

Testimony before the House Subcommittee on Criminal Justice, Drug Policy, and Human Resources

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Wednesday, May 15th,
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Introduction

I am a Reproductive Specialist and Scientist that has dedicated the last 24 years of my life in helping infertile couples have children and complete their biological cycle (see Attachment). In January 2001, we have announced the possibility of using reproductive regeneration technologies as a means of treating infertility, and our intention to develop these technologies in a safe and responsible manner. However, we have received great opposition from fellow scientists, news media and the general public. It seems that the great opposition is due to the lack of complete understanding and comprehension of what in actuality human cloning really is all about. The British Medical Association however, has so appropriately stated: "Public hostility to human reproductive cloning may be based on an illogical transient fear of a new technology". Much of the confusion is caused by the variance in opinions coming from different scientific sources, politicians, news media and Hollywood. Due to the limited knowledge of these technological and medical procedures in the Scientific Community, we have organized, hosted and attended meetings involving scientists from all over the world to discuss and debate the issues of human reproductive regeneration (1). We have even presented our intentions before the Congress of the United States last year.

Do You Care About Infertility?

Infertility affects approximately 10-15% of couples of reproductive age throughout the developing world. Assisted Reproductive Technologies (ART) have played a major role in treating various causes of infertility. In fact, about 65% of the couples who seek medical help will eventually succeed in having a child. However, in cases where there are no sperm or eggs present (possibly due to loss of testicular or ovarian function), the only options these couples face are sperm donation, oocyte donation or adoption. These are difficult choices for couples to make and many do not want to use sperm or egg sources other than their own or do not wish to consider adoption. Reproductive regeneration (RR), which is synonymous to reproductive cloning, can therefore play a very real role in the treatment of severe male or female infertility in couples that wish to have their own biological children.

After a lot of time, money and suffering, many of the infertile couples have been able to have children using present IVF techniques. Personally, it has given me great satisfaction to assist them in the creation of their own families. However, some of these infertile couples have not been able to experience the joy of creating their own families because the present technologies are not advanced enough to help them. For them, human reproductive cloning is the only way they can have their own children. As a Reproductive Specialist and a scientist who cares about their plight, I am trying to develop safe techniques of human cloning so they can have the healthy babies they want. Mr. Chairman, am I wrong in wanting to help couples become parents?

If you care about these unfortunate infertile couples, why are you considering legislation that would make both them and the people that are trying to help them, criminals? Criminalizing human reproductive cloning in the United States will only make it less safe and more costly for these infertile couples. They will be forced to travel outside the United States to pursue their dream of creating a family. After all, according to the Americans with Disabilities Act (ADA), infertility is a disability and reproduction is a major life activity for the purposes of the ADA (*Bragdon v. Abbott*, 118 S.Ct 2196; 1998). In light of this, it is the right of each and every American citizen to bear a child.

Cloning cannot be Curbed

Mr. Chairman, experts state repeatedly that history proves the point very clearly that scientists will clone even if President Bush and the Congress forbid it. The House of Representatives may vote against human cloning but that will not stop scientists from doing it and people from wanting it. The American Society for Reproductive Medicine (ASRM) of which I am a long standing member of, recently stated that "thousands of years of human experience have shown us that governments cannot bottle up human progress, even when you want to" and that "there is every reason to believe that if passed, this kind of prohibition would not be effective". In another case made by a infertility patient, who wants her own genetic baby so badly that she would go wherever she had to, in order to clone either herself or her husband "if they called me right now and said, 'We're paying for everything and giving you the chance to have your own genetic child,' I would be on a plane so fast it's not even funny," she said. In the words of a bioethicist "The best way to control this research is to fund it by the federal government, because then you create rules," and in my words Mr. Chairman, this Genie is out of the bottle and it keeps getting bigger by the hour. There is no way that this Genie is going back into the bottle. Let us find ways to develop it properly and disseminate it safely.

Banning human reproductive cloning in the United States will not stop human cloning. In fact, the first cloned pregnancy may have occurred already. If you institute a ban, all that will happen is exactly what happened when the first IVF baby was born in 1978. The United States banned IVF when it first came out and then after several years, decided it had made a mistake and spent the next several years catching up with the technology that was advanced in other countries. The only people that suffered were the infertile U. S. couples who were unable to have children or had to travel outside of the United States to receive these treatments. Let us show the proper compassion for

those suffering American infertile couples. Let us give them some hope and let us not turn our backs on them. They deserve something better than that.

If you are concerned about the risks of human cloning, the proper approach is to fund it and then institute regulations that will insure that human cloning is done properly with a minimum of risk for the baby just as is done in other medical or drug innovations. This is what our team is working on and we will not go forward with human cloning until the risks are comparable with other IVF procedures. Of course, because of the present political climate in the United States, we have been forced to look elsewhere in the world for a proper venue. We have no intentions of doing this in the USA whether any legislation is passed for or against this technology. Furthermore, Mr. Chairman, we have no intentions of breaking the laws of this country or any other country to accomplish this. We are law abiding citizens of this great Nation of ours, but we are a compassionate group of people that wish to help our fellow man and woman have the gift of life. The gift of life that most of us have been so fortunate to have, enjoy and take for granted. Let us not be so uncompassionate and so insensitive to tell those people that we are not willing to listen to them and unwilling to help them. This is not what our Country's constitution and principles are based on. We believe in creating families, not preventing them. In God we trust!

Reproductive Regeneration as a Means of Infertility Treatment

The incidence of developmental abnormalities following natural sexual reproduction in humans is 3% and is significantly higher when maternal age is over 40. As recently reported in the New England Journal of Medicine, the risks are even greater from IVF and other more advanced ART procedures yielding more than 30,000 children per year in the USA. It is vividly clear that thousands of potential parents accept these risks to conceive a child. If human reproductive regeneration is banned as a reproductive technique on safety grounds, then we may find ourselves in the untenable position of having banned all reproductive techniques which suffer equal or higher risks, thereby, possibly even banning natural sexual reproduction with its 3% risk, a situation that the majority of people would consider ridiculous. It appears reasonable to suggest that the incidence of developmental abnormalities as to the safety of human reproductive regeneration is negligible when compared to current risks associated with IVF and other ART procedures.

It is quite evident to us along with other competent human reproductive specialists that with further elucidation of the molecular mechanisms involved during the processes of embryogenesis, careful tailoring of subsequently developed culture conditions and manipulation strategies, and appropriate screening methods, will eventually allow infertile couples to safely have healthy, genetically related children through SCNT methods.

The opponents of Human Cloning or Reproductive Regeneration

The most prominent opponents to human reproductive regeneration and spokesmen for animal cloning are Drs. Ian Wilmut from the Roslin Institute and Rudolph Jaenisch from the Massachusetts Institute of Technology (MIT), who have misled and have misdirected the public and its leadership

for their very own gains, whatever those gains might be. They have repeatedly stated that the application of animal cloning technologies to humans, is extremely dangerous, not because of ethical and social implications, but because of the foreseeable possibility that cloning humans might result in a very high incidence of developmental abnormalities, large offspring syndrome (LOS), placental malfunctions, respiratory distress and circulatory problems, the most common causes of neonatal death in animals (2). They also noted that the rate of success as an ART method is extremely low, being only 3%. Furthermore, they state that because since the production of Dolly the sheep in 1995, they have not improve on these technologies themselves, they have concluded that reproductive regeneration is not safe and efficient for use in humans, and would like for the world to believe this. Let us examine the facts as they appear.

If one reviews the animal cloning literature, one can deduce that the poor cloning success rates noted by the "animal cloners" are mainly due to experiments that were (i) poorly designed, (ii) poorly executed, (iii) poorly approached, and (iv) poorly understood and interpreted. These experiments were mostly done under non-sterile and uncontrolled environments and having a "hit-and-miss" type of outcome. Also, when the cloned animals died, no clear view of their cause of death was ascertained. In short, their experimentation methods lacked the seriousness of purpose that is vital when performing similar studies in humans. Furthermore, the same scientists responsible for Dolly, the sheep, now plan to utilize similar crude technologies to experiment on cloned human embryos for medical purposes.

According to a recent article in Time Magazine (3), Wilmut and Jaenisch stated "animal cloning is inefficient and is likely to remain so for the foreseeable future". On the contrary, a number of studies have already demonstrated far higher rates of success and, in some cases, matching or exceeding successes noted in human IVF today. Also, if history is any indicator, one can reasonably expect that further refinements to the cloning process will improve efficiency rates. Scientists have reported success rates of 32% in goats and 80% in cows since 1998, as opposed to the poor 3% success rate Wilmut obtained when cloning Dolly in 1995. Furthermore, scientists at Advanced Cell Technologies in Worcester, Massachusetts, in association with others, have recently produced 24 cloned cows, that were all normal and healthy and have survived to adulthood (4). Despite the overwhelming data that exists showing refinements in the RR technology that yield improving success rates, Wilmut and Jaenisch still insist that it is inefficient based upon their poor success using very crude and uncontrolled experimental techniques , almost seven years ago. One can only but question their motives for their illogical arguments. They do not seem interested in developing and refining techniques, but they rather seem to have immense private interests and want to patent and control the technologies for themselves. Interestingly enough, the Roslin Institute scientists who cloned Dolly the sheep have changed their agenda on the cloning subject and have stated recently that they plan to seek permission to experiment on cloned human embryos for medical purposes. What are their true motives?

Animal Cloning vs. Human Reproductive Regeneration

It has been very clearly shown that animal cloning and its difficulties appear to be species-specific,

and the data cannot be extrapolated with a great degree of accuracy to the human species. In a recent study by scientists from Duke University Medical Center, it was demonstrated that it may be technically easier and safer to perform somatic cell nuclear transfer (SCNT) in humans than in sheep, cows, pigs, and mice because humans possess a genetic benefit that prevents fetal overgrowth, one of the major obstacles encountered in cloning animals (5).

The genetic benefit is based on the fact that humans and other primates possess two activated copies of a gene called insulin like growth factor II receptor (IGF2R). Offspring receive one functional copy from each parent as expected. However sheep, pigs, mice and virtually all non-primate mammals receive only one functional copy of this gene because of a rare phenomenon known as genomic imprinting in which the gene is literally stamped with marking that turn off its function. Since humans are not imprinted at IGF2R, then fetal overgrowth would not be predicted to occur if humans were cloned. If this theory is correct, the incidence of developmental abnormalities following human SCNT would be significantly lower. Also, the authors concluded that the data showed that one does not necessarily have these problems in humans. This is the first concrete genetic data showing that the cloning process could be less complicated in humans than in sheep.

The political Status on Cloning

In the United States, the House passed in July, 2001 the Weldon Bill or the Human Cloning Prohibition Act of 2001 (bill H.R. 2505). This bill would prohibit any person or entity, in or affecting interstate commerce, from (i) performing or attempting to perform human cloning, (ii) participating in such an attempt, (iii) shipping or receiving the product of human cloning, or (iv) importing such a product. The bill currently pending in the US Senate, S 790, written by Sen, Sam Brownback (R Kansas), would criminalize all cloning with a fine of up to \$1 million and 10 years in prison and it is almost identical to the bill (H.R. 2505) passed by the House in July 2001. The Council of Europe has introduced a protocol that prevents any abuses of such techniques by applying them to humans, banning "any intervention seeking to create a human being genetically identical to another human being, whether living or dead". Finally, the Protocol leaves it to countries' domestic law to define the scope of the term "human being". In April 24, 2001, England has banned "reproductive regeneration" but not "therapeutic cloning".

The political situation with cloning in general remains very fluid, mainly because of the inability of the politicians to understand, comprehend and act decisively on the issues that cloning presents to society. After all, their inability to act decisively may have a great deal to do with their resistance to debate and face the facts that humans will be cloned.

Recent Statements by President Bush

In his speech to the American public, President Bush made an appeal for a global ban on cloning, whether it be for therapeutic or reproductive cloning, on the basis that we should not use people for "spare parts" and we should not "manufacture people". Reproductive cloning does neither. As opposed to therapeutic cloning which results in the inevitable death of an embryo once the stem cells

have been removed, reproductive cloning aims to protect and preserve life in allowing the embryo to grow and be implanted into the uterus for a subsequent pregnancy. From an ethical point of view, there is no destruction of life.

Quoting President Bush: "Life is a creation, not a commodity. Our children are gifts to be loved and protected, not products to be designed and manufactured. Allowing cloning would be taking a significant step toward a society in which human beings are grown for spare body parts, and children are engineered to custom specifications; and that's not acceptable." And that's not acceptable to us either, Mr. Chairman! We agree with President Bush and uphold the sanctity of human life. Reproductive cloning does not involve the destruction of human embryos, nor does it modify or "engineer" the genetic code to custom specifications. Reproductive cloning involves employment of similar technology used for Intra cytoplasmic Sperm Injection (ICSI), which is routinely employed in IVF centers throughout the World. The only difference is that instead of using a sperm cell from the father, scientists can use a somatic cell nucleus and inject it into the mother's anucleated egg. The resulting embryo would have its genetic makeup from the father, but the expression of the genetic code and characteristics and personality of the baby born will be completely different and unique. Reproductive cloning is nothing more than another modality for the treatment of human infertility in giving the gift of life to a childless couple that have exhausted all other choices for having a child. What is so wrong about this?

Is History Repeating Itself?

This is not the first time that the scientific community has had to deal with controversial issues regarding new technologies. Exactly the same events happened with IVF in the Kennedy Institute in Washington in 1978. Professor Robert Edwards and Dr. Patrick Steptoe were faced with such criticism from hundreds of reporters, senators, judges, scientists and doctors, when they proposed the idea of in-vitro fertilization. The language and accusations were the same as what we face today, including "they ignored the sanctity of life, performed immoral experiments on the unborn", "subject to absolute moral prohibition", "no certainty that the baby won't be born without defect" and to "accept the necessity of infanticide. There are going to be a lot of mistakes" (6-11).

Twenty-four years later, the exact opposite of everything the "experts" predicted happened. IVF has become an acceptable and routine treatment of infertility worldwide. The abnormalities that were expected to have been unacceptable proved to be the same, if not less than with natural conception (11). Ironically, those critics of IVF have become the "pioneers" of IVF. These same critics might have delayed the introduction of IVF but their actions mostly harmed patients, and also the medical and scientific community. I am certain that the reproductive cloning procedures will follow in the same footsteps. Recently, I have had the opportunity to openly debate Professor Robert Winston from the UK, on the issue of human reproductive cloning at an Oxford Union Debate at Oxford University. Ironically enough, he was one of the leaders originally opposed to IVF, and who is currently a leading IVF specialist in Britain. The technology that he was vehemently opposed to, almost twenty-five years ago, is now the very same technology that he uses to earn a living. Once reproductive regeneration is commonplace in the ART treatment market, will he, along with all the

other critics, "jump" on the bandwagon and offer this new technology in their own IVF centers? I believe so. They have done it before and they can do it again. Mr. Chairman, we can not afford to behave this way and most importantly wish to repeat the same mistake.

Conclusion

As Professor Robert Edwards, the great English scientist who helped create the world's first test-tube baby in 1978, so eloquently prophesied recently "Cloning, too, will probably come to be accepted as a reproductive tool if it is carefully controlled" (12). No doubt, humans will be produced via reproductive regeneration. Recent scientific and technological progress demonstrates that very clearly. Similar to IVF, the technology of reproductive regeneration will advance, techniques will be improved, and knowledge will be gained. Reproductive regeneration's difficult questions can be answered only through a dedicated pursuit of knowledge and an exercise of our willful rationality, and in the end, the answer to the debate over human nature may be simply that man's nature is the product of his own will.

Mr. Chairman, science has been very good to us and we should not abandon it now. Consider why America has the best medical care in the world. It is because we have the freedom to investigate, research and market the latest medical techniques, all within proper procedures and safeguards. This is not the time to panic and try to turn back the clock. The Genie is already out of the bottle. Let's make sure it works for us, not against us. Let's do it here. Let's do it right.

By banning cloning, America will be showing the world that she is hesitant and/or reluctant to take the lead in this new arena of technological advancement. The world today is looking at the most powerful nation on Earth for leadership on this issue, and walking away from it by banning it is not a sign of leadership, but cowardice. Do not let the future of this technology slip away through our fingers, because we are too afraid to embrace it. I believe that it is the right of the American people to choose whether or not they want to have this technology available to them. Let us educate ourselves and debate the issues and not make irrational decisions based upon fear of a new technology. Banning this technology would only give our enemies license to use it to their advantage. Let us learn from history and forge ahead in this brave new world as leaders, not spectators, the American way.

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ATTACHMENT

PANAYIOTIS MICHAEL ZAVOS, Ed.S., Ph.D.

A SHORT BIOGRAPHY

Born February 23, 1944, in a small village of Tricomo in Famagusta, Cyprus, Panayiotis Michael Zavos is the second youngest son of Michael and Theodora Zavos. He comes from a very successful family, holding numerous national and international companies and institutions. He grew up in Tricomo, and attended the Agricultural Gymnasium of Morphou (High school) in the city of Morphou. He worked at the Agricultural Research Institute of Cyprus as a Research Assistant and served as a Lieutenant in the Cypriot Army from 1963-1966. He immigrated to the United States for University studies in 1966.



Dr. Panayiotis Zavos received his B.S. in Biology-Chemistry in 1970, his M.S. in Biology-Physiology in 1972 and Education Specialist in Science (Ed.S.) in 1976 from Emporia State University in Emporia, Kansas. He earned his Ph.D. in Reproductive Physiology, Biochemistry and Statistics in 1978 from the University of Minnesota in the Twin Cities, Minnesota. He received the Distinguished Alumnus Award and the Graduate Teaching Award from Emporia State University and the Student Leadership Award from the University of Minnesota.

Dr. Zavos has a long career as a reproductive specialist and he has devoted more than 25 years to academia and research. He is the chief scientist in the development of several new and innovative technologies in the animal and human reproductive areas with worldwide implications. He has authored or coauthored more than 400 peer-review publications, along with a number of solicited reviews, book chapters and popular press releases. He has presented more than 300 abstracts and other presentations at a large number of national, international and professional scientific meetings all over the world. Dr. Zavos' studies and findings have been reported in the local, national and international press. He served as an ad hoc reviewer for the NIH and other scientific groups.

Dr. Zavos is currently serving as a Board Member of the Middle East Fertility Society, and is a past Board Member of the China Academy of Science. He was awarded the first ever Honorary Professorship by the Chinese Academy of Science awarded to an American by Chinese Scientists. He has given plenary lectures nationally and internationally at a number of Scientific Societies meetings, has been and continues to be a visiting scientist for a number of international collaborations and exchanges.

Dr. Zavos has numerous scientific collaborations nationally and internationally and his publications have appeared in eight languages. He is a member of the American Society for Reproductive Medicine (ASRM), the American Society of Andrology (ASA), the European Society for Human Reproduction and Embryology (ESHRE), the Middle East Fertility Society (MEFS), the Japanese Fertility Society, the International Society of Cryobiology Sigma XI, Gamma Sigma Delta and a number of other Scientific and Professional Societies. He has served on a large number of

committees for the International Society of Cryobiology, ASRM, MEFS, ESHRE and others.

Professor Zavos has received a great deal of media coverage both within the scientific and reproductive arena and the mainstream press for his many scientific accomplishments and pioneering ventures. He has made many television and radio appearances including: NPR Radio, 60 Minutes with CBS, Twenty-Twenty with ABC, Dateline NBC, Face the Nation, BBC World, Tech TV, Nightline, Fox TV, World News Tonight, Good Morning America ABC, The Early Show, CBS This Morning, CNN News, CNN, CNN International, Reuters, HBO, The View with Barbara Walters, National Geographic, Televisione svizzera (Swiss TV), Cyprus Broadcasting Corporation, Antena TV of Cyprus and Greece, Tokyo Broadcasting System International, NHK Television (Japan), Nippon Television of Japan, TV Asahi (Japan), ZDF TV (Germany), Deutsche Welle TV (Germany), Nine Network TV (Australia), National TV (Israel), Live Talk with Sabine Christiansen (Germany) and a great deal of other local and regional TV programs throughout the US, Canada and Europe, too numerous to mention.

Dr. Zavos is recognized worldwide as a leading researcher and a strong authority in the areas of male reproductive physiology, gamete physiology, male infertility, Andrology and other ART procedures including the development of in-vitro round spermatid manipulations (ROSI procedures). Dr. Zavos is also recognized as an international authority on smoking and its effects on human reproductive performance.

Dr. Zavos founded and serves on various companies as:

1. Founder, The Zavos Organization, www.zavos.org
2. President and CEO of Zavos Diagnostic Laboratories, Inc., a private corporation that markets infertility products and technologies, in the USA and worldwide, www.zdline.com
3. Founder, Director and Chief Andrologist of the Andrology Institute of America, www.aia-zavos.com
4. Founder, Repromed International, dealing with Oocyte Donation Services and ART technology development, www.repromedinternational.com
5. Founder and Executive Director of the Home Fertility Network, www.homefertility.com
6. Founder, SpermRus, for "Online" Semen Analysis, www.spermrus.com
7. Founder and Executive Director, Online Domains R Us, www.onlinedomainsrus.com
8. Co-Founder and Associate Director of the Greek-American Andrology Institute of Athens, Greece
9. Professor Emeritus of Reproductive Physiology-Andrology at the University of Kentucky, in Lexington, KY, USA
10. Honorary Professor, China Academy of Science