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The Historical Development of Cloning Technology and the Role of Regulation in Ensuring Responsible Applications

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I. Introduction

On December 27, 2002 a company called Clonaid announced the birth of a cloned human.¹ Clonaid announced the birth of a second child on January 4, 2003.² Clonaid was founded by the leader of a religious sect known as the Raelians. This individual, a French expatriate named Claude Vorilhon, also goes by the name Rael.³ He and his group are probably the most vociferous and well-known advocates of applying cloning technology to human beings.

What motivates the desire to make human clones? Vorilhon, reportedly born out of wedlock, was abandoned by his parents at an early age.⁴ While cloning may be an attractive option for those in similar situations, aversion to the so-called traditional concept of parentage, where one is reared by biological parents, is not the only reason why people might be interested in cloning as a potential reproductive means. Other motivations include the desire to see a clone of oneself grow to adulthood,⁵ the lack of any other reproductive option,⁶ and the need to compensate for the loss of a loved one.⁷

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¹See *The White House Bulletin*, CNN LIVE TODAY, 10:00, December 27, 2002, Transcript # 122702CN.v75.

²See LONDON FREE PRESS, January 5, 2003, at A8.

³See *id.*

⁴See Rick Ross, *The True Story of "little Claudy" Vorilhon, now known as "His Holiness Rael"* (March 2003), at <http://www.rickross.com/reference/raelians/raelians77.html>.

⁵See Richard Dawkins, *What's Wrong With Cloning?*, in CLONES AND CLONES 54-66 (Martha C. Nussbaum and Cass R. Sunstein, eds., 1998).

⁶See *The First Human Cloning Company*, at <http://www.clonaid.com/english/pages/services.html> (last visited May 14, 2003).

⁷*Id.*

Vorilhon and the Raelians, on the other hand, have leached upon a motivation that has tantalized human beings since the dawn of civilization – the desire for immortality.⁸ In the aftermath of the recent cloning debacle that witnessed the announcement of cloned children and subsequent months of hemming and hawing by the Clonaid spokespeople, the pseudo-religious branch of Vorilhon’s activities under the guise of the Raelian religion appears to have backed away from an overt connection to cloning. If the Raelian organizational website is to be used as an indicator of the group’s focus, cloning is no longer the central emphasis of this religion, at least for the moment.⁹ The website information conveys the belief that aliens were originally responsible for life on Earth via DNA seeding.¹⁰ The website also goes so far as to assert that, in a Raelian utopia, biotechnology will be used for the betterment of the human condition, but no specific mention of cloning is made within the pages.¹¹

At the same time, it would seem that a hot-button issue such as human cloning is too attractive of a potential publicity vehicle to abandon altogether, especially for such an attention-hungry organization as the Raelians and, perhaps more precisely, a self-aggrandizing machinator recently characterized in the mainstream scientific community as “charlatans.”¹² Thus, it comes as no surprise that, despite the present dissociation from the primary website text of language related to human cloning, there are still mentions of cloning, such as an advertisement for a book entitled, “Yes to Human Cloning.”¹³ This link from the Raelian homepage leads to a shopping page.¹⁴ The book synopsis reveals the promise of eternal life through cloning and memory transfer. The Raelian group still maintains a vested interest in the exploitative power of human cloning, if

⁸See *Raelian Leader Says Cloning First Step to Immortality*, CNN.COM, December 28, 2002; *Probing Asian Clone Link*, CBSNEWS.COM, January 4, 2003, at <http://www.cbsnews.com/stories/2003/01/03/tech/main535105.shtml> (last visited May 14, 2003) (quoting Vorilhon as saying, “I think it’s a big step for human beings in the future. It will bring us eternal life. That’s the best thing that can happen to humanity. We can not only cure all diseases but also it will give us eternal life”).

⁹See *The Raelian Revolution*, at <http://www.rael.org/english/index.html> (last visited May 14, 2003).

¹⁰See *id.*

¹¹See *id.*

¹²See Gretchen Vogel, *Misguided Chromosomes Foil Primate Cloning*, 300 SCIENCE 226, 227 (2003) (quoting Professor Gerald Schatten as saying, “This reinforces the fact that the charlatans who claim to have cloned humans have never understood enough cell or developmental biology.”).

¹³See *The Raelian Revolution*, at <http://www.rael.org/english/index.html> (last visited May 14, 2003).

¹⁴See *id.*

not so much in the actual benefits.

A brief visit to the website of Clonaid, another one of Verhilon's endeavors, verifies this conclusion. Here, the company bills itself as "The First Human Cloning Company."¹⁵ The company has been described as the "scientific arm" of the Raelians.¹⁶ Among the services offered for sale are Insuraclone, Ovulaid, and Clonapet. Insuraclone offers to preserve a client's cells in a cryogenic state, the idea being that, in the event of future advances in biotechnology, healthy cells could be used to address various medical problems. Ovulaid targets infertile women seeking to purchase eggs for the purpose of conceiving a child. The precise mechanism of conception is not entirely clear from the website's description. On the one hand, one would think that Clonaid would be trying to sell the ability to make one's own clone. A reading of the text under Ovulaid, however, gives one the impression that the point here is to try to sell the clone of a different person. The product description reads that customers will have the option of "choosing their future babies from a catalog showing the pictures of the donor egg women..."¹⁷ One cannot help but wonder whether Clonaid is purposefully confusing the distinction between an egg donor and a donor of genetic material, since, under the current understanding of cloning technology, these are two separate categories. Of course, for a company integrally associated with a cult of flying saucers and little extraterrestrial founder beings, it is not difficult to imagine a fast and loose treatment of scientific understandings.

What makes the Raelians and more particularly Clonaid alarming, however, is not the tendency to turn away from science fact and embrace science fiction when convenient. Rather, the cause for elevated attention arises from the potential for this group to undertake genuine scientific endeavors. The technology required to undertake cloning attempts, while specialized and expensive, is not inaccessible.¹⁸ A brief examination of

¹⁵See *The First Human Cloning Company*, at <http://www.clonaid.com/english/pages/home.html> (last visited May 14, 2003).

¹⁶See Press Release, Cult's human 'cloning machine' goes on display at the Science Museum (Jan. 22, 2003), *available at* http://www.sciencemuseum.org.uk/corporate_commercial/press/ShowPressRelease.asp?Show=166 (last visited May 14, 2003).

¹⁷See *The First Human Cloning Company*, at <http://www.clonaid.com/english/pages/services.html> (last visited May 14, 2003).

¹⁸For instance, one can go onto the Internet and find lists of vendors for the most delicate and expensive instrument required, the microinjector apparatus. See *ISC Buyers' Guide – Microinjection Apparatus*, at

the Clonaid website reveals that the company has at least a partial complement of the equipment needed to carry out cloning attempts.¹⁹ Furthermore, several species of mammals have already been successfully cloned. Cloning has been achieved in sheep, mice, cows, and other mammals. However, these attempts have typically experienced failure rates of 97%.²⁰ The unsuccessful attempts result in death during pregnancy and even at birth, accompanied by physical abnormalities.²¹ If for no other reason than safety and the need to prevent biological mishaps, any attempts to clone humans must now be stopped.

At the same time, it would be a fruitless and wasteful expenditure of resources to impose a ban on the technology that has made human cloning almost feasible. In examining the justifications for this statement, this paper will trace the history of advances in cloning technology and the motivations for making these advances. For the most part, human cloning was not an end, or even a consideration, for early researchers who made the key discoveries; rather, the focus was upon cloning animals for commercial or scientific purposes. As a result, this research was not heavily scrutinized by the public and the regulatory community until relatively late in the discovery process.

II. The History of Cloning Technology

A. From Frog Eggs to Farm Animals

The beginnings of cloning research trace back to the first studies in embryology, when scientists studied frog

<http://www.iscpubs.com/bg/us/prod/prod1939.html> (last visited May 14, 2003)

¹⁹See The First Human Cloning Company, at <http://www.clonaid.com/english/pages/products.html> (last visited May 14, 2003); Promotional Video, *id.* at <http://www.clonaid.com/common.ressources/video/promo.ram> (last visited May 14, 2003).

²⁰See Anne McLaren, *Cloning: Pathways to a Pluripotent Future*, 288 *SCIENCE* 1775, 1779 (2000).

²¹*Id.*

eggs to determine developmental processes. The reasons for using amphibian eggs instead of mammalian ones were eminently practical. A frog's egg measures approximately 2 millimeters in diameter, which, although small, is nonetheless visible to the naked eye.²² On the other hand, a human egg is considerably smaller – at 100 micrometers, measuring approximately 5-10% of the diameter of the frog egg.²³ The early stages of frog development take place outside of the parents' bodies. This made it possible for the developmental cycle to be observed under laboratory conditions, with a microscope. A further advantage of studying frog was that they produce an abundant number of eggs. One frog produces up to thousands of eggs at a time.²⁴ For the early scientists studying embryology, studying frog development was simply the only practical choice.

In 1938, Hans Spemann proposed a cloning experiment.²⁵ Spemann, who had performed several notable experiments with salamander embryos, had become fascinated with the potential of taking a nucleus from a developed organism and transplanting it into an egg cell to see whether a normal embryo would develop.²⁶ During the course of his career, Spemann was the first person to demonstrate definitively that an organism at the two-celled stage could be divided into two single-celled entities, and that each of those cells would develop into an individual organism.²⁷ The method by which Spemann accomplished this was nothing short of ingenious. Like many scientific breakthroughs, Spemann's methodology was refreshingly elegant. Spemann used a very fine thread of hair and, under a microscope, wrapped the thread around a salamander embryo that was at the two-cell stage. The cells split into two individual cells, and each of those cells developed into a viable salamander. Spemann, however, did not figure out an effective way to transfer a nucleus from

²² See "Evolution of Cells," Biology 255, Miami University, at http://www.bio.miami.edu/tom/bil255/bil255goods/01_cells.html (updated Aug. 26, 2002).

²³ See Sizes of Things, Biological Sciences 101, University of Nebraska, at <http://niko.unl.edu/bs101/notes/sizes.html> (last visited May 14, 2003).

²⁴ See GINA KOLATA, CLONE: THE ROAD TO DOLLY, AND THE PATH AHEAD 44 (1998).

²⁵ See McLaren, *supra* note 20, at 1777.

²⁶ See *id.*

²⁷ See KOLATA, *supra* note 24, at.

one cell into an egg cell. With respect to cloning, his historical role was to propose the basic idea. Other scientists, in Spemann's tradition, devised clever ways to carry out his conceptual imaginings.

The first cloning experiments in frogs were performed in 1950 by Robert Briggs and Thomas J. King.²⁸ The types of cells used were not from fully grown frogs, but rather blastula cells. These blastulas contained approximately 10,000 cells overall, and while they were not as far along in development as the adult frog, differentiation of the cells had already begun.²⁹ In other words, the embryo at this point had already advanced to the stage such that each individual cell could not, if separated from the rest of the embryo, give rise to another organism.

Conceptually, the frog embryo experiment was straightforward. The nucleus of an unfertilized egg cell was removed using a glass pipette having a much smaller diameter than that of the egg cell. Next, the nucleus of a blastocyst cell was transferred into the egg. The overall blueprint followed the plan that Spemann had laid out some dozen years earlier. However, Briggs and King still had to contend with the major obstacle confronting Spemann, that is, how to remove from a cell a nucleus, without destroying that nucleus.³⁰

The techniques employed by the first experimenters in retrieving the nucleus which contained the full complement of genetic information for the clone are quite similar to the ones used by modern day researchers. The underlying idea is that the nucleus lies within the cell and needs to be taken out of the cell. What Briggs and King did was to take a glass pipette with a very small diameter, smaller than that of the blastula

²⁸See *id.* at 63.

²⁹See *id.*

³⁰See McLaren, *supra* note 20, at 1778.

cell.³¹ Next, that pipette was used to suction up the cell, akin to how one would use a straw to suction up a small ice cube. The vacuum pressure exerted upon the wall of the cell caused the cell membrane, the outside layer of the cell, to burst open. At this point, the pipette was used to collect the cell nucleus, located in its own compartmentalized unit.³² Of course, for the pipette to do this, its diameter was necessarily wider than that of the nucleus. By using a pipette with these specifications – a diameter greater than that of the nucleus but less than that of the cell membrane – Briggs and King were able to do what Spemann could only conceptualize. Since then, scientists have been able to retrieve the nuclei of various types of cells for cloning experiments.

Those early frog embryo experiments, using nuclei obtained from early-stage blastula cells, ultimately proved successful. Of the 197 blastula nuclei transferred to frog eggs, 27 developed into tadpoles.³³ However, the true efficacy of this technique in cloning fully grown frogs had yet to be proven. Blastula cells, though no longer totipotent stem cells,³⁴ are nonetheless found considerably earlier in development than are the cells from a fully grown adult organism. The research of Briggs and King, although cause for optimism, was still only the beginning of attempts to clone organism from fully differentiated adult cells.

This message became all the more clear when researchers following up on the work encountered difficulties when attempting to use the same cloning techniques on more fully developed cells. To be sure, not all of the subsequent experiments yielded negative results. For instance, researchers were able to repeat the

³¹ See KOLATA, *supra* note 24, at 64.

³² See *id.*

³³ See *id.* at 65

³⁴ Totipotent stem cells are defined as:

Stem cells which are capable of forming every type of body cell. Each totipotent cell could replicate and differentiate and become a human being. All cells within the early embryo are totipotent up until the 16 cell stage or so.

See General Term: Totipotent Stem Cells, at <http://www.counterbalance.net/biogloss/totistem-body.html> (last visited May 14, 2003).

experiments on different frog species,³⁵ a result that lent support to the biological universality of the ability to clone from blastula cells. Still, the researchers were not demonstrating the results in non-amphibians, and so making broader generalizations proved to be a tenuous proposition at best. More importantly, the efforts to apply the methods to cells that were further along the developmental chain yielded sobering results. The upshot of this body of findings was that, the further along in development of the organism from which the genetic material was transferred, the less likely the chances of producing viable clones.

By the end of the 1960s, progress on the advancement of cloning technology in frogs had slowed down considerably. It was generally conceded that the nuclei from differentiated frog embryo cells at an early stage such as the blastula could be transferred to enucleated egg cell to produce viable organisms. These organisms could advance to the tadpole stage, certainly, and probably develop further to the fully grown adult frog.³⁶ However, with respect to using nuclei from a fully grown adult frog, the furthest that cloning experiments could get were organisms that developed to the tadpole stage.³⁷ No one was able to produce experimental results in which fully differentiated cell nuclei, taken from adult cells, could be used to generate fully grown frogs. At this point did the state of cloning advancement remain for the next few decades. Understandably, regulation of the research was not stringent at this point, as it was confined to frogs, although the publication of a photograph of 30 cloned frogs in 1977 did cause a bit of a public stir.³⁸

B. From Frogs to Mice

The science of cloning from adult cells did not witness any verifiable breakthroughs in the 1970s and 1980s.

³⁵ See KOLATA, *supra* note 14, at 66

³⁶ See *id.* at 69.

³⁷ *Id.*

³⁸ See McLaren, *supra* note 20, at 1775.

Save for a widely publicized claim in 1978 regarding human cloning, which later proved to be publicly discredited in the legal system, and another more favorably received though ultimately discredited claim of mouse cloning in 1981, cloning technology did not witness major substantive events in the aftermath of the frog cloning experiments initiated by the work of Briggs and King.

The 1978 hoax was propagated by a science journalist who claimed that an anonymous millionaire had approached him in an effort to clone an heir for himself. David Rorvik, who had reported for such publications as *Time* magazine and the *New York Times*, claimed that he had agreed to the rich man's request and proceeded to initiate a successful effort to recruit the necessary personnel and create the desired clone. Interestingly enough, events surrounding the 1978 announcement contain several parallels to the thus-far unconfirmed claims of similar nature made by the present-day orchestrations of Claude Vorilhon and his eager band of Raelian followers. Like the attention-hungry Vorilhon, Rorvik discovered that the cloning vehicle could be used to travel on the fast track to public notoriety. Similarly to Vorilhon, Rorvik subsequently discovered that the path also led to the type of infamy characterized by widespread and deserved mocking. Along the way to this ignoble end, Rorvik, like Vorilhon's cohorts at Clonaid, provided various excuses and pretenses with respect to why substantive verification of claims to human cloning could not be provided. As in the past several months with Clonaid, Rorvik felt the sudden urge to protect the privacy of the putatively cloned individual and other interested parties, despite having notified the international community of their existence. In Rorvik's case, this had taken the form of a work of "non-fiction" entitled "In His Image: The Cloning of a Man."³⁹ Vorilhon was perhaps more guarded in the sense that the announcement took place in the form of a press conference, yet the salient fact was that the announcement was made, and to an international audience.

³⁹DAVID M. RORVIK (1978)

Another similarity to present day events was the fact that Rorvik was met with skepticism by the scientific community. Much like Vorilhon has recently been met with debunkers, naysayers followed closely in the wake of the 1978 claim. In Rorvik's case, however, the degree to which his attackers proceeded was untempered by present-day advances in the state of cloning technology. These doubters attended a Congressional hearing that Rorvik first delayed and ultimately failed to make. Perhaps the general tenor of the attitude toward Rorvik and his fantastical claims is most politely expressed by relating that the most favorable comment made by one of the scientists was that Rorvik's book was "mildly amusing."⁴⁰ All agreed, however, that his was a work of science fiction, the imaginings of a strangely misguided professional who had, until that point, managed to develop a solid reputation as a credible science journalist.

Vorilhon differs from Rorvik in that the former's background does not have a caché that lends itself to a presumption that reports of scientifically legitimate breakthroughs may actually be legitimate. Vorilhon happened upon the subject of cloning following failed stints as a singer and as a publisher of an automobile racing magazine.⁴¹ The foray into human cloning extended from the career move that transitioned Vorilhon out of the relatively narrow roles of entertainer and publisher, and into the more generally-encompassing position of cult leader. With such a scientifically inauspicious beginning, it perhaps comes as a surprise that Vorilhon and his Raelian followers were not met with at least an equal degree of skepticism as that encountered by Rorvik. Vorilhon, however, has benefited from awareness of advances in cloning technology that have made the public and scientific community more guarded, and justifiably so, in voicing vehement doubt as to the probability of claims reporting the successful development of human clones from fully-differentiated adult cells.

⁴⁰ See KOLATA, *supra* note 14, at 103.

⁴¹ See Rick Ross, *The True Story of "little Claudy" Vorilhon, now known as "His Holiness Rael"* (March 2003), at <http://www.rickross.com/reference/raelians/raelians77.html>.

The relevant developments in cloning technology have only been in the public consciousness for the past five years. Biologically immediate precursors to these advances date back two decades, however. In early 1981, an announcement of cloned mice was made by the highly respected researcher Karl Illmensee. These mice were supposedly cloned from embryo cells, and so did not have the full effect of cloning from a fully grown adult cell. However, the scientific community recognized this as a major breakthrough. Unfortunately, despite many efforts to repeat the experiments, no one was able to replicate the reported results. In addition, suspicions arose within the scientific community as to the integrity of the experiments involved in the original claims.⁴² As it turned out, some in the scientific community came to believe that the original reports of mouse clones were at best suspect, and that Illmensee had not developed the requisite techniques for attempting such experiments.

Following these events, other researchers did manage to advance the state of the technology insofar as introducing a mouse nucleus into a fertilized mouse egg was concerned. In the first of this series of experiments, the nucleus from a fertilized mouse egg was transferred to another fertilized mouse egg through the use of an inactivated virus to fuse the introduced nucleus with the host egg cell. This experiment met with success, producing viable offspring mice. However, while the technique for manipulating mice nuclei and egg cells had advanced, this did not represent progress on the front of mouse cloning, because differentiated cells had not been used in these experiments. When the experiments shifted from using fertilized eggs as the donor cells to using donor cells that were further along the developmental pathway, the results dramatically shifted. No viable mice offspring were produced, and the results were even considerably less promising than the limited success of the frog experiments. Whereas the frog researchers were able to make tadpoles from early embryonic cells, the mice researchers were unable to achieve more than a few cellular divisions using

⁴²See KOLATA, *supra* note 14, at 130-144.

cell nuclei from the two-cell embryo stage, which, next to the fertilized egg, is the earliest stage of biological development. The researchers subsequently reported the impossibility of creating mammalian clones in the December 1984 issue of the prominent research periodical *Science*.⁴³ For some time afterwards, the focus of the research-oriented developmental and molecular biologists shifted away from cloning.⁴⁴ The public eye, already not overly-focused on what seemed to be a tangentially-relevant scientific endeavor, shifted even further away from developments in mammalian cloning research.

C. From Sheep to Cows

The cloning of mammals using fully differentiated adult cells caught the larger scientific community by surprise. In the aftermath of the unencouraging mouse experiments of the 1980s, scientists focused on research had shifted away from the pursuit of clones and instead embraced other subjects such as the characterization of the many genes involved in regulating cell growth and activity. Still, experimental work on cloning did not cease. It simply became relegated to one of the less luminous circles of science, where agricultural research funded by private interests reside. The two groups that pushed the boundaries of cloning research were located on opposite sides of the Atlantic, one in Wisconsin and the other in England. Of the Wisconsin group, Gina Kolata, a noted science correspondent for the *New York Times*, writes, “The only true surprise was that its researchers were so amazingly successful in the face of enormous inexperience with the new techniques needed for cloning.”⁴⁵ This group, working with funding from W. R. Grace and Company, was attempting to clone cows for the purpose of commercial applications, namely, to profit from

⁴³ See *id.* at 146.

⁴⁴ See *id.* at 132.

⁴⁵ See *id.* at 159.

the sale of cloned prize animals. The group succeeded in their attempts in the Fall of 1986, and published their results in the subsequent year.⁴⁶ Despite the prevalent report that mammalian clones were a biological impossibility, this group successfully cloned cows using early-stage embryonic cells. In addition to the practical problems in working with adult cows, the group was able to surmount such obstacles as to how to fuse the donor nuclei with the host egg cell and how to keep the newly-created embryos viable until they were ready for surgical transplantation into the surrogate mother cow. The latter problem was solved by implanting the new cow embryos into sheep oviducts. To the first question of method of fusion, the Wisconsin team used an apparatus that gave off an electrical pulse to facilitate nucleus to egg cell fusion. This solution proved to be quite significant to the development of cloning technology, as the method was also later used by Wilmut and Campbell to reinitiate the cell cycle of egg cells into which new nuclei had been injected.⁴⁷

Working at the same time as the Wisconsin group on the problem of mammalian cloning was Steen Willadsen. Willadsen came up with the innovation of using unfertilized host eggs instead of host eggs that had already been fertilized prior to introduction of the new nucleus. This led to the birth, in 1984, of lambs that had been created using this technique in conjunction with the same cell fusion technique used in the earlier mouse experiments, the same experiments used for support of the declaration that cloning mammals was impossible. Shortly thereafter, Willadsen happened upon using electrical pulses to fuse the introduced nucleus with the host egg cell, similar to but independent of the same technique employed by the Wisconsin group. At roughly the same time that the mainstream research scientists were abandoning cloning research, Willadsen and the Wisconsin group, working in relative obscurity, were expanding the frontiers.

⁴⁶See *id.* at 167.

⁴⁷See text accompanying notes 48-52, *infra*.

Willadsen and the Wisconsin group published their findings in 1986 and 1987, respectively. Although neither of the two had employed differentiated cells taken from fully grown adults in the creation of their clones, their results were significant enough to displace the assertion that mammals could not be cloned. The Wisconsin group continued to research ways in which cows could be cloned, and Willadsen began to work in the same field when he moved to the United States to work for a company interested in marketing clones of prize cattle.

Despite the encouraging results, the scientific advance in the state of cloning knowledge subsequently slowed. In a demonstration of how commercial interests can drive science, progress on cloning technology came to a standstill when the monetary motive behind cloning cows proved not to be as lucrative as originally thought. By the early 1990s, the original researchers involved in pushing the state of cloning science forward in the previous decade had moved on to other projects. At this point, the state of the technology remained at the point where it was possible to take early-stage embryo cell nuclei and make clones, but it was not possible to do the same using cell nuclei from fully-grown adults.⁴⁸

This all changed with the cloning efforts of Ian Wilmut and Keith Campbell. In 1996, they reported work in the journal *Nature* that they had successfully cloned sheep from cells that had, in a laboratory culture, differentiated from early embryo cells.⁴⁹ However, this announcement was met mostly with indifference from the scientific community. For the people who did pay attention to the result, the reaction was more akin to skepticism than optimism.⁵⁰ Because the cells used by Wilmut and Campbell were derived directly

⁴⁸ Although anecdotal accounts suggest that cells from embryos as far along in the developmental stage as one week had been successfully used to create clones, this research was never published. See *id.* at 187.

⁴⁹ See Keith H. S. Campbell et al., *Sheep Cloned by Nuclear Transfer from a Cultured Cell Line*, 380 *Nature* 64 (1996).

⁵⁰ See KOLATA, *supra* note 14, at 215.

from early embryo cells, it was thought possible that the cloning had actually been performed using non-differentiated genetic material, which was not an advance from earlier experiments. In fact, this result was of enormous significance, and it was in the following year that the pair announced results that cloning using genetic material from a fully grown parent had been achieved.

The innovation employed by Wilmut and Campbell in successfully cloning an adult sheep was the same one they used in the 1996 Nature article. However, what made the next experiment different was that, instead of using early embryo cells that had already differentiated, they used cells from udder cell tissue that had been stored in deep-freeze conditions. This tissue came from a sheep that had already died three years before Wilmut and Campbell attempted to make the clone.⁵¹ Thus, when Dolly was born in July 1996,⁵² her biological mother had long since passed away.

The announcement of Dolly's birth caught the attention not only of the scientific community, but of the international public. An adult mammal had been cloned, and it was time to consider the potential ramifications, namely, the possibility that humans could also be genetically duplicated. The most timely questions dealt with issues of feasibility and failure rates. The ensuing inquiries revealed that the cloning attempts leading up to Dolly's birth indicate that cloning, while technically possible, was by no means efficient or safe. Beginning with 277 udder cells, Wilmut and Campbell transferred the nuclei from those cells to egg cells. Using their novel technique of starving the donor cells to the point where they entered the G₀ (quiescent) phase of the cell cycle,⁵³ and then introducing a series of electric pulses to the newly-injected eggs to induce further development, the scientists were able to obtain 29 embryos. They transferred these embryos to surrogate mothers that were also sheep, but had noticeably different physical characteristics than the original sheep from whom the udder cells had been taken. Ultimately, only one lamb, the soon-to-be-famous Dolly, was born.

⁵¹See *id.* at 216

⁵²See *id.* at 219

⁵³See Keith H. S. Campbell et al., *Sheep Cloned by Nuclear Transfer from a Cultured Cell Line*, 380 Nature 64 (1996).

To reiterate the point concerning failure rates, it is not this single success that gives immediate pause regarding reproductive cloning. Even before considering the gravitic ethical issues associated with such a practice, issues of safety and efficacy warn against attempting to apply these techniques to humans. It is the 276 failed Dolly's that fueled and continue to feed the fire of criticism based strictly upon the feasibility of this reproductive technique. Of the hundreds of eggs used for the Dolly experiments, barely 10% of them made it to the early embryo stage,⁵⁴ and fewer still made it to one week, where development reaches the blastula stage in sheep.⁵⁵ Ultimately, there was only successful attempt from the creation of 29 embryos. The efficacy of this technique has not been demonstrated in humans, nor any kind of primate. However, even if scientists successfully clone, for instance, a chimpanzee, it would, without a doubt, be unacceptable to both proponents and opponents of human cloning to have a failure rate of 28 out of 29 embryos. This is notwithstanding the fact that roughly ten times this amount of egg cells would be required to duplicate the conditions of the original lamb cloning experiments. These egg cells, of course, would have to come from human egg donors.

One counterstrain of thought to the belief that cloning is simply too dangerous to be practiced on humans argues that, in some respects, cloning is actually safer than other forms of reproduction. Critics point to failure rates for early *in vitro* fertilization attempts and note that this technique, in its early stages, failed rather frequently. Lee Silver, a prominent biologist, points out that the success rate for the Dolly experiments, is far greater than the success rates of early human *in vitro* fertilization efforts.⁵⁶ Furthermore, cloning from the cells of a grown adult sidesteps the most common cause of birth defects, which is an incorrect number of chromosomes. During the creation of sex cells, sperm and eggs sometimes end up with too few or too many

⁵⁴ See KOLATA, *supra* note 14, at 218. *But see id.* at 239 ("Some cloning critics have said that it is clear from the Dolly experiment that cloning is unsafe because Ian Wilmut started out with 277 eggs and ended up with a single sheep. But, Silver noted, only 13 of those eggs developed into embryos and 12 of the 13 were miscarried early in pregnancy.")

⁵⁵ See ANS 431: Early Embryonic Development, at <http://www.siu.edu/~tw3a/431emb.htm> (last visited May 14, 2003).

⁵⁶ See LEE SILVER, REMAKING EDEN: CLONING AND BEYOND IN A BRAVE NEW WORLD (1998).

chromosomes.⁵⁷ Most of the time, if these sex cells are involved in fertilization, there will be a miscarriage. However, those individuals who do survive to birth have such genetic irregularities as Down's syndrome and Tay-Sachs disease.⁵⁸ Regardless of the merits of this argument, the fact that it and other human cloning-related discussions were being entertained in the mainstream indicated that the public consciousness had been raised. Serious discussions over policy was to follow, followed later still by substantive action in the legislative and regulatory realms.

D. Of Mice and Humans?

Potentially diminished risks of genetic irregularities may cause some to point to reproductive cloning as a safer alternative to traditional reproductive practices. Certainly, the safety disincentive has not completely dampened enthusiasm for the technology. The high probability of a substantial failure rate for initial human cloning attempts has not prevented all attempts to experiment with this technique. As discussed at the outset of this paper, Clonaid, the brainchild of Claude Vorilhon, claims to have actually created viable human clones. But Clonaid, despite being subject to a good deal of justified skepticism, has not been alone in its putative efforts to clone using adult human cells as the source of genetic material. Outside the thus-far unverified claims of Clonaid, at least one entity has gone so far as to attempt to create human embryos using human donor egg cells and genetic material from human adults.

In the United States, the only credible claim to human cloning attempts to date have involved a company called Advanced Cell Technology. In the November 24, 2001 issue of *Scientific American*, members of this company reported their results in an effort entitled, "The First Human Cloned Embryo."⁵⁹ This piece

⁵⁷ See KOLATA, *supra* note 14, at 238.

⁵⁸ See *id.* at 238-239.

⁵⁹ See Michael West et al., *The First Human Cloned Embryo*, *SCIENTIFIC AMERICAN* (Nov. 24, 2001), available at http://www.sciam.com/print_version.cfm?articleID=0008B8F9-AC62-1C75-9B81809EC588EF21 (last visited May 14, 2003).

reports the group's efforts throughout the entire process, from recruiting egg donors to culturing one of the embryos to the six-cell stage. The group reportedly undertook the first cloning attempt in July 2001⁶⁰ After injecting 71 eggs with genetic material from differentiated adult cells, the members of Advanced Cell Technology succeeded in inducing three of those cells to divide. None of these three embryos divided past the early embryonic stages, with the most advanced one reaching the six-cell stage.

The success of Advanced Cell Technology's attempts were founded upon earlier work on mouse cloning done at the University of Hawaii. In 1998, two years after the birth of Dolly, Teruhiko Wakayama and his laboratory successfully cloned mice using a novel source for the injected cell nucleus. Instead of using cells from skin tissue, Wakayama and cohorts used cumulus cells, adult cells which surround the egg. Cumulus cells have all of the genetic material of other differentiated adult cells, but they tend to be considerably smaller than the average adult cell. For this reason, it was possible for these cells to be injected into the eggs whole, without undertaking the extra step of removing the nucleus. According to the Scientific American article, Wakayama was affiliated to Advanced Cell Technology after the successful mouse cloning trials at the University of Hawaii.⁶¹ When the human cloning attempts were performed, some egg cells were injected with fibroblast (skin cell) nuclei, and other egg cells were injected with whole cumulus cells. All three of the embryos that the company created used the cumulus cell injection method.

In another set of experiments, the members of Advanced Cell Technology utilized a technique known as parthenogenesis to make embryos. Parthenogenesis makes use of the genetic material found in an egg cell. Until late in the maturation cycle, the egg cell possesses the same amount of genetic material as a normal cell found elsewhere in the body. However, an immature egg cell with the full complement of genetic material, under normal conditions, cannot divide in the same manner an embryo does to result eventually in an organism. By chemically altering the environment surrounding an unfertilized egg, West and his group

⁶⁰*See id.*

⁶¹*See id.*

successfully induced parthenogenesis, causing the egg cell to undergo changes that resulted in division into an embryo. Six of these egg cells developed to the blastula stage, considerably further than the six-cell stage of the most advanced cloned embryo. Although parthenogenesis makes use of the genetic material found in the egg, it is not cloning. The genetic material resulting from parthenogenesis, although very similar to that found in an adult somatic cell with a full complement of DNA, is not identical to it. The reason is that, during formation of sex cells, the genetic material in a person's body is mixed up in a process known as gene shuffling. Whereas a normal body cell contains the genetic material prior to shuffling, a parthenogenetically activated cell contains DNA that has been reordered.⁶²

The rationale for performing parthenogenesis experiments speaks to a fundamental difference between the aims of Advanced Cell Technology and the interests represented by Clonaid. The former seek to utilize the capabilities of cloning technology for medically therapeutic purposes, whereas the latter wish to make genetic replicas of people. Although it would be ideal for medical purposes to have identically matching tissue on the genetic level, highly similar genetic material will also serve a therapeutic end. For example, a patient who requires an organ transplant may have a narrow chance of finding a matching donor, but if technology can be used to produce organs from parthenogenetically activated cells, then the chances of producing tissue that will not be rejected by the body's immune system might increase considerably. But for those seeking to pursue reproductive cloning, a close genetic match might not suffice. West and the others at Advanced Cell Technology, by taking parthenogenetically activated tissue to the blastula stage, brought the state of technology that much closer to the point where embryonic stem (ES) cells can be obtained from a person's own cells.

⁶²*See id.*

E. Embryonic Stem Cells

So what are the advantages to researchers at the present moment of using ES cells? To gain a full appreciation of the benefits, it is useful to understand the distinction between ES cells and other cells found during embryonic development. When an egg is fertilized, the cell that results is a zygote, the first cell of the embryo. At this point, that single cell is totipotent. In other words, the cell can (and does) develop into any other type of cell in the adult body. When the cell divides, it becomes two cells attached to each other. At this point, both of these cells are still totipotent. In fact, the cells undergo several more divisions until they become a solid mass of cells attached to each other. This mass of cells is known as a morula, from the Latin *morum*, which means blackberry. One can imagine a morula as being similar to a microscopic blackberry, with the cells on the outside forming the little bumps that gives the fruit its surface texture.

The cells of the morula are also totipotent. Potentially, every one of these cells can develop into any type of tissue. However, in the next stage, the morula begins to fold inward and the cells, which are still dividing, begin to differentiate, or divide into cells that are no longer totipotent. One can imagine this process by thinking of the making of a pot from a round ball of clay. This structure becomes closed off, in a manner akin to extending the sides of the pot such that they close off the center opening. At this point, the embryo is called a blastula, and can be appropriately described as a hollow mass of cells. It is from within the blastula that embryonic stem cells are found. However, at this point, the cells of the embryo are no longer totipotent. Rather, they are pluripotent, unable to divide into every type of tissue found in the adult.

Still, the pluripotent ES cells retain the capacity to become most other types of adult tissue. The types of cells that ES cells cannot become are trophoblasts, which eventually form the fetal portion of the placenta, the biological structure through which nutrients are exchanged between the mother and child. Other than the trophoblasts, it is thought that ES cells can develop into all of the other types of adult tissues. This

ability to divide into all other types of cells and tissues is what makes ES cells so critically important to future scientific developments. From a strictly medical standpoint, research in ES cells could ultimately lead to the day where a paralysis victim could be given a new spinal cord or someone who had experienced a massive heart failure could be given a new heart. What distinguishes these applications from present similar endeavors, however, is that if doctors use ES cells created from a patient's own cells, the immunochemical rejection associated with current transplants would not be an issue.

Given the above description of the developmental process, one natural question to ask is why ES cells, as opposed to cells that are found earlier in development, must be used for research purposes. The answer is that scientists do not know how to culture the earlier totipotent cells, whereas the knowledge to maintain ES cells in a laboratory environment does exist. For mice, scientists have long been maintaining ES cell lines and using these cells to investigate the function of various mouse genes.⁶³ The advantage of having many ES cells available in petri dish cultures is that the genetic material of some of these cells can be altered. However, the process by which the genetic is altered requires a very large amount of cells, because only a very small proportion of the cells are successfully altered. Once researchers identify the cells that have been successfully changed, these cells can be reintroduced into the biological context by combining them with cells of a different developing mouse embryo. What happens afterwards is that the adult mouse has some cells that are from its original parents, and some cells that are from the altered ES cells. The hope is that some of the ES cells are present in the gametes, or sex cells, so that when these mice are mated with other mice, some of the offspring will have the altered genetic material in all of their cells. The mice with fully altered genetic material can then be used for further studies.

Embryonic stem cell technology has the potential to treat many diseases and medical needs. The ability of these cells to grow into most any type of tissue found in the adult body presents the opportunity to grow

⁶³See KOLATA, *supra* note 14, at 197.

cardiac muscle for heart problems and neural cells for such conditions as Alzheimer's and Parkinson's.⁶⁴ Given the shortage of organs available for transplant,⁶⁵ the potential to use ES cells to grow into any type of tissue may solve a longstanding medical quandary. As with any type of tissue transplant, organs derived from ES cells run the risk of being rejected by the recipient. If the ES cells are derived using nuclear transfer, with the nucleus originating from one of the organ recipient's cells, then the problem of incompatibility disappears.

One of the ethical dilemmas in pursuing this course of treatment is that, currently, the derivation of ES cells requires the creation of an embryo, and development of that embryo to the one-week old stage. In the process of cultivating the ES cells, the embryo is destroyed. Some find this to be an intolerable violation and termination of life. Another moral problem is that such medical technology, were it available, using ES cells derived from the patient's genetic material, could be used to create genetic clones of people. The next section examines regulatory efforts to prevent this eventuality.

III. Efforts to Prevent and Sanction Human Cloning

To this point, there has been no broad ban passed on human cloning on the federal level.⁶⁶ There has been a limited ban placed upon experimentation with cloning or embryonic stem cells.⁶⁷ With respect to most research, the control mechanism has been through regulation of federal funds. Congress placed a ban on NIH-

⁶⁴See Anne McLaren, *Stem Cells: Golden Opportunities With Ethical Baggage*, 288 *SCIENCE* 1778 (2000).

⁶⁵See Jennifer Ryan and Dorsey Edwards, *Can a Website Solve the Organ Shortage Crisis in America?*, WUSA 9 – Health, Feb. 26, 2003, at http://www.wusatv9.com/health/health_article.asp?storyid=15133 (last visited May 14, 2003) (stating that “[s]eventeen Americans die every day waiting for an organ transplant”).

⁶⁶See AAAS Policy Brief: Human Cloning, American Association for the Advancement of Science, *available at* <http://www.aaas.org/spp/cstc/issues/cloning.htm> (updated Jan. 2003) (last visited May 14, 2003).

⁶⁷See AAAS Policy Brief: Stem Cell Research, American Association for the Advancement of Science, *available at* <http://www.aaas.org/spp/cstc/issues/stemcells.htm> (updated Aug. 14, 2002) (last visited May 14, 2003).

funded human embryo research in 1995, and that ban has been in effect in each year's appropriations bill ever since.⁶⁸ However, this mechanism does not speak to private individuals and corporations such as Clonaid and Advanced Cell Technology. The regulatory structure here remains murky and awaits further clarification via Congressional legislation or Executive order, but the FDA appears to be the existing regulatory agency with sufficient resources and recognition to address private efforts.⁶⁹ It is conceded that the FDA possesses oversight authority of tissues used for transplant,⁷⁰ from which may arise regulatory authority over human cloning attempts.

On a practical level, the FDA has been largely successful in preventing or discouraging human cloning attempts in the United States. Clonaid is no stranger to regulatory efforts by the FDA. The company website acknowledges that, in 2001, representatives from the government made "several visits" to the company's facilities.⁷¹ Following these visits, the company decided to relocate to "another country where human cloning is legal."⁷² According to Bernard Stone, a spokesman for the Agency, in 2002 the FDA investigated and shut down a Clonaid laboratory in Nitro, West Virginia.⁷³ After the December 2002 announcement, the FDA had began another investigation into the organization.⁷⁴

At the same time, not all attempts in the United States to apply cloning technology to humans have been prevented. As seen in the previous section, the FDA did not stop Advanced Cell Technology from undertaking a series of attempts to create a human embryo using cloning technology.⁷⁵ However, actions taken subsequent to the reporting of these experiments may have deterred further attempts, at least for the time being. During

⁶⁸ See *id.*

⁶⁹ See, e.g., Regulating Human Cloning, American Association for the Advancement of Science, Apr. 3, 2003, available at <http://www.aaas.org/spp/cstc/issues/cloningreport.pdf> (last visited May 14, 2003).

⁷⁰ *Id.* at 7.

⁷¹ See The First Human Cloning Company, A Historical Background, at <http://www.clonaid.com/english/pages/history.html> (last visited May 14, 2003).

⁷² *Id.*

⁷³ See Linda Greenhouse, *F.D.A. Exploring Human Cloning Claim*, THE NEW YORK TIMES, Dec. 30, 2002, at A10.

⁷⁴ See *id.*

⁷⁵ See II.D, *supra*.

a January 2003 panel on human cloning, CEO Michael West described the attempts of FDA regulators to inspect and shut down the company's facilities.⁷⁶ In the aftermath of these inspections, Advanced Cell Technology has not reported further attempts to extend their previous line of research involving human cloning and embryonic stem cells.

General public sentiment against such attempts provide another source of regulation. This has manifested itself in litigation brought on behalf of cloned individuals, despite the unconfirmed existence of these children. Bernard Siegel filed a suit against Clonaid in Florida court, claiming that Eve is an abused child.⁷⁷ The rationale behind this suit was that cloning technology is too unreliable and stands too great of a chance for birth defects to ensure the birth of healthy children. Hence, to subject an individual to this high possibility of death or defect is tantamount to abuse.

For the time being, these official and private regulatory efforts may be enough to prevent further human cloning attempts in the United States. Based upon current scientific understandings and social conventions, it is necessary that an effective ban on human cloning be made at this point. Such cloning attempts are highly unlikely to succeed, and any measure of success will be accompanied by many more highly undesirable outcomes. And if technology ever exists to carry out the process of taking a nucleus from an adult human's differentiated cell, creating an embryo, harvesting the ES cells, and coaxing these cells to grow into tissues to be used for medical therapy of the same person, moral qualms will still plague application. Until such time that science reaches the point where ES cells can be derived without going through the intermediate step of creating embryos, or social attitudes toward creating embryos strictly for medical purposes change, it unlikely that this technology will be widely accepted in the United States.

⁷⁶ See Human Cloning Panel, Harv. J. Law & Tech., Jan. 21, 2003, *available at* http://media.law.harvard.edu:8888/ramgen/jolt/spring_03/2003-01-22_h102_0630-0730.rm (last visited May 14, 2003).

⁷⁷ See Russ Mitchell, CBS Early Show interview with Bernard Siegel, Jan. 2, 2003.

IV. Conclusion

When news of the first successful cloning of a mammal using the genetic material of an adult sheep reached the public, the policy-making and -effecting mechanisms were too late to stop the advent of this technology. In the six years since this first successful cloning attempt, the state of knowledge has advanced yet further, and techniques have improved. The technical problems more specific to cloning humans have become clearer, in the form of cloning research on other primates.⁷⁸ As is the wont of researchers, these problems have been met with proposed solutions.⁷⁹ Advances in knowledge of basic cellular mechanisms, though broader-ranging in application than cloning, also contribute to our ability to make genetic duplicates of any organism. Doubtlessly, research will continue and may well eventually reach the point where human cloning is possible. This eventuality should not lead us to condemn the original discoveries, for advances in knowledge and technology are not, in and of themselves, deleterious. While retrospection is oftentimes described as clear-sighted, the problem with looking back in the scientific and technological contexts is that policy regulates application of principles rather than the direction of discovery. Oftentimes, no one even anticipates a particular manner in which a new discovery can be applied. Asking policymakers and regulators to prevent all future innovations that may have potentially negative applications is basically asking them to make time stand still. The only way to prevent any conceivably harmful eventuality would be to have everyone sit on their hands and do nothing. Instead of focusing our efforts on soothsaying and its attendant frustrations, we should concentrate on ensuring that existing technology is harnessed in a beneficial manner.

For human cloning, this means that regulators must act to prevent all possible attempts at this time.

While the technology exists to perform the procedure, our current understanding of cell programming and

⁷⁸ See Calvin Simerly et al., *Molecular Correlates of Primate Nuclear Transfer Failures*, 300 SCIENCE 297 (2003).

⁷⁹ See *id.*

development is not sufficient to ensure success, much less safety. There are also threshold questions that need to be resolved, questions that implicate our conceptions of sentience and life. Now that technology has opened the door, regulation must earnestly work to ensure that our application of these profound discoveries does not create a Pandora's Box of ethical and biological catastrophes.