[ORAL ARGUMENT SCHEDULED FOR DECEMBER 6, 2010]
No. 10-5287

IN THE

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

DR. JAMES L. SHERLEY, *et al.*,
Appellees,

v.

KATHLEEN SEBELIUS, in her official capacity as Secretary of the Department of Health and Human Services, *et al.*,
Appellants,

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BRIEF OF *AMICUS CURIAE* PROFESSOR MAUREEN L. CONDIC, PH.D., IN SUPPORT OF PLAINTIFFS-APPELLEES AND AFFIRMANCE

Nikolas T. Nikas, AZ Bar No. 011025
*Dorinda C. Bordlee, LA Bar No. 20115
BIOETHICS DEFENSE FUND
6811 E. Voltaire Avenue
Scottsdale, AZ 85254
(480) 483-3597

* COUNSEL OF RECORD

Attorneys for Maureen L. Condic, Ph.D.

CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to D.C. Circuit Rule 28(a)(1), the undersigned counsel certifies as follows:

A. Parties and *Amici*. All parties, intervenors and *amici* appearing before the District Court and in this Court are listed in the Brief for Appellees (Dkt. 1274222) filed on October 24, 2010. Disclosure statements for proposed amicus Dr. Maureen Condic are provided immediately following this Certificate and incorporated herein.

B. Rulings Under Review. The rulings under review are the August 23, 2010, Order and Memorandum Opinion of the District Court issuing a preliminary injunction. *Sherley v. Sebelius*, 704 F. Supp. 2d 63 (D.D.C. 2010) (Chief Judge Royce C. Lamberth). The order and opinion appear at page 226 of the Joint Appendix (JA).

C. Related Cases. This matter has previously come before this Court in *Sherley v. Sebelius*, No. 09-5374 (June 25, 2010). The opinion is available at 610 F.3d 69 and at page 214 of the Joint Appendix. Counsel is not aware of any other related cases within the meaning of D.C. Circuit rule 28(a)(1)(c).

Respectfully submitted,

/s/ Dorinda C. Bordlee

_____

*Dorinda C. Bordlee
BIOETHICS DEFENSE FUND
6811 E. Voltaire Avenue
Scottsdale, AZ 85254
(480) 483-3597

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES, RULES AND REGULATIONS

LEGISLATIVE MATERIALS

* Authorities chiefly relied upon are marked with an asterisk.

OTHER AUTHORITIES

GLOSSARY

ASC	adult stem cell
Dickey-Wicker Amendment	Consolidated Appropriations Act, 2010, Pub. L. No. 111-117, § 509(a)(2), 123 Stat. 3034.
The Government	The Defendants-Appellants
hESC	human embryonic stem cell
Human Subject Regulations	45 C.F.R. 46, Subpart A
ICM	inner cell mass
iPSC	induced pluripotent stem cell
JA	Joint Appendix
NIH Guidelines	National Institute of Health Guidelines for Human Stem Cell Research

INTERESTS OF *AMICUS CURIAE*[1]

Maureen L. Condic, Ph.D., a research scientist, is Associate Professor of Neurobiology and Anatomy at the University of Utah School of Medicine.[2] Dr. Condic is the author of over 50 peer-reviewed studies and reviews. Her teaching focuses primarily on embryonic development. In 2008, Dr. Condic authored a scientific white paper entitled, *When Does Human Life Begin? A Scientific Perspective* (attached as Appendix A). Dr. Condic is familiar with the NIH regulations both in her capacity as medical school faculty, as well as from her own research involving human research subjects. In an ongoing collaborative project, Dr. Condic is studying the properties of human amniotic fluid stem cells with the long-term goal of determining whether these stem cells can be used to treat congenital heart disease in newborn human babies or in late-term human fetuses. In 1999, Dr. Condic was awarded the Basil O'Connor Young Investigator Award for her studies of peripheral nervous system development. In 2002, she was named a McKnight Neuroscience of Brain Disorders Investigator, in recognition of her research in the field of adult spinal cord regeneration. Dr. Condic submits this brief in the interest of informing this Court's legal analysis with the objective science underlying the controverted issue.

---

[1] Pursuant to Cir. Rule 29(b), the parties have consented to the filing of this brief.

[2] This brief is presented solely on behalf of Dr. Maureen L. Condic; it in no way represents the views or opinions of the University of Utah or its employees.

INTRODUCTION

Modern science is well suited to clarify the factual predicates that underlie a normative debate. The plain language of the Dickey-Wicker Amendment, properly relied on by the lower court, reflects the Congressional adoption of a normative principle, namely, that of respect for the consciences of citizens who do not want their tax dollars used to support research that makes them complicit in the knowing destruction of human lives. It does this by referencing laws that protect "*human subjects*" in taxpayer funded research.

The factual predicate of this legal norm is that human embryos are human subjects, i.e., human beings, and not merely collections of cells. This factual predicate is confirmed by the empirical scientific evidence presented in the interest of informing this Court's review of how the challenged National Institute of Health Guidelines for Human Stem Cell Research (NIH Guidelines) violate the human subject regulations incorporated by reference in the Dickey-Wicker Amendment.

Part A of Section I summarizes the empirical conclusions of a cogent scientific white paper authored by Amicus Dr. Maureen L. Condic entitled, *When Does Human Life Begin: A Scientific Perspective* (2008) (attached as Appendix A). The white paper presents this Court with a concise yet comprehensive review of the human biology underlying the ethical and legal norms embodied in the Dickey-Wicker Amendment. Using universally accepted criteria, the white paper

establishes that from a scientifically well-defined moment of sperm-egg fusion – and *a fortiori* at the blastocyst stage when the embryo may be destroyed to derive embryonic stem cells – a human embryo is a distinct, individual human being, and not a mere collection of human cells.

Part B of Section I then sets forth the text of the two human subject protections that Congress references in the Dickey-Wicker Amendment as the standard to be applied to federally funded research that endangers human subjects at the embryonic stage of life. These two provisions, 45.C.F.R. 204(b) and Section 289g(b) of the Public Health Act, demonstrate that human subjects at the embryo stage (even those "no longer needed") are not to be subjected in federally funded research to risks greater than that allowed for research on fetuses *in utero* who are intended to be brought to term.

Section II addresses the implausibility of the government's attempt to bifurcate human embryonic stem cell (hESC) research when it purports that its funding for one aspect of the research does not implicate the integral first phase of destroying the human embryo to derive the hESCs. The inextricable continuity of both phases of the research is made especially clear in light of the NIH Guidelines' detailed provisions that predicate eligibility for funding on the hESC researcher himself providing documentation of the parents' "voluntary written consent for the human embryos to be used for *research* purposes."

Both the law and the underlying science demonstrate that the lower court properly applied the Dickey-Wicker Amendment "as its language is most naturally read, and in accordance with what that language makes clear is its basic purpose." *Barber v. Thomas*, 130 S. Ct. 2499, 2509 (U.S. 2010).

ARGUMENT

I. The challenged NIH Guidelines squarely undermine the normative core of the Dickey-Wicker amendment, and the underlying human subject protections it references.

In this litigation, the defendants-appellants ("the government") offer a construction of the Dickey-Wicker Amendment that renders it meaningless to justify the federal funding of research that inherently involves, depends on, and promotes the destruction of living human embryos.[3] Through this misconstruction, the government seeks judicial sanction of a policy that erodes the legitimacy of representative democracy in our nation's science policy; namely, that the scientific community *alone* should determine what research should be supported with taxpayer funds, even if such research unavoidably requires the destruction of

[3] *Amicus* agrees with the lower court's ruling that human embryonic stem cell research is "research in which" human embryos are destroyed, based, *inter alia*, on the text of the NIH Guidelines highlighted in Section II, *infra*. *See* District Court Memorandum Opinion (August 23, 2010), at JA 235-239.

vulnerable human subjects in blatant contradiction of legally enacted research norms.

The only rationale offered by President Barack Obama in his March 9, 2009 Executive Order is that there is "broad agreement in *the scientific community* that [embryonic stem cell] research should be supported by federal funds."[4] In his remarks, the President elaborated: "Promoting science. . . is about letting scientists like those here today do their jobs, free from manipulation or coercion, and listening to what they tell us, even when it's inconvenient. . . ."[5]

The notion that "the scientific community" alone should determine what research should be supported with taxpayer funds undermines the legitimate role of democracy in defining the moral and ethical boundaries of biomedical research on human subjects.[6] In fact, the current administration has never even raised, much

---

[4] Executive Order No.13,505, 74 Fed. Reg. 10,667 (March 9, 2009))(emphasis added).

[5] REMARKS OF PRESIDENT BARACK OBAMA – AS PREPARED FOR DELIVERY – SIGNING OF STEM CELL EXECUTIVE ORDER AND SCIENTIFIC INTEGRITY PRESIDENTIAL MEMORANDUM , Washington, D.C., March 9, 2009.

[6] *See generally*, O. Carter Snead, *Science, Public Bioethics and the Problem of Integration*, 43 U.C. DAVIS L. REV. 1529, 1531 (2010)(quoting Einstein's statement, "Science can only ascertain what is, but not what should be, and outside of its domain[,] value judgments of all kinds remain necessary." Albert Einstein, "Science and Religion," in Daniel Bronstein, Approaches to the Philosophy of Religion: A Book of Readings (New York, Ayers Publishing, 1954), at 68-69).

less engaged the central moral question posed by embryonic stem cell research, namely, the moral status of the human embryo used and destroyed in this context. By elevating the financial demands of hESC scientists above the codified will of the people, the challenged NIH Guidelines violate the normative core of the human subject protections expressly cited in the Dickey-Wicker Amendment. The "scientific community alone" policy ignores the right of all men and women in a democracy, as exercised by their representatives in Congress, to set reasonable ethical limitations on biomedical research – especially when it impacts the American ideals of human dignity, human equality, and the integrity of science.

This shared responsibility is clearly reflected in the Dickey-Wicker Amendment's funding restriction on "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 C.F.R. § 46.204(b) and section 498(b) of the Public Health Service Act (42 U.S.C. § 289g(b))."[7]

In support of the lower court's ruling, *Amicus* herein brings this Court's attention to the citations within the Dickey-Wicker Amendment. These citations are of notable significance because they refer to laws that protect human subjects

[7] Consolidated Appropriations Act, 2010, Pub. L. No. 111-117, § 509(a)(2), 123 Stat. 3034, 3280-81 (the "Dickey-Wicker Amendment").

in federally funded research. *Amicus* first presents the underlying scientific facts establishing that a human embryo is indeed a human subject, followed by a review of the text of the two codified research norms that are applied to human beings at the embryonic stage of life by the Dickey-Wicker Amendment.

A. Modern embryology establishes that the life of a new human embryo begins at a scientifically well-defined moment, and that the human embryo is a distinct, individual, human organism; i.e., a new human being, and not a mere collection of cells.

Debates concerning the practice and funding of human embryonic stem cell research are often perceived as thorny because of the widespread misperception that we do not or cannot know when the life of an individual human being begins as a matter of empirical fact. Yet if this view is correct, we are left with a serious ethical dilemma: while no one objects to the destruction of ordinary human cells for biomedical research, the destruction of *human beings* to obtain biological material for research is a matter of grave moral and legal consequence.[8] As a

[8] *See* YUVAL LEVIN, IMAGINING THE FUTURE: SCIENCE AND AMERICAN DEMOCRACY (2008); Robert P. George and Christopher Tollefson, EMBRYO (2008); *see also* Albert R. Jonsen, THE BIRTH OF BIOETHICS 90-100 (1998), recounting the history of the1974 legislation that created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was charged to conduct a "comprehensive study of the ethical, legal, and social implications of advances in biomedical research" involving human subjects. The Commission ultimately produced *The Belmont Report*, which became the basis for federal regulations at 45 CFR 46, Subpart A "to cover all biomedical researchers who received federal funds for their work." The human subject regulation

matter of logic, there must be some non-arbitrary scientific criteria to determine when living human cells give rise to a new individual human being.

These criteria are presented in the white paper authored by Amicus Dr. Maureen Condic, *When Does Life Begin: A Scientific Perspective* (2008)(attached as Appendix A).[9] This white paper provides a concise yet comprehensive assessment of the foundational question of when, as a matter of developmental biology, the life of a new human being begins. The conclusions unambiguously support the factual premise underlying the Dickey-Wicker Amendment. After all, its references to "human subject" regulations are coherent only if the protected research subject – the human embryo – is indeed a human being and not a mere collection of human cells.

In specific, the review of modern embryology found in the attached white paper provides this Court with the objective conclusions of two central questions regarding the biological beginning of human life: (1) in the course of sperm-egg interaction, when is a new cell formed that is distinct from either sperm or egg?

---

pertaining to human fetuses is cited in the Dickey-Wicker Amendment, as discussed in Section IB, *infra*.

[9] Maureen L. Condic, Ph.D., *When Does Human Life Begin? A Scientific Perspective,* Westchester Institute White Paper (October 2008), available at http://www.westchesterinstitute.net/images/wi_whitepaper_life_print.pdf

And (2) is this new cell a distinct individual human organism (i.e., a new human being), or merely a new kind of human cell?[10]

Based on universally accepted scientific criteria, the white paper sets forth the unequivocal conclusion that a new cell, the human zygote, comes into existence at a precise moment of sperm-egg fusion, an event that occurs in less than a second. Upon formation, the zygote immediately initiates a complex sequence of events that establish the molecular conditions required for its own self-directed development. The behavior of the one-cell embryo and its molecular composition are radically unlike that of either sperm or egg separately, and are characteristic of a human organism.[11]

As the human embryo matures, it continues to meet the distinguishing feature of an organism or being; self-directed interaction of parts in the context of a coordinated whole.[12] In contrast, collections of human cells (such as skin cells) are alive and carry on the activities of cellular life, yet fail to exhibit coordinated interactions directed towards any higher level of organization. Collections of cells

[10] *Id.* at 5.

[11] *Id.* at 7.

[12] *Id.* at 6.

do not establish the complex, interrelated cellular structures (tissues, organs, and organ systems) that exist in a whole, living human being.[13]

Thus, from the beginning – and *a fortiori* at the blastocyst stage, when the embryo might be destroyed to derive embryonic stem cells – the human embryo is a living, individuated human being.[14] Yet, *amici* in support of the government seem to disregard the biological status of the embryo based, *inter alia*, on the size of the human being at this stage of life:

> Human embryonic stem cells (hESCs) are derived from blastocysts, which are pre-implantation embryos that develop within five days after fertilization of an egg by a sperm. **A blastocyst is smaller than the period at the end of this sentence**.[15]

---

[13] *Id.*

[14] *Id.*

[15] Brief of *Amici Curiae* the State of Wisconsin, et al. Supporting Reversal of the Preliminary Injunction, *Sherley, et al. v. Sebelius, et al.* (No. 10-5287) (Dkt. 1272219) (filed 10/18/2010), at 27. (emphasis added). *Amici* supporting the government also use misleading terminology in their claim the blastocysts used for hESC line derivation are "not viable" unless they are implanted. *Id*. The term "viable" more aptly reflects an internal state of being compatible with long term survival in an appropriately supportive environment. No human being of any age is able to survive in all environments; *e.g.*, on the moon or at the bottom of the ocean. The human embryos subject to the derivation phase of hESC research are actively alive and generally have no internal state or condition of genetic defect that will produce their imminent death. As discussed in Section B, *infra*, the relevant human subject protections require that these human embryos not be subjected to risks greater than that allowed for research on fetuses *in utero* that are intended to be brought to term.

This flawed argument was squarely addressed by a colloquium of scholars including scientists and philosophers:

> The embryo is a being: that is to say, it is an integral whole with actual existence. The being is human; it will not articulate itself into some other kind of animal. Any being that is human is a human being. **If it is objected that, at five days or fifteen days, the embryo does not look like a human being, it must be pointed out that this is precisely what a human beings looks like – and what each of us looked like – at five or fifteen days of development.** Clarity of language is essential to clarity of thought.[16]

As established by the empirical evidence in Appendix A, a human embryo is a human organism, and the life of a new human being commences at a scientifically well-defined moment. This unambiguous scientific finding supports the factual premise underlying the "human subject" laws referenced in the Dickey-Wicker Amendment – that the human embryo is indeed a human being.

[16] Ramsey Colloquium, *The Inhuman Use of Human Beings: A Statement on Embryo Research*, 49 FIRST THINGS 17, 18 (January 1995), available at http://www.firstthings.com/ftissues/ft9501/articles/ramsey.html (last checked October 17, 2010).

B. The Dickey-Wicker Amendment's reference to certain "human subject" protections is consistent with Congress' implicit recognition that a human embryo is a human being.

The legitimate role of Congress in defining the legal and ethical boundaries of research involving human subjects is not an issue that originated with the administration of President George W. Bush. In fact, it was the persistence of Senator Walter Mondale (D-MN) and Senator Edward Kennedy (D-MA) that resulted in the 1974 legislation establishing the National Commission for the Protection of Human Subjects.[17] Congressional hearings held between 1968 and 1973 by Senators Mondale and Kennedy were prompted by "medical advances [that] raise grave and fundamental ethical and legal questions for our society. Who shall live and who shall die?"[18] The hearings addressed the ethics of biomedical advances such as genetic engineering and organ transplantation, and were especially driven by reports on human research subject abuses such as the Tuskegee Syphilis Study[19] and the emerging practice of "fetal research."[20]

---

[17] For a history of the Mondale and Kennedy hearings leading to the enactment of the National Research Act, Pub. L. No. 93-348 (1974), *see* Albert R. Jonsen, THE BIRTH OF BIOETHICS 90-106 (1998).

[18] *Id.* at 91 (citing Statement of Senator Mondale, U.S. Senate Subcommittee on Government Research, Committee on Government Operations, *Hearings on S.J. Resolution 145*, 90th Congress, 2nd session, 1968, p 1-3.)

[19] *Id.* at 96 (A hearing called by Senator Kennedy on April 30, 1973, focused on the news story of a federally funded experiment that deprived a group of rural, African-American men of treatment for syphilis over a 30-year period.)

The Mondale and Kennedy hearings ultimately resulted in the enactment of 45 C.F.R. 46, Subpart A ("Human Subject Regulations") that governs "research that is conducted on human beings if it is funded by one of 18 federal agencies."[21] Enacted in 1974, the Human Subject Regulations are a body of research standards with roots in numerous international agreements, such as the Nuremberg Code and the Declaration of Helsinki, as well as in domestic policies adopted by the U.S. Department of Health and Human Services (HHS) following cases involving research that harmed human subjects.[22] Since 1974, HHS has promulgated and

---

[20] *Id.* at 94 (recounting how the Federal Research Act was prompted in part by Eunice Shriver's efforts to stop fetal research after she read a news report about an NIH advisory panel report "'encouraging the use of newly delivered live fetuses for medical research before they died.'" Delivered intact as the result of a late abortion, the fetus could be briefly maintained alive "while studies were done that might improve the care of future mothers and children. In the article, one scientist commented, "'I don't think it's unethical. It's not possible to make this fetus into a child, therefore, we can consider it as nothing more than a piece of tissue.'")(*quoting* Victor Cohen, *Live fetal research debated*, WASHINGTON POST, April 10, 1973, at A1, A9.)

[21] U. S. Congressional Research Service, *Federal Protection for Human Research Subjects: An Analysis of the Common Rule and Its Interactions with FDA Regulations and the HIPPA Privacy Rule*, (RL32909; June 2, 2005), by Erin D. Williams, at 6, *available at* http://www.fas.org/sgp/crs/misc/RL32909.pdf.

[22] *Id.* at 1, 70; *See generally* Nathan A. Adams IV, et al, *Specially Respecting the Living Human Embryo by Adhering to Standard Human Subject Experimentation Rules*, 11 YALE J. HEALTH, POLICY, LAW & ETHICS 111 (2001).

amended additional regulations for the protection of human subjects in "vulnerable populations," including pregnant women and fetuses.[23]

Advances in biomedical technology made the practice of conducting research on human embryos *in vitro* and destroying them to obtain human embryonic stem cells possible in the 1980s and 1990s. Human embryonic stem cells were first isolated and grown briefly in the laboratory in 1994, and first successfully maintained long-term in the laboratory by in 1998.[24]

Respecting the consciences of citizens who do not want their tax dollars used to support research that makes them complicit in the knowing destruction of vulnerable human lives in the fatal practice of conducting research on human embryos *in vitro*, Congress authorized the 1996 budget rider known as the Dickey-Wicker Amendment.[25]

The Dickey-Wicker Amendment, in relevant part, prohibits the use of federal funds for:

> (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death

---

[23] U.S. Congressional Research Service, *supra* n. 21, at 6.

[24] JA at 260, citing Bongso, *et al.*, *Human Reproduction* 9, 2110 (1994) and Thomson, *et al.*, *Science* 282, 1145 (1998).

[25] June Mary Zekan Makdisi, *The Slide from Human Embryonic Stem Cell Research to Reproductive Cloning: Ethical Decision-Making and the Ban on Federal Funding*, 34 RUTGERS L.J. 463, 477 (2003).

> greater than that that allowed for research on fetuses *in utero* under **45 CFR 46.204(b)** and **section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b))**.[26]

Despite various attempts to change its language, Congress has included the Dickey-Wicker Amendment in every Health and Human Services ("HHS") appropriations bill since 1996 and has not altered the Amendment in any material respect. JA 54–55. For example, an ultimately defeated amendment was offered by Congresswoman Lowey that would have authorized federal funding for research on "spare" embryos just as proposed by the challenged NIH Guidelines in this case. Rising on the floor of the Congress in opposition to the Lowey Amendment, Congressman (now Senator) Roger Wicker, the co-author of the Dickey-Wicker Amendment, reminded the Congress why the budget rider had been passed and should not be changed:

> What the Lowey amendment would do, however, is cause our Government to embark into an area of research which we have never, never before been willing to do as a government. As the chairman of the subcommittee stated, this is a very sensitive issue. It is also a very important issue for millions of Americans. As a matter of fact, 76 percent of Americans oppose funding for the type of research that the Lowey amendment would sanction. This goes to the very profound questions of human life and to very sensitive questions of bioethics.
>
> Proponents of the Lowey amendment say there is a distinction between spare embryos and embryos created for research purposes. But the leading experts say there is no distinction. Let me quote Dr.

[26] Consolidated Appropriations Act, 2010, Pub. L. No. 111-117, § 509(a)(2), 123 Stat. 3034, 3280-81 (the "Dickey-Wicker Amendment")(emphasis added).

> Robert Jansen of the National Health and Medical Research Council. He says,
>
> > *It is a fallacy to distinguish between surplus embryos and specially created embryos in terms of embryo research. The reason I say this is that any intelligent administrator of an in vitro program can, by minor changes in his ordinary clinical way of doing things, change the number of embryos that are fertilized.*
>
> . . . . [L]et us respond to the 76 percent of Americans who say, 'Do not use tax dollars to fund embryo research.' [27]

The two federal laws referenced as standards by Congress in the Dickey-Wicker Amendment show a clear intent to protect human embryos as human subjects, i.e. human beings.

The first federal regulation cited in the Dickey-Wicker Amendment, 45 C.F.R § 46.204(b), is found within Part 46 in Title 45 of the Code of Federal Register, under the title, "Protection of *Human Subjects*,"[28] revealing Congress' understanding that the human embryo is a human subject. This regulation is found under Subpart A, which is entitled "Basic HHS Policy for Protection of *Human Research Subjects*." The following is the text, substituting the phrase "human embryo" for the phrase "pregnant women and fetuses" as required by the Dickey-Wicker Amendment:

---

[27] 142 Cong. Rec. H7340 (1996) (Statement of Rep. Wicker).

[28] 45 C.F.R § 46 (2009)(emphasis added).

> §46.204 Research involving [human embryos]
>
> [Human embryos] may be involved in research if all of the following conditions are met:
>
> (b)The risk to the [human embryo] is caused solely by interventions or procedures that hold out the prospect of **direct benefit** for the [human embryo]; or, if there is no such prospect of benefit, the risk to the [human embryo] is not greater than **minimal *and*** the purpose of the research is the development of important biomedical knowledge **which cannot be obtained by any other means**.[29]

The risks to the human embryo involved in the necessary first phase of human embryonic stem cell research, namely the removal of the inner cell mass which destroys a living human embryo, violate the requirements of this human subject regulation.[30] There is no "prospect of direct benefit" to the human embryo, nor is the risk of death "minimal." Moreover, the speculative argument that hESC research is necessary to develop "important biomedical knowledge which cannot be obtained by any other means," fails to meet the *conjunctive* requirement that "the risk to the [human embryo] is not greater than minimal."[31]

---

[29] 45 C.F.R § 46.204(b) (2009)(emphasis added)(substituting the statutory word "fetus" with "human embryo" as required by the terms of Dickey-Wicker).

[30] *See* Section II, *infra*, explaining that hESCs are ***laboratory produced cells, not natural cells.***

[31] Proponents of human embryonic stem cell research frequently choose to ignore the effective performance of immune-matched ASCs and iPSCs methods that do not require the destruction of human embryos, asserting that because they don't know which stem cell is best, research on all types of stem cells must go forward.

The second federal law cited in the Dickey-Wicker Amendment defeats the faulty rationale that the risk is minimal to the embryo because the embryo is going to die anyway. This invalid rationale forms the basis of the challenged NIH Guidelines' authorization of funding for research on "hESCs . . . derived from human embryos created using in vitro fertilization for reproductive purposes and were no longer needed for that purpose."[32]

This provision of the NIH Guidelines is in clear violation of the second federal statute referenced in the Dickey-Wicker Amendment in its provision that human embryos not be "knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under. . . 42 U.S.C. 289g(b)."[33] The text of this statute requires that "fetuses intended to be aborted" be given the same human subject protections as "fetuses intended to be carried to term":

> **(b) Risk standard for fetuses intended to be aborted and fetuses intended to be carried to term to be same**
>
> In administering the regulations for the protection **of human research subjects** which –

This argument presupposes moral neutrality of all methods, disregarding the destruction of human beings at the embryonic stage of life that is necessary to the derivation phase of human embryonic stem cell research (which must be documented with the NIH by hESC researchers, *see* Section II, *infra*).

[32] Nat'l Insts. of Health Guidelines for Human Stem Cell Research, 74 Fed. Reg. 32,174 (July 7, 2009).

[33] § 509(a)(2), 123 Stat. at 3280–81.

> (1) Apply to research conducted or supported by the Secretary;
> (2) Involve living human feuses in utero; and
> (3) Are published in section 46.208 of part 46 of title 45 of the Code of Federal Regulations;
>
> Or any successor to such regulations, the Secretary shall require that **the risk standard** (published in section 46.102(g) of such part 46 or any successor to such regulations) **be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.**[34]

Substituting the term "human embryo" for the term "human fetuses" in the above statute, as required by the terms of the Dickey-Wicker amendment, results in an unambiguous conclusion: "Excess" human embryos abandoned in fertility labs are entitled to the *same* human subject protections in federally funded research as human embryos intended to be transferred to the mother's womb and carried to the fetal and infant stage of human development.

This is confirmed by the following statement made during the 1996 floor debate of the Dickey-Wicker Amendment, regarding an ultimately rejected amendment that would have allowed federal funding for the same kind of research authorized by the challenged NIH Guidelines:

> The supporters of [the Lowey] amendment claim that this funding will be used only to do experiments on ''spare'' embryos that would be discarded anyway. We, as a Congress, have already addressed this question. In 1985, Congress was made aware of abuses in some NIH research programs. These programs were conducting risky experiments on unborn children who were scheduled for abortions. At

[34] 42 U.S.C. § 289g (b)(emphasis added).

> that time we wisely enacted a law **insisting that federally funded research should treat these children the same as children intended for live birth.** This law protects human embryos in the womb at every stage and is still in effect today. **There is no reason that it should not be extended to protect human embryonic children outside the womb**.[35]

The foregoing establishes that human subjects at the embryo stage (even those considered "spare") are to be treated in federally funded research with no greater risk of harm or death than human subjects at the fetal stage intended to be brought to birth.[36] Thus, it would be a clear violation of the federal laws examined above if NIH were to issue guidelines authorizing taxpayer funding of ultra-hazardous, non-therapeutic research on unborn children under the condition that the mother gave her "proxy" consent. Yet, the challenged NIH Guidelines do just that with respect to human embryos. As discussed more fully below, the NIH Guidelines explicitly predicate federal funding on the requirement that the human embryonic stem cell (hESC) researcher himself submit written compliance to the NIH stating that the hESCs were derived from human embryos destroyed with the proxy consent of his or her biological parents. Because proxy consent is obviously not necessary if the subject of the research is merely cells or tissues, the challenged

---

[35] 142 Cong. Rec. H7342 (1996) (Statement of Rep. Vucanovich).

[36] 42 U.S.C. 289g (b) (as cited in the Dickey-Wicker Amendment, §509(a)(2), 123 Stat. at 3280-81)(providing risk standards are "the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.")

NIH Guidelines implicitly acknowledge that the subject to be destroyed via proxy consent is a human subject.[37]

[37] This raises grave implications if the lower court is reversed, because no court has ever approved proxy consent for research that is ultra-hazardous and non-therapeutic to the human subject, even with parental consent. *See, e.g., Grimes v. Kennedy Krieger Inst.*, 782 A.2d 807 (Md. 2001), where researchers associated with Johns Hopkins University subjected otherwise healthy children to the probability of lead poisoning to assess the effect of various levels of lead dust abatement. The Court found inadequate disclosure of these health risks to the children's parents, and added:

> [I]n our view, **parents** whether improperly enticed by trinkets, food stamps, money or other items, **have no more right to intentionally and unnecessarily place children in potentially hazardous non-therapeutic research surroundings,** than do researchers. In such cases, **parental consent, no matter how informed, is insufficient**.
> *Id.* at 177 (emphasis added).

See also, T.D. v. New York State Office of Mental Health, 626 N.Y.S.2d 1015 (N.Y. Sup. Ct. 1995), aff'd, 650 N.Y.S.2d 173 (N.Y. App. Div. 1996), finding that a state agency could not authorize non-therapeutic experiments on mental patients including both adult and minor subjects, reasoning that

> **The benefits of, and needs for, the medical research at issue are clear and evident; but at what cost** in human pain and suffering **to those subjects who are not capable of expressing either their consent or objection** to participation?. . . . .[H]owever laudable the ends which defendants seek to achieve may be, those results must be gained through means within their grant of authority and which properly safeguard the rights of the [the human subjects].

Id. at 177 (emphasis added). This Court should likewise decline the government's invitation to become the first court to approve a research policy that requires proxy consent of parents for ultra-hazardous, non-therapeutic research on human subjects.

II. The express terms of the NIH Guidelines demonstrate that destruction of human embryos "for research purposes" is an integral part of human embryonic stem cell research, not merely a separate preparatory step.

The foregoing review brings us to the critically relevant issue at the core of this litigation: whether human embryonic stem cell research is *"research in which"* a human subject at the embryo stage of life is "destroyed, discarded, or knowingly subjected to risk of injury or death."[38] In support of the lower court's ruling that the fatal derivation phase is part of hESC "research," it should first be noted that the derivation of hESCs is indeed a *research* process, not simply a preparatory act of removing cells from a human embryo. In fact, hESCs are ***laboratory produced cells, not natural cells.*** The only cells known beyond a shadow of a doubt to produce *all* cells of the human body (i.e. to be *truly* pluripotent) are cells *within the embryo* that actually perform this job in normal development. These cells, known as "inner cell mass" or ICM, are the cells from which hESCs are produced in the laboratory. Studies by independent groups have shown hESCs are not identical to ICM cells.[39] Thus, derivation is the necessary first step in hESC *research*.

---

[38] § 509(a)(2), 123 Stat. at 3280–81 (emphasis added).

[39] *See, e.g.*, R.A. Reijo Pera, et al., *Gene expression profiles of human inner cell mass cells and embryonic stem cells*, 78 DIFFERENTIATION 18-23 (July 2009); T.C. Brink et al., *The origins of human embryonic stem cells: a biological conundrum*, 188 CELLS TISSUES ORGANS 9-22 (2008).

This is confirmed by the express language in the NIH Guidelines, quoted below, characterizing the derivation phase as "research." And the continuity of both phases of the research is made especially clear with the NIH Guidelines' funding requirement that the *hESC researcher himself* must provide extensive documentation of the "voluntary written consent for the human embryos to be used for ***research*** purposes":

> A. Applicant institutions proposing research using hESCs derived from embryos donated in the U.S. on or after the effective date of these Guidelines may. . . establish eligibility for NIH funding by submitting an assurance of compliance with Section II (A) of the Guidelines, along with supporting information demonstrating compliance for administrative review by the NIH. For the purposes of this Section II (A), **hESCs should have been derived from human embryos**:
>
> 1. That were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose;
>
> 2. That were donated by individuals who sought reproductive treatment . . .and who gave voluntary written consent for the human embryos **to be used for *research* purposes**.
>
> 3. For which all of the following can be assured and documentation provided, such as consent forms, written policies, or other documentation, provided [a long list of other requirements that the hESC researcher must document such as the absence of cash or in kind payment for the donated embryos].[40]

[40] 74 Fed. Reg. 32,170, 32,174-75 (emphasis added).

Thus, as a condition of eligibility for taxpayer funding, the NIH Guidelines clearly and extensively implicate the complicity of the researcher in the time, place and manner of how the hESCs were derived from human embryos donated by their parents "for research purposes." This unequivocally supports the lower court ruling.[41]

The impact of the NIH proxy consent provisions is illustrated in an October 3, 2010 story covering the announcement by the University of Michigan that it had created the state's first embryonic stem cell line. Explaining that the university plans to adding it new hESC line to the "National Institutes of Health Embryonic Stem Cell Registry,"[42] the report gave a concrete example of how the challenged NIH Guidelines directly induce the university to actively recruit fertility patients to sign NIH compliant consent forms for the destruction of their offspring "for research purposes:"

> The couple who donated the embryo to U-M is unaware theirs became the first embryonic stem cell line, Smith said. They are among 5 couples who have donated about 20-30 embryos to U-M **since January, when U-M developed consent forms to comply with federal, state and university guidelines.**

---

[41] For an analysis of other express provisions within the NIH Guidelines that support the lower court's ruling, *see* Brief of *Appellees* Dr. James L. Sherley, et al., *Sherley v. Sebelius* (No. 10-5287) (Dkt. 1272219) (filed 10/18/2010), at 14-24.

[42] Kim Kozlowski, *U-M stem cell milestone advances research, controversy*, THE DETROIT NEWS (Oct. 3, 2010), at http://detnews.com/article/20101003/LIFESTYLE03/10030305/1040/

> It is believed that all of its donor embryos are genetically normal, so U-M is **now working to get couples to donate embryos** that are genetically abnormal.[43]

The level of NIH complicity in creating demand for and then regulating the circumstances of the destruction of human subjects "for research" makes the government's position completely untenable. The law, the underlying science, and the inevitable impact of the NIH Guidelines demonstrate that the lower court properly applied the Dickey-Wicker Amendment "as its language is most naturally read, and in accordance with what that language makes clear is its basic purpose." *Barber v. Thomas*, 130 S. Ct. 2499, 2509 (U.S. 2010).

[43] *Id.*

CONCLUSION

Amicus herein joins appellees in asking this Court to affirm the preliminary injunction issued by the district court and to dissolve the stay pending appeal.

Respectfully submitted,

*/s/ Dorinda C. Bordlee*_____

Nikolas T. Nikas, AZ Bar No. 011025
*Dorinda C. Bordlee, LA Bar No. 20115
BIOETHICS DEFENSE FUND
6811 E. Voltaire Avenue
Scottsdale, AZ 85254
(480) 483-3597

* COUNSEL OF RECORD

Attorneys for Maureen L. Condic, Ph.D.

DATED: November 1, 2010

CERTIFICATE OF COMPLIANCE

Pursuant to Rule 32(a)(7(C) of the Federal Rules of Appellate Procedure, I hereby certify that this brief complies with the type-volume limitations set forth in that rule. This brief contains 6,128 words (exclusive of the cover, table of contents, table of authorities and appendix). I relied on my word processor, Microsoft Word 2007, to obtain the count.

In addition, this brief complies with the typeface requirements of Fed. R. App. P. 35(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionally spaced typeface using Microsoft Word 2007 in Times New Roman 14 pt.

DATED: November 1, 2010

/s/*Dorinda C. Bordlee*
Dorinda C. Bordlee
Counsel for *Amicus* Dr. Condic

APPENDIX A

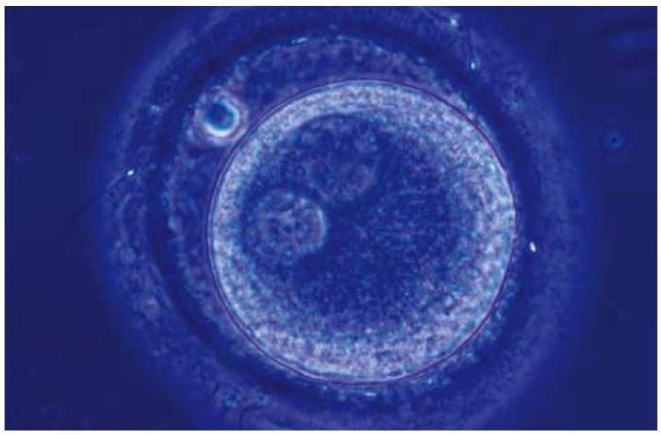
Maureen L. Condic, Ph.D., *When Does Human Life Begin? A Scientific Perspective,* WESTCHESTER INSTITUTE WHITE PAPER (October 2008), available at http://www.westchesterinstitute.net/images/wi_whitepaper_life_print.pdf

THE WESTCHESTER INSTITUTE
FOR ETHICS & THE HUMAN PERSON

WHITE PAPER
Volume 1, Number 1
October 2008

When Does Human Life Begin?

A Scientific Perspective



Maureen L. Condic
Senior Fellow
Westchester Institute for Ethics & the Human Person

Associate Professor of Neurobiology and Anatomy
at the University of Utah School of Medicine

Foreword by

Richard John Neuhaus
Editor in Chief, *First Things*

When Does Human Life Begin?

A Scientific Perspective

Maureen L. Condic

Westchester Institute White Paper Series
Volume 1, Number 1

The Westchester Institute for Ethics & the Human Person
P.O. Box 78, 582 Columbus Ave.
Thornwood, NY 10594

Copyright © 2008 by The Westchester Institute for Ethics & the Human Person

Printed in the United States of America

All rights reserved. No part of this publication may be used or reproduced in any manner without the written permission of the Westchester Institute for Ethics & the Human Person, except in the case of brief quotations embodied in critical articles and reviews.

Cover Art
Copyright © 2008 by Richard G. Rawlins, Ph.D. - Custom Medical Stock Photo
All Rights Reserved

The cover photograph shows a light micrograph of a cryopreserved, unicellular human zygote approaching syngamy. Human embryos, such as this one, are routinely created by *in vitro* fertilization in efforts at assisted reproduction, and are sometimes designated for research in which they are deliberately destroyed. Given the current state of biotechnology, most photos of human embryos in circulation today are made possible by these situations which of themselves are unnatural to human embryos. The Executive Director of the Westchester Institute, while authorizing the use of this photo, wishes to express his own moral objection to the *in vitro* production of human embryos.

CONTENTS

Westchester Institute White Paper

When Does Human Life Begin?
A Scientific Perspective

FOREWORD

It is really far past time to clear the air of the smog that obscures and confuses debates about abortion, embryonic research, cloning, and related issues.

Among the chief obfuscations and confusions is the claim that we do not know when human life begins. This frequently takes the form of claiming that the question is a matter of faith or religious belief. Nothing could be farther from the truth, as is lucidly and convincingly demonstrated in this White Paper.

When a human life begins is a question of science. The ethicist Peter Singer of Princeton University is famous, or notorious, for his advocacy of selective infanticide for babies who are born and then found to be defective in a way that makes them unwanted. Most people will find that argument morally abhorrent. But Singer is right about one thing. As he has said on many occasions, he and the pope are in complete agreement on when human life begins.

The debate in our society and others is not over when human life begins but is over at what point and for what reasons do we have an obligation to respect and protect that life. Before we can get to that argument, however, we need to clear the smog surrounding the question of when human life begins. This White Paper makes an invaluable contribution to that end.

It is sometimes said that the abortion debate is about "values" rather than "facts." An honest debate about abortion, however, is about values based on facts. If we don't get the facts right, we will not get our values right. Establishing by clear scientific evidence the moment at which a human life begins is not the end of the abortion debate. On the contrary, that is the point from which the debate begins.

Throughout history, there have been many societies that have decided that some human lives are more worthy of respect and protection than other human lives. While some such decisions are repugnantly racist, as in the case of Nazi Germany, or ideological, as in the case of Soviet and Maoist communism, others have made the decision on more sophisticated, even apparently humane, grounds. That is certainly true in the case of most of those who support an unlimited abortion license in our society. What we should not evade or obscure is the nature of the decision under discussion.

Finally, Christians believe that all truth is one because God, who is the source and end of all truth, is one. On the question at hand, as on other questions, there is no tension, never mind conflict, between science and faith. Faith and science, when rightly understood, are in the service of truth. This White Paper is not an exercise in theology. Nor is it an exercise in ethics or moral reasoning. It is a scientific examination of facts which, when clearly understood, provide the subject matter upon which other forms of reasonable reflection—medical, moral, legal, political, and theological—can then be brought to bear. All who are involved in these debates should be grateful to the Westchester Institute for Ethics & the Human Person for providing this important clarification of what it is that we are debating.

Richard John Neuhaus
Editor in Chief
First Things

INTRODUCTION

It is my great pleasure to introduce Dr. Maureen Condic's "When Does Human Life Begin?" as the first White Paper of the Westchester Institute for Ethics & the Human Person. Each contribution to this new White Paper series intends to offer a cogent and measured argument on a question of great moment, and Dr. Condic's inaugural paper provides us with nothing less.

Though human reason is not dependent upon biological findings for its certainty that a new human life wholly begins at some discrete moment, it is nonetheless dependent on the careful investigations of biologists like Dr. Condic to determine precisely where and when that discrete moment occurs.

In this White Paper, Dr. Condic challenges some of the conventional wisdom about that moment and argues that a coherent and non-arbitrary analysis of the scientific data forcibly points to the conclusion that a new human life commences at the precise moment when the membranes of the sperm and egg cells fuse. Specifically, she critiques the more common position that human life begins about 24 hours later during an event called syngamy (the breakdown of the two pronuclear membranes in the new cell, which results from the fusion of sperm and egg).

In this way, Dr. Condic accomplishes in the field of developmental biology exactly what the Westchester Institute hopes to foster in the realm of ethical reflection: namely, rigorous advancement of the discussion regarding unsettled questions of paramount moral concern.

With Dr. Condic's contribution, we are proud and delighted to launch our White Paper series.

Fr. Thomas Berg, L.C., Ph.D.
Executive Director
The Westchester Institute for Ethics & the Human Person

ACKNOWLEDGEMENT

The Westchester Institute is profoundly grateful to Antoine Puech, whose generosity has made this publication possible.

Westchester Institute White Paper

When Does Human Life Begin?
A Scientific Perspective

SUMMARY

Resolving the question of when human life begins is critical for advancing a reasoned public policy debate over abortion and human embryo research. This article considers the current scientific evidence in human embryology and addresses two central questions concerning the beginning of life: 1) in the course of sperm-egg interaction, when is a new cell formed that is distinct from either sperm or egg? and 2) is this new cell a new human organism—i.e., a new human being? Based on universally accepted scientific criteria, a new cell, the human zygote, comes into existence at the moment of sperm-egg fusion, an event that occurs in less than a second. Upon formation, the zygote immediately initiates a complex sequence of events that establish the molecular conditions required for continued embryonic development. The behavior of the zygote is radically unlike that of either sperm or egg separately and is characteristic of a human organism. Thus, the scientific evidence supports the conclusion that a zygote is a human organism and that the life of a new human being commences at a scientifically well defined "moment of conception." This conclusion is objective, consistent with the factual evidence, and independent of any specific ethical, moral, political, or religious view of human life or of human embryos.

Westchester Institute White Paper

When Does Human Life Begin?
A Scientific Perspective

HOW HAS THE BEGINNING OF LIFE BEEN DEFINED?

The question of when human life begins is one of considerable ethical, legal, and political importance, particularly for public policy debates over abortion and embryonic stem cell research. Recently, a number of our nation's most prominent political leaders have weighed in on this question, proposing two very different sorts of answers. On the one hand, Nancy Pelosi, the Speaker of the House of Representatives, stated, "I don't think anybody can tell you when … human life begins."[1] Her sentiment has been echoed by Senator Biden,[2] who said that he believes life begins at conception, but that this is merely a religious opinion that could not legitimately be the basis for public policy. In contrast, Senator McCain has confidently stated that life begins "at the moment of conception,"[3] although he did not offer a precise definition of when this moment occurs.

1 Nancy Pelosi, *Meet the Press* interview with Tom Brokaw, August 24, 2008. Transcript available at http://www.msnbc.msn.com/id/26377338/page/3/ (accessed 9/12/2008; transcript on file with author).

2 Joseph Biden, *Meet the Press* interview with Tom Brokaw, September 7, 2008. Transcript available at http://www.msnbc.msn.com/id/26590488/page/4/ (accessed 9/12/2008; transcript on file with author).

3 John McCain, *Saddleback Presidential Forum* interview with Rick Warren, August 16, 2008. Transcript available at http://transcripts.cnn.com/TRANSCRIPTS/0808/17/se.01.html (accessed 9/12/08; transcript on file with author).

Modern science indicates that the beginning of life occurs sometime after the fertilization of an ovum by a sperm cell, yet fertilization itself is surprisingly difficult to define.

When in the course of prenatal development a new human being comes into existence is not an easy question to answer; indeed, it has been answered in many ways throughout history, based on the understanding of human development available at any given time. Advances in the study of human embryology have sharpened our focus to an increasingly narrow developmental time-frame. Modern science indicates that the beginning of life occurs sometime after the fertilization of an ovum by a sperm cell, yet fertilization itself is surprisingly difficult to define. The events immediately following the fusion of sperm and egg—and prior to the first cell division (an approximately 24-hour period also referred to as the first cell cycle)—have typically been viewed as part of the "process" of fertilization (see Figure 1, p. 17). At some point during this period, an embryo forms, but precisely when this occurs has been the subject of considerable disagreement and debate.

The point at which fertilization ends and embryonic development commences is commonly placed at "syngamy," the time when the membranes surrounding the nuclei derived from the sperm and the egg break down in preparation for the first cell division (see Figure 1E, p. 17). Indeed, many textbooks devoted to the topic of human embryology,[4] as well as the legal codes of a number of countries[5] and states within the USA,[6] define the completion of fertilization and beginning of life in this manner. Yet this is not the only point at which life is said to begin. Recently,[7] it has been asserted that the life and moral status of the embryo begin at the eight-cell stage, because zygotic transcription (the active utilization of embryonic genes) commences at this time; and prior to this moment, whatever is happening in the "fertilized egg" [8] is being driven by maternal factors.[9] Some push the onset of life to even later, to the formation of specific structures or the onset of specific developmental processes.[10]

4 For example: "Fertilization is a complex sequence of coordinated events that begins with contact between a sperm and an oocyte…and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote" [Keith L. Moore and T.V.N. Persaud, *The Developing Human*, 7th ed. (Philadelphia: Saunders-Elsevier, 2003), 31]; "At this point, [syngamy] the process of fertilization can be said to be complete and the fertilized egg is called a zygote" [Bruce M. Carlson, *Human Embryology and Developmental Biology*, 3rd ed. (Philadelphia: Mosby-Elsevier, 2004), 36].

5 International Consortium of Stem Cell Networks, "Global Regulation of Human Embryonic Stem Cell Research and Oocyte Donation" http://www.stemcellcentre.edu.au/PDF/Global_Regulation_HESC_Research_Oocyte_Donation.pdf (accessed October 6, 2008).

6 For example: VA. CODE ANN. S 20-156 (2004): "'Embryo' means the organism resulting from the union of a sperm and an ovum from first cell division until approximately the end of the second month of gestation."

7 Philip G. Peters, Jr., "The Ambiguous Meaning of Human Conception," *University of California-Davis Law Review* 40 (2006):199-228.

8 Referring to the product of sperm-egg fusion as a "fertilized egg" is misleading; once an egg is fertilized, it ceases to be an egg. This term avoids the central question of what kind of cell is produced by fertilization.

9 There is good evidence from mouse and from human embryos that the zygotic genome becomes active before the first cell division: Luke Martin-McCaffrey et al., "RGS14 is a Mitotic Spindle Protein Essential from the First Division of the Mammalian Zygote," *Developmental Cell* 7, no. 5 (November 2004): 763-9; Asangla Ao et al., "Transcription of Paternal Y-linked Genes in the Human Zygote as Early as the Pronucleate Stage," *Zygote* 2, no. 4 (November 1994): 281-7; Robert Daniels et al., "XIST Expression in Human Oocytes and Preimplantation Embryos" *American Journal of Human Genetics* 61, no. 1 (July 1997): 33-9; Richard M. Schultz, "Regulation of Zygotic Gene Activation in the Mouse," *Bioessays* 15, no. 8 (August 1993): 531-8; Christine Bouniol, Eric Nguyen, and Pascale Debey, "Endogenous Transcription Occurs at the 1-cell Stage in the Mouse Embryo," *Experimental Cell Research* 218, no. 2 (May 1995): 57-62; Anthony T. Dobson et al., "The Unique Transcriptome Through Day 3 of Human Preimplantation Development," *Human Molecular Genetics* 13, no. 14 (July 2004):1461-70.

10 It is commonly claimed that life begins with the formation of the inner cell mass of the embryo (~four days post fertilization), or when the embryo implants in the uterus (~5-6 days post fertilization), or at the onset of gastrulation (~two weeks after fertilization).

The fact that life is truly a continuum further complicates the question of when a new life commences. Most human beings are produced from the union of two preexisting cells: sperm and egg. Sperm and egg cells were, in turn, generated from living cells that preceded them in the testes and ovaries, and so forth, back indefinitely to the beginning of all life. In light of the continuous nature of living cells, defining the beginning of a new organism as the onset of zygotic transcription or the breakdown of nuclear membranes is intellectually and scientifically unsatisfying. These are arbitrary points along a continuum of life—points that are likely to vary considerably across closely related species and across individuals of the same species. Such definitions are logically akin to linking the beginning of "personhood" to the eruption of teeth in an infant or to the onset of menses in an adolescent—they are arbitrary, variable, and not indicative of any fundamental change in the entity under consideration.

The continuum of cellular life—with living cells giving rise to new types of cells and, ultimately, to new individuals—has led some to conclude that the question of "when life begins" is unanswerable. Because cellular life exists in a continuum, this line of reasoning concludes, there can be no meaningful point at which a "new" human life is said to begin. Yet if this view is correct, we are left with a serious ethical dilemma: while no one objects to the destruction of ordinary human cells for biomedical research, the use of *human beings* for such purposes is universally condemned. Clearly, some non-arbitrary criteria must be established to determine when living human cells give rise to a new individual human being.

WHAT IS THE SCIENTIFIC BASIS FOR DISTINGUISHING DIFFERENT TYPES OF CELLS?

Science relies on detailed observation to determine when a change in cell type has occurred. Throughout embryogenesis, cells continuously change from one type to another, and these transitions can be reliably detected. Scientific distinctions are made between various cell types, based on two relatively simple criteria: cells are known to be different from each other because they have different composition (i.e., different genes are expressed, different proteins produced, etc.) and because they exhibit distinct types of cell behavior. For example, a transient embryonic population of cells, known as neural crest cells, produces a variety of different cell types during development, including the progenitors of all the sensory neurons of the body. As neural crest cells convert into this new cell type (sensory neural progenitors), they undergo a number of observable changes: they stop migrating, begin a period of more active cell proliferation, begin to express different genes, and assume a different cellular morphology. These changes are the basis for asserting that neural crest cells and sensory neural progenitors are *distinct* cell types.

When cells are classified into specific types, differences in either composition or behavior are the bases for all *scientific*, as opposed to *arbitrary*, distinctions. If, for example, scientists were to propose that during embryonic development a novel cell type exists between a neural crest and a sensory neural progenitor cell, they would have to *prove* this assertion by pointing to specific material or behavioral characteristics that distinguish this cell both from the cell that gave rise to it and from the cell it subsequently generates—or risk having their assertions dismissed as mere fantasy.

In considering the question of when the life of a new human being commences, we must first address the more fundamental question of when a new cell, distinct from sperm and egg, comes into existence: when during the interactions of sperm and egg do we observe the formation of a new cell with both a material composition and a developmental pathway (i.e., a pattern of cell behavior) that are distinct from the cells giving rise to it? These two criteria (unique composition and behavior) are used throughout the scientific enterprise to distinguish one cell type from another—and if we reject them as the basis for making such distinctions, the only alternative is to make an essentially arbitrary decision.

HOW DOES THE ZYGOTE DIFFER FROM SPERM AND EGG?

The basic events of early development are both reasonably well characterized and entirely uncontested. Following the binding of sperm and egg to each other, the membranes of these two cells fuse, creating in this instant a single hybrid cell: the zygote or one-cell embryo (see Figure 1A). Cell fusion is a well studied and very rapid event, occurring in less than a second.[11] Because the zygote arises from the fusion of two different cells, it contains all the components of both sperm and egg, and therefore the zygote has a unique molecular composition that is distinct from either gamete.

Subsequent to sperm-egg fusion, events rapidly occur in the zygote that do not normally occur in either sperm or egg. The contents of what was previously the sperm, including its nucleus, enter the cytoplasm of the newly formed zygote. Within minutes of membrane fusion, the zygote initiates changes in its ionic composition[12] that will, over the next 30 minutes, result in chemical modifications of the zona pellucida, an acellular structure surrounding the zygote (Figure 1B). These modifications block sperm binding to the cell surface and prevent further intrusion of additional spermatozoa on the unfolding process of development. Thus, the zygote acts immediately and specifically to antagonize the function of the gametes from which it is derived; while the "goal" of both sperm and egg is to find each other and to fuse, the first act of the zygote is immediately to prevent any further binding of sperm to the cell surface. Clearly, then, the prior trajectories of sperm and egg have been abandoned, and a new developmental trajectory—that of the zygote—has taken their place.

Fig 1A Sperm-Egg Fusion

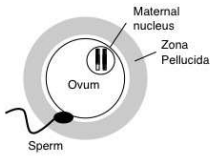


Fig 1B Zygote Formation

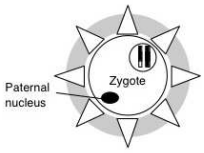


Fig 1C Early Acts of the Zygote

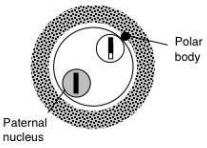
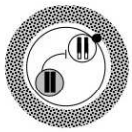


Fig 1D Onset of Zygotic Transcription



11 Ulyana Vjugina and Janice P. Evans, "New Insights into the Molecular Basis of Mammalian Sperm-Egg Membrane Interactions," *Frontiers in Bioscience* 13, no. 2 (January 2008): 462-76; Meital Oren-Suissa and Benjamin Podbilewicz, "Cell Fusion During Development," *Trends in Cell Biology* 17, no. 11 (November 2007): 537-46.

12 Llewellyn J. Cox et al., "Sperm Phospholipase Czeta from Humans and Cynomolgus Monkeys Triggers Ca2+ Oscillations, Activation and Development of Mouse Oocytes," *Reproduction* 124, no. 5 (November 2002): 611-23; Christopher M. Saunders, Karl Swann, and F. Anthony Lai, "PLCzeta: A Sperm-Specific PLC and its Potential Role in Fertilization," *Biochemical Society Symposia* 74 (2007): 23-36.

maternally derived DNA.[21] This differential transcription again indicates that the two halves of the genome interact prior to syngamy, even though they are located in physically separate compartments within the zygote.

Gradually, the two pronuclei move towards the center of the cell, in preparation for the first cell division (i.e., mitosis) of the zygote (Figure 1E). Immediately prior to cell division, syngamy occurs. Although syngamy is often characterized as the "uniting" of the two halves of the genome to generate a single diploid nucleus, in fact, syngamy is little more than the breakdown of the nuclear membranes that separate the two pronuclei. No "single" nucleus is formed at this point since there is no nucleus at all. The maternally and paternally derived chromosomes are merely present in the same general region of the cytoplasm. This physical co-localization is required for accurate segregation of the chromosomes during cell division, so that both cells of the two-cell embryo inherit identical DNA. Following nuclear membrane breakdown (i.e., "syngamy"), the first mitotic division of the zygote takes place, thus completing the first cell cycle and generating the two-cell embryo (Figure 1F).

From this time forward, although many complex interactions will occur between cells as the mature body is gradually produced, on the intracellular level DNA replication and cell division will proceed in more or less the standard way that is common to all body cells. Thus, the events of the first cell cycle, which modify the DNA contributed by sperm and egg to enable the participation of this DNA in embryonic development, are unique to the zygote and to the first cell cycle (i.e., the first day following sperm-egg fusion).

Based on this factual description of the events following sperm-egg binding, we can confidently conclude that a new cell, the zygote, comes into existence at the "moment" of sperm-egg fusion, an event that occurs in less than a second. At the point of fusion, sperm and egg are physically united—i.e., they cease to exist as gametes, and they form a new entity that is materially distinct from either sperm or egg. The behavior of this new cell also differs radically from that of either sperm or egg: the developmental pathway entered into by the zygote is distinct from both gametes. Thus, sperm-egg fusion is indeed a scientifically well defined "instant" in which the zygote (a new cell with unique genetic composition, molecular composition, and behavior) is formed.

IS THE ZYGOTE MERELY A NEW HUMAN CELL OR IS IT A NEW HUMAN INDIVIDUAL?

The events immediately following sperm-egg fusion provide incontrovertible evidence that a new human cell, the zygote, is produced by this event. Yet, these observations do not address whether the life of a new human individual has commenced. Is the zygote merely a new kind of cell, or is it a new *human being*—a distinct, individual human organism?

17 Gemma Capmany et al., "The Timing of Pronuclear Formation, DNA Synthesis and Cleavage in the Human 1-cell Embryo," *Molecular Human Reproduction* 2, no. 5 (May 1996): 299-306.

18 Pierre Comizzoli et al., "Onset of the First S-phase is Determined by a Paternal Effect During the G1-phase in Bovine Zygotes," *Biology of Reproduction* 62, no. 6 (June 2000): 1677-84; J. Schabronath and K. Gärtner, "Paternal Influence on Timing of Pronuclear DNA Synthesis in Naturally Ovulated and Fertilized Mouse Eggs," *Biology of Reproduction* 38, no. 4 (May 1988): 744-9.

19 See footnote 9.

20 Toshio Hamatani et al., "Dynamics of Global Gene Expression Changes During Mouse Preimplantation Development," *Developmental Cell* 6, no. 1 (January 2004): 117-31; Toshio Hamatani et al., "Global Gene Expression Profiling of Preimplantation Embryos" *Human Cell* 19, no. 3 (August 2006): 98-117. See also Diane M.Worrad, Prahlad T. Ram, and Richard M. Schultz, "Regulation of Gene Expression in the Mouse Oocyte and Early Preimplantation Embryo: Developmental Changes in Sp1 and TATA Box-binding Protein, TBP," *Development* 120, no. 8 (August 1994): 2347-57, and references therein.

21 Fugaku Aoki, Diane M. Worrad, and Richard M. Schultz, "Regulation of Transcriptional Activity During the First and Second Cell Cycles in the Preimplantation Mouse Embryo," *Developmental Biology* 181, no. 2 (January 1997): 296-307; Marie Wiekowski, Miriam Miranda, and Melvin L. DePamphilis, "Requirements for Promoter Activity in Mouse Oocytes and Embryos Distinguish Paternal Pronuclei from Maternal and Zygotic Nuclei," *Developmental Biology* 159, no. 1 (September 1993): 366-78; Pierre G. Adenot et al., "Differential H4 Acetylation of Paternal and Maternal Chromatin Precedes DNA Replication and Differential Transcriptional Activity in Pronuclei of 1-cell Mouse Embryos" *Development* 124, no. 22 (November 1997): 4615-25.

Fig 1E Syngamy

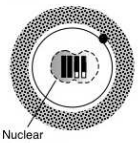
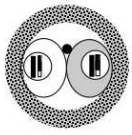


Fig 1F Two-Cell Embryo



The question of precisely when a new human organism comes into existence wasn't a matter of practical importance until the advent of *in vitro* fertilization and human embryo research. Consequently, scientists, philosophers, and bioethicists have not considered this question in great detail until recently; and appealing to experts (embryologists and ethicists alike) yields a plethora of opinions, often with very little factual evidence to support them. To address this question based on the scientific evidence, it is important to distinguish clearly between human cells and human organisms.

An organism is defined as "(1) a complex structure of interdependent and subordinate elements whose relations and properties are largely determined by their function in the whole and (2) an individual constituted to carry on the activities of life by means of organs separate in function but mutually dependent: a living being."[22] This definition stresses the interaction of parts in the context of a coordinated whole as the distinguishing feature of an organism.

22 http://www.merriam-webster.com/dictionary/organism (accessed 10/1/2008; definition on file with the author). The second definition is also given verbatim by the National Library of Medicine, administered by the National Institutes of Health (http://www.nlm.nih.gov/medlineplus/mplusdictionary.html).

The key feature of a human pattern of development is its organization towards the production of a mature human body.

Based on this definition, it has been proposed that human beings (including embryonic human beings) can be reliably distinguished from human cells using the same kinds of criteria scientists employ to distinguish different cell types: by examining their composition and their pattern of behavior.[23] A human being (i.e., a human organism) is composed of characteristic human parts (cells, proteins, RNA, DNA), yet it is different from a mere collection of cells because it has the characteristic behavior of an organism: it acts in an interdependent and coordinated manner to "carry on the activities of life." In contrast, collections of human cells are alive and carry on the activities of cellular life, yet fail to exhibit coordinated interactions directed towards any higher level of organization. Collections of cells do not establish the complex, interrelated cellular structures (tissues, organs, and organ systems) that exist in a whole, living human being. Similarly, a human corpse is not a living human organism, despite the presence of living human cells within the corpse, precisely because this collection of human cells no longer functions as an integrated unit.[24]

Is a human zygote a human organism? For developing humans, the behavior and structures associated with adult stages of life are not yet fully manifest (embryos neither look like nor act like mature human beings). However, developing human beings are composed of characteristic human parts and they exhibit a *human* pattern of developmental behavior. *The key feature of a human pattern of development is its organization towards the production of a mature human body.*

23 Maureen L. Condic and Samuel B. Condic, "Defining Organisms by Organization," *National Catholic Bioethics Quarterly* 5: 331-353.

24 Maureen L. Condic, "Life: Defining the Beginning by the End," *First Things* 133: 50-54.

From the moment of sperm-egg fusion, a human zygote acts as a complete whole, with all the parts of the zygote interacting in an orchestrated fashion to generate the structures and relationships required for the zygote to continue developing towards its mature state. Everything the sperm and egg do prior to their fusion is uniquely ordered towards promoting the binding of these two cells. Everything the zygote does from the point of sperm-egg fusion onward is uniquely ordered to *prevent* further binding of sperm and to promote the preservation and development of the zygote itself. The zygote acts immediately and decisively to initiate a program of development that will, if uninterrupted by accident, disease, or external intervention, proceed seamlessly through formation of the definitive body, birth, childhood, adolescence, maturity, and aging, ending with death. This coordinated behavior is the very hallmark of an organism.

Mere human cells, in contrast, are composed of human DNA and other human molecules, but they show no global organization beyond that intrinsic to cells in isolation. A human skin cell removed from a mature body and maintained in the laboratory will continue to live and will divide many times to produce a large mass of cells, but it will not re-establish the whole organism from which it was removed; it will not regenerate an entire human body in culture. Although embryogenesis begins with a single-cell zygote, the complex, integrated process of embryogenesis is the activity of an organism, not the activity of a cell.

Based on a scientific description of fertilization, fusion of sperm and egg in the "moment of conception" generates a new human cell, the zygote, with composition and behavior distinct from that of either gamete. Moreover, this cell is not merely a unique human cell, but a cell with all the properties of a fully complete (albeit immature) human organism; it is "an individual constituted to carry on the activities of life by means of organs separate in function but mutually dependent: a living being."[25]

WHY ISN'T SYNGAMY THE BEGINNING OF A NEW HUMAN LIFE?

Syngamy, the breakdown of nuclear membranes in preparation for cell division, is commonly held to be the point at which the zygote is formed and life begins. This definition does not deny that a new cell with unique composition and behavior is formed at sperm-egg fusion (a "pre-zygote," perhaps), but it fails to specify the nature of this cell. The reasons for identifying syngamy as the beginning of life are two-fold. First, syngamy is the last event associated with the first cell cycle and thus represents the completion of this unique period of development. After this point, many interesting and complex interactions occur, but the cells of the embryo behave in manners that are also seen in other, more mature body cells. Thus, according to some, syngamy marks the end of the "process" of fertilization and the onset of a developmental trajectory driven by the zygote itself. Second, many believe that syngamy represents

25 See footnote 22.

the "fusion" of the maternally and paternally derived half-genomes, and the generation of the mature, diploid genome that is unique to the new individual. Both of these assertions are scientifically inaccurate.

Compared with the changes in both material composition and developmental trajectory that occur at the fusion of sperm and egg, syngamy is fundamentally an arbitrary definition for the beginning of life.

Compared with the changes in both material composition and developmental trajectory that occur at the fusion of sperm and egg, syngamy is fundamentally an arbitrary definition for the beginning of life. From a biological perspective, the breakdown of nuclear membranes at syngamy is a relatively mundane event along an *already progressing* developmental trajectory. The material composition of the cell does not change from the instant prior to syngamy to the instant after it takes place. There is no substantive change in the behavior of the cell at syngamy; all the preparations for cell division (DNA replication, assembly of the mitotic spindle, chromatin condensation) are already underway as the pronuclei move together. Indeed, nuclear membrane breakdown is not a unique, "zygote-forming" event, but rather it is part of every round of cell division that occurs through life. The zygote is the same cell—and it continues doing exactly what it was doing (i.e., preparing to undergo cell division) both before and after the pronuclei come into physical proximity. The developmental program observed during the first cell cycle (including the breakdown of nuclear membranes at syngamy) is clearly initiated by the fusion of the sperm and egg, and it progresses seamlessly from that instant forward.

The assertion that the mature, diploid genome forms at syngamy is also scientifically untenable. The definitive diploid genome is formed at the completion of meiosis. As detailed above, although syngamy appears to result in the "fusion" of the two pronuclei, the maternally and paternally derived DNA interact extensively prior to syngamy. The physical proximity of the two halves of the genome achieved after nuclear membrane breakdown is biologically irrelevant to the ongoing interaction of the DNA contained within the genome.[26] Moreover, the "mingling" of the DNA that occurs at syngamy is in some ways quite superficial. There is good evidence that full mingling of the maternal and paternal DNA strands is not completed during the first cell cycle, but rather that chromatin derived from each parent occupies distinct domains within the nucleus until at least the four-cell stage.[27] Thus, syngamy does not fully establish the normal state of a diploid nucleus (as is seen in mature somatic cells, with random mixing of DNA strands derived from both parents), further compromising syngamy as a definition of when the life of a new individual begins.

26 A good analogy for the communication between the maternally and paternally derived halves of the genome is the communication of two Internet-linked computers with different data sets that are executing a common program. The computers will transmit information and mutually modify each other's function via electronic signals that are carried by data cables or telephone lines. The mechanism of this indirect communication will not be substantially different for computers separated by a few feet than for those separated by a few thousand miles; computers located in the same room are not somehow more "united" by virtue of their physical proximity than are computers located in different countries. Similarly, DNA communicates indirectly and remotely via DNA-binding proteins, and this communication is not dependent on physical proximity. So long as the two halves of the genome are contained within a single cell (i.e., there is a common mechanism for communication between different elements of the genome), interaction between maternally and paternally derived DNA happens indirectly through transcription and translation of DNA binding proteins, mechanisms that do not require the DNA to be "united" within a single nuclear membrane.

27 Wolfgang Mayer et al., "Spatial Separation of Parental Genomes in Preimplantation Mouse Embryos," *Journal of Cell Biology* 148, no. 4 (February 21, 2000): 629-34; Seungeun Yeo et al., "Methylation Changes of Lysine 9 of Histone H3 During Preimplantation Mouse Development," *Molecules and Cells* 20, no. 3 (December 2005): 423-8; Fatima Santos et al., "Dynamic Reprogramming of DNA Methylation in the Early Mouse Embryo," *Developmental Biology* 241, no. 1 (January 2002): 172-82; Jacqueline Bomar et al., "Differential Regulation of Maternal and Paternal Chromosome Condensation in Mitotic Zygotes," *Journal of Cell Science* 115, no. 14 (July 15, 2002): 2931-40.

The essential problem with the view that life begins at syngamy is the notion that a cell can change from one type (a "pre-zygote" that exists following sperm-egg fusion but prior to syngamy) into another type (the zygote that exists after syngamy) without any actual change in the material state or behavioral trajectory of the cell. This argument is simply not consistent with the scientific method. To assert that life begins at syngamy is to propose some form of mysticism: although a zygote cannot be distinguished in any significant manner from the "pre-zygote" that precedes it, the cell is now a zygote simply because one asserts that it is.

Regardless of how intuitively plausible syngamy may seem as a marker for the onset of a new cell (the zygote), without a demonstrable change in the material and/or the behavioral state of the cell—that is, without credible scientific *evidence* that a new cell type comes into existence at this point—one simply cannot assert that syngamy marks the beginning of a new human cell type, much less a new human being.

WHAT ARE PARTHENOTES, HYDATIDIFORM MOLES, AND CLONES?

Defining the beginning of life as the point at which a new, single-cell organism with unique composition and behavior is formed raises concerns about a number of entities that appear to be closely related to embryos. In particular, parthenotes, hydatidiform moles, and human clones raise issues that need to be carefully considered.

Cloning presents a challenge to the proposed definition of when life begins because cloning does not involve the union of sperm and egg.

In many animal species, mature egg cells can be induced to divide in the absence of sperm by external administration of an electrical pulse or a chemical stimulus that mimics some aspects of fertilization. Depending on the species, such "parthenotes" will progress through a sequence of developmental events that are quite similar to the development of a zygote. Indeed, in some species of animals, parthenotes occur spontaneously and can mature to fully formed adults.[28] However, for most species, including all mammals thus far studied, parthenotes do not develop normally or survive to birth.

Are parthenotes organisms? In the case of mammals, although parthenotes are similar to zygotes in certain respects, there are significant differences. Parthenotes contain only maternal chromosomes and, therefore, have a composition that is distinct from a zygote. Importantly, there is no strong evidence that human parthenotes exhibit globally coordinated activity of parts to generate an integrated pattern of development.[29] The fact that certain aspects of early zygotic behavior can be mimicked

28 Christoph Vorburger, "Geographic Parthenogenesis: Recurrent Patterns Down Under," *Current Biology* 16, no. 16 (August 22, 2006): R641-3; Robert G. Edwards, "The Significance of Parthenogenetic Virgin Mothers in Bonnethead Sharks and Mice," *Reproductive BioMedicine Online* 15, no. 1 (July 2007): 12-5; T. V. Groot, E. Bruins, and J. A. Breeuwer, "Molecular Genetic Evidence for Parthenogenesis in the Burmese Python, Python Molurus Bivittatus," *Heredity* 90, no. 2 (February 2003): 130-5; G. Cassar, T. M. John, and R. J. Etches, "Observations on Ploidy of Cells and on Reproductive Performance in Parthenogenetic Turkeys," *Poultry Science* 77, no. 10 (October 1998): 1457-62.

29 See discussion of human parthenogenesis in Mahendra Rao and Maureen L. Condic, "Alternative Sources of Pluripotent Stem Cells: Scientific Solutions to an Ethical Dilemma," *Stem Cells and Development* 17, no. 1: 1-10.

artificially in the laboratory by delivering electrical or chemical stimulation to an oocyte in no way compromises the account of when life begins during the interaction of sperm and egg. An electrically stimulated egg is different in material composition from a bona fide zygote, and (on a molecular level) its "behavior" shows it to be quite distinct from a zygote.[30]

A parallel, yet opposite case is presented by complete hydatidiform moles, a type of tumor that arises as a consequence of abnormal fertilization. Most commonly, hydatidiform moles form when a normal sperm fertilizes an oocyte that has abnormally lost its own genetic material. This event results in a tumor-forming cell with only paternally derived chromosomes. Hydatidiform moles grow quite rapidly and in some ways mimic a normal pregnancy (indeed, they are often referred to as a "molar pregnancy"). However, because hydatidiform moles contain only paternally derived chromosomes, they are distinguishable from zygotes based on their molecular composition. Moreover, hydatidiform moles behave quite differently from embryos: they grow as a chaotic mass of disorganized cells and tissues, all of which are unrelated to each other or to anything resembling a whole. Despite the fact that hydatidiform moles are generated from human gametes, they do not exhibit an embryonic pattern of organization or molecular composition; they are a collection of human cells, but not a human organism.

Finally, cloning, or somatic cell nuclear transfer (SCNT), presents a challenge to the proposed definition of when life begins because cloning does not involve the union of sperm and egg. In SCNT, the nucleus of an egg is removed and a mature body (somatic) cell is then fused to the empty egg, generating a hybrid cell that contains the genetic information of the body cell. In rare cases (usually less than one in a hundred transfers) the body cell nucleus is reprogrammed by the egg cytoplasm to a state that is capable of supporting a relatively normal pattern of embryonic development. Although human cloning has only recently been reported,[31] it is likely that improvements in the cloning technique will enable human clones to be reliably generated through SCNT.

Does generation of a cloned human embryo or live human baby by SCNT compromise the definition of when a life begins? No. Upon transfer of a somatic nucleus to an empty egg cell, a new cell is generated that has a material composition and a developmental trajectory different from those of either of the two cells that produced it. In the rare cases where this hybrid cell goes on to produce a normal pattern of development, its behavior demonstrates that it is an organism.[32] The production of human embryos via cloning indicates that although gametes are naturally disposed to generate a new organism upon fusion, embryos can also be generated under other, highly artificial circumstances. Cloning simply indicates that there is more than one way to make a zygote; it does not alter the analysis of natural fertilization or compromise our ability to determine precisely when fertilization results in an organism that is both materially and behaviorally distinct from the gametes that give rise to it.

30 The question of whether human parthenotes can, in rare cases, exhibit an organismal pattern of development remains controversial, mostly due to a lack of rigorous scientific observation. While it is clear that human parthenotes do not develop normally, considerable caution is in order. Although stimulated egg cells do not differ in molecular composition from unstimulated eggs, they *do* exhibit a radical change in developmental trajectory—or behavior. Should it be demonstrated that parthenotes have some degree of coordinated development, it would raise the concern that they may be severely defective human organisms.

31 Andrew J. French et al., "Development of Human Cloned Blastocysts Following Somatic Cell Nuclear Transfer with Adult Fibroblasts," *Stem Cells* 26, no. 2 (February 2008): 485-93.

32 In cases where the development of the cell produced by cloning is abnormal or where the clone does not survive, interpreting the nature of the cell produced by SCNT is problematic. If such clones exhibit any degree of normal, "organismal" coordination, caution would dictate they should be considered defective organisms.

DOES A HUMAN BEING CONTROL ITS OWN DEVELOPMENT OR IS IT "MANUFACTURED"?

Why has it been so difficult to define when a human life begins? Why has the view that life begins at syngamy (or at even later developmental stages) been so compelling for so many scientists and physicians? Those who advocate syngamy as the beginning of life appear to find it intuitively obvious that syngamy completes the unique events of the first cell cycle and produces "full union" of the gametes; until syngamy occurs, the "process" of fertilization is still underway. Those who advocate an even later point for the onset of life do so on the basis of a similar argument: the embryo has not yet fully formed until specific structures or processes are in place; until these "defining" events occur, the process of fertilization (or of embryo formation) is still underway. Clearly, if fertilization is seen as a process rather than as an event, then prior to the completion of this process the zygote is not yet fully present. Based on this view, the cell that results from the fusion of sperm and egg is not a new individual but, as expressed recently by a colleague, merely "a unique human cell in the process of becoming a new human, but not there yet." [33]

This way of thinking about human development is compelling to many because it is similar to our thinking about the much more familiar process of manufacturing. A car is not a car until it rolls off the assembly line—until then it is a bunch of parts in the process of becoming a car, but not there yet. Similarly, a cake is not a cake until it comes out of the oven—until then it is a variously gooey mass of flour, sugar, eggs, and butter that is gradually becoming a cake.

The embryo is not something that is being passively built by the process of development, with some unspecified, external "builder" controlling the assembly of embryonic components. Rather, the embryo is manufacturing itself.

However, a profound difference exists between manufacturing and embryonic development. The difference is who (or what) is doing the "producing." The embryo is not something that is being passively built by the process of development, with some unspecified, external "builder" controlling the assembly of embryonic components. Rather, *the embryo is manufacturing itself.* The organized pattern of development doesn't produce the embryo; it is produced *by* the embryo as a consequence of the zygote's internal, self-organizing power. Indeed, this "totipotency," or the power of the zygote both to generate all the cells of the body and simultaneously to organize those cells into coherent, interacting bodily structures, is the defining feature of the embryo.[34]

33 Micheline Mathews-Roth, M.D., Harvard University (personal communication).

34 Identical twins demonstrate that totipotency may be preserved in all the cells of a human embryo, up to the two-cell stage, or even later (identical quintuplets are extremely rare, but have been observed). The phenomenon of twinning does not alter the importance of the zygote's producing its own development based on an internal developmental program. Twinning merely indicates that when cells of the early embryo are separated, they retain this internal developmental potency and are able to regenerate the missing cellular components to produce a complete pattern of human development.

An additional problem with comparing embryogenesis to manufacturing is that, unlike the building of an automobile, there is no actual endpoint to the "building" of a human being. Human development is an *ongoing* process that begins with the zygote and continues seamlessly through embryogenesis, fetogenesis, birth, maturation, and aging, ending only in death. If the zygote is a manufactured "product" of an ongoing developmental process, at what point along this continuum does a human being actually exist? Why is a cell that has undergone syngamy a human zygote and not merely a "unique human cell in the process of becoming a new human, but not there yet"? Indeed, why consider the entity present at the end of embryogenesis or at birth a human being, and not merely "a unique collection of human cells in the process of becoming a new human, but not there yet"? Once a concession has been made to the concept of manufacture and to an arbitrary point at which development has proceeded "far enough" along the assembly line to generate a human being, the precise positioning of this point becomes purely a matter of preference, convenience, and the power to enforce one's view.

In contrast, if the embryo comes into existence at sperm-egg fusion, a human organism is fully present from the beginning, controlling and directing all of the developmental events that occur throughout life. This view of the embryo is objective, based on the universally accepted scientific method of distinguishing different cell types from each other, and it is consistent with the factual evidence. It is entirely independent of any specific ethical, moral, political, or religious view of human life or of human embryos. Indeed, this definition does not directly address the central ethical questions surrounding the embryo: What *value* ought society to place on human life at the earliest stages of development? Does the human embryo possess the same right to life as do human beings at later developmental stages? A neutral examination of the factual evidence merely establishes the onset of a new human life at a scientifically well defined "moment of conception," a conclusion that unequivocally indicates that human embryos from the zygote stage forward are indeed living individuals of the human species—human beings.

AUTHOR

Dr. Condic is an Associate Professor of Neurobiology and Anatomy at the University of Utah School of Medicine, with an adjunct appointment in the Department of Pediatrics. She received her undergraduate degree from the University of Chicago, and her doctorate from the University of California at Berkeley. Since her appointment at the University of Utah in 1997, Dr. Condic's primary research focus has been the development and regeneration of the nervous system. In 1999, she was awarded the Basil O'Connor Young Investigator Award for her studies of peripheral nervous system development. In 2002, she was named a McKnight Neuroscience of Brain Disorders Investigator in recognition of her research in the field of adult spinal cord regeneration. In addition to her scientific research, Dr. Condic participates in both graduate and medical teaching. She is director of the University of Utah School of Medicine course in Human Embryology. She has published and presented seminars nationally on issues concerning science policy and the ethics of biological research. Dr. Condic currently resides in Salt Lake City with her husband and four children.

Maureen L. Condic, Ph.D.
Department of Neurobiology and Anatomy, University of Utah School of Medicine
Salt Lake City, UT 84132-3401
mlcondic@neuro.utah.edu

GLOSSARY *

* All definitions are taken from the NIH-administered medical dictionary, (accessed 10/1/08; definitions on file with author; http://www.nlm.nih.gov/medlineplus/mplusdictionary.html) with minor modifications for clarity, as indicated by italics.

centromere: the point or region on a chromosome to which the spindle attaches during mitosis and meiosis–also called kinetochore.

chromatin: a complex of a nucleic acid with basic proteins (as histone) in eukaryotic cells that is usually dispersed in the interphase nucleus and condensed into chromosomes in mitosis and meiosis.

chromosome: any of the usually linear bodies of the cell nucleus of eukaryotic organisms that take up basophilic stains and contain most or all of the genes of the organism; *a condensed form of chromatin found prior to cell division. When chromosomes have replicated, but are still attached at the centromere, they are called sister chromatids.*

demethylation: the process of removing a methyl group from a chemical compound. *Methyl groups bound to DNA generally inhibit DNA function.*

diploid: having the basic *(haploid)* chromosome number doubled. *Diploid is the normal state for somatic (i.e., body) cells.*

DNA: any of various nucleic acids that are usually the molecular basis of heredity, that are constructed of a double helix held together by hydrogen bonds between purine and pyrimidine bases, which project inward from two chains containing alternate links of deoxyribose and phosphate, and that in eukaryotes are localized chiefly in cell nuclei—also called deoxyribonucleic acid.

embryo: an animal in the early stages of growth and differentiation that is characterized by cleavage, the laying down of fundamental tissues, and the formation of primitive organs and organ systems; especially the developing human individual from the time of *fertilization* to the end of the eighth week after conception *(cleavage commences immediately after fertilization at the two cell stage).*

eukaryote: any of a domain (Eukarya) or a higher taxonomic group (Eukaryota) above the kingdom that includes organisms composed of one or more cells containing visibly evident nuclei and organelles.

fertilization: the process of union of two gametes whereby the somatic chromosome number is restored and the development of a new individual is initiated.

gamete: a mature male or female germ cell *(sperm or egg)* usually possessing a haploid chromosome set and capable of initiating formation of a new diploid individual by fusion with a gamete of the opposite sex—also called sex cell.

gene: a specific sequence of nucleotides in DNA that is located usually on a chromosome and that is the functional unit of inheritance controlling the transmission and expression of one or more traits by specifying the structure of a particular polypeptide and especially a protein or controlling the function of other genetic material – also called determinant, determiner, factor.

genome: one haploid set of chromosomes with the genes they contain.

haploid: having the gametic number of chromosomes or half the number characteristic of somatic cells.

histone: any of various simple water-soluble proteins that are rich in the basic amino acids lysine and arginine and are complexed with DNA.

hydatidiform mole: a mass in the uterus that consists of enlarged edematous degenerated chorionic villi, growing in clusters resembling grapes, that typically develops following fertilization of an enucleate egg, and that may or may not contain fetal tissue.

meiosis: the cellular process that results in the number of chromosomes in gamete-producing cells being reduced to one half and that involves a reduction division in which one of each pair of homologous chromosomes passes to each daughter cell and a mitotic division.

mitosis: a process that takes place in the nucleus of a dividing cell, involves typically a series of steps consisting of prophase, metaphase, anaphase, and telophase, and results in the formation of two new nuclei each having the same number of chromosomes as the parent nucleus.

nucleus: a cellular organelle of eukaryotes that is essential to cell functions (as reproduction and protein synthesis), is composed of nuclear sap and a nucleoprotein-rich network from which chromosomes and nucleoli arise, and is enclosed in a definite membrane.

organism: an individual constituted to carry on the activities of life by means of organs separate in function but mutually dependent: a living being.

ovum (oocyte, egg): a female gamete—especially a mature egg that has undergone reduction, is ready for fertilization, and takes the form of a relatively large inactive gamete providing a comparatively great amount of reserve material and contributing most of the cytoplasm of the zygote.

parthenote: *an individual formed by* development of an unfertilized, usually female, gamete that occurs especially among lower plants and invertebrate animals.

pronucleus: the haploid nucleus of a male or female gamete (as an egg or sperm) up to the time of fusion with that of another gamete in fertilization.

protamine: any of various strongly basic proteins of relatively low molecular weight that are rich in arginine and are found, associated especially with DNA, in place of histone in the sperm of various animals.

RNA: any of various nucleic acids that contain ribose and uracil as structural components and are associated with the control of cellular chemical activities—called also ribonucleic acid. Messenger RNA is an RNA produced by transcription that carries the code for a particular protein from the nuclear DNA to a ribosome in the cytoplasm and acts as a template for the formation of that protein—also called mRNA.

SCNT/Cloning: *Somatic cell nuclear transfer (SCNT)*; transplanting nuclei from body *(i.e., somatic)* cells to enucleated eggs.

sister chromatid: *see chromosome.*

sperm (spermatozoa): *a sperm cell*; a motile male gamete of an animal usually with rounded or elongate head and a long posterior flagellum.

syngamy: sexual reproduction by union of gametes. *Commonly used to refer to the break-down of nuclear membranes of the pronuclei approximately 24 hours after sperm-egg fusion.*

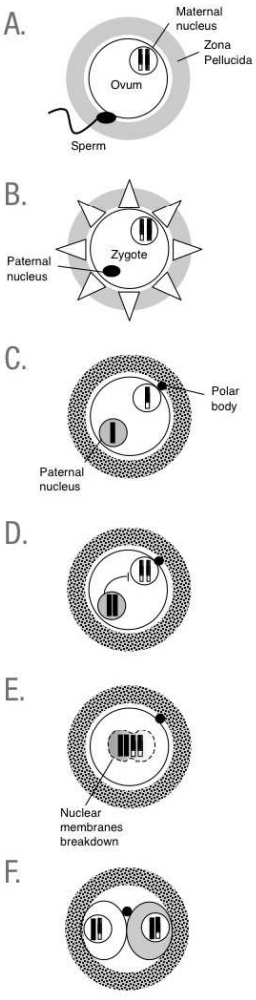
transcription: the process of constructing a messenger RNA molecule using a DNA molecule as a template with resulting transfer of genetic information to the messenger RNA.

translation: the process of forming a protein molecule at a ribosomal site of protein synthesis from information contained in messenger RNA.

zona pellucida: the transparent more or less elastic noncellular glycoprotein outer layer or envelope of a mammalian ovum.

zygote: a cell formed by the union of two gametes; broadly, the developing individual produced from such a cell.

FIGURE 1



A. Sperm-egg fusion: Prior to fusion, the maternal nucleus is arrested at meiosis II. Sister chromatids (one pair illustrated) are non-identical due to genetic recombination during oogenesis.

B. Zygote formation: The zygote forms immediately upon sperm-egg fusion. Factors from the sperm initiate completion of meiosis II in the maternally derived nucleus. Within 1-3 minutes, changes in cellular calcium initiate the cortical reaction of the zygote, making the cell refractory to fusion with other sperm.

C. Early acts of the zygote: Within 30 minutes, meiosis II is complete, establishing the final diploid genome of the zygote. Sperm binding sites in the zona pellucida are destroyed. Both nuclei undergo decondensation. Paternal DNA is more rapidly and more extensively demethylated than maternal DNA.

D. Onset of zygotic transcription: DNA replication begins at 8-10 hours, converting both nuclei to a (2N) state. Transcription commences immediately following DNA replication. The paternal nucleus suppresses transcription in the maternal nucleus.

E. Syngamy: After approximately 20-25 hours, the pronuclei move together and their nuclear membranes break down. The chromosomes align and mitosis begins immediately.

F. Two-cell embryo: Cell division generates a two-cell embryo. Transcription increases and development beyond this stage depends on zygotic transcription. Evidence suggests that each cell is biased towards distinct developmental paths, and that they interact coordinately to orchestrate subsequent development.

SELECT BIBLIOGRAPHY

Anderson, Ryan T., and Maureen L. Condic, "Professor Lee Silver's Vast Scientific Conspiracy." *First Things:* On the Square. January 14, 2008. http://www.firstthings.com/onthesquare/?p=946.

Berg, Thomas. "The Personhood of the Human Embryo." *Homiletic and Pastoral Review* 103, no. 7 (April 2003): 10-19.

Berg, Thomas V., and Maureen L. Condic, "Emerging Biotechnologies, the Defense of Embryonic Human Life, and Altered Nuclear Transfer." *Linacre Quarterly* (forthcoming).

Condic, Maureen L. "Alternative Sources of Pluripotent Stem Cells: Altered Nuclear Transfer." *Cell Proliferation* 41, Suppl. 1 (2008): 7-19.

---. *The Beginning of Life: A Perspective from Science.* DeVos Medical Ethics Colloquy. Grand Rapids: Van Andel Press, 2007.

---. "Life: Defining the Beginning by the End." *First Things* 133: 50-54.

Condic, Maureen L., and Samuel B. Condic. "Defining Organisms by Organization." *National Catholic Bioethics Quarterly* 5, no. 2: 331-53.

Condic, Maureen L., and E. J. Furton. "Harvesting Embryonic Stem Cells from Deceased Human Embryos." *National Catholic Bioethics Quarterly* 7, no. 3: 507-525.

George, Robert P., and Alfonso Gomez-Lobo. "The Moral Status of the Human Embryo." *Perspectives in Biology and Medicine* 48, no. 2 (Spring 2005): 201-10.

George, Robert P., and Patrick Lee. "The Embryo Question I: Acorns and Embryos." *New Atlantis* 7 (Fall 2004 – Winter 2005): 90-100.

George, Robert P., and Christopher Tollefsen. *Embryo: A Defense of Human Life.* New York: Doubleday, 2008.

Hurlbut, William, Robert P. George, and Markus Grompe. "Seeking Consensus: A Clarification and Defense of Altered Nuclear Transfer." *Hastings Center Report* 45 (September-October 2006).

Lee, Patrick. *Abortion and Unborn Human Life.* Washington, DC: Catholic University of America Press, 1996.

Lee, Patrick, and Robert P. George. "The First Fourteen Days of Human Life." *New Atlantis* 13 (Summer 2006): 61-7.

Rao, Mahendra, and Maureen L. Condic. "Alternative Sources of Pluripotent Stem Cells: Scientific Solutions to an Ethical Dilemma." *Stem Cells and Development* 17, no. 1: 1-10.

THE WESTCHESTER INSTITUTE
FOR ETHICS & THE HUMAN PERSON

The Westchester Institute for Ethics & the Human Person is a research institute conducting interdisciplinary, natural law analysis of complex, contemporary moral issues as yet unresolved among Judeo-Christian scholars.

Anchored in the classic perennial and Catholic view of the human person, our moral inquiries are first and foremost of a scholarly nature. However, we pursue answers to disputed questions with an eye toward enriching the quality of contemporary moral discourse and fostering sound prudential judgment in cultural and political matters.

We are currently dedicated to the following issues:

- The genesis of human life and the moral status of the human embryo
- The search for scientifically and morally feasible alternatives to embryo-based biomedical research
- The use of emergency contraception in rape protocols
- The determination of human death and end-of-life issues
- The relationship between religion, science, and reason as sources of moral insight for modern society

The Westchester Institute and its scholars have become a distinguished resource and point of reference for think-tanks, centers for applied research, and institutes of public policy analysis.

www.westchesterinstitute.net

CERTIFICATE OF SERVICE

I hereby certify that on November 1, 2010, a copy of the foregoing BRIEF AMICUS CURIAE OF PROFESSOR MAUREEN CONDIC IN SUPPORT OF APPELLEES was electronically filed with the Clerk of the Court by the appellate CM/ECF system and by hand-delivery of 8 copies to the Clerk's Office.

I further certify that the BRIEF AMICUS CURIAE OF PROFESSOR MAUREEN CONDIC was served on the following by the CM/ECF system:

Thomas G. Hungar, Esq.
Gibson, Dunn & Crutcher, LLP
1050 Connecticut Avenue, NW
Washington, D.C. 20036-5306
thungar@gibsondunn.com

Bradley Jason Lingo, Esq.
Gibson, Dunn & Crutcher, LLP
1050 Connecticut Avenue, NW
Washington, D.C. 20036-5306
blingo@gibsondunn.com

Samuel B. Casey, Esq.
Advocates International
9691 Main Street, Suite D
Fairfax, Virginia 22031
sbcasey@advocatesinternational.org

Steven H. Aden, Esq.
Alliance Defense Fund
801 G. Street, NW, Suite 509
Washington, D.C. 20001
saden@telladf.org

Thomas M. Johnson, Esq.
Gibson, Dunn & Crutcher, LLP
1050 Connecticut Avenue, NW
Washington, D.C. 20036-5306

tjohnson@gibsondunn.com
Beth S. Brinkmann, Esq.
Deputy Assistant Attorney General
U.S. Department of Justice
Civil Division, Appellate Staff
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001
beth.brinkmann@usdoj.gov

Mark B. Stern, Esq.
U.S. Department of Justice
Civil Division, Appellate Staff
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001
mark.stern@usdoj.gov

R. Craig Lawrence, Esq.
U.S. Attorney's Office
Civil Division
555 4th Street, NW
Washington, DC 20530
craig.lawrence@usdoj.gov

Stephanie Robin Marcus, Esq.
U.S. Department of Justice
Civil Division, Appellate Staff
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001
stephanie.marcus@usdoj.gov

Abby Christine Wright, Esq.
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001
Abby.Wright@usdoj.gov

Jon E. Pettibone, Esq.
Quarles & Brady
411 East Wisconsin Avenue, Suite 240
Milwaukee, WI 53202-4497

john.pettibone@quarles.com
Andrew T. Karron, Esq.
Arnold & Porter
555 Twelfth Street, NW
Washington, DC 20004
andrew.karron@aporter.com

Robert Charrow, Esq.
Greenberg Traurig LLP
2101 L Street, NW
Washington, DC 20037
charrowr@gtlaw.com

Service was also accomplished on the following by U.S. Mail:

Beth S. Brinkmann
U.S. Department of Justice
(DOJ) Civil Division, Appellate Staff
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

Robert Phillip Charrow
Greenberg Traurig, LLP
2101 L Street, NW
Suite 1000
Washington, DC 20037

Ronald C. Machen, Jr.
U.S. Attorney's Office
(USA) Appellate Division
555 4th Street, NW
Washington, DC 20530

DATED: November 1, 2010

/s/*Dorinda C. Bordlee*
Dorinda C. Bordlee
Counsel for *Amicus* Dr. Condic