University of Chicago Legal Forum

Volume 2022 Article 14

2023

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I. INTRODUCTION

In 2006, Dr. Shinya Yamanaka captured the attention of the scientific community by publishing a paper where he showed he could reverse time and turn ordinary adult cells into a coveted and controversial resource: stem cells.[1] He then captured the attention of the entire world when, in 2012, he shared a Nobel Prize in Physiology or Medicine for this same work.[2] By that time, the American preoccupation with stem cells, and the human embryos that had until then been the primary source of stem cells, had generated a flurry of regulation by both the federal and state governments. Scientists used Dr. Yamanaka's discovery to create a new kind of human cell that has substantially the same properties as embryonic stem cells, known as an induced pluripotent stem cell ("iPSC").[3] They have used these new cells to create models of human embryos, sometimes called embryoids,[4] to research human embryo development and potential future treatments for complications in early pregnancy.[5] This research raises not only complex moral issues

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[1] Kazutoshi Takahashi & Shinya Yamanaka, *Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors*, 126 CELL 663 (2006).

[2] Press Release, The Nobel Assembly at Karolinska Institute, The Nobel Prize in Physiology or Medicine 2012 (Oct. 8, 2012), https://www.nobelprize.org/prizes/medicine/2012/press-release/ [https://perma.cc/DEJ3-6KXN].

[3] Katherine Brind'Amour, *Induced Pluripotent Stem Cells*, EMBRYO PROJECT ENCYCLOPEDIA (May 6, 2010), https://embryo.asu.edu/pages/induced-pluripotent-stem-cells [https://perma.cc/VG32-YM3Z].

[4] Kirstin R.W. Matthews & Daniel Morali, *National Human Embryo and Embryoid Research Policies: A Survey of 22 Top Research-Intensive Countries*, 15 REGENERATIVE MED. 1905, 1912 (2020).

[5] *See generally*, SIOBHAN ADDIE ET AL., EXAMINING THE STATE OF THE SCIENCE OF

but also a legal quandary on how to integrate such research into the pre-existing regulatory scheme. This Comment will address the latter thorny question of how to properly define what is an "embryo." Ultimately, it proposes an understanding of the term embryo that provides the greatest ability for scientists to capitalize on Dr. Yamanaka's work.

Stem cell research first garnered national and legislative attention during the Clinton presidency when the Human Embryo Research Panel recommended creating and destroying human embryos solely for research purposes.[6] Congress strongly and swiftly disagreed. They attached a rider to the appropriations bill, commonly referred to as the Dickey-Wicker Amendment, which prohibited the government from funding research in which an "embryo" was created or "destroyed, discarded, or knowingly subjected to risk of injury or death" purely for research purposes.[7] This Amendment has been attached to every subsequent Department of Health and Human Services (HHS) appropriations bill.[8]

Although later Presidents have used their authority over the National Institutes of Health (NIH) to expand and contract the scope of this statutory prohibition, it remains a substantial impediment to certain kinds of research seeking access to the approximately $41.7 billion dollars of funding NIH spends annually on medical research.[9] For this reason, resolving whether embryoid models using iPSCs constitutes research in which "embryos are destroyed, discarded, or knowingly subjected to risk of injury or death," or whether iPSCs embryoid models constitute "the creation of a human embryo or embryos for research purposes" will significantly determine both the course and speed this research can take.[10]

In the absence of strong federal regulation, states have passed their own legislation which has established both the legality and the eligibility of state funding for research involving human embryos.[11] These laws

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MAMMALIAN EMBRYO MODEL SYSTEMS: PROCEEDINGS OF A WORKSHOP (2020); *see also* Jianping Fu et al., *Stem-cell-based Embryo Models for Fundamental Research and Translation*, 20 NATURE MATERIALS 132 (2021).

[6] As opposed to embryos created but ultimately unused during fertility treatments. *See* NAT'L INSTS. OF HEALTH, REPORT OF THE HUMAN EMBRYO RESEARCH PANEL, 44–45 (Sept. 1994); *see also* J. BENJAMIN HURLBUT, EXPERIMENTS IN DEMOCRACY: HUMAN EMBRYO RESEARCH AND THE POLITICS OF BIOETHICS 108–31 (2017).

[7] H.R. 2880, 104th Cong. (1996); *see also* Balanced Budget Down Payment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

[8] Matthews & Morali, *supra* note 4, at 1908.

[9] *What We Do: Budget*, NAT'L INSTS. OF HEALTH (June 29, 2020) https://www.nih.gov/about-nih/what-we-do/budget#note [https://perma.cc/C88V-7RAX].

[10] Balanced Budget Down Payment Act, I § 128(1).

[11] Kirstin R.W. Matthews & Erin Yang, *Politics and Policies Guiding Human Embryo Research in the United States*, BAKER INST. FOR PUB. POL'Y 20–24 (2019).

run the spectrum from completely prohibitive to wholly permissive.[12] They were motivated by different ethical concerns, are part of different substantive areas of law, and have a unique understanding of what an embryo is. Nonetheless, these laws are united by the task of specifically defining what a human embryo is and setting the boundaries of what can and cannot be done in research.

Part II of this Comment will first take a historical look at the regulation of stem cells. It will explain stem cells generally and pluripotent stem cells specifically. It will then briefly trace the major historical steps in regulating stem cell research on the federal level and identify the current federal policy as it relates to research involving embryoids created from iPSCs. Finally, Part III will begin by closely examining the text in an attempt to resolve the ambiguity in the law. It will then provide greater context for the federal law by identifying and categorizing the major concerns which motivated states to independently regulate research involving embryos or stems cells. It will assert that there are only certain types of embryo creation and embryo destruction that have grabbed the attention of state legislatures. Ultimately, this Comment will argue that the embryoids created from iPSCs should not be considered embryos for purposes of federal law. Instead, their use in research should be subject only to state and federal cloning laws. It will draw upon the initial concerns of the Dickey-Wicker Amendment, an analysis of state laws, and an examination of the incentives the current federal law creates to conclude that the Amendment's main purpose was to prohibit the creation or destruction of only those embryos which have the characteristic of being viable, should the embryo be implanted in utero. To the extent embryoid models lack this quality, they should not be considered embryos for purposes of this law, and to the extent they develop into something that becomes viable, they are prohibited by the federal cloning ban.

II. STEM CELLS AND THEIR HISTORY OF FEDERAL REGULATION

A. What is a Stem Cell?

Stem cells are unique among cells precisely because they are not yet unique. Instead, stem cells have the potential to become many different types of cells in the human body.[13] The adult human body has a supply of somatic stem cells, which can develop into a limited number

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[12] *Id.*

[13] *Stem Cells: What They Are and What They Do*, MAYO CLINIC (June 8, 2019), https://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/in-depth/stem-cells/art-20048117 [https://perma.cc/3DK8-QYZ8].

of different cell types and help replenish old cells when they die.[14] More importantly for this Comment, there is an even more special kind of stem cell, pluripotent stem cells, which can develop into any kind of cell type in the human body—hence the name, pluri-(many)-potent-(able to become).[15] The first kind of pluripotent stem cells to be discovered were embryonic stem cells ("ESCs"). Although scientists had long understood that such cells existed, they were not able to isolate and identify these cells until the late 1970s and early 1980s.[16] However, the discovery of these stem cells came with significant ethical questions about how to appropriately use them in research, especially human embryonic stem cells. This is because, at the time, the only way to isolate these stem cells for research was through a process that destroyed a developing human embryo.[17] Many politicians, pundits, and philosophers took the view that it was ethically impressable to destroy these embryos, even if the goal of the research was to develop medical treatments and cures.[18]

B. Early Regulation in the United States

Beginning in 1975, federal regulation required that all research on in vitro human embryos be approved by an ethics advisory board ("EAB").[19] However, after the creation of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in 1978, Congress found the work of EAB to be redundant, assuming that this new commission would encompass much of the work of the advisory board.[20] As such, the dissolution of the EAB in 1980 effectively removed the federal government from the field of regulating embryo research.[21] Despite the ever-increasing supply of frozen embryos from in vitro fertilization (IVF) and major scientific discoveries about embryo development after the dissolution of the EAB, the federal government's policy towards embryo research remained largely nonexistent as it considered IVF generally to be a matter of private

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[14] *Adult Stem Cells*, NATURE REVS. MOLECULAR CELL BIOLOGY (Feb. 28, 2022), https://www.nature.com/collections/hzwmqpdpnd/ [https://perma.cc/V4X2-XT5X].

[15] Antonio Romito & Gilda Cobellis, *Pluripotent Stem Cells: Current Understanding and Future Directions*, STEM CELLS INT'L, 1, 1–2 (2016).

[16] PHILIP BALL, HOW TO GROW A HUMAN: ADVENTURES IN HOW WE ARE MADE AND WHO WE ARE 144–45 (2019). Biologist Martin Evans also received a Nobel Prize for his work at Cambridge in 1981 for successfully culturing embryonic stem cells from the blastocyst embryos of mice. *Id.*

[17] ERIN WILLIAMS & JUDITH JOHNSON, CONG. RSCH. SERV., RL33554, STEM CELL RESEARCH: ETHICAL ISSUES 1 (2006).

[18] *See generally* LeRoy Walters, *Human Embryonic Stem Cell Research: An Intercultural Perspective*, 14 KENNEDY INST. ETHICS J. 3 (2004).

[19] 45 C.F.R. § 46.204 (2000).

[20] Hurlbut, *supra* note 6, at 77. This was not entirely the case as the commission was focused on broader ethical questions, such as defining death.

[21] *Id.* at 96–97.

moral judgment.[22] Yet, President Clinton took up the issue soon after taking office.[23] Clinton established the Human Embryo Research Panel (HERP) in 1993 to develop a series of recommendations to the Director of NIH on the use of federal funds to support research involving human embryos.[24] In 1994, the panel released its report and concluded that the government should be allowed to fund projects that not only use human embryos created as part of IVF but also research that created embryos specifically for research purposes—at least under certain, highly restrictive circumstances.[25] This report alarmed Congress, despite the fact Clinton ultimately rejected this last recommendation, and prompted it to attach strings to HHS funding which forbade the use of NIH funds for embryo research.[26]

C. Dickey-Wicker Amendment

Before President Clinton could act on the advice of HERP, Congress decided to preemptively address the issue of funding for embryo research. Republicans on the House Appropriations Committee attached a rider to The Balanced Budget Down Payment Act, I,[27] named after its principal authors, Jay Dickey and Roger Wicker. The Amendment, which has been attached to every HHS appropriations bill since 1996,[28] is as follows:

> SEC. 128. None of the funds made available [in this Act] may be used for–
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> (1) the creation of a human embryo or embryos for research purposes; or
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> (2) 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 CFR 46.208(a)(2) and 42 U.S.C. 289g(b).

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[22] *Id.* at 104–05.

[23] *Id.* at 107–09.

[24] *Id.* at 108–09.

[25] *See* REPORT OF THE HUMAN EMBRYO RESEARCH PANEL, *supra* note 6, at 44–45. HERP proposed that human embryos should be allowed to be developed for research only when: (1) "the research by its very nature cannot otherwise be validly conducted" and (2) when the creation of embryos "is necessary for the validity of a study that is potentially of outstanding scientific and therapeutic value." *Id.*

[26] O. Carter Snead, *Science, Public Bioethics, and the Problem of Integration*, 43 U.C. DAVIS L. REV. 1529, 1546 (2010).

[27] H.R. 2880, 104th Cong. (1996).

[28] Matthews & Morali, *supra* note 4, at 1908.

> For purposes of this section, the phrase 'human embryo or embryos' shall include any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes.[29]

Notwithstanding Congress's attempt to settle the issue, President Clinton soon sought a way around this incredibly expansive prohibition.

The HHS General Counsel issued an opinion that allowed for federal funds to be spent on research that used pluripotent cells,[30] so long as the research itself did not destroy the embryo. The opinion considered these new cell lines as not *themselves* embryos within the meaning of the Dickey-Wicker Amendment, even if they had been derived from an embryo.[31] More precisely, the General Counsel argued that "embryos" were, per the statute's definition, "organisms." They went on to assert that these cells were not "organisms" as understood by the scientific community because they were not by themselves "whole bod[ies]."[32] This allowed the government to fund research in which private funds had been used to create new pluripotent stem cell lines.

Before this interpretation could become effective, President George W. Bush was elected and advanced a similar but distinct interpretation. While he agreed that the Dickey-Wicker Amendment could be read to allow the federal government to fund research using then-existing iPSC lines, on August 9, 2001, Bush announced that only research that did not create future incentives for the destruction of human life in the embryonic stage of development would be funded.[33] This permitted funding for nonembryonic (adult) stem cell research and for research involving embryonic stem cell lines that had been derived from human embryos and were created before the announcement.

Following his election, on March 9, 2009, President Barack Obama issued Executive Order No. 13505 to overturn the Bush interpretation of the Dickey-Wicker Amendment.[34] The order stated:

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[29] Balanced Budget Down Payment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

[30] At this point derived from human embryos. *See* James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCI. 1145, 1145–47 (1998).

[31] Memorandum from Harriet S. Rabb, Gen. Couns. of the Dep't of Health and Hum. Servs., to Harold Varmus, Dir. of the Nat'l Insts. of Health, Federal Funding for Research Involving Human Pluripotent Stem Cells, 2–3 (Jan. 15, 1999) (citing N. CAMPBELL, BIOLOGY, 8–9 (4th ed., 1996)).

[32] *Id.*

[33] *Fact Sheet: Advancing Stem Cell Research While Respecting Moral Boundaries*, THE WHITE HOUSE: PRESIDENT GEORGE W. BUSH (June 20, 2007), https://georgewbush-whitehouse.archives.gov/news/releases/2007/06/20070620.html [https://perma.cc/5C7B-FT5X]; *see also* O. Carter Snead *The Pedagogical Significance of the Bush Stem Cell Policy: A Window into Bioethical Regulation in the United States*, 5 YALE J. HEALTH POL'Y L. & ETHICS 491, 493–96 (2005).

[34] Exec. Order No. 13505, 74 Fed. Reg. 10667, § 1 (Mar. 9, 2009).

> Research involving human embryonic stem cells and human non-embryonic stem cells has the potential to lead to better understanding and treatment of many disabling diseases and conditions. Advances over the past decade in this promising scientific field have been encouraging, leading to broad agreement in the scientific community that the research should be supported by Federal funds.[35]

The purpose of the order was to "remove [presidentially imposed] limitations on scientific inquiry, to expand NIH support for the exploration of human stem cell research, and in so doing to enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind."[36] As such, the Secretary of HHS, acting through the Director of NIH, was given 120 days to issue new guidance on embryonic research.[37]

NIH's new guidelines for human embryonic stem cell ("hESC") research became effective on July 7, 2009. These guidelines embraced a very narrow understanding of the Dickey-Wicker Amendment which allowed the government to fund research using many more embryonic stem cell lines.[38] "These guidelines [ ] recognize the distinction . . . between the derivation of stem cells from an embryo that results in the embryo's destruction, for which federal funding is prohibited, and research involving hESCs that does not involve an embryo nor result in an embryo's destruction, for which federal funding is prohibited."[39] The guidelines established a federal registry for these stem cell lines and a set of criteria by which new cell lines could be added to this list.[40] The criteria included, for example, "hESCs should have been derived from human embryos . . . that were created using in vitro fertilization for reproductive purposes and were no longer needed for this purpose."[41]

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[35] *Id.*

[36] *Id.*

[37] *Id.* § 3.

[38] *See generally* Raynard Kington, *NIH Guidelines for Human Stem Cell Research*, NAT'L INSTS. OF HEALTH (July 7, 2009), https://stemcells.nih.gov/research-policy/guidelines-for-human-stem-cell-research [https://perma.cc/D2YQ-XVQK].

[39] *Id.* at 4. "For the purpose of these Guidelines, 'human embryonic stem cells (hESCs)' are cells that are derived from the inner cell mass of blastocyst-stage human embryos, are capable of dividing without differentiating for a prolonged period in culture and are known to develop into cells and tissues of the three primary germ layers. Although hESCs are derived from embryos, such stem cells are not themselves human embryos." *Id.* at 5.

[40] *Id.* at 2.

[41] *Id.* at 6.

Soon after NIH promulgated these guidelines, a group of Christian researchers and activist organizations sued the agency because they believed the policy was immoral. In *Sherley v. Sebelius*,[42] Drs. James Sherley and Theresa Deisher sought to enjoin the new NIH guidelines from taking effect, arguing that the Dickey-Wicker Amendment prohibited funding for hESC research.[43] On appeal, case was ultimately decided using a *Chevron* analysis,[44] which turned on the ambiguity of the word "research"—and not the ambiguity in the word "embryo"—in the Amendment's prohibition of "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death."[45] Ultimately, the court found that the definition of research was "flexible enough" to support either party's interpretation but that, because NIH's interpretation was "reasonable," NIH was entitled to *Chevron* deference.[46] The court also emphasized that Congress has "reenacted Dickey-Wicker unchanged year after year with full knowledge that HHS has been funding [h]ESC research since 2001 . . . when President Bush first permitted federal funding for ESC projects."[47] As such, Congress likely "intended the Agency's interpretation, or at least understood the interpretation as statutorily permissible."[48] Bound by this interpretation, the district court granted the government's motion for summary judgment,[49] and the D.C. Circuit affirmed on appeal.[50] The Supreme Court denied certiorari on January 7, 2013.[51]

Although both the Trump and Biden Administrations have made small adjustments to policies like the use of fetal tissue in research,[52]

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[42] 644 F.3d 388 (D.C. Cir. 2011).

[43] *Id.* at 389–90.

[44] *Id.* at 393–97. For a more detailed discussion of how lawyers and judges apply the *Chevron* analysis, *see* Cary Coglianese, Chevron*'s Interstitial Steps*, 85 GEO. WASH. L. REV. 1339 (2017).

[45] 644 F.3d at 393–97. The two scientists asserted the research which had developed the original cell line by destroying human embryos should be considered part of any later research projects while NIH asserted that later research projects were distinct for purposes of the Dickey-Wicker Amendment. *Id.*

[46] *Id.* at 393–94.

[47] Sherley v. Sebelius, 644 F.3d 388, 396 (D.C. Cir. 2011) (internal quotation omitted).

[48] *Id.* (quoting Barnhart v. Walton, 535 U.S. 212, 220 (2002)).

[49] Sherley v. Sebelius, 776 F.Supp.2d 1, 24–25 (D.D.C. 2011).

[50] Sherley v. Sebelius, 689 F.3d 776, 785 (D.C. Cir. 2012), *aff'g* 776 F.Supp.2d 1 (D.D.C. 2011), *cert. denied*, 568 U.S. 1087 (2013).

[51] Sherley v. Sebelius, 568 U.S. 1087 (2013).

[52] Meredith Wadman, *Trump Administration Restricts Fetal Tissue Research: National Institutes of Health Staff Projects Killed, Future University Studies Will Get New Ethics Review*, SCI. INSIDER (June 5, 2019), https://www.science.org/content/article/trump-administration-restricts-fetal-tissue-research [https://perma.cc/6EXU-XVHV]; Kelly Servick, *Biden Administration Scraps Human Fetal Tissue Research Restrictions: Internal NIH Research May Resume, and Funding Applications Will No Longer Face Trump-era Ethical Review*, SCI. INSIDER (Apr. 16, 2021), https://www.science.org/content/article/biden-administration-scraps-human-fetal-tissue-research-restrictions [https://perma.cc/PG8Y-U9YW].

the 2009 NIH guidelines remain the final official federal word on the regulation of using human embryos and embryonic stem cells for research.

D. Induced Pluripotent Stem Cells

Confronted with increasingly strict regulation and outright bans across the world,[53] scientists began to search for more ethical and more legal ways to source and research stem cells. In 2006, their prayers seemed to have been answered by Dr. Shinya Yamanaka with his paper *Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors*.[54] Dr. Yamanaka had discovered a way to take differentiated adult cells and revert them to a pluripotent state.[55] Human cells are defined not only by the genes they contain—all our cells have the same genetic blueprint—but also by which genes are expressed in a given cell. In a certain sense, the type of cell is defined by which parts of the genetic code are "turned on" and which are "turned off." Yamanaka found that embryonic stem cells have certain parts of the genetic code—gene factors—which were turned on in stem cells more than in somatic—differentiated—cells.[56] Using a virus, he injected a cocktail of these genes into somatic cells and discovered they gained pluripotent potential.[57] Over time he was able to refine his cocktail to only four gene factors and showed it was possible to induce this pluripotency in not only mouse but also human somatic cells.[58]

Pluripotency means that the cell can be converted into one of three germ layers. The differentiation from a ball of undefined cells, the blastula, into three distinct layers of cells, germ layers, is the first step in differentiation and embryonic development.[59] Each of these three types of germ layers go on to become different parts of our bodies—our skin,

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[53] *See generally* Matthews & Morali, *supra* note 4.

[54] Takahashi & Yamanaka, *supra* note 1. Dr. Yamanaka had been seeking a way around Japan's restrictive laws on the source of embryonic stem cells and the need for governmental approval of embryonic stem cell research. *See* [Act on Regulation of Human Cloning Techniques], Law No.146 of 2000 (Japan) *unofficial translation in* www.cas.go.jp/jp/seisaku/hourei/data/htc.pdf [https://perma.cc/892X-WWFP]; *see also* [Ministry of Education, Culture, Sports, Science and Technology: Guidelines on the Derivation and Distribution of Human Embryonic Stem Cells], Public Notice No. 86 of 2010 (Japan), *tentative translation in* https://www.lifescience.mext.go.jp/files/pdf/n743_00.pdf [https://perma.cc/8L77-3CXK].

[55] *See generally* Takahashi & Yamanaka, *supra* note 54.For a more accessible explanation of Takahashi & Yamanaka's research, consult Ball, *supra* note 16, at 152–58.

[56] Takahashi & Yamanaka, *supra* note 54.

[57] *Id.*

[58] Ball, *supra* note 16, at 157–58.

[59] Claudia Winograd, *Germ Layer*, ENCYCLOPEDIA BRITANNICA (May 26, 2020), https://www.britannica.com/science/germ-layer [https://perma.cc/4DZY-578D].

hair and nerves, our inner organs, and our intestinal tract. An important caveat, however, is that pluripotent cells are not, in fact, toti-(all)-potent cells. Some of the cells that originally form from the dividing, recently fertilized egg do not become part of the embryo itself but, instead, go on to form the umbilical cord and placenta.[60] This fact has been, at times, used to argue that embryoids made from induced pluripotent stem cells, unlike embryos, could never develop into a human being, even if an embryoid were implanted in utero. The problem with this argument is that it is not entirely clear that this is true. It may be possible that, under the proper conditions and with sufficient care, such an embryoid could be successfully implanted in utero and carried to term. The only way to know with certainty is to try. Nonetheless, such an experiment is doomed to fail Institutional Review Board ("IRB") approval,[61] and, as Dr. Carrie D. Wolinetz, then Acting Chief of Staff and Associate Director for Science Policy at NIH, has stated, is "an experiment that NIH would never support."[62] Nevertheless, this leaves the biological and therefore ethical status of embryoids created from iPSCs uncertain.

While NIH has not promulgated comprehensive guidelines on the use of iPSCs in research, it has formally restricted their use in two circumstances:

> The following uses [of] . . . human induced pluripotent stem cells, are prohibited:
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> - Research in which hESCs or human induced pluripotent stem cells are introduced into non-human primate blastocysts.
> - Research involving the breeding of animals where the introduction of hESCs or human induced pluripotent stem cells may contribute to the germ line.[63]=

Furthermore, NIH, through Dr. Wolinetz, has shared its "current thinking" on how it handles research involving iPSC embryo model systems. In a blog posted on October 10, 2019, Dr. Wolinetz answered the

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[60] Ball, *supra* note 16, at 144.

[61] "Under FDA regulations, an Institutional Review Board is group [sic] that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects." *Institutional Review Boards (IRBs) and Protection of Human Subjects in Clinical Trials*, U.S. FOOD AND DRUG ADMIN. (Sept. 11, 2019), https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/institutional-review-boards-irbs-and-protection-human-subjects-clinical-trials [https://perma.cc/38F7-M7SX].

[62] Carrie D. Wolinetz, *Sharing Our Current Thinking: Models Containing Aspects of Human Embryos*, NAT'L INSTS. OF HEALTH (Mar. 11, 2021), https://osp.od.nih.gov/2021/03/11/human-embryo-development/ [https://perma.cc/KT45-G7BQ].

[63] NIH GRANTS POLICY STATEMENT § 4.1.13.1 (Oct. 1, 2020), https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.13_human_stem_cell_research.htm [https://perma.cc/P8Q8-3UDX].

question "[c]an research involving various models of aspects of human embryo development be supported by NIH?" with the answer, stating it briefly, of "it depends."[64] After reviewing the proceedings of the January 2020 National Academies of Science, Engineering, and Medicine's state of the science workshop to "identify and better understand some of the unknowns associated with this nascent field of research,"[65] Dr. Wolinetz clarified NIH's "current thinking" on "models containing aspects of human embryos."[66] In a blog posted on March 11, 2021, Dr. Wolinetz identified a list of questions NIH considers when reviewing applications for NIH funding on a case-by-case basis. These questions included:

- What stage, or aspect, of embryonic development is being modeled?
- What cell types, structures, and functions are present in the model? For example,
    - Does the model contain all components of the epiblast lineage (i.e. the three "germ layers" that collectively form the embryo)?
    - Does the model contain any extraembryonic lineage cell types (i.e. cells that contribute to the yolk sac, placenta, or other tissues that support development of the embryo)?
    - Are there other materials or growth factors present that might substitute for the functions of the extraembryonic lineages?
- Is the spatial orientation of the components similar to, or different from, an actual embryo?
    - Are the cells in a single monolayer or in a more complex structure?
    - How is the shape similar to or different from that of the embryo?
- Can the model maintain its organizational structure? Does it change to look like the next stage in normal development?
- Would the researcher watch for any unanticipated events, such as the unexpected appearance of other cell types or structures?[67]

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[64] Carrie D. Wolinetz, *A Quick Word About Human Embryo Model Systems*, NAT'L INSTS. OF HEALTH (Oct. 10, 2019), https://osp.od.nih.gov/2019/10/10/a-quick-word-about-human-embryo-model-systems/ [https://perma.cc/EM8C-P2WQ].

[65] *Id.*

[66] *Wolinetz*, *supra* note 62.

[67] *Id.*

While this list is not comprehensive or part of official guidance, it makes clear that NIH considers just how embryo-like the proposed embryoid would be. This ensures that, "as a steward of taxpayer funds," NIH is not running afoul of the "long-standing statutory limitation on funding research involving human embryos," i.e., the Dickey-Wicker Amendment. [68] It is also clear that the answer can sometimes be that a model is indeed too embryo-like.[69]

E. Other Federal Law and Regulation

As a final note on federal regulation of stem cell research, it is important to observe that the Dickey-Wicker Amendment is not a monolithic anomaly in the restriction of research involving developing human cells. Instead, it overlaps with many different laws and regulations on scientific research. Most central to this discussion are restrictions on cloning and restrictions on the use of fetal tissue.

> The term cloning describes a number of different processes that can be used to produce genetically identical copies of a biological entity. The copied material, which has the same genetic makeup as the original, is referred to as a clone. Researchers have cloned a wide range of biological materials, including genes, cells, tissues, and even entire organisms, such as a sheep.[70]

While the Dickey-Wicker Amendment prohibits funding research in which an embryo is created or destroyed, it does not expressly address cloning. President Clinton found this to be unacceptable, first because the Dickey-Wicker Amendment did not apply to all agencies, and second because "current restrictions on the use of Federal funds for research involving human embryos do not fully assure" that federal funds would not be used to clone human beings.[71] On March 4, 1997, he, therefore, issued a memorandum to the heads of all executive departments and agencies forbidding the use of federal funding on research involving

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[68] Wolinetz, *supra* note 64.

[69] Nidhi Subbaraman, *Studies of Embryo-like Structures Struggle to Win US Grants*, 577 NATURE 459 (2020).

[70] *Cloning Fact Sheet*, NAT'L HUM. GENOME RSCH. INST. (Aug. 15, 2020), https://www.genome.gov/about-genomics/fact-sheets/Cloning-Fact-Sheet [https://perma.cc/Q43J-69SA]. This final example is a reference to Dolly the sheep, which was a cloned sheep produced by Scottish biologists in 1997 and which engendered a worldwide debate around cloning technology. This event led many states and the federal government to (re)consider their position on cloning.
Judith L. Fridovich-Keil, *Dolly: Cloned Sheep*, ENCYCLOPAEDIA BRITANNICA (Dec. 22, 2021), https://www.britannica.com/topic/Dolly-cloned-sheep [https://perma.cc/6MSV-5YBL].

[71] Memorandum on the Prohibition on Federal Funding for Cloning of Human Beings, 3 Weekly Comp. Pres. Doc. 281 (March 4, 1997). *See also* Thomas V. Cunningham, *What Justifies the United States Ban on Federal Funding for Nonreproductive Cloning?*, 16 MED. HEALTH CARE & PHIL. 825 (2013).

the cloning of human beings.[72] "I want to make it absolutely clear," he announced, "that no Federal funds will be used for human cloning."[73] This prohibition remains in effect to this day. The significance of this prohibition on cloning is relevant to embryoids created through induced pluripotent stem cells. This is because, should such an embryoid, given yet unknown assistance by researchers, develop into a child, that child would be a clone—their genetic material would be the same as that of the original adult cell used to create the iPSC.[74]

A second significant area of federal law that abuts the Dickey-Wicker Amendments are federal laws and regulations restricting fetal tissue use in experimentation. Their linkage comes from the fact that embryonic stem cell lines can and have frequently been derived from fetal tissues.[75] NIH defines fetal tissue as "tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion or stillbirth. This definition does not include established human fetal cell lines."[76] While a detailed discussion of this body of law is beyond the scope of this Comment, the practical and ethical proximities between the destruction of an embryo and the use of fetal tissue for research purposes make an overview relevant. Under 42 U.S.C. § 289g-1 the Secretary of NIH "may conduct or support research on the transplantation of human fetal tissue for therapeutic purposes."[77] Fetal tissue can be used in research "regardless of whether the tissue is obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth," so long as it is obtained with the informed consent of the donor—i.e., previously pregnant adult—and various other constraints.[78]

The Dickey-Wicker Amendment works in conjunction with, and is foundational to, these two other areas of law. Thus, an understanding of the Amendment and its terms, such as "embryo," should be considered alongside these other laws. More importantly for this Comment, these other federal laws track distinctions and concerns raised by states as they regulate embryonic stem cell research. These two bodies of law can help provide context which clarifies the Dickey-Wicker Amendment.

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[72] Memorandum on the Prohibition on Federal Funding for Cloning of Human Beings, *supra* note 71.

[73] *Id.*

[74] *See generally* Zhaohui Kou et al., *Mice Cloned from Induced Pluripotent Stem Cells (iPSCs)*, 83 BIOLOGY OF REPRODUCTION 238 (2010).

[75] Meredith Wadman, *The Truth about Fetal Tissue Research*, 528 NATURE 178 (2015).

[76] NIH GRANTS POLICY STATEMENT § 4.1.14 (Oct. 1, 2020), https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.14_human_fetal_tissue_research.htm [https://perma.cc/6AF8-NN3H].

[77] 42 U.S.C. § 289g-1 (2020).

[78] *Id.*

III. STATE LAWS AND THE CONCERNS UNDERLYING EMBRYO RESEARCH REGULATION

NIH is not the only regulator of U.S. research. Many (though not all) states have engaged in regulating stem cell and embryo research.[79] However, there is no consistent policy among states; rather, each uses different language to accomplish different substantive outcomes. The diversity of these laws means that the type of research conducted across jurisdictions varies widely. Notably, the use of terms like "embryo" and "live fetus" in these statutes makes it equally unclear whether these laws, like the Dickey-Wicker Amendment, apply to embryoid models derived from iPSCs.

Nevertheless, an examination of state laws reveals that those states whose legislatures have in some way addressed embryonic research generally fall into a few categories, motivated by generalizable concerns. Furthermore, these concerns track the concerns raised by the Dickey-Wicker Amendment over the "creation" and "destruction" of human embryos for research purposes.[80] This is illustrated by the fact that some states have made their regulations concomitant with the regulation of abortion or the use of fetal tissue after abortions, while others have paired the regulation of embryonic research with the regulation of cloning.

Twenty-nine states have passed laws directly or indirectly addressing research involving human embryos. While it is almost impossible to create a schema that effectively captures all these state laws, states generally fall into two categories: prohibitive[81] and permissive.[82] That said, only some laws directly regulate embryonic stem cell research. Other state laws apply more tangentially while still providing an illuminating definition of terms like embryo, fetus, and "conceptus" as part of regulating either cloning or fetal tissue research. All of these laws can be used to understand what the Dickey-Wicker Amendment does, or at least should, mean by "embryo" and whether that term included embryoids formed from iPSCs.

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[79] Matthews & Yang, *supra* note 11, at 20–24.

[80] Balanced Budget Down Payment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

[81] These include Arizona, Arkansas, Florida, Iowa, Louisiana, Maine, Minnesota, North Dakota, Oklahoma, South Dakota, and Utah.

[82] These include California, Connecticut, Illinois, Indiana, Maryland, Massachusetts, Michigan, Missouri, New Jersey, New York, and Virginia.

A. Restricting Research: "Embryo" as a Single-Celled Organism

Several states have expansively defined "embryo" to include even a single-celled organism and are generally prohibitory in nature. Montana's definition is typical of these states: "'[e]mbryo' means an organism of the species Homo sapiens from the single cell stage to [eight] weeks of development."[83] Other states have followed a similar line of reasoning by defining an embryo or fetus as the product of fertilization.[84] Louisiana has further clarified the ethical and legal status of embryos by stating a human embryo "is an in vitro fertilized human ovum, with certain rights granted by law, composed of one or more living human cells and human genetic material so unified and organized that it will develop in utero into an unborn child."[85] Furthermore, an "in vitro fertilized human ovum exists as a juridical person until such time as the in vitro fertilized ovum is implanted in the womb; or at any other time when rights attach to an unborn child in accordance with law."[86] Many states that take this approach incorporate this definition as either part of a ban on research that destroys embryos in the process[87] or as part of regulations on the use of fetal tissue from abortion.[88] This focus on conception, from the single cell forward, and its proximate location to regulations on abortion or fetal tissue suggests that many of the states enacted laws to protect embryos that might otherwise have had the capability to become fully formed adults. These laws indicate a strong conviction that there is something unique about human conception from the beginning, but in so doing, seem to place a lesser value on

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[83] MONT. CODE ANN. § 50-11-101 (2021); *see also* ARK. CODE ANN. § 20-16-1001 (2022); OKLA. STAT. ANN. tit. 63, § 1-270.2 (West 2022); S.D. CODIFIED LAWS § 34-14-20 (2022); LA. STAT. ANN. § 9:121 (2022).

[84] *See, e.g.*, a Minnesota statute which prohibits "the use of a living human conceptus for any type of scientific, laboratory research or other experimentation" defines "human conceptus" as "any human organism, conceived either in the human body or produced in an artificial environment other than the human body, from fertilization through the first 265 days thereafter." MINN. STAT. § 145.421–422 (2021); *see also* a Nebraska statute defining a human embryo as "the developing human organism from the time of fertilization until the end of the eighth week of gestation and includes an embryo or developing human organism created by somatic cell nuclear transfer." NEB. REV. STAT. § 71-8802 (2022); OHIO REV. CODE ANN. § 2919.14 (West 2022).

[85] LA. STAT. ANN. § 9:121.

[86] *Id.* at § 9:123.

[87] ARIZ. REV. STAT. ANN. § 36-2313 (West 2022); S.D. CODIFIED LAWS § 34-14-16 (2022). These bans often mirror the language of the Dickey-Wicker Amendment. *See, e.g.*, "No state facilities, no state funds, fees, or charges, and no investment income on state funds shall be used to destroy human embryos for the purpose of research." NEB. REV. STAT. § 71-8806 (2022).

[88] *See*, *e.g.*, an Ohio statute declaring "no person shall experiment upon or sell the product of human conception which is aborted." OHIO REV. CODE ANN. § 2919.14 (West 2022); *see also* 11 R.I. GEN. LAWS § 11-54-1 (2022); N.D. CENT. CODE ANN. § 14-02.2-01(1) (West 2021); S.D. CODIFIED LAWS § 34-14-20; N.M. STAT. ANN. § 24-9A-1 (West 2022); IND. CODE §§ 16-18-2-128.5, 35-46-5-3 (2022); FLA. STAT. ANN. § 390.0111(6) (West 2022).

organisms not created through fertilization/conception, such as those created through cloning.

B. Permitting Embryonic Stem Cell Research

Taking a different tack, Massachusetts, which specifically allows for and funds embryonic stem cell research,[89] incorporates the fertilization framework by defining embryos as "an organism of the species homo-sapiens [ ] formed by fertilization" but expands it to incorporate organisms formed by "somatic cell nuclear transfer, parthenogenesis or other means."[90] This approach is shared by Missouri, whose constitution defines a "blastocyst" as "a small mass of cells that results from cell division, caused either by fertilization or somatic cell nuclear transfer, that has not been implanted in a uterus" and defines "human embryonic stem cell research" as "any scientific or medical research involving human stem cells derived from in vitro fertilization blastocysts or from somatic cell nuclear transfer."[91]

Many states have defined embryos or included stem cell research in the same substantive law that bans or limits funding for cloning. For example, New York has created the Empire State Stem Cell Board, which oversees and provides funding for stem cell research in the state.[92] Yet, that same statute later clarifies that "[n]o grants made available in the fund from any source shall be directly or indirectly utilized for research involving human reproductive cloning."[93] Likewise, in Illinois, "[r]esearch involving the derivation and use of human embryonic stem cells . . . shall be allowed to receive public funds through a program established specifically for the purpose of supporting stem cell research in Illinois."[94] However:

> [n]o person may clone or attempt to clone a human being. For purposes of this Section, 'clone or attempt to clone a human being' means to transfer to a uterus or attempt to transfer to a uterus anything other than the product of fertilization of an egg of a human female by a sperm of a human male for the purpose

[89] MASS. GEN. LAWS ch. 111L, § 3 (2022).

[90] MASS. GEN. LAWS ch. 111L, § 2 (2022). Somatic cell transfer and parthenogenesis are both ways of creating clones. For more information consult John P. Rafferty, *Parthenogenesis*, ENCYCLOPAEDIA BRITANNICA (Apr. 7, 2020), https://www.britannica.com/science/parthenogenesis [https://perma.cc/UG2R-ELGR]; David Stocum, *Somatic Cell Nuclear Transfer*, ENCYCLOPAEDIA BRITANNICA (Mar. 4, 2020), https://www.britannica.com/science/somatic-cell-nuclear-transfer [https://perma.cc/G99X-L977].

[91] MO. CONST. art. III, § 38(d) (2006).

[92] N.Y. PUB. HEALTH LAW § 265-a (McKinney 2022).

[93] *Id.*

[94] 410 ILL. COMP. STAT.110/5 (2022).

> of initiating a pregnancy that could result in the creation of a human fetus or the birth of a human being.[95]

Both Michigan and Missouri have amended their constitutions through public referenda to allow human embryonic stem cell research explicitly but also have laws prohibiting cloning.[96] Prohibitions on cloning, either accompanied by a definition of human embryo or otherwise tied to embryonic stem cell research, can also be found in Montana,[97] Iowa,[98] Oklahoma,[99] Virginia,[100] and Arkansas.[101] It is clear that for many states, and theoretically the citizens of those states, one of the main concerns with embryonic stem cell research and the use of embryos in research generally is the possibility of creating a fully autonomous clone.

C. Shared State Preoccupations

While an examination of state laws reveals just how differently states have chosen to approach this complicated issue in their individual labs of democracy, two main preoccupations emerge. First is the idea that there is something unique about conception or fertilization and that from that moment on, an embryo is formed—i.e., an embryo can be a single-celled organism.[102] These laws protect the product of this unique event from destruction and are thus concerned with the destructive nature of the research.[103] Second, this examination reveals that states, like President Clinton, are deeply worried about embryos when they are or have the potential to become developed clones. States are concerned with the creation of something. While embryoids created from induced pluripotent stem cells do have identical genetic material to the adult somatic cells from which they were created, NIH clearly does not consider them to be "clones" for purposes of the cloning prohibition. Otherwise, it would not fund any research involving embryoid models.

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[95] 410 ILL. COMP. STAT. 110/40 (2022).

[96] MO. CONST. art. III, § 38(d); MI. CONST. art. I, § 27 (2008).

[97] MONT. CODE ANN. § 50-11-103 (2021).

[98] IOWA CODE ANN. § 707C.4 (West 2022).

[99] OKLA. STAT. ANN. tit. 63, § 1-270.2 (West 2022).

[100] VA. CODE ANN. § 32.1-162.22 (2022).

[101] ARK. CODE ANN. § 20-16-1001 (2022).

[102] This understanding of embryo seems to fly in the face of the approach taken by the NIH, which analyzes research proposals based on how embryo-like the embryoids are. Surely, the NIH could not and does not consider a single cell to be sufficiently embryo-like to preclude research involving such organisms.

[103] *E.g.*, ARIZ. REV. STAT. ANN. § 36-2311 (2022) ("'Destructive human embryonic stem cell research' means any research that involves the disaggregation of any human embryo for the purpose of creating human pluripotent stem cells or human pluripotent stem cell lines.").

IV. A BETTER INTERPRETATION OF THE DICKEY-WICKER AMENDMENT AND THE MEANING OF "EMBRYO"

The creation of embryoids from induced pluripotent stem cells for scientific research raises serious biological, ethical, and legal questions. Chief among these questions is whether embryoids should be treated the same under federal law as embryos created through traditional fertilization methods. At stake is access to some of the approximately $41.7 billion dollars of funding NIH spends annually on medical research.[104] To answer this question, it is important to consider the history and motivation of the Dickey-Wicker Amendment itself and the ex-ante incentives interpreting embryoids as embryos create for future research. It is also useful to see the animating goals and fears that have driven Americans, acting through their state legislatures, to create additional law around embryonic stem cell research. Taken together, these considerations should lead NIH to not consider embryoids "embryos" for purposes of federal funding restrictions. Embryoids do not raise the same concerns that first animated Congress to act, nor do they raise the same kinds of fears that states seem to be preoccupied by in subsequent legislation. Finally, to do otherwise would dampen innovative research and let go unrewarded the fruits of an international quest to find more ethical sources of stem cells for significant medical research.

A. The Text of the Dickey-Wicker Amendment

The strongest argument that embryoids created from induced pluripotent stem cells should be considered embryos for purposes of the Dickey-Wicker Amendment is from a literal reading of its text: "[T]he creation of a human embryo or embryos for research purposes" or "research in which a human embryo or embryos are destroyed" shall not be funded.[105] The law goes on to define an "embryo" as "*any* organism not protected as a human subject under 45 CFR 46, as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, *or any other means* from one or more human gametes or human diploid cells."[106] This language looks intentionally all-inclusive. Not

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[104] *What We Do: Budget*, *supra* note 9.

[105] Balanced Budget Down Payment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

[106] NIH GRANTS POLICY STATEMENT § 4.2.5 (Oct. 1, 2020), https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4.2.5_human_embryo_research_and_cloning_ban.htm?Highlight=4.2.5 [https://perma.cc/8YZ8-8LRM] (emphasis added). "45 CFR 46" refers to part 46 of title 45 of the Code of Federal Regulations which constitutes basic HHS policy for the protection of human research subjects. The definitions section defines "human subject" as "a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens." 45 C.F.R. § 46.102(e) (2022). 45 C.F.R.

only does it cover embryos created through fertilization with the use of gametes,[107] and cloning techniques using diploid cells,[108] but also leaves open the category of techniques used to create embryos. This sweeping language would suggest that Congress intended for the prohibition to evolve with science and that creating an embryo from adult cells reverted to stem cells is within the statute's general, if not specific, intent.

Nevertheless, the language of the statute is unclear in several places. This Comment primarily concerns itself with the meaning of "embryo;" however, the significance of the word "create" may also help define what is being created. In this way, whether forming an embryoid model out of iPSCs is "creating" an embryo may resolve whether they should be considered embryos in the first place. The Merriam-Webster dictionary provides two definitions that point in opposite directions for the purposes of this analysis. It first defines the verb "create" as "to bring into existence."[109] This may indicate that embryoids are distinct from embryos because it could be argued that scientists have not "brought them into existence" in a meaningful way. Instead, they simply arranged pre-existing induced pluripotent stem cells into a particular arrangement. These cells, in turn, were developed from the cells of a pre-existing adult. From this perspective, the act of "creation" that relates to these embryoid models is the moment of fertilization creating the embryo that developed into the adult who donated their cells for this research. If this is so, then embryoids are not creations and should not be considered subject to the Dickey-Wicker Amendment.

Yet, the dictionary supplies a second definition that seems to support the opposite inference. Definition two says that "to create" is "to invest with a new form, office, or rank," "to produce or bring about by a course of action or behavior."[110] This indeed does seem to describe well what the scientists are doing by compiling iPSCs into embryoid models. Through layering and combining these cells—a specific course of action—they are giving these cells a new form that makes them behave like cells in an embryo, which is the entire purpose of these experi-

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§§ 46.201–207 provides additional protections for women and fetuses. This section defines a "fetus" as "the product of conception from implantation until delivery." 45 C.F.R. § 46.202(c) (2022).

[107] Gametes are cells used in sexual reproduction such as sperm and eggs. For more information consult, Joan Lackowski, *Gamete*, ENCYCLOPAEDIA BRITANNICA (Feb. 24, 2020), https://www.britannica.com/science/gamete [https://perma.cc/8JPH-9YK5].

[108] Diploid cells are nonreproductive cells that have a full complement of genetic material. Kara Rogers, *Chromosome Number*, ENCYCLOPAEDIA BRITANNICA (Feb. 24, 2020), https://www.britannica.com/science/chromosome-number [https://perma.cc/8TXC-V8XT].

[109] *Create*, MERRIAM-WEBSTER'S COLLEGIATE DICTIONARY (11th ed. 2012); *see also* MERRIAM-WEBSTER (last visited Feb. 21, 2021), https://www.merriam-webster.com/dictionary/create [https://perma.cc/4DZY-578D].

[110] *Id.*

ments. If this is the controlling understanding of what it means to create, then embryoids perhaps should be considered embryos because they are being created.

The definition of embryo provided by the statute itself sheds light on the proper way to interpret the word "embryo" and the acts that can "create" them. The statute defines an embryo as something "that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells." Embryoids and the induced pluripotent stem cells that comprise them are *not* derived from fertilization, parthenogenesis, or cloning. Thus, if they are to be considered embryos, they must be derived by "any other means." Of course, read literally this would include the process of inserting certain genetic factors into a cell through a virus to change the expression of its genetics and revert it to a pluripotent state. This is a means and therefore could be considered part of any means. However, courts have not always construed clauses such as "or any other means" so literally. Instead, they generally rely on the cannon of *ejusdem generis* to provide further meaning.

Ejusdem generis means "of the same kind" and instructs that, "where general words follow specific words in an enumeration describing a statute's legal subject, the general words are construed to embrace only objects similar in nature to those objects enumerated by the preceding specific words."[111] This canon of construction remains a loadstar of the Supreme Court and lower courts throughout the nation.[112] Perhaps the most commonly cited Supreme Court decision deploying the canon is *Circuit City Stores, Inc. v. Adams*.[113] In that case, the Court deployed the canon to interpret the meaning of an exception from the Federal Arbitration Act which extended to "seamen, railroad employees, or any other class of workers engaged in foreign or interstate commerce."[114] The Court used the canon to narrow the class of "workers engaged in foreign or interstate commerce" not to include all people whose jobs involve such commerce but only to those workers whose work is significantly like that of seamen and railroad employees. The Court stated that the residual clause should be "controlled and defined by reference to the enumerated categories of workers which are recited just before it."[115] Under this canon, it could be argued here that the term

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[111] Norman Singer & Shambie Singer, *Ejusdem Generis*, *Sutherland Statutory Construction* § 47:17 (7th ed. 2021).

[112] *See, e.g.*, Gooch v. United States, 297 U.S. 124, 128 (1936); Ali v. Fed. Bureau of Prisons, 552 U.S. 214, 218 (2008); *Ex parte* Emerald Mountain Expressway Bridge, L.L.C., 856 So.2d 834, 842 (Ala. 2003).

[113] 532 U.S. 105, 114 (2001).

[114] *Id.*

[115] *Id.* at 116.

"any other means" should be limited to only those processes of "deriving" embryos which is substantially like "means" previously mentioned—fertilization, parthenogenesis, and cloning.

There is a commonality between these three processes of creating human embryos which is not shared by turning an adult somatic cell into an induced pluripotent stem cell: all these other processes require the use of a human egg cell. During fertilization, a human sperm cell containing half of a full complement of genetic material injects itself into a human egg cell containing the other half of the genetic material that becomes the full genetic complement of the embryo.[116] The parthenogenic process, which has been used by scientists to develop human stem cells without fertilization, involves an unfertilized egg being exposed to an electrical or chemical shock that "activates" the egg into developing as if it were fertilized.[117] Finally, cloning generally refers to the process of somatic cell transfer. In this process, the nucleus of somatic cells, which contains all the cell's genetic information, is inserted into an egg cell that previously had its own nucleus removed.[118] Thus, using the canon of *ejusdem generis*, for something to be considered an embryo, it must have been "derived" by a process that includes the use and manipulation of a human egg cell. That is to say the means of fertilization, cloning, and parthenogenesis constrain the meaning of "any other means" to only those involving human egg cells just as "seamen and railroad worker" constrained who could be considered "any other worker" involved in interstate commerce in *Circuit City*.[119] Under this interpretation of the Dickey-Wicker Amendment, embryoid models should not be considered embryos subject to the funding restriction because the iPSCs that make up a model are not derived by manipulating a human egg cell.

While this argument has some appeal, the Supreme Court has repeatedly instructed that canons of statutory interpretation cannot be used to defeat the obvious purpose or intent of the legislation.[120] The repeated use of the word "any"—i.e., "any organism," and "any means"—seems to point to a more expansive understanding of both the terms "create" and "embryo" than the one suggested from an *ejusdem generis* analysis. It is not obvious what the statute's purpose is from the text alone. Therefore it is important to look at the statute's history and

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[116] Alberto Monroy, *Fertilization*, ENCYCLOPAEDIA BRITANNICA (Feb. 18, 2020) https://www.britannica.com/science/fertilization-reproduction [https://perma.cc/B76C-22NY].

[117] *See generally* Rafferty, *supra* note 90; Qingyun Mai et al., *Derivation of Human Embryonic Stem Cell Lines from Parthenogenetic Blastocysts*, 17 CELL RSCH. 1008 (2007).

[118] Stocum, *supra* note 90.

[119] *Circuit City*, 532 U.S. at 115.

[120] *Gooch*, 297 U.S. at 128 (listing Supreme Court cases to that effect).

surrounding legislation in order to clarify the intent of Congress when it enacted this law.

B. The Single Cell?

When looking to state laws, it may first appear that many states understand what an embryo is in a way that is inconsistent with the current understanding held by NIH, but in fact, their understanding is harmonious. Key among these apparent differences is the fact that many states define an embryo as including a "single cell."[121] This seems to fly in the face of the interpretation of "organism" adopted by President Bush's NIH that embryonic stem cells themselves are not the kinds of "organisms" that are protected under the Dickey-Wicker Amendment.[122] Yet the justifications for these seemingly different understandings match in a way to make them more congruous. President Bush did not consider embryonic stem cells to be organisms because they are not complete and whole in and of themselves.[123] This rests on the idea that embryonic stem cells are pluri—but not toti—potent and, therefore, will likely not develop into a fetus and then a child without assistance. This is consistent with the understanding of those states which ascribe special significance to fertilization and conception. Embryos created from fertilization are totipotent, even at the single cell stage, and therefore have the potential to become a "whole and complete" organism described by the Bush Administration in a way that embryonic stem cells from stem cell lines never could.

Thus, both states and the federal government are more focused on the destruction of an embryo, or its creation for later destruction, than the creation itself. Put another way, although the Dickey-Wicker Amendment addresses both the creation and destruction of embryos, the federal government seems to only care about their creation in so far as they lead to the destruction of embryos. The government seems to take the view that there is nothing inherently wrong with the creation of embryos themselves, only what happens to them after their creation. This is especially clear from the states that include research regulations as part of either abortion regulation or regulation of fetal tissue use, which are even more clearly focused on embryo destruction.

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[121] *See, e.g.*, MONT. CODE ANN. § 50-11-101 (2021).

[122] Snead, *supra* note 33, at 493–96. I am using the Bush interpretation of the Dickey-Wicker Amendment because the Bush administration has interpreted the statute to make ineligible the largest amount of scientific activity for funding, and therefore NIH's then-understanding is most likely to find that embryoids should be considered embryos.

[123] *Id.*

Induced pluripotent stem cells are no more totipotent than embryonic stem cells. Embryoids created from these cell lines cannot themselves develop into people. As such, they do not raise the same creation concerns that animate both state and federal law. Therefore, while state laws defining embryos as including single-celled organisms might suggest NIH should adopt this interpretation as well, NIH's current organism understanding of embryos addresses some of the underlying concerns. It, therefore, need not adopt this interpretation entirely. Nevertheless, this only addresses whether a single iPSC should be considered an embryo in and of itself. It does not address whether models made from these stems should be considered embryos under the Dickey-Wicker Amendment. The original concerns of Congress when it first passed the Dickey-Wicker Amendment as well as the concerns that animated similar state laws, will make it clear that NIH should not consider embryoids to be embryos.

C. "Destruction" and "Creation"

Embryoids made from iPSCs are far removed from what had motivated Congress to create the restrictions on federal funding of research involving human embryos. The Congress that first attached the Dickey-Wicker Amendment was reacting directly to Clinton's HERP proposal to allow embryos to be created for research purposes. The intent was to keep scientists from fertilizing human eggs to create embryos for research. This is evidenced by the fact that Congress has consistently added this Amendment, without modification, even though embryoid models have existed for years. Both Presidents Bush and Obama referenced iPSCs as part of the developing alternatives to ESC research, which their administrations were pursuing.[124] This indicates that Congress has been aware of these emerging forms of research but has chosen not to extend protections from embryos to embryoid models.

NIH has taken a more nuanced approach in addressing whether embryoids should be considered embryos, as evidenced by Dr. Wolinetz's blog posts.[125] Its answer to the question is effectively "it depends."[126] As previously stated, iPSCs are pluripotent but not totipotent. That is, while it is an open question of what they may be able to do when given additional materials and environments, if left in a single layer in a petri dish, they will never develop into something like a human fetus. However, embryoids made from iPSCs are not monoliths. Each is unique, and each seems to fall differently between the polarities

[124] Hurlbut, *supra* note 6, at 263, 272.

[125] Wolinetz, *supra* note 64.

[126] *Id.*

created by Bush's distinction of "organism" versus cells. The more "organismal," the more likely NIH considered them embryos for purposes of the Dickey-Wicker Amendment. NIH takes a fact-specific investigation into how biologically similar an embryoid is to an embryo and how likely it would be to develop into a fetus and mature human if it were implanted in utero.[127]

First, this approach somewhat misses the point of embryoid models. It is crucially important for scientists to work with models that accurately reflect the subject they are trying to study. Under this approach, the closer an embryoid is to modeling an embryo, the farther away it is from federal funding and the less likely the research will be carried out in the first place. Second, this fact-specific approach lacks a clear measuring stick. It is entirely unclear whether an embryoid model implanted in utero would develop into a child. If even the most sophisticated model could not develop into a child, then all models would lack the special quality of the ability to become an autonomous human which states and the federal government seem to value. Finally, the more an embryoid model has the capability of developing into an autonomous human, the more it is in danger of becoming a clone. This is the second major concern identified in both state and federal laws that address embryonic research.

There is already a prohibition on the federal government from using funds to create clones. As President Clinton said, "I want to make it absolutely clear that no Federal funds will be used for human cloning."[128] This is because cloning raises a plethora of moral and even legal concerns.[129] These concerns also led states to regulate embryonic research to forbid the creation of clones.[130] While it is clear that the American people, acting through their federal and state governments, disfavor the practice of cloning, the Dickey-Wicker "restrictions on the use of Federal funds for research involving human embryos do not fully assure" clones will not be created.[131] Hence the additional restriction.

The creation of a clone is the kind of "creation" concern that animates the laws restricting "the creation of a human embryo or embryos for research purposes."[132] Embryoids share the same genetics as the adult cells that were used to create the induced pluripotent stem cells

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[127] *Id.*

[128] *Id.*

[129] For a more detailed discussion, *see generally* KERRY L. MACINTOSH, HUMAN CLONING: FOUR FALLACIES AND THEIR LEGAL CONSEQUENCES (2013).

[130] *See supra*, Part II.0 (discussing cloning laws).

[131] Memorandum on the Prohibition on Federal Funding for Cloning of Human Beings, *supra* note 71.

[132] Balanced Budget Down Payment Act, I, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996).

that comprise the embryoid and are, therefore, in a certain sense, already clones. Certainly, if an embryoid were to be created in such a way as to develop into an autonomous human, then that human would be a clone. However, embryoids cannot develop into autonomous humans, and research that would implant an embryoid in utero to test that hypothesis would be disallowed by other existing laws. Because the "creation" concerns in the Dickey-Wicker Amendment are already covered by laws restricting cloning, the statute should not be understood to restrict the creation of embryo-like models. Instead, it should be understood as prohibiting the creation of those things that are clearly embryos themselves and that will later be destroyed in research. This would allow for the maximum amount of scientific development while still staying true to fears which motivated Congress and thus their specific intent when passing the law. Therefore, all embryoid research should fall outside the scope of the Dickey-Wicker Amendment.

Identifying when an embryoid is a clone does raise several of the same concerns and difficulties as determining whether an embryoid should be considered an embryo.[133] A thorough comparative analysis of these two inquiries is beyond the scope of this Comment. Instead, this Comment asserts that there is likely to be significant daylight between the quality and quantity of research that can be done under the current line drawn at "embryo" and the proposed line at "clone." In this daylight, significant scientific discoveries would be lost by needlessly restricting research that neither involves the destruction of an embryo inherently capable of becoming a human nor creates a clone of another human being.

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[133] There should of course be ethical norms and institutional practices (but not laws) which limit research involving iPSCs models generally just as there are in other types of research. iPSCs have been used to create not only embryoids, which model embryos, but also organoids, which model organs. Some have created organoids made of neurons which form brain-like structures. Ball, *supra* note 16, at 166–67. Are these entitled to protections because these might be considered to have proto-human consciousness? Is the mere fact that these embryoids could experience something like pain significant? If they developed a "heartbeat," would that be significant, considering recent abortion legislation in states like Texas? Even if they are not embryos for purposes of the Dickey-Wicker Amendment, should these models follow the international standard of having a fourteen-day limit on how long they will let develop during research? *See generally*, Matthews & Morali, *supra* note 4. If, however, they are allowed to extend beyond the fourteen-day limit, then a new ethical limitation may need to be developed. This may solve several problems as there is an international push to allow research past the fourteen-day mark. *Id.*

V. CONCLUSION

The Dickey-Wicker Amendment prohibits two things: (1) "the creation of a human embryo or embryos for research purposes" and (2) "research in which a human embryo or embryos are destroyed."[134] Analyzing the history of the Amendment and looking to state laws that also regulate research involving embryos, it is clear that the destruction of embryos that Congress was concerned about was the destruction of embryos that would, if implanted in utero, have developed into a human. This approach also reveals two different creation concerns. First, the Amendment was concerned with the creation of these otherwise developmentally sufficient embryos for the sole purpose of their destruction. Second, embryonic research regulation more generally demonstrates a concern that embryonic research will create viable clones.

Embryoid models created from induced pluripotent stem cells are distinct from the kinds of embryos that Congress hoped to protect. Most importantly, they very likely cannot, on their own, develop into a human because they lack the totipotent potential of embryos that were created by fertilization. Thus, they do not raise the same destruction or creation-for-destruction concerns that motivated Congress to act. While it is true that embryoid models implanted in utero may be able to develop into a cloned human, that is, again, very unlikely. However, research that would yield such an outcome is already prohibited by restrictions on cloning. The meaningful dissimilarity between embryoid models made from induced pluripotent stem cells and embryos should lead the NIH to not consider them covered by the Dickey-Wicker Amendment and to fund such research involving such models accordingly.

The interpretation of the Dickey-Wicker Amendment that it does not cover embryoids does not leave a wild frontier open. Instead, it allows scientists to receive funding for research that has the potential to dramatically increase both our understanding of human development and the efficacy of fertility treatment while restricting it to research that does not create a clone.

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[134] Balanced Budget Down Payment Act, I § 128.