# Regulating (for the Benefit of) Future Persons: A Different Perspective on the FDA's Jurisdiction to Regulate Human Reproductive Cloning

*Gail H. Javitt*[*] *and Kathy Hudson*[**]

*The Food and Drug Administration (FDA) has taken the position that human reproductive cloning falls within its regulatory jurisdiction. This position has been subject to criticism on both procedural and substantive grounds. Some have contended that the FDA has failed to follow administrative law principles in asserting its jurisdiction, while others claim the FDA is ill suited to the task of addressing the ethical and social implications of human cloning.*

*This Article argues that, notwithstanding these criticisms, the FDA could plausibly assert jurisdiction over human cloning as a form of human gene therapy, an area in which the FDA is already regarded as having primary regulatory authority. Such an assertion would require that the FDA's jurisdiction extend to products affecting future persons, i.e., those not yet born. This Article demonstrates, for the first time, that such jurisdiction was implicit in the enactment of the 1962 Kefauver-Harris Amendments to the Federal Food, Drug, and Cosmetic Act and that the FDA has historically relied on such authority in promulgating regulations for drugs and devices.*

---

[*]Policy Analyst, Genetics and Public Policy Center; Adjunct Professor, University of Maryland Law School; J.D., Harvard Law School; M.P.H., Johns Hopkins School of Hygiene and Public Health; Former Greenwall Fellow in Bioethics and Health Policy, Johns Hopkins and Georgetown Universities.

[**]Director, Genetics and Public Policy Center; Associate Professor, Department of Pediatrics, Johns Hopkins School of Medicine; Ph.D., Molecular Biology, University of California at Berkeley; M.S. in Microbiology, University of Chicago.

Special thanks to Joan Scott, Susannah Baruch, Alta Charo, and Richard Merrill for their helpful comments on various drafts of this article, and to Erica Stanley, J.D., and Julie Albertus for their assistance with citations. Address all correspondence to Gail Javitt, Genetics and Public Policy Center, 1717 Massachusetts Avenue, NW, Washington, D.C., 20036, or gjavitt1@jhu.edu. This paper was written with the generous support of The Pew Charitable Trusts. The opinions expressed in this paper are those of the authors.

## I. INTRODUCTION

Since 1998, the FDA has taken the position that human reproductive cloning using somatic cell nuclear transfer ("SCNT") is within the scope of the agency's statutory authority.[1] Consistent with this stance, the agency has made public its view that any researcher seeking to conduct clinical investigations to clone a human being will first be required to submit an investigational new drug application (IND) to the agency.[2] Further, since the FDA believes human reproductive cloning raises safety concerns that remain unresolved, the agency has stated that it will not approve such an application, "until those [concerns] are appropriately addressed in the IND."[3] In short, the FDA has invoked its statutory and regulatory powers in an attempt to administratively prohibit human reproductive cloning in the United States.[4]

Previous commentators have addressed both the manner and substance of the FDA's approach to human reproductive cloning, and have also questioned the agency's institutional capacity to undertake this endeavor. Professor Richard Merrill, noted legal scholar and former FDA chief counsel, has criticized the agency's failure to follow procedural requirements in asserting jurisdiction, and has questioned whether the FDA's institutional structure and traditional oversight functions are adequately suited to mediating the societal conversation concerning the ethics of reproductive cloning.[5] Merrill has also noted the absence of a clearly articulated legal basis for the FDA's jurisdiction,[6] and has concluded, most recently in testimony before the President's Council on Bioethics,[7] that the FDA "has not yet put forward its best case" for its legal authority to regulate cloning.[8]

The purpose of this Article is to continue the rich dialogue concerning the appropriate oversight of human reproductive cloning, and to explore at greater length the most plausible basis—i.e., the "best case"—for the FDA's assertion

---

[1]*See, e.g.*, Rick Weiss, *Human Clone Research Will Be Regulated: FDA Asserts it Has Statutory Authority to Regulate Attempts at Human Cloning*, WASH. POST, Jan. 20, 1998, at A1 (asserting FDA's statutory authority to regulate human cloning).

[2]*See, e.g.*, Letter from Stuart L. Nightingale, M.D., FDA Assoc. Comm'r for Med. Affairs, to colleagues, *at* http://www.fda.gov/oc/ohrt/irbs/irbletr.html (Oct. 26, 1998) (stating that to pursue human cloning research scientists first must submit IND).

[3]*Id.*

[4]*See* Richard A. Merrill & Bryan J. Rose, *FDA Regulation of Human Cloning: Usurpation or Statesmanship?*, 15 HARV. J.L. & TECH. 85, 100, 124 (2001) (noting *in terrorem* effect of FDA's claim of jurisdiction).

[5]*Id.* at 97–98, 133–39; Richard A. Merrill, *Human Tissues and Reproductive Cloning: New Technologies Challenge FDA*, 3 HOUS. J. HEALTH L. & POL'Y 1, 68–73, 76–78 (2002) [hereinafter Merrill, *Human Tissues and Reproductive Cloning*].

[6]*See* Merrill, *supra* note 4, at 105–06, 147.

[7]The Council was established by President Bush on November 28, 2001 by Executive Order No. 13, 237, 3 C.F.R. 821 (2002).

[8]The President's Council on Bioethics, *Session 5: Biotechnology and Public Policy: Role of the Food and Drug Administration (FDA)*, *at* http://www.bioethics.gov/transcripts/jan03/session5.html (Jan. 17, 2003) (transcript).

of jurisdiction over human reproductive cloning. This Article will argue that the FDA could plausibly choose to regulate SCNT as a form of gene therapy. Regulating SCNT in this manner would be consistent with the FDA's existing definitions for gene therapy. However, whereas current gene therapy protocols seek to deliver genetic material to an existing human being for that person's benefit, the target of SCNT is an enucleated egg (i.e., an egg from which the original nucleus has been removed) that is intended to develop into a born human being following gestation. The FDA's regulation of reproductive cloning as a form of gene therapy would therefore need to presume that the agency's regulatory jurisdiction extends to evaluating the safety and effectiveness of products administered prior to birth, and indeed, prior to gestation.

This Article argues that, although the FDA's regulations for gene therapy have thus far been focused predominantly on the protection of currently living persons, the FDA's assertion of jurisdiction over SCNT for the benefit of a future person would nevertheless be consistent with the agency's historical oversight of products that have the potential to affect future persons. Additionally, it would comport with the legislative history and purpose of the Federal Food, Drug, and Cosmetics ("FD&C") Act.[9]

## II. BACKGROUND

### *A. What Is Cloning?*

The scientific methods that are used in mammalian SCNT cloning have been exhaustively documented.[10] In brief, SCNT entails removing the original nucleus from an egg cell and replacing that nucleus with one from a somatic cell, such as a skin cell. The egg cell, now containing a *new* (for the egg cell) nucleus, is then induced to divide under laboratory conditions to form an embryo.

What happens next determines whether the process will be termed *research* cloning or *reproductive* cloning. The embryo may be used to derive stem cells, which are progenitor cells with the capacity to generate a wide

---

[9] 21 U.S.C. §§ 301–397 (2000).

[10] *See, e.g.*, COMM. ON SCI., ENG'G, & PUB. POLICY, THE NATIONAL ACADEMIES, SCIENTIFIC AND MEDICAL ASPECTS OF HUMAN REPRODUCTIVE CLONING 25, 39 (2002) (documenting human reproductive cloning using SCNT); András Dinnyés et al., *Somatic Cell Nuclear Transfer: Recent Progress and Challenges*, 4 CLONING & STEM CELLS 81, 82 (2002) (noting successes and problems cloning various species); Angelika E. Schnieke et al., *Human Factor IX Transgenic Sheep Produced by Transfer of Nuclei from Transfected Fetal Fibroblasts*, 278 SCIENCE 2130 (1997) (documenting "nuclear transfer from stably transfected somatic cells [to] . . . transgenic livestock"); Calvin Simerly et al., *Molecular Correlates of Primate Nuclear Transfer Failures*, 300 SCIENCE 297, 297 (2003) (documenting SCNT in nonhuman primates).

variety of specialized cells.[11] Scientists believe that embryonic stem cells may, in the future, be used as therapies for human diseases such as Parkinson disease[12] and diabetes.[13] Alternatively, the embryo could be implanted into a uterus. If the embryo is successfully gestated, the result is an organism that is a virtually identical genetic copy (with the exception of the mitochondrial DNA) of the source of the somatic cell.[14]

Reproductive cloning using SCNT has been used to produce a variety of animals,[15] including sheep,[16] mice,[17] cows,[18] and most recently, a mule.[19] However, SCNT is a very inefficient procedure, as most embryos created via SCNT do not implant, and most of those that do implant do not complete gestation.[20] Moreover, live-born cloned animals have significant health problems.[21] To date, there has been no documented case in which a human being was produced through reproductive cloning, although a sect known as

---

[11]James A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCIENCE 1145, 1145–47 (1998).

[12]Jong-Hoon Kim et al., *Dopamine Neurons Derived from Embryonic Stem Cells Function in an Animal Model of Parkinson's Disease*, 418 NATURE 50, 50 (2002).

[13]Shimon Efrat, *Cell Replacement Therapy for Type 1 Diabetes*, 8 TRENDS MOLECULAR MED. 334, 336–38 (2002).

[14]*See generally* John A. Robertson, *Liberty, Identity, and Human Cloning*, 76 TEX. L. REV. 1371, 1387 (1998) (examining demand for human cloning); Dan W. Brock, *Human Cloning and Our Sense of Self*, 296 SCIENCE 314, 314 (2002) (discussing potential of cloning to undermine sense of self or identity).

[15]Don P. Wolf et al., *Nuclear Transfer Technology in Mammalian Cloning*, 32 ARCHIVES MED. RES. 609, 610–11 (2001).

[16]Elizabeth Pennisi & Gretchen Vogel, *Clones: A Hard Act to Follow*, 288 SCIENCE 1722, 1722–23 (2000).

[17]*Id.* at 1727.

[18]*Id.* at 1724.

[19]Constance Holden, *First Cloned Mule Races to Finish Line*, 300 SCIENCE 1354, 1354 (2003).

[20]Pennisi & Vogel, *supra* note 16, at 1722.

[21]*See, e.g.*, Kontad Hochedlinger & Rudolf Jaenisch, *Nuclear Transplantation: Lessons From Frogs and Mice*, 14 CURRENT OPINION CELL BIOLOGY 741, 744–45 (2002) (pointing to subtle abnormalities of cloned animals); Birgit Kühholzer-Cabot & Gottfried Brem, *Aging of Animals Produced by Somatic Cell Nuclear Transfer*, 37 EXPERIMENTAL GERONTOLOGY 1315, 1316 (2002) (discussing aging variations between cloned species); Wafa C. Slimane-Bureau & W. Allan King, *Chromosomal Abnormalities: A Potential Quality Issue for Cloned Cattle Embryos*, 4 CLONING & STEM CELLS 319, 320 (2002) (discussing chromosomal abnormalities in cloned animals); Y. Tsunoda & Y. Kato, *Recent Progress and Problems in Animal Cloning*, 69 DIFFERENTIATION 158, 159–60 (2002) (discussing recent problems with animal cloning); Gretchen Vogel, *Dolly Goes to Greener Pastures*, 299 SCIENCE 1163, 1163 (2003) (discussing death of first cloned mammal); R. Yanagimachi, *Cloning: Experience From the Mouse and other Animals*, 187 MOLECULAR & CELLULAR ENDOCRINOLOGY 241, 244–46 (2002) (discussing defects in gene expression). Dolly, the first mammal to be cloned from an adult cell, had arthritis and other problems indicating that she may have been aging prematurely. Vogel, *supra*. It is still unclear whether the unique circumstances of her conception had anything to do with her early death (she was euthanized after contracting a viral disease). *Id.*

the Raelians[22] has made unsubstantiated claims that they have produced children using this method.[23] Researchers have been attempting to generate cloned human and nonhuman primate embryos, and with one recent notable exception reported in *Science*, have had little success.[24] Some argue there are insurmountable biological barriers preventing successful cloning of humans and other primates, while others believe these to be only technical barriers.[25]

### *B. The FDA's Position on Cloning*

As others have noted previously, the FDA's method of publicly communicating its intent to regulate, and thereby prohibit, reproductive cloning via SCNT has been astonishingly informal and uninformative.[26] The FDA's first statements regarding cloning emerged not in the Federal Register (the traditional forum for reporting federal administrative agency regulatory activities), but rather in the context of a Washington, D.C.-based public radio talk show on which then Acting FDA Commissioner Michael Friedman was the guest on January 12, 1998.[27] Friedman stated that human cloning is an "investigational technology" and therefore cannot be attempted unless the researcher has submitted an "investigational application," i.e., an IND application.[28] Additionally, he stated that the FDA would ask the prospective researcher what scientific data that researcher possessed to show that the process was safe, and ensure that the individuals involved had the proper

---

[22]*See, e.g.*, Eleanor Cowie, *Is This a Picture of Cloned Baby?*, HERALD (Glasgow), Mar. 26, 2003, at 13 (discussing Clonaid claims of cloning success).

[23]Tim Rutten, *Cloning for Dollars: Sordid Tales of Hard-Sell Tactics*, L.A. TIMES, Jan. 8, 2003, at E2.

[24]*See* Woo Suk Hwang et al., *Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst*, SCIENCE (forthcoming 2004), *available at* www.scienceexpress.org (reporting derivation of cloned embryonic stem cells from human embryo). This experiment was notable in its ability to develop the embryo to a much later stage than had been previously reported. *See* Jose B. Cibelli et al., *Somatic Cell Nuclear Transfer in Humans: Pronuclear and Early Embryonic Development*, 2 e-BIOMED: J. REGENERATIVE MED. 25, 28 (2001) (reporting that three somatic-cell-derived human embryos developed up to six-cell stage); Panayiotis M. Zavos, *Human Reproductive Cloning: The Time Is Near*, 6 REPRODUCTIVE BIOMEDICINE ONLINE 397, 397–98 (2003) (reporting creation of "first human cloned embryo for reproductive purposes," stating that cloned embryo reached eight- to ten-cell stage before being cryopreserved for future analysis).

[25]Rick Weiss, *Study Shows Problems in Cloning People: Researchers Find Replicating Primates Is Harder Than for Other Mammals*, WASH. POST, Apr. 11, 2003, at A12; Calvin Simerly et al., *supra* note 10, at 297 ("With current approaches, NT to produce embryonic stem cells in nonhuman primates may prove difficult—and reproductive cloning unachievable."). *But see* Hwang et al., *supra* note 24.

[26]*See, e.g.*, Merrill & Rose, *supra* note 4, at 98–99, 105 (discussing first signs of FDA regulation).

[27]Interview by Diane Rehm, WAMU radio station, with Michael Friedman, Acting FDA Commissioner, Washington, D.C. (Jan. 12, 1998).

[28]*Id.*

training.[29] Friedman affirmed that "we believe we have jurisdiction over [human reproductive cloning]."[30] In response to the interviewer's suggestion that individuals who wanted to conduct human cloning would do so without seeking the FDA's permission, Friedman responded that such action would be "a matter of breaking the law."[31] Friedman defended the agency's cautious approach stating that "the risks that are attendant, the kind of birth defects that a developing child might run the risk of, the damage to that individual and to others, is not well-evaluated right now."[32]

The FDA first stated its position publicly in writing several months after the Friedman interview. In a "Dear Colleague" letter signed by then Associate Commissioner Stuart Nightingale, the agency alerted institutional review boards ("IRB"s) that the FDA "has jurisdiction over clinical research using cloning technology to create a human being," under both the Public Health Service ("PHS") Act and the FD&C Act.[33] Based on its claim of jurisdiction, for which no further elaboration was provided, the agency stated that "the appropriate mechanism to pursue a clinical investigation using cloning technology is the submission of an IND to the FDA."[34] However, "[s]ince the FDA believes that there are major unresolved safety questions pertaining to the use of cloning technology to create a human being, until those questions are appropriately addressed in the IND, the FDA would not permit any such investigation to proceed."[35] A similar letter was sent to the research community.[36]

In March 2001, Dr. Kathy Zoon, who was then director of the FDA's Center for Biologics Evaluation and Research ("CBER"), testified before the U.S. House of Representatives' Committee on Energy and Commerce, specifically, the Subcommittee on Oversight and Investigations.[37] She reiterated that the use of cloning technology to clone a human being would be subject to both the biologics provisions of the PHS Act and the drug and device provisions of the FD&C Act.[38] She also restated the requirement for an

---

[29]*Id.*

[30]*Id.*

[31]*Id.*

[32]*Id.*

[33]*See* Letter from Stuart L. Nightingale, *supra* note 2.

[34]*Id.*

[35]*Id.*

[36]Letter from Kathryn C. Zoon, Ph.D., Director, Center for Biologics Evaluation and Research, Food and Drug Administration, to Associations, *at* http://www.fda.gov/cber/ltr/aaclone.htm (Mar. 28, 2001).

[37]*Issues Raised by Human Cloning Research: Hearing Before the House Subcomm. on Oversight and Investigations of the Comm. on Energy and Commerce*, 107th Cong. 78–81 (2001) (statement of Kathryn C. Zoon, Director, Center for Biologics Evaluation and Research, Food and Drug Administration), *available at* http://www.fda.gov/ola/2001/humancloning.html (Mar. 28, 2001).

[38]*Id.* at 79.

IND submission in advance of any attempt to clone a human being.[39] She cited the FDA's past statements regarding human somatic-cell therapy, gene therapy, and tissue-based products without expressly stating whether, how, and to what extent such statements would be applied to reproductive cloning.[40]

Finally, the Web site for CBER—the Center within the FDA that regulates biological products—purports to explain the FDA's regulation of human cloning.[41] Perplexingly, the Web site asserts that SCNT is "not reproduction since a sperm cannot be used with the technique."[42] Rather, "it is an extension of technology used not only in research but also used to produce medically relevant cellular products such as cartilage cells for knees, as well as gene therapy products."[43] The Web site implies that SCNT would be subject to regulation in accordance with the agency's "comprehensive plan for the regulation of cell and tissue based therapies," which the agency announced on February 28, 1997.[44] As will be discussed below, that plan did not itself establish new regulations, but rather presented a framework comprising several different potential regulatory elements that would require development and implementation through notice and comment rulemaking.

In summary, the FDA has alluded to several possible regulatory *categories* that could, in theory, encompass cloning, including tissue-based therapies, cellular therapies, and gene therapy, but has not provided any rationale for how reproductive cloning fits, conceptually or definitionally, within any of these categories. The agency's reference to its IND regulations implies that it considers some aspect of the process to involve a *drug*, and, specifically, a *new drug*. The FDA has not, however, articulated what component or components of cloning constitute that drug. CBER's fairly recent assertion that the use of cloning technology to clone a human being is not *reproduction* is, at the least, puzzling. The ordinary meaning of reproduction encompasses both sexual and asexual replication, but CBER's assertion implies that reproductive cloning is not even an asexual form of reproduction. Such an implication raises some difficult questions. For example, if cloning is not reproduction, what would be the status of the resulting child? If the cloned child is not a product of reproduction, then what is it?

CBER's claim that reproductive cloning is not reproduction, along with its failure to identify the component of cloning that constitutes a drug, underscores the fact that the FDA has, in all of its iterations of what might be termed policy, assiduously avoided answering the central question of what precisely is the subject of its jurisdiction, or, in statutory parlance, the *article*

---

[39]*Id.*

[40]*Id.*

[41]Center for Biologics Evaluation and Research, *Use of Cloning Technology to Clone a Human Being*, *at* http://www.fda.gov/cber/genetherapy/clone.htm (last updated Dec. 27, 2002).

[42]*Id.*

[43]*Id.*

[44]*Id.*

that it seeks to regulate. As will be discussed in the next Part, defining the article in cloning is essential to justifying a legal theory in support of that article's regulation. Thus far, the FDA appears to be floundering for a regulatory *hook*; it is positing a desired regulatory result that is in search of a cogent legal theory.

While the FDA's activities to date have had their intended effect (namely, to deter would-be cloners from, at least publicly, undertaking efforts to clone a human being), and while it is unlikely that any of the odd cast of would-be human cloners thus far assembled would bring a legal challenge to the FDA's activities,[45] it is nevertheless a worthwhile endeavor to explore the legal basis for the FDA's actions.

First, although quasi-science fiction now, it does not strain credulity to posit that human reproductive cloning techniques could be successful within the next few decades. Significant new developments in basic science have led to new understandings about how to create and manipulate human gametes—only recently, scientists have discovered how to create artificial mouse eggs from embryonic stem cells.[46] At the same time, the field of reproductive medicine continues to develop clinical techniques for overcoming infertility, commonly known as assisted reproductive technologies, or ART.[47] The combination of advances in these two disciplines means both that the technical hurdles that need to be overcome may in fact be resolved in the future, and that the clinical incentives to undertake cloning—namely, overcoming infertility—are in place. Second, as a matter of legal principle, it damages the federal division of power established by the U.S. Constitution when an administrative agency proceeds without proper regard for the requirements of administrative

---

[45]*See, e.g.*, CNN.com, '*Raelian' Biochemist Insists She Will Clone Human* (June 20, 2003), *at* http://www.cnn.com/2001/HEALTH/06/30/clone.lab.txt/ (citing Clonaid scientist Brigitte Boisellier as stating that she is reluctant to challenge FDA's jurisdiction in court). Panayiotis Zavos' work to generate human cloned embryos for reproduction has been conducted outside the United States. *See* Zavos, *supra* note 24, at 398.

[46]Karin Hubner et al., *Derivation of Oocytes from Mouse Embryonic Stem Cells*, 300 SCIENCE 1251, 1252–56 (2003).

[47]ART is a broad term that encompasses a variety of medical techniques used to assist couples in becoming pregnant. Examples of ARTs include in vitro fertilization ("IVF"), gamete intrafallopian tube transfer ("GIFT"), zygote intrafallopian tube transfer ("ZIFT"), and intracytoplasmic sperm injection ("ICSI"). *See, e.g.*, Kate Hardy et al., *Future Developments in Assisted Reproduction in Humans*, 123 REPRODUCTION 171, 171–72 (2002) (discussing strategies for improving ART efficiency). In 2001, the most recent year for which data are available, more than 40,000 babies were born as a result of ART procedures. *See* Nat'l Ctr. for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 2000 Assisted Reproductive Technology Success Rates, http://www.cdc.gov/reproductivehealth/ART01/section1.htm (last reviewed May 13, 2003). This number represents close to one percent of all live births for that year. *See* HHS News, *Women Are Having More Children, New Report Shows Teen Births Continue to Decline* (Feb. 12, 2002), *at* http://www.cdc.gov/nchs/releases/02news/womenbirths.htm (reporting 4,058,814 births in United States in 2000).

law,[48] which the FDA has, at least arguably, done in the case of cloning.[49] Furthermore, a court, in reviewing the FDA's decision on cloning, would likely not give deference to the agency's substantive position on cloning if the agency had not first engaged in a formal rule-making process.[50] Failure to comply with the Administrative Procedure Act ("APA") requirements could itself provide the basis for invalidating FDA action.[51] Finally, substantive

---

[48]The U.S. Constitution divides the authority of the federal government into three branches: the executive, the legislative, and the judicial. Article I provides that all legislative powers "shall be vested in a Congress of the United States." U.S. CONST. art. I, § 1. Article II directs the executive branch to "take Care that the Laws be faithfully executed." *Id.* art. II, § 3. Under the "non-delegation doctrine," courts historically held broad grants of legislative or judicial authority to executive branch agencies to be an unconstitutional violation of the separation of powers. *See* Sandra B. Zellmer, *The Devil, the Details, and the Dawn of the 21*st *Century Administrative State: Beyond the New Deal*, 32 ARIZ. ST. L.J. 941, 957–59 (2000). Criticisms of delegation of authority to executive branch agencies are based on the concern that agency officials are not elected by and are less accountable to the public. *Id.* at 953. Some have argued that agencies constitute an illegitimate "fourth branch" of government. *Id.* at 950. Nevertheless, agencies have become an essential adjunct to statutory implementation, filling in the interstices of broad legislative mandates. Courts have responded to the non-delegation problem by requiring that statutory language provide principles to guide agency action and procedural safeguards to protect the public from arbitrary or abusive decisions. *Id.* at 958, 963. In addition, the Administrative Procedure Act, enacted in 1946, sought to constrain the actions of administrative agencies and to ensure transparency and accountability to the public by requiring, inter alia, that agencies engage in formalized rulemaking processes and include the public in their deliberations. *Id.* at 954, 963.

[49]Merrill, *Human Tissues and Reproductive Cloning*, *supra* note 5, at 71–77.

[50]In *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 843, 866 (1984), the Supreme Court held that an administrative agency's interpretation of an ambiguous statute will prevail provided that it is reasonable. This principle, known as *Chevron* deference, gives wide latitude to agency actions that purport to implement the statutes they are charged with administering. *See, e.g.*, Jonathan T. Molot, *Reexamining Marbury in the Administrative State: A Structural and Institutional Defense of Judicial Power Over Statutory Interpretation*, 96 NW. U. L. REV. 1239, 1242, 1320–37 (2002). In recent years, however, the Court has issued rulings that limit the application of *Chevron* deference only to agency actions that have the force of law, i.e., actions undertaken following notice-and-comment rulemaking or formal adjudicatory proceedings. *See, e.g.*, United States v. Mead Corp., 533 U.S. 218, 226–27, 230–31 (2001) (noting that lack of notice-and-comment rulemaking or formal adjudication is not dispositive); Christensen v. Harris County, 529 U.S. 576 (2000) (holding Department of Labor opinion letter is not entitled to *Chevron* deference). *See also* James V. DeLong, *The Chevron Doctrine: Running Out of Gas*, 23 REGULATION 5, 5–6 (2000) (calling limiting of *Chevron* deference a "seismic" shift in balance of power); James A. Lastowka & Arthur G. Sapper, *The Supreme Court Substantially Cuts Back on Chevron Deference:* United States v. Mead Corp., *533 U.S. ___ (2001) (No. 99-1434, June 18, 2001)* (summarizing developments from *Chevron*, *Christensen*, and *Mead*), *available at* http://www/emlf.org/lastowka.htm; Molot, *supra*, at 1269. To the extent that FDA's position on cloning has been articulated solely in an informal manner (which statements on talk shows and in letters to interested parties would undoubtedly be), it is unlikely that a court would give deference to the agency's position if it were challenged.

[51]The Administrative Procedure Act authorizes a court to "hold unlawful and set aside agency action" that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A) (2000). Courts have invalidated agency actions that have a binding effect on third parties for failure to first engage in notice-and-comment

grappling with these issues can only refine the FDA's regulatory efforts, not only over cloning, but also over related technologies. If a careful analysis reveals that the FDA lacks authority currently, and there is consensus that it would be in society's interest for the FDA or some other entity to be afforded additional authority, then now, before the technology is "out of the barn," is the time to address such deficiencies.

## III. FDA REGULATION UNDER THE FEDERAL FOOD, DRUG AND COSMETIC ACT AND THE PUBLIC HEALTH SERVICE ACT

This Part discusses the different categories of products under the FDA's jurisdiction, and the statutory definitions of these categories. As will be demonstrated, defining the regulatory category of a product is an essential prerequisite to FDA regulation, and something that the FDA has repeatedly avoided in the case of cloning.

### *A. Drugs*

The FD&C Act, enacted in 1938 and amended numerous times since, authorizes federal regulation of "drugs" and other products.[52] This authority has been delegated to the Commissioner of the FDA.[53] The statute defines the term "drug" to include an article that is intended either "for use in the diagnosis, cure, mitigation, treatment, or prevention of disease,"[54] or "to affect the structure or any function of the body."[55] A "new drug" is a drug that is "not generally recognized . . . as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof."[56] The FD&C Act prohibits the interstate distribution of any new drug that has not been approved by the FDA.[57]

The extent and manner of the FDA's regulation of any product under the agency's jurisdiction, including drugs, depends on the intended use of the product.[58] Historically, the FDA has determined a product's intended use based

---

rulemaking. *See, e.g.*, Croplife America v. EPA, 329 F.3d 876, 884 (D.C. Cir. 2003) (holding that EPA must comply with notice-and-comment requirements to effect dramatic change).

[52]21 U.S.C. §§ 301–397 (2000).

[53]21 C.F.R. § 5.10 (2003).

[54]21 U.S.C. § 321(g)(1)(B).

[55]*Id.* § 321(g)(1)(C).

[56]*Id.* § 321(p)(1).

[57]*Id.* § 331(d).

[58]The FD&C Act directs the FDA to reject an NDA if the data fail to demonstrate that the drug is "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof." *Id.* § 355(d)(1). FDA regulations define "intended use" as "the objective intent of the persons legally responsible for the labeling of drugs." 21 C.F.R. § 201.128. This intent is "determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article." *Id.* For example, objective intent may be demonstrated through "labeling claims, advertising matter, or oral or written statements by

primarily on the "manufacturer's objective intent, as evidenced by labeling, promotional, and other relevant materials for the product."[59] Courts have also recognized the FDA's authority to look beyond a manufacturer's express claims and consider more subjective evidence of intended use, such as the foreseeable or actual use of the product.[60]

As discussed in greater detail in Part V, the 1962 amendments to the FD&C Act ushered in the modern era of drug approval. The FDA's approval process for a new drug typically begins when a sponsor of the new drug submits an IND to the agency.[61] The IND must be submitted in advance of any human testing of a new drug.[62] It must contain information from laboratory and animal testing sufficient to permit the FDA to assess the safety of the proposed clinical study.[63] Unless the FDA objects, the study that is the subject of the IND may proceed thirty days after the IND is filed with the agency.[64]

Clinical testing of drugs typically occurs in three phases.[65] During Phase I, the drug is tested on a small number (twenty to eighty) of patients or healthy volunteers in order to study how the drug is tolerated, metabolized, and excreted.[66] Phase I studies are not generally designed to assess drug efficacy, although they may provide some initial evidence in this regard.[67] Phase II studies are larger, generally involving anywhere from fifty to 200 patients, and represent the first time when both safety and effectiveness are evaluated.[68] Finally, Phase III trials may include between "several hundred to several thousand subjects,"[69] and are intended "to confirm and expand upon the safety and efficacy data obtained from the first two phases."[70]

---

such persons or their representatives" or "may be shown by the circumstances that the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised." *Id.*

[59]Robert P. Brady et al., *The Food and Drug Administration's Statutory and Regulatory Authority to Regulate Human Pluripotent Stem Cells*, *in* 2 NAT'L BIOETHICS ADVISORY COMM'N, ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH: COMMISSIONED PAPERS, B-1, B-4 (2000), *available at* http://www.georgetown.edu/research/nrcbl/nbac/briefings/may99/fda.pdf.

[60]*Id.* (citing Action on Smoking & Health v. Harris, 655 F.2d 236, 240–41 (D.C. Cir. 1980); Nat'l Nutritional Foods Ass'n. v. Matthews, 557 F.2d 325, 334 (2d Cir. 1977)).

[61]21 U.S.C. § 355(i); 21 C.F.R. § 312.20(a).

[62]21 C.F.R. §§ 312.20(b), 312.23(a)(iii).

[63]*Id.* § 312.23(a)(3)(iii), (a)(3)(iv), (a)(5)(v), (a)(8), (a)(10)(iv).

[64]21 U.S.C. § 355(i)(2).

[65]21 C.F.R. § 312.21.

[66]*Id.* § 312.21(a).

[67]*Id.*

[68]*Id.* § 312.21(b).

[69]*Id.* § 312.21(c).

[70]Investigational New Drug, Antibiotic, and Biological Drug Product Regulations; Procedures for Drugs Integrated to Treat Life-Threatening and Severely Debilitating Illnesses, 53 Fed. Reg. 41,516, 41,518 (Oct. 21, 1988) (codified at 21 C.F.R. § 312.21(c)). These phases are not statutorily required, and they are by no means absolute: indeed, some officials within the FDA have tried to get away from the Phase I, II, III terminology because of concerns that it conveys an unduly mechanistic description of the process. For example, a 1997 Guidance

Once clinical trials have been successfully completed, the sponsor of the new drug may submit a new drug approval application ("NDA").[71] The NDA must contain information from clinical trials demonstrating that the drug is safe and effective when used for the condition described in the labeling.[72] FDA approval of the drug permits it to be marketed under the conditions specified in the grant of approval.[73] Promotion of a drug for uses other than those that are approved constitutes a violation of the statute.[74]

### *B. Biological Products*

The FDA also has authority to regulate biological products pursuant to the PHS Act.[75] Section 262 of the PHS Act defines a "biological product" as a "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings."[76] To market a biological product, the manufacturer must first submit a biologics license application ("BLA") to the FDA.[77] The BLA must contain data from clinical trials demonstrating that it is "safe, pure, and potent."[78]

The FDA has historically taken the position that products regulated as biologics pursuant to section 262 of the PHS Act meet the definition of drugs and are therefore also subject to the provisions of the FD&C Act, such as the requirement to demonstrate safety and effectiveness.[79] Since the FD&C Act contains many additional regulatory provisions not present in the PHS Act, such as the authority to require an IND, this position has permitted the FDA to regulate biological products to the same extent it regulates drugs. The FDA's historical understanding was formalized by an amendment to the FD&C Act in

---

Document suggested that a Phase II study be referred to as "therapeutic exploratory" and a Phase III study be referred to as "therapeutic confirmatory." Jennifer Kulynych, *Will FDA Relinquish the "Gold Standard" for New Drug Approval? Redefining "Substantial Evidence" in the FDA Modernization Act of 1997*, 54 FOOD DRUG L.J. 127, 143 (1999). Nevertheless, the terminology appears to remain the standard in the scientific and legal literature and common parlance, as well as the FDA's own regulations. *See* 21 C.F.R. § 312.21.

[71]21 U.S.C. § 355(b)(1) (2000); 21 C.F.R. pt. 314.

[72]21 U.S.C. § 355(b)(1).

[73]21 C.F.R. § 314.105(a).

[74]21 U.S.C. § 331(d).

[75]Public Health Service Act, 42 U.S.C. §§ 201–300 (2000).

[76]*Id.* § 262(i).

[77]*Id.* § 262(a)(1)(A); 21 C.F.R. pt. 601 (2003) (describing application procedure for Biologics license).

[78]42 U.S.C. § 262(a)(2)(B)(i)(I).

[79]Human Drugs Which Are Biological Products, 37 Fed. Reg. 4004, 4005 (Feb. 18, 1972); Procedures for Review of Safety, Effectiveness, and Labeling, 37 Fed. Reg. 16,679, 16,679 (Aug. 14, 1972); 38 Fed. Reg. 4,319, 4,321 (Feb. 8, 1973); John P. Swann, *Sure Cure: Public Policy on Drug Efficacy Before 1962*, *in* THE INSIDE STORY OF MEDICINES 223, 230 (Gregory J. Higby & Elaine C. Stroud eds., 1997).

1997.[80] The import of the "dual" status of biological products in the context of reproductive cloning is that even products that the FDA regulates as biologics must meet the statutory definition for drugs in order to be subject to requirements under the FD&C Act.

As discussed below, the phrase "analogous product" has been broadly construed by the FDA to govern many biologically derived products not explicitly identified in the definition, including gene therapy. Over the past several years, the FDA has, through the process of rulemaking and informal communications, articulated an additional product category subject to its jurisdiction, which it has described as "human cells, tissues, and cellular and tissue based products" ("HCT/P"s).[81] This category has been defined to include both products regulated as human tissue and "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient."[82] While the detailed implementation of this plan is ongoing, in general terms the regulatory framework would assign cellular and tissue-based products to different regulatory categories (e.g., drug, device, biologic, or tissue) based on several factors.

The import of the previous description in the cloning context is that FDA regulation of products is category driven. The statutory framework is designed such that the FDA's first question in determining whether it can lawfully regulate a product and the manner in which it can regulate a product, is to determine into what category the product best fits. This is the crucial step that the FDA has not yet taken with regard to cloning. As is discussed in the next Section, the FDA could plausibly argue that cloning is relevantly similar to gene therapy, which the FDA has already determined fits within the categories of drug or biological products.

### *C. FDA Regulation of Gene Therapy*

Gene therapy is an investigational technique that involves the transfer of a segment of DNA into an individual's cells and the expression of that DNA in the body.[83] The goal—largely unrealized to date—is to overcome the effects of an individual's incorrectly functioning genes through the introduction of an additional gene. The additional gene could correct the defect by, for example,

---

[80]42 U.S.C. § 262(j). This section provides: "The Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301–397] applies to a biological product subject to regulation under this section, except that a product for which a license has been approved under subsection (a) shall not be required to have an approved application under section 355 of Title 21." *Id.*

[81]*See* Food and Drug Administration, *Proposed Approach to Regulation of Cellular and Tissue Based Products*, *at* http://www.fda.gov/gdlns/celltissue.pdf (Feb. 28, 1997).

[82]Human Cells, Tissues, and Cellular and Tissue-Based Products, 21 C.F.R. § 1271.3(d)(2) (2003).

[83]ROBERT L. NUSSBAUM ET AL., THOMPSON & THOMPSON, GENETICS IN MEDICINE 269–70 (6th ed. 2001).

*replacing* the nonfunctioning gene with a functioning one,[84] or by causing cells containing deleterious genes such as those that cause cancer, to self-destruct.[85]

Researchers have encountered many difficulties along the path to the clinical use of gene therapy. In particular, gene-delivery issues, that is, how to transfer the segment of DNA into target cells in a manner that allows integration and/or gene expression without disrupting other processes, have continued to pose challenges.[86] Researchers have attempted a variety of gene-transfer methods. Most of the current gene therapy approaches make use of viral vectors.[87] These are viruses that have been altered to remove their pathogenic properties, but which retain the ability to infect cells and transmit a gene into the target cell.[88] In effect, they act as molecular taxicabs. Other, nonviral approaches are also under investigation.[89] Recent progress in specifically targeting transferred genes for integration into particular sites in the genome of human stem cells suggests that some of the major technical challenges to human gene therapy can be overcome.[90]

Gene therapy can, at least in theory, be directed to either *somatic* (nonreproductive) or *germ* (reproductive) cells of the body. Gene therapy that targets somatic cells is intended to alter only the DNA of the recipient of the gene therapy and not his or her progeny.[91] In contrast, germline gene therapy is intended to modify sex cells (sperm and egg) and thereby affect the genome of subsequent offspring.[92] Because germline gene therapy can affect future

---

[84]*See, e.g.*, Alan Fischer et al., *Gene Therapy of Severe Combined Immunodeficiencies*, 2 NATURE REVIEWS IMMUNOLOGY 615, 615–20 (2002) (describing clinical trials involving insertion of corrective transfer genes into abnormal cells).

[85]Frank McCormick, *Cancer Gene Therapy: Fringe or Cutting Edge?*, 1 NATURE REVIEWS CANCER 130, 130 (2001) (describing possible methods of gene therapy which target and suppress cancerous cells).

[86]Erika Check, *Gene Therapy: A Tragic Setback*, 420 NATURE 116, 116 (2002) [hereinafter Check, *A Tragic Setback*] (discussing patient treated with replacement gene which led to leukemia-like condition); Erika Check, *Gene Therapy: Shining Hopes Dented—But Not Dashed*, 420 NATURE 735, 735 (2002) (same).

[87]*See, e.g.*, Matthias Dobbelstein, *Viruses in Therapy—Royal Road or Dead End?*, 92 VIRUS RES. 219, 220 (2003) (listing recent uses of viruses in gene therapy); Cathryn Mah et al., *Virus-based Gene Delivery Systems*, 41 CLINICAL PHARMACOKINETICS 901, 901 (2002) (discussing various vector systems used in gene therapy).

[88]Check, *A Tragic Setback*, *supra* note 86, at 116.

[89]Dobbelstein, *supra* note 87, at 242.

[90]*See* Thomas P. Zwaka & James A. Thomson, *Homologous Recombination in Human Embryonic Stem Cells*, 21 NATURE BIOTECHNOLOGY 319, 320 (2003) (discussing advances in homologous recombination in human embryonic stem cells—a practice that "will be important for . . . modifying specific ES cell-derived tissues for therapeutic applications in transplantation medicine").

[91]NUSSBAUM ET AL., *supra* note 83, at 269.

[92]*See generally* Mark S. Frankel & Audrey R. Chapman, HUMAN INHERITABLE GENETIC MODIFICATIONS: ASSESSING SCIENTIFIC, ETHICAL, RELIGIOUS, AND POLICY ISSUES 2–3 (2000), *available at* http://www.aaas.org/spp/dspp/sfrl/projects/germline/report.pdf (discussing germline therapy as form of inheritable genetic modification which might correct or prevent genetic disease in future progeny).

generations, the National Institutes of Health's (NIH) Recombinant DNA Advisory Committee (RAC) has refused to consider protocols intentionally targeting germline cells and will not review protocols involving genetic modification of embryos prior to implantation.[93] However, there has been some concern that somatic-cell targeted vectors may inadvertently enter the germline.[94] Both the NIH and the FDA require that investigators monitor whether vectors enter germ cells,[95] and, in the past, the FDA has placed a clinical hold on a protocol following evidence of possible germline transmission of a viral vector.[96]

Since 1984, the FDA has taken the position that gene therapy is subject to regulation by the agency.[97] Moreover, the FDA has consistently expressed the view that gene therapy can be regulated within the existing statutory framework for drugs and biological products.[98] The FDA defines gene therapy as:

> [A] medical intervention based on modification of the genetic material of living cells. Cells may be modified *ex vivo* for subsequent administration to humans, or may be altered *in vivo* by gene therapy given directly to the subject . . . . The genetic manipulation may be intended to have a therapeutic or prophylactic effect, or may provide a way of marking cells for later identification.[99]

---

[93]*See* NAT'L INST. OF HEALTH, DEP'T OF HEALTH AND HUMAN SERVS., GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT DNA MOLECULES app. M (Apr. 2002), *available at* http://www4.od.nih.gov/oba (stating "RAC will not at present entertain proposals for germ line alterations" and "it is premature to undertake any in-utero gene transfer clinical trial").

[94]*See, e.g.*, Eliot Marshall, *Gene Therapy: Panel Reviews Risks of Germ Line Changes*, 294 SCIENCE 2268, 2268 (2001) (hypothesizing FDA's reluctance to allow continued somatic-cell gene therapy research without requiring more tests of germline effects); Eliot Marshall, *Viral Vectors Still Pack Surprises*, 294 SCIENCE 1640, 1640 (2001) (noting case where FDA asked researchers to put clinical trial on hold after viral vector was detected in patient's semen).

[95]Biological Response Modifiers Advisory Committee, Briefing Document for May 10, 2002; *Issues Pertaining to Inadvertent Germline Transmission of Gene Transfer Vectors*, *available at* http://www.fda.gov/OHRMS/DOCKETS/ac/02/briefing/3855B2_01.pdf.

[96]*See generally id.* (stating FDA will mandate clinical hold on studies causing inadvertent germline transmission when sex cells from fractionated semen tests positive for vector sequences); *see also Gene Therapy and the Germline*, 5 NATURE MED. 245, 245 (1999) (reviewing concern over gene therapy vectors that make their way to gonads).

[97]*See* Richard A. Merrill & Gail H. Javitt, *Gene Therapy, Law and FDA Role in Regulation*, *in* 1 ENCYCLOPEDIA OF ETHICAL, LEGAL, AND POLICY ISSUES IN BIOTECHNOLOGY 321, 328 (Thomas J. Murray & Maxwell J. Mehlman eds., 2000).

[98]*Id.*; Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53,248, 53,251 (Oct. 14, 1993).

[99]CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, DEP'T OF HEALTH AND HUMAN SERVS., GUIDANCE FOR HUMAN SOMATIC CELL THERAPY AND GENE THERAPY 3 (March 1998), *available at* http://www.fda.gov/cber/gdlns/somgene.pdf.

The definition indicates that the FDA considers human gene transfer, even when it is not intended for therapeutic purposes, to meet the definition of gene therapy. The FDA considers both the DNA segment and the delivery system (e.g., viral vector) to be "products" subject to regulation as biologics.[100] These products also simultaneously meet the definition of "drugs" because they are either intended to prevent or treat a disease, or are intended to affect a structure or function of the body.[101] Thus, like other drugs, gene therapy products cannot be administered to a human being unless the entity seeking to administer them has submitted an IND to the FDA.[102]

As of September 2000, there were more than 200 active gene therapy INDs under the FDA's oversight.[103] These protocols target only the somatic cells of the body.[104] Although gene therapy was originally conceived as a means to treat or correct rare diseases caused by *monogenic* or single-gene defects, the vast majority of protocols have targeted widespread diseases such as AIDS, cancer, and heart diseases—illnesses for which the genetic basis is far more complex and varied.[105] In recent years the NIH has also approved gene therapy trials in healthy volunteers as a means to assess the effect of viral vectors and establish a baseline before measuring therapeutic effect.[106]

In addition to the FDA, the Recombinant DNA Advisory Committee ("RAC") of the NIH also plays a role in the regulation of gene therapy.[107] Over time, the RAC has redefined its role regarding human-gene therapy and has moved from independent review and approval of individual gene therapy protocols to consideration of the ethical implications of new uses of human-gene transfer.[108] Gene therapy protocols that are funded by the NIH or conducted at or sponsored by NIH-funded institutions must be submitted to the RAC.[109] The NIH maintains a registry of these protocols.[110] Submission to the

---

[100]Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg., *supra* note 98, at 53,251.

[101]*Id.* at 53,249.

[102]*Id.* at 53,250.

[103]U.S. Food & Drug Admin., Dep't of Health and Human Servs., *Human Gene Therapy and The Role of the Food and Drug Administration* (Sept. 2000), *available at* http://www.fda.gov/cber/infosheets/genezn.htm.

[104]*See supra* notes 94–95 and accompanying text.

[105]Merrill & Javitt, *supra* note 97, at 333 (citation omitted).

[106]Jeffrey L. Fox, *Green Light for Gene Therapy in Healthy Volunteers*, 15 NAT. BIOTECHNOL. 314 (1997).

[107]Merrill & Javitt, *supra* note 97, at 328.

[108]*See, e.g.*, *id.* (explaining that RAC was preserved despite FDA's successful acquisition of primary role in gene therapy regulation because "number and fervor of comments" opposing elimination of RAC prompted NIH to simply amend RAC functions from review of individual gene therapy protocols to include "identifying novel social and ethical issues relevant to specific human applications of gene transfer"); *see also* Joseph M. Rainsbury, *Biotechnology on the RAC—FDA/NIH Regulation of Human Gene Therapy*, 55 FOOD DRUG L.J. 575, 590–92 (2000) ("The RAC continues today primarily as a sounding board for novel gene therapy protocols.").

[109]NAT'L INST. HEALTH, *supra* note 93, §§ I-A-1, -C-1, -D.

RAC is voluntary for protocols that are funded solely with private funds and not conducted at or by an institution receiving NIH funding.[111] The RAC reviews registered protocols to determine if they raise unique and/or novel issues, and facilitates public discussion of such protocols.[112] Issues requiring public discussion may include the use of new vectors or other gene-delivery systems, application of gene therapy to new diseases, and other novel uses. For example, in 1997 the RAC sponsored the first Gene Therapy Policy Conference to discuss the use of gene therapy for "enhancement,"[113] meaning for use in non-life-threatening conditions such as baldness. The RAC has also served as a forum for discussing potential in utero gene therapy protocols.[114] As discussed previously, the RAC has stated that it will not at present entertain proposals for germline gene-transfer experiments,[115] a position that the FDA considers to constitute a reason for caution, although the agency has issued no formal position with regard to the germline gene transfer.[116] The RAC is widely seen as having a crucial role in providing a public forum for discussion and debate concerning particular applications of human-gene transfer.[117]

## IV. WHY REPRODUCTIVE CLONING CAN CONCEPTUALLY BE CONSIDERED A FORM OF GENE THERAPY

Like gene therapy, reproductive cloning involves the transfer of genetic material to affect the genotype,[118] and sometimes the phenotype,[119] of a human

---

[110]The list of protocols can be obtained at http://www4.od.nih.gov/oba/rac/PROTOCOL.pdf.

[111]*See* NAT'L INST. HEALTH, *supra* note 93, § IV-D (stating individuals and other entities not covered by NIH Guidelines are encouraged though not required to follow established standards).

[112]Rainsbury, *supra* note 108, at 590.

[113]Office of Recombinant DNA Activities, 62 Fed. Reg. 44,386 (Aug. 20, 1997) (notice of conference).

[114]*See* Jennifer Couzin, *RAC Confronts in Utero Gene Therapy Proposals*, 282 SCIENCE 27 (1998) (mentioning meeting in which RAC discussed protocols for in utero gene therapy); Recombinant DNA Research: Proposed Actions Under the Guidelines, 60 Fed. Reg. 57,528, 57,530 (Nov. 15, 1995) (announcing presentation on issues associated with use of in utero gene therapy).

[115]*See* NAT'L INST. HEALTH, *supra* note 93, at app. M.

[116]Telephone interview with Dr. Philip Noguchi, Director, Division of Cellular and Gene Therapies (Nov. 18, 2003).

[117]*See, e.g.*, Merrill & Javitt, *supra* note 97, at 322, 328 (stating that FDA and NIH recognize RAC's role in providing public forum for discussion of social and ethical issues raised by gene therapy).

[118]*See* EBERHARD PASSARGE, COLOR ATLAS OF GENETICS 387 (Mary Fetter Passarge & Eberhard Passarge trans., Thieme ed., 1995) (defining genotype as "all or a particular part of the genetic constitution of an individual or a cell").

[119]*See id.* (defining phenotype as "the observable effect of one or more genes on an individual or a cell").

being.[120] Just as gene therapy involves the transfer of human genetic material using either a viral vector or a genetically modified cell, cloning involves the transfer of genetic material by inserting a nucleus from another person's somatic cell.[121] Furthermore, just as the article subject to FDA regulation in gene therapy is the genetic material and the vector used to introduce it, the article in cloning can be thought of as the nucleus and the genetic material contained therein.

However, rather than being a partial modification to an existing genome, cloning replaces the genome entirely.[122] Indeed, because cloning affects both the somatic and germ cells of the future person, it can conceptually be thought of as both somatic and germline gene therapy. This is because the transferred nucleus contains the entire genetic makeup of the future individual, and this genetic information can be transmitted to subsequent offspring of that future person through his or her reproductive cells.

Cloning also raises safety concerns similar to those raised by gene therapy—and in particular by germline gene therapy.[123] Like gene therapy, potential harms from cloning may be experienced by the recipient of the DNA, and also potentially by future individuals when the transferred DNA is transmitted to future generations. Furthermore, these harms may also arise from the manner in which the imported DNA expresses itself in its new environment.

It might be argued that cloning, for the most part, has not been construed as a *therapeutic* procedure, that is, as a means to cure or prevent illness, and therefore cloning is not an appropriate candidate for FDA regulation. While it is true that cloning could be used as a means to avoid illness, such as parents using cloning as a way to avoid passing on genetic defects, it is unlikely that this would be the only, or even primary, motivation. Even if the technique were first limited to this circumstance, its uses would likely expand once the technique was proven successful. Nevertheless, a therapeutic or preventive intent is not a prerequisite to FDA regulation. The FD&C Act defines drugs, including biological products, to include both therapeutic products and those that "affect the structure or function of the body."[124] Undoubtedly, the transfer of a nucleus affects both the structure and function of the future individual. Moreover, the harms that have been posited with respect to human cloning will be experienced primarily, and perhaps entirely, by this future person.

A more difficult question, and one that will be explored in the following Part, is whether the FDA's jurisdiction extends to articles whose sole intended

---

[120]*See supra* notes 10–14 and accompanying text.

[121]*See id.*

[122]*See id.*

[123]*See* Joe Cummins & Mae-Wan Ho, *First GM Humans Already Created*, INST. SCI. SOC'Y (May 2, 2001), *available at* http://www.isis.org.uk/first_gm_humans.php (noting that germline therapy essentially changes human gene pool which impacts human progeny).

[124]21 U.S.C. § 321(g)(1)(C) (2000).

effect will be experienced by future persons. Whereas most products are intended to exert their effect on a currently living person, the technique of cloning takes place in an egg cell, and is intended to dictate the genome of a future person. Even germline gene therapy, as currently conceived, is intended to affect both a currently living person and any subsequent offspring of that person. By contrast, cloning affects the genetic makeup of only the future person and any offspring of that individual.

The FDA's assertion of jurisdiction over cloning, therefore, must of necessity presume the FDA's ability to regulate articles that are intended to affect future persons. The following Part argues that, while the FDA's jurisdiction has not typically been construed in this manner, there is ample precedent that establishes the FDA's ability to assert jurisdiction on behalf of future persons.

## V. FDA JURISDICTION TO REGULATE ON BEHALF OF FUTURE PERSONS

### *A. Thalidomide and the Kefauver-Harris Amendments of 1962*

The FD&C Act[125] has been amended eighty-eight times since its enactment in 1938.[126] As initially enacted, the FD&C Act was fairly modest in scope. The Kefauver-Harris Amendments of 1962, however, radically transformed the FDA's authority over drugs and arguably gave rise to the modern clinical trial.[127] These amendments changed what had been a system of pre-market notification to one of pre-market approval. Under the former system, a drug manufacturer merely had to notify the FDA of its intention to market a new drug, and could go forward unless the FDA disapproved the NDA within a limited time period after filing.[128] In contrast, pre-market approval prohibits the manufacturer from marketing the product unless the FDA has granted approval,[129] and the statute specifies that the FDA must respond to an application within 180 days.[130] Furthermore, the amendments required that the manufacturer submit evidence demonstrating both the safety

---

[125]21 U.S.C. §§ 301–397 (2000).

[126]E-mail from Suzanne Junod, FDA History Office, to Gail H. Javitt (Oct. 10, 2003) (on file with author).

[127]*See, e.g.*, Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1766–67 (1996) [hereinafter Merrill, *The Architecture of Government Regulation of Medical Products*] (asserting that 1962 amendments reversed burden of proof, making FDA responsible for judging "whether new drugs worked" and thus "transformed the way in which drugs are developed, tested, and marketed").

[128]Joel E. Hoffman, *Administrative Procedures of the Food & Drug Administration*, *in* FUNDAMENTALS OF LAW AND REGULATION 13, 23 (David G. Adams et al. eds., 1997).

[129]21 U.S.C. § 355(a).

[130]*Id.* § 355(c).

and the effectiveness of the new drug.[131] For the first time, the amendments established concrete standards of evidence for new drug approval. As amended, the statute provides that the NDA must contain "substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof."[132] The statute defines "substantial evidence" as:

> [E]vidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.[133]

While bills to amend the FD&C Act to expand FDA authority had been circulating in Congress following its passage in 1938,[134] it was a tragedy of massive proportions that spurred Congress to substantially amend the law. That tragedy was brought about by the drug thalidomide. Thalidomide was introduced in the late 1950s by the German firm Chemie Grunenthal, and was widely marketed as a sedative in Western Europe, England, Canada, Brazil, Japan, and other countries.[135] However, when given to pregnant women early in pregnancy, it caused a severe developmental defect known as phocomelia—a condition wherein the limbs are shortened or nonexistent, and the hands and feet are attached close to the body.[136] At the time Congress was considering the 1962 amendments, it was estimated that 3500 to 5000 malformed babies had been born as a result of prenatal exposure to the drug.[137]

The American company Wm. S. Merrell filed an application with the FDA in 1960 to market the drug under the trade name Kevadon.[138] The indication for which the company sought approval from the FDA was reduction of nausea associated with pregnancy.[139] At that time, the evidence demonstrating limb defects had not yet been reported. However, other safety

---

[131]21 U.S.C. § 355(b)(1)(A); Merrill, *The Architecture of Government Regulation of Medical Products*, *supra* note 127, at 1764–65.

[132]21 U.S.C. § 355(d)(5).

[133]*Id.* § 355(d).

[134]Food and Drug Administration, Dep't of Health and Human Servs., *The Story of the Laws Behind the Labels*, *available at* http://vm.cfsan.fda.gov/~lrd/histor1a.html (relating preventative amendments enacted between 1938 Act and 1960) (last updated Apr. 6, 1999).

[135]S. REP. NO. 87-1744, at 40 (1962), *reprinted in* 1962 U.S.C.C.A.N. 2884, 2905.

[136]*Id.*

[137]*Id.*

[138]*Id.* at 2906.

[139]*Id.*

concerns kept the FDA from approving the application.[140] Ultimately the company withdrew the application after reports emerged linking the product to birth defects.[141] Because the drug was not approved, only seventeen "thalidomide babies" were born in the United States. The mothers of these babies had either obtained the drug overseas, through doctor's samples, or through clinical trials.[142]

Legislative history clearly evidences Congress' concern with the near miss of thalidomide.[143] Congress sought to "give physicians of the FDA adequate time to appraise the safety and effectiveness of drugs,"[144] without what was, in essence, ad hoc agency stalling of the company's application for approval.[145]

Though not expressly mentioned during congressional consideration of the 1962 amendments, perhaps because it was so obvious to the legislators, the underlying assumption was that the FDA's jurisdiction extended to review of product safety relative to persons other than the intended recipients. There is no suggestion in the medical annals or in the legislative history that thalidomide was unsafe for the women who ingested it or that it was ineffective in aiding sleep and relieving nausea. The reason for its demise had nothing to do with its lack of safety or effectiveness for the intended recipients and everything to do with its devastating effects on third parties, that is, the developing fetuses, who were inextricably linked to a subset of intended recipients (i.e., pregnant women). This devastating impact was sufficient to warrant the FDA's prohibition of the drug in the marketplace, and was the driving force behind strengthening the FDA's regulatory oversight of drugs.[146] Thus, at least as far back as 1962, there has been a tacit presumption that the FDA's regulatory jurisdiction over articles intended "for use in man" includes

---

[140]*Id.*

[141]*Id.* at 2907.

[142]FRANCIS FUKUYAMA, OUR POSTHUMAN FUTURE 201 (2002); Cori Vanchieri, *Preparing for Thalidomide's Comeback*, 127 ANNALS OF INTERNAL MED. (Nov. 15, 1997), *at* http://www.acponline.org/journals/annals/15nov1997/currthal.htm.

[143]1962 U.S.C.C.A.N. at 2907–08.

[144]*Id.* at 2905.

[145]*Id.* at 2908.

[146]In recent years, thalidomide has made a comeback of sorts as evidence increases that it may be effective in treating a variety of serious diseases such as AIDS, cancer, and leprosy. *See* Michael Kranish, *New Use is Found for Thalidomide: Fighting Cancer*, BOSTON GLOBE, Oct. 20, 2002, at A28 (describing FDA grant of permission to company for use of thalidomide to treat leprosy patients, subject to safeguards to ensure use of birth control among those treated); Herbert Burkholz, U.S. Food & Drug Admin., *Giving Thalidomide a Second Chance*, *available at* http://www.fda.gov/fdac/features/1997/697_thal.html (listing warnings given to women participating in thalidomide clinical trials). In 1998, the FDA approved the drug for treatment of Hansen's disease (leprosy) but placed stringent labeling and monitoring requirements on the manufacturer. *FDA Moves Closer to Approving Thalidomide* (Sept. 22, 1997), *available at* http://www.cnn.com/HEALTH/9709/22/thalidomide/index.html (anticipating approval for treatment of leprosy but only under extremely tight restrictions).

both current and future persons, and that its mandate extends to protecting the safety of future persons who may be exposed to a regulated product, even when they are not the intended recipient of that product.

Several of the FDA's regulatory actions since 1962 similarly rely on this presumption. Some of these examples are reviewed briefly below. That the FDA has undertaken these actions does not, of course, prove that it can legally do so, but does provide evidence that the presumption has become an entrenched facet of the FDA landscape, and one that has never been challenged.

### *B. Pregnancy Labeling Requirements*

The FD&C Act requires that all drugs be accompanied by labeling that summarizes essential scientific information needed for their safe and effective use.[147] FDA regulations, first promulgated in 1979, provide that:

> [U]nless a drug is not absorbed systemically and is not known to have a potential for indirect harm to a fetus, its labeling must include a "Pregnancy subsection" containing information on the drug's teratogenic effects and other effects on reproduction and pregnancy, and, when relevant, effects on later growth, development, and functional maturation of the child.[148]

The regulation also requires that each product be classified under one of five pregnancy categories (A, B, C, D, or X) on the basis of risk of reproductive and developmental adverse effects or, for certain categories, on the basis of such risk weighed against potential benefit.[149] A drug's pregnancy category is identified at the beginning of its pregnancy labeling subsection.[150]

Information on possible teratogenicity, while no doubt important, cannot be considered necessary for the "safe and effective" use of the drug, if safety and effectiveness is construed to apply only to the individual for whom the drug is intended. While the FDA has sometimes articulated the justification for requiring such labeling as providing the physician with information necessary to make treatment decisions for pregnant women, such an explanation begs the question. The information is not needed to assure the safe and effective use in the woman, but to avoid harm to the fetus. While such information may affect a woman's willingness to take the drug, it is not needed to assure safe and effective use in the woman once administered. This leads to one of two possible conclusions: (1) the fetus is so integrally connected to the woman that something unsafe to the fetus is per se unsafe to the mother, or (2) the FDA

---

[147] 21 U.S.C. § 352(f) (2000).
[148] 21 C.F.R. § 201.57(f)(6) (2003).
[149] *Id.*
[150] *Id.*

considers the safety of the drug to the unintended recipient, who may experience an injury that is manifested following birth, to be relevant to the overall safety and effectiveness of the drug. While some have argued, for example, in the context of a woman's right to choose abortion, that the fetus is part of the woman,[151] such an argument does not lead to the conclusion that harm (such as genetic damage) to the fetus automatically causes a physical injury to the mother. Thus, the second possible conclusion is more logical, whereby the FDA takes into account harm to unavoidable yet unintended recipients when evaluating a drug's safety and effectiveness.

### *C. Regulation of Devices Used in In Vitro Fertilization*

The FD&C Act establishes FDA jurisdiction over medical devices. A medical device is defined as an article "intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease"[152] or "[an article] intended to affect the structure or any function of the body" and "which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes."[153]

Among other products, the FDA classifies as medical devices "instrumentation intended for use in in vitro fertilization (IVF) and related assisted reproduction technology (ART) procedures, including but not limited to gamete intrafallopian transfer (GIFT), embryo transfer (ET), and intracytoplasmic sperm injection (ICSI)."[154] Specific instrumentation regulated by the FDA includes: "(1) needles; (2) catheters; (3) accessories; (4) microtools; (5) micropipette fabrication instruments; (6) micromanipulators and microinjectors; (7) labware; (8) water and water purification systems; and (9) reproductive media and supplements."[155]

---

[151]*See, e.g.*, Connecticut v. Sandoval, 821 A.2d 247, 267 (Conn. 2003) (upholding defendant's conviction on count of first-degree assault for secretly inserting labor-inducing drugs into his pregnant girlfriend to cause miscarriage, on basis that fetus is part of mother's body and therefore can be subject to assault); Kayhan Parsi, *Metaphorical Imagination: The Moral and Legal Status of Fetuses and Embryos*, 2 DEPAUL J. HEALTH CARE L. 703, 709, 718–28 (1999) (discussing metaphor of fetus as appendage, in which "the nonviable fetus is little more than a form of the pregnant woman's bodily tissue: it is part of the woman without separate identity or status." This metaphor was used in cases from the late nineteenth and early twentieth centuries to deny fetus standing to sue separately from mother for negligently inflicted prenatal injuries because fetus was viewed as part of mother.).

[152]21 U.S.C. § 321(h)(2) (2000).

[153]*Id.* § 321(h)(3).

[154]Reclassification and Classification of Medical Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures, 63 Fed. Reg. 48,428, 48,428 (Sept. 10, 1998).

[155]Reclassification of Medical Devices Used for In Vitro Fertilization and Related Assisted Reproductive Procedures, 62 Fed. Reg. 46,686, 46,687 (proposed Sept. 4, 1997).

Medical devices may be subject to both pre-market review and post-marketing requirements. The types of requirements to which a device, including those used in ART, will be subject depends on its classification. The FDA classifies medical devices into Class I, Class II, or Class III, depending on the degree of risk posed by the device.[156] Class I devices are those for which "general controls" (e.g., prohibitions against misbranding or adulteration) are sufficient to provide reasonable assurance of the safety and effectiveness of the device.[157] Class II involves devices for which "special controls" (e.g., performance standards, post-market surveillance) are required in order to provide reasonable assurance of safety and effectiveness.[158] Finally, Class III devices are those for which insufficient information exists to demonstrate that general or special controls will provide reasonable assurance of safety and effectiveness.[159] Additionally, such devices purport to be life supporting and of substantial importance in preventing impairment to health, or otherwise present an unreasonable risk of injury or illness.[160]

Any device that has not previously been marketed in the United States, regardless of classification, is considered a Class III device and the manufacturer must file a pre-market approval application ("PMA").[161] Like the NDA, the PMA must contain data from clinical trials demonstrating the safety and effectiveness of the device.[162] However, if the device is "substantially equivalent" to a device in commercial distribution in the United States prior to May 28, 1976, a PMA is not required.[163] Proponents of devices that meet the requirements for substantial equivalence do not need to submit a PMA or conduct clinical safety and effectiveness trials, but rather need only submit data demonstrating their substantial equivalence to the previously marketed device.[164] This latter process, termed a "510(k) application," is significantly faster and less expensive, and is used for the majority of devices currently on the market.[165]

Devices specifically intended for IVF and embryo transfer were not developed until after 1976.[166] The FDA initially classified such devices as

---

[156]21 U.S.C. § 360(c)(a).

[157]*Id.* § 360(c)(a)(1)(A)(i).

[158]*Id.* § 360(c)(a)(1)(B).

[159]*Id.* § 360(c)(a)(1)(C).

[160]*Id.*

[161]*Id. See* Howard M. Holstein & Edward C. Wilson, *Developments in Medical Device Regulation, in* 2 FUNDAMENTALS OF LAW AND REGULATION 275–76 (David G. Adams et al. eds., 1997).

[162]21 U.S.C. § 360(c)(a)(3)(A), (k).

[163]21 U.S.C. § 360(f), (i).

[164]21 U.S.C. § 360(k); 1 C.F.R. 807.81, .87. *See* Holstein & Wilson, *supra* note 161, at 275–77 (explaining 510(k) process).

[165]Benjamin A. Goldberger, *The Evolution of Substantial Equivalence in FDA's Premarket Review of Medical Devices*, 56 FOOD DRUG L.J. 317, 318, 323 (2001).

[166]Reclassification of Medical Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures, *supra* note 155.

Class III, and rejected claims that they were "substantially equivalent" to pre-1976 devices.[167] According to the FDA, use of such instruments for IVF constituted a new indication and therefore a PMA was required.[168]

In 1988, the FDA convened an expert advisory panel to assist the agency in devising a regulatory strategy for these devices and to determine what data would be required to evaluate their safety and effectiveness.[169] In assessing the appropriate classification, the panel reviewed both risks to the woman undergoing the procedure and to the gametes or embryo:

> Gamete or embryo damage could occur which would render them viable but damaged, or nonviable. This could occur with the knowledge of the gynecologist, so that affected gametes or embryos would not be used in the procedures, or without the knowledge of the gynecologist, in which case damaged or nonviable gametes or embryos could be used in assisted reproductive procedures. This could result in cycles lost or potential development of damaged embryos, which may result in later loss of pregnancy or congenital defects.[170]

The panel concluded that reclassification could take place if "certain recognized testing, specifications, and/or labeling requirements were imposed."[171] In September 1998, the FDA reclassified some of these instruments from Class III to Class II. The FDA's basis for this reclassification was its conclusion that the devices at issue had a long and well-established history of safe and effective use.[172] Those devices that did not have such a history remained regulated as Class III devices.

Like the thalidomide example, the FDA's regulation of IVF/ART-related devices demonstrates the agency's concern not only for the current patient upon whom the devices will be used, but also for the future person that may result from the procedures. The agency's analysis of the appropriate degree of regulatory oversight takes into account both potential risks to the woman and potential harms to the gamete or embryo that may result in injuries to a future person.

---

[167] *Id.*
[168] *Id.*
[169] *Id.*
[170] *Id.* at 46,689.
[171] *Id.* at 46,687.
[172] Obstetric and Gynecologic Devices; Reclassification of Medical Devices Used for In Vitro Fertilization and Related Assisted Reproduction Procedures, 63 Fed. Reg. 48,428, 48,428–29 (Sept. 10, 1998) (codified at 21 C.F.R. §§ 884.6100–.6190) (final rule).

### *D. Ooplasm Transfer*

In 2001, scientists at a medical institution in New Jersey announced that they had assisted in producing babies through a process known as ooplasm transfer.[173] Ooplasm transfer involves the insertion of ooplasm[174] from a healthy donor egg (the ooplasm) into an egg from a woman with infertility problems. While the nuclear genetic material contained in the healthy egg is not transferred, the ooplasm that is transferred contains mitochondria,[175] cellular structures containing a few genes that provide the energy for the cell.[176] The resulting egg contains mitochondria from both the ooplasm donor and the recipient egg.[177] For this reason, the researchers presented it as the "first case of human germ line genetic modification."[178] Investigators theorize that the transferred mitochondria may help restore normal growth in developmentally compromised oocytes and thereby improve IVF outcomes, although they do not know the mechanism by which this may occur.[179] The babies born following this procedure have three genetic parents, since they carry mitochondrial DNA from the ooplasm donor and the egg donor (the mother), and nuclear DNA from the mother and the father.[180]

In July 2001, the FDA sent a letter to researchers advising them that the FDA "has jurisdiction over human cells used in therapy involving the transfer of genetic material by means other than the union of gamete nuclei," including ooplasm transfer, since it involves the transfer of mitochondrial DNA.[181] The letter stated that ooplasm transfer constitutes a clinical investigation requiring the submission of an IND to the FDA before the procedure is allowed in human beings.[182] Since the FDA has significant concerns about the use of

---

[173]*See* Jason Barritt et al., *Mitochondria in Human Offspring Derived from Ooplasmic Transplantation*, 16 HUM. REPROD. 513, 513 (2001) ("Ooplasmic transfer from fertile donor oocytes into developmentally compromised oocytes from patients with recurrent implantation failure has led to the birth of 15 healthy babies."); *see also* Eric Parens & Eric Juengst, *Inadvertently Crossing the Germ Line*, 242 SCIENCE 397, 397 (2001) (editorializing that though use of ooplasm in recent experiment achieved admirable therapeutic result, procedure's side effect of germline modification crossed line that RAC thought "too important to cross inadvertently" and should have been subject of public discussion first); Gina Kolata, *Babies in Fertility Method Have Genes From 3 People*, N.Y. TIMES, May 5, 2001, at A11 (noting birth of fifteen babies resulting from injection of healthy cytoplasm into eggs of infertile women).

[174]Ooplasm is defined as the cytoplasm of an egg. U.S. Nat'l Library of Med., *Medline Plus Health Information*, *at* http://medlineplus.gov/ (last visited Sept. 19, 2003).

[175]Barritt et al., *supra* note 173, at 515.

[176]Kolata, *supra* note 173.

[177]Barritt et al., *supra* note 173, at 513.

[178]*Id.*

[179]*Id.*

[180]*Id.*

[181]Letter from Kathryn C. Zoon, Ph.D., Director, Center for Biologics Evaluation and Research, Food and Drug Administration, to Sponsors/Donors (July 6, 2001), *at* www.fda.gov/cber/ltr/cytotrans070601.htm.

[182]*Id.*

ooplasm transfer,[183] it is unlikely that such an application would be approved, and the pronouncement has therefore had the effect of halting the use of the procedure. The letter also mentioned cloning, thereby reiterating the FDA's previously announced IND requirement for cloning.[184]

While the letter did not articulate specific safety or effectiveness concerns, others have indicated concern about the dangers of "heteroplasmy," that is, the mixing of ooplasm, and specifically mitochondria, from more than one individual.[185] According to the FDA, "it is clear that stringent mechanisms have evolved to insure homogeneity of mitochondrial genotypes at the initiation of human development. The FDA has concerns about the safety of perturbing this process."[186] Moreover, ooplasm transfer "changes the genetic makeup of the resulting offspring. Appropriate follow-up of children born after ooplasm transfer and their progeny must therefore be considered carefully."[187] The FDA has stated its belief that "further public discussion is necessary to: 1) evaluate the potential risks of this procedure, 2) recommend how safety should be monitored, [and] 3) assess how efficacy might best be determined . . . ."[188]

Since ooplasm transfer occurs outside the body, the actual transfer poses no risk to the mother. While in theory the heteroplasmic embryo could pose harm to the mother once implanted, it is clear from the FDA's discussions of the procedure that a significant, if not the primary, concern relates to the effect on the children born as a result of the procedure. Thus the FDA must, necessarily, be interpreting its jurisdiction to include oversight of these future individuals.

The above examples all demonstrate that the FDA has historically viewed its jurisdiction to include future persons who are intentionally or foreseeably exposed to FDA-regulated products. The FDA's regulation of reproductive cloning would be consistent with this view. Reproductive cloning, like ooplasm transfer, is a form of gene therapy, indeed, of *genome* therapy, since it transfers an entire genome to influence the genetic makeup of a future person. As such, it has the ultimate effect on the structure or function of that future person's body. Like its concerns with the teratogenic effects of drugs, IVF/ART devices, and ooplasm transfer, the FDA's concerns with this technique relate to the impact of the genome transfer on future persons.

---

[183]Biologics Response Modifiers Advisory Comm., *Briefing Document for Day 1, May 9, 2002; Ooplasm transfer as method to treat female infertility* 4, *at* http://www.fda.gov/OHRMS/DOCKETS/ac/02/briefing/3855B1_01.pdf.

[184]Letter from Kathryn C. Zoon, *supra* note 181.

[185]*See* James M. Cummins, *Mitochondria: Potential Roles in Embryogenesis and Nucleocytoplasmic Transfer*, 7 HUM. REPROD. UPDATE 217, 217–24 (2001) (discussing "risk [of] complex and unpredictable outcomes emerging from disharmonious nuclear-cytoplasmic interactions"); Biologics Response Modifiers Advisory Comm., *supra* note 183, at 3–4.

[186]Biologics Response Modifiers Advisory Comm., *supra* note 183, at 4.

[187]*Id.*

[188]*Id.*

### *E. Implications for the "Beginnings of Life" Debate*

It might be argued that, in order for the FDA to regulate cloning under the theory outlined above, the agency must, at least implicitly, take the position that the embryo created through cloning constitutes a human being. Such an assertion would of course be consistent with the views of those who, for religious or other reasons, believe that embryos have the moral status of a person.[189] However, for those who do not share this view, and who, moreover, fear that this view could lead to the restriction of reproductive rights for women,[190] the FDA's need to conclude that an embryo is a human being as a basis for regulation would be a powerful disincentive to permitting the FDA's regulation.

The FDA's jurisdiction to regulate cloning as a form of gene therapy does not, however, require the conclusion that the embryo or fetus is a living human being prior to being born; indeed, it need not change the terms of the "beginnings of life" debate at all. This is because, regardless of one's position on the beginnings of human life, there is a basis for concluding that the FDA has jurisdiction to regulate for the benefit of future persons when the intervention is one made to protect an intended or unintended recipient. Thus the person on whose behalf the FDA is regulating pursuant to the cloning procedure is not the embryo. Rather, it is the person who is intended to be or may be expected to be born as a result of that procedure.[191] The FDA's regulatory hook is not that the embryo or fetus is a life. Rather, it is that, whatever one's opinion on that issue, the transfer of the genome will alter the structure or function of the person who is born as a result of the procedure.

---

[189]*See, e.g.*, Sacred Congregation for the Doctrine of the Faith, Ctr. for Bioethics and Human Dignity, *The Gift of Life (Donum Vitae)* (Nov. 19, 2001), *at* http://www.usccb.org/prolife/tdocs/donumvitae.htm ("From the moment of conception, the life of every human being is to be respected in an absolute way."); Francis J. Beckwith, *Abortion, Bioethics and Personhood: A Philosophical Reflection*, Ctr. for Bioethics and Human Dignity (Nov. 19, 2001), *at* http://www.cbhd.org/resources/bioethics/beckwith_2001-11-19.htm ("[B]ecause the functions of personhood are grounded in the essential nature of humanness, and because human beings are persons that maintain identity through time from the moment they come into existence, it follows that the unborn are human persons of great worth because they possess that nature as long as they exist.").

[190]Kristen Philipkoski, *Cloning Bill Bans Abortion Too?*, WIRED NEWS, May 30, 2002, *at* http://www.wired.com/news/print/0,1294,52838,00.html (reporting concern by some that legislation banning cloning will give greater protection to clonal embryos than to sexually produced embryos, thereby weakening protections for abortion).

[191]Nor does the FDA's jurisdiction to regulate on behalf of future persons mean that the agency is bound to consider only the well-being of the future person in the course of its regulatory deliberations. As with any product, the FDA may take into account, as part of its safety and effectiveness calculus, risks to all parties foreseeably affected. In the case of pregnancy in particular, the FDA must consider both the existing person (the gestating woman) and the future person when undertaking safety and effectiveness analyses of new products.

## VI. CONCLUSION

The goal of this Article is modest—to articulate the best argument for the FDA's legal jurisdiction over cloning. The Article argues that the FDA has jurisdiction to regulate cloning as a form of gene therapy. It demonstrates the scientific and regulatory similarities between gene therapy and cloning, and concludes that cloning is the ultimate form of gene therapy, in that it replaces not only one or a few genes but rather the entire genome. Further, the Article provides evidence demonstrating that the FDA has historically viewed its responsibility to assure safety and effectiveness to encompass the evaluation of harms to future persons who are potentially at risk from exposure to FDA-regulated products prior to gestation or birth.

In limiting this Article to this modest objective, the authors are by no means unmindful of the many difficult and complex issues that remain. First, there is the issue of the FDA's arguable failure to articulate its jurisdiction in a manner consistent with administrative law precepts. Moreover, asserting that the FDA can, as a legal matter, regulate cloning leaves to one side the question of whether it should. Calls for caution in this latter arena have come from many quarters, and deserve serious attention.[192] Indeed, cloning raises not only complex scientific challenges but also serious ethical concerns. Even if it were demonstrated to the FDA's satisfaction that cloning is a safe and effective means of producing offspring, the question would still remain whether this technology is "good for society," taking into account the many possible constructions of that word. Some, both inside and outside the agency, have argued that while the FDA is widely regarded as having expertise to evaluate scientific data and to determine whether a product is safe and effective, the agency's mission and staff are not well suited to make judgments concerning the broader social and ethical implications of new technologies and products. Whether the FDA is the appropriate arbiter of the ethical dimensions of new medical technologies, and whether other institutions that exist now, or that could be created in the future, would be more suited to that role, remains an open question that warrants broad public discussion.

---

[192] *See, e.g.*, The President's Council on Bioethics, *supra* note 8; FUKUYAMA, *supra* note 142, at 212–16; Merrill & Rose, *supra* note 4, at 133–39. *See also* Elizabeth C. Price, *Does the FDA Have the Authority to Regulate Human Cloning?*, 11 HARV. J.L. & TECH. 619, 641 (1998) (arguing that Congress did not intend to grant FDA authority to regulate human cloning aimed at producing children).