

Dr. BUSTILLO.—favor of——

Senator BROWNBACK. I understand.

Dr. BUSTILLO.—reproductive cloning.

Senator BROWNBACK. I understand we are talking about reproductive cloning. But when does gene imprinting occur?

Dr. BUSTILLO. It depends on the gene, but I think usually very early.

Senator BROWNBACK. Are you not given the very first gene pool as what you start with? And does it change——

Dr. BUSTILLO. That is——

Senator BROWNBACK.—at a very——

Dr. BUSTILLO.—correct. But again, when we are talking about stem cells, we are talking about a cell that is undifferentiated——

Senator BROWNBACK. I understand, but——

Dr. BUSTILLO.—not imprinted——

Senator BROWNBACK. Well, then maybe I just need to be much more clear with you on my question. If Dolly has genetic problems—she is given a genetic pool from the very outset that does not change, so if she has genetic problems, she has them as a therapeutic clone or as a reproductive clone if she has a genetic defect in this system. Is that correct?

Dr. BUSTILLO. No, sir, because it is a——

Senator BROWNBACK. Okay, but——

Dr. BUSTILLO.—different——

Senator BROWNBACK.—when does the gene change?

Dr. BUSTILLO. It is one cell versus an organism, so it is a very different situation.

Senator BROWNBACK. Is the gene pool any different?

Dr. BUSTILLO. Well, yes, it is different in that it does not—in some cases, it does not have, you know, the immunologic signals, et cetera, so it depends on the cell. Yes, it is very different.

Senator BROWNBACK. So the gene pool that Dolly had as a one-cell embryo is different from what she has as an adult.

Dr. BUSTILLO. No, but the gene pool of Dolly as an organism and the interaction between the genes and the different cells between the different organ systems is a whole different situation from taking a few cells from a five day old embryo and generating stem cells that are undifferentiated.

Senator BROWNBACK. Is it possible that Dolly had genetic defects as a one-cell embryo?

Dr. BUSTILLO. Yes, it is very possible.

Senator BROWNBACK. Isn't it even likely?

Dr. BUSTILLO. It is likely, because, again, Dolly, again, was generated from an adult somatic cell, and we are not talking about doing that with therapeutic cloning utilizing stem cell generation from normally in vitro fertilized embryos. It is a different experiment.

Senator BROWNBACK. Are you comfortable with the level of knowledge we have of therapeutic cloning amongst animals today——

Dr. BUSTILLO. I think——

Senator BROWNBACK.—that this is a technology to be transferred to humans?

Dr. BUSTILLO. I think, in certain areas, I think it is very promising and probably ready for some early human experiments, like Parkinson's disease.

Senator BROWNBACK. And you are comfortable with what we know in the animal to transfer it into the human model today?

Dr. BUSTILLO. I am not an expert on Parkinson's disease or in this area, but I think it is, again, promising, and I think what we need is more research utilizing human tissues. I know we are not ready to institute medical therapy utilizing therapeutic cloning today.

Senator BROWNBACK. Okay.

Thank you, panelists, very much for your interest and your information, and we appreciate very much your coming here and testifying today.

I would call up our next panel, Ms. Alta Charo, Associate Dean for Research and Faculty Development, University of Wisconsin Law School, Mr. Andrew Kimbrell, International Center for Technology Assessment, and Mr. Richard Doerflinger, Associate Director for Policy Development, U.S. Conference of Catholic Bishops.

I was just informed that a witness in that first panel, Lynne Millican, is in at Union Station, so we may add her to you as a panel when she comes on forward.

Ms. Charo, thank you very much for joining us today, and the floor is yours.

STATEMENT OF R. ALTA CHARO, J.D., ASSOCIATE DEAN, PROFESSOR OF LAW AND BIOETHICS, UNIVERSITY OF WISCONSIN LAW AND MEDICAL SCHOOLS

Ms. CHARO. Thank you very much, Senator Brownback, and thank you for the opportunity to discuss with you a shared goal of preventing irresponsible efforts to use cloning to produce children.

As you know, Congress has repeatedly tried to bolster the FDA's already successful efforts to prohibit reproductive cloning, but each effort has become bogged down in a related, but distinctly separate, debate concerning the use of cloning for nonreproductive research or therapeutic purposes, and I urge you today to separate those two debates.

S. 303 bans reproductive cloning with stiff penalties for those scientists and doctors who might dare to make such an attempt by transferring a cloned embryo into a woman's body, and it builds on

the extensive existing regulation of cloning research by adding even further regulatory safeguards.

Now, if and when cloning research is done in humans for therapeutic ends—that is, to produce embryos whose stem cells will be transplanted back into the donor to repair damaged organs—it is clearly and indisputably covered by the FDA regulations on cell-based therapy and transplantation, regulations that already apply to privately funded activity and that, by virtue of the congressional delegation of power to FDA, answers some of the very questions raised earlier today about the appropriate transition from animal to human research and the scaling of human research under close monitoring.

FDA's regulations cover myriad aspects of the work, from the labs where it is done to the collection of the eggs, the nuclear transfer procedure, the derivation of stem cells, and, finally, the transplant back to the donor. The regulations also require that every aspect of the work be carried out under the strict oversight of an institutional review board. Those IRBs ensure that reimbursement to egg donors is reasonable and poses no risk of donors being tempted to abandon their own good judgment. The IRBs also review the scientific basis for determining the risks and benefits that will be described to these women and the actual documents that will embody the information for their use when they give their informed consent. IRBs also monitor the research while it goes on, with periodic updates to guard against unexpected side effects. This is the same comprehensive scheme of protections used generally for human subjects research in the United States.

Now, S. 303 would build on this very extensive set of current regulations that governs all publicly or privately transplant-related work by extending the common rule to even privately funded work that does not involve transplantation as an end point. Under S. 303, even basic research that involves only developing stem cell lines for work in the laboratory would still require informed consent from egg donors and oversight by IRBs so that no aspect of cloning work, whether for therapeutic or purely research purposes, could proceed unmonitored.

Now, given the extensive existing and proposed regulation, I believe that prohibiting all cloning research is unduly burdensome and, in addition, subject to constitutional challenge. For 30 years, courts and scholars have discussed the scope of the First Amendment and its protection of scientific research as part of the freedom of thought, inquiry, and dissemination of knowledge that is at the core of that aspect of the Bill of Rights. Thought and the testing of thoughts through science facilitates the dissemination of ideas just as much as monetary contributions to political campaigns facilitates the expression of political ideas. And indeed, in many cases, research is, in and of itself, a form of political expression.

In other places and other times, governments have sought to ban the dissection of the human body because it would interfere with deeply felt notions of the body as a reflection of the divine order; or sought to ban investigation of the orbits of the planets, as it would interfere with essential views about the place of humankind in the universe. So, too, does investigation of the origins of life, of the secrets of conception and development, threaten our deepest

views concerning the sources of life. But the First Amendment exists precisely to protect the development and dissemination of knowledge and truth and opinion so that it may be tested and retested over time in the marketplace of ideas.

Certainly, of course, protected activities are still subject to reasonable regulation; but where prohibitions are designed merely to guard against the development of knowledge for fear it might someday be used in controversial ways, it runs afoul of the very basis of the First Amendment protection of inquiry.

And where prohibitions are designed to guard against violating the rights of embryos, they run athwart of the legal reality that federal law does not grant embryos the same rights as live born children. Indeed, the Supreme Court has repeatedly reiterated its view that even while science and theology and philosophy continue to debate the biological and moral status of the embryo, the Constitution does not grant them the rights of persons under the law. Any federal law that goes beyond reasonable regulation and instead entirely bans nonreproductive research and therapeutic cloning applications, therefore, is vulnerable to challenges in interference in the First Amendment rights of patients, doctors, and scientists, a challenge that might well result in an injunction on the enforcement of the entire federal law during the many years that judicial review runs its course.

I, therefore, urge the Congress to focus on legislation that prevents the unsafe practice of reproductive cloning. I also urge it to adopt the additional regulatory protections for nonreproductive research uses of cloning, as proposed in S. 303, so the public is reassured that every measure has been taken to guide the research in a responsible way.

A debate on embryo research, generally, or on nonreproductive cloning research, in particular, can always proceed separately, to be debated on its own merits and ultimately to be tested on its own terms before the constitutional authorities of the Nation.

Thank you very much, Senator Brownback.

[The prepared statement of Ms. Charo follows:]

PREPARED STATEMENT OF R. ALTA CHARO, J.D., ASSOCIATE DEAN, PROFESSOR OF LAW AND BIOETHICS, UNIVERSITY OF WISCONSIN LAW AND MEDICAL SCHOOLS

Mr. Chairman and Members of the Committee,

My name is Alta Charo, and I am a professor of law and bioethics at the University of Wisconsin. Thank you for this opportunity to discuss with you a shared goal, the goal of preventing irresponsible experimentation that involves the use of somatic cell nuclear transfer (that is, cloning) to produce a live-born child.

Because cloning is not, and may well never be, a safe method for conceiving children, there is virtually perfect consensus that such attempts ought to be discouraged. The Federal Food and Drug Administration has already taken a first and definitive step toward this goal, by announcing that it views attempts to use somatic cell nuclear transfer to create a child to fall within the scope of its regulatory authority, and by further announcing that this technique may not legally be used in the United States for this purpose.

While scholars may argue about the precise statutory language behind this action, it is a fact that FDA has already enforced its authority, by investigating alleged attempts to use cloning to produce a live-born child, and by issuing warning letters to those suspected of being most likely to try this unsafe experiment. The small number of eccentric scientists who claim an interest in pursuing this effort have reacted by moving their activities to other countries, and by acknowledging in the press that they understand that cloning to produce a live-born child is illegal in the United States, thus confirming the effectiveness of FDA's enforcement efforts.

The Congress has repeatedly demonstrated its interest in bolstering FDA's already successful efforts, whether by re-affirming and particularizing its jurisdiction over this activity or by banning the practice directly by legislative action. In each effort, however, Congress has become bogged down in a related but distinctly separate debate concerning the use of cloning for research or therapeutic purposes.

I urge you today to separate these two debates, both to protect the valuable scientific and medical advances that may emerge from non-reproductive cloning research, and to pave the way to effective action to discourage attempts to use this technique to produce children.

S. 303, introduced and co-sponsored in the Senate by Members such as Senators Hatch, Feinstein, Kennedy, and Specter would prohibit all efforts to use cloning to produce children. Stiff penalties are applied to those who would dare to make such an attempt. The simple act of transferring a cloned embryo into a woman's womb becomes definitive proof of the attempt and triggers criminal penalties for those doctors or scientists who make the attempt.

Critics of this approach express concern that such legislation would be difficult to enforce, and urge Congress to ban basic research lest it lead to the prohibited act of transferring a cloned embryo into a womb for development. But criminal law is almost always grounded in a theory of deterrence. We do not prohibit the manufacture of guns in order to guard against the possibility of their future misuse in homicide. Rather, we criminalize misuse of guns and prosecute the offenders accordingly.

Critics of this approach also worry that this leaves other, non-reproductive forms of research unregulated, and fear it may lead to exploitation of egg donors or the diversion of this research toward eugenic ends. But these critics overlook both the extensive existing regulation of cloning research and the additional regulatory safeguards that have been proposed in new legislation before the Senate.

If and when cloning research is done for therapeutic ends, that is, when it is done to produce embryos whose stem cells will be transplanted back into the donor in an effort to repair or regrow damaged tissues of the brain, the heart and other organs, it is clearly and indisputably covered by the FDA regulations on cell-based therapy and transplantation. These regulations cover all such research, even when it is done with private funding.

FDA's regulations cover myriad aspects of the research, from the laboratories where it may be done, to the collection of eggs, to the nuclear transfer procedure, to the derivation of stem cells, to the final transplant back to the donor. And FDA regulation also requires that every aspect of the work be carried out under the strict oversight of an Institutional Review Board (IRB), whose job is to guarantee that eggs are donated only after voluntary and fully informed consent.

IRBs ensure that reimbursement to egg donors for their time and inconvenience is reasonable and poses no risk of donors being tempted to abandon their own good judgement. And IRBs review the scientific basis for the information given to egg donors about the risks associated with egg donation, as well as the actual documents they will be given to ensure that their consent is genuinely informed. IRBs also monitor research, with periodic updates to guard against unexpected side-effects in donors or unexpected problems in the laboratory management of the cloned materials and stem cells. This is the same, comprehensive scheme of protections used generally for human subjects research, and our experience in the United States demonstrates that research with human subjects, is not only extremely safe, it is far safer than the ordinary practice of medicine.

This system of protections is supplemented with an extra layer of safeguards whenever genetic engineering is introduced into research. If and when cloning research comes to involve genetic manipulation of any sort involving the embryo or its stem cells, it will also be screened by the Federal Recombinant DNA Advisory Committee, which has long functioned as the gatekeeper to gene therapy. This Committee's charge is broad, and it is empowered to examine every aspect of research to ensure its safety for all participants.

S. 303 would extend this comprehensive system of protections to all cloning research, by extending the Common Rule for human research protections even to privately funded research that does not involve transplanting the resulting stem cells back into the donor. Unique to cloning research is the possibility of cloning tissue from women who suffer from breast cancer or autoimmune diseases, so that specialized stem cell lines that exhibit these diseases can be grown in the laboratory for further research and testing. No other source of stem cells, neither those from surplus IVF embryos at infertility clinics nor those from bone marrow or other sources of adult stem cells can be used for this crucial research. Here, S. 303 would require informed consent from egg donors and oversight by IRBs, so that no aspect of

cloning work, whether for therapeutic or purely research purposes, would proceed unmonitored.

Given the extensive regulation that already exists, and the proposals for extending that regulation even further, outright prohibitions or moratoria on cloning research are unduly burdensome and subject to constitutional challenge.

For thirty years, federal courts and nationally recognized scholars have discussed the scope of the First Amendment and its protection of scientific research as part of the freedom of thought, inquiry, and dissemination of knowledge that is at the core of that aspect of the Bill of Rights. Research is an integral part of the scientific method, a form of inquiry that fits uniquely within the purposes, histories, and structures of the First Amendment. Thought and the testing of thoughts through science facilitates the dissemination of ideas just as much as monetary contributions to political candidates facilitates the expression of political ideas.

Indeed, in many cases, research is in and of itself a form of challenging political ideas. In other places and other times, governments have sought to ban the dissection of human bodies, because it would interfere with deeply felt notions of the body as a reflection of the divine order, or have sought to ban investigation of the orbits of the planets, as it would interfere with essential views about the place of humankind in the universe. So, too, does investigation of the origins of life, of the secrets of conception and development, threaten our deepest views concerning the sources of life. But the First Amendment exists precisely to protect the development and dissemination of knowledge and truth and opinion, so that they may be tested and retested over time in the marketplace of ideas.

Certainly, even protected activities are subject to reasonable regulation to avoid interfering with the rights of others. But where prohibitions are designed merely to guard against the development of knowledge, for fear it might someday lead to new and controversial ways to manipulate cells and genes, they run afoul of the very basis of the First Amendment protection of inquiry, association, and dissemination.

And where prohibitions are designed to guard against violating the rights of embryos, they run athwart of the legal reality that federal law does not grant embryos the same rights as live-born children. Indeed, the Supreme Court has repeatedly reiterated its view that even while science, theology and philosophy continue to debate the biological and moral status of the embryo, the Constitution does not grant them the rights of other persons under the law.

Any federal law that goes beyond reasonable regulation of cloning research and enacts a temporary or permanent ban on this form of scientific inquiry is thus vulnerable to challenge in court as an interference with the First Amendment rights of patients and researchers. Such challenges might well result in an injunction to forbid enforcement of the federal law until judicial review has been completed, a process that can take years. During such a hiatus, the federal law is inoperative, thus thwarting Congressional efforts to use legislation to prevent reproductive uses of cloning.

If the Congress wishes to take action with regard to reproductive cloning, I urge it to focus on legislation that prevents that unsafe practice.

I also urge it to adopt the additional regulatory protections proposed in S. 303 for research and therapeutic applications of cloning, so that the public can be reassured that every measure has been taken to guide this research along a responsible path.

A separate debate, on embryo research generally or non-reproductive cloning research in particular, can always proceed separately, to be debated on its own merits, and ultimately to be tested on its own terms before the constitutional authorities of the nation.

Senator BROWNBACK. Thank you very much.

Mr. KIMBRELL.

STATEMENT OF ANDREW KIMBRELL, EXECUTIVE DIRECTOR, INTERNATIONAL CENTER FOR TECHNOLOGY ASSESSMENT

Mr. KIMBRELL. Thank you very much, Mr. Chairman, for the opportunity to speak today, and I also thank you for having a hearing on this very important subject that I think too often has been ignored in the multiyear debate now that we have had in Congress on cloning, the very crucial issue of the women's health implications of both research and reproductive cloning.

I am an attorney and the executive director of the International Center for Technology Assessment. But also, for ten years I served

as the chairman of the National Coalition Against Surrogacy, where I, firsthand, litigated on behalf of dozens of women across the country who were victimized by commercialized childbearing. And so I saw firsthand what these fertility drugs can do and what this process can do, both physically and psychologically, to women around the country.

Now, I have submitted a more detailed statement for the record, Mr. Chairman. I would like to just summarize and perhaps focus on a couple of the points that have been made and see if I can be of some help on this.

Senator BROWNBACK. Your statement will be in the record.

Mr. KIMBRELL. Thank you.

Perhaps, first, in that there seems to be, sort of, a cost-benefit analysis going on here, I wonder how many Senators would answer a certain pop quiz correctly, Mr. Chairman, and that would be, "How many stem cells have been garnered from cloned human embryos as we sit here today?" And this is by peer-reviewed studies, which show how many. And the answer, Mr. Chairman, is zero. Zero. With all the testimony I have heard in five years, and I've testified myself, about all these cures—I have heard scientists come here for five years—the number of stem cells that have been garnered from cloned human embryos is zero.

And I think this is essential for a couple of reasons as we look toward this, because I think that we are seeing recent science that suggests that—exactly as you were suggesting, Mr. Chairman, in that Dolly was the 277th try and the horrible birth defects that were testified in the Senate about—that research is showing that something happens during the cloning process.

Dr. Yenich has a recent study, peer reviewed, that says there is silencing of certain genes once a cell, an embryo, is cloned. And I think we may be looking, in the future, at a scenario where it is understood that cloning harms embryos in a way that will never allow them—never allow them—to be a consistent source of stem cells.

So at the outset, I would suggest that we separate these two debates. I am here representing a coalition of environmentalists and feminists and over a hundred others who have signed on for a ban on reproductive cloning and a moratorium on research cloning. Many of them support expanded stem cell research. But to confuse the stem cell debate with the cloning debate, when right now we have zero stem cells coming from embryo cloning, to me is disingenuous at best, and it has been done time and time again.

There are a couple of other points that I think are very, very important to make here, and one has to do with the enforcement. The Hatch bill, S. 303, seeks to both halt reproductive cloning and encourage research cloning. And if you look at that bill and the definitions of that bill, there is a definition of a "cloned embryo" as an unfertilized blastocyst.

And let us consider this term for a moment, an "unfertilized blastocyst." This appears to me to be intentionally misleading. "Unfertilized" seems to me that it would be unviable, or could never become a child. We know that is not true. If that "unfertilized blastocyst" were transplanted into a woman's womb, it, indeed, would grow into a child—perhaps not a healthy child, as

we have learned from the Dolly experience, but it would become a child. And second of all, there seems to be the idea that because it is a blastocyst, it is not an embryo, and that is not correct. Of course it is an embryo.

As a matter of fact, and this is absolutely critical—and before the Senate, the Department of Justice testified last year that once a cloned embryo has been created, it is indistinguishable, biologically, from a normal fertilized embryo. All right? Once the cloned embryo is created, it is indistinguishable from a fertilized embryo.

Now, think about the enforcement issues this raises once, as in the Hatch bill, thousands, perhaps millions, of these cloned embryos are created, once they are out there, once they are in an IVF clinic, once they are transported, shipped, frozen, which this bill allows, 303. They will be indistinguishable from other embryos, biologically. That is an enforcement nightmare. Imagine trying to enforce firearms or drugs if once they were created, they became literally invisible and were allowed to be shipped, transported, frozen.

So the question is, in S. 303, where they try and enforce their ban on reproductive cloning by basically saying that the illegal act is the transferring of this embryo into a woman, how are we going to know which kind of embryos are being transferred into a woman? At that late stage, how do you even know whether it is a cloned embryo or a conventional fertilized embryo? There is no way to know.

Additionally, the idea of having a police force that is going into doctors' offices around the country to try and find out whether the transfer to a woman was from a cloned or a fertilized embryo is not only a huge invasion of privacy, but is obviously, from an enforcement standpoint, ridiculous. But even if you had that police force, they would not be able to tell, right? Because they would not be able to distinguish that embryo from a normal embryo.

So this term "unfertilized blastocyst" hides the fact that these embryos, indeed, are identical, and that the only way—the only way—you can have responsible legislation in this area is at the supply level. In that once they are created, they are indistinguishable from other embryos, clearly the only way to stop this is at the supply level; in other words, to either ban the process of creating cloned embryos or to have it so restricted and so monitored that we have custody of each and every embryo created. Otherwise, no one—you, me, no one in this room, no scientist—can tell us which embryos are out there and what is being done with them. As such, the enforcement scheme, as laid out in 303, is legally incoherent, scientifically incoherent, and will do nothing to halt reproductive cloning.

Now, adding insult to injury, 303 then has a provision that seems to admit that there are some enforcement problems here and says one year after the bill has been passed, they want a report on exactly what enforcement is happening or not happening.

Mr. Chairman, I would suggest that the time to do studies on enforcement is not after a harmful practice has been allowed to be disseminated and perhaps creating its harm in this invisible way throughout the country, but before we allow a harmful practice to ever be sanctioned by law. The idea of having a bill that says,

"Let's look at enforcement a year after we allow this process," again, is legally incoherent, and I cannot understand it.

Now, Ms. Charo mentioned that the—correctly, I think—that 303 relies on these institutional review boards for a case by case study and approval of research cloning. Let me read you a 1998 report by the HHS office, the Inspector General's report to the HHS, on the efficacy of institutional review boards in monitoring and reviewing these kinds of human subject experiments. In this report, the Inspector General found, "that the IRBs reviewed too much, too quickly, with too little expertise, that they conducted minimal continuing review of approval research, that they faced conflicts of interest that threatened their independence, provided far too little training for investigators and board members." A 2000 report looking at how these reforms were possibly carried out, they basically said, "minor changes, but these problems still exist, are endemic to these IRBs and have not been cured."

Well, I find it very troubling, Mr. Chairman, that the core, the backbone, of regulations, S. 303, is these IRBs that HHS, for the last five years, has been saying are not working.

A couple of final points. One of the first opportunities I had in Washington many, many years ago, was working with then-Representative Al Gore to help create and then pass the Organ Transplant Act. This, as you know, is the act that prohibits the sale of organs in the United States. And as such, we faced a very difficult question about what kind of reasonable compensation people should be given for organ donation. One of the considerations we had at that time was whether "time and inconvenience," those terms, should be used for something that you could recompense people who had donated their organs. We rejected it at that time, because we viewed it as I think it is, a loophole for virtually any kind of payments you want to give.

Now, a couple of years ago, a spokesman for the infertility industry admitted that time and inconvenience was simply, "semantics." It means "payment."

So the fact that we are talking about—in S. 303, the fact that they are saying you cannot have valuable consideration to these egg donors, but you can pay them for their time and inconvenience, according to the infertility industry, itself, is semantics. "Payment" and "time and inconvenience" are the same thing.

And let me read you from the marvelous legal scholar, George Annas on this, on the term "inconvenience" as used in this valuable consideration for paying for women's eggs. This is George Annas now, "Of course, you're not really buying a woman's inconvenience. It's a bogus argument that you're not actually selling these eggs. Clearly, donors are selling their reproductive capacity. And if you can sell your egg, then shouldn't you sell your child, too?"

Again, in contrast to this, I urge the Committee to look at the Organ Transplant Act, where we do not allow this huge loophole that has been allowed in this bill.

A couple of final points, if I could. One is this idea that we are restricting science and that that is a possible offense to the First Amendment. One of my privileges as an attorney has been to do numerous litigations under the Animal Welfare Act. In order to protect animals from cruel experiments, experiments that offend

both their dignity and their physical and psychological wellbeing, we have numerous restrictions on experiments that can be conducted in virtually every area of medicine. Numerous. None of those has ever been subjected, to my knowledge, to any kind of constitutional attack, and I think anybody who thought that they could do that would not be taken seriously, legally. If, to protect animals, we can have significant restrictions on research, I do not know why we cannot do the same thing for women's health.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Kimbrell follows:]

PREPARED STATEMENT OF ANDREW KIMBRELL, EXECUTIVE DIRECTOR, INTERNATIONAL CENTER FOR TECHNOLOGY ASSESSMENT

Mr. Chairman and Members of the Committee:

My name is Andrew Kimbrell. I am the Executive Director of the international Center for Technology Assessment, an attorney and author of *The Human Body Shop: the engineering and marketing of life* (Harper Collins 1991, 3rd Edition 1998). I am here today as part of a broad coalition of progressive environmental, consumer and women's health groups who agree that responsible policy on the matter of human cloning requires a ban on reproductive cloning and a moratorium on human cloning for research. The potential impacts to women of human reproductive cloning, but especially, human research cloning have received insufficient attention in the cloning debate, and I'm grateful to the Committee both for recognizing the importance of this issue and providing me the opportunity to testify today. I'd like to begin by summarizing the physical and psychological risks to women posed by human reproductive and research cloning. I will then provide a brief analysis of S. 303, introduced by Senators Hatch and Feinstein and explain why, as currently written, this bill would neither effectively ban human reproductive cloning nor provide adequate protection to women.

The Impacts of Human Cloning to Women

Human cloning is a process in which a nucleus from a human somatic cell is fused with an enucleated human egg cell to produce a cloned embryo. The technical term for this process is "somatic cell nuclear transfer." There are two potential uses of cloned embryos produced by nuclear transfer, each of which pose significant risks to women. In the case of human reproductive cloning, cloned embryos would be transferred into a woman's uterus, and, if brought to term, would result in a child that would be a genetic duplicate of the nuclear donor. In the case of human cloning for research purposes, these cloned embryos would be used to develop stem cell lines for regenerative tissue research. The following describes the risks to women posed by each of these two types of human cloning.

Human Reproductive Cloning

Human reproductive cloning is widely condemned and has been outlawed by more than 30 countries. Many scientists agree that reproductive cloning is an inherently unsafe procedure that could only he made "safe" by carrying out extensive, unethical experimentation on women. The physical risks associated with this procedure cannot be overstated. Almost all cloning experiments in mammals have resulted in miscarriages, stillbirths, and deformities. Many efforts to clone mammals have resulted in abnormally large fetuses, often up to twice the average size. In humans, "large offspring syndrome" of this magnitude could be fatal to a surrogate mother as well as to the fetus. Finally, experiments in mammals have been highly inconsistent and unpredictable. As such, endless experimentation with mice, sheep, cats, even monkeys may never provide us the level of confidence required to attempt this procedure in humans.

As many scientists, health professionals, ethicists and others have noted, these insurmountable risks, alone, warrant a permanent ban on human reproductive cloning. In addition, reproductive cloning poses significant psychological and social risks to women. Surrogate mothers who would have to undergo the stillbirths and miscarriages and witness the deformities involved in attempting to create a successful clone would suffer an enormous emotional and psychological toll. In addition, if reproductive cloning were allowed, an increase in demand for surrogate mothers would exacerbate an already coercive market in the buying and selling of women's wombs. That demand would likely be met by low-income women, pressured into selling their bodies as "mother machines" to those who can afford the price.

Human Embryo Cloning for Research

The impacts to women (and social consequences, generally) posed by human research cloning have been less widely discussed, but are nonetheless compelling. They include the following:

- *Research cloning is a highly inefficient process, which would require an unlimited supply of human eggs*. It has been estimated that research cloning might be able to provide up to 1.7 million therapies per year. Assuming a highly optimistic success rate of 1 stem cell culture per 5 cloned embryos, and one cloned embryo per 10 eggs, these therapies would require 85 million eggs, or 8.5 million egg donors.
- *Egg donation is a burdensome, risky, and painful procedure.* Egg donation is not a simple process; it lasts several weeks, and includes repeated injections of fertility hormones and super-ovulatory drugs and finally, surgery. Risks associated with egg extraction include a potential link to ovarian cysts and cancers, severe pelvic pain, abdominal bleeding, and ovarian hyperstimulation syndrome, a potentially life-threatening condition.
- *An explosion in demand for human eggs would exacerbate the coercive nature of the lucrative egg donation industry.* Currently, compensation to women for egg "donation" is uncapped, and ranges from an average payment of $5,000–$6,000 to as high as $80,000. The increase in egg demand created by research cloning is likely to increase the price of eggs and coercive potential of the egg market.
- *The burden of egg supply will likely fall on underprivileged women.* There are no federal standards concerning limitations on the number of times a woman can donate eggs. Low-income women may feel obliged to choose repeated egg donation as a source of income.
- *Research cloning will result in a loss of choice for women.* Researchers can clone embryos from any number of body cells. A woman's cells could be removed for the creation of any number of cloned embryos without her knowledge or choice.
- *The perfection of techniques to create cloned human embryos through research cloning would make it far more likely that reproductive cloning will occur.* The major barrier to successful reproductive cloning lies not in implantation, but in the development of the ability to clone embryos free of reprogramming errors. Allowing the creation of cloned embryos would encourage the perfection of this technical barrier, after which uterine implantation would be a trivial step. As such, research cloning is the gateway for eventual reproductive cloning and its profound impacts on women's health described above.
- *Perfection of research cloning techniques will also open the door to creating "designer babies."* Inheritable genetic modification, or germline engineering, is a process that involves changing genes that are passed on to future children. This technique has been used to create "transgenic" animals for commercial and research purposes, and some scientists and others are advocating its acceptance and use in humans. Perfection of research cloning techniques is necessary for "designer babies" to become commercially practicable. Allowing genetic "enhancements" in humans would unleash a powerful new eugenics, and could lead to unacceptable forms of genetic discrimination and inequality, not unlike those that many advocates for women's health and rights have worked so hard to overcome.

A Misguided Legislative Approach: S. 303

On February 5, 2003, Senators Hatch (R–UT), Feinstein (D–CA), Specter (R–PA), Kennedy (D–MA), Harkin (D–IA), and Miller (D–GA) announced the introduction of S. 303, a new bill to address the issue of human cloning. At a hearing held by the Senate Committee on the Judiciary on March 19, Senator Hatch stated that the purpose of the bill is twofold: (1) To stop any attempts to facilitate the birth of a cloned baby; and (2) to allow a promising form of stem cell research to go forward under "strict ethical guidelines." A closer examination of S. 303 reveals that neither of these goals will be accomplished by this bill. In particular, the bill, as currently written, will not effectively prevent human reproductive cloning, nor will it adequately protect women. CTA is preparing a thorough, in-depth analysis of this deeply flawed and misguided legislation, which it will provide the Committee in the near future. However, today I would like to focus on just a few of the more egregious failings of S. 303.

S. 303 Fails To Effectively Prevent Human Reproductive Cloning:

Among the changes from last year's incarnation of this bill is its use of the term "unfertilized blastocyst" to describe a cloned human embryo. The use of this term appears to be intentionally misleading. It suggests that, once created, clonal embryos (i.e., "unfertilized blastocysts") could he distinguished from "fertilized" embryos, namely those created from the union of an egg and a sperm. Additionally it seems to suggest that the "unfertilized blastocyst" is in some way not viable, that if it were transferred to a woman's womb it would not result in a child. It is true that a cloned embryo is not fertilized in the traditional sense, by way of the union of an egg and sperm. However a cloned embryo is potentially as viable as a conventional embryo and if implanted in a womb could result in a cloned child. Moreover, and very importantly, once created a cloned embryo ("unfertilized blastocyst") cannot be distinguished from a "fertilized" embryo. To repeat once an embryo is cloned it is biologically identical to a fertilized embryo and cannot be distinguished from a fertilized embryo nor identified as a cloned embryo.

This important fact, purposely obscured by S. 303, underscores the enormous challenge in enforcing any restriction on the sale or use of cloned embryos *after* they have been created. The bill allows for the production of an endless supply of cloned human embryos without acknowledging that once they are produced they are biologically identical to conventional embryos and will be virtually impossible to find. This simple fact demonstrates that any attempt to regulate the use of cloned embryos after they have been created is legislating the impossible. Imagine trying to regulate the use of drugs or firearms if they became invisible once they were created and you get the scope of the difficulty in enforcing the ban on reproductive cloning attempted by S. 303.

Clearly the only coherent approach to halting reproductive cloning is at the supply level, that is to either ban or significantly restrict the creation of cloned embryos. S. 303 does the reverse. it encourages the creation of cloned embryos but does not in any way provide direct oversight of the number of facilities creating human cloned embryos, limit the number of clonal embryos created, or create a strict chain of custody requirement for each individual cloned human embryo produced for research purposes. As such, there is no way to ensure that cloned embryos purportedly produced for research purposes are not subsequently transferred to a woman's uterus. This potential that these embryos will be used for reproductive cloning is exponentially increased because the bill explicitly allows for: (1) Freezing; (2) transport; and (3) export of cloned human embryos. *Without either a ban on the production of cloned embryos or a highly restricted production of cloned embryos that is subject to a rigorously enforced system of monitoring that tracks the chain of custody of each and every cloned human embryo produced, there can be no way to ensure that attempts to clone human beings are not being undertaken*. S. 303 provides for neither of these alternatives and therefore will completely fail in its stated purpose of halting human reproductive cloning and will also fail in preventing the serious impacts on women's health which reproductive cloning will bring.

Rather than addressing this enforcement issue directly, S. 303 calls for a series of reports on enforcement mechanisms found in state or international laws to be completed one year after the bill has been passed. This is incomprehensible. Allowing human cloning to proceed for a year, or potentially several years, while various enforcement schemes are reviewed and studied in order to arrive at adequate enforcement is legally incoherent. The whole point of regulatory legislation is to develop an effective enforcement regime *before* allowing a certain potentially harmful activity to proceed, *not after* it has been disseminated and creates the harm the legislation was intended to avoid.

S. 303 Fails to Provide Adequate Protection to Women Egg Donors:

The bill assigns the primary load of protecting women in research cloning to existing human subject protection regulations. Yet it is probable that these regulations would not even apply to egg donors or somatic cell donors. This is because these donors would not be "research subjects" as contemplated under the regulations; instead, they are "donors" of biological material, not a class currently covered under the regulations. Even if these regulations did apply, companies involved in cloning embryos could avoid these requirements by obtaining human eggs and cells from outside sources and not directly from the donors. In addition, standards of Investigational Review Board (IRB) review are not the most efficient or practical way to provide consistent protection to these participants. Decisions about the appropriate process for extracting and using human eggs and somatic cells in research should not be made on an individual, case-by-case basis, or left to the whim of a given IRB. Instead, federal standards should be developed that are specific to women's health concerns.

I would add that the bill's reliance on IRBs as the primary means to monitor and control human cloning activity also ignores serious issues that have been raised about these Boards. A number of recent major failures in human research protection have led me, and many in the scientific community, to believe that most of the important issues raised in the 1998 HHS Office of Inspector General Report "Institutional Review Boards: A Time for Reform" have yet to be effectively addressed.

In this 1998 report the Inspector General found that IRBs:

- reviewed too much, too quickly, with too little expertise;
- conducted minimal continuing review of approved research;
- faced conflicts that threatened their independence; and
- provided too little training for investigators and board members.

They also found that neither IRBs nor HHS devoted much attention to evaluating IRB effectiveness.

In a follow up investigation in 2000, the OIG found that while several promising steps had been taken by NIH and FDA, few of the recommended reforms had been enacted. Of particular continuing concern to the IG were the areas of:

- flexibility and accountability;
- oversight and human protections;
- board and investigator education;
- conflicts of interest;
- workload; and
- federal oversight.

Virtually the same list as in 1998. Given these findings, if we are serious about ensuring that reproductive cloning cannot occur, and that women's health be protected IRBs are not any kind of answer for at least the foreseeable future.

Let me conclude with S. 303's handling of the exploitation of women in the egg donation process. There can be no doubt that the endorsement of research cloning in S. 303 would stimulate a major expansion in the market for women's eggs. At the same time, the bill does not adequately address the coercive aspects of the egg donation industry, which would be exacerbated by a massive increase in the demand for women's eggs. While the bill prohibits the purchase or sale of human eggs for use in embryo cloning research "for valuable consideration", it does so with a large loophole. While "valuable consideration" is prohibited the bill does allow for payment to egg donors for the "time or inconvenience" associated with the donation. This vague provision has been used for years by institutions around the country to allow them to pay tens of thousands of dollars to egg donors. Ultimately, there is little real difference between paying for eggs or for the "time and inconvenience" of their removal. "It's almost a matter of semantics," admits Joyce Zeitz, former public relations coordinator for the American Fertility Society. Legal scholar George Annas sees the term "inconvenience" as nothing more than a ruse: "Of course, you're not really buying a woman's inconvenience. It's a bogus argument that your not actually selling these eggs. Clearly, donors are selling their reproductive capacity. And if you can sell your egg, then why shouldn't you sell your child too?" In contrast to S. 303 language, I would point out that the U.S. Organ Transplant Act prohibiting sale of organs does not have the "time and inconvenience" loophole. I would further note that S. 303 contains no caps on the number of times a woman can donate/sell eggs. As such, economically disenfranchised women are likely to become repeat donors.

In sum, if passed S. 303, will encourage unlimited production of unidentifiable cloned embryos. This will not halt but rather facilitate human reproductive cloning and thus will completely fail to adequately protect women's health from the dangers of all forms of human cloning. The bill is deeply flawed both in concept and in its specifics. It is simply irresponsible legislation.

Thank you.

Senator BROWNBACK. Thank you, Mr. Kimbrell.

Mr. Doerflinger?

STATEMENT OF RICHARD M. DOERFLINGER, DEPUTY DIRECTOR, SECRETARIAT FOR PRO–LIFE ACTIVITIES, U.S. CONFERENCE OF CATHOLIC BISHOPS

Mr. DOERFLINGER. Thank you, Mr. Chairman.

Human cloning is an unethical and dehumanizing procedure; and, ironically, the most startling evidence of its dehumanizing as-

pects can be found in some proposals ostensibly aimed at preventing human cloning. A case in point, in my view, is the Hatch-Feinstein Human Cloning Ban and Stem Cell Research Protection Act, S. 303. The bill is gravely deficient in at least eight ways. I say "at least," because I had one day to write the testimony. I will find 20 more tomorrow.

Very briefly, first, the bill is offered under false pretenses. In fact, it does not ban human cloning at all, for any purpose. "Human cloning" is defined by the National Academy of Sciences as the production of an organism that has the same nuclear genome as another organism. And contrary to the fertility doctor who testified earlier, there is a virtually unanimous consensus among Congress, the NIH, the National Bioethics Advisory Commission, and many others that the embryo, even at the earliest stage, is an organism of the human species. That is not a moral or political statement; it is simply basic science. In fact, there is a great deal of law on stem cell research right now that is based on the legal opinion that a stem cell is not an organism, but an embryo is. When you produce that embryo, you have done human cloning. S. 303 does nothing whatever to place any limits on cloning, for any purpose or no purpose.

Two, what it does ban is embryo transfer, which is a distinct procedure also defined by the National Academy of Sciences. And that creates a great many problems, some of which Mr. Kimbrell has just gone over. The bill's penalties are directed not at irresponsible cloning researchers, but at anyone engaged in trying to implant such an embryo in a woman's womb—presumably, by the language of the bill, including the woman herself. In fact, everyone else could simply evade penalties under the law by training the woman to transfer the embryos to her own womb. If the woman is exempt from penalties, then the law simply evaporates. It is simply a regulation on who can do human cloning, rather than on whether you can do it at all, even reproductive cloning.

S. 303 recognizes the enforcement problem here that, as Mr. Kimbrell said, you simply cannot tell, even if you were standing right over the shoulder of the fertility physician, whether any given embryo about to be transferred to a woman is from cloning or fertilization. You cannot even do it with all the prenatal diagnostic tests that we have now—because we do not have a test, for example, for the disorderly gene imprinting and gene expression that are found in cloned embryos. And so the Act tries to resolve this by forbidding researchers to conduct human cloning research in the same place where IVF is done in assisted reproduction.

That only confirms what the Justice Department has said in its House testimony some time ago. You cannot enforce this bill without placing new and unprecedented restrictions on assisted reproduction techniques that are widely accepted. Whether you are banning the location of an IVF clinic, or banning the location of a cloning research facility, is simply going to depend on which one got there first. You cannot operate the second one in the same place as the first one. This would be the first federal law in history that bans the location of IVF clinics in certain places.

Third, the bill allows research that will facilitate what its sponsors claim to oppose—that is, cloning to produce children. My

longer statement has quotes from people who favor research cloning, confirming that, of course, if you allow cloning for research it will facilitate and bring closer the day when this procedure is refined and people can conduct it for reproductive purposes. In fact, some of the organizations supporting S. 303 have exactly that view themselves—that when research cloning is allowed to make the procedure, "safer," they might then support reproductive cloning as well.

Fourth, the bill allows—and this is a very odd clause—it allows exporting of cloned embryos to other countries, but only if they do not—I have to read this, because the double negatives are a little odd—it forbids exporting of cloned embryos, called unfertilized blastocysts, to a foreign country only if such country does not prohibit human cloning. So the only circumstance in which you can export cloned embryos to another country is where they will be used for illegal activity. We are pretending to ban even reproductive cloning, and then facilitating it in violation of other countries' laws elsewhere. I do not think that will increase our standing abroad.

Fifth, the bill has a number of careless and incoherent passages that end up potentially restricting activities that are not human cloning at all. One I would like to mention briefly is this "unfertilized blastocyst" term which is defined in such a way that it fails even to make the distinction between an embryo and a stem cell. "Any intact cellular structure," made by nuclear transfer is covered. And so the very sort of things that some people have talked about to bypass the moral problem of cloning, ways of adapting the procedure so that, from the outset, it only makes stem cells instead of an organism, an embryo, that then has to be killed for its stem cells, would be as restricted by this bill as actually making an embryo is. This is not a defect in the Brownback bill.

Sixth, regarding protection of women, this bill is really a Potemkin Village. It is very carefully crafted so that it takes the whole body of current law and regulation on human subjects research, finds the areas that would actually have some relevance to cloning research, and then makes sure they are *not* applied. The only regulations it does apply are rather vague and general provisions that, in fact, do not have much of anything to do with cloning, for reproduction or research. It does not apply, for example, the protections for unborn children in pregnant women. It does not apply the current federal law that has been in place for six years on embryo research. It only applies these vague informed consent standards, and these provisions on compensation for time or inconvenience. I have a hard time with the idea of the "inconvenience" of getting ovarian cancer.

Here is something that the National Bioethics Advisory Commission said about the IRB system. Professor Charo was a member of the commission at the time. "In our view, IRBs should appreciate that, for some components of a study, participants might incur risks with no personal potential benefit. For these elements"—and that is what happens with egg donation for cloning research—"For these elements, there should be some limitation on the amount of social and physical risk that can be imposed, regardless of the participant's willingness to participate or the monetary or other enticement being offered." That is the advice that this bill ignores. It

thinks that if you throw in some compensation and have people sign a form, then this inherently ethically questionable practice of having women undergo the risks of these egg donation practices for no possible benefit to themselves is perfectly all right.

The bill's reference to FDA oversight is even more unpersuasive, because it requires you to treat the cloned embryo as a biological product, as a commodity to be regulated, presumably in order to prevent harm to others. So it has nothing to do with the ostensible purpose of the bill in terms of its stance against reproductive cloning, which was to protect the safety of the child who is going to be receiving birth defects and miscarrying from being cloned. You cannot call the child a dangerous biological product, and say it is the person to be protected from risk at the same time.

There are many other defects here, but I want to end with just this one, because it is not widely known here. This bill is already obsolete. The biotechnology movement has moved on. There are eight states now where state biotechnology alliances are supporting bills that have language like the following. "It is the public policy of this state to promote research involving the derivation and use of human embryonic stem cells, human embryonic germ cells"—those can only be obtained from fetuses eight weeks old—"and human adult stem cells from any source, including somatic cell nuclear transplantation." Now, that language is no accident. It has been simultaneously introduced in eight states in the last couple of months.

The researchers have looked at the field, and they have found what anyone can find by looking at the medical literature. There are only two studies in all the vast sea of medical literature that showed any therapeutic benefit from cloning in animals; and one of them required taking the clone to the fetal stage, and the other required taking it to the newborn stage.

They are already moving on past this bill, the 14-day limit on maintaining embryos—morally reprehensible though that is because, for the first time in history, the Federal Government would actually define a class of humanity it is a crime not to destroy at a certain stage. That limit is going to be infinitely flexible, because tomorrow the researchers will come back and say, "We need 20 days, we need 30, we need a hundred." They are already saying it in the laboratory of the states, and we should beware of something that is far too much of a free fall even to be called a "slippery slope." We are already there. They are already taking these animal studies, and saying that the human model for therapeutic cloning may have to exploit human beings into much later stages than the embryonic.

Embryonic stem cells have been found to have many serious problems in terms of integrating with tissues, in terms of tumor formation and overproliferation. And the logical way, unfortunately, for the researchers to get more usable cells is to grow those cells to a later stage in the original organism, and then destroy that organism.

Mr. Chairman, we should ban human cloning, but we should do it by banning human cloning. Legislation which allows the practice, and then seeks to destroy the humans thus produced so that we can pretend we have banned cloning, is worse than doing nothing.

I urge Congress to oppose S. 303 and to approve the Brownback-Landrieu bill, S. 245. Thank you.

[The prepared statement of Mr. Doerflinger follows:]

PREPARED STATEMENT OF RICHARD M. DOERFLINGER, DEPUTY DIRECTOR, SECRETARIAT FOR PRO-LIFE ACTIVITIES, U.S. CONFERENCE OF CATHOLIC BISHOPS

I am Richard M. Doerflinger, Deputy Director of the Secretariat for Pro-Life Activities at the U.S. Conference of Catholic Bishops. I also serve as Adjunct Fellow in Bioethics and Public Policy at the National Catholic Bioethics Center. It is on behalf of the bishops' conference that I wish to speak to you today about the moral challenge presented by radically different congressional proposals on human cloning.

The sanctity and dignity of human life is a cornerstone of Catholic moral reflection and social teaching. We believe a society can be judged by the respect it shows for human life, especially in its most vulnerable stages and conditions.

Human cloning is sometimes presented as a means for creating life, not destroying it. Yet it shows disrespect toward human life in the very act of generating it. Cloning completely divorces human reproduction from the context of a loving union between man and woman, producing children with no "parents" in the ordinary sense. Here human life does not arise from an act of love, but is manufactured to predetermined specifications. A developing human being is treated as an object, not as an individual with his or her own identity and rights. As one group of scientific and other experts advising the Holy See has written:

> In the cloning process the basic relationships of the human person are perverted: filiation, consanguinity, kinship, parenthood. A woman can be the twin sister of her mother, lack a biological father and be the daughter of her grandmother. *In vitro* fertilization has already led to the confusion of parentage, but cloning will mean the radical rupture of these bonds. [1]

Such moral concern transcends denominational bounds and has been eloquently expressed by some of our country's most respected philosophers and ethicists. Writes Professor Leon Kass of the University of Chicago, now chairman of the President's Council on Bioethics:

> Human cloning would . . . represent a giant step toward turning begetting into making, procreation into manufacture (literally, something "handmade") . . . [W]e here would be taking a major step into making man himself simply another one of the man-made things. [2]

From the dehumanizing nature of this technique flow many disturbing consequences. Because cloned humans are produced by a means more suited to more primitive forms of life—a means which involves no loving relationship, no personal investment or responsibility for a new life, but only laboratory technique—they would be uniquely at risk of being treated as "second-class" human beings.

The very scenarios often cited as *justifications* for human cloning are actually *symptoms* of the moral problem it creates. It has been said that cloning could be used to create "copies" of illustrious people, to replace a deceased loved one, or even to provide a source of spare tissues or organs for the person whose genetic material was used for the procedure. In each proposal we see a utilitarian view of human life, in which a human being is treated as a means to someone else's ends instead of as a person with his or her own inherent dignity. This same attitude lies at the root of human slavery.

Let me be perfectly clear. In reality a cloned human being would not be, in any sense, an "object" or a substandard human being. Whatever the circumstances of his or her origin, he or she deserves to be treated as a human person with an individual identity. But the depersonalized technique of manufacture known as cloning disregards this dignity and sets the stage for further exploitation. Cloning is not wrong because cloned human beings lack human dignity—it is wrong because they *have* human dignity, and deserve to come into the world in ways that respect this dignity. Each child has a right to be conceived and born as the fruit of a loving union between husband and wife, to be loved and accepted as a new and distinct individual.

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[1] Reflections from the Pontifical Academy for Life, "Human Cloning Is Immoral" (July 9, 1997), in *The Pope Speaks,* vol. 43, no. 1 (January/February 1998), p. 29. Also see: Congregation for the Doctrine of the Faith, *Donum Vitae* (Instruction on Respect for Human Life in its Origin and on the Dignity of Procreation) (March 10, 1987), I.6 and II.B.

[2] Leon R. Kass, "The Wisdom on Repugnance," in *The New Republic, June 2, 1997, p. 23.*

Ironically, the most startling evidence of the dehumanizing aspects of cloning is found in some proposals ostensibly aimed at *preventing* human cloning. Some Members of Congress favor legislation that would not ban human cloning at all—but would simply ban any effort to allow cloned human beings to survive. In these proposals, researchers are allowed to use cloning for the unlimited mass production of human embryos for experimentation—after which they are required to destroy them. Enactment of such a proposal would mark the first time in history that the U.S. government defined a class of human beings that it is a crime *not* to destroy.

Specifically I have been asked to comment on the two pending federal bills now offered as a response to human cloning: the Hatch/Feinstein "Human Cloning Ban and Stem Cell Research Protection Act" (S. 303), and the Brownback/Landrieu "Human Cloning Prohibition Act" (S. 245).

Let me begin with the bill that is, in my view, offered under false pretenses—the bill that, despite its title, is not a ban on human cloning at all.

S. 303 (Hatch/Feinstein)

This bill is gravely deficient in at least eight ways.

1. **It does not, in fact, ban human cloning at all.** The National Academy of Sciences (NAS) has defined "cloning" as the production of "an organism that has the same nuclear genome as another organism."[3] As Congress has formally acknowledged since 1996, the early embryo produced by fertilization *or* cloning is an organism of the human species.[4] The National Institutes of Health (NIH), and President Clinton's National Bioethics Advisory Commission (NBAC), have acknowledged the same fact.[5] To produce that embryo—using, for example, the somatic cell nuclear transfer procedure used to make Dolly the sheep—is to conduct human cloning, whatever else one may plan to do with that embryo afterwards. This is scientific fact, not ethics or politics. It was, in fact, a unanimous point of agreement in the recent report on cloning by the President's Council on Bioethics, whose Members otherwise disagreed sharply on moral and policy issues.[6] S. 303 does nothing whatever to ban the use of the cloning procedure to create human embryos, for *any* purpose (or even to restrict someone's ability to create them for no discernible purpose at all).

2. **What it does ban is "embryo transfer," a distinct procedure already in use by fertility clinics across the world for many years; and this creates serious legal and enforcement problems.** The NAS defines "embryo transfer" as "the introduction of a preimplantation embryo into the uterus for growth and development."[7] S. 303 bans *this* procedure, *if* it involves an embryo produced earlier by cloning (page 2 lines 10–13). This has certain consequences:

(A) The bill's penalties are directed not against irresponsible researchers engaged in human cloning, but against those engaged in implanting or attempting to implant the cloned embryo in a womb—presumably including the woman herself. (If the penalty did *not* apply to the woman, of course, this would create an enormous loophole—the law could be completely evaded by having the woman herself conduct the embryo transfer, a realistic possibility if she has any training as a fertility doctor or technician.)

(B) Such a law is inherently almost impossible to enforce, because at this stage of embryonic development there is no reliable way for law enforcement to distin-

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[3] National Academy of Sciences, *Scientific and Medical Aspects of Human Reproductive Cloning* (National Academy Press 2002), p. E–4.

[4] See the Dickey amendment enacted as part of the annual Labor/HHS appropriations bills since 1996: "'human embryo or embryos' includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells." The current version of this amendment is Sec. 510 of Pub. L. 108–7, the Omnibus Appropriations Act of 2003 (enacted Feb. 20, 2003).

[5] NBAC defined "embryo" as "the developing organism from the time of fertilization until significant differentiation has occurred . . ." NBAC, *Cloning Human Beings* (Rockville, MD: June 1997), Vol. I, p. A–2. This term encompasses the cloned embryo: "The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg involves the creation of an embryo, with the apparent potential to be implanted *in utero* and developed to term." Id., p. 3. Similarly, the NIH defines "embryo" as follows: "In humans, the developing organism from the time of fertilization until the end of the eighth week of gestation." NIH, *Stem Cells: Scientific Progress and Future Research Directions* (U.S. Department of Health and Human Services: June 2001), p. F–3.

[6] The President's Council on Bioethics, *Human Cloning and Human Dignity* (Washington, DC: July 2002), pp. 54–55.

[7] NAS, note 3 supra, p. A–2.

guish cloned embryos from fertilized embryos.[8] Even to initiate such scrutiny would require delaying embryo transfer until the results of all relevant tests were obtained, at which time the embryo in question (whether cloned or fertilized) would most likely be dead. In this context it is important to note that while cloned animal embryos seem much more likely to suffer from serious problems of disorderly gene expression than embryos created by union of sperm and egg, these problems are not detectable by any prenatal diagnostic test in current use.[9]

(C) The bill recognizes this problem, and tries to resolve it by forbidding researchers to conduct human cloning research at the same laboratory where "assisted reproduction" occurs (page 10 lines 19–24). But of course this begs the question, which is: How do you tell which of the two is being done at any given time? And how would you create a closed system to prevent cloned embryos from being brought from one laboratory to the one next door?[10]

3. **This bill allows cloning research that will facilitate what its sponsors claim to oppose—that is, cloning to produce born children.** Again, this is widely acknowledged by experts who *support* cloning for research in general and S. 303 in particular. For example, researchers and ethicists who support cloning for research purposes (which they call CRNT for "cell replacement through nuclear transfer") admit that "the techniques developed in CRNT research can prepare the way scientifically and technically for efforts at reproductive cloning."[11] Similarly, the ethics committee of the American Society for Reproductive Medicine (ASRM), which supports S. 303, has stated regarding human cloning for research purposes:

> If undertaken, the development of SCNT [somatic cell nuclear transfer] 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.[12]

To be sure, this does not create an intractable conflict for ASRM itself in terms of supporting S. 303, because ASRM does *not* support a permanent ban on (even) "reproductive" cloning.[13] The conflict is between the public statements of the bill's supporters in Congress, and the real-world impact of the legislation they support.

4. **The bill allows exporting of cloned embryos to facilitate violations of other countries' laws.** Incredibly, the bill forbids exporting of cloned embryos ("unfertilized blastocysts") to a foreign country only "if such country does not prohibit human cloning" (page 3 lines 19–21). Under S. 303, cloned embryos *can* be exported to foreign countries that do prohibit "human cloning" as defined by the bill, where they will be used in *illegal* efforts to initiate pregnancies with cloned embryos. Thus the bill would facilitate abroad what it purports to make illegal here.

5. **Through careless and incoherent drafting, the bill potentially restricts activities that are not human cloning.** To mention only a few:

(A) "human somatic cell"—defined to include "*any* human cell other than a haploid germ cell" (page 2 lines 14–16), so that it includes even the one-celled embryo. It will be a crime to implant in a uterus any embryo produced by transferring the nucleus from one single-celled embryo into another embryo or an unfertilized egg. By most definitions this is not cloning; it is a nuclear transfer technique used in some fertility clinics in an effort to circumvent mitochondrial disease (by replacing the defective mitochondrial DNA found in the protoplasm of the woman's own egg), to allow women with this disease to have healthy children. S. 303 bans this

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[8] See Written Statement of Daniel J. Bryant, Assistant Attorney General, before the Subcommittee on Criminal Justice, Drug Policy and Human Resources of the House Committee on Government Reform, May 15, 2002 (*www.house.gov/weldon/issues/doj.htm).*

[9] For example, see: Testimony of Dr. Mark E. Westhusin before the House Energy and Commerce Subcommittee on Oversight and Investigations, March 28, 2001; R. Jaenisch and I. Wilmut, "Don't Clone Humans!", 291 *Science* (30 March 2001), p. 2552.

[10] This provision illustrates the truth of the Justice Department's testimony: One cannot enforce this ban without imposing new and unprecedented restrictions on fertility procedures already widely practiced in this country. For the provision is double-edged: Its text says that one may not conduct cloning research in a laboratory where eggs are subjected to assisted reproduction procedures (page 10 lines 21–24); but its heading calls for "separation of in vitro fertilization laboratories" from locations where cloning research is conducted (page 10 lines 19–21). If a laboratory started conducting cloning research first, in vitro fertilization is banned there. This would be the first federal law to restrict where one may establish a private fertility clinic.

[11] Lanza et al., "The ethical validity of using nuclear transfer in human transplantation," 284 (24) *Journal of the American Medical Association* (Dec. 27, 2000), pp. 3175–9 at p. 3178.

[12] Ethics Committee of the American Society for Reproductive Medicine, "Human somatic cell nuclear transfer (cloning)," 74 (5) *Fertility and Sterility* (Nov. 2000), pp. 873–6 at p. 873.

[13] "There is not yet clear consensus that reproductive SCNT in cases of infertility serves a compelling need . . . Nor is there clear consensus on a compelling need to bar the technique." Id., p. 875. ASRM can support S. 303, consistent with its own policy, because the bill's authorization for research cloning will help make its ban on "reproductive cloning" a temporary one.

nuclear transfer procedure itself (page 9 line 23 to page 10 line 2), and also bans transferring any of these repaired embryos to a woman's womb (page 3 lines 13–14, in light of the definitions on page 2).

(B) "unfertilized blastocyst" (page 3 lines 3–9)—This is apparently intended as a demeaning reference to cloned embryos, but the word "blastocyst" is inaccurately used here to refer to the one-celled embryo initially produced by cloning, and even to the 14-day-old cloned embryo (whose further survival is made illegal by S. 303).[14] More broadly, "unfertilized blastocyst" is defined as any "intact cellular structure" produced by somatic cell nuclear transfer, so the bill bans transferring this product to a woman's womb *whether it is an embryo or not*. For example, if researchers develop a way to modify the egg or the somatic cell in advance, so that the initial product of this technique is not a living organism but a culture of stem cells (as some researchers say they may be able to do), this would be covered by the ban. Placing, say, endothelial stem cells produced by this hypothetical technique into a woman's womb to help heal her endometrial tissue would not be forbidden by any moral principle of which I am aware—but under a literal reading of this bill, it could provoke a ten-year prison sentence.

(C) "the functional equivalent of a uterus" (page 2 line 13)—This odd phrase is not defined, leaving room for much confusion. For example, S. 303's prime sponsor has repeatedly said there is no such thing as the functional equivalent of a uterus, because the function of a uterus is to turn the new embryo into a "human life" and no artificial environment can fulfill this task:

> After many conversations with scientists, ethicists, patient advocates, and religious leaders and many hours of thought, reflection, and prayer, I reached the conclusion that human life does not begin in the petri dish. I believe that human life requires and begins in a mother's nurturing womb.[15]

If, on the other hand, the phrase "functional equivalent" is to have any application, one can only guess how effective an artificial environment must be to qualify as a "functional equivalent" of a uterus. Certainly a Petri dish itself does not qualify, for then even cloning for research (which requires developing the cloned embryo to the blastocyst stage in that dish) would be banned. Perhaps a "functional equivalent" is an environment that could sustain the cloned embryo to live birth, because any womb that fails to do so would not fulfill the usual "function" of a womb. In that case, one may transfer the embryo to any artificial environment that would fall short of this function to any extent—in other words, at present one may transfer the embryo to any and all artificial environments. This will be important in the likely event (discussed below) that the bill's "14-day rule" for maintaining a cloned embryo is later changed.

6. **The bill erects a Potemkin village, a mere facade, of protection against research risks for human subjects involved in cloning research.** Title II of the bill (page 8 ff.) claims to expand current regulations on federally funded research involving human subjects (Subpart A of 45 CFR Part 46), so they will now apply to all "research involving nuclear transplantation" (even if privately funded). This one-sentence expansion of federal regulations into the private sphere raises a number of serious legal and jurisdictional issues that cannot be explored in depth here.[16]

However, assuming that the goal here is to place real ethical limits on human cloning for biomedical research, that goal is not met at all. Three distinct classes of humans may be involved in cloning research—the embryos created by cloning, the women solicited for their eggs, and the patients who donate body cells in the hope of receiving a genetically compatible stem cell treatment—and this Title lets them all down:

(A) **There is no ethical limit on what one may do to cloned embryos outside the womb**, because there are no such limits in federal human subjects regula-

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[14] In embryology the "blastocyst" is the embryo from four to around seven days old.

[15] Statement of Senator Orrin Hatch before the Senate Commerce Subcommittee on Science, Technology and Space, January 29, 2003.

[16] One threshold question would be: What activities involving nuclear transplantation will count as "research"? The question is now easily answered operationally in the case of federally funded research, because each research proposal must be submitted to the Federal Government in the form of a grant request. Potential grantees have an interest in arguing that what they wish to do *is* research. Is any current federal definition of "research" clear and specific enough to be applied to those conducting privately funded activities, even when the researchers will have an interest in *denying* that they are conducting "research" (so they can exempt themselves from this Title of the bill)? Does this bill really intend to say that if a project is *not* research—if cloning is used to produce human embryos simply for sport, or in order to "farm" them for strictly commercial purposes, such activity is exempt from these restrictions?

tions. To be sure, there are limits—in fact, there is an absolute ban—on federally funded research that harms or destroys human embryos, specifically including cloned embryos.[17] However, that is statutory language, not part of the Code of Federal Regulations, so it will not apply. This is, of course, by design—if S. 303 *did* extend Congress's policy on federally funded human embryo research to the private sector, the research favored by supporters of S. 303 would be illegal. This raises a very odd contradiction: Congress will enshrine as permanent law whatever regulatory language happens to have been written by the staff of the Executive branch up to the moment when this bill is enacted (page 9 lines 15–22)—but Congress will ignore its own statutory language that has been duly enacted and signed into law by Democratic and Republican presidents every year for the past six years, although *it is the only federal policy that directly relates to the issue at hand*. The only relevant provision that S. 303 itself provides on this point is in direct contradiction to current federal policy on embryo research—that is, the provision requiring all cloned embryos to be destroyed at the age of 14 days (page 10 lines 3–7). In federally funded projects, of course, Congress *forbids* researchers to destroy or harm cloned human embryos.

(B) **Title II places no ethical limits on what may be done to human subjects who may be the recipients of stem cells from cloned embryos.** The bill's expansion of federal human subjects regulations into the private sector applies only to "research involving nuclear transplantation" (that is, the act of creating cloned embryos). Since 1999, the law on federally funded research involving human embryos has been construed *not* to apply to activities using stem cells derived from those embryos.[18] The sponsors of S. 303 certainly agree with this legal opinion, which allows the Federal Government to fund embryonic stem cell research even when it cannot fund the research in which the embryos are created or destroyed. S. 303 actually reinforces this distinction, by explicitly defining the "unfertilized blastocyst" produced by nuclear transplantation to *exclude* any stem cells derived from this blastocyst (page 3 lines 6–9). So the considerable risks involved in placing embryonic stem cells from cloned embryos into patients—an activity that in animals can produce tissue rejection, overproliferation, and tumor formation—are completely unaddressed by this bill.[19]

(C) **Title II places only the vaguest and most inadequate limits on what can be done to women selected as "donors" of eggs.** Again, current federal regulations contain *no* specific guidance on the standards for donating eggs to make embryos, for the obvious reason that it has been a *de facto* federal policy for 23 years *not* to fund human in vitro fertilization research. The regulations contain some vague and general guidelines regarding risks, informed consent, and approval by institutional review boards (IRBs). But egg donation for the purpose of creating embryos for research is one of those practices that the entire IRB system is supposedly designed to discourage—that is, the practice of involving human subjects in research that imposes significant risks upon them but can be of no benefit to them as individuals. S. 303 wrongly seems to assume that a signature on a consent form (page 10 lines 9–13) and compensation for "time or inconvenience" (page 9 lines 12–14) will justify researchers in subjecting women to serious risks, including a potentially increased risk of ovarian cancer, in the name of progress. This approach ignores what Professor Alta Charo and the other members of the National Bioethics Advisory Commission warned in 2001, when they issued a report on the *inadequacy* of current safeguards against such exploitation of human subjects:

> **No matter what potential benefit is offered to individual participants or society at large, the possibility of benefit from one element of a study should not be used to justify otherwise unacceptable elements** . . . In our view, IRBs should appreciate that for some components of a study, participants might incur risks with no personal potential benefit . . . For these elements, there should be some **limitation on the**

[17] See the Dickey amendment, note 4 supra.

[18] HHS General Counsel Harriet S. Rabb, Memorandum to NIH Director Harold Varmus on "Federal Funding for Research Involving Human Pluripotent Stem Cells," Jan. 15, 1999.

[19] The NIH notes: "The potential disadvantages of the use of human ES cells for transplant therapy include the propensity of undifferentiated ES cells to induce the formation of tumors (teratomas)." NIH, note 5 supra, p. 17. In short, "undifferentiated embryonic stem cells are not considered as suitable for transplantation due to the risk of unregulated growth." Id., p. 97. Also see S. Wakitani et al., "Embryonic stem cells injected into the mouse knee joint form teratomas and subsequently destroy the joint," 42 *Rheumatology* (2003), pp. 162–5. And recent studies indicate that even stem cells from cloned embryos, supposedly a genetic match, may be rejected by recipients' bodies. See Y.L. Tsai et al., "Plasticity, Niches, and the Use of Stem Cells," 2 *Developmental Cell* (June 2002), pp. 707–712 at p. 710.

> **amount of social and physical risk that can be imposed, regardless of the participants' willingness to participate or the monetary (or other) enticement being offered**.[20]

This NBAC report also called attention to serious deficiencies in the IRB system itself as it currently exists, including the conflicts of interest that often allow IRBs to represent the interests of their own research institution rather than those of vulnerable human subjects:

> In recent years, increasing strains on the system have **undermined the practice of independent review.** IRBs are **overburdened** by the volume of research coming before them, a strain that is compounded by concerns about training of IRB members and **possible conflicts of interest.** In addition, the constantly changing nature of research challenges existing notions about what constitutes risks and potential benefits . . . Today, investigators and IRBs are rightly **confused** over issues as basic as which areas of inquiry should be reviewed and who constitutes a human participant.[21]

The Commission even noted with concern that "**there are no clear criteria** for IRBs to use in judging whether the risks of research are reasonable in terms of what might be gained by the individual or society." [22]

It is difficult to reconcile this pointed and well-deserved critique of the current system with the enthusiastic endorsement given to it by Professor Charo in her testimony before this Subcommittee today. How can this new, complex and ethically controversial field of human cloning research—research that may endanger women and desperately sick patients as well as embryonic humans—be adequately addressed by a system so often found incapable even of meeting its current obligations to protect human subjects in traditional medical research?

(D) **Title II's reference to FDA oversight is confusing, unpersuasive and incoherent.** At an earlier hearing before the House of Representatives, Members of Congress of both parties found the claim of FDA jurisdiction over human cloning to be unpersuasive.[23] At the very least, any such claim must address a very basic threshold question. In order to claim that FDA regulations can be applied to research involving "nuclear transplantation" (page 9 lines 19–20), what kind of entity does the cloned embryo have to be? These regulations do not cover medical techniques or procedures as such, but relate to "products" such as "foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products" (21 CFR § 56.101(a)). Assuming that the cloned embryo is not a food additive or a drug, he or she must be a "biological product"—a commodity to be tested for its dangers to others. Not only is this a false, demeaning and dehumanizing label for a fellow member of the human species, but it directly contradicts the sponsors' alleged rationale for banning "reproductive" cloning—that is, the risks to the child, including the massive risk of miscarriage and birth defects. One and the same entity cannot be the innocent victim of the experiment, and at the same time be the dangerous "biological product" from whom others must be protected by the Food and Drug Administration.

(E) **The bill's policy on research involving the cloned child in the womb raises especially disturbing moral and legal issues.** While current federal regulations on protection of human subjects do not cover the embryo outside the womb, they do protect the embryo and fetus implanted in the womb as well as the pregnant woman (45 CFR §§ 46.201 to 46.207). However, S. 303 refuses to expand to the private sector these specific protections for the cloned unborn child or the woman

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[20] NBAC, *Ethical and Policy Issues in Research Involving Human Participants* (Bethesda, Maryland: August 2001), p. iii (emphasis added).

[21] Id. p. iii, vii (emphasis added). For an extreme recent case of "conflict of interest," see the findings of Maryland's highest court in *Grimes* v. *Kennedy Krieger Institute*, 782 A.2d 807 (Md. 2001). The court found that the IRB at Johns Hopkins University had "abdicated" its responsibility to protect children from research risks, and had shown itself "willing to aid researchers in getting around federal regulations designed to protect children used as subjects in nontherapeutic research" (that is, research that would not benefit those particular children). No one who has read this decision will want to entrust all ethically controversial research decisions solely to IRBs.

[22] Id., p. xvi (emphasis added).

[23] Hearing before the House Energy and Commerce Subcommittee on Oversight and Investigations, March 28, 2001. The opening remarks by Committee Chairman Rep. Billy Tauzin were characteristic of Members' reactions: "The FDA argues these old federal laws regulating new drugs cover a human cell or a human fetus. I frankly do not find it obvious that a human fetus is a drug."

who may bear him or her—for these are found in Subpart B of Part 46, and Title II expands the reach only of Subpart A (see page 9 line 18).[24] Researchers who were not themselves involved in the illegal act of transferring the cloned embryo to a uterus would surely be interested in observing any special risks or other developments arising from the first human clonal pregnancy. Apparently S. 303 refuses to expand protections for pregnant women and their cloned unborn children in order to avoid a direct contradiction: The existing federal regulations forbid federally funded researchers to impose significant risks of harm and death on the unborn human subject (see 45 CFR § 46.204), but sponsors of S. 303 want to ban "maintaining" the cloned unborn child for more than 14 days in *any* environment except a deep freezer (page 10 lines 3–7). It seems this latter requirement can only be obeyed by forcing an abortion about one week after implantation (which usually occurs about six days after the embryo is formed). This raises a moral and perhaps even constitutional nightmare, and directly contradicts federal policies that have sought to protect fetuses and pregnant women from harmful research since 1975.

7. **Most generally, this bill's policy on the human embryo ratifies one gravely demeaning view that lies at an extreme end of the spectrum in our divided and pluralistic society: The embryo as commodity, as nothing more than disposable property to be manufactured and discarded to suit the desires of others.** It is important to note this, because supporters of cloning for research have wrongly applied this "pluralistic society" argument against the Brownback bill.[25] The fact is that a complete ban on cloning, already approved by a number of states as well as foreign countries, can be supported and is supported by Americans with a wide array of views on the moral status of the embryo—those who, like myself, hold that each and every member of the human species deserves to be protected as a human person; those who, like some ethicists, columnists and others, hold that the embryo (if not a "full" person) is at least a developing human life that deserves respect and should not be created solely to be destroyed;[26] and those who are agnostic on the status of the embryo but recognize that a complete ban on cloning is the only effective and enforceable way to prevent cloning for babymaking as well as further assaults on human dignity.[27] By contrast, the enactment of S. 303 would assume, and seek to promote, a national consensus that the cloned embryo has *no* moral status whatever, or has the status of a being whose survival is an active threat to the public good. No other view is consistent with a policy that this embryo may be created at will, but that government can *mandate* its destruction at a certain stage.

Under S. 303 it would be a federal offense to let such an embryo survive, or to show this fellow human being any degree of respect. Dr. Charles Krauthammer has observed:

> Creating a human embryo just so it can be used and then destroyed undermines the very foundation of the moral prudence that informs the entire enterprise of genetic research: the idea that, while a human embryo may not be a person, it is not nothing. Because if it is nothing, then everything is permitted. And if everything is permitted, then there are no fences, no safeguards, no bottom.[28]

I am confident that Congress will not enact such a gravely immoral policy and that President Bush would refuse to sign it.

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[24] Transferring such an embryo to the womb is of course illegal under S. 303, and those who perform this activity would be prosecuted and imprisoned. If the woman is not herself punished, she will still be potentially available as a subject for observational research on human clonal pregnancies (research conducted by researchers other than the original felons). If she, too, is imprisoned, however, she might be protected by the federal regulations providing additional protections for prisoners subjected to research (Subpart C, 45 CFR §§ 46.301 to 306)—if not for the fact that S. 303 excludes Subpart C as well.

[25] See Testimony by Dr. Paul Berg ("We take considerable pride in being a pluralistic society"), Dr. Harold Varmus ("(W)ho has such moral standing that they [sic] would impose on our multiethnic, pluralistic society an ethical standard that only a minority would endorse?"); and Dr. Thomas Murray ("Respecting the diversity of beliefs about families, about women, men, children—and embryos—honors our most noble traditions") before the Senate Judiciary Committee, March 19, 2003.

[26] "We can debate all day whether an embryo is or isn't a person. But it is unquestionably human life, complete with its own unique set of human genes that inform and drive its own development. The idea of the manufacture of such a magnificent thing as a human life purely for the purpose of conducting research is grotesque, at best." Editorial, "Embryo Research Is Inhuman," *Chicago Sun-Times*, October 10, 1994, p. 25.

[27] See "Statement of Dr. Krauthammer," in The President's Council on Bioethics, note 6 supra, pp. 277–285.

[28] Id., p. 285.

8. **Finally, this bill as written cannot achieve its stated objective of advancing therapies, and the biotechnology lobby has already moved on to broader policies for exploiting cloned humans at the fetal and newborn stages.** The sponsors of this bill have apparently failed to notice that only two animal studies have claimed to show any "therapeutic" benefits from cloning for research. One study, seeking to provide kidney tissue for cows, found it necessary to develop the cloned cow embryos to the *fetal* stage so they could be aborted for their partly formed kidney tissue.[29] The other, seeking to remedy an immune deficiency in mice, found it necessary to produce a *newborn* mouse whose *adult* stem cells could be transplanted into the original mouse.[30] These and other studies have found embryonic stem cells to be enormously difficult to culture, to control, and to develop into usable cells that will integrate with the host animals' cells; they have found these cells to have a disturbing tendency to form lethal tumors in recipients' bodies; and they have found that even embryonic cells from cloning can be rejected by the recipients' bodies, perhaps because of inherent differences between embryonic and adult cells.[31] Reading the handwriting on the wall, state biotechnology alliances have conducted simultaneous campaigns in several states to pass legislation authorizing

> research involving the derivation and use of **human embryonic stem cells, human embryonic germ cells, and human adult stem cells from any source, including somatic cell nuclear transplantation.**[32]

Embryonic germ cells, of course, are harvested at the fetal stage (at around 8 weeks' gestation), while adult stem cells are harvested from infants and children. In this new generation of cloning legislation, the old distinction between "therapeutic" cloning and "reproductive" cloning has been obliterated: Researchers will conduct "reproductive" cloning (developing cloned embryos to at least the fetal stage) to achieve "therapeutic" cloning (producing usable stem cells for supposed therapies).

At present S. 303 punishes efforts to maintain the cloned embryo past the 14th day. But this is an arbitrary limit, and Congress will be hard pressed to find a *principled* reason not to extend this to 20 days, or 30, or 100, if (as now seems more than likely) researchers report that such an extension is necessary to fulfill the "promise" of "therapeutic cloning." In the laboratory of the states, this broader agenda has already been launched.

S. 245 (Brownback/Landrieu)

By contrast, S. 245 has none of the serious problems outlined above. Very briefly, this bill:

1. Does ban human cloning, as that is accurately and scientifically defined.

2. Imposes its penalties on irresponsible researchers, not on vulnerable women, and avoids the moral, legal and constitutional problems raised by efforts to "ban" pregnancy and birth.

3. Effectively attacks the threat of "reproductive cloning" at its root, by preventing the production of cloned human embryos.

4. Bans shipping, receiving or importing of cloned human embryos for any purpose, preventing any collusion by the U.S. Government with those who wish to violate other countries' laws against cloning.

5. Is carefully crafted to avoid interference with any activity other than human cloning.

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[29] R. Lanza et al., "Generation of histocompatible tissues using nuclear transplantation," 20 *Nature Biotechnology* (July 2002), pp. 689–96. The authors wrote: "Because the cloned cells were derived from early-stage fetuses, this approach is not an example of therapeutic cloning and would not be undertaken in humans." Id, p. 689. Now lead researcher Robert Lanza has reversed his stand, insisting that this study is indeed a model for "therapeutic cloning." See Do No Harm: The Coalition for Research Ethics, "Reality Check: Proof of 'Therapeutic' Cloning?", March 10, 2003 (*www.stemcellresearch.org/pr/pr20030310.htm).*

[30] W. Rideout et al., "Correction of a Genetic Defect by Nuclear Transplantation and Combined Cell and Gene Therapy," 109 *Cell* (April 15, 2002), pp. 17–27. For a critique of this study see Americans to Ban Cloning, "Why the 'Successful' Mouse 'Therapeutic' Cloning Really Didn't Work," April 2002 (http://cloninginformation.org/info/unsuccessful__mouse__therapy.htm).

[31] See note 19 supra.

[32] Such language was enacted into law in California in September 2002. Virtually identical language has been proposed in: Illinois (HB 3589, introduced February 2003), Maryland (HB 482, introduced February 2003), New Jersey (S. 1909, introduced September 2002), New York (A. 1819, introduced January 2003), Pennsylvania (HB 422, introduced February 2003), Texas (SB 1034, introduced March 2003), Vermont (H. 326, introduced in 2003), and Washington (SB 5466, approved by Committee March 2003).

6. Directly protects all humans who would be harmed by the practice of human cloning (embryos, patients, and women who might be exploited for their eggs), by banning the practice for any purpose.

7. Respects the diversity of American views on the human embryo, by enacting only those provisions necessary to ban human cloning and leaving other research (including embryonic stem cell research that does not involve cloning) to be addressed by other proposals.

8. Prevents future "slippery slopes" that would require us to demean and exploit ever wider classes of our fellow humans as sources of body parts.

This is a case in which *how* we achieve an important goal is at least as important as whether we achieve it. We should ban human cloning—by banning the use of the cloning procedure to create new developing humans in the first place, as in the Brownback/Landrieu cloning ban (S. 245). Legislation which allows the practice, and then seeks to dehumanize and destroy the humans thus produced so we can pretend we have banned cloning, is worse than doing nothing. I urge Congress to oppose S. 303, and to approve the genuine ban on human cloning offered by S. 245.

Senator BROWNBACK. Thank you very much, Mr. Doerflinger.

We have now been joined by Ms. Lynne Millican. She is a patient/advocate, had difficulty getting in this morning, and, I think, was not feeling quite the best, and we are very appreciative of your willingness to come and testify this morning in spite of how you have been feeling. Thank you for joining us, and the floor is yours.

STATEMENT OF LYNNE MILLICAN, R.N., B.S.N., PARALEGAL, BOSTON, MASSACHUSETTS

Ms. MILLICAN. Well, I am honored to be here, and I did have great difficulty in getting here.

I actually should not have to be here. I underwent fertility treatment to have a baby. However, I think I am more like egg donors than anybody else, because the extent of my disease was such that I needed a hysterectomy. I never expected to have children. I just wanted to make sure that I would not be 40 years old and look back and think, "What if I had tried?"

So that is the context that I underwent this treatment, and I was given the drugs Lupron and Pergonal. Before I took these drugs, I had endometriosis, misdiagnosed which resulted in infertility, a knee injury, colds, flus, and usual childhood illnesses. Since Lupron, it has been a nightmare. Everybody wants to promote research, but who is looking out for the harm that is being caused by this? I am just one—there are thousands of Lupron victims, and they are one of the reasons why I am here today, because when I was vomiting at 5 o'clock this morning, all I could think of is if I do not come here and tell you people about all of these sick women out there, I would never be able to live with myself.

I am a registered nurse, but I cannot help these people. I have had difficulty getting help myself. In 1995, after six years of going through this, I testified at the Massachusetts Health Care Committee, because when I realized, in 1990, that there were no regulations, no laws, no protections, no nothing, no consumer advocacy, no governmental assistance, no state assistance, no consumer agency assistance, I wound up getting involved in drafting a piece of legislation, a first-in-the-Nation bill in Massachusetts that would require fertility clinics to have a license to operate. I provided written and oral testimony every year.

In 1995, at that time, I sat down at my computer and I typed in single space on continuous computer paper every doctor's office

visit, surgery test, lab, procedure that I had, and this is just to 1995. This paper is seven and a half feet tall. And I am just one victim.

If you go on the National Lupron Victims Network, yesterday morning there were over 2 million hits, and the counter just started January 1st, 2000. Lupron is not FDA approved for fertility treatment. It is a pregnancy category-X drug, according to the FDA. It is a hazardous drug according to NIH and OSHA. It is a reproductive and developmental teratogen. It has been referred to as a toxicant. I was told it was safe and effective and used successfully throughout the world. I run into women who never heard this risk information. This is unacceptable.

The *Boston Globe,* in August of 1996, quoted the Nation's largest volume fertility clinic, a physician, as stating, "Women do not need to know that Lupron is not FDA-approved for fertility treatment." I disagree.

I have had adenoma, breast cysts, cardiac arrhythmias, dizziness, edema, fatigue, gastritis, gastroesophageal reflux disease, hyperlipidemia, immune system abnormalities, joint pain, knee pain, lymphadenopathy, myalgia, neuralgia, osteopenia, now I have severe osteoporosis. My dentist said my jaw is dissolving. I have lost one tooth, and the rest of them are loosened.

I am not alone. Initially, I did think I was alone. I would ask all the doctors, "I just took Lupron. Is this related to Lupron?" They'd say: "No, nothing to do with it. Just coincidence. It is just your time." Well, it is not my time.

Candice Hedin, of Marlboro, Mass., seven years ago took Lupron for fertility treatment, with Clomid. She suffered multiple unexplained serious illnesses. She has been hospitalized for unexplained chest pain, inability to breathe, about 15 times. She has hives inside her mouth and throat, open sores. She cannot eat or drink anything. She gets hospitalized.

Wendy Camacho, Cherry Hill, New Jersey, took Lupron for IVF years ago. As she puts it, "my IVF baby is now nine and my health is a mess. It has been downhill since. I have seen neurologists, rheumatologists, orthopedists. None of them have any answers for me. I have severe fatigue, fibromyalgia, trouble sleeping, nightmares, gross motor skills are disintegrating fast." I could go on and on, and these are just a few people——

Senator BROWNBACK. Would you——

Ms. MILLICAN.—that I put in.

Senator BROWNBACK.—would you submit those for the record?

Ms. MILLICAN. I have.

Senator BROWNBACK. Okay, I just want to make sure that we have those in the record, those of other people, other statements from individuals.

Ms. MILLICAN. I included them within my own statement.

Senator BROWNBACK. Good.

Ms. MILLICAN. There is much more that I could have put in my statement. Time did not permit.

I do not feel that any victim should ever have to do what I have had to do. I brought this just simply as a display.

I had to file my own lawsuit without a lawyer. I am not a lawyer. There is nobody to help these people. Although I do have to say

now—you know, I started this in 1989—now there are lawsuits that are being filed.

TAP has been sued for product liability. They are being settled. I do know that cases are being consolidated, and I do foresee a class action looming large. TAP has been declared a criminal enterprise based upon its scheme with physicians and billing fraud and kickbacks and—they just paid the largest fine in history at the time, $875 million. They allegedly have been maintaining a registry of babies exposed, inadvertently exposed, to Lupron, and they have a registry of over a hundred babies. That data is as of 1992. Somebody needs to find out how these babies are. TAP Pharmaceuticals maintains that there are no birth defects attributable to the drug.

I know women myself with adverse pregnancy: birth outcomes after Lupron, and there are women on the Internet who report similar problems. There are problems with all of these drugs. I am especially concerned about Lupron, because I do believe that it is an especially toxic drug. But I have concerns about other drugs, as well. There has been no long-term epidemiologically sound research looking into the long-term health effects of any of these drugs.

And where are you going to get these eggs from? You are going to get them from women who think they are doing a good thing, maybe who need some money. I have seen egg donor ads in Boston, "We're on the T." Poor women who do not have cars, who need money, who are going to be going for this, and they need to know about the risks. And where are they going to hear it from? Only from somebody like me or other victims. And I do not get an opportunity to do this, because I am sick a lot of the time. But where are these women going to hear about this? The fertility industry is not telling them. I call them a bunch of "reproductive endo-criminologists."

There is a lot more that I have to say, but——

[The prepared statement of Ms. Millican follows:]

PREPARED STATEMENT OF LYNNE MILLICAN, R.N., B.S.N., PARALEGAL, BOSTON, MASSACHUSETTS

Mr. Chairman, and Members of the Committee:

I am honored for the invitation to speak to you today on this very important issue. And although I am a registered nurse, I am here before you because of personal experiences as a patient undergoing superovulation during in vitro fertilization (IVF) attempts at several Boston fertility clinics over a decade ago—and because of what I've learned in the interim. My focus will be upon the adverse effects to the eggs, embryos, fetuses and women from one particular and commonly used drug, Lupron (leuprolide acetate), which is not FDA approved for fertility treatment; as well as addressing the risks from other fertility drugs and the assisted reproductive technology (ART) procedures in general.

For ease of reading and reference, this paper will be arranged under the following 13 headings:

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3. On The Count Of Eggs And Money—p. 5
4. A Brief Overview of the "Hazardous", "Commonly Prescribed" Agent Lupron—p.12
5. Impact of Lupron Upon Women's Brains, Bodies, and Bones—p.14
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11. Considering Cloning? Consider the Myths of Hype, and The Realities of Scientific Misconduct—p.36
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1. Preliminary Comments

The drugs and fertility agents and the processes used in superovulation regimes for fertility treatments are exactly the same as that used to obtain women's eggs for cloning research (although numerous variations of the protocols exist within the core group of 'fertility drugs'). Cloning cannot take place without women's eggs, and therefore the information I have to offer concerning the risks of fertility treatment have direct application to the process of therapeutic cloning. It has been estimated that some 8 million eggs per year may be necessary to sustain therapeutic cloning research—how many women would that entail? My research into the medical literature revealed the maximum top three reports of numbers of eggs retrieved at one time as being: 91 eggs from one woman at one time (Source, 1995), 71 eggs from one woman at one time (Lewit, 1995), and 56 eggs from one woman at one time (Lim, 1995). Since this research will require millions of eggs, this demand translates into the need to obtain as many eggs as possible from each woman per attempt. To quote from the consent form for egg donation for purposes of stem cell research at Advanced Cell Technology: "The idea is that the greater number of fully mature eggs, the greater the chance of successfully utilizing them in this research." (ACT)

A dozen years ago, an article examined "[t]he risks associated with ovulation induction", identifying that "epidemiologic studies are needed to determine the true risks associated with exposure" to the older, 'traditional' fertility drugs (St. Clair Stephenson, 1991). More than a decade later, the question is still being asked: 'Are we ignoring potential dangers of in vitro fertilization and related treatments?' (Winston, 2002). Costly complications from ART were, in part: a high incidence of first and second trimester bleeding, spontaneous abortion, toxemia, fetal growth restriction, anemia, anesthetic complications, ovarian hyperstimulation syndrome, culture medium infections (hepatitis and AIDS), visceral and vascular injuries, pathogenic infections, and breast and ovarian cancer. (Schenker, 1994). I believe it was Mirabella's August 1993 issue which carried 'A Doctor's Story', about a physician who took Clomid and was diagnosed with breast cancer. Large scale, epidemiological sound studies remain lacking on these earlier drugs, and yet in the interim years, the newer fertility 'agents' have been added and have themselves become 'traditional', standard, chemicals used in ovulation induction—but again, this standard has developed without any epidemiologically sound, long-term, safety data. It is noteworthy that while Lupron has become 'standard' within superovulation regimes, it is administered at various doses for various times, varying even within the various patients, and has varying effects.

There have been a number of past, as well as a flurry of recent, published reports of birth defects in babies born from superovulation, IVF and other variants of ART, and it is widely acknowledged that critical long-term studies of the risks of ART are lacking (i.e., among others: Kola, 1988; Fischel, 1989; Saunders, 1989; Tanbo, 1995; Silver, 1999; Aboulghar, 2001; Mitchell, 2002; BBC, 2002; Sutcliffe, 2002; Skloot, 2003). Titles often tell the story: "Ocular Manifestations in Children Born After In Vitro Fertilization' (Anteby, 2001), 'Congenital malformations in infants born after IVF: a population-based study' (Ericson, 2001), 'Hormone and Fertility Drug Use and the Risk of Neuroblastoma: A Report from the Children's Cancer Group and the Pediatric Oncology Group' (Olshan, 1999), 'Congenital malformations in infants born after IVF: a population-based study' (Ericson, 2001), 'Brain worry over IVF children' (Health, 2002), 'Low and very low birth weight in infants conceived with use of assisted reproductive technology' (Schieve, 2002), 'The Risk of Major Birth Defects after Intracytoplasmic Sperm Injection and in Vitro Fertilization' (Hansen, 2002), 'In Vitro Fertilization May Be Linked To Bladder Defects' (Trock, 2003), 'Some Studies Sees Ills for In Vitro Children' (Mestel, 2003), 'Incidence of retinoblastoma in children born after in-vitro fertilisation' (Moll, 2003). March 2002 brought headline news that the highly promoted and touted low incidence of birth defects from IVF (always stated as "similar to the general population, about 2–3 percent") was now being reported as 9 percent—much higher than the general population. And now March 2003 brings news that IVF babies are at increased risk for urologic birth defects (Wood, 2003).

The American Society for Reproductive Medicine, in its Annual Meeting in 2002, released the following statement on October 14, 2002: "Studies Show Children of ART Develop Normally" (ASRM, 2002—note link of 'kidsareallright'). Figures don't

lie, but liars figure. (In 1990, the Federal Trade Commission brought complaints against 4 fertility providers for false claims in fertility treatment success rates [FTC, 1990]). To quote the New York Times: "Since the 1970's, fertility clinics have created almost a million children through experimental technologies. They've used untested and unregulated procedures . . . Where is Washington in all of this?" (Skloot, 2003).

Online transcripts from the FDA's Reproductive Health Drugs Advisory Committee Public Meeting, held October 18, 1999, identified "the need for pregnancy registries of babies born resulting from such [ART] treatment. These drugs include GnRH agonists and antagonists, human menopausal gonadotropins, purified urofillitropin, recombinant follicle stimulating, chorionic gonadotropin, and progesterone". The United Kingdom recently announced plans to study 68,000 people born as a result of ART (Kaiser, 2002). Will the percentage of birth defects from ART continue to climb in the U.K., and the U.S., with further study? Do human embryos really need to be grown in human ovarian cancer cell lines (see Ben-Chetrit, 1996)? "Abnormal embryos" have been implanted into women (Munne, 1995)—what kind of consent did that experiment entail? One treatment, using intravenous immunoglobulin (IVIG), has raised questions about the "ability to screen for any diseases that could crop up 20 or 30 years down the road. Some doctors have even gone so far as to denounce [the] practice not as medicine, but witchcraft." (Arnot, 2000).

Children have been born from co-culture with animal sera that could potentially contain prions, viruses, and/or unknown infectious agents—and my questions from the mid 1990's about risks from such co-cultures to embryos, children, and women went unanswered. In 2002, the FDA sent a 'Dear Colleague' letter, announcing that the transfer of such co-cultured embryos "constitute[d] a clinical investigation involving xenotransplantation" (Letter, 2002), but no enforcement action would be based on already existing embryos; and FDA and U.S. Public Health Service guidance documents recommend, among others, "follow patients for their lifetimes and counsel them to be alert to any unusual symptoms . . . [and] they and their intimate contacts should defer from donation of blood and other tissues." (CBER, 2002). Vero cells, from African green monkey kidney cells, have been used frequently in human embryo co-culture (i.e., see Veiga, 1999). In an online 1994 report of ART practices, it was stated that "[a]lthough the firm of Merieux refuses to accept any responsibility for the use of these [Vero] cells for the culture of human embryos, they are already widely used for this purpose by many specialists in medically assisted procreation . . ." (Report, 1994). Who is minding this store?

The nation's highest volume clinic was one of 10 participating clinics in a 1988 national study that attempted to look at the long-term health consequences of ART and drugs on the women and offspring—however the study made no mention of GnRHa's—the results were touted as 'reassuring', yet results were inconclusive (although "warrant[ing] epidemiologic study"), and with too few study subjects (NICHHD, 1992). Of note, this writer, who developed multiple health problems, was a fertility patient at this clinic during this study—but was never asked to participate in this study. More significantly, another patient who was asked and did participate in this study (and shared her study documents with me) was subsequently dropped from the study following her hospitalization for severe ovarian hyperstimulation syndrome during her fertility treatment—in which she went into kidney failure and nearly died.

Many follow-up studies I've read of ART children do not identify the specific drugs received. My own experiences highlight the lack of informed consent that women experience when they "agree" to take fertility drugs. The best illustration of this is found in the *Boston Globe's* quote of the Director from Boston IVF, the 'nation's largest volume fertility clinic' (one of the two clinics I attended) who proclaimed "women do not need to know about the lack of FDA approval [of Lupron for fertility treatment] . . ." (Kong, 1996) Years later, this clinic would receive "$180,000 over two years to cover the cost of providing the embryos" "to Harvard University scientists for stem cell research. . . . Harvard researchers plan to offer the new stem cells to any interested scientist at no cost, with no commercial restrictions. . . ." (Mishra, 2001)

The profit within the fertility industry that exists today, as well as the hyped potential profit of therapeutic cloning tomorrow, along with lack of informed consent, the risks, and inherent exploitation all point to this issue having very serious ramifications upon many lives.

A recent Popular Science article unintentionally highlights the issue of consent: in the March 2003 series, the McNamara's were featured as they had undergone experimental fertility treatment using cow uterus to grow their embryos. This Popular Science piece examined the risks of ART, and the McNamara's conclusion at the end

of this article was "Yeah, there is [a possibility of long-term effects] . . . But . . . we would still have done it." (Skloot, 2003). However, Popular Science held a Popular Science Infertility Chat on America Online, and, in fact, the McNamara's stated in the chat—after they had read the article—that "I think it's important to point out that the information in the article wasn't available when we made our decisions. . . . Honestly, if it was presented in a way that it would cause trauma to our offspring, we probably wouldn't have done it." (Chat, 2003)

2. Dead Women Don't Talk

Not until long after my fertility treatment did I learn that, before my treatment, there were questions raised and warning given regarding the fertility industry's use of lack of informed consent, deceptive advertising and manipulated statistics. The first survey in the world of IVF clinics was done by two journalist/authors, Gena Corea and Susan Ince, and this survey revealed that while half of responding clinics had claimed high success rates, they had, in fact, produced not one baby (Corea, 1987). In 1992 I had begun legal action against my fertility treatment providers, and in 1997, Gena Corea (see also Corea, 1985) provided a statement to me intended for inclusion into the Offer of Proof for my medical malpractice tribunal (*Millican* v. *Harvard Community Health Plan*, Boston IVF, Natalie Schultz M.D., Brian Walsh M.D., Mahmood Niaraki M.D., Selwyn Oskowitz M.D., Michael Alper M.D.) The following 5 paragraphs are from that statement:

" . . . A lack of informed consent to IVF has been a constant and continuing problem with IVF from its earliest days when Lesley Brown, pregnant with the first IVF baby, Louise, was under the misapprehension that hundreds of such babies had already been born. She had no idea that she was in such an experimental program. . . ."

" . . . The exact number of women who have died in in vitro fertilization programs is not known. However I have information on the deaths of ten women: in Germany, Brazil, Israel, Spain, and Martinique (in all these countries, I have tape-recorded interviews with the physicians and/or relatives of the dead women), and in Australia, New Zealand and Canada. Women entering IVF programs do not know of these deaths. Even physicians practicing IVF do not know of most of the deaths or their causes. With the exception of the Israelis, the IVF teams involved are not writing reports on the deaths for their professional publications nor are they delivering papers on the deaths at international meetings . . . No professional or governmental organization is recording the deaths in a data bank."

"Some Brazilians know of the first death—of a woman named Zenaide Maria Bernardo, whose daughter and physician I interviewed in, respectively, Araraquara and Sao Paulo, Brazil. They know of her death because it occurred during a course on IVF for physicians and the course was a huge media event, covered by Globo, a national television station and the fourth largest in the world. The death could hardly be covered up when the television cameras were rolling. But aside from these Brazilian citizens, few in the public know of any IVF deaths."

"To date, IVF deaths are known to have occurred due to hyperstimulation of the ovaries through the administration of hormones; anesthesia for laparoscopy; infection following laparoscopy; bleeding following laparoscopy; bleeding following ultrasonically-guided puncture of egg follicles; and ectopic pregnancy."

"Physicians and the public relations firms hired by the IVF industry often give women the impression that IVF is a low-risk procedure. How do they know it is low-risk? I have interviewed physicians around the world on IVF deaths and without exception, I have known of, and had documentation on, more IVF deaths than any of them claimed to. Why is that? If scientists doing IVF do not know of the deaths their programs are causing, why don't they? What are the mechanisms by which this information has been obscured? Through their journals and conferences, physicians share information on every slight change in drug protocol for inducing artificial ovulation. Shouldn't information on deaths, injuries, psychotic breaks, lengthy recoveries also be shared? It's not. . . ."

3. On The Count of Eggs and Money

Early articles describe Lupron's application in ovulation induction regimes as "in special situations" (Blankstein, 1988), yet Lupron "began to be widely used for IVF in 1989" (Martin, 1994). By 1990 fertility industry figures, GnRHa's were utilized in 97 percent of reported assisted reproductive technology cycles (MRI, 1992), with Lupron identified as the "prevalent choice" and most frequently prescribed GnRHa in this country (Keenan, 1991; Martin, 1994). The fertility industry had already achieved the recognition of being more than a billion dollar industry by 1990 (Talan, 1990), and sounding like a trumpet, a 1991 publication proclaimed "Chronic indications for GnRH agonist therapy among IVF/GIFT patients are likely to increase sig-

nificantly in the immediate future." (Gordon, 1991). Early on, Lupron's use had been described as increasing the use/purchase of Pergonal (manufactured by Serono) by 50 percent (Keenan, 1991), and it was known that "[t]he direct financial cost of cycles incorporating adjunctive leuprolide therapy was 40 percent greater than the cost of cycles in which no leuprolide therapy was used." (Dodson, 1991). At this time, the failure rates for IVF were around 80–85 percent: "rarely has a technology that has had such dismal success rates been so quickly accepted." (Raymond, 1993).

When I complained to my Harvard HMO about their use of this experimental drug, their response was an illustration in how definitions can easily be changed; they state that institutional review board (IRB) review was unnecessary because Lupron was not being used in "research", but rather Lupron was being used in a "therapeutic" manner. The Office for Protection from Research Risks has received reports from major research institutions of "startling ignorance" of IRB policies regarding informed consent in reproductive research (Ellis, 1995).

Because of my nightmare experiences as a fertility consumer, I became involved in drafting a first in the nation bill which would have required fertility clinics to have a license to operate, and which would have mandated informed consent of ART risks (Millican (2), 1992; Lasalandra, 1995). My collaborator in drafting this bill, Linda DeBenedictis, had also attended Boston IVF and had also been mandated to switch to Lupron—and her story was told over a 3 part series on Boston TV news. Doctors from Boston IVF told the DeBenedictis' that 3 eggs had fertilized and 3 embryos were ready for implantation the next morning. Upon arrival at the clinic the next morning, there were not 3 embryos for implantation—there were no embryos for implantation. The clinic maintained there had been an "error in communication", and that no embryos had fertilized (WHDH, 1989).

From 1992–1999, I provided verbal and written testimony to the MA. Health Care Committee in support of this bill (MA. H. 3308), and these documents are a testament to my experiences, my learning curve, and the mounting evidence against Lupron. My 1992 written testimony states: " . . . nearly every IVF clinic has mandated that women take Lupron—or they will not be allowed to cycle . . . Women are told that Lupron results in better quality and better quantity of eggs." In 1995, my testimony states I was told that I "must use Lupron" if I wanted to undergo IVF. Women reported successful IVF births without Lupron, yet were made to use Lupron nonetheless, and reported subsequent failure in these switched cycles. Other women using Lupron complain of failure to suppress and canceled IVF cycles, premature leutinization, and poor quality eggs with Lupron (see Chetkowski, 1989; Schoolcraft, 1991). The internet posts of women identify the badgering, and coercion, and manipulation, and threats used to convince women into taking Lupron for a variety of indications—many refer to their doctor as trying to "shove it down [their] throat".

Later I would learn that the first survey in the world of IVF clinics was conducted in 1986 (Raymond, 1993), revealing deceptive success rate claims and manipulated figures (Corea, 1987). As a result, the 101st Congress held hearings in the Subcommittee on Regulation, Business Opportunities, and Energy, House of Representatives, in which data from 191 fertility clinics was published. This clinic specific information shows a significant number of these reporting fertility clinics had recently "switched" and/or "began to use" Lupron in their superovulation regimes—without any IRB review (Hearing, 1989). One reporting clinic provided testimony identifying Lupron as "a costly, experimental medicine . . ." (Kemmann, 1989).

One of the fertility clinics that I attended in 1990, Brigham & Womens, had as its protocol in its IVF brochure that "Lupron is only used in certain diagnosis", but in 1991 this clinic changed its brochure to read "Lupron is widely prescribed". I would later learn that the director of this IVF clinic, Dr. Andrew Friedman, had been a lead Lupron investigator, had received numerous grants and funds from Lupron's manufacturer, Takeda Abbott Pharmaceuticals (TAP), and had published extensively on Lupron. Dr. Friedman was ultimately found guilty of falsifying and fabricating approximately 80 percent of the data in four Lupron studies, two of which had been published and were subsequently retracted. Friedman had "altered and fabricated information in patient medical records, falsified research notes by changing dates and changing and adding text", and fabricated notes and fabricated patients for clinical visits that had not taken place. (Federal Register, 1996; see also Lasalandra, 1998; Millican, 1998; Kong, 1999).

My 1995 written testimony in support of MA. H 3308 identified "manipulated figures" in a fifth Friedman Lupron study (Millican, 1995). To the best of my knowledge, while confidential Harvard documents state further investigation into other Friedman Lupron data should be explored, no investigation has been conducted beyond the four, identified, fraudulent Friedman Lupron studies. Two years after the Federal Register publication of Friedman's fraud, the MA. Board of Registration

'acted' by temporarily suspending his medical license, however the published and cited bogus data is irretrievable. And in fact, one fraudulent and retracted Friedman Lupron study was cited as a credible reference and data source in an article published on Medscape (Women's Health) in August 2001 (Data, 2001). In a similar faux pas, FDA Consumer magazine recently had to provide a correction to an article in which it erroneously stated GnRHa's would "shrink fibroids"—a statement told repeatedly to women despite the fact Lupron has only been approved for "the anemia associated with fibroids, when iron therapy alone has been ineffective". The indication of Lupron's use to "shrink fibroids" received the FDA's rejection in the past, and no FDA approval has ever been granted for this indication. (FDA, 2002)

NBC Dateline did a story January 2, 2000 about severe side effects experienced by women taking Lupron for endometriosis (adverse events such as joint pain, numbness, memory loss, irregular heart beat, suicidal depression, whole body swelling, grand-mal seizures). Quoting from the Dateline story transcript: "[Dateline] asked TAP about the complaints of these women, given TAP's marketing of Lupron as "perhaps making miracles possible." While the company declined an on-camera interview, [Dateline] met with several top executives, who told [Dateline] the preponderance of evidence suggests that Lupron works, otherwise women wouldn't continue to use it." Dateline's story concluded with "[Lupron] is also widely and routinely used for women going through fertility treatments." (Dateline, 2000).

In 2001, the U.S. Attorney's office in Boston would land the largest fine in history—$875 million—from TAP for its lucrative, unethical, illegal, conspiratorial scheme involving urologists and kickbacks, gifts, trips, TV's, computers, VCR's, as well as gifts of free samples of Lupron which were then billed to Medicare. Confidential documents of Lupron's "return to practice" scheme were revealed during Chairman Bliley's hearings (Oversight Hearings). This prosecution resulted in TAP officially earning the title of "a criminal enterprise", and a decade earlier TAP had profitably tarnished itself with receipt of Notices of Adverse Findings from the FDA due to its incessant and "deliberate campaign to promote this product [Lupron] for a wide range of unapproved uses." (FDA, FDC; 1990). "In addition to offering inducements to hospitals and doctors, TAP was encouraging its salespeople to approach patients in support groups." (Pitchmen, 2002). And I aware of one gynecologist who TAP approached and indicated he could clear $98,000 to his income by prescribing Lupron.

Government documents of the TAP prosecution reveal that TAP also attempted to make deals involving the costs of gynecological uses of Lupron. And, incredulously, these government documents state that "Lupron depot 3.75 mg is indicated for treatment of . . . infertility". This statement contradicts the FDA's lack of approval of Lupron for the indication of infertility, but the presence of this erroneous and promotional language within these government documents well illustrates the extent of pervasive influence of the industrial mantra that 'Lupron is standard in fertility treatment' (U.S.A., 1998). The rationale for so many unreasonable heated decrees of "you must take Lupron if you want IVF (to get good quantity and quality eggs)", "you must take Lupron for your endometriosis (if you ever want to get pregnant)", "you must take Lupron for your fibroids (or you'll bleed to death or have to have a hysterectomy)" was now as clear as a solid gold bell struck with a silver spoon.

Fertility clinics have been generating in the multi-million dollar annual surplus range, and years ago claimed a 37.5 percent profit margin and physician salaries up to one million (Gabriel, 1996). For quite some time, reproductive endocriminology has enjoyed the label of a multi-billion dollar industry. In such an area of 'obscene profiteering', every attempt at regulation has met with stiff opposition. The MA. bill (H. #3308) has habitually died and been refiled each session, although it has not been refiled this year to date. And I understand a recent provision by Senator Frist to study the adverse health effects of ART on women and babies was also defeated (Skloot, 2003). Patient protections are nowhere to be found, while patent and industry protections abound—and market/ing forces rather than science dictate the 'standard of care'.

When discussions of the lack of regulation within the fertility industry arise, the industry refers to the Federal bill, the 'Fertility Clinic Success Rate and Certification Act of 1992', as the answer. Yet this Act, Public Law 102–493 (signed into law by President George H.W. Bush on October 24, 1992), does not contain any language whatsoever to address or mandate informed consent to the risks of the drugs and procedures. And, in H.R. 4772 (which directs the Secretary of the Department of Health and Human Services to develop a model embryo laboratory certification program for the states), there are "Limitations" (in 'Section 3:i') which declare: "(1) In developing the certification program, the Secretary may not establish any regulation, standard, or requirement which has the effect of exercising supervision or con-

trol over the practice of medicine in assisted reproductive technology programs; [and] (2) In adopting the certification program, a state may not establish any regulation, standard, or requirement which has the effect of exercising supervision or control over the practice of medicine in assisted reproductive technology programs.

This language, which was crafted at the behest of the industry (Lawrence, 1993), appears from my vantage point to illustrate the Lupron loophole well—'you can tell us what to do, as long as you don't tell us what we can't do . . . including patentable, profitable, ventures involving injecting hazardous drugs without informed consent.' What we have here is unconscionable stealthcare: an entire 'profession' and industry utilizing hazardous and untested drugs and procedures upon vulnerable women attempting to conceive, without informed consent, under the guise of "science" and "under the law". For a preyed upon victim to have to try to sort this out without advocacy, and to have to learn how and then search applicable law to try to make sense of this outrageousness, is patently absurd. Judge Learned Hand precisely captured the essence of this matter: " . . . there are precautions so imperative that even their universal disregard will not excuse their omission" (T.J. Hooper, 1932).

Of critical note is the increasing number of states that have passed legislation that mandates insurance coverage for fertility treatment—in essence, promoting further use of experimental agents such as Lupron (and in the case of MA., it would appear that the state has become complicitous in the advancement of human experimentation in light of failure to pass informed consent legislation). These states have been, and/or are being, lobbied heavily by RESOLVE, Inc., an organization that alleges to "educate, support, and advocate" for the infertile, yet was taking thousands of dollars from TAP Pharmaceuticals as early as 1989 (before any female indication had ever been FDA approved for Lupron). RESOLVE, Inc. admits to receiving hundreds of thousands of dollars from numerous fertility drug manufacturers in its itemizations in Annual Report disclosures, however RESOLVE claims in published Boston reports that RESOLVE "does not receive any funding from drug companies" (Seiffert, 2000).

RESOLVE has a history of opposing regulation of the fertility industry, including MA. H #3308 (Millican (1), 1992), and of "mov[ing] quickly to downplay" information pertaining to risks from fertility drugs and treatment (Dezell, 1994). And, in similar fashion, the Endometriosis Association (EA), which testified at the FDA on behalf of, and claims an active role in the approval of, Synarel, the first GnRHa FDA approved for use in women with endometriosis—with the EA providing testimony to the FDA on behalf of Lupron as well . . . yet the EA has also received thousands upon thousands upon thousands of dollars from GnRHa manufacturers, including TAP (see *www.lupronvictims.com*, 'Endometriosis', for partial list of specific years, companies, and dollar donation amounts). Another younger endometriosis association, founded in 1997, the Endometriosis Research Center (ERC), like the EA, publicizes clinical drug trials for endometriosis. The "ERC March 2000" was "presented by the ERC and Amgen Praecis" (manufacturer of a GnRH antagonist) (ERC, 2001); and an ERC Board Member and Director of Operations is also the "co-ordinator of the AstraZeneca [manufacturer of Zoladex] Pharmaceutical Corporation website, the Endometriosis Zone" (Operations, 2003). While the disease of endometriosis and the havoc it wreaks needs as much attention as possible, the eternal presence of conflicts is quite troubling.

For years the FDA has been making annual seizures at ports of unlabeled and illegal fertility medications, including Lupron. I have also seen a publicly posted note on a fertility message board advertizing an ultrasound machine, and media reports have been made in the past of 'black market' Lupron and sales. Just what type of underground market exists out there? Just how many people are lining their plush pockets while their victims simply line and pile up?

'Follow the money' is an apt adage for this unregulated billion-dollar industry and all its associates groups. The value of eggs and embryos for research was clearly identified in the transcripts of the National Institutes of Health's 1994 Human Embryo Research Panel Hearings, wherein the profit from human embryo research in the form of vaccines, hormones, proteins, stem cells, gene therapy, cell lines, organogenesis, ectogenesis, parthenogenesis, chimeras, patents, etc. was amply highlighted. There were a few voices of caution: i.e., Dr. Van Blerkom stated "The [medical] literature is the quality of the science in the field, and without offending anybody who might have a vested interest, I think the quality of science in this field has been awful, in this country at least, from the very beginning, awful because there are reports that get into journals based on handfuls of patients." And C.A. Tauer stated "I think the fact that the research enterprise has gone on out there without peer review and without the appropriate safeguards is something very bad that has happened." (NIH, 1994)

One patent relating to assessing eggs and pre-implantation embryos noted that "[s]ignificant improvements in ovulation induction, oocyte retrieval, and in vitro culture techniques have resulted in an abundance of embryos per patient or experimental animal." (Assignee, 1996). One gross eggsample of commercialism at its highest level of crass was the website auction of the eggs of "beautiful young models for as much as $150,000 a pop" (Oldenburg, 1999). Hundreds of "egg donor wanted" ads litter the nation's newspapers and college campuses, with financial enticement as high as $50,000 for Ivy league eggs (Padawer, 2002) and $100,000 for the preference of 'proven college-level athletic ability' (Enge, 2000)—and the industry proclaims the "shortage of egg donors"—yet it would seem that the published medical literature tells a different story.

In curiosity, I added the number of human oocytes and embryos identified in a mere, random, 20 pages in just *one* of the numerous relevant medical journal publications available, and arrived at a total of 7,845 human oocytes [eggs] and 266 human embryos used in research in these few pages. These 20 pages contained roughly 80 abstracts, published in just *one* supplement of this *one* journal, from just *one* month, in just *one* year (Journal, 1995). This genetic 'research material' is described in the published medical literature as "coming from the IVF program", "surplus", "left-over", "discarded", "extra", "spare", "clinic", "donated", "research", "abnormal", "fertilized", "unfertilized", "nontransferable", "suboptimal", "nonviable", and "aspirated". In Britain's *The Times,* an article entitled 'Scientists pillaging foreign embryos' qualified that "the stem cells are derived from an anonymous embryo in the United States, left over from an IVF procedure." (Hawkes, 2000). And, again for curiousity, I tallied the incidence of 'egg donor wanted' ads published in the *Boston Globe* for the month of February 2001; and found 'egg donor wanted' ads published on February 4th, 6th, 7th, 8th, 11th, 14th, 18th, 20th (twice), 21st, 22nd, 25th, and 27th.

The *Washington Post* reported in 1998 on 'Experimenting with eggs': " . . . No one was paying attention . . . The research required many eggs to practice on, said [][one] clinic's director, so doctors there turned to women who were donating eggs to infertile women and used some of the leftover eggs for their research. 'We call it sharing with the lab' he said." (Weiss, 1998). And there are few embryologists who admit to "hav[ing] played around with embryos after hours." (Rogers, 2001).

The same researcher who recruited egg donors for Advanced Cell Technology's human embryo cloning endeavors has a mobile embryology lab—"a conventional-looking recreation vehicle with a connected trailer. Inside is nearly all the gear needed for in-vitro fertilization." (MSNBC, 2002). Currently this mobile embryology lab is utilized to serve HIV+ clients who wish IVF, but it is noted that such a traveling lab "could potentially provide location-flexible ART for under served populations" (Foundation, 2002). In the matter presently before Congress, there is discussion that if therapeutic cloning were allowed, it should be removed from the fertility clinic setting. Are traveling embryology vans, pulling trailers and driving throughout the streets of the country, the answer? With the value of human eggs as research material increasing, imagine the obscene profit that an unscrupulous scientist could envision with a mobile IVF unit traveling the country, trafficking in underground egg sales.

The profoundly significant and despicable thefts ("conversion", "sharing") of women's ova and embryos by Drs. Ricardo Asch, Sergio Stone and Jose Balmaceda at the University of California at Irvine (Regents; Press; 1995) should be a serious reminder to the utter (and anesthetized) ease with which such menacing maneuvers can be executed. (And Dr. Asch had co-authored studies of Lupron, "which was kindly provided by Abbott" [Guerrero, 1993]). The contemptible violations of stealing women's eggs and embryos should highlight the profitability of schemes to procure women's eggs and embryos for use in research and/or covert 're-sale'. Dr. Asch reportedly 'left his office daily with briefcase stuffed with thousands of dollars'. And attention should be directed to the drug protocol(s) used—medications administered "deliberately" "so there would be a surplus of eggs" (Challender, 1995). Who is exerting any oversight over the field of reproductivity? Who would exert oversight over therapeutic cloning—this same industry?

The conflicts within this arena are excessive and have had a tremendously negative impact upon care. For one example, I pursued initial rheumatology work up for bone pain post-Lupron at the renowned hospital which had first prescribed Lupron to me, and during the course of my visits I was met with the standard "(pain) has no connection to Lupron". Years later I would read that the head of this department had been a long-term highly paid consultant and scientific advisor for Lupron's manufacturer (with compensations rising each of the many years displayed)—and I've seen this doctor's signature on the contract where the pledge is taken to 'defend the company's products at all times in all ways'. In retrospect, I'm able to say 'no

wonder no one there wanted to even hear about any connection between Lupron and problems'—but how many other patients know of conflicts of interest in their circumstance(s) . . . and who will tell them?

4. A Brief Overview of the "Hazardous", "Commonly Prescribed" Agent Lupron

Lupron, referred to as a GnRHa (gonadotropin releasing hormone analog/agonist [and also previously referred to as LHRH]), will be the focus of my comments as it is one of the most commonly used agents, but it should be recognized that numerous other GnRHa's as well as the newer GnRH antagonists are being used in superovulation of women—and the risks from all of these agents should be taken into consideration. Thousands of women have become seriously ill after taking Lupron (and there have also been complaints about other GnRHa's, such as Buserelin, Synarel and Zoladex); and the alleged safety and mechanism of action of these drugs needs attention. A National Lupron Victims Network (NLVN) was founded in 1993, and when I learned of their existence in 1994, they were the only entity who was interested in the results of my searches into the medical literature; and this information, along with many other sources of information, continues to serve as the 'clearinghouse' of information on the risks of Lupron at their website, *www.lupronvictims.com*. The NLVN began a visit counter on January 1, 2000: as of 3/25/03 there were 2,119,422 hits made to this site. While the NLVN provides detailed information on Lupron, other internet sites contain public message boards about problems after Lupron, i.e., Delphi message boards such as 'Julie's After Lupron Page' (Julie's Page), and AOL message boards, among many others.

The initial patent filed for Lupron involved ovulation induction (Patent #4,005,063), and Lupron has been used in drug company funded studies to induce ovulation (i.e., Segal, 1992). Lupron has become the "standard of care" for some 15 years, for a variety of reasons, including to maximize number of eggs produced. A multitude of many, including numerous Internet pharmacy websites, hawk Lupron as a "fertility medication" . . . yet the FDA has never approved Lupron for infertility, or fertility treatment, or IVF treatment, or any variant of IVF or ART. According to the Physician's Desk Reference, the FDA classifies Lupron as a Pregnancy Category X drug, meaning any woman who is or who may become pregnant should not use. Lupron is a known teratogen (Shephard, 1992), and Lupron is a known developmental and reproductive toxicant (Scorecard). NIH and OSHA place Lupron (leuprolide) on its list of hazardous drugs (NIH, OSHA). Yet, inexplicably, medical literature reports Lupron to be the most commonly prescribed and "prevalent choice" of GnRHa used in fertility treatment (Keenan, 1991; Martin, 1994).

Medical literature regularly refers to Lupron as an antineoplastic and chemotherapy, with some references characterizing Lupron as an antineoplastic hormone. Yet, according to deHaen modified American Hospital Formulary System, Lupron is not listed in the antineoplastic/hormone category (Classification No. 10:00.10, as are the drugs Tamoxifen, Megestrol, Flutamide)—but rather Lupron is listed in the antineoplastic/OTHER category (Classification No. 10:00.12, listed along with Interferon) (deHaen, 1995). No one seems to know what the "other" in Lupron is! But it is known that Lupron was originally approved out of the FDA's Office of Biologics Research and Review. (NDA [New Drug Application] 19–010).

Clinical studies conducted by the manufacturer to evaluate Lupron's efficacy (and 'not' safety) in fertility treatment and in IVF occurred between 1988 through 1992, according to Abbott Annual Reports (see also FDC, 1988). The "IVF clinical trials" and "fertility treatment clinical trials" using Lupron "were discontinued", according to the manufacturer (Abbott correspondence, 1995), and I've been unable to learn whether these Lupron IVF and Lupron fertility trials were discontinued because of efficacy reasons, safety reasons, both reasons, or other reasons.

Lupron has never gained FDA approval for any type of fertility treatment, however, Lupron did gain FDA approval for use in women for pain management of endometriosis in 1990—yet the clinical studies for these approvals are a joke—conducted on a handful of women, by paid investigators, and with an endpoint of establishing Lupron's efficacy in pain management of endometriosis while the women in these studies were simultaneously allowed to take narcotics, including Dilaudid and parenteral narcotics. These women were also expected to 'recall and record their adverse events at the end of the study month', yet were not informed that Lupron was known to affect memory (NDA 19–010; see also Newton, 1996). Problems with this trial alone could fill this document—never mind attempting to address the numerous and gross problems evident within other Lupron NDA's.

Lupron is alleged to cause menopausal symptoms such as hot flashes and headaches, and Lupron's categorization as a "hormone" is an allusion that is frequently conveyed to women. Women are often told by the physician, and TAP continues to

state, that side effects to Lupron disappear after the 'drug' is stopped. Yet FDA documents for the endometriosis NDA identify that the majority of hot flashes occurred *after* stop of study (NDA 20–011). One clinical trial evaluating memory loss and cognitive effects of Lupron in young women undergoing IVF showed that "[72 percent] showed difficulty with memory while on leuprolide" and there was "no correlation between estradiol levels and tests results on any test" (Varney, 1993); and another study showed 11 percent continued with memory complaints 6 months after stop of study (Newton, 1996). In the March 1984 FDA's toxicological reviews of Lupron, it is stated that "[rat] testes showed various degrees of testicular degeneration which were detectable within 2 days. The severity of the lesions were greater in the testes of rats sacrificed 7 days after cessation of treatment indicating that the effects continued after drug withdrawal. . . ." (Jordan, 1984).

Women are told that Lupron will "shut down their system", allowing "control" over their system, and that the side effects are related to menopausal symptoms. But in fact, it was known prior to my 'treatment' with Lupron (but not disclosed to me) that Lupron causes a "hypophysectomy" (Holmes, 1988)—which, by definition, is "destruction or removal of the pituitary"; and it was known (but not disclosed to me) that "sustained treatment with GnRH agonists most likely abolishes pituitary function" (Bischof, 1988). I would also later learn that in the original rat studies submitted to the FDA for Lupron's initial approval of palliative prostate cancer, all rats at all doses developed pituitary adenomas (tumors)—and it was stated that "there is no obvious reason to suggest that the same process could not occur in humans" (NDA 19–010).

Years following these Lupron animal studies, it would be reported "[w]e cannot exclude that [GnRHa] may cause not only adenomas in rat pituitary glands as reported previously, but also a (nodular) hyperplasia of the pituitary gland in man." (Radner, 1991) While the industry maintains that the hot flashes from Lupron are due to lack of estrogen, women complain of hot flashes while on Lupron but not achieving 'suppression' (termed "Lupron escape"), and women complain of hot flashes while on Lupron plus estrogen, and women complain of hot flashes after stopping Lupron that do not go away. Years later, I'd read that it is the "interference with the pulsatile pattern of GnRH that causes flushes" (van Leusden, 1994)—thus, the alteration, impairment, destruction, of the pituitary (as never explained to me or others). To quote one investigator: "GnRH analogs are not like any other medication currently available for treatment of disease. As we continue to learn more about these analogs' mechanisms of action, it is increasingly apparent that they do not just affect the gonadal [sex] hormones, but are powerful modulators of autonomic neural function." (Mathias, 1995)

5. Impact Of Lupron Upon Women's Brains, Bodies, and Bones

By way of understanding the significance of this information, the hypothalamus and pituitary are considered the master glands of the body, and both are directly connected to each other by neurons and blood supply; and are responsible and required for proper functioning of the autonomic nervous system (involving hunger, thirst, temperature, heart rate, blood pressure), and the production of numerous hormones necessary for life. GnRH, gonadotropin releasing hormone, which is made by only around 1000 neurons in the hypothalamus (Wierman, 1995), is sent to the pituitary and causes the secretion of (among others) the hormones necessary for normal ovulation (leutenizing hormone [LH] and follicle stimulating hormone [FSH]). Lupron is a synthetic copy of the GnRH found in pig and sheep, except that Lupron has an added, unnatural amino acid substitution inserted into the structure of the molecule, causing it to become an 'analog' of GnRH and far more potent than the original molecular structure. Which brings me to several pertinent comments made by the FDA that sum up some of the problems and concerns with the use of such a new molecular entity:

One year prior to Lupron's initial FDA approval for palliative treatment of prostate cancer, members of the FDA's Center for Drugs and Biologics wrote an article entitled 'Trends in Drug Development with Special Reference to the Testing of LHRH [GnRH] Analogues'—stating "[c]onceivably, LHRH analogues may be antigenic . . . [and] may even cause immune-related disorders. . . . The long-term safety of LHRH analogues have not yet been fully investigated, especially when we are dealing with structures drifting farther and farther from the original molecule." (Gueriguian, 1984).

Lupron's structure indeed differs from the original structure in that it contains an UN-natural amino acid, making the 'drift' of Lupron, in my opinion, far from the original 'natural' (pig/sheep) structure. Bear in mind that other GnRHa's have modifications of the original GnRH molecule with their own unnatural substitutions at different and differing places along the structure of the original GnRH molecule—

and the newest 'models', the GnRH antagonists, are even further modified. It would seem that there was recognition by these FDA members that 'tinkering' with this molecule raised long-term safety issues for human health.

Five years following the publication of 'Trends in Drug Development with Special Reference to the Testing of LHRH Analogues', prior to any FDA approval of any GnRH analog use in women, the FDA Medical Review Officer of GnRH drugs for gynecology closed her comments at a public hearing with her "experience in observing the course of GnRH analog research over the past year." These were Dr. Ragavan's comments in 1989: "Most of the studies that have been presented for [GnRH] analog research are presently being conducted in young women for benign indications. . . . The number of studies trying to use these drugs has by no means slowed down recently. Industrial sponsors have been quick to fund these studies on the drugs seeing a potential market. . . . [The Committee] may wish to consider the ethical issues of continued intellectual searches for the use of analogs and the possible risks associated with such studies in this study population. We have always used with extreme caution in our abilities to render men hypogonadal albeit for different reasons. And have reserved this treatment for life threatening conditions in the male, such as prostate cancer. Should we use the same caution in women, especially when we treat benign chronic non-life threatening conditions such as endometriosis? In fact, I propose for you an even more caution in this population who must live with the consequences of treatment for a very long time." (Ragavan, 1989)

In 1994, the FDA issued recommendations (authored by FDA Medical Officer Reviewers of either Lupron's prostate or endometriosis NDA's) that "only pertain to GnRH analogs and should not be considered as guidance for the testing of any drug classes"; and with acknowledgment of "unpublished work" from TAP Pharmaceuticals, these Reviewers recommended: "At necropsy, special attention should be given to the anterior pituitary, adrenal, pancreas, testes, and ovaries, since an increased incidence of neoplasia in these organs has been associated with GnRH agonist treatment. . . . Following restoration of fertility after cessation of treatment, the possibility exists that some germ cells may have been permanently affected by drug treatment. It is therefore important to investigate the effects of fetal morphology (teratogenicity) and on postnatal development of the offspring." (Raheja, 1994).

An FDA Medical Officer, in reviewing a proposed study for Lupron in high risk breast cancer patients stated the "[d]evelopment of this drug as a general contraceptive should meet with substantial reservations . . . it is an adventure into the unknown", and a Committee Chairman recommended "find out what its [Lupron plus oral contraceptives] long-term effects were, and then consider it for a larger population." (FDC, 1994)

Medical literature reports that the use of GnRHa's in IVF has caused neurological symptoms—migraines, numbness and tingling, paresthesia and weaknesses and sensory ataxia—"Transient cerebral ischemia is one possibility that may explain the symptoms . . . a direct effect of potent GnRHa on the central nervous system resulting in neurological effects independent of the hypothalamic-pituitary-gonadal axis is possible . . . [and] it is quite possible that mild cases with minor symptoms have escaped notice; thus, the occurrence of this type of complication may be far more common that we realize." (Ashkenazi, 1990). Of note within the latter article's Medline abstract on PubMed is the mesh heading: "Nervous System Diseases/chemically induced".

Another study using Lupron and Synarel, for endometriosis alone or with infertility, was titled "Memory complaints associated with the use of gonadotropin-releasing hormone agonists: a preliminary study" (Newton, 1996). "Profound luteinizing hormone suppression after stopping the gonadotropin-releasing hormone-agonist leuprolide acetate" is another study's title (Sungurtekin, 1995).

In 1995, the first bone biopsy was done on the bones of young women receiving GnRHa therapy for endometriosis, and results showed that after 6 months of GnRH use in young women, there was "severe disruption of the cancellous microstructure" of the bone, and the "results suggest that bone loss induced by GnRH analogs may be associated with adverse effects on cancellous microstructure which are unlikely to be reversed following cessation of therapy." (Compston, 1995; See reprint of bone biopsy results before and after GnRHa at *www.lupronvictims.com*—'Effects on bone').

Ovarian enlargement and development of ovarian cysts frequently occurs during superovulation, with ovarian cyst formation "occur[ring] in up to 35 percent of women receiving leuprolide acetate" (Serafini, 1988; Gocze, 1993). And during clinical trials of Lupron's use in endometriosis, it is noted that no difference in ovarian enlargement/decrease was noted compared to control patients (NDA 20–011), yet in a separate study (co-authored by a Lupron endometriosis clinical trial investigator)

it was noted that "significant changes were noted" and "the identifiability of the ovaries [by MRI] was significantly poorer . . . The effects of [Lupron] therapy on the normal uterus and the ovaries were statistically significant", predicting an "experienced radiologist should expect to be able to identify the ovaries on only 70 percent of the images." (Zawin, 1990)

In the Journal of American Medical Association, a letter reported "[p]ossible ocular adverse effects associated with leuprolide injections", and noted "11 reported cases of pseudotumor cerebri" (Fraunfelder, 1995) Thousands of women (and men as well) have contacted the NLVN, filled out surveys detailing their medical complaints after Lupron, and continue to report adverse events post-Lupron to the FDA, to TAP, to doctors, to lawyers, to legislators, to federal, state, and consumer agencies, and to the media). The FDA and TAP continue to receive these reports, and women continue to receive Lupron, without receiving informed consent.

6. Known Effects Of Lupron On Eggs, Embryos, and Babies

Ovarian cyst formation "occurs in up to 35 percent of women receiving leuprolide" (Serafini, 1988). Even though Lupron is allegedly prescribed to prevent ovarian hyperstimulation syndrome, the use of Lupron (including the sole use of Lupron alone, with no other fertility drugs) has caused the life threatening condition of 'severe ovarian hyperstimulation syndrome' (Yeh, 1989; Barbieri, 1991; Hampton, 1991; Droesch, 1994; Weissman, 1998). "[U]nacceptable level[s] and variability of stimulation prior to suppression" was encountered early with Lupron's use in ovulation induction regimes (Meldrum, 1988), and aberrant estradiol flares and an inability of Lupron to establish "any ovarian response" were noted elsewhere (i.e., Chetkowski, 1989; Penzias, 1992, 1994). Lupron is commonly used during the superovulation regime prior to egg aspiration/donation, and one study using Lupron in an egg donor program concluded that "continuous postaspiration GnRHa [Lupron] may be beneficial for oocyte donors whose ovaries are hyperstimulated". In this latter egg donor study utilizing Lupron, 1 of 6 patients required hospitalization. (Ng, 1995). "Fertility clinics will not be informing their patients that in Collingswood N.J. there flourishes a National Lupron Victims Network." (Millican (3), 1995)

Published medical reports have noted the occurrence of abnormal human pregnancy outcomes associated with the use of Lupron—43.5 percent in one 1996 study (Karande, 1996). Another report, using the 'long Lupron protocol', showed a 38 percent abortion rate (Shanis, 1995), and a study of 'low responders' using Lupron showed a 66.6 percent spontaneous first trimester abortion rate (Droesch, 1989). In 'healthy women undergoing ovarian stimulation' using Lupron in another study, another 66.6 percent abortion rate was noted (Minaretzis, 1995). Another study's title states "Exposure to [Lupron] in Early Pregnancy is Associated With High Pregnancy Wastage That Could be Related to the Length of Exposure" (Sasy, 1997).

What are the known effects of Lupron upon eggs? In a 1994 study of chickens using Lupron, 1 out of 25 of the hens died, and at the end of the 30-day experiment, all egg shells had thinned (Burke, 1994). A study using two GnRHa's (including Lupron) involving rabbit ovaries, concluded "GnRHa act directly in the rabbit ovary . . . increasing oocyte [egg] degeneration" (Yoshimura, 1991). In studies involving Lupron in human fertility cycles, it was reported that "some retrieved oocytes exhibit incomplete nuclear and cytoplasmic maturation after the use of this agonist [Lupron]" (Racowsky, 1997) as well as "maturational asynchrony between oocyte cumulus-coronal morphology and nuclear maturity" (Hammitt, 1993). In 'Designs on Life', by Robert Lee Hotz, it was revealed that "[s]cientists . . . noticed that Lupron embryos were different. They grew faster, developed more rapidly. They were more fragile when frozen and less likely to survive thawing. Nobody knew why or what it meant for the long-term health of the woman or any resulting child." (Hotz, 1991)

According to the 1998 text, 'Drugs in Pregnancy and Lactation', TAP communicated in 1992 that it was "maintaining a registry of inadvertent human exposure during pregnancy to leuprolide and currently has over 100 such cases. No cases of congenital defects attributable to the drug have been reported . . ." (Briggs, 1994). And "[f]etal growth retardation was observed with increased frequency among the offspring of rats or rabbits treated during pregnancy with subcutaneous doses of leuprolide similar to those used in humans." (Friedman JM, 1994). In a study using Lupron and other GnRHa's on rabbit eggs, "[t]he rates of normal fertilization and early embryonic development were significantly reduced in the oocytes matured by GnRHa", and it was noted that "one cannot exclude the possibility that GnRHa in pharmacological dosages may be cytotoxic against oocytes." (Yoshimura, 1992)

In a patent for embryo culture composition, it is noted that "culture of primate embryos in the presence of a GnRH agonist . . . unexpectedly dramatically reduces the rate of embryo attachment and cell differentiation." (Hearn, 2000). Using

Lupron in fertility cycles, "some retrieved oocytes exhibit incomplete nuclear and cytoplasmic maturation after the use of this agonist" (Racowsky, 1997). Growth retardation has been noted in young monkeys given Lupron (Golub, 1997).

But TAP has maintained a registry from over a decade ago of more than 100 Lupron exposed babies in which no "attributable" defect has allegedly been found Perhaps someone needs to investigate the veracity of this data. There have been accounts by women, including on the internet, reporting birth defects in babies conceived on or after stopping Lupron—including Lupron use for fertility as well as use for endometriosis. It is not uncommon to see an internet infertility message board note stating "I have one Lupron 2-week kit for sale. I just lost my third baby and can't go through this any more". Public posts have described babies conceived spontaneously within several months of stopping Lupron, and born with birth defects such as Total Anomalous Pulmonary Venous Return, a heart defect. I personally know women who conceived babies from IVF using Lupron whose children have anatomic anomalies and developmental delays, and I know women who conceived babies after using Lupron for endometriosis who've experienced loss of child, developmental delays, esophageal stricture, attention deficit, and serious seizure disorders. I personally know 3 women, with 5 children (conceived on Lupron either through IVF or unintentionally during Lupron for endometriosis) who have serious seizure disorders, and I have heard of other similar cases. Internet message boards about parenting problems with ART children show notes of ART children undergoing a variety of tests (i.e., CAT scans) and surgeries (i.e., open heart) and being prescribed a variety of drugs for a variety of ailments including poor muscle tone, jerkiness, choking, esophageal stricture, spinal cord abnormalities, GERD (gastroesophageal reflux disease).

The first published long-term study of babies born after accidental exposure to GnRHa's revealed that 4 out of 6 babies have severe neurodevelopmental abnormalities, and the conclusion of this study was that "[t]his observation . . . justifies the need for long-term follow-up of more children previously exposed to GnRHa" (Lahat, 1999). When Lupron is used in superovulation regimes, upwards of 1 mg/day will be injected for several weeks to one month or more, and to within days of egg retrieval. Women are given both the daily Lupron and depot Lupron (monthly formulation) for superovulation regimes (i.e., Ruhlmann, 1993)—yet Lupron depot brochures for endometriosis and fibroids state barrier contraception should be used during depot Lupron and that pregnancy should not be attempted until 2 months after therapy (meaning 3 months from the last injection). Again—TAP Lupron depot brochures advise barrier contraception during Lupron and recommend pregnancy not be attempted until 3 months after last injection, yet TAP has funded studies using Lupron depot and Lupron daily in infertility and IVF. Regardless of daily or depot Lupron use, women are told that Lupron will be out of their system before any fertilized egg is implanted—yet published medical literature by, among others, a TAP Medical Director, identified that detectable levels of Lupron remained after 11 weeks following the last injection. (Miller, 1990)

Women are prescribed anywhere from 10–45 days of Lupron during one superovulation regime (see, i.e., Nader, 1988), often being put on prolonged Lupron—a "delay". (Damario, 1997). And women are frequently prescribed birth control pills before Lupron to prevent Lupron-induced ovarian cysts that are known to develop. One woman from the 'Surrogates' Corner', having already given birth twice to twins in the past as a surrogate, describes how she's working with a new couple: " . . . I have been on Lupron since May 26 . . . I can't take much more Lupron!"—the date of her note was July 28th (Surrogate, 2000). A woman could receive a range of 5–22.5 mgs in one 'fertility' cycle with Lupron if using Lupron 0.5 mg per day, or she could receive a range of 10–45 mgs in one 'fertility' cycle if using Lupron 1 mg per day. Some women are prescribed more, some less, in a superovulation regime. Women receiving Lupron for endometriosis receive 3.75 mg per month in one injection—for a total of 22.5 mgs in 6 months of treatment (a limit recommended by the FDA due to occurrence of bone loss). The woman who undergoes one "controlled ovarian hyperstimulation" regimen may be very well be exposed to more Lupron than a woman undergoing six months of treatment for endometriosis.

While the endometriosis patient may undergo more than 6 months of Lupron 'treatment', women who undergo fertility treatment are well known to be 'frequent fliers' (given the failure rate and need for repeated IVF trials to attempt 'success'). One published study reported a woman undergoing superovulation 18 times (Check, 1988). Women who take Lupron for fibroids use 3.75 mgs per month for 3 months—although variations in dose and duration are often reported. Consider that men in the final stages of prostate cancer are currently prescribed Lupron 7.5 mg per month (depot), and not the daily Lupron, yet the daily Lupron was the initial form of Lupron first approved by the FDA (for palliative treatment of prostate cancer).

Currently, daily Lupron is rarely used in prostate cancer, but it is this daily Lupron that is most frequently prescribed in superovulation regimes, despite discontinued clinical trials and despite never having gained FDA approval for fertility or IVF.

7. Examples of Iatrogenic Illnesses Induced By Exposure

In 1999, the FDA reported on their review of MedWatch Reports for adverse events from Lupron. The FDA reviewed more than 6000 reports, concluding "there were high prevalence rates for serious side effects". The FDA's action was to reexamine the product label, "to ensure that these events are adequately addressed." (Lazar, 1999). It is my understanding that the FDA was to undertake another review. In the meantime, what, if anything, has been done "to ensure that these events are [] addressed"? After FOX 25's 2 part series on the adverse effects of Lupron, FOX informed Senator Kennedy of their series and quoted the Senator as stating he found their "report on possible side effects of Lupron was troubling. Physicians have an obligation to inform patients of the risks of drugs they prescribe, and promotion of potentially risky 'off-label' uses of products by manufacturers is illegal and unethical." (Kennedy, 1999)

The medical literature offers numerous examples of iatrogenic illnesses following exposure to GnRHa's. For example, in a 1990 study utilizing GnRHa in IVF treatment, one of a group of women who had developed severe ovarian hyperstimulation syndrome and liver function abnormalities, had a liver biopsy performed (at the end of surgical removal of conceptus due to intrauterine death 2 months into the pregnancy). This liver biopsy showed "a striking abnormality consisting of macrovesicular fatty infiltration around and linking the portal tracts. This appearance could not be classified into any well-recognized clinical entity." (Forman, 1990).

These, and other, clinical reports are disturbing, especially as they pile on top of one another. Case report or study titles often tell the story: 'Adverse effects of leuprolide acetate depot treatment' (Friedman, 1993), 'Neuropsychologic Dysfunction in Women Following Leuprolide Acetate Induction of Hypoestrogenism' (Varney, 1993), 'Angina and myocardial infarction with use of leuprolide acetate' (McCoy, 1994), 'Memory complaints associated with the use of gonadotropin-releasing hormone agonists: a preliminary study' (Newton, 1996), 'Leuprolide Causes Pure Red Cell Aplasia' (Maeda, 1998), 'Transient thyrotoxicosis and hypothyroidism following administration of the GnRH agonist leuprolide acetate' (Kasayama, 2000), 'A case of atypical absence seizures induced by leuprolide acetate' (Akaboshi, 2000). Case reports of Lupron-treated fibroids having "striking vascular changes and histologic features of vasculitis and atherosclerosis" note that "[t]he florid and rapid development of vascular inflammation, fibrinoid deposits, and thrombosis after leuprolide acetate therapy ["rarely seen in non-leuprolide treated {fibroids}"] suggest an immune-mediated process. . . . these observations are significant and worrisome if such changes affect other organs." (Mesia, 1997). Lupron has been listed among those medications that may cause lupus. (Greenberg, 1999).

Problems associated with Lupron are also identified in the titles of male uses of Lupron as well, i.e. 'Leuprolide therapy for prostate cancer. An association with scintigraphic "flare" on bone scan' (Johns, 1990), 'Sudden death due to disease flare with luteinizing hormone-releasing hormone agonist therapy for carcinoma of the prostate' (Thompson, 1990), 'Possible Ocular Adverse Effects Associated With Leuprolide Injections' (Fraunfelder, 1995), 'Pituitary apoplexy after leuprolide administration for carcinoma of the prostate' (Morsi, 1996; multiple other similar case reports have been published), 'Localized Amyloidosis of the Seminal Vesicle: Possible Association With Hormonally Treated Prostatic Adenocarcinoma' (Unger, 1997), 'Incidence of bone fracture in patients receiving luteinizing hormone-releasing hormone agonists for prostate cancer' (Hatano, 2000), 'Altered cognitive function in men treated for prostate cancer with luteinizing hormone-releasing analogues and cyproterone acetate: a randomized controlled trial' (Green, 2002).

In the animal testing data submitted for Lupron's initial approval, the FDA Review and Evaluation of Pharmacology and Toxicology Data states, among others: " . . . There are other, inconsistent, effects of Leuprolide in the various toxicology studies but potentially the most serious effect of Leuprolide, in my view, is its effect on spinal column bone marrow. This increased fat deposition and subsequent hypocellularity was explained as a physiological response to the drug. . . ." (Jordan, 1984). Years later, other animal testing would reveal "[a]lterations in thymic and bone marrow lymphocyte subpopulations in GnRH agonist [Lupron] treated prepubertal female mice" (Rao, 1993).

Many, many relevant studies and case reports are left unmentioned here. Many effects of Lupron, such as upon the bone, heart, immune, and other systems, have barely, if at all, been touched upon. But it is the people with real names, real faces, and real pain that is most upsetting. Many women, and sometimes family of these

women, have contacted me over the years with varied complaints following Lupron—always looking for help. It is extremely difficult for me to hear these horror 'stories'.

As a former full-time career R.N. who has been able to effectively advocate for any patient, and did so for many patients in the past, after Lupron I suddenly found myself in a land somewhere beyond the upper level of nowhere—and all rules had changed. It was an awful moment when I realized that I was not alone and there were many other Lupron victims—comforted by company, but horrified at the scope involved. All other victims were echoing my words that "after lupron" thus and such started. And all other victims have interesting doctor 'stories' to tell. My experiences were simply inexplicable at times, and I quickly learned (but fiercely resisted) the fact that Lupron was not open for substantive discussion. I would self-triage my own various symptoms and prioritize before arriving at the doctor's office, otherwise s/he would be overwhelmed. One physician replied after I reported dizziness, pedal edema (swelling in feet), and gastric pain, that "those are bullshit symptoms". That atrocious answer and behavior is never a correct response to any patient, and after I changed doctors a small gastric bleed was diagnosed. These few personal details barely convey the level of destruction this drug and the subsequent unmerry-go-round has had upon my life and the lives of countless others. Here is a glimpse into the experiences of some other women who want you to know that they're hurt and they want attention paid to this public health issue.

Candace Hedin, of Marlboro MA., was told seven years ago, at age 25, that she'd need Lupron prior to undergoing fertility treatment with Clomid. Candace was put on Lupron for six monthly shots, and has suffered with multiple, unexplained, serious illnesses since. She's been hospitalized for unexplained chest pain and inability to breath about 15 times, and each time it just "goes away after 3 or 4 days" until the next time "it" returns. Candace also has extensive and extreme hives, including inside her mouth and throat, which become open sores and she cannot eat or drink anything—resulting in hospitalizations for dehydration. She also reports continued vaginal bleeding despite having undergone a total hysterectomy and a battery of tests (including full body CAT scan) to establish the reason(s) for this bleeding, and all tests have been inconclusive. In addition, her mammogram is normal, her prolactin level is normal, but she lactates daily. "Nobody's even looking at any of this—I can't get any diagnoses! All they tell me is my immune system stinks—I'm allergic to my own body is the diagnosis. My toenails are coming out and now my fingernails are coming out too!" Candace's husband says "How can you take a girl, at 25, who'd never had any medical problems, and suddenly become so sick and debilitated—we've gone to 5000 medical doctors and they say 'think of something that might have caused all these things to suddenly come about' and I tell them 'Ya!—she took lupron and she's been sick ever since'—but they say Lupron doesn't have anything to do with it. I think I'm watching my wife die in front of my eyes and no one wants to do a thing about it." (personal communications)

Wendy Camacho of Cherry Hill NJ took Lupron for IVF years ago, and as she puts it "my IVF baby is now 9 and my health is a mess . . . it has been downhill since." Wendy writes "I have seen neurologists, rheumatologists and orthopedists, and none of them have any answers for me. I have been experiencing severe fatigue (diagnosed as fibromyalgia), trouble sleeping, nightmares, gross motor skills are disintegrating fast. I am unable to work as a waitress anymore because my arms can't balance anything, and my legs give out from under me at will. I also have severe osteoarthritis. During a routine eye exam, at which I was diagnosed with cataracts (rare at age 38), I was asked by the doctor if I ever took fertility drugs. When I said yes, I was told I was one of many, but she said she didn't know enough about it to go into detail. . . . I now have the corneas of a 6 year old boy. . . . I was diagnosed with MS, benign remittent, Thank God. I awoke one morning with a very weakened left side. EMG showed I have only 35 percent strength on that side. I have spent ages going to doctors. . . . I would tell everyone—RUN in the opposite direction from Lupron." (personal correspondence)

Linda DeBenedictis, a teacher from MA., mandated to use Lupron without rationale, has testified at the MA. Health Care Committee regarding the health problems she's experienced. At the 1995 hearings for MA. H #3308, at the close of her testimony, Linda stood up, faced the crowd, and removed her wig. She is totally bald, and has lost every single hair on her entire body (FOX News, 1999). [Unlike other chemotherapy/antineoplastics, hair growth had not returned years after Lupron.]

Gilda Radner posthumously is associated with ovarian cancer awareness, however little focus has been placed upon her fertility treatment. In her book 'Its Always Something', Gilda questioned red meat and hair dyes, among other potential causes for her ovarian cancer—but never questioned her use of fertility drugs.

And Barbara Mays, and her offspring, are two others whom I believe deserve consideration as victims of fertility treatment: Barbara Mays was infertile for 10 years, underwent fertility treatment, and ultimately gave birth to a baby born with a heart defect. The Mays baby was intentionally switched in the hospital nursery, and the Mays went home with a healthy baby (named Kimberly 'Mays') who had been born to the Twiggs. The baby that the Twiggs took home, the biological child of the Mays, died at age 9 from congenital heart problems. Several years ago, a national news broadcast aired an interview with the dying LPN who admitted she was instructed to switch the babies and remained silent for fear of losing her job, but no rationale was offered for the switch. Based upon historical fact and my observations of the machinations of this industry, the field of reproductive endocriminology can be characterized as utilizing a multitude of slick maneuvers to deny, disinform, mislead, discount, dismiss, diminish, and suppress risks. The U.S. investigation of TAP's billing practices revealed that a computer program given by TAP to many doctors in the country (some 10,000 urologists received gifts from TAP), which computated the amount of money per Lupron prescription the doctor could earn, also harbored a 'secret key'—and in the event the secret computer program was in danger of discovery, a secret key was struck and !presto! all incriminating information disappeared. Given the history of the fertility industry, it appears plausible that !presto! any incriminating association between the use of fertility treatment and congenital birth defects could disappear if you 'remove' the association by 'simply' switching babies.

In a 1996 *Boston Globe* story, available industry figures (for 1993) showed that more than 50,000 assisted reproduction procedures were performed, and about 8,500 came home with babies—noting that "thousands of others bring home only disappointment and a lingering anxiety about the aftereffects of treatment." Susan McCarthy, attending Boston IVF, had 34 eggs ripen at once—which "led to kidney failure, and she developed a massive, life-threatening infection. She was hospitalized for days, connected to tubes delivering intravenous antibiotics and draining the fluid that was swelling her abdomen, making her look four months pregnant. 'I felt terrible for the longest time . . . And it's not just that. I don't have anything to show for it. . . . ' [Susan] recalls "ovarian hyperstimulation was mentioned by the clinic staff. But the risk was dismissed with the comment 'it never happens' "(Kong, 1996).

The story also described an egg donor, Debra Christensen of Divide, CO., who took Lupron, and suffered ovarian hyperstimulation, ripening 30 eggs, and experiencing a lot of pain. Following soon after Debra's egg donation, she became pregnant and experienced problems with this, her 3rd child, that she hadn't experienced before—"The placenta grew into her uterine lining, huge uterine cysts developed and her son had to be delivered two months prematurely. Nine months later, when the cysts had swollen her uterus to about six times normal size, Christensen—at 32—had to have her uterus and ovaries removed." (Kong, 1996)

According to Stanford Magazine, Calla Papademas, a 22-year old Stanford graduate "slipped in and out of a coma in the intensive care unit at Stanford Hospital" after responding to an egg donor ad "promising $25,000 or more" and agreeing to donate her eggs for a $15,000 fee. . . . A few days after Calla began the drug regimen [Lupron], a benign, undetected tumor on her pituitary gland—which Calla's doctors believe was stimulated by the Lupron—grew at a furious rate and ultimately ruptured, causing a massive stroke. Calla suffered brain damage and lasting weakness on her left side. Her academic and career plans were derailed, and she and her family incurred $100,000 in uninsured medical bills. . . ." (Hamilton, 2001)

In my own situation, within months of stopping Lupron I began to experience a variety of ailments, was unable to work for 3 years (and have yet to be able to return to full-time employment since Lupron), lost my job and home, and slowly came to the terrifying realization that I was in for the fight of my life at a time in which I had never felt sicker or had so many health problems. Six years later, in 1995, in preparation for written testimony in support of MA. H #3308, I audited my health records and compiled a chronological list. All doctors visits, surgeries, labs, tests, procedures, ultrasounds, etc. were typed, in single space, on continuous computer paper—and the end product was 7½ feet tall. This sheet of paper represented: adenoma (tumor), breast cysts, cardiac arrhythmias, dizziness, edema (swelling), fatigue, gastritis, gastro-esophageal reflux disease (GERD), hyperlipidemia, immune system abnormalities, joint pain, knee pain (exacerbated), lymphadenopathy (swollen glands), myalgia (muscle pain), neuralgia (nerve pain), osteopenia, and spasms, to name a few. And, most importantly, knowing the many serious health problems of so many other very sick women post-Lupron, I consider myself to be one of the 'luckier' and 'healthier' victims—causing me to fight even more.

All my symptoms/diagnoses/diseases have been acknowledged as adverse events reported to the FDA following Lupron, yet none of my symptoms or diagnoses or

diseases have ever been reported to the FDA as adverse events from Lupron. Since 1995 this list has grown: arthritis, ascites (abnormal collection of fluid in abdomen), adrenal problems (abnormal cortisol and ACTH levels—workup ongoing), degenerative disk disease, "dissolving jaw" per dentist, enlarged liver (pre-Lupron operative reports indicate normal liver), fibromyalgia-like syndrome, lesions in nerves in arms, lesions on skin, scoliosis (presently "mild", and childhood screenings and pre-Lupron X-Rays evidence normal spinal curvature), the osteopenia has now progressed to severe osteoporosis, telemetry monitoring of cardiac status (pulse noted at 38, blood pressure roughly 60/42) raised the specter of a pacemaker should I become symptomatic, and a few other problems I can't recall at the moment. In the last seven months, I've been hospitalized twice, and officially rang in this spring at the endocrinologists office, reviewing recent abnormal cortisol and ACTH levels, and heard orders I've never heard in my life: "[I] need to avoid stress".

For 'fun' during recent hospitalizations for gastritis, I'd ask the nurses to explain the following: at times (not always) when they'd check my resting pulse and the machine would register a heart rate of, say, 41—I'd ask "do you know how I can make my pulse go down?" I'd get out of bed and momentarily jog in place and the pulse oximeter would go *down* to 38. When they'd wonder what would make that happen, Lupron and autonomic nervous system dysfunction becomes the topic. Invariably, I've met nurses, phlebotomists, ultrasonographers, and fellow patients who've been prescribed Lupron without informed consent of the risks. And I've met a number of doctors who report seeing patients in their own practice with similar "bone, gastric, and cardiac problems after Lupron".

Nurses are also not informed, despite OSHA recommendations, to use two pair of chemotherapy gloves and a chemotherapy gown (among other precautions) when *handling* and administering Lupron. And any healthcare worker who is planning on conceiving or fathering a child is advised to avoid *handling* the hazardous drug Lupron at least 3 months prior to conception attempts (AHFS, 1999). Three years ago, I conducted a survey of random U.S. healthcare institutions, inquiring what policy and procedure they had for the administration of Lupron by healthcare workers. 100 percent of the respondents stated they had no such policy or procedure (unpublished data). I've met, talked to, and read online plenty of women complaining about Lupron, and I've never once seen anyone say their doctor or nurse was gowned and double-gloved during their injection. TAP states in its product literature that there are no hazardous components to Lupron. Would you consent to an injection of a hazardous agent for a benign condition from a gowned and double-gloved health worker?

Many women undergoing 3 months of treatment for fibroids or 6 months of treatment for endometriosis with Lupron have been complaining about post-Lupron problems for years, and again, sometimes these women can receive less Lupron than someone undergoing repeated IVF or egg donation. Some women use Lupron for endometriosis and IVF, as in my situation. And some women have also been maintained on Lupron for years on end. Dr. Mercola states Lupron for endometriosis "could be the Kiss of Death . . . Lupron is a disaster drug that in no way shape or form treats the cause of the problem. I have seen it absolutely devastate many women's lives. It is one of the few drugs that I actually cringe when patients tell me that they have taken it. It is my experience and belief that this drug causes permanent neurological damage. This drug needs to be avoided at all costs." (Mercola, 2002)

Paula Andrade, an R.N. from Methuen MA., provided a statement of her experiences as supportive testimony for my 1997 Offer of Proof for my medical malpractice tribunal: "Four years ago I took a GnRH analogue [Lupron and Synarel] for problems with endometriosis. I took the medication for 5¾ months. The week before I was due to discontinue the medication I became ill. I experienced flu like symptoms with severe muscle pain, paresthesias, and bone crushing fatigue. Four weeks later I developed a host of neurological problems including vertigo, nausea, loss of balance, blurred vision, muscle twitching, and fasciculations with difficulty walking and constant muscle stiffness. Since then I have been seen by several neurologists and rheumatologists who remain baffled by my condition. I haven't been able to receive any help within the medical community. Prior to taking the medication I was an active and healthy individual who had worked as an RN for many years. I took care of my home and family. Since the medication I have been unable to work and have difficulty performing daily activities. I have spoken with other women from around the United States who have taken this medication and are now suffering with similar problems and whose lives have been drastically altered. I swear under the pains and penalty of law that the above statements are true." Today Paula says she hasn't seen a doctor in years—"For what—they can't find out what's wrong and

nothing they did changes the way I am, so what good is it to keep going?" (personal correspondence and communications)

Lisa Plante, Fall River, MA., was a former congressional staffer who was prescribed Lupron for presumed endometriosis—and Lisa and I traveled to Washington together last year to speak to Senate staff on the issue of Lupron and its connection to cloning. Lisa experienced extreme and unbearable bone and joint pain from the time of her first of three injections, and this pain has gradually worsened. Eight years later Lisa says "I now have arthritic bones, very bad bone loss, constant bone pain and joint pain, and basically feel like I have aged 30 years since Lupron. I have not been able to live a normal life with my family because of this bone pain and want others to be fully informed of the dangers of Lupron. Women must not be put at risk like this and MUST NOT be used as guinea pigs!" Lisa recently went on a long promised overseas vacation with her family, fearing that her future might prevent her from ever going—and during this trip Lisa spent 50 percent of her time in the hotel bed, in pain. Lisa is not able to travel here today. (personal correspondence and communications)

Paulette Wilson, Newport News, VA, took two monthly injections of Lupron for endometriosis, and after the second shot she "woke up with chest pain and needed to go to the emergency room." She was told she had 'reflux disease', a gastrointestinal disorder. "I never had any problem like that before. . . . Tests showed that I had acid burns from my esophagus to my rectum." Paulette now lives with severe pain, which sometimes affects her entire body. Paulette also has been diagnosed with fibromyalgia (Regush, 2002) and liver problems (personal correspondence).

Jeanne Wolf, from Orange County, NY, had to have her gallbladder removed after Lupron, and was diagnosed with gastritis for years until stomach testing showed that she had gastroparesis—her stomach was paralyzed and was not emptying food. "I am waiting for these bastards to pay for what they poisoned me with. Funny thing is I was given the poison because they said I had endometriosis, well I obtained my laparoscopy biopsy results and no endo was ever found! My body and mind will never be the same." (personal correspondence)

Melanie Waldman Lloyd, Corvallis, OR, took Synarel to treat her endometriosis prior to attempting pregnancy, and subsequently developed immune problems, suffered 8 miscarriages due to antibody formation, has developed thyroid problems, eye problems affecting eye muscles and seeing double, and now takes an IV treatment every 2 months (which runs at cost some $600 per dose). Melanie writes "My health is ruined from this drug. . . . No one should take this drug without knowing the risks." (personal correspondance)

Melody Hampton, Mt. Victory, OH, more than 7 years after Lupron, continues to experience tremendous headaches, rash, joint pain, nausea, heart palpitations, high white cell count, bone loss, high blood pressure, blood in urine, atrophy of muscles, leg swelling—all beginning shortly after her first Lupron injection. (personal correspondance; Regush, 2002)

Kimberly Bradford of FL, also started complaining right after her first injection, and continues with complaints a decade later. Kimberly suffered a miscarriage following her use of Lupron, experienced intense migraines, and has neuropathy and Adie syndrome in her right eye. She started to trip over everything and began to notice a smell of "burning" which led to an MRI of her brain. An MRI "showed lesions on my brain. There was a question of "demyelinating lesions" or MS, and Kimberly has come to call this "my spot"—"it's in the white matter, in the middle, near the pituitary gland, but not in an area they can biopsy without causing more injury." When Kimberly's doctor was filling out her Family Medical Leave Act paperwork, he stated that "this all started when [Kimberly] unknowingly got [her]self involved with the FDA's phase IV clinical trial of Lupron." Kimberly says: "I did not know until my own research that I was part of a clinical trial. I never signed a consent for this." (Bradford, 2002). [Kimberly is not the only patient with a diagnosis of brain lesions following Lupron use].

Diane DeFeo, a teacher from Yonkers, NY, lost two teaching jobs as a result of being on Lupron. Diane writes "This was disabling. I was exhausted and still experiencing pain, had migraines, mood swings, bone and muscle aches and pains, not to mention that I gained 35 pounds. I have lapses of memory I call "lupron moments." I was constantly dizzy. And I waited for the symptoms of Lupron poisoning to diminish. Seven years later I still experience effects from this drug. And TAP Pharmaceuticals, the company that manufacturers this poison, simply—this is evil at work. The physicians that continue to prescribe this drug knowing the possible repercussions are the most evil of all. I pray for the day when people will take us seriously and that women do not need to suffer permanent illness and damage. (personal correspondance).

Julie Johnson, Chicago, IL., relates how her doctor told her "its lupron or hysterectomy, so I agreed to the lupron. I had my first shot at the end of October 1996, and I was fine—for about 20 hours. Then I developed a terrible pain at the injection site and I could not move, walk, or sit, but my doctor said it was not the Lupron and I probably hurt my back and it eventually eased with a dull ache remaining at that site." She received a second shot and experienced achiness but attributed it to the flu and received her third shot, to awake the next day with hives. "And then my knees started to ache, and every morning for the next week I woke up with pain in another part of my body. By New Years I hurt very badly—even wiggling my toes to slip on shoes was excruciating. The pain went on for months and months and I noticed that I was losing strength in my legs." Julie continues to suffer from fibromyalgia, has lost her libido and has dealt with chronic depression since Lupron. She tells of her phone calls to TAP, in which "he refused to listen to me—I've often wondered, if they refuse to listen or take this type of information from the women who have taken lupron—how will they know what type of problems lupron causes?" (personal correspondance). Julie is the founder of 'Julie's After Lupron Page', on Delphi.com, a public internet message board where Lupron victims share information and experiences. (Julie's Page).

Susan Hayward, Lake Havasu City, AZ, says "I would rather suffer with my initial diagnosis, endometriosis, than what this drug has done to the rest of my body and life". Susan relates how, in attempts to maintain her career amidst endometriosis, 2 doctors administered a total of either 19 or 20 Lupron injections over a five year period. "When I first started using the drug I had to purchase it like any other prescription. Later, both doctors had me skip going to the pharmacy and they obtained the drug for me. I believe I was sold prescription samples. The kickback schemes involved with TAP and physicians are well documented . . .". Since Lupron, Susan reports experiencing "vertebrae bone loss diagnosed as degenerative disk disease, arthritis, myalgia, bone pain, fatigue, swelling in hands and feet, severe allergies, nausea, weight increase, severe memory loss, vision changes, sleep changes, rapid heart beat, and abdominal pain. . . . After taking Lupron, I don't go a day without pain and am under constant doctor care to control pain and autoimmune problems. I left my home and moved to Arizona where I didn't know a soul so I could get relief from the arthritis problems. . . . The total lack of support from the medical profession is appalling, and all lawyers say 'without a doctor saying your problems are related to Lupron you don't have a case'. . . . I lost my career and am disabled, but more than that it has robbed me of any faith in our system of justice and what is right." Susan points out that her disability has resulted in "approximately $900,000 disability costs being paid by Social Security and the Federal Retirement Program, plus factor in the increased insurance premiums from hundreds of thousands in medical bills from hospitalizations, surgeries and tests." (personal correspondence; see also Lazar, 1999).

Judy Norsigian, Co-director of the Boston Women's Health Book Collective, also provided a statement for my 1997 Offer of Proof in my medical malpractice tribunal: " . . . No fewer than 15–20 women have called our Women's Health Information Center over the past 5–6 years about totally debilitating and frightening reactions to this drug . . .".

In 1995 Donna Kuha, of MA., entered one of Dr. Andrew Friedman's Lupron clinical trials for fibroids—"The doctor told me it would be good for me. . . . He didn't tell me of any possible danger. . . . I sure didn't expect a stroke." Donna Kuha, "who lost the use of a hand and most of the use of one leg, is one of a disturbing number of patients who have been harmed by clinical trials." (Lasalandra (2), 1998; personal communications, 1998). Publicly available court records in Kuha's medical malpractice trial, containing medical records, indicate Donna suffered her first stroke while in the Lupron clinical trial, and she suffered another stroke subsequent to Lupron discontinuation, as well as developing a seizure disorder. In my professional opinion, the medical records within these court documents compel one to entertain 'the magic clot theory' and are deserving of a close and critical review. According to the public records, Donna's expert medical witness concluded that a drug other than Lupron caused her stroke, and twenty-one pages into this plaintiff's medical expert's curriculum vitae it is learned that he's been an Abbott consultant since "1987 through present", and had served on Abbott Young Investigator Award Advisory Board in 4 previous years. (Kuha, 1997). Donna suffered her first stroke in March, 1995—just prior to Lupron's FDA approval for 'anemia associated with fibroids when iron therapy alone is ineffective'. (NDA 19–943)

The *Boston Herald* did a 3-part series on Lupron, the second part entitled 'Women seek answers on drug's suspected side effects'. A dozen women were interviewed for this story, which began "Hundreds of women nationwide, with nowhere else to turn, are forging a campaign against a drug they believe has ruined their health and

their lives." Quoting one victim in the series: "My knees tremble a lot and get very weak, and I have to use a cane now to go up and down the stairs," says Kimberly Savino, 17, of Easton, who was prescribed Lupron last year for a gynecological problem. Before taking the drug, Savino said she often rode horses and jogged. Today, three months after stopping Lupron, the teenager has trouble even walking and has been diagnosed with a degenerative arthritis, which usually develops over many years. Her mother is worried—and suspects Kimberly's strange bone problems were triggered by Lupron. "It's very hard to see her, all of a sudden, moving around like an old lady with a cane," said Susan Savino. "Now we don't know if she is going to end up in a wheelchair. This shouldn't be happening to someone who is 17." (Lazar, 1999)

This shouldn't happen to anyone at any age. And problems with Lupron appear throughout all ages and all indications. For example, a public internet post from another mother about her 15 year old daughter who at age 5½ was treated with Lupron for 3½ years. The mother reports her daughter had no problems on Lupron, but writes that "her period has never been real regular . . . she has been having severe pains in her leg joints. Started in the knees and have moved to the hips. . . . Now she is having similar pains in her elbows and shoulders. She was always a small girl until about the same time as the pain started, she gained almost 50 pounds and can't seem to get it off. Does anyone out there know if this could be some long term affects of Lupron???? We have had her to 2 different doctors and they can't seem to figure out what is going on. . . ."

Numerous men have reported a multitude of adverse events following their use of Lupron for palliative treatment of prostate cancer (Abend, personal communication, 1994). Zoladex (goserelin) is another GnRHa used in prostate cancer, as well as used in endometriosis and infertility. Lupron, Zoladex, and Synarel are all advertised as "fertility medications" (Fertilitext, 2003; Members, 2003), yet no GnRH analog has been approved for fertility treatment or IVF or any variant of infertility treatment. In an overseas IVF study using GnRHa's Zoladex and Buserelin with clomiphene (CC) and hMG, "[i]f no selection against chromosomally abnormal oocytes takes place at the time of fertilization, more abnormal oocytes are harvested with GnRHa/hMG protocols than with CC/hMG." (DeSutter, 1992). Studies in pregnant baboons using Zoladex resulted in numerous abortions and stillbirths and neonatal death (Kang, 1989).

Debbie Arnason wants you to know about her husband's experience with Zoladex treatment: "Arne Arnason of Naples FL was diagnosed with prostate cancer about 18 months ago and was put on Zoladex 3-month depots with resulting side effects of debilitating hot flashes, extreme weakness, breathing difficulties, irritability, bone mineral density loss, hip, back and joint pain as well as muscle pain. He was unable to work. With each successive treatment, the symptoms became worse. We truly believe the 3rd and last shot was unnecessary—this treatment aged him 20 years in 9 months, requiring 2 ER visits, one for arrhythmia and one for a retinal tear. Arne continues to have symptoms related to the calcium imbalances the Zoladex created—he was referred for surgery of the neck to remove his parathyroid gland. It's just been one scary thing after another. No one warned us of any of this!! I had to do all my own research. We feel for people who don't know the awful consequences of the use of this goserelin acetate drug, Zoladex by AstraZeneca (similar to Lupron)". (Arnason, personal communications and correspondence) [AstraZeneca "is in negotiations with U.S. state and federal authorities over the potential settlement" involving "improper claims for its prostate cancer treatment Zoladex, in a ruse similar to that of TAP . . ." (Pharmafocus, 2003; Church, 2002)].

8. Rita Abend, D.D.S.—Her Story & The Inception Of The NLVN

The following is testimony of Linda Abend, D.D.S., dated December 5, 1997, and submitted into the public record as expert witness testimony within my Offer of Proof in my medical malpractice tribunal (*Millican* v. *Harvard Community Health Plan*, Boston IVF, Natalie Schultz M.D., Brian Walsh M.D., Mahmood Niaraki M.D., Selwyn Oskowitz M.D., Michael Alper M.D.; No. 92–2140A). At that time, in 1997, there was no medical expert that I could locate who was willing to publicly address Lupron's causality to adverse health problems. Linda Abend's testimony is reprinted below in its entirety:

"Dear Tribunal Members: Many years ago I founded The National Lupron Victims Network to inform people about the risks involved in taking the drug Lupron. The network does not accept any money from either victims or external sources. All of our information is available for free on the internet. I hope that the information I have found in my years of research will help other people so that they are fully informed of the risks involved in taking Lupron."

"Women and men from all over the world have contacted the network. Nearly all of the people I have spoken to were not informed of the risks involved in taking Lupron. The majority of the people who continue to have medical problems after taking Lupron are finding that they are having an unusually hard time getting adequate medical care."

"The individual case that I have the greatest knowledge of is that of my sister, Dr. Rita Abend. Before Rita took Lupron, difficulty in obtaining medical care was something neither Rita nor I could comprehend. Once she took Lupron everything changed. While on Lupron Rita experienced horrendous side-effects. Doctors had never informed Rita of any risks. Ultimately, we realized that she probably would never receive the medical care that she so desperately needed."

"Since taking Lupron, Rita has been diagnosed with seizures, autonomic nervous system dysfunction and myeloma/plasmacytomas (a rare form of bone marrow cancer). All of these diagnoses were given and then rescinded at one time or another. Results on her blood laboratory reports and numerous pages of medical documents were whited-out, and vials of blood lost by a physician before they even left his office. Doctor after doctor has refused to treat her including one who plainly stated that it would not be in his best interest to do so. Rita went all over the country in search of medical care after taking Lupron. Rita, like many others who took Lupron, could not get honest medical care after taking Lupron. And without honest medical care and doctors to testify, due process in the courts is an impossibility."

"In one instance, Rita had to obtain a court order in order to get her medical records from one doctor, Orin Devinsky. Devinsky had threatened to "destroy" the continuous audio-visual video tapes that he had made of her electroencephalograms (EEGs) during a 9 day hospital stay in a specialized epilepsy unit, approximately two weeks after stopping Lupron. (Rita spent three of these days in intensive care). Despite the fact that these tapes had over 600 computerized "events" (alerting the viewer to abnormal brain activity) Devinsky wanted to destroy them. During the hospital stay Devinsky learned that Rita's IQ had dropped to 97 on an IQ test and her manual dexterity was in the bottom 8 percent of the nation. Instead of informing us of this drastic decline after taking Lupron, he informed us that the tests came back "normal". Although Devinsky's admitting diagnosis was "convulsions" (based on an EEG), he claimed that this was all a mistake and in the end nothing was wrong with Rita. Even with the court order Devinsky did not turn over all of the medical records. He claims to have "lost" some tapes."

"Instead of offering Rita anti-seizure medication, Devinsky tried to coax Rita into taking a derivative of pentamethylenetetrazole (PTZ), insisting that it was perfectly safe and that no one had ever been hurt by it. Rita refused the PTZ. After researching PTZ I discovered that PTZ is no longer given to humans since it is not safe. It has been found to cause seizures and effects the autonomic nervous system. It is used in the laboratory to make animals epileptic for experimentation purposes. When Rita finally found a doctor to monitor her seizure condition caused by Lupron, she was offered not one, but four anti-seizure medications."

"In another instance, Rita was experiencing extreme pain in her hip. An x-ray revealed that she had lost 30–50 percent of her bone density at the head of her femur. Lupron is known to cause bone loss at the head of the femur. Rita was instructed to use a walker because her hip could fracture from the loss of bone. Rita was referred to a specialist. He refused to treat her. He refused to run a single test, not even a blood test. Rita was left in bed suffering with excruciating pain for one year, unable to get up without the use of a walker."

"Today, my sister, a once actively employed, vital, energetic and intelligent woman who graduated from New York University Dental School, is now totally and permanently disabled. It is hard to say which is most difficult for Rita; relinquishing her dental license, relinquishing her drivers license, accepting the fact that comprehensive medical care (no testing, no answers) will always be denied because she took Lupron, or that justice will probably not prevail if one has been injured by Lupron."

"Doctors who prescribe Lupron are denying people the accurate information they need in order to make an informed decision. Once people become ill on Lupron, these physicians are denying the temporal relationship between Lupron and the onset of symptoms. They even deny information in respected peer-reviewed medical journals. For example, two studies reported memory loss with Lupron occurring in 72 percent and 75 percent of the studied populations. Both studies were published in the Journal of Assisted Reproduction and Genetics, and Fertility & Sterility, respectively. The percentages reported are quite high. In fact, if an individual does not experience memory loss with Lupron that individual is in the minority. Yet, doctors who prescribe Lupron are continuing to deny that Lupron causes memory loss. Doctors who prescribe Lupron are also denying that Lupron can cause other side-

effects that have already been ackowledged in the medical literature and printed in the package insert. They deny the correlation of side-effects while on Lupron. They deny the correlation when one stops taking Lupron and the side-effects persist."

"I certainly do not want to leave you with the impression that I believe all physicians are bad. There are many good, caring physicians out there treating people with all kinds of medical problems. But when Lupron victims turn to physicians for help and answers they get a deaf ear and the run-around. Lupron victims are not victims of Lupron alone, but are also victims of a medical system that has failed them. And without medical care and doctors to testify, they are unable to obtain justice in the courts. If you have any questions, please feel free to contact me. Respectfully, Linda Abend, D.D.S., Founder, The National Lupron Victims Network."

Although Linda Abend closed this 1997 statement with an invitation for contact, attempts to contact the NLVN (by myself, other victims, lawyers, and media) have been in vain. Phone calls go unanswered and certified mail to their long-held address returned "unk". No new information has been posted at the NLVN website for years, and the private NLVN message group (where there had been postings by hundreds of members) has long been inaccessible. Thousands of women contacted the NLVN and had filled out the detailed questionnaire that the NLVN had mailed out, and was processing, in the 1990's. Now, the question is not only what happened to all that information—but what has happened to Rita, Linda, and the NLVN?

9. The State Of The ART, And The Art Of Stating

In February 1995 I noticed a surrogate ad running in a college newspaper, offering $17,000 plus expenses to carry the gift of life for an infertile couple, and I called the ad. A Dr. Radecki answered the phone, and I heard all about the wonders of IVF and "there were no long-lasting risks" and "no one ever suffered serious harm from the drugs." On March 21, 1995, I was surprised to see CBS Evening News interviewing this Dr. Radecki—and became even more surprised to learn that Dr. Radecki was not a fertility doctor—he was a psychiatrist who had lost his license for sexually abusing his patients. By the end of March 1995, Dr. Radecki had closed shop—the telephone number for the surrogate ads was disconnected, the ads were gone, and he was under siege for misrepresentation.

A TAP advertisement in a fertility journal gives a glimpse into the sly canvas upon which the industry paints its picture: This TAP Lupron ad read: "Remote Control: Your patient with endometriosis doesn't have to remember her daily therapy—Lupron Depot 3.75 mg remembers it for her. . . . She only needs to remember six monthly visits." (Ad, 1992). Nowhere does the consumer learn that memory loss has been known to be "a commonly observed" side effect to Lupron, or that patient noncompliance with daily Lupron could likely have been related to a memory disorder (listed as a known adverse event to Lupron), or that clinical trials conducted for Lupron depot approval utilized methodologically flawed study design that was conducive to subjects forgetting adverse events (surveyed every 30 days).

In 1990, several Brigham & Womens physicians (including the lead author who would later admit to falsifying and fabricating approximately 80 percent of 4 Lupron studies) would write "not since the development of oral contraceptives has there been so much excitement and enthusiasm among basic scientists, clinical investigators, and practitioners of reproductive medicine." (Friedman, 1990). A coauthor in the latter article, Robert Barbieri M.D., has also been a lead investigator for Lupron, authoring or co-authoring (including with Friedman) many Lupron or GnRHa studies and books, and has received TAP funds for numerous studies, and serves also as a Medical Advisor on TAP's Lupron endometriosis website.

In 1997, Dr. Barbieri, representing the industry, testified in opposition to the MA. bill which would have mandated state regulation and informed consent of the risks of ART. Following the hearing, when I asked Dr. Barbieri why memory loss, along with all of the other hundreds of reported side effects, was not included in their IVF Clinic's consent form, he subsequently forwarded their consent form with an attached, handwritten note stating: "Here is a copy of our current Lupron consent form for IVF. I am going to ask Dr. Hornstein to add memory loss as a potential side effect. I don't think we can add 300 side effects. Do you have 3 or 4 others that would be important to add?" That such a lead and allegedly prestigious Lupron investigator should query me as to what adverse events are important to include within their Lupron informed consent document (presumably approved by an IRB) is troubling, disgraceful, and the epitome of the 'state of this art'.

"Inclusion of patients with a poor response to GnRHa therapy has not always occurred in outcome analysis in the published medical literature." (Redwine, 1994). Conflicts of interest are extensive, troubling, and have far reaching consequences upon standards of care and the state of science. Two cases in point: Another lead Lupron investigator alleged in a study that reduced bone mass was associated with

endometriosis (Comite, 1989), yet another investigator with contrasting findings reported that "One explanation for the difference between the results of this study and those of Comite et al. is that they included women who previously had been treated with GnRH agonists and these agonists are associated with bone loss." (Dochi, 1994). (See *www.lupronvictims.com*, 'Endometriosis' for further elaboration on these studies). Claims of the disease endometriosis being associated with bone loss, while deliberately omitting patient's prior use of GnRHa (which is known to causes bone loss), is a perilous concept of manipulating iatrogenic, adverse, drug effects into a disease-related non-tort phenomenon—and deserves attention.

A 2002 Human Reproduction article, 'High rates of autoimmune and endocrine disorders, fibromyalgia, chronic fatigue syndrome and atopic diseases among women with endometriosis: a survey analysis', co-authored by the President of the Endometriosis Association, failed to mention GnRHa's within the article (Sinaii, 2002). The survey upon which the article is based, which was sponsored by Zeneca (1998), does contain reference to GnRHa use in survey participants. Despite the presence of a National Lupron Victims Network, with many women complaining of autoimmune and endocrine disorders, fibromyalgia, chronic fatigue syndrome, etc. post-Lupron, this article makes no mention of these adverse advents.

I do not think any of this is funny—but if there were ever a game involving Lupron and/or GnRHa titled something like 'Patent—Conflict . . .Yea or Nay', I'd participate. For example: Issue—Person involved with the testing of animals and Lupron and FDA approval submission . . . Yea Patent! Yea Conflict! Issue—Person heading major reproductive research unit and member of RESOLVE's Advisory Board . . . Yea Patent! Yea Conflict! Issue—Member of major Institutional Review Board, who has performed numerous TAP-sponsored Lupron studies, and published numerous articles on Lupron . . . Yea Patent! Yea Conflict! Issue—Individuals promoting awareness of risks of Lupron and ART . . . Patently NayNay!

10. The Check Is In The Fe/male

"GnRH and its analogs have led to exciting new avenues of therapy in virtually every subspecialty of internal medicine as well as in gynecology, pediatrics, and urology . . . virtually every subspecialty of medicine will be touched by the GnRH analogues . . ." (Conn, Crowley; 1994).

The following is a fairly comprehensive, alphabetical, list of clinical uses, case reports, or studies involving Lupron's use in unapproved and off-label indications. These uses were mostly found within published medical literature, although some were noted within patents, or advertisements for clinical trials, and one was a personal clinical observation. Citations have been omitted for brevity, but are available upon request.

A:adjuncts for IVF; adjunct to fibroid surgery; anovulation; autism [management of sexual behaviors]; acute intermittent porphyria; Alzheimer; adenomyosis; severe adenomyosis; adhesions; amenorrhea [functional]; angiomyxoma of vulva; autoimmune disease; autonomic neuropathies; 'add-back' regimen [estrogen/progestin with lupron]; advanced breast cancer.

B:before hysterectomy for leiomyomas; benign prostatic hyperplasia; benign prostatic hypertrophy; birth control; breast cancer; breast cancer prevention; bioavailability following nasal and inhalation delivery to healthy humans.

C:catamenial insulin reaction; catamenial pneumothorax; chronic intestinal pseudo obstruction [in patient with heart-lung transplant]; cluster headaches; colorectal cancer, congenital adrenal hyperplasia with oligomenorrhea; contraception; cryptorchidism; controlled ovarian hyperstimulation in normal, abnormal and poor responders; combination therapy with flutamide and castration; colonic endometriosis; comparison of suppressive capacity of different GnRHa's in women; comparison of hCG versus lupron for releasing oocytes.

D:dysfunctional uterine bleeding prior to hysterectomy.

E:egg donation; endometrial ablation; endometrial cancer, endometrial glandular hyperplasia; endometrial hyperplasia without atypia; endometrial cancer; endometrial stromal sarcoma; epithelial ovarian cancer; exhibitionism; effect of very high dose in prostate cancer; effects in animal and man; effect on embryos ("accelerated development"); endometrial preparation for transfer of frozen-thawed pre-embryos in patients with anovulatory or irregular cycles; effects on follicular fluid hormone composition at oocyte retrieval for IVF; effect on hair growth and hormone levels in hirsute women; effects on glucose metabolism in a diabetic patient; equivalency of hMG and FSH stimulation following suppression; effect on LH surge; effect on adrenocorticotropin and cortisol secretion in premenopausal women; effect on seminal vesicles; effects of lupron on luteal-phase hyperprolactinemia during ovarian stimulation.

F:fallopian tube obstruction; functional ovarian hyperandrogenism, functional abdominal pain from functional bowel disease; fibrocystic breast disease; first cycles of IVF/GIFT; follicular development and oocyte maturation.

G:GIFT.

H: Headache, Huntington's Disease (for exhibitionism), hyperandrogenism, hysteroscopic surgery; hilus cell hyperplasia within ovarian cyst wall; hypermenorrhea in premenopausal women with acute leukemia; hypermenorrhea with severe thrombocytopenia; hypergonadotropic hypogonadism; hypergonadotropic amenorrhea; hypothalamic-pituitary axis disease; hypothalamic hamartomas and sexual precocity; hirsutism; moderate and severe hirsutism; hysteroscopic surgery; benign symptomatic hyperandrogenism in a postmenopausal woman; hidradenitis suppurativa.

I: infertility; IUI; IVF; IVF–ET in insulin-dependent diabetics; irritable bowel syndrome; intravenous leiomyomatosis with cardiac extension; intranasal lupron for endometriosis; intranasal/sc lupron for fibroids.

K:Kallmann syndrome.

L: leuprolide flare regime for IVF/GIFT & embryo cryopreservation; lupron screening test for IVF; luteal phase lupron flare protocol; luteinized unruptured follicle syndrome; leiomyosarcoma; leiomyomatosis peritonealis disseminata.

M:male contraception; 'male' factor infertility (female is treated—male is not); Meniere's Disease; menstrual migraines; motility disorders.

O:ovarian cysts; ovarian cysts after ovarian transposition; ovarian epithelial tumors; ovarian granulosa cell tumor; ovarian hyperthecosis; advanced epithelial ovarian carcinoma; ovulation induction; ovarian stimulation; ovarian stimulation with lupron and norethindrone in IVF/GIFT; ovarian hyperstimulation; oocyte release; ovarian hyperstimulation syndrome; severe ovarian hyperstimulation; oocyte donation, oocyte donation [post-menopausal]; operable breast cancer; ovarian carcinoma [refractory]; ovarian remnant syndrome [diagnostic].

P:pancreatic cancer; paraphilias; Parkinson's Disease symptoms, pedophilia, pelvic pain not associated with endometriosis; pituitary metastatic mass; polycystic ovarian disease; PMS; protection against chemotherapy-induced testicular damage; postpartum depression; premenopausal breast cancer; post-menopausal breast cancer [advanced]; pre-implantation [embryonic] diagnosis; prevention of hypermenorrhea in premenopausal women undergoing bone marrow transplantation; prostate cancer (Stage C adenocarcinoma]; endometroid adenocarcinoma of prostate; pseudo intestinal blockage, psychosis in PMS, resistant paraphilia, pulmonary endometriosis; pulmonary tuberous sclerosis; pulmonary delivery of leuprolide in health male volunteers; pre-myomectomy; poor prognosis patients for IVF/poor responders; preservation of fertility in a woman with menorrhagia; pharmacokinetic studies in humans [iv and sc]; preoperative treatment of complicated myomata; pre-surgical treatment of fibroids.

R:resectoscopic endometrial ablation; rectal endometriosis; routine pituitary suppression before ovarian stimulation.

S:sexual offenders; sexual precocity; Sickle-cell anemia associated priapism; surrogacy, SUZI; steroid-cell tumor (advanced); systemic lupron erythematosis; submucous myomas; sexual behavior disorders; syndrome of familial virilization, insulin resistance, and acanthosis nigricans; stimulation test in Tourette's syndrome; small cell carcinoma of prostate.

T:transgender adjunct, testicular function effects; transdermal vs. subcutaneous leuprolide—a comparison; triggering follicular maturation.

U:urinary retention in prostate cancer; ureteral obstruction caused by endometriosis; urinary retention due to benign prostatic hyperplasia.

W:with or without medroxyprogesterone in treatment of fibroids.

Z:ZIFT

And the following list is simply an odd collection of TAP-funded Lupron studies that were jotted down along the way. This list should not be construed as any formal, complete, or even partial, audit of the numbers of published TAP funded Lupron studies. Even if the total tally of TAP funded Lurpron grants and investigators could be counted today, that figure would be obsolete with the next publication of TAP funded Lupron studies. But here's a few examples, with duplicative years indicating separate studies.

In Alabama, there was one of 13 investigative sites conducting TAP funded research; in Arizona, TAP funded a symposium; in California, numerous investigators for numerous indications; in Colorado, 5 physicians received TAP funds; in Connecticut, another one of the 13 investigative sites conducting TAP funded Lupron research; in Florida, another one of the 13 investigative sites conducting TAP funded Lupron research, and in Florida, a TAP sponsored educational program at Walt Disney for unapproved female uses (FDA memo by David Banks, 1990); in Illinois,

numerous investigators supported by grants from either Abbott or TAP or both, in 1988, 1989, 1991, and another one of the 13 investigative sites conducting TAP funded Lupron research; in Kansas, another one of the 13 investigative sites conducting TAP funded Lupron research; in Massachusetts, another one of the 13 investigative sites conducting TAP funded Lupron research, and in Massachusetts in 1987 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1988 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1989 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1989 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1990 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1991 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1995 numerous investigators conducted TAP funded Lupron research, and in Massachusetts in 1997 Brigham & Women's website identified two grants were funded by TAP; in Maryland, another one of the 13 investigative sites conducing TAP funded Lupron research; in North Carolina, numerous investigators (including an FDA Advisory Committee member) received funding from TAP, and had Lupron "generously provided" by TAP for a study involving ovulation induction; in New York, another one of the 13 investigative sites conducting TAP funded Lupron research; in Pennsylvania, another one of the 13 investigative sites conducting TAP funded Lupron research; in Tennessee, one physician was on TAP's Speaker's Bureau and is an "active contributor" to the EA (personal correspondence, 1998); in Texas, another one of the 13 investigative sites conducting TAP funded Lupron research; and in Texas an educational grant from TAP to numerous investigators; and in Washington, another one of the 13 investigative sites conducting TAP funded Lupron research.

11. Considering Cloning? Consider The Myths of Hype & The Realities of Scientific Misconduct

It is outrageous to hype cloning research, which will involve superovulation with drugs such as Lupron, as probable cures for diabetes, Parkinson disease, Alzheimer, etc.—when women who've received Lupron have now iatrogenically DEVELOPED these and other diseases. It is appalling that this debate has not centered on the adverse health effects of superovulation and Lupron upon the women, and especially the reports of adverse pregnancy and birth outcomes associated with treatment.

Without proper long-term follow-up study of the reports of adverse health outcomes to the superovulated women and without proper long-term follow-up of the adverse pregnancy and adverse birth outcomes in the babies conceived and exposed to drugs such as Lupron, how can you propel recklessly forward to create a massive demand for more superovulation of women for research eggs?

The message of research and biotech has resulted in the impression of hope, promise, cure, and benefit. My personal experience can be summed up by the words hype, myth, research fraud, conflicts of interest, and injury . . . and all without any medicolegal advocacy for the injured victim. It is a myth that public safety is being protected by the FDA, evidenced by the fact that some 20 million people have taken drugs that have been recalled—drugs that were initially deemed 'safe and effective during study', only to later learn that data identifying serious problems, including deaths, had been suppressed.

Somewhere it is written that it was a "comforting but erroneous myth" that research involving drugs and devices still serves medicine. Time magazine's 4/22/02 cover, of a woman crouched within a laboratory cage, epitomized the story within, depicting yet another research debacle in which data identifying adverse side effects was kept secret—and only revealed by a whistleblower (Lemonick, 2002). Time also noted that there were more than 60 institutions that "failed to protect human subjects adequately." Other recent articles have identified the dramatic disparity in research results and reporting, depending on who is paying for the research—with contracts allowing pharmaceutical companies control over disclosure of bad data. Furthermore, large sums of money in the form of grants, stock options, company ownership, patents, consulting agreements, scientific agreements, speaking engagements, symposiums, trips, gifts, etc. (which are disclosed in less than ½ of 1 percent [Stolberg, 2001]), have created an environment conducive to suppressing bad data and inducing outright fabrication of data. It would be nice to think that ethical behavior is the norm, but a review of recent news compels one to notice the increasingly rampant unethical machinations of research medicine.

To date there have been a number of renowned reproductive physicians/surgeons who have been found to have fabricated and/or falsified data: Dr. Andrew J. Friedman, a lead investigator for Lupron, recipient of many TAP grants to study Lupron, and director of Brigham & Women's IVF Program (where this writer was mandated to use Lupron), was found to have falsified and fabricated approximately 80 percent

of the data in 2 published, and 2 unpublished Lupron journal articles (Federal Register, 1996). Is it any wonder that during the time Dr. Friedman was director of Brigham & Women's IVF Program, the criteria for the administration of Lupron with IVF changed from "Lupron is only used in certain diagnoses" to "Lupron is widely prescribed"? Where is the data to justify such widespread application of a hazardous, reproductive and developmental toxicant?

There has also been the brothers Drs. Nezhat (one of whom serves as a Scientific Advisor for the EA, according to the EA website) who have been found to have fabricated research involving laparoscopic surgery for endometriosis, resulting in the retraction of two published journal articles (Nezhat; 1991, 1992). An attorney, as a result of litigation (on behalf of a client who believed she had signed an informed consent form to authorize surgery but had instead signed a waiver of right to receive informed consent), doggedly pursued to have this bogus published surgical procedure data examined—and only after 6 years was the data finally produced, examined, and retracted. In one study, more than half of the patients were used for premarket testing of a new, non-FDA approved, circular stapling device. "The Doctors Nezhats' retracted bowel surgery articles are included in Ethicon's coursebook for surgeons. . . . While the Doctors Nezhat reported no "short or long term ill effects" with this new technique, there were significant complications in these subjects, some severe. A portion of one woman's bowel died during surgery, another's anastomosis (where bowel is rejoined) massively hemorrhaged a few days post-op requiring repair, one patient's bowels fell into the toilet post-operatively, several patients had bowel leaks in the staple line, several patients were incontinent of feces, some could no longer evacuate normally, etc. Yet, the operation was promoted for 185,000 women by Johnson and Johnson based on the Doctors Nezhats' research" (Attorney James J. Neal, 2003: *www.mdjdfraud.com*; see also Neal, 2002).

The father of GIFT, gamete intrafallopian transfer, Dr. Cecil Jackobson, rounded off his accomplishments with 52 convictions of perjury and fraud. He had been substituting his own sperm for that of some 75 women's husbands' sperm resulting in these women (initially) unknowingly giving birth to children fathered by this 'expert'. To quote USA Today, " . . . His case taught a valuable lesson about the fertility industry: Self-regulation is not enough. . . . Many of his most offensive acts were legal—like donating his own sperm. The only way Jacobson was stopped was on federal wire, mail fraud and perjury charges. . . ." (USA Today, 1992).

The "Dyno Gyno", Dr. Niels Lauersen (and a cohort) were convicted of billing fraud, "falsif[ying] bills to get $2.5 million in payments from insurers for a variety of fertility procedures" (Barrett, January 2001), and Dr. Lauersen was "jailed as flight risk" (Barrett, March 2001). Dyno Gyno loyalists attempted to assign this fraudulent billing as nothing but 'an attempt to provide otherwise denied procedures', causing "prosecutors [to] fume that the case is not about health-care policy, but a thief with a medical degree and a lab coat." (Barrett, 2000). Of note is an aside mentioned in the latter article, which relates one loyal Lauersen patient's position that women's health issues don't get enough insurance coverage. The aside is a description of this patient, "whose three children all needed special attention from the doctor due to different complications at birth." (Ibid). No further elaboration is made on these "birth complications", and the implications of such "complications" appear to be unrecognized.

And the story of Dr. Asch, et al. is well known: Dr. Asch, who was overdosing women in superovulation to steal their eggs and then sell them to researchers and other unsuspecting women, reportedly often left his office with a briefcase stuffed with thousands of dollars in cash—while he was also preaching and publishing on the psychological effect of egg donation on women (Lessor, 1993).

A renowned group of fertility experts published a study, a report of "the first case of human germline genetic modification resulting in normal healthy children" (Barritt, 2001), however the expert group "failed to disclose that along with 15 healthy babies it produced two fetuses with a rare genetic disorder. Experts are horrified because the fault can be passed to future generations" (Hill, 2001). The fertility clinic and fertility experts report published claims of healthy children from their procedure . . . yet the Washington Post reported "[i]nternal documents from Saint Barnabas explicitly acknowledge that the novel technique may be causing the problem . . ." (Weiss, 2001). The 'Birth Defects Research for Children' points out that "the two cases of Turner's syndrome should have been mentioned in the report so that doctors and others would be aware of all the facts" (Birth Defects, 2001). The group would later report that the "children born after IVF with cytoplasmic transfer have been carefully evaluated and one 18-month-old child was recently diagnosed with a pervasive development disorder . . . a broad spectrum of disorders with mixed prognosis. . . . . Because the procedure is experimental, protocols have been supervised and re-evaluated in 1999 and 2001. . . . However, this research

has been suspended since early July 2001, pending clarification of new requirements suggested by the Federal Food and Drug Administration." (Institute, 2001). Six years prior, in an abstract published by one of this group, 4 abnormal embryos were implanted into women—and this act brought little, if any, attention from anyone or anywhere. (Munne, 1995). At St. Barnabas' webpage on egg donation (in which Lupron is used), the question of "What are the risks of being an egg donor" is answered . . . "Donors may risk psychological distress if they are rejected from the program . . ." (St. Barnabas, 2001).

Falsified and suppressed data (which can set, alter, and impact standards of care), along with conflicts of interest and abuses of human subjects in research endeavors are poisoning medicine systemically. Shouldn't you begin to address the forces that result in profit via dictation of data and spin and to-hell-with 'first do no harm'? And should you really open the reproductive research doors wider to the inevitable abuses in human embryo cloning research? The criminal penalties of jail and fines of at least $1 million that President Bush has proposed should be applied not just to the use or importation of cloning technology, but rather should be applied like a heavy wet blanket over every research discipline in medicine in attempts to quash this destructive slow burn.

12. The Marginalization of Victims and Lack of Medico-Legal Advocacy

The consumer who has been victimized by the fertility industry and/or Lupron has no recourse. Consumer protections are woefully lacking in the fertility research enterprises today—and there is no reason to assume that adequate 'measures' will take place or be enforced in the cloning arena. Start cleaning up the mess in today's fertility clinic before you create nightmares at the human embryo farms.

Who or what is in place *now* to assist the injured egg donor, or the harmed fertility patient—and whomever or whatever is offered as an answer to that question, please then answer what are they doing *now* about Lupron victims? My complaints to the FDA about Lupron and lack of informed consent promulgate the mantra that the FDA has no supervision over the practice of medicine, which falls to state Boards of Medicine. State Boards of Medicine state a doctor can prescribe any drug they want off-label, and drugs are under the purview of the FDA. The Department of Public Health has no jurisdiction over fertility clinics, so refers one to the Board of Registration in Medicine. The FTC round-robins the consumer to the FDA. And there you go, round and round . . . no informed consent, no advocacy, no accountability, no protection. The consumer is left stranded, while profits and abuses exponentiate, and her medical needs, costs, tests, and doctor/hospital visits accumulate.

Fiscal prudence would seem to imply that insurance companies would audit their costs of members 5 years prior to and then 5 years post Lupron, for expenditure comparison. My medical bills, and the medical bills of others, both before and after Lupron, speak for themselves. After enjoying a full-time salary for many years, it would be 8 years post-Lupron before I had earned a total of my formerly annual years salary. Illnesses, medical costs, inability to work, no medical or legal advocacy—all are extreme hindrance to the effort, energy and time necessary to mobilize for survival. Eggs donors, et al. beware! My advice to those considering undergoing superovulation and Lupron is: first, establish independent wealth in the event you become disabled; second, you will not be able to recognize lack of informed consent or be able to rely on the information or advice given to you, therefore some type of healthcare degree, preferably M.D., is necessary; third, having advanced chemistry will be especially helpful, so bone up there also; fourth, you may need to become quite familiar with the legal system and you might be on your own—so prepare yourself beforehand to save yourself a lot of grief; fifth, make sure you have family and friends available who can help you as you may find you are in need; sixth, make sure you can type real fast as you may find yourself having to write thousands of letters; and seventh, buy a head-phone because you will need to talk to as many people as you can.

It is "very bad", indeed, that reproductive experimentation has been conducted without informed consent, and with 'treatment' using hazardous agents propagandized as safe and as science—but is neither. "It no longer appears possible to consider the marketing of new drugs for stimulating the gonadicpituitary axis unless they have been tested within the framework of IVF" (Buvat-Laborie, 1988). The Health, Education, and Welfare Department, in 1979, advised that a global study be undertaken to establish the safety of IVF, and although no such undertaking was done, it was proclaimed at the 1994 Human Embryo Research Panel Hearings that former concerns about IVF's safety had been abated. The March 2000 study indicating a 9 percent rate of major birth defects from IVF represents a substantial increase from former reports. Dolly, the cloned sheep, became lame and was

euthenized. And there are thousands of Lupron victims who appear to have no voice, and are crying out for medical care and legal representation.

The FDA has had a "fatal erosion of integrity" (Horton, 2001), and conflicts of interest on 18 FDA Advisory Committees were revealed several years ago. (Cauchon, 2000; Mercola(2), 2000). The protections allegedly in place for federal research subjects were recently shown to have failed—and in private research enterprise the consumer is just plain out of luck. Conflicts of interest abound in clinical trials—"Let's be realistic" said [the] commissioner of the FDA, "Profits do drive this business" (Agnew, 2000). Where are the consumer protections?

While there has been some litigation recently, in the early 1990's there was little legal recourse available, and I am aware of 2 other women who attempted to bring their own lawsuit involving Lupron pro se because they couldn't find an attorney. I searched high and low, east and west, north and south, individual and firm and agency alike. Never having been inside a law library and needing to know everything about a foreboding and alien process with requirements and deadlines I'd yet to learn creates a most precarious and unfortunate position. Having to learn how to draft a complaint, and having to figure out the problem in terms of legal issues, identify the law and find other case law, file motions to compel, file answers and promulgate interrogatories and requests for production of documents, undergo 7 motions for summary judgment and a medical malpractice tribunal—without any attorney or real guidance beyond cursory advice by attorneys over the phone. I was told by numerous attorneys "you most definitely have a case, but without laws and standards—its a legal vacuum" and then years later, "if you can find the expert, I'll take the case".

Not until my case approached the MA. Appellate level did I pursue obtaining a paralegal certificate, but clearly, without counsel, and without laws and regulations, I understood that I had limited abilities to do justice to the case or the issue. I tried over and over, again and again, to find an attorney, each attempt to no avail—and it was very unnerving to try to prepare an appeal to the MA. Supreme Judicial Court pro se. Incredibly, a final online internet plea for some legal guidance was seen by an appellate attorney with endometriosis, Barbara Sosin, from Chicago IL. Barbara's reproductive endocrinologist "fired [her] because [she] refused to take Lupron". This doctor told her "I've been so patient with your irrational refusal to take this medication, and there's nothing more that I have to offer you". Therefore, through just a few phone calls of my presenting the legal issues, cases, and facts, Attorney Sosin was able to help me assemble this information in the most appropriate format, and I was very grateful for that last minute support. But, nonetheless, from start to almost finish (some 8 years), traveling that road alone is unacceptable; and was not the way for such an important matter to have had to be handled. Filing a case pro se is something that no victim should *ever* have to do.

Many product liability cases have been filed against TAP regarding adverse events to women following Lupron—and quietly settled. Through the grapevine, I became aware of 5 cases in the latter 1990's, and obtained court records for *Villarreal* v. *TAP* (Sacramento County, CA., No 528453; 1993), and *Gantner* v. *TAP* (Cook County, Il, No. 96L11379; 1997)—and have since become aware of a separate, additional settled case, and there are many potential-plaintiffs searching for counsel. I am aware that cases are being consolidated, and do foresee a class action suit looming on the horizon. But it has taken a very long time to get to that point, and an awful lot of wonderful, innocent, misled people have been hurt. My lawsuit was initially filed in 1992, and was terminated at the MA. Supreme Court level in 2000, the day Boston papers broke the Lupron urology kickback scam story—but I left nearly 1000 pages of medical, scientific, pharmaceutical, and governmental documents involving Lupron's risks for the next victim/case.

Since then, and after 11 years of seeing untold numbers of doctors and specialists, I finally received documentation that my "multiple medical problems [are] consistent with case reports following Lupron exposure . . . [and have] an extremely complex, multifaceted, constellation of medical problems." I'd like to quote the final paragraph from my MA. Supreme Judicial Court appeal: "Moreover, Defendants claims of lupron's 'menopausal' action does not correlate with known science. (Appendix p. 290 & 293). And studies for lupron's use in IVF were "discontinued". (Appendix p. 358). Therefore, her IVF treatment with lupron was not grounded in reliable scientific methodology. The opinions of the *Defendants*, as well as the accepted 'standard of care' regarding the use of lupron, cannot meet the threshold requirements of Daubert and is "junk science", creating a genuine issue of material fact for a jury. (*Daubert* v. *Merrell Dow Pharmaceuticals* . . .)" (*Millican* vs. *Harvard Community Health Plan*, Boston IVF, Natalie Schultz MD, Brian Walsh MD, Mahmood Niaraki MD, Selwyn Oskowitz MD, Michael Alper MD. Docket No. 98–P–1472.)

An online investigation of Lupron (*www.redflagsweekly.com*), as well as the NLVN, myself, other victims, and media such as FOX News and Dateline, have challenged TAP to produce data and to answer questions—but there has been no response from TAP. The FDA was to take another look at its damaging 1999 review, but no word has been heard. The NIH just conducts more Lupron studies, while shielding consumers from its webpages for its Hazardous Drug List and Material Data Safety Sheets (MSDS). The MSDS for Lupron, available to all hospitals and healthcare institutions, states that leuprolide acetate is "hazardous per OSHA criteria", and identifies that "women of childbearing potential must be excluded from working directly with product." This is information necessary for consumers to make an informed decision about 'treatment' with a hazardous, toxic substance. Questions were posed to several NIH Lupron investigators inquiring whether their Lupron trials followed NIH and OSHA guidelines in use of protective gear for healthworkers administering Lupron, and these questions were responded to by several NIH investigators—however, the replies do not answer the question as to whether NIH Lupron clinical trials follow NIH guidelines (personal communications). More than thirty years after the debacle of DES, the CDC (in 2003) began a campaign to inform people about the potential health effects of DES (*www.cdc.gov/DES*). The CDC's annual report of fertility clinic data has been questioned in the past, and issues regarding its reliability have again been raised, pointing out its "lack of reliable information", citing data that is up to 3 years old, and clinic success rates that are "too easy to fudge" (Report, 2002).

In one aspect of my 'fertility treatment nightmare', the dates and details of an office visit were deliberately altered in the computer through collusion and deliberative machinations by several of the defendants in my case—and my HMO had steadfastly denied that I had ever received treatment or prescriptions on that date (*Millican* v. *Harvard Community Health Plan*, Boston IVF, Natalie Schultz M.D., Brian Walsh M.D., Mahmood Niaraki M.D., Selwyn Oskowitz M.D., Michael Alper M.D.; see also Donahue, 1996). Given the ease with which my computer record data was deleted and altered, along with numerous other experiences, as well as the known fraudulent Lupron data, and recent newsreports on fraudulent research elsewhere, "data" coming from self-interested parties should always be viewed as potentially unreliable, to say the least.

A few more comments from Gena Corea's supportive statement for my lawsuit are pertinent here: "After discussing the death of a woman in the IVF program in a Seville clinic with Dr. Francesca Martinez of the IVF program at Instituto Dexeus in Barcelona, Spain, I said to her: If it's so difficult for you, who are practicing IVF, to find information on women who died of IVF, how can you say what the risks of IVF are? She replied that she and her colleagues knew what happened in their own center and they had many cases—2,000. So she is telling potential IVF candidates what the risks of IVF are based on her own clinic's experience. This is a pitiful situation." And Gena concludes by saying "I don't know what will happen with Ms. Millican's complaint. What often occurs in such situations is that women, with only their own limited financial resources, without even an attorney, doing the labor themselves when they come home tired from their jobs, seek justice. Few can do it. Few can break silence on the abuse to which they have been subjected. But it is vital to talk back, to insist one's reality into the fictional never-never land of miracle babies and ecstatic, unharmed mothers. I applaud [those women] for speaking [t]he[i]r truth."

The answers do not lie in continued exposure to Lupron, which would definitely occur should the Senate pass any bill allowing therapeutic cloning research. Does Lupron sound like the kind of drug you want to give to young healthy women who are 'offering' to donate eggs? Does Lupron sound like the kind of drug you would want to take for any benign condition, without informed consent? It appears that the majority of women whose eggs are harvested used Lupron. How many women know Lupron has never been approved for fertility? How many women know the facts and the tragedies mentioned in these pages? If millions of women are needed to meet the demand for research 'material', what will these women be told? My advice to them is—instead of asking questions to the Industry . . . read the Congressional Record.

13. A Request To Congress Asking For An Investigation Into Lupron and ART

In closing, the data in this paper barely scratches the surface of problems associated with Lupron and ART, and Committee Members should know that there are unknowns and redflags beyond those described in this submission. Time limits did not prevent further detail or elaboration, and wish to add that any references or further information are available upon request.

For all of the above stated reasons, I would respectfully urge the Committee to ban reproductive and therapeutic cloning.

And I would like to also respectfully urge the Committee and Congress to undertake a formal investigation into Lupron and its victims, as well as investigating the long and short term safety of ART drugs and procedures on women and offspring.

Respectfully submitted.

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Senator BROWNBACK. Well, thank you for making it in and for coming here to give your personal testimony and also the statements of other people who have contacted you.

You mentioned the National Lupron Victims Network on the Internet——

Ms. MILLICAN. Yes.

Senator BROWNBACK.—and that a number of suits have been filed against Lupron.

Ms. MILLICAN. Yes, they have.

Senator BROWNBACK. And those are being settled? Have any of them been tried yet? Do you know?

Ms. MILLICAN. To my knowledge, none have been tried, no.

Senator BROWNBACK. Okay.

Ms. MILLICAN. They are all settled.

Senator BROWNBACK. Mr. Kimbrell, this hearing is primarily about the issue of egg donation and an egg market and its impact on women. And as I have heard you speak over the years on this topic, that has been an area that your group has been as focused on as anybody in the starting of a new bio-industrialization. Have you done any studies, do you know of any economists who have looked at any studies, as to what price would need to be paid to get a million qualified women to be able to donate eggs? Do you know of anybody who has looked at that and the numbers associated with it?

Mr. KIMBRELL. You know, it is hard to say. And let me just—I have this in the record, but I will show it here. We talked about this earlier. I thought it might be good to have an example right in front of us. We got this last month from the *Stanford Daily*. This is an ad that was put in the newspaper, the *Stanford Daily*. It says, "Special egg donor needed"—let's see here—"height approximately 5'9" or taller, Caucasian, SAT score around 1250 or high ACT, college student or graduate, under 30, athletic, no genetic medical issues, compensation $80,000."

[The information referred to follows:]

EGG DONOR NEEDED
LARGE FINANCIAL INCENTIVE
Intelligent, Athletic Egg Donor Needed
For Loving Family
You must be at least 5' 10"
Have a 1400+ SAT score
Possess no major family medical issues
$50,000*
Free Medical Screening
All Expenses Paid
For More Information
Please Contact Darlene Pinkerton
Hitt & Pinkerton, Attorneys At Law
(800) 264-8828 or (619) 234-6640
TomEsquire@aol.com

SPECIAL
EGG DONOR
NEEDED

Preferred Donor will meet the following criteria:

Height Approximately 5'9 or Taller

Caucasian

S.A.T. Score Around 1250 or High A.C.T.

College Student or Graduate Under 30

Athletic

No Genetic Medical Issues

COMPENSATION $80,000

Paid to you and/or the charity of your choice

All related expenses will be paid in addition to your compensation

(Extra compensation available for someone who might be especially gifted in athletics, science/mathematics or music)

For more information or to obtain an application please contact Michelle at the Law Offices (800) 808-5838 or email EggDonorInfo@aol.com

*This ad is being placed for a particular client and is not soliciting eggs for a donor bank.

Senator BROWNBACK. Wow.

Mr. KIMBRELL. "Extra compensation available for someone who might be especially gifted in athletics, science, mathematics, or music."

So it is pretty hard, Senator, to really see what, you know, the price will be or will not be, but I will tell you, for whoever is tempted by these ads, and we know they are always targeted, as was surrogate motherhood, always targeted to poor women. You know,

wealthy women do not sell their reproductive heritage. They do not sell their bodies. They do not sell their eggs. These are poor women. These are basically turning the poor women of this country and around the world into "mother machines."

So what amount would actually be required, perhaps in an economy that is not that good, to encourage these women? I do not know. But I do wish that a part of the informed consent of these women will be to listen to Ms. Millican and what has happened to her. I think we should make that legislatively part of consent, because I think a great many women have come into this—and we interviewed numbers of them, both in the surrogate motherhood when we wrote our book and in reports on this and the egg donation, and they had no idea. They thought they were trying to do a good thing for somebody else, they desperately needed the money, and the screening that was talked about before is minimal, at best, and the real reason they are there, quite often, is because they are in desperate need of money, and so informed consent virtually never happens. And so I think that, again, a requirement that they hear the kind of health effects that they could suffer would be key.

Senator BROWNBACK. When you were doing the Organ Donor Bill, I was taken by your statement about no payments for the donations allowed, and it strikes me that that has worked just fine—I mean, that people continue to donate organs and they do not seek the compensation for it.

Mr. KIMBRELL. That is right. And then, of course, any of us who—and I hope all of us do—give blood know that that works just fine, too. It is an extraordinarily important thing we can all do.

Yes, when we first passed that bill, Senator, there was a lot of discussion about black market organs in this country and that it would not work, and it has worked very, very well, indeed.

And I think that, again, the important point here when we're looking at 303 is that second provision that says "time and inconvenience." A number of States have that same provision, and they do not prevent ads like this. It is a loophole. "Inconvenience," as George Annas, in the quote that I cited before, means virtually nothing. It means that you can pay anything you want for, "inconvenience."

I certainly second Mr. Doerflinger's point that it is also hard to calculate, when you hear what Ms. Millican was saying and you know the cancer risks involved, exactly how far you take that term, "inconvenience."

But, yes, I think it is very instructive to compare this with NOTA, the Organ Transplant Act, and note how this bill has been purposely changed to allow for this loophole.

Senator BROWNBACK. Ms. Charo, you have served on the National Bioethics Board previously, is that correct?

Ms. CHARO. That is correct.

Senator BROWNBACK. I am sure this has to be troubling to you about bidding for women's eggs. Was that issue handled by the National Bioethics Board when you were serving on it, and did it take a position against the compensation of women for the donation of eggs?

Ms. CHARO. First, before I answer, if I may, I would like to also indicate I did have a longer statement and ask that it be put in the record, if I may.

Senator BROWNBACK. Without objection.

Ms. CHARO. And one other quick clarification. With respect, I think Mr. Doerflinger lacks the anatomy that every woman in the room has to know that it is really not possible to transfer embryos into yourself.

[Laughter.]

Ms. CHARO. But putting that aside—and I say that with respect and affection, because Richard and I have dealt with each other.

With response to your question about egg donation, specifically, the National Bioethics Advisory Commission, which did do a report on stem cell policy—a report from which I recused myself due to the possible appearance of a conflict of interest, as I was at the University of Wisconsin—did not touch directly on the question of sale of human eggs. However, I would note that in many cases what we have been hearing today are descriptions of a market that takes place in the context of eggs being sought for reproductive purposes. That is, somebody—we do not know who—has the misguided belief that SAT scores are inheritable and, therefore, is offering a high price to somebody who they think could transmit that SAT score to an offspring. That is not the kind of incentive structure that would exist if you are looking for people to donate or provide eggs in other ways for a research context in which the eggs are not going to be used for reproductive purposes and there is no expectation of a long-term outcome, only be used for stem cells.

Second, the American Society for Reproductive Medicine has set a $5,000 limit on what is expected to be a notion of "reasonable compensation," a notion that is also reflected——

Senator BROWNBACK. Is that——

Ms. CHARO.—in the National——

Senator BROWNBACK. Excuse me. Is that a hard limit? And that does not carry the weight of law, does it?

Ms. CHARO. It does not carry the weight of law. This is a professional society guideline——

Senator BROWNBACK. Just a recommendation.

Ms. CHARO.—as I understand it. And I will happily stand corrected by those who know it more precisely. But these guidelines have——

Senator BROWNBACK. I am sorry. If I could, I want to be——

Ms. CHARO. Sure.

Senator BROWNBACK.—clear on this. That is a recommendation of that group that the compensation not be above $5,000?

Ms. CHARO. That is correct. That is——

Senator BROWNBACK. Okay.

Ms. CHARO.—correct. And——

Senator BROWNBACK. Can I get to the very specific point? Because I really want to get—and then I will give you time——

Ms. CHARO. Sure.

Senator BROWNBACK.—to answer the rest of this. But have you seen any studies, anybody calibrate, saying if we want to get simply a million women to donate eggs—say, we are three, five years down the road, this has come along great, we want to do this for

diabetes, for ALS or something, but we want to get a million women to donate eggs—what is the market? What are we going to have to pay to get—as I understand from the testimony earlier, you are going to probably have to go through 10 million women to find 1 million who would be qualified if you have got this ten to one ratio.

Ms. CHARO. Well, actually——

Senator BROWNBACK. And you are going to have to——

Ms. CHARO. Right.

Senator BROWNBACK. I mean, there is going to have to be a pretty heavy recruitment, I think, if—the experience under anybody's scenario is a pretty difficult one to go through this, for a woman to go through it. Have you seen any numbers on this?

Ms. CHARO. There are no numbers, because the scenario is not realistic. I think the premise is the problem, Senator Brownback. I do not share the premise. And I think this is what Dr. Bustillo was trying to get at, as well.

The way this research will proceed, first on the therapeutic arm and on the purely research laboratory study arm, is that it starts very small, with very small numbers of people under close control by the Food and Drug Administration, in which they are looking at the animal data, whether it's ready for laboratory work with human materials, and you start with very small numbers of people. And as you continue to do the work and slowly scale up as you perfect your techniques, you are simultaneously developing methods by which you no longer need as many eggs for the next stage, per procedure, as you did in the first stages of research.

So the scenario of using millions of women——

Senator BROWNBACK. Then you paint——

Ms. CHARO.—at an early stage for all diseases, I do not think is realistic vision.

Senator BROWNBACK. Then you paint for me—we have got a hundred million people with these diseases we are going to cure with the cloning——

Ms. CHARO. No, I do not think a hundred million people are going to be the patient population for therapeutic cloning, either.

Senator BROWNBACK. What is the——

Ms. CHARO. This would be one——

Senator BROWNBACK. What is the patient population going to be?

Ms. CHARO. No, it is the patient population people with the diseases, but for each——

Senator BROWNBACK. Okay, well, what is it——

Ms. CHARO.—person, there are——

Senator BROWNBACK.—going to be? Please——

Ms. CHARO. There are many——

Senator BROWNBACK.—come up with the number, if you can, or a round figure for me, if you can. What is the patient population going to be?

Ms. CHARO. We do not know that yet, because the research is just beginning. The point is, for every disease, whether it is heart disease or Parkinson's, there are multiple therapies. It is not one therapy that is used for every person. Different things work in different people, and therapeutic cloning may work for some subset of that patient population.

I do not think I have ever heard any responsible doctor or scientist suggest that this therapy will be used for every patient——

Senator BROWNBACK. Well, why——

Ms. CHARO.—with every one of these diseases, and that's another reason why the numbers——

Senator BROWNBACK.—do they keep saying, then——

Ms. CHARO.—can become misleadingly large.

Senator BROWNBACK.—we are going to—we have got all these cures for—and then they list a litany of diseases that are going to be cured by therapeutic cloning, the same list that was put forward in the fetal tissue debate that we are going to cure with that, the same list that was put forward in embryonic stem cell. I mean, at some point in time there has to be some coming up with, "Here is the product of what we have done."

Ms. CHARO. Oh, but I think it is unfair, with research aspects of human cloning, to ask for an actual approved, FDA-reviewed and -approved, therapy to emerge within five years.

When Jamie Thompson said what he did about Parkinson's at that hearing, what he was talking about was, "When would we be able to move into clinical trials for Parkinson's disease?" And he predicted five to ten years out. It is now five years out, as you correctly note.

Senator BROWNBACK. And there is no——

Ms. CHARO. And we are now at——

Senator BROWNBACK.—limitation on therapeutic cloning to date, is there?

Ms. CHARO. We are now at the stage at which we have successfully seen human embryonic stem cells—and, remember, he was not talking about cloning them; he was talking about stem cells from extra IVF embryos—so we have now seen those stem cells successfully differentiated into neurological tissue. And the next step is to see whether or not that tissue can be developed to the appropriate stage for transplant into a patient. That requires lab work, animal work, and, eventually, human trials. We still have another five years on his prediction to see if we can get that next stage of the work done to the point where the FDA would permit that work to go on.

The FDA, remember, keeps a very tight lid on all of this. It requires licensing of establishments that do this kind of research. It has an extremely tight tracking and monitoring system so it can track viral transmissions as well as everything else in its comprehensive tissue action plan, and it has comprehensive donor suitability requirements. That is, it has already issued Federal regulations—proposed, interim, and finalized—that cover every aspect of this but keep it moving slowly and responsibly.

Senator BROWNBACK. I want to ask Mr. Doerflinger or Mr. Kimbrell about this issue. I think both of you were around Washington when the fetal tissue debate started going, and I believe fetal tissue was stated that it was going to cure a myriad of diseases at that time. And these are actually even cells that were further developed; they are less primitive than the embryonic, the therapeutic embryonic.

These are a couple of quotes from *New York Times* of some extensive studies on fetal tissue impact in Parkinson's patients, which

were, "Disastrous side effects. Absolutely devastating. It was tragic. Catastrophic. It's a real nightmare, and we can't selectively turn it off," because the cells were, as I understand, uncontrollable. Instead of making brain cells, they make various different tissues or tumors.

Were people saying, at this same time, we were going to do with fetal tissue what is being proposed with therapeutic cloning?

Mr. KIMBRELL. Yes, Senator. I was working with then-Senator Humphrey and Senator Kennedy to try and get adequate regulation at that time on fetal tissue research.

To step back just a second, though, just so we can get some clarity on a prior issue, I would note that 18 months ago, Michael West, of Advanced Cell Technology, at a Senate hearing, predicted that within six months, his company would be ready to create stem cells from cloned human embryos that would save 3,000 lives a day. And he warned that for those—and, Senator, you may be one of these that was suggesting a six month moratorium on this—that that would cause the loss of perhaps as many as a half million lives.

So I did want to just clear the record that these claims have been made, and, at that time, Senator Harkin said, "Thank you. Now at least we have some—I am quoting—real numbers." So these claims have been made, and I just wanted to clear that piece of it up.

And yes, indeed, I think one of the things we have to be very careful with here that I have seen in 15 years of working on these issues, and this includes fetal tissue research and somatic gene therapy research, is hype over healing. Quite often, what we have seen is, with a lot of hype, some early investment capital, and some sometimes overly ambitious researchers, the real victims have been those who are suffering from these diseases.

And this happened with fetal tissue. The claims were extraordinary. We were talking about claims, at that time, or the researchers were, of a hundred million lives being saved by fetal tissue research. They pushed it through, despite the best efforts of many in this body. We were not able to get adequate regulation. We were not able to impose a moratorium. And you see what has happened. Approximately 15 to 20 percent of all patients that have been given these fetal tissue for Parkinson's have uncontrolled motion 24 hours a day. They cannot feed. They cannot speak properly. And that has led to this front page *New York Times* story saying, "My God, what have we done?" Many of these researchers are now saying we should never have done it.

So, again, before we jump into these predictions such as the one that Dr. West made at a prior Senate hearing, we need to realize that the real victims, quite often, of this hype over healing turn out to be those who are suffering from those diseases, themselves, and I think that it is the responsibility of this body and every legislative body to look out after their interests and realize that those interests are not always being served by those who are pushing these technologies.

Senator BROWNBACK. Good. I want to thank—Mr. Doerflinger, yes, do you have a statement?

Mr. DOERFLINGER. I wanted to say something about that issue, too. The fetal tissue did have very mixed and often devastating ef-

fects. I think what the federally funded research showed was that there seemed to be some benefits only in younger patients with Parkinson's. None of the patients over 60 years old were really helped. And I think about 15 percent had these devastating side effects that made them worse.

There was one study in the Journal of Neurology, May of 1996, that may be an even more disturbing sign of what we may face with embryonic cells. That was the story of a man who went to China for his fetal tissue transplant for Parkinson's. He was dissatisfied with the slow pace of progress in this country. They seem to have implanted in him some cells that were somewhat earlier in gestational age than the usual eight weeks. What happened to him was that he seemed to get some benefit from it, but within a year he had mysteriously died. And on autopsy, what they found was that bone and skin and hair tissue had proliferated in the middle of his brain and filled up the ventricles of his brain and killed him, cut off his breathing reflex among other things.

So having failed with fetal tissue, it does not seem logical to me to say, "What we need is earlier cells, embryonic stem cells," that now, in animal trials, are proving to have a very disturbing tendency, when tried for Parkinson's, when tried for spinal cord injury in rats, for example, when tried in knee repair in mice—one of the studies quoted in my testimony—have the very disturbing tendency to form tumors, and even, in one of the rat experiments, to simply kill 20 percent of the rats in the study.

We are finding, at this point, almost an obsession with this as the Holy Grail for medical cures. And it is really tending to divert people away from things that are far less morally controversial that are far, far closer to actually helping human patients.

There was almost no news in most news sources about the first clinical trial of a patient with Parkinson's disease using his own adult neural stem cells. But that man, three years later, has 83 percent reversal of his symptoms in a study by Dr. Michel Levesque, and they are trying for broader clinical trials and approval from the FDA for that.

There are so many things moving forward that do not require having to worry about lethal tumor formation, having to worry about harvesting women's eggs, having to worry about overproliferation and uncontrolled growth in patients' bodies, that it is becoming increasingly clear this whole agenda of therapeutic cloning—in which as Mr. Kimbrell noted, they still have not managed to make a single cloned human embryo that survived long enough to get any embryonic stem cell—is becoming an enormous digression away from medical progress that we could otherwise have.

Mr. KIMBRELL. Mr. Chairman, just one quick note on that. Since I am here representing Friends of the Earth and Greenpeace and other environmental groups, let me note that as of this morning's E-mail, I saw a peer-reviewed study that associates Parkinson's with early exposure to pesticides. I would suggest that it might be reducing our exposure to pesticides might be a far better place to start than trying to harvest fetal tissue.

Senator BROWNBACK. Well, you are all very kind to come forward and to testify. Ms. Millican, in particular, I am appreciative of you

fighting through your difficulties to be here today. We do all want to find cures, and we want to do it as best we possibly can for everybody who is involved.

The record will stay open for the requisite number of days. I do appreciate all the witnesses for coming here.

The hearing is adjourned.

[Whereupon, at 11:30 a.m., the hearing was adjourned.]

A P P E N D I X

PREPARED STATEMENT OF HON. RON WYDEN, U.S. SENATOR FROM OREGON

Chairman Brownback, in any new field of research, it is important to oversee closely the clinical practices of researchers to assure that abuses do not occur. We have done this in the past with *in vitro* fertilization, and I think we can do it in the future to produce vitally important therapeutic nuclear transfer treatments safely.

In 1992, when *in vitro* fertilization was a relatively new technology, I authored the Fertility Clinic Success Rate and Certification Act. This remains the only federal legislation regulating these clinics. My legislation provided women and their families the information that they needed to make educated choices about embryo clinics by requiring the publication of clinic success rates. In addition, individuals can now also learn who accredits the clinic they are considering. All this information is available on the U.S. Centers for Disease and Control website and the information is updated annually. My legislation also called for the creation of a state model regulatory program for certification of embryo laboratories. This was accomplished in 1999, when the U.S. Department of Health and Human Services published a state model regulatory program. Combining consumer information, the state model regulatory program and the guidelines that this medical field had developed for itself, I think IVF has been a clear success story for the treatment of women.

We can continue this kind of successful oversight in therapeutic nuclear transfer research and its applications to the treatment of disease and injuries. As I stated clearly in this Subcommittee's January 29th hearing, I support the strong ethics requirements—which would be enforced by the Department of Health and Human Services—contained in the bipartisan legislation "The Human Cloning Ban and Stem Cell Research Protection Act of 2003," S. 303. These provisions require informed consent, prohibit the purchase or sale of an egg cell, and apply all of the existing federal ethical research standards to nuclear transfer treatments. Tough penalties give this law teeth, but do not stand in the way of the many medical advances that can be made through nuclear transfer.

It is important to remember that this research will help women. Nuclear transfer technology is crucial to treating diseases which affect women disproportionately or exclusively. By increasing our understanding of how cells predisposed toward diseases like ovarian cancer develop, we can learn how to fight these diseases. Promising treatments for osteoporosis, arthritis, and autoimmune diseases could be supplied by replacing damaged tissues with cells grown through nuclear transfer. Women would directly benefit from such advances, and would be helped as well as the primary care givers for those who suffer from chronic diseases.

I hope we can work together to protect women's health at the same time that we allow for careful progress in nuclear transfer research.

RESPONSE TO WRITTEN QUESTIONS SUBMITTED BY HON. FRANK LAUTENBERG TO RICHARD M. DOERFLINGER

Question. If the egg could be manipulated so that it could not implant and therefore would not have the potential to become a child, would you still oppose any research or therapeutic cloning?

Answer. First, a clarification: No mere egg can implant in a womb. If we are discussing the new embryo created by human cloning, which is no longer simply an egg, then in our view that embryo deserves respect as a new developing member of the human species—a human life with potential, not only a potential life. The cloned human deserves that respect because he or she is already a human life here and now, not only because of what he or she may become in the future.

An embryo with no ability to implant in the mother's womb will not survive very long. Nor will a newborn infant who has no ability to ingest his or her mother's milk or other nutrients. But we would not say of the infant that he or she is less than

human due to the lack of potential to become an adult, and we should not say of the embryo that he or she is less than human due to the lack of potential to survive long enough to be born. In either case, deliberately manipulating these humans in order to deprive them of these abilities needed for survival would be gravely immoral in itself. So my answer to the question is in the affirmative.

There may, in fact, be ways to modify the nuclear transfer procedure so that it produces stem cells without ever producing a living human organism (that is, an embryo) in the first place. The Brownback/Landrieu cloning ban (S. 245), which we support, explicitly allows for this, and bans only the use of the somatic cell nuclear transfer procedure to create a human embryo. But an embryo that has been unethically manipulated to be short-lived is still a human embryo.

PREPARED STATEMENT OF KIMBERLY BRADFORD, ORLANDO, FLORIDA

My name is Kimberly Bradford, I'm 34, the mother of one 7 year old son and have been very ill for the past 10 years due to the use of Lupron for Endometriosis. When we are younger, in our late teens, in high school and college we start thinking, dreaming about what our life is going to be like. We start setting goals. All of mine were cut short. Lupron robbed me of the good health I once had. It stole my ability to participate in most physical activities. It took my ability to think clearly and make rational decisions. At times it took my ability to move at all and left me paralyzed.

I am very grateful for the one child I was able to have . . .I had some VERY good surgeons who made that possible. I had several operations that led to my ability to bear my one and only child.

I lost my first child. I got pregnant four months after my last Lupron shot. I thought enough time had passed, I was wrong. The toxin was not gone, considering how sick I was I should have known but all I could see what the need to have a child. This is the same need that MANY women have when they undergo infertility treatment and agree to use Lupron, even though it is NOT approve for such use. How Lupron became used for this I can't imagine. It's toxin is so sickening. I know they use Lupron for superovulation, a procedure that Puts women's lives in jeopardy. The use of Lupron to gain eggs for stem cell research is wrong! The same diseases that they are trying to cure, Lupron is causing!

It is risking the health of the women who innocently volunteer for this, not to mention possible passing on a toxin contained in the egg itself.

My Whole Story:

My diagnosis of Endo came in October of 92, but my ordeal started when I was 11. Like most of us I had the usual, painful period then painful ovulation. My period kept getting longer and longer despite being on birth control pills at age 16. I complained to my GYN for years about the pain, but it was not until I had a class II pap (Dyplasia) that she finally listened. She wanted to do a biopsy and laser my cervix so she agreed to do a Lap at the same time. I was 24 at the time of my lap. I worked in the same hospital as my doctor so she knew me by name. She was also my mothers doctor. Needless to say I trusted her. I think she agreed to do the lap to try and prove me wrong. I had been doing research on my pain and knew I had Endo. Well, I had it. It was covering my bladder. This explained why I always thought I had a bladder infection or UTI only to have the tests come back negative. It also explained why Sex hurt so much. She told my parents afterwards that she didn't remove any, she told us it was inoperable and wanted to put me on a drug called Lupron. I had to watch a video prior to getting an injection. It was made by TAP holdings, the pharmaceutical CO that makes Lupron. In the video was this very perky women spewing the benefits of Lupron and how you can find relief for up to a WHOLE YEAR. A year sounded like a long time then. . . . Little did I know. The only info I could find on Lupron was mostly for men with Prostate cancer. It was listed in the PDR but that doesn't really give you an idea on how "real" people react. I gave up my search and took the drug. I mean after all I trusted my doctor. I was told about the pseudo-menopause symptoms, hot flashes and such. She also told me to drink milk, but not to worry about it too much because of my age.

I started complaining right after my first injection. The hot flashes were horrible. My poor mother felt so sorry for me she stopped taking her hormones so we could "flash" together. It was winter so at least we could just go outside and melt snow. But this was fun compared to the rest. . . . I started bruising really bad, like just from wearing shoes. No one could even touch me without an imprint of their finger or hand showing up on my skin. I called the doctor, the one I trusted, and was told "don't go horseback riding" She said it as if it was part of my daily routine.

I felt like I was in a "fog." I couldn't think. Decision's like what color sweater to wear became a major ordeal. When I looked in the mirror I always expected to see someone else. I felt 80. Everything hurt, like someone drained my blood and replaced it with acid.

The shots were given by one of the nurses in her office. When I received my records in the mail a few months ago the notes were filled with stuff like "Kim is very excited planning her wedding," NO complaints, nothing medical! Nothing I said was documented. I did complain!! About headaches, insomnia, joint pain, pain at the injection site for days, I was told that none of these things could be caused by Lupron and not to worry about them. I was left believing that I just had an overactive imagination. My doctor did only one exam during those 6 months and it was really bad! I wanted to kick her in the face. I told her it hurt and she said "what about sex?" Was she kidding? I couldn't stand the Q-tip never mind actually having sex. She said "everything looks great, you're going to be just fine." I was so naive. I wanted so badly to believe her. I tried to put it out of my mind, after all I had a wedding to plan. All my energy went to that and just trying to get thorough a week of work without missing too much time. I got married on June 5, 1993, one month after my last injection. 400 invited guests, family, friends, members of his family I had not met yet . . .they all witnessed my total emotional breakdown. It was REALLY awful! I can't even bear to watch the video as all you see is my head bobbing as I cried, I should have bought stock in Kleenex. I must have gone through 4 boxes during the service. I could not even say my vows because I was crying so hard. My husband thought I wanted out. I did but only to put an end to the embarrassment. We could not kiss because I had to blow my nose, as if no one would notice. Somehow we got through the night. Next came the honeymoon and a week of unbelievable pain. I kept quiet, I was supposed to be OK, this was just in my head. . . .

When we got back we moved from Maryland to Virginia, about 3 hrs away. By August I couldn't stand the pain anymore. I finally broke down and told my husband everything. I told him he could leave me if he wanted. I was not the same person he thought he had married and I was not sure if I would ever be the same. The pain was getting worse, not better as the doctor had promised. I called her, desperate for answers. Her reply "there is nothing more I can do for you, find another doctor." I was devastated, but I needed help so I searched for a new doctor. I finally found one who specialized in high risk pregnancy and GYN disorders.

She met with my husband and I for over an hour. She had lots of questions. The biggest being "why was the Endo not removed"? Good Question!!! I was told it was inoperable. This was the beginning of an eye opening experience. I finally realized that my doctor of nine years had deceived me. Anyway, the new doctor wanted to do another lap. I had it in October 93. Almost exactly a year from the first one. Despite my old doctors promises of Lupron helping me, it actually made it worse!!! It had gone from just my bladder to my bladder, cul de sac, ovaries, and tubes. Basically there was a little bit everywhere and I would not have been able to have children without her intervention. She removed all she could and did a LUNA as well but could not get to as much of the nerve as she would have liked. We had no time to waste planning a pregnancy. My husband knew when we got married that our window of opportunity for children would be small. We got the green light and I was pregnant by January 94. Sadly, Our happiness did not last long. I miscarried in March.

I shut myself off from the rest of the world for a while. That summer I drank . . . a lot . . . Looking back it wasn't fully out of depression it was also to hide my other problems. It was easier to hide my dizziness and stumbling and visual problems if I had a few drinks than to admit there was something else wrong with me. Somehow we got through it and by September I was pregnant again. This time I told no one until I was past the point of my last miscarriage. I was so fearful of losing this one I would wake up thinking I was in labor, pushing and everything. The pain was pretty intense the first couple of months, but it did give me an excuse again for my klutziness. Then around 3½ months an amazing thing happened, I felt great!!!! For about 5 months I was almost pain free, symptom free, headache free. WOW! My son was born on May 11, 1995. I nursed for about 3 months then tried to go back on birth control pills. But surprise, I could not remember to take them everyday. I talked to my doctor and finally decided that Depo Provera may be the best choice. It offered me a chance to "save" my uterus until I was ready to have another one. I wouldn't get a period so the pain I had with them and ovulation would be gone. At the time it made sense. But with it I also lost my excuses for not facing the other problems my body was having. And just to prove it they started knocking me on my butt. I started to get sinus infections. I should say again, my VERY first sinus infection ever came after my second injection. I never had allergy

problems before. After months of trying different antibiotics my doctor finally sent me to an allergy specialist. That's when I found out I now had an IGA deficiency. Which had been checked by the doctor I saw for the infections I got while on Lupron? My IGA at that time was low, but still in normal range. Basically your body has five different Ig's for different systems in your body. They are the "brains" behind your white blood cells and tell your white blood cells what to attack when you have an infection. I don't have enough to fight infections in my respiratory system. I also learned that when I get a sinus infection I am more susceptible to other infections like strep throat and bacterial laryngitis. They put me on Prednisone and a long course of Biaxin. Still it took months to get well. I was miserable and thought for sure I was going to lose my mind!!! When the infections finally settled down I went back to work for the Orthopedic practice I was with before I had my son. He was almost two and I thought he needed to be with children his age, rather than a mother who was sick all the time. It didn't take long for myself and others to realize something was wrong. I mean you can only walk into so many walls before someone asks if you're alright. My right foot has a tendency to "disappear" on me at times. I hardly noticed my tripping over it anymore, but others noticed. I started getting these intense migraines with an Olfactory aura. Everything smelled like it was burning. My PCP thought I should have an MRI of my brain. I had it on a Thursday. That evening I got a call from my doctor. They wanted to do more. I needed to go back to the hospital in the morning for more MRIs. Then when we got home I got another call. They still wanted more, so back we went. Since it was a Friday and I was scarred to death at this point my PCP gave me her home number to call if I needed anything. She also wanted to see me Monday morning. She didn't have the results but thought I should see a Neurologist. The one she had called in to read my MRI was not in my insurance plan, so she went through the book and found one that could see me right away. I can tell you this was the single most humiliating experience in my entire life!!!!! He came into the exam room abruptly, he did not even introduce himself. He picked up my chart and looked at me and said "So you're feeling dizzy, what does that mean? Look at the wall, is the wall spinning or are you spinning" I was speechless!!! I was also very scared, I still didn't have the results of my MRI, but I had brought the films with me and he proceeded to read them by holding them up to the light above his head, no light board. The whole time he is looking at them he's saying "Well you get headaches because, unfortunately, you are a women." I kid you not he really said this!!!! Then he looks at my eyes and asks if I had been checked for syphilis. I had enough and left. What a jerk!!!!!!!

I took my MRI films back to the hospital and called my PCP to tell them what happened. That doctors name is no longer in their book!! They still had not received a report on my MRI. In the mean time I went to an ENT to rule out Menergies disease. The doctor was very nice and said I had classic vertigo but did not know why. He said maybe it was just a virus and would go away. At this point all I could do was hope and pray. I made an appointment to see him back in three weeks. He said he would run more tests if nothing had improved. About one week before my follow-up with him I got a call from my PCP. She said she really wanted me to see another Neurologist. I got nervous and told her I was willing to go out of my Insurance network if she could get me in. The best the Neuro's office could do was 2 months away. I took it and kept my appointment with the ENT. This is when I learned what everyone already knew. My MRI showed lesions on my brain. There was a question of "demylinating lesions" or M.S. I don't remember the drive back to my office that day. Only my supervisor driving me home. And the look on my husbands face when he came home and found me curled up on the kitchen floor. We had tried to convince ourselves that no news was good news. I kept thinking "this is not real, this is not happening to me, to us." I kept calling the Neurologists office in hopes of a cancellation or something. I was very angry, how could everyone just expect me to put my brain on hold?

When I finally saw him he showed me the area everyone was fussing about. I have come to call it "my spot." It is an area about the size of a quarter on the left side of my brain. It's in the white matter, in the middle, near the pituitary gland, but not in an area they can biopsy without causing more injury. He wanted to do a battery of tests, lab work, visual evoke potentials and a spinal tap. So far so good, then about four days after my spinal tap on a Saturday morning my husband tried to hand me the phone. It was my parents. I could hardly move the right side. I couldn't grip the phone with my right hand. I couldn't talk, just slur. My husband was scarred, I was worse. I tried to get up, the right side of my body felt like it weighed 300 lbs. We called the neurologist and he met us in the ER. He did some tests and seemed worried. He decided that I should stay in the hospital for a few days and take IV steroids, salumedrol. He also thought that I may still be leaking

spinal fluid and should have a blood patch, and more MRIs. While I was in the hospital he got the results of my Spinal tap, No M.S. But that did not help tell us what was going on. They took me to the O.R. and did the blood patch, YUCK!!!! And then off to MRI to do more MRIs and a MRA to check for stroke. Lesions still there but nothing else. After four days I still did not have the use of my right hand. Two days after I got home I started to swell. I though I was having a reaction to something, but did not know to what. As I swelled it felt like every cell in my body was exploding. I called the Neuro just to have him refer me back to my PCP. They wanted to see me first thing in the morning, but that meant still getting through the night. I should have gone to the ER but instead just sat up all night. I felt like I had been hit by a Mac truck. When I woke in the morning I looked like I had the chicken pox, but I could finally move my hand. My stomach hurt pretty bad but I thought it was just from the swelling as everything else hurt as well. When I got to my PCP's office she did an exam, made an appointment for me with a dermatologist for the rash and to top it all off she explained that the stomach pain could possibly be from the steroids. I have stomach problems anyway and she was afraid it ripped a hole in my stomach. So back to the hospital for an Upper GI. That turned out OK, no holes. She gave me darvocet for pain. That to go along with the bag of Meds I already had from the Neurologist: Fiorocet, imitrex, erogot, Noratryptoline, Inderol, and midrin. I am a walking pharmacy. Now I add Zantac back to my list.

My Neurologist thought it would be a good idea for me to get another opinion since he was still not sure what to pinpoint everything to. So I took my MRIs and records to The Medical College of Virginia (MCV), to the Neurology department. There I was examined by three students, one resident and one fully certified physician. After two hours of questions and following pen lights they finally looked at my MRIs. The doctor turned to everyone in the room and said "Do you see it?" I felt like a lab rat!! "WELL" he finally gets back to me "The good news is you don't have M.S., the bad news is I think you have Lupus"? When will this nightmare ever end??????? It took a while to let this "new" diagnosis set in. Then to organize it in my mind as to how they could go from one end of the spectrum to another. I started to do some research and it seems that Lupus and M.S. have a lot of the same symptoms. Even the treatment is the same. Change your diet, get more exercise, take steroids when you have a "flare." Someone at work recommended a Rheumotologist and I made an appointment. He is known for having the longest living Scleroderma patient and very well respected in our community. Unfortunately it made his ego quite large. He, like ALL the other doctors spent a great deal of time with me during the initial evaluation. He ordered his own round of blood work and checked all my joints and muscles. He told me to bring my husband with me for the follow-up because he wanted him to understand EVERYTHING that was happening. A month later we found ourselves in the exam room with the doctor telling us that as far as the question of Lupus goes my SED RATE was OK so we should talk about something else for now . . . Fibromyalgia. I sat there for a half hour and only heard about 3 words he said. Rub here, Rub there, get more exercise, see me in a month . . . Now this time I am sure I was losing my mind!! I have to be, that is the only explanation for what has been happening to me the past few years. I went back for the follow up and with a list of questions. None of which were answered. He seemed uninterested in the Neurological things that were happening. I was worried about this happening in public or while I was alone with my son, what would happen to him??? Then it happened. I picked him up from pre-school and wanted to buy him a new pair of shoes. I was carrying him because it was a busy parking lot and he is very active. We had to walk up about 5 concrete steps to get into the shopping center. On the second step my right foot just "disappeared" and down we went. His back slammed into the concrete as did my right knee. He's screaming, I'm dazed and hurt and people are running at us, out from the stores. This has to be a nightmare. I shut my eyes and tried to wish it all away. It didn't work. We finally got up. His back was OK, just a little scrape and a lot of scared. I looked around and could not remember where I parked the car. Then I saw it but it kept getting farther and farther away. My heart raced and I felt cold sweat just pouring out of me. An anxiety attack on top of it all. The doctor heard none of this. He said "perhaps you're not getting enough sleep . . . he handed me a prescription for Flexeril and Ambien . . . "see me back in a month or two". I wanted to scream! I finally sought out a counselor and saw her for about 6 months, once a week. It felt so good to be told that I wasn't crazy, I really needed to hear that. It also felt good to be treated like my problems were important. She never once said the old "it could be worse, you could have X, Y or Z." She was just as appalled at the way I had been treated and shuffled around from doctor to doctor, none of them taking into account the other's findings. She helped me come to terms with things I already knew, but could not except. There is no going back, I can't turn back the clock and

not take Lupron, it's already done. There most likely is no cure for what is wrong with me, but there can be peace. It's just finding a way to obtain it. She gave me the courage to do my own research and ways of reaching out to others who this has happened to. She helped me find my voice. Now I am able to share my story, this story, with others and possibly prevent this from happening to someone else. This is my path to peace. Through this search I have found that My illness is probably not M.S. or Lupus . . . but something else, something somewhere in-between. I have begun seeking out other doctors. Ones to help me deal with the pain I have daily. Most of my physical pain is on the right side. There are signs of Arthritis in my neck, right hand and elbow and right knee. I also still see the Neurologist to keep an eye on the lesions and help with headaches. I see a Neuro-opt, one of my Neuro's partners to keep track of the Neuropathy and Adie syndrome in my right eye. My husband has been VERY supportive. He bought me this computer to help me research. He has gone to the library with me and tries to find contacts who may be able to help us. He kept me grounded when I found the information on the NLVN. He was with me when we brought all this to the attention of my PCP and was told by them that "the only way for the medical community to know these things is when a group of people search each other out and find that they have the same problems and the only common denominator is a certain drug . . . in this case LUPRON." He filled out my FMLA stating that this all started when I unknowingly got myself involved with the FDA's phase IV clinical trial of LUPRON. I did not know until my own research that I was part of a clinical trial. I never signed a consent for this. I am just a sure that the doctor who gave it to me NEVER filled out the MEDWATCH forms or reported any of my problems with this drug. I called TAP in the beginning just to see what they would say. I asked if they were going to do any long term studies on Lupron. They told me "Maybe in another 20–25 years, look how long it took them to find out about DES." I can't wait that long. For now I will continue to spread this story to as many people as I can. I will continue to have a battery of tests done every couple of months. I will continue to try to find doctors who have some answers. I will continue to take various combinations of medications to try to keep my illness as stable as possible. I will try to continue to be the best mother and wife as I can be. I will continue my search for peace. . .

To those of you who made it this far in this story and are facing problems from taking Lupron, please know that you are not alone in your fears or concerns about what this drug has done to you. There is a lot of information out there and a few very good sources of support. If there is anything I can do to help you, just ask!

There is info available on Medscape and from the National Library of Medicine at pubmed. Dateline aired a show on Lupron on January 2, 2000. They interviewed 9 women who all have permanent damage from taking Lupron. One of those women, started a website to offer support: Julie's After Lupron Forum I believe 8 of the 9 women post there as well as many, many others. There is also a petition: Lupron Petition. Kay Lazar, a reporter for the Boston Herald, wrote a 2 part article on our Lupron Damage in August 1999. If anyone would like the links or the articles, just ask. Until we find a lawyer who will take our case our own stories are the most powerful tool we have.

If you have not taken Lupron yet and are trying to decide please do your research before you do anything that could alter your life forever. I know that Endometriosis is VERY painful. I still have it. I know that pain can cloud our judgment. The promises of a Painfree period of time. The HOPE it brings to be Painfree is a very persuasive reason for taking it. Please do not take what I have said lightly. I am not the only one. This is only one story, I am only one person. All I ask is that you search. Search your heart, your mind and weigh the price of your soul . . . .

Good luck to all!

Adendum

It is now July of 1999 and some things have changed for me since I ended this story. But of course, there really is no end . . . My husband was offered a promotion that could not be turned down. We moved to Orlando, FL in February of this year. We are now settled in our new house and my son has started in Montessori school. Before we moved I asked for recommendations for a GYN and have found a really good one. I had stopped taking Depo Provera in January of 1998, in hopes of having another baby. It took 14 months for my period to return. And it came with vengeance!! My Endo pain has been increasing every month. I told my GYN at the first visit my problems from Lupron. He had me start taking Prenatal vitamins to boost my immune system. He also referred me to a Reproductive Endocrinologist. We have met with him once and his acknowledgment of my Lupron trouble has been the best I have received. He added more B–6 and evening primrose oil to my list of meds. The bad news is he has diagnosed me with secondary infer-

tility. He does not think I am ovulating at all and when he did an internal sonogram he did not like the looks of my ovaries. I will have an HSG next month and possibly start fertility drugs. His biggest concern with these meds is that they DO make Endo worse. They are all high in estrogen, which most of you know feeds the endo. He is also concerned about what other antibodies Lupron may have caused me to develop, so I will be tested for those soon. My pregnancy, if it happens, must also be followed by a Neurologist. I have an appointment with one soon. Basically I am starting from ground 0. Being a "new" patient, filling out endless forms, explaining my condition(s) and it's cause, hoping they believe me or at least understand. Not to mention waiting MONTHS for that new patient slot to open up.

It's now the end of August. I've had the HSG, it wasn't good and it hurt like Hell! He was able to force the Dye through. I emphasize "force." Rob and I have talked and all this pressure to try and get pregnant has been wearing me down. It's felt like something I have to do, like having to do the laundry or dishes. The reality is we don't know if I am even healthy enough to have another child. My Endo pain is controlling me right now. I can feel it building up on my bladder. It hurts to pee and I feel like I have to go all the time. I went and had a check for a UTI, almost hoping that is all it was . . . no such luck. I am going to go with Lap #3 and see how I feel afterwards.

November 10, 1999

I am now almost 2 weeks post Laperoscopy. DR found more Endo and adhesions. Also said my uterus was VERY red and not the color of salmon it should be. He also said my right ovary spasms when he touched it. I know that sounds kinda gross . . . Well, I don't know what any of this means just yet. My follow up with him is on the 15th. I am not recovering as quickly as I should. I can't seem to shake the "flu" like symptoms and fatigue. I had a few complications after surgery. My blood pressure dropped and heart rate dropped very low. They had to keep waking me up. Plus I had trouble peeing. Don't understand why it never occurred to them that I might have a UTI since I had a low grade fever and pain. The pain meds they were giving me came by the way of hip injection. Well, one struck a nerve and now my leg feels like I have a HUGE gaping wound in it. It hurts to shave. Supposedly this will slowly go away. I hope so!!! I am not feeling well today! I am nauseous and my stomach hurts, right around my uterus.

I have received more published articles on Lupron. Two from the Boston globe from 1996. It details two women taking Lupron for infertility and it caused hyperstimulation of the ovaries. They both almost died. The others are from the HERS foundation from back in 1989–1990. The founder of this group had all the research info on Lupron prior to it's approval. She has proof to show that they knew of the dangers of this drug before it got approved. She also gives her strong opinion that Lupron will turn out to be worse than Thalidomide or DES ever was. For my son's sake (he is a post Lupron baby) I pray to GOD every night that he is spared! It is bad enough that he got me for a Mom.

November 20, 1999

Had my Post op on Monday. It didn't go so well. Since he was unsure about my uterus he took biopsies of it in different places. Turns out it is ALL Endo with the added probability that I now also have Adenomyosis. This is when Endometriosis is found embedded in the uterine muscle and the ligaments that attach it. He feels bad for second guessing and not removing what he could. I am still kinda numb and don't really know how to react to all this. He also showed me a cyst he ruptured and the "redness" where all the nerves are hyperstimulated from the endo and told me I have some PCS (pelvic congestion syndrome). This he explained is from an injury to the uterus. Most likely from delivering my son. I will start continuous BC Pills for now, try to buy some time while I sort through all this.

June 2000

Had another appointment with the GYN. I wanted to see the pictures again. UGH! All that endo still there. So far the Continuous Loestrin Fe has been helping. At least as far as no added ovulation or period pain. He brought up the "H" word. He wanted to tell me what his thoughts on it are. Wanted to tell me that he has turned women away because he did not feel a hyst was the right choice for them. He says he does NOT believe in just yanking out a women's organs. Then he said whenever I was ready, so was he. . .

November 2000

Here I am one year post op and all was going relatively well until I got home from a long summer vacation. Apparently at some point during my long trip up the east coast I got bit by a deer tick and developed Lymes disease. I have spent 5 of

the last 8 weeks on antibiotics. I still have Lupron to thank for my poor immune system. It makes everything so much harder to fight. The lymes got into my joints and I have a stress fracture in my rt foot. That pain started 3 weeks ago. Then to top it all off the antibiotics weekend the pill enough to cause some severe pain. After being in bed for 2 days with a migraine my neurologist called in some vicodin. Rob picked it up for me and my plan was to take 2 and hop in the tub for a good long soak. Except that as soon as I actually go up the pain began. By the time I knelt to start the water I knew I was not going to get back up. The pain took my breathe away and I could not even yell to Rob for help. Zak found me on the bathroom floor whimpering. I HATE that he saw me like this. I hate even more that he had to come with us to the ER. Odd but in all my years with endo this was my first trip to the ER because of it. It took 2 shots of demerol to calm me down and be able to tell them what was wrong. When someone came in to check my uterus, I think I could have kicked him into the next room! The pain was incredible. They gave me another shot before sending me on my way. Nothing they can do for me there. I went to see the GYN the next day and the word Hysterectomy was tossed around again. He gave me more pain med and told me to return in 3 weeks. WELL I'm not going to make it to 3 weeks. Zak came into my room 2 nights ago looking for the dog and when I got up to help him the pain started again. This time the pain was alone. I made it to the bathroom in time to pass a few large clots and am still bleeding today. I have an appointment Friday morning. . . . If I can just make it through the holidays. . . .

Jan 2001—Another Laperoscopy only reinforces Pelvic Congestion and Adenomyosis is worse. A hyst is unavoidable and Dr. doubts I will get much relief.

November—Have Ovarian Vein Embolization. DO NOT Recommend!!!! AWFUL procedure! 7 hours, through Jugular, AWAKE no less. . . filling left ovarian veins with Coils, Balloons and glue. . .

This procedure caused MAJOR pain and problems. Large Endometromas grew in left ovary. At scheduled Ultrasound in January they have ruptured. Talk about pain!!! Dr. does not know what to do. For the first time he is at a loss for a plan. My endo is beyond his capabilities. There is more to it but I'm running out of room.

March 2002—Fly to California to see Dr. Andrew Cook. . . I honestly believe this man saved my life. I had a hysterectomy and Bowel resection. He FULLY understands all problems from Lupron and did a LOT of testing for problems he is aware of. Specifically Allergy related. . . I am allergic to ALL my hormones and 6 of 9 foods tested for.

This Doctor was amazing! WWW.PELVICPAIN.COM. . . now if I can get the rest of my pain under control. . .If my hands could stop hurting for just one day. . . Or my head . . . That would be really nice! I am actually not sure what I would do with no pain in my life. I have lived with it for so long now . . .I do NOT remember what it is like to live without pain. Maybe someday. . .

PREPARED STATEMENT OF MELODY HAMPTON

My name is Melody Hampton. My testamony is part of the testimony Lynne Millican gave to the Senate Subcommittee. I would like to add a few things. I am now 44 years old and I feel 94. I am sick all the time and a lot of days I just hardly can move due to the stiffness and pain in my body. I ask you to please do what ever you can to stop Lupron from being put into anyones body. I do not know what can be done for us who have the drug in our bodies already, but please don't let others be hurt like this. I will die knowing Lupron ruined my body and my life as I knew it. For me not to plead for others would be a sin. Thank you in advance for your efforts.

PREPARED STATEMENT OF SUSAN HAYWARD, LAKE HAVASU CITY, ARIZONA

My name is Susan Hayward and I moved to Lake Havasu City, AZ two years ago from Massachusetts where I was born. In 1997 at the age of 42, I became disabled from the U.S. Postal Service. I have been receiving Social Security Disability Payments and Disability from the Office of Personnel Management under the FERS program. I worked my entire life up until the point where I became disabled, 28 years straight, with the last 10 with the Federal Government. I had a great job with a private office making good wages. It was a career and I planned to work there until retirement in my 60s.

The reason I am writing to you is because I want to offer my experience with the drug Lupron to bring awareness of the harmful side effects of this prescription drug. In my situation, I was administered 19–20 injections of Lupron as treatment for

endometriosis. The recommended dosage is 6. When you examine marketing techniques of the manufacturer, Abbott Laboratories and Takeda Pharmaceuticals, TAP, then you can understand why doctors continued to prescribe the drug. Samples were offered to physicians who were able to bill patients and insurance companies for hundreds of dollars. The total for my prescriptions is approximately $7,000 alone. Two doctors gave me my injections and they had something in common; both had me skip going to the pharmacy and they obtained the drug for me. When I first started using the drug I had to purchase it like any other prescription. Later, I believe I was sold prescription samples. The kickback schemes involved with TAP and physicians are well documented in the litigation resulting in the largest fine in U.S. History against a drug company. We are all paying the price for this so TAP and doctors could profit.

Please think for a moment about the costs of lost productivity from my being disabled: approximately $900,000 disability costs being paid by Social Security and the Federal Retirement Program. Factor in the increased insurance premiums from hundreds of thousands in medical bills from hospitalizations, surgeries and tests. None of this considers the personal loss of my Thrift Savings Plan, the loss of contributions to the economy in commuting costs from using an automobile to buying lunches, or what this has done to me physically and emotionally.

My motives are not monetary. I simply want to warn other individuals how dangerous Lupron is so they too don't become ill or disabled. I feel that my life has already been ruined, but perhaps I can help another person from having their life destroyed. Against the advice of lawyers I went public with my story in the Boston Herald in 1999. By publishing my story I could compromise any future legal case, but it was too important for me to warn others.

I have written to Hillary Clinton when she was in the White House, Senator Ted Kennedy, and my local State Representative in the past. My understanding of such abuses TAP makes is that individuals hide behind the guise of a corporation and are not accountable, all in the promotion of capitalism and profit. If one of those people at TAP thought they'd go to jail for selling poison to the public, they wouldn't be marketing this drug. There is a history in this country of exposing the public to dangerous drugs, pharmaceutical giants making huge profits with full knowledge of the harm they are causing, and by the time litigation catches up with the profiteers they have bailed out and reorganized. The paltry settlements offered through class actions are eaten up by lawyers and never truly compensate the victims for the amount of damage. The pharmaceutical lobby in Washington, DC is quite powerful and has strong influence over political voting. Understandable when you consider how much money they've made from all the profits. Who is watching out for the citizens when you have this dragon to slay? The FDA has done little to help claiming there is no other drug available that will do what Lupron does. My firsthand experience is that I would rather suffer with my initial diagnosis, endometriosis, than what this drug has done to the rest of my body and life. What I believe is that TAP will not stop selling Lupron until it no longer is profitable. The only way to make it unprofitable is through a barrage of litigation or a huge class action suit. But TAP has even found a way around that. All the successful lawsuits against TAP brought on behalf of victims for the damage it causes are SEALED with secrecy agreements. This makes it that much more difficult for victims to argue a new case and delaying a class action. If we can't find out what constitutes successful litigation then we get stalled, the statute of limitations runs out, lawyers don't have the resources to start a class action, and all these victims linger in silence. Unlike other pharmaceutical lawsuits where there is a direct cause and effect, i.e., Fen-Fen and heart disease, Lupron causes a syndrome with a host of symptoms that are very easy to blame on something else and difficult to prove. The ailments often don't show up in tests until much later if at all, so we get grouped into garbage diagnoses such as chronic fatigue, fibromyalgia, and degenerative disk disease. TAP continues to create more profits and victims with few obstacles.

Please consider who the people are that are using Lupron and how TAP has consistently tried to find new ways to market it. Originally it was developed for men with late stage prostrate cancer. Any cry of foul play would be discounted by this group because "they are dying anyway." Who knows how many of these men suffered more problems than they already had and nobody listened. Women desperate to have a baby were given Lupron for invitro fertilization. Many were so happy to finally have a child that they overlooked the health problems these children face. TAP decided they could use it for treatment of endometriosis. It doesn't cure it and causes a rapid regrowth once it's stopped. Like myself, most of these women are suffering with incredible pain and having to fight to receive the proper treatment, painkillers and surgical excision requiring a skilled surgeon. Fibroids temporarily shrink in some cases but still need to be removed. If they aren't there is rapid regrowth.

Lupron only postpones the inevitable so why are they giving it to us? The FDA claims there is nothing else doctors can offer. TAP says we need it so they can profit. It doesn't make sense if it doesn't help, and it actually causes us harm. Precoscious puberty is being treated with Lupron with younger victims without the opportunity to gain an education before their memories are compromised. The memory problems can best be described as Swiss Cheese, neither long or short term, more like holes with total blanks. It is my understanding this is some form of seizure where thought processes are interrupted mid sentence and you draw a complete blank. Sex offenders are given probation if they take the drug as a form of chemical castration. The majority of the public hold sex offenders with disdain, so who is going to be looking out for their interests? Are there other markets for TAP to sell Lupron? I assume they are lobbying for cloning so they can sell more in IVF to harvest doner eggs. With each new group of users it lends credibility to the use of Lupron i.e., they've been using it for years to treat prostate cancer so it's safe for treatement of endometriosis. In reality, it should not be prescribed for anyone who isn't terminal, and then only as a last resort. That's what it was developed for and that's the only way it should be used.

As a way to offer greater understanding of what Lupron can do to someone's life, I'd like to offer background on my situation and illustrate the difficulties this drug has caused.

Like many people in this country, I was born into a lower middle class family. There were difficulties in my parents' marriage and I ended up being raised by my grandparents with 3 siblings with help from public assistance, or welfare. This humbled me a great deal and I learned a good work ethic early. We were raised with strong morals and religious background.

My whole life I aspired to be a success and have a normal lifestyle. I knew education was important and had planned to attend college after high school, but the year I qualified for a free college education was in 1973 when Richard Nixon cut the welfare bill. A lot of hope went away when that happened but I started working and eventually went through college attaining my Bachelor's in Business 10 years later and even took a post graduate course at Harvard. I worked full time during those years with the exception of one when I was writing my thesis, and worked part time instead.

Upon completion of college I decided on a career in the U.S. Postal Service. I was very proud to work in the largest mail processing facility in my area. We were voted #1 in the country for customer satisfaction and I met the Postmaster General. There was a tremendous sense of pride for all the employees but with me, it was even more so because I tied a lot of my sense of self esteem and worth in with my job and accomplishments.

A few years into my career I applied for a managerial promotion and wasn't awarded it. The person who received the promotion had a high school diploma and military background as a prison guard in the Coast Guard. The next several years I endured extreme stress at the hands of this professionally jealous supervisor. I sought assistance from the American Postal Workers' Union, higher level management including the Plant Manager, EEO, and the Employee Assistance Program. By the time I was allowed to report to a different supervisor, I had developed endometriosis.

What followed was years of pain and surgeries. I needed my job in order to support myself and lived in fear that I would not be able to maintain the schedule from illness. I sought treatment in Boston at University Hospital, now a part of Boston Medical Center. I assumed I would receive the best care with the newest techniques. The doctor who treated me was well known for his research and after a few months and diagnosis, placed me on Lupron. Between October 1992 and October 1997 I received 19–20 injections of the drug from my doctor in Boston and my local gynecologist. Both doctors knew of each other and the number of shots I was receiving. Instead of finding a solution for the pain the doctors would put me right back on Lupron until the bone loss was too great.

People ask me how I could allow the doctors to give me so much Lupron. It's a multifaceted issue. From my background you can see that my sense of self worth directly correlated to my accomplishments at work. I struggled to get myself educated and gain a career. It took many years for me to attain the level I was at and I was in the career I chose to be. This was my lifelong plan and goals. How could I maintain that if I was always sick? I had to do everything I could in order to keep working for the financial and emotional benefits. Eventually it got to the point where I could no longer do it. Later on I was diagnosed with post traumatic stress disorder.

The main symptoms that I attribute to my using Lupron are the vertibrae bone loss diagnosed as degenerative disk disease, arthritus, myalgia, bone pain, fatigue,

swelling in hands and feet, severe allergies, nausea, weight increase, severe memory loss, vision changes, sleep changes, rapid heart beat, and abdominal pain. During the first doses of Lupron I developed panic attacks which I never had. The first few years after using Lupron I had horrendous migraines. Before I took Lupron I had none of these conditions; I was a normal woman in her 30s with endometriosis. After taking Lupron, I don't go a day without pain and am under constant doctor care to control pain and autoimmune problems. I left my home and moved to Arizona where I didn't know a sole so I could get relief from the arthritus problems. It was worth the chance that maybe I could gain my health back and be able to work again. That is all I've ever wanted when you consider where I came from.

I'd like to outline the frustration we Lupron patients suffer at the hands of the medical establishment. The symptoms and diagnostic tests don't always show what we experience and often we have to be tactful in how we approach doctors. If you mention Lupron sometimes they brush us off because they know it's a bad situation and fear being dragged in a lawsuit. What's the alternative, not tell them? Others dismiss you like you are making the whole thing up in your head like a hypocondriac. In 6 years of dealing with my health problems post Lupron, I have yet to find an MD who believes my problems are caused by it. You don't take a healthy woman in her 30s to a woman with a host of medical issues in her 40s by endometriosis alone. Stress didn't cause my back to become herniated in 3 places. I didn't move to Arizona for arthritus relief because I don't have it, but that's what my tests say. The total lack of support from the medical profession is appauling, and there are thousands of people who need this documented. We need to know which tests to have, the proper pain relief medications, what we can do to help ourselves. Right now all we are doing is muddling along trying to help each other and most of us have no medical background. I attempt reading studies and biology reports that I struggle to understand because I know there are answers. Isn't that what we pay doctors to do? We don't all become doctors because we get sick, but that's what we are expected to do when it comes to Lupron.

The other side of the equation is the legal establishment. I've contacted half a dozen lawyers and they all say the same thing; without a doctor saying your problems are directly related to the use of Lupron, you don't have a case. This is a need for an expert witness. It costs thousands to hire one. Most of us don't have the resources and law firms won't proceed without the guarantee of a positive outcome in the case. Another issue is the recommendation of only 6 doses of Lupron during the course of a lifetime. I had two doctors who ignored that and when presented to a lawyer they said it's a matter of opinion regardless of it being in the Physicians Desk Reference. That attitude has resulted in people like me with multiple injections over the course of years. Patients have no recourse and doctors don't face any consequences. With all the sealed verdicts and secrecy agreements, it makes it very difficult to obtain legal representation within the window of opportunity the statute of limitations allows. Once a class action does finally open up the lawyers will be looking for a percentage of ALL claims, probably a third of any settlement. Class actions are historically lower awards than a regular court case because there are so many litigants and often they drive the company into bankruptcy. As one lawyer put it, you are likely to receive a dime on a dollar. Class actions have administators too and they also take a portion. The true victims in these cases rarely get compensated for what they endure, while the tag-a-longs get rewarded handsomely. My feelings are to forget the money, let's stop poisoning new people, but that won't happen without TAP feeling the financial pinch.

I have mentioned what this whole experience with Lupron has done to me physically and the frustrations I continue to endure with the legal and medical professionals, but I want to stress what this has done to me personally. Yes, I lost my career and am disabled, but more than that it has robbed me of any faith in our system of justice and what is right. How disheartening do you think it is for me knowing they are poisoning innocent teens because their bodies are developing too quickly? I worry so much about other people and what will happen to them knowing what this has done to me. How can everyone turn a blind eye to what is going on here? Do the lobbyists hold that much influence that people toss their morals out the window? Isn't that why people go into politics to begin with, to make a difference for the good of all? I know in my heart there are caring people in this world who just don't understand this situation with Lupron. I want as many people to know about it as possible so they can warn people not to take it, and hopefully someone will become motivated enough to do something to help the ones like myself who are just too sick to do anything about it.

Also on a personal level, I enjoy travel more than any other passtime. Now I can no longer carry a bag or wheel a suitcase because my back can't sustain it. I was lucky enough to visit Europe before I stopped working and at the time, I kept think-

ing I better go now while I can. Thank goodness I had the insight to know to go when I did because I could never travel long distance again. This is the most enjoyable aspect of my life and now it's gone caused by the bone damage Lupron gave me.

The most frustrating aspect of this whole situation is the fact that people have known about this for a very long time. I uncovered data published in 1990 warning about Lupron and feel it is important to incorporate it into this letter. It is obvious to me that the FDA is not protecting the public. TAP continues to find new ways to market this dangerous prescription drug and the doctors don't delve into it deeply enough to understand exactly what it does to our pituitary gland, hypothalmus, and adrenal systems that make us have problematic autoimmune responses. The economic costs will be catastrophic with millions of victims should this continue unbridled. It will make my loosing my Thrift Savings Plan look like a drop in the bucket.

In closing I'd like to express my appreciation for you taking the time to listen and showing interest. We need caring individuals to take a stand against this multi-national corporation harming us so more people won't suffer. I am sincerely grateful for anything you can do to help.

PREPARED STATEMENT OF MELANIE WALDMAN

I am one of the women named in the testimony about Lupron. I am not looking for a lawsuit, reparations, etc., I just beg that someone does something to stop this drug from being used without more information to all parties.

Before taking the spray version of Lupron (synarel) I was an architect and able to work full time. Since my health was destroyed by this drug I have not been able to work. I am fortunate that I am married and that my husband is able to support us on his salary. I am also fortunate that his health insurance coverage allows no more than 1,000 dollars out of pocket expenses because without that we would never be able to afford the IV treatments for the resulting joint pain that keep me functioning at all. I also know the drug is commonly used off label for people like me who suffer from endometriosis. (the ironic piece is that I'm used to it hoping to increase my chances to get pregnant and it destroyed my ability to carry a pregnancy, I am also lucky that we were able to afford to adopt a child) yet Doctors are not aware that so many of us have horrible permanent side effects. It seems like this issue falls throughout the regulatory cracks. The FDA has not approved it for this use, the manufacturer promotes it but is not responsible for its off label repercussions and the Doctors. have no way to find out the facts.

In a time with more important issues like war and the economy, I am sure this issue doesn't seem pressing, but I ask that you do your best to see that something is done to prevent more woman from being needlessly harmed.

PREPARED STATEMENT OF LISA A. PLANTE, FORMER U.S. CONGRESSIONAL STAFF PERSON

My problems with Lupron started when I was wrongly diagnosed with endometriosis (all I had was adhesions) I was suffering from years of pain with adhesions attached to many internal organs. After many surgeries due to cysts I still experienced much pain.

I asked a young doctor (OBGYN) to please make me better so I could live normally, enjoy my family and 2 children. This particular doctor said I would have to try Lupron before he did anything invasive. I was never properly diagnosed with endo before my injections of Lupron but was absolutely desperate to get better and decided to trust this doctor's advice.

Immediately after having the first injection of Lupron I experienced terrible bone & joint pain, chest pain, depression, insomnia, foggy brain. . . etc., the doctor said it would be temporary and to stick with more monthly injections..

I questioned doctor prior to Lupron injections on a pamphlet an organization (NLVN) was leaving in libraries that a friend had given me. The doctor asked to keep the pamphlet and told me not to worry that it was probably a competing drug company. I spoke with people who warned me of Lupron but thought they were spewing lies for one reason or another. I decided to trust my doctor in thinking he would never give me something that would harm me. I desperately wanted to work with him in getting me better and took 3 more injections of Lupron.

I was encouraged to take more injections of Lupron but abdominal pain was unbearable plus the side effects . . . this was a nightmarish time. . .

The doctor and his partner decided to take out my only remaining ovary plus the adhesions. After adhesion removal, I felt better in the abdomen but continued to

have bad side effects from Lupron. After 8 years, I still have bone and joint pain, foggy brain, chest pain, bloating . . . My teeth have thinned out tremendously, hips hurt, arms & joints are weak and sore. I do excercise a little, which helps some but feel like a very old lady at age 46.

I don't think the doctor meant to cause me any harm and realize the constraints of many doctors these days but to give this drug out to just anybody is not a good idea. I especially don't think it's good to use in helping women's fertility! My gosh, where is the common sense?

dates took Lupron:

Lupron Depot 3.75 kit TAP—1/20/1995
Lupron Depot 3.75 kit TAP—2/27/1995
Lupron Depot 3.75 kit TAP—3/29/1995
Lupron Depot 3.75 kit TAP—4/28/1995

PREPARED STATEMENT OF J. WOLF

Dear Senator,

I was given your name by someone who is aggressively trying to help those of us who were poisoned by Lupron, I appreciate you reading this, my experience with this drug. I went to my doctor complaining of cramps, I was told to have an exploratory laparoscopy, when this was completed, I went back to the doctor and was told I had endometriosis. I was a little mystified since that is related to infertility and other symptoms that I did not have but he was my doctor and I had no reason to doubt his findings. He prescribed Lupron injections and told me it was a safe drug and I would only experience mild menopause symptoms with the loss of my menstrual cycle but all would return to normal as soon as the injections were stopped so I began them Sept. 1996. I returned to his office for monthly injections until Nov. 1996, when I began to complain of worsening pain, the injections were stopped and I became worse. I repeatedly went back to the doctor sometimes doubled over in pain (which was not there before Lupron). He did another laparoscopy with no findings and I was then sent to a gastroentologist for which he referred me also with no findings from the endoscopy and colonoscopy he performed, I kept going back in major pain (not present before Lupron) He then started to patronize me insinuating this was a women's problem and maybe in my head and suggested I go get the nerve in my gut cut, in other words, let's stop the pain without finding the cause, I began to doubt this doctor, I requested all my medical records from his office and to my shock found that the laparoscopy he performed before Lupron showed NO endometriosis and neither did the biopsy! By now it's the end of 1997 and I'm suffering to no end. I realized I may have been used for this experimental drug on women and I believe it was because of my insurance that I was placed on this drug, had I not been able to afford it I don't think I would be suffering right now. I took matters into my own hands and started all over again seeing a different set of doctors, I went through a series of tests all over again when a doctor suggested I get a nuclear stomach emptying test. This test showed an extremely delayed emptying (normal stomach is less then 60 minutes and mine was 500 minutes!!). I finally had a diagnosis to go with the pain, I saw several doctors that took several more tests and I was told I had gastroparisis (a paralyzed stomach). With research and many questions I learned that this does not go away and I'd have it for the rest of my life, I knew Lupron did this to me because I never had stomach problems before Lupron so I requested the test again a few months later, my theory was since Lupron did this to me perhaps as it leaves my system I will improve, I was right 4 months later it was better, I repeated it a total of 4 times in two years each getting a little better as the Lupron was further from my system, I began to research Lupron and to my horror found it was used for prostate cancer and on sex offenders to castrate them, I was not told this by my doctor nor was I allowed to see the paper work accompanying this drug because it was giving to me at the doctors office. Given these facts I would have chose NOT to take this drug, I was deceived in the worse way possible first by a doctor who gave me a drug with no known medical diagnosis and then by the drug company for not disclosing the facts, side effects, uses, ect. . . , I am left with a stomach that will never be the same, my personality has changed, I have weight issues that I never had before, with a paralyzed stomach the food just sat there for days causing my gallbladder to become so infected I had to have it removed, I had doctors tell me I needed a hysterectomy and almost removed all my women parts for no reason, I had a doctor tell me to get the nerve in my stomach cut to "shut me up", my hair has fallen out, my menstrual cycle is now painful, I have fits of rage from my hormones being sent into overdrive and suffer from major depression, I was basically castrated myself because Lupron has

murdered my sex drive. I am not the same person and know I will never get back the person I was before this poison, I want help, I need help, This drug is a danger and it shouldn't be given, The drug company needs to be held accountable for the pain it caused and will cause in the future. I only hope you can do something because as I understand a new generation of Lupron babies will be popping up soon as the gynecological field is pushing this drug to desperate infertile women without knowing the ramifications of it's use!

Thank You,

PS: Please be advised I have my test results and all records proving everything said in above statement.

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