UIC John Marshall Journal of Information Technology & Privacy Law

Volume 16
Issue 4 *Journal of Computer & Information Law - Summer 1998*

Article 7

Summer 1998

Everybody's Got Something to Hide Except Me and My Patented Monkey: Patentability of Cloned Organisms, 16 J. Marshall J. Computer & Info. L. 971 (1998)

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EVERYBODY'S GOT SOMETHING TO HIDE EXCEPT ME AND MY PATENTED MONKEY:[1] PATENTABILITY OF CLONED ORGANISMS

I. INTRODUCTION

Imagine having a twin sibling. Now imagine having twenty identical twin siblings. Initially this sounds like something straight from the pages of a George Orwell novel.[2] Rather, this incredible scientific achievement comes not from the pages of Orwell's *Animal Farm*, but from the pages of the highly respected scientific journal *Nature*.[3] In the February 27, 1997 issue, Dr. Wilmut and his colleagues reported the successful cloning of a living, breathing animal.[4] A lamb named "Dolly" was the first animal cloned from the mammary cell of a 6-year-old ewe in the last trimester of pregnancy.[5]

Dolly is no longer alone. In the July 23, 1998 issue of *Nature* two groups of scientists reported the successful cloning of healthy and fertile female mice.[6] Scientists at the University of Hawaii and an international team assembled from the United States, Japan, Italy, and the United Kingdom implemented a technique similar to that which produced Dolly and applied it not to farm animals, but to laboratory mice.[7] The short gestation period of mice will dramatically enhance the pros-

1. *See* JOHN LENNON & PAUL MCCARTNEY, *Everybody's Got Something to Hide Except Me and My Monkey*, *on* THE BEATLES WHITE ALBUM (EMI Records 1968).

2. *See* GEORGE ORWELL, 1984 (1986). *See also* GEORGE ORWELL, ANIMAL FARM (1946). (Orwell wrote several novels dealing with a variety of psychosocial, political, and humanistic themes). Two of the more famous satirical lines in ANIMAL FARM are: "All animals are equal, but some animals are more equal than others" and "Four legs good, two legs bad." *Id.* at 14, 62.

3. *See* I. Wilmut et al., *Viable Offspring Derived from Fetal and Adult Mammalian Cells*, 385 NATURE 810 (1997). This group from the Roslin Institute in Edinburgh, Scotland reported for the first time in the February 27, 1997 edition of the scientific journal NATURE, the successful cloning and birthing of a live sheep. *See id.*

4. *Id.* at 810.

5. *See id.*

6. *See* T. Wakayama et al., *Full-Term Development of Mice from Enucleated Oocytes Injected with Cumulus Cell Nuclei*, 394 NATURE 369 (1998).

7. *See id.*

pect of determining the technical and biological factors that contribute to mammalian cloning.[8]

In 1998, the image of a pasture covered with identical sheep and cattle is far from Orwellian, it is reality.[9] Cloning is conceivable for any breed of livestock. It may be possible to produce animals with traits dramatically superior to their traditionally bred ancestors. Cloning technology allows for the possibility of developing leaner, healthier, and more efficient herds than those achievable through traditional breeding techniques.[10] Cloning applications are numerous, including possibilities such as transplantable organ procurement (xenotrans-plantation)[11] and the propagation of animal species facing extinction.[12]

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8. *See* Davor Solter, *Dolly is a Clone—and No Longer Alone*, 394 NATURE 315 (1998)

9. *See generally* ORWELL, *supra* note 2. *See also George Orwell* (visited Oct. 14, 1997) <http://www.geocites.com/WallStreet/6325/>. Mr. Orwell's thought provoking, yet cynical introspection towards the future of societies, governments, and politics gave rise to the perhaps overused adjective "Orwellian" to describe artifacts of society that are, at times, difficult to accept and understand. *See also* Henry Gee, *Biotechnology: Cloning Sheep* (visited Oct. 13, 1997) <http://www.nature.com/Nature2>. Dr. Gee suggests that making copies of a "prize herd specimen" would require nothing more than "harmlessly removing some cells from the animal, injecting the nuclei of these cells into egg cells whose own nuclei had been removed, and implanting the altered egg cells into surrogate animals." *See id. See also* Wilmut, *supra* note 3, at 810. Dr. Gee's summary is a simplified method of that described by Dr. Wilmet et al., in their groundbreaking cloning work. *See id.*

10. *See* Jonathan MacQuitty, *Boon for Barnyard Biotechnology*, 15 NATURE 265, 306 (1997).

11. *See* Michael Thomas et al., *Adrenocortical Tissue Formed by Transplantation of Normal Clones of Bovine Adrenocortical Cells in scid Mice Replaces the Essential Functions of the Animals' Adrenal Glands*, 3 NATURE MED. 978 (1997). Xenotransplantation utilizes animal organs for transplantation into humans experiencing organ failure. *See id.* Baboon bone marrow was introduced into a patient with advanced AIDS, pig neural cells were injected into the brains' of patients with Parkinson's disease, pig pancreatic cells were given to patients with pancreatic failure, and pig livers have sustained patients suffering from liver failure. *See* David Sachs, *Xenographs, Cloning and the Immune System*, 3 NATURE MED. 951, 953 (1997). Pigs are frequently used as donor animals in xenotransplantation because the size of their organs is comparable to human organs. *Id.* Theoretically, scientists could clone human genes, introduce them into an animal, and then clone a specific animal (like a pig) for the purpose of transplanting its organs into humans awaiting a compatible human organ. *See id.*

12. *See Potential Benefits of Plant and Animal Cloning* (visited Aug. 7, 1997) <http://www.ncgr.org/gpi/odyssey/dolly-cloning_benefits.html>. Potential benefits of plant and animal cloning include the following: a) pharmaceutical industry application through the utilization of genetically engineered animals to express a human protein (like insulin) and then cloning this organism, thereby creating an aggregate human insulin producing "factory"; b) improving medical research through the mass production of identical subjects via cloning, thereby decreasing the variability observed among test subjects from the same species and subsequently decreasing the need for larger tests group to achieve statistical significance; c) expanding agricultural capabilities to produce adequate supplies of food for the growing global population; and d) increasing the numbers of endangered species by cloning those species at the highest risk of extinction. *See id.*

Numerous biotechnological advances have occurred in the last thirty years.[13] Each year, hundreds of articles disseminating the results of laboratory work worldwide document the advances made by the scientific community in manipulating genetic material in organisms.[14] The power of biotechnology has positively impacted society through improvements in the treatment of disease,[15] the development of ultra-effective medications,[16] and the production of high-yield, pest-resistant crops.[17]

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13. *See* Bruno W.S. Sobral, *Biodiversity: Perspectives and Technological Opportunities—High Throughput Screening Technologies* (visited Oct. 13, 1997) <http://www.bdt.org.br/bdt/paper/padctbio/cap8/2/bruno.html> (DNA-based genetic markers (isozymes), Markert and Moller, 1959; in situ hybridization techniques, Gall and Pardue, 1969; Restriction Fragment Length Polymorphism ("RFLP") technology, Pinkel, 1986; single-copy DNA sequence isolation and identification techniques, Harper and Sanders, 1984; Polymerase Chain Reaction ("PCR"), Saiki, 1985; Short Tandem Repeats ("STRs"), Jacob et.al. and Edwards et. al., 1991; and Advanced Fragment Length Polymorphism ("AFLP") technology, Zabeay and Vos, 1993).

14. *See* L.B.K. Herzing et al., *Xist has Properties of the X-Chromosome Inactivation Centre*, 386 NATURE 272 (1997); K. Kaupman et al., *Expression Cloning of GABA-B Receptors Uncovers Similarity to Metabolic Glutamate Receptors*, 386 NATURE 239 (1997); T. Koga et al., *Transposable Element in Fish*, 383 NATURE 30 (1996); L.R. MacGillivray & J.L. Atwood, *A Chiral Spherical Molecular Assembly Held Together by 60 Hydrogen Bonds*, 389 NATURE 469 (1997); T. Misteli et al., *The Dynamics of a pre-mRNA Splicing Factor in Living Cells*, 387 NATURE 523 (1997); T. Murphy et al., *Endosome Dynamics Regulated by a Rho Protein*, 384 NATURE 427 (1996); G.J. Raymond et al., *Molecular Assessment of the Potential Transmissibilities of BSE and Scrapie to Humans*, 388 NATURE 285 (1997); O.C. Steinbach et al., *Somatic Linker Histones Cause Loss of Mesodermal Competence in Xenopus*, 389 NATURE 395 (1997); J.F. Tomb et al., *The Complete Genome Sequence of the Gastric Pathogen Helicobacter Pylori*, 388 NATURE 539 (1997); H. Yamagata et al., *Mutations in the Hepatocyte Nuclear Factor-1-alpha Gene in Maturity-Onset Diabetes of the Young (MODY3)*, 384 NATURE 455 (1996);

15. *See Identifying Human Disease Genes by Positional Cloning* (visited Oct. 12, 1997) <http://www.ncgr.org/gpi/odyssey/dolly-cloning/nuclear_transfer.html>. Using positional cloning ("PC") techniques in 1993, a collaborative group of medical scientists linked Hunington Disease, a neurological disorder that has plagued mankind for centuries, to chromosome 4. *See id.* Other diseases attributable to genetic mutations include breast cancer, Alzheimer's disease, and polycystic kidney disease, all cloned via PC. *See id. See also Transgenic Technology* (visited Aug. 7, 1997) <http://www.ncgr.org/gpi/odyssey/dolly-cloning/nuclear_transfer.html>. Diseases such as cancer can be studied more liberally by inserting a human cancer gene into a mouse. *See id.* The mouse (oncomouse) then expresses the cancer gene, allowing for broad experimentation of potential therapeutic methodologies. *See id. See also* U.S. Patent 4,736,866, *infra* note 34 (describes the patent issued for the oncomouse).

16. *See* Philippe Ducor, *Recombinant Products and Nonobviousness: A Typology*, 13 SANTA CLARA COMPUTER & HIGH TECH. L.J. 1, 3-4 (1997). Modern tools of biotechnology have yielded therapeutic medicines such as Factor VIII, erythropoietin ("EPO"), human growth hormone ("hGH"), tissue plasminogen activator ("t-PA"), granulocyte colony-stimulating factor ("G-CSF"), and hepatitis B vaccine. *See id.*

17. *See* Juan J. Estruch et al., *Transgenic Plants: An Emerging Approach to Pest Control*, 15 NATURE 546 (1997); David G. Scalise & Daniel Nugent, *International Intellectual Property Protections for Living Matter: Biotechnology, Multinational Conventions and the*

Recombinant DNA technology is said by some to hold the greatest promise for demonstrating a positive scientific impact on society.[18] Recombinant DNA technology, known as genetic engineering, is defined as the ability to construct new DNA molecules from different base sequences from a variety of source organisms.[19] Scientists can isolate, modify, and recombine genetic sequences with a host animal and produce a variety of compounds in greater concentrations and with the highest purity.[20] Gene manipulation enables the transformation of organisms into biological factories, capable of producing unique and sensitive bioactive materials with relative ease.[21]

Utilizing genetic manipulative techniques, scientists recently produced a cloned animal.[22] Since late 1996, several groups of scientists independently demonstrated the possibility of cloning an entire organ-

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Exception for Agriculture, 27 CASE W. RES. J. INT'L L. 83, 84 (1995); Phil Oger et al., *Genetically Engineered Plants Producing Opines Alter Their Biological Environment* (visited Oct. 13, 1997) <http://bio-tech.nature.com/cgi-bin/wilma.cgi/v15n4.868630590.html>.

18. *See* BENJAMIN LEWIN, GENES III, 353 (3d ed. 1987). Recombinant DNA technology allows scientists to construct hybrid DNA molecules by utilizing the power of restriction enzymes that act on nucleic acids. *See id.* DNA or deoxyribose nucleic acid is an informational macromolecule that is composed of four nucleotides: adenine (A); guanine (G); cytosine (C); and thymine (T). *Id.* at 42-48. It gets some of its unique properties from its double-helix structure that allows it to unwind during duplication. *Id.* at 49-51. DNA can be thought of as a genetic blueprint of an organism. *See id.* Nucleic acids are responsible for maintaining and conveying genetic information, while the proteins they code for are responsible for providing the means of executing this genetic information. *Id.* at 7. Proteins are synthesized from a series of amino acid building blocks. *See id.* The sequence in which the individual building blocks are joined together is the critical factor that determines the property of the resulting molecule. *Id.* at 4-13. *See also In re O'Farrell*, 853 F.2d 894, 895-899 (Fed. Cir. 1988). Judge Rich does an excellent job of establishing the basic scientific principles required for a cursory understanding of biotechnology and recombinant DNA techniques. *See id.*

19. *See* LEWIN, *supra* note 15, at 634.

20. *See id.*

21. *See* Ducor, *supra* note 16.

22. *See* Wilmut, *supra* note 3. Cells were extracted from the udder of the adult ewe and the nucleus from these cells was extracted (a process referred to as enucleation). *Id.* at 813. The nucleus contains the DNA or genetic blueprint. *See also* Brian C. Cannon, Note, *Toward a Clear Standard of Obviousness for Biotechnology Patents*, 79 CORNELL L. REV. 735, 737 (1994). The researchers then fused the mammary cell nuclear material into the unfertilized, enucleated egg of another sheep. Wilmut, *supra* note 3, at 813. This hybrid embryonic cell was then transferred into the womb of a third surrogate mother sheep. *See id.* The scientists revealed their accomplishment after Dolly was born and reached a healthy age of seven months. *Id.* at 810. In the same month Dolly was announced, "Gene" the bull-calf was born in DeForest, Wisconsin. *See ABS Global Announces Birth of Cloned Calf and Formation of Infigen To Commercialize Novel Technology* [hereinafter *Cloned Calf*] (visited Oct. 12, 1997) <http://www.infigen.com/0807-news.html>. Gene is the first known calf to be born from cloning technology developed by ABS Global, Inc. *See id.* Utilizing a slightly different technique, yet conceptually the same idea, the ABS scientists successfully cloned and implanted a calf embryo. *See id.* ABS researchers waited until

ism.[23] Cloning technology may be the most impressive advancement in genetic engineering made in this decade.[24] Commercially, the scientific value of cloning is worthless, without patent protection.

What patent protection will be offered cloned organisms is yet undetermined. When compared to other fields of art, patent law in the area of biotechnology is in its early stages of development.[25] The advent of cloning technology will continue to challenge the Patent and Trademark Office ("PTO") and the courts' ability to keep patent law in-step with emerging biotechnologies.[26]

Undoubtedly, inventive scientists will continue to seek and obtain patent protection for cloning methods.[27] This comment, however, examines the legal issues surrounding the patentability of the cloned organism. Section II provides a brief history of the technology that lead to cloning. It also serves as a basic primer on the scientific principles of biotechnology, and concludes with an examination of recent Federal Court decisions in the area of biotechnology. Section III analyzes how the PTO is likely to respond to patent applications for cloned organisms and the position the Federal Courts should take when interpreting patents issued for cloned organisms. This article then concludes with the assertion that, although patents will be issued for narrowly filed applications for cloned organisms, their issuance will present difficulties in demonstrating nonobviousness and enablement requirements for inventors seeking patent protection for cloned organisms.

Gene was born and matured to five-months-old before they announced their achievement. *See id.*

23. *See* Wilmut, *supra* note 3; Wakayama, *supra* note 6; *Cloned Calf, supra* note 22.

24. *See* Robert Winston, *The Promise of Cloning for Human Medicine* (visited Oct. 13, 1997) <http://194.216.217.166/reg/bmj/archive/7085e.htm> (espousing the potential benefits of cloning on the progress of medicine).

25. *See* Jeremy Cubert, *U.S. Patent Policy and Biotechnology: Growing Pains on the Cutting Edge*, 77 J. PAT. & TRADEMARK OFF. SOC'Y 151, 152 (1995).

26. *Id.* at 152-53.

27. *Id.* at 157-58. Due to the lack of predictability, the inherent nature of biotechnology has led the Patent and Trademark Office [hereinafter PTO] to implement higher standards of review for "method of making" patent applications than those applied to other aspects of patenting genetic sequences. *See id.*

> Biotechnology relies for the most part on the use of standard methodology. For example, a standard technique used for production of a recombinant protein involves splicing the gene coding for the protein into bacterial plasmid vectors. Plasmid vectors are small, self-replicating circular pieces of DNA that are used as recipients for foreign DNA. After the DNA is spliced into the vector, the vector is placed into bacterial cells. The bacteria now have the DNA instructions to produce the protein product of interest.
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> Thus, even if the gene is new and nonobvious and the resulting protein is new and nonobvious, the method of using a patentable product to produce a patentable product may be obvious (and therefore, unpatentable due to obviousness).

Id. at 158.

II. BACKGROUND

A. BIOTECHNOLOGY: A BRIEF HISTORY

The essential attributes of the gene were defined more than a century ago by Gregor Mendel, a nineteenth-century Austrian monk with a keen interest in botany.[28] His work in pea plants established the fundamental concepts of heredity.[29] In the 1930s, Boris Ephrussi undertook to establish the relationship between genes and enzymatic function.[30] These experiments, conducted with fruit flies, resulted in the discovery of naturally occurring mutations.[31]

In 1945, the gene phenomenon crossed into the area of molecular biology with the help of Erwin Schrodinger, who realized that the then current view of chemistry and physics was inadequate to account for the properties of genetic material.[32] In less than forty years, scientists were able to account for the properties of genetic material. Scientists' understanding of the genetic code has progressed to the point where genetic material can be isolated and removed from one organism and inserted (recombine) it into a bacterium such that the bacterium expresses the inserted gene (recombinant DNA).[33] The first successful products of the genetic engineering process were protein drugs, such as insulin and growth hormone.[34]

Scientists developed recombinant DNA technology in bacterium and then applied this knowledge to the process of inserting foreign DNA from

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28. *See* LEWIN, *supra* note 18, at 19-20. Mendel is recognized as the father of modern genetics. *See id.* His classical pea plant experiments established the gene as the essential component involved in the transmission of information from parent to offspring. *See id.*

29. *See id.*

30. *See* LUBERT STRYER, BIOCHEMISTRY, 833 (3d ed. 1988). Dr. Ephrussi was instrumental in discovering mitochondrial DNA. *See id.*

31. *See id.*

32. *See* LEWIN, *supra* note 18, at 1. Schrodinger hypothesized that further characterization of genetic material would reveal that new laws of physics will enable a better understanding the function of the gene. *See id.* Schrodinger made the following assumptions in 1945:

> "[Genes are] incredibly small groups of atoms, too small to display exact statistical laws, do play a dominating role in the very orderly and lawful events within a living organisms . . . . The gene is much too small . . . to entail an orderly and lawful behavior according to physics."

Id.

> We shall assume the structure of the gene to be that of a huge molecule, capable only of discontinuous change, which consists in a rearrangement of the atoms and leads to an isomeric molecule. The rearrangement [mutation] may affect only a small region of the gene, and a vast number of different rearrangements may be possible.

Id. at 3.

33. *See* STRYER, *supra* note 30, at 136-37.

34. *Id.* at 137-38.

one animal, known as transgenes, into another animal, creating a transgenic animal.[35] Philip Leder of Harvard University and Timothy Stewart of Genetech contributed to this cutting-edge work in the early 1980s.[36] In June of 1984, this scientific team submitted an application to the Patent and Trademark Office entitled, *Transgenic Non-Human Mammals*.[37] Dr. Leder's invention was a mouse transformed to express human cancer, creating a "super mouse" that allowed for the investigation of human cancer therapies in mice.[38]

While the first transgenic "super mice" emerged in the early 1980s, this technology advanced to provide for the engineering of mice to produce human tissue plasminogen activator ("tPA"), a potential treatment for heart attack patients.[39] More recently, a patent issued for a transgenic mouse designed to study the effects of estrogen and other sex hormones in the protection against such diseases as osteoporosis, breast cancer, and cardiovascular disease.[40] Since the Leder patent issued in

35. *See* Thomas T. Moga, *Transgenic Animals as Intellectual Property (Or the Patented Mouse that Roared)*, 76 J. PAT. & TRADEMARK OFF. SOC'Y 511, 517 (1994).

36. *See id.*

37. *See* Philip Leder and Timothy A. Stewart, *Transgenic Non-Human Mammals*, U.S. Patent No. 4,736,866 (Apr. 12, 1988) [hereinafter Patent '866]. The invention described in Patent '866 comprises a strain of transgenic mice carrying an activatable transgene that induces the development of tumors with high frequency. *See id.* Transgenic animals are created by introducing exogenous (foreign) DNA sequences (plasmids) into the germ line via addition to the egg. *See* LEWIN, *supra* note 18, at 736. Plasmids carrying the gene of interest are injected into the nucleus of the oocyte (immature egg) or into the pronucleus (chromosomal capsule) of the fertilizied egg. *Id.* at 634. Plasmids are autonomous (capable of transposition) self-replicating extrachromosomal circular DNA. *Id.* at 731. Following the aforementioned injection of the plasmids into the nucleus of the egg, the egg is implanted into a pseudopregnant mouse (chemically induced to develop thick lining of the utereus capable of sustaining a fertilized egg). *Id.* at 634. Following the birth of the baby mouse, a test is administered to determine if the engineered mouse is expressing the desired protein, indicating a successful plasmid-mediated genetic transfection. *See id.*

38. *See* Patent '866, *supra* note 37. Patent '866 claims, in part, "[a] transgenic nonhuman eukaryotic animal whose germ cells and somatic cells contain an activated oncogene sequence introduced into the animal, or an ancestor of the animal, at an embryonic stage." *See id.*

39. *See* STRYER, *supra* note 30, at 256. Plasma proteins contain plasminogen which, when activated, becomes a substance called plasmin. *See id.* Plasmin is an enzyme that digests the fibrin threads of a blood clot. *See id.* This becomes especially important in patients in post-operative cardiovascular surgery settings where circulating platelets will recognize a reconstructed nacesent or donor artery as injured and attempt to "heal" this region by forming a blood clot (thrombus) which subsequently attracts the other cells that respond to injured cells. *See id.* By introducing exogenous (extra) tPA, plasminogen is activated and plasmin is freed to "attack" the forming thrombus before it has a chance to block the artery, thereby causing an stenosis, which could lead to an infarction, or heart attack. *See id.*

40. *See* Kenneth S. Korach, *Mutant Mice Having a Deficit of Functional Estrogen Receptors*, U.S Patent No. 5,650,550 (July 22, 1997) [hereinafter Patent '550]. This patent,

1988, nearly all patents issued for transgenic organisms claim non-human animals engineered to investigate human disease.[41]

B. Basic Scientific Concepts

A fundamental principle of biology is the fact that DNA automatically controls the formation of another nucleic acid, ribonucleic acid (RNA), which spreads through a cell and controls the formation of specific proteins.[42] Some proteins are structural proteins, which in association with various lipids,[43] form the structures of the various organelles.[44] Notwithstanding the structural properties of proteins, the majority of proteins are enzymes that catalyze different chemical reactions within cells.[45] Enzymes are required to promote reactions that both supply the cell with energy and synthesize other chemicals utilized by the cell to support itself.[46]

Genes are contained in long, double-stranded, helical molecules of DNA.[47] The importance of DNA lies in its ability to control the formation of other substances in the cell.[48] It does this by means of a so-called genetic code.[49] When the two strands of a DNA molecule split apart, this separation exposes the base for duplication.[50] The genetic code consists of successive triplets of bases, each three successive triplets constitute a

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entitled, describes an invention that claims, in part, "[A] mutant non-human vertebrate . . . which mutation is introduced into the vertebrate, or an ancestor of the vertebrate, at an embryonic stage, and which mutation produces a phenotype . . . ." *See id.*

41. *See* U.S. Patents cited *infra* note 91 (patents have issued for transgenic animals that were designed specifically for studying the treatment of diseases such as polio, HIV, Alzheimer's, epilepsy, and osteoporosis).

42. *See* Lewin, *supra* note 18, at 90-93.

43. *See* Stryer, *supra* note 30, at 288-89. Lipids are the primary structural element of the cell wall. *See id.* Essentially all physical structures of the cell are lined by membranes composed primarily of lipids and proteins. *See id.* The lipids of the membranes provide a barrier that prevents free movement of water and water-soluable substances from one cell compartment to another. *See id.*

44. *See* Lewin, *supra* note 18, at 423-27. Organelles are highly organized physical structures of great import to cell function. *See id.* Perhaps the most important organelle is the mitochondria. *See id.* The main function of mitochondria is to supply the cell with energy via the metabolic conversion process known as oxidative phosphorylation. *See id.* Other important organelles include the cell membrane, nuclear membrane, endoplasmic reticulum, and lysosomes. *See id.*

45. *Id.* at 4. An enzyme's primary role is to encourage metabolic reactions in converting raw material into substances that maintain cellular function. *See id.*

46. *See id.*

47. *Id.* at 42-48. All genes contain DNA, but not all DNA is contained within a gene. *See id.*

48. *See id.*

49. *See* Lewin, *supra* note 18, at 48.

50. *See id.*

code word, referred to as a codon.[51] The successive triplets control the amino acid chain formation sequence of a protein molecule synthesized in the cell.[52]

The cloning of a DNA fragment allows scientists to produce infinite amounts of identical DNA from a single original molecule.[53] A clone is defined as a large number of cells or molecules identical to an original ancestral cell or molecule.[54] Following foreign DNA incorporation, bacterial plasmids[55] and phages[56] (host organisms) continue their usual lifestyle, thereby facilitating the continuous production (cloning) of the foreign DNA.[57] However, in work recently completed in Scotland and the United States, scientists successfully replicated a cluster of pre-fetal material and reimplanted these cells back into the womb of its maternal

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51. *See id.* A codon of GGC codes for the amino acid proline; AGA codes for the amino acid serine; and CTT codes for the amino acid glutamic acid. *See id.* A segment of DNA with -GGC-AGA-CTT- will eventually result in a segment of amino acids in protein form in exactly the same sequence exhibited by the initial strand of DNA. *See id.*

52. *Id.* at 31-32. Since almost all DNA is located in the nucleus of the cell and yet most of the functions of the cell are carried out in the cytoplasm, some means must be available for the genes of the nucleus to control the chemical reactions of the cytoplasm. *See id.* This is achieved through the intermediary of another type of nucleic acid, ribonucleic acid (RNA). *See id.* The formation of RNA is controlled by DNA in the cell nucleus in a process called transcription, whereby the code is transferred to the RNA. *See id.* The newly transcribed RNA is then transported from the nucleus into the cytoplasmic cavity where it controls protein synthesis. *Id.* at 89-90. During the synthesis of RNA, the two strands of the DNA molecule separate temporarily; one strand acting as a template for RNA synthesis. *See id.* The code triplets in the DNA cause the formation of complementary code triplets in the RNA and these codons control the sequence of amino acids in a protein chain to be synthesized later in the cytoplasm. *See id.* When one strand of DNA is used in this manner to cause the formation of RNA, the opposite strand remains inactive, but realigns itself with the other DNA strand after transcription is complete. *See id.*

53. *See id.*

54. *See Human Genome Project*, 20 LOS ALAMOS SCIENCE 16 (1992).

> The Human Genome project provides four separate definitions for the term "clone," two of which are relevant and are as follows: "1) A population of genetically identical unicellular organisms or viruses arising from successive replications of a single ancestral unicellular organism or virus, . . . and 4) A population of identical cells arising from the culture of a single cell of a certain type, such as a human fibroblast or a rodent-human hybrid cell containing a full set of rodent chromosomes and a single human chromosome."

Id.

55. *See* STRYER, *supra* note 30, at 127. A plasmid is an autonomous self-replicating extrachromosomal circular DNA. *See id.*

56. *Id.* at 128. A phage is a bacterial virus. *See id.*

57. *Id.* at 130. The cellular genome is a general term for the area in which the genetic material or genes of a cell is located and it is essentially indefinite in size. *See id.* The number and location of individual sequences can be changed by duplication, deletion, and rearrangement. *See id.* Therefore, it requires a generalized mechanism for packaging its DNA, insensitive to the total content or distribution of sequences. *See id.*

counterpart.[58] By doing so, these scientists have opened the door to the possibility of cloning nearly any organism.[59]

Initially, one recognizes the impact that such technology can have on modern agricultural advances. Moreover, scientists could reduce the possibility of the extinction of endangered species. The vast number of applications that these techniques provide raises many legal issues surrounding the patentability of a man-altered and nearly man-made genome. Each year the courts' and the Patent and Trademark Office encounter new issues concerning the patentability of biotechnology inventions. Trends that shed light on the patentability of cloned organisms are visible from the judicial branch and the agency entrusted to patent inventions.

C. Current Trends In Biotechnology Patent Law

Along with the other eighteen enumerated powers of Article I, the Framers of the Constitution had the insight to include intellectual property protection in Section 8: "[t]o promote the Progress of Science . . . by securing for limited Times to . . . inventors . . . the exclusive Right to their . . . Discoveries."[60] Since that time, the statutory provisions of patent law have undergone relatively minor changes.[61] This is due, in part, to the flexibility the system offers.[62] However, some patent attorneys might suggest that the attractiveness of this flexibility soon wears thin when either prosecuting a complicated biotechnology application or litigating a complex biotechnology patent case.[63] The potential for difficulties is extremely high when grappling with the patentability of cloned organisms.

Prior to 1980, the PTO declined to issue patents for living organisms.[64] The policy resulted from the agency's "longstanding belief that

58. *See* Wilmet, *supra* note 3, at 810; Wakayama, *supra* note 6; *Cloned Calf, supra* note 22.

59. *See* Winston, *supra* note 24. Dolly the lamb and Gene the bull-calf are not actually identical clones. *See id.* The enucleation step fails to alter the mitochondria of the enucleated/renucleated cell. *See id. See also* Lewin, *supra* note 18, at 31-32, 423-27. A portion of the genetic material in most cells, albeit slight, comes from the cytoplasmic mitochondria. Winston, *supra* note 24. *See also* Lewin, *supra* note 18, at 31-32, 423-27. Mitochondria are an important consideration when contemplating aging, due to the oxidative stress-induced mutations experienced by cells throughout their lifetimes. *Id.* at 31-32.

60. *See* U.S. Const. art I, § 8, cl. 8.

61. *See* Lorance L. Greenlee, *Biotechnology Patent Law: Perspective of the First Seventeen Years, Prospective on the next Seventeen Years*, 68 Denv. U. L. Rev. 127, 128-35 (1991).

62. *See id.*

63. *See id.*

64. *See* Moga, *supra* note 35, at 514.

living organisms were unpatentable products of nature."[65] This changed when the Supreme Court reviewed the rejection of a patent sought for a genetically engineered bacteria in *Diamond v. Chakrabarty*.[66]

Writing for a five-justice majority, Chief Justice Burger defined the patent issue narrowly and stated that the issue was not necessarily whether living organisms were patentable, but whether Chakrabarty's invention satisfied the "manufacture" or "composition of matter" requirements of the patent statute.[67] Justice Burger found the discussions in Congress during the recodification of the patent laws in 1951 particularly persuasive, directing attention to Congress' intent to "include anything under the sun that is made by man" as patentable subject matter.[68] Accordingly, the Supreme Court held that "[t]he language of . . . section [101] fairly embrace[d] respondent's invention,"[69] and thereby granted Chakrabarty a patent for his bioengineered bacteria.[70]

Following the lead of the Supreme Court, the Patent and Trademark Office, in 1987, issued a new ruling that declared nonnaturally occurring, living organisms patentable.[71] The new ruling served as a regulatory codification of the Supreme Court's interpretation of Title 35, section 101.[72] According to this interpretation, living organisms different from those occurring in nature are patentable under Title 35.[73] Thus, scientists seeking patent protection for their organism-based inventions need no longer struggle with the subject matter restriction on patenting living organisms, but still must satisfy the formidable obstacles that remain in

65. *See id. See e.g.* Parker v. Flook, 437 U.S. 584 (1978); Gottschalk v. Benson, 409 U.S. 63 (1978) (in two separate cases, the Supreme Court held in 1978 that "laws of nature, physical phenomena, and abstract ideas are not patentable").

66. *See* Diamond v. Chakrabarty, 447 U.S. 303 (1980).

67. *Id.* at 307.

68. *Id.* at 309. In testimony before Congress, P.J. Federico, a draftsman of the 1952 recodification, stated that "[U]nder section 101 a person may have invented a machine or manufacture, which may include anything under the sun that is made by man. . . ." *Hearings on H.R. 3760 Before Subcomm. No. 3 of the House Comm. on the Judiciary*, 82nd Cong. 37 (1951) (statement of P.J. Federico).

69. *See Chakrabarty*, 447 U.S. at 318.

70. *Id.* at 303. The Patent and Trademark Office's rejection of Chakrabarty's patent application was affirmed by the Patent Office Board of Appeals, but reversed by the Court of Customs and Patent Appeals. *See id.* The Supreme Court granted *certiorari* and affirmed the decision of the Court of Customs and Patent Appeals. *See id.*

71. *See* Donald J. Quigg, *Commissioner's Notice of Apr. 7, 1987*, 1077 OFF. GAZ. PAT. OF. 24 (Apr. 21, 1987). The Patent and Trademark Office [hereinafter PTO] interpreted the holding in *Chakrabarty* with great breadth and the Commissioner issued a formal ruling, stating that "[t]o the extent that the claimed subject matter is directed to a non-human 'nonnatural occurring manufacture or composition of matter—a product of human ingenuity' . . . such claims will not be rejected under 35 U.S.C.A. 101 as being directed to nonstatutory subject matter." *See id.*

72. *See id.*

73. *See id.*

the patent statute. These obstacles include the requirement of utility,[74] the necessity of showing nonobviousness,[75] and the obligation to draft an application such that one skilled in the art could practice the invention.[76]

1. *Utility*

Title 35 is the heart of patent law.[77] Section 101 of Title 35 states that, "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."[78] Simply stated, an invention must be useful to others to be patentable.[79]

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74. *See* 35 U.S.C.A. § 101 (1994). To meet the utility requirement of § 101, a claimed invention must be a "new and useful process, machine, manufacture, or composition of matter, or any new and useful process thereof." *See id.*

75. *See* 35 U.S.C.A. § 103 (1994). The nonobvious requirement of § 103 limits patent protection to inventions that would not "have been obvious at the time the invention was made to persons having ordinary skill in the art to which said subject matter pertains." *See id.*

76. *See* 35 U.S.C.A. § 112 (1994). The first paragraph of § 112 sets forth that each application prosecuted before the PTO must "contain a written description of the invention, and of the manner and process of making and using it, in such, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . ." *Id.*

77. *See* 35 U.S.C.A. § 101-376 (1994). Sections 101 through 376 pertain exclusively to the patent laws of the U.S. *See id.*

78. *See* 35 U.S.C.A. § 101 (1994).

79. Interview with Dr. Helgi Oskarsson, *infra,* note 112. Whether the real world includes the scientific public and the laboratory is unclear. *See id.* While a scientist may view his life work, culminating into something he thinks is patentable, useful to himself and his colleagues, such an achievement may not satisfy the requirement of real-world utility. *See id.* Inventions with no utility outside the experimental scientific domain are barred from patent protection. *See* Brenner v. Manson, 383 U.S. 519 (1966). However, the question of utility in the patent prosecution process is rebuttable. *See* James R. Nelson, *Prosecuting Biotechnology Patent Applications*, 464 PLI/PAT 633, 637 (1996). The inventor may submit the following in an attempt to overcome an Examiner's lack of utility assertions:

> a) literature references demonstrating that one skilled in the art would be convinced of the asserted utility, e.g., a reference demonstrating that the assays used in the specifications are "art recognized" ways of screening for the asserted utility;
>
> b) a declaration or affidavit including evidence that there is a reasonable correlation between a disclosed in vivo utility and an in vitro test result, Cross v. Izuka, 224 U.S.P.Q. 739, 747 (Fed. Cir. 1985), or between an in vivo result in an animal model and results in man, if the latter is what is effectively being claimed Ex parte Aggarwal, 23 U.S.P.Q. 2d 1334 (Bd. Pat. App. & Int'f 1992); and/or
>
> c) a declaration or affidavit including additional test results demonstrating the asserted utility in the claimed subject matter.

Id. at 637.

2. *Nonobviousness*

Once a patent application establishes the utility of an invention, the next hurdle is obviousness. To obtain a patent for a novel invention, an applicant must show that the "differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains."[80] In determining obviousness, a court must determine: 1) the scope and content of the prior art; 2) the differences between the prior art and the claims at issue; and 3) the level of ordinary skill in the pertinent art.[81]

A court also may consider "secondary considerations" which include: 1) commercial success; 2) long felt but unsolved needs; and 3) the failure of others to solve the problem.[82] Section 103 is not difficult for those to which the statute is aimed to protect and it requires "clear and convincing evidence of unobvious results in order to overcome a prima facie case of obviousness."[83]

3. *Enablement*

Enablement may be the trickiest issue when considering the patentability of cloned organisms. Section 112 of Title 35 requires that, to be patentable, specifications of patent must enable any person skilled in the art to which it pertains to make and use the claimed invention without undue experimentation.[84] The purpose of Section 112 is to facilitate the teachings of the patent by the inventor such that a person skilled in the art could follow and repeat the invention without wasting "undue" time and resources.[85] An inadequate enablement results in a rejection by the

80. *See* 35 U.S.C.A. § 103 (1994).

81. *See In re O'Farrell*, 853 F.2d 894, 902 (1988); Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966) (the *Graham* test serves as the controlling test for obviousness); Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 958 (Fed. Cir. 1986).

82. *See, e.g., Graham*, 383 U.S. at 17-18; Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co., 730 F.2d 1452, 1461 (Fed. Cir. 1984); Cable Elect. Products, Inc. v. Genmark, Inc., 770 F.2d 1015, 1027 (Fed. Cir. 1985); Safety Car Heating & Lighting Co. v. General Elect. Co., 155 F.2d 937, 939 (2d Cir. 1946).

83. *See Ex parte Thim*, 22 U.S.P.Q.2d 1941, 1944 (Pat. App. 1992) (the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences affirmed the PTO examiner's rejection of the Thim patent application based on the conclusion "that the yield achieved using yeast as an expression vehicle is not so significantly superior that it overcomes the prima facie case of obviousness").

84. *See* 35 U.S.C.A. § 112 (1994).

85. *See* Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1571 (Fed. Cir. 1991), *reh'g denied* 18 U.S.P.Q.2d 1896 (Fed. Cir. 1991); United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989).

Patent and Trademark Office for an otherwise patentable invention.[86]

Recent Patent and Trademark Office history demonstrates numerous patents issued for transgenic animals.[87] Presuming that an application for a newly cloned creature passes the requirements of utility, nonobviousness, and enablement, the path appears open for patent protection.[88] The basic scientific concepts that apply to creating a transgenic animal and a cloned animal are virtually identical.[89]

In addition to the technical similarities between transgenic animals and cloned animals, claims in patents issued for transgenic animals usually include patent protection for the subject animal as well as an ancestor of the transgenic animal.[90] Thus, not only were the specific animals patented, but all of the subsequently bred offspring received patent protection as well.[91] This aspect of patenting transgenic animals has important implications to the patentability of cloned organisms.

III. ANALYSIS

Just as scientists face new challenges to utilize their expanding set of technological tools,[92] the Federal Courts must face unique challenges

86. *See* Nelson, *supra* note 79, at 639-655.

87. *See* Kathryn M. Albers, *Transgenic Mice Which Overexpress Nerve Growth Factor*, U.S. Patent 5,602,309 (Feb. 11, 1997) [hereinafter Patent '309]; Barbara Cordell, *Transgenic Mice Displaying the Amyloid-Forming Pathology of Alzheimer's Disease*, U.S. Patent No. 5,387,742 (Feb. 7, 1995) [hereinafter Patent '742]; Michael J. Dewey, *Alpha-1-Acid Glycoprotein Transgenic Mice*, U.S. Patent No. 5,648,597 (July 15, 1997) [hereinafter Patent '597]; Paulus Krimpenfort & Antonius Berns, *Transgenic Mice Depleted in Mature T-Cells and Methods for Making Transgenic Mice*, U.S. Patent 5,434,340 (July 18, 1995) [hereinafter Patent '340]; Paulus Krimpenfort & Antonius Berns, *Transgenic Mice Depleted in Mature T-cells and Methods for Making Transgenic Mice*, U.S. Patent No. 5,175,384 (Dec. 29, 1992) [hereinafter Patent '384]; Paulus Krimpenfort and Antonius Berns, *Transgenic Mice Depleted in a Mature Lymphocytic Cell-type*, U.S. Patent No. 5,591,669 (Jan. 7, 1997) [hereinafter Patent '669]; Nils Lonberg and Robert M. Kay, *Transgenic Non-Human Animals for Producing Heterologous Antibodies*, U.S. Patent No. 5,625,126 (Apr. 29, 1997) [hereinafter Patent '126]; Vincent Racaniello et al., *Transgenic Mouse Expressing DNA Sequences Encoding the Human Poliovirus Receptor*, U.S. Patent No. 5,631,407 (May 20, 1997) [hereinafter Patent '407]; Thomas E. Wagner & Xiao-Zhuo Chen, *Virus-resistant Transgenic Mice*, U.S. Patent No. 5,175,385 (Dec. 29, 1992) [hereinafter Patent '385]; *See also* Patent '550, *supra* note 40; Darwin J. Prockop et al., *Transgenic Mice Expressing a Mutated Human Collagen Gene*, U.S. Patent No. 5,663,482 (Sept. 2, 1997) [hereinafter Patent '482].

88. *See* 35 U.S.C.A. §§ 101, 103, 112 (1994).

89. *See* Patent '866, *supra* note 37 and *Cloned Calf*, *supra* note 22 (the techniques and processes utilized for producing a transgenic mouse are strikingly similar to those utilized for developing a cloned calf).

90. *See* Patent '866, *supra* note 38 (the '866 patent claims "[a] . . . non-human . . . animal . . . or an ancestor of the animal, at an embryonic stage").

91. *See id.*

92. *See* Sobral, *supra* note 13.

resulting from expanding biotechnology.[93] This is especially true in the area of patent law, and more specifically, patent law as it relates to cloned organisms.

Examining the patent landscape in an attempt to locate an ideal location to place patents for cloned organism reveals transgenic animal patents as offering the most analogous situation.[94] When comparing the two years prior to 1995 with the two years following 1995, one notices a dramatic increase in the patents issued for transgenic animals.[95] Pat-

93. *See* MacGillivray et al., *supra* note 14, at 469. The numerous examples of the diverse nature of current ongoing research illustrate the potential for continual increases in patent applications to the PTO. *See id.*

94. *See* Patent '385, *supra* note 88. This patent claims in part, "[a] transgenic mouse whose somatic and germ cells contain and express a gene coding for human beta interferon at a level sufficient to provide antiviral activity in said mouse, said gene having been introduced into said mouse or an ancestor of said mouse at an embryonic stage . . . ." *See id. See also* Patent '384, *supra* note 88. This patent claims, in part, "[a] transgenic mouse having a phenotype characterized by the substantial absence of mature T-cells otherwise naturally occurring in said mouse, said phenotype being conferred by a transgene contained in the somatic and germ cells of said mouse . . . ." *See id. See also* Patent '742, *supra* note 88. This patent claims, in part, "[a] transgenic mouse whose cells contain a DNA sequence, comprising . . . [a] nerve tissue specific promoter; and a DNA sequence . . . wherein the promoter and DNA sequence . . . are . . . linked . . . and integrated in the genome of the mouse and expressed . . . . " *See id. See also* Patent '340, *supra* note 88. This patent claims, in part, "[a] transgenic mouse having a phenotype characterized by the substantial absence of mature T-cells otherwise naturally occurring in said mouse . . . being incapable of mediating T-cell maturation in said transgenic mouse." *See id. See also* Patent '669, *supra* note 88. This patent claims, in part, "[a] transgenic mouse having a phenotype characterized by a disruption of the . . . endogenous heavy chain and an absence of plasma B cells producing naturally occurring mouse antibodies . . ." *See id. See also* Patent '309, *supra* note 88. This patent claims, in part, "[a] transgenic mouse whose somatic and germ cells contain and express a gene coding for mouse nerve growth factor, said mouse exhibiting hyperinnervation when compared to a normal mouse, and said gene having been introduced into fertilized mouse embryo . . . ." *See id. See also* Patent '126, *supra* note 88. This patent claims, in part, "[a] transgenic mouse containing in its genome a transgene comprising in operable linkage a plurality of human V genes . . . in response to antigenic stimulation." *See id. See also* Patent '407, *supra* note 88. This patent claims, in part, "[a] transgenic mouse which has stably integrated into the genome of its somatic and germ cells the DNA sequence . . . which encodes a human poliovirus receptor, wherein expression of said DNA sequence results in the mice becoming susceptible to polio virus infection." *See id. See also* Patent '597, *supra* note 88. This patent claims, in part, "[a] transgenic mouse or progeny thereof whose somatic and germline cells contain a stably integrated DNA sequence selected from the . . . rat AGP gene which is expressed in the mouse to produce rat alpha-1-acid glycoprotein . . . ." *See id. See also* Patent '550, supra note 40. This patent claims, in part, "[a] mouse homozygous for a targeted disruption in exon-encoding DNA of the estrogen receptor gene, wherein said targeted disruption . . . is characterized by a lack of estrogen responsiveness"). *See also* Patent '482, *supra* note 88. This patent claims, in part, "[a] transgenic mouse whose somatic and germ cells contain at least one endogenous, normal gene for type I procollagen, and a . . . mini-gene . . . wherein expression of said . . . mini-gene . . . results in the formation of abnormalities in the skeleton of the mouse . . ." *Id.*

95. *See supra* note 94. *See also infra* notes 96-98.

ents issued since 1995 include: one for a transgenic pig,[96] a transgenic bovine,[97] and many for transgenic mice.[98] Accordingly, the patents issued over the last two years demonstrate a trend in the Patent and Trademark Office of accepting the patentability of transgenic animals.[99] Moreover, an issued patent is presumed valid.[100] Therefore, the trend of patenting transgenic animals has as its likely successor the patenting of cloned animals.

The trend toward the patentability of transgenic animals started in late 1992, when the Patent and Trademark Office ended a four and one-half year drought on transgenic patent approval.[101] By granting three separate inventors patents, the agency acknowledged the utility, nonobviousness, and enabling characteristics of the inventors' applications.[102] Furthermore, the patents issued not only provided protection for the specific animals, but extended patent protection to their respective offspring

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96. *See* Robert F. Seamark and Julian Wells, *Transgenic Pigs*, U.S. Patent No. 5,573,933 (Nov. 12, 1996) [hereinafter Patent '933]. This patent claims, in part, "[a] method for preparing a transgenic pig which overexpresses porcine growth hormone . . . ." *Id.*

97. *See* Herman A. DeBoer et al., *Method of Producing a Transgenic Bovine or Transgenic Bovine Embryo,* U.S. Patent No. 5,633,076 (May 27, 1997) [hereinafter Patent '076]. This patent claims, in part, a method whereby a genetically altered cattle results from a manipulated embryo that has undergone transplantation into the womb of a cow. *See id.*

98. *See* Patent '385; Patent '384; Patent '742; Patent '340; Patent '669; Patent '309; Patent '126; Patent '407; Patent '597; Patent '550; and Patent '482 *supra* note 88. *See also* Cornelius P. Terhorst & Baoping Wang, *Transgenic Immunodeficient Animal Models*, U.S. Patent No. 5,530,179 (June 25, 1996) [hereinafter Patent '179]; *See also* Nils Lonberg & Robert M. Kay, *Transgenic Non-Human Animals Capable of Producing Heterologous Antibodies of Various Isotypes*, U.S. Patent No. 5,661,016 (Aug. 26, 1997) [hereinafter Patent '016]; Beatrice Mintz, *Transgenic Animal Model System for Human Cutaneous Melanoma*, U.S. Patent No. 5,550,316 (Aug. 27, 1996) [hereinafter Patent '316].

99. *See supra* notes 94, 96-98.

100. *See* 35 U.S.C.A. § 282 (1994). "A patent shall be presumed valid. Each claim of a patent . . . shall be presumed valid . . . the burden of establishing invalidity of a patent or any claim therof shall rest on the party asserting such invalidity." *See id. See also* Roper Corp. v. Litton Sys., Inc., 757 F.2d 1266, 1270 (Fed. Cir. 1985). "A patent is born valid. It remains valid until a challenger proves it was stillborn or had birth defects, or it is no longer viable as an enforceable right." *Id.* at 1270.

101. *See* Terri A. Jones, *Patenting Transgenic Animals: When the Cat's Away, the Mice Will Play*, 17 VT. L. REV. 875, 921-22 (1993). The PTO issued a patents to the following individuals on Dec. 29, 1992: Dr. Philip Leder, inventor of the Harvard Mouse, was granted U.S. Patent No. 5,175,384 for his mouse designed that is susceptible to the development of benign prostatic hypertrophy (a form of prostate problems exhibited in older men); Drs. Paulus J.A. Krimpenfort & Antonius J.M. Berns for a mouse developed to investigate the rejection phenomenon observed during tissue transplantation; and Drs. Thomas E. Wagner and Xiao-Zhuo Chen for a mouse genetically engineered to examine viral infection resistance. *See id.*

102. *See* 35 U.S.C.A. §§ 101, 103, 112 (1994).

as well.[103]

This aspect of patenting transgenic animals has important implications relating to the patentability of cloned organisms. Transgenically created animals are deemed unnatural by definition of patent law.[104] Since naturally propagated offspring of unnaturally occurring (transgenic) animals are patentable, then it follows that unnaturally propagated (cloned) offspring of unnaturally occurring (transgenic) animals are patentable as well.

The similarities between transgenic organisms and cloned organisms far outweigh the differences, but any inventor seeking patent protection for a cloned organism will have to meet the well-established requirements.[105] The three threshold requirements for the patentability of any invention are utility, nonobvious, and enablement.[106] Applying these thresholds to the biotechnological field of wholesale genomic cloning presents special circumstances of first impression.[107] This analysis reviews the standards applied during the adolescence of biotechnology patent law and concludes with a prospective look at these standards as applied to the patentability of non-human cloned genomes.[108]

A. Section 101: Utility Requirements

The modern era of patent law had its genesis in *Diamond v. Chakrabarty*.[109] In 1980, the United States Supreme Court decided the *Chakrabarty* case which deemed microorganisms as patentable inventions where such organisms resulted from manufactured or genetically engineered matter.[110]

Not all claims asserting the patent rights based on engineered structure are automatically protected by current patent law.[111] Inventors of modified natural products must distinguish their invention from that

103. *See* Patent '866, *supra* note 38 (the '866 patent claims "[a] . . . non-human . . . animal . . . or an ancestor of the animal, at an embryonic stage").

104. *See* Diamond v. Chakrabarty, 447 U.S. 303 (1980). *See also Quigg, supra* note 71 (Commissioner Quigg released a statement acknowledging the patentability of man-altered, naturally occurring organisms and deemed them unnatural because they did not occur in nature without mans' genetic manipulation).

105. *See* 35 U.S.C.A. §§ 101-376 (1994).

106. *See* 35 U.S.C.A. §§ 101, 103, 112 (1994). The standards applied in every patent prosecution are utility, nonobviousness, and enablement. *See id.*

107. *See I.B.M. U.S. Patent Database* (visited Oct. 24, 1997) <http://www. ibm.com/patents> (search revealed no patents issued for cloned organisms).

108. *See* 35 U.S.C.A. § 101, 103, 112. The standards applied in every patent prosecution are utility, nonobviousness, and enablement. *See Id.*

109. *See Chakrabarty*, 447 U.S. at 303.

110. *Id.* at 316.

111. *Id.* at 315.

which occurs naturally.[112] However, the Patent and Trademark Office has allowed claims directed towards manipulated nucleotide sequence ligations to demonstrate this distinction.[113] From a modern technical standpoint, this is not a scientific hardship in some instances.[114] Nevertheless, it may be quite impressive when one recognizes the technical difficulty in satisfying Section 101 by engineering a product that both distinguishes itself from that occurring in nature and maintains its desired activity.[115]

Section 101 imposes the following standard to determine utility: "[T]he test is whether one with ordinary skill in the art to which the invention pertains would question the assertions of utility, and if so, whether the inventor has supplied such evidence through tests or otherwise as would convince such a person of the invention's asserted utility.[116]"

For biotechnology patent applications before the Patent and Trademark Office, examiners interpret "utility" as a "practical utility" or real-world utility.[117] Accordingly, if an inventor can establish that his or her invention will serve some practical application in the real world, it will at least past the muster of Section 101.[118]

The Harvard mouse had no trouble meeting the utility requirement in that the mouse was more susceptible to cancer, thereby making it an

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112. *See id.*

113. *See Transposon-Containing DNA Cloning Vector and Uses Thereof*, U.S. Patent No. 5,645,991 [hereinafter Patent '991]; *Heterologous Polypeptides Expressed in Filametous Fungi, Processes for Making Same, and Vectors for Making Same*, U.S. Patent No. 5,578,463 [hereinafter Patent '463]; James R. Bunzow et al., *Cloned Genes Encoding the D.Sub.1 Dopamine Receptor*, U.S. Patent No. 5,389,543 (Feb. 14, 1995) [hereinafter Patent '543]; *Cloning of a Gene Encoding for the Growth Hormone Releasing Hormone Receptor*, U.S. Patent No. 5,644,046 [hereinafter '046]. *See id.*

114. *See* ROBERT L. DRYER & GENE F. LATA, EXPERIMENTAL BIOCHEMISTRY, at 250 (1989).

115. Interview with Dr. Helgi Oskarsson, M.D., Dept. of Internal Med., Univ. of Iowa (Sept. 22, 1997) [hereinafter Oskarsson]. From a laypersons standpoint, the biotechnology techniques may seem overwhelming and extremely difficult. *See id.* While the processes do require an intimate familiarity with proper technique, these types of procedures have become routine for thousands of scientists in hundreds of labs throughout the nation and the world. *See id.*

116. *See id.* The difficulty lies not within the mechanics of the technique itself, but in modifying a sequence of DNA, introducing it into the target cell, and behave in manner consistent with the scientists expectations and experimental design. *See id.* Therefore, to develop a new, non-naturally occurring cell type and inducing it to produce a biologically useful and commercially viable product is easier said than done. *See id.*

117. *See* CHISM, PATENTS, at 4.36.1 (1987).

118. *See* Oskarsson, *supra* note 115 (discussing a scientist's perspective on patentability of biotechnology under the utility requirement).

ideal model to test innovative cancer therapies.[119] While the study of terrible diseases is an important and very useful application of genetic engineering, the same could be said for a cloned organism. The capability of making hundreds of copies is more useful than the, at times, unpredictable results demonstrated by transgenic animals.[120] Accordingly, from a utility standpoint, the transgenic animals are in no better position than their cloned counterparts. Thus, the standard imposed by the utility requirement will not act as a barrier to the patentability of cloned organisms.

B. UNIQUENESS/NONOBVIOUSNESS: TRANSGENIC ANIMALS

While *Chakrabarty* opened the door to modern biotechnology patent law, it failed to address one issue: whether scientific developments resulting in man-made, non-human animals, not occurring in nature, were patentable under Section 101.[121] This, however, was determined in *Ex Parte Allen,* but in an interesting context.[122] The organism subject to patent scrutiny in *Ex Parte Allen* was a type of oyster that, due to its infertile state, was edible twelve months of the year.[123] Unfortunately for Allen, this fertility information was so well known by those skilled in the art that it rendered the invention obvious, and therefore, unpatentable under Section 103.[124]

The first patent issued asserting protective rights over a genetically unique and distinguishable transgenic mouse occurred in 1988.[125] From a basic standpoint, this genetic line of mice was no different than a genetic cell line with a modified genome.[126] This differs from cloning be-

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119. *See* Michael B. Landau, *Multicellular Vertebrate Mammals as "Patentable Subject Matter"* Under 35 U.S.C.A. § 101 (1994)*: Promotion of Science and the Useful Arts or an Open Invitation for Abuse?* 97 DICK. L. REV. 203, 209 (1993).

120. *See* Stephen G. Whiteside, Ph.D. *Patents Claiming Genetically Engineered Inventions: A Few Thoughts on Obtaining Broad Property Rights*, 30 NEW ENG. L. REV. 1019, 1027 (1996).

121. *See* Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980).

122. *See Ex parte Allen*, 2 U.S.P.Q.2d 1425 (P.T.O. Bd. Pat. App. & Int. 1987) (non-transgenic oysters were properly rejected from obtaining patent rights on grounds of obviousness; improper rejection on ground of living, natural entity).

123. *Id.* at 1431.

124. *See* 37 C.F.R. § 1.101 (1995); United States Dep't of Commerce, Patent & Trademark Office, MANUAL OF PATENT EXAMINING PROCEDURE § 702, 706 (6th ed. 1995) [hereinafter MPEP].

125. *See* Patent '866, *supra* note 37. See also LEWIN, *supra* note 18, at 736. Transgenic animals are created by introducing exogenous (foreign) DNA sequences into the germ line via addition to the egg. *See id.*

126. *See* Kate H. Murashige, *Genome Research and Traditional Intellectual Property Protection—A Bad Fit?*, 7 RISK: HEALTH, SAFETY AND ENV'T 231, 236 (1996). Drs. Venter and Adams, on behalf of the National Institutes of Health [hereinafter NIH] filed applications with the PTO seeking patent protection on several thousand nucleotide sequences

cause each transgenic "copy" of the transgenic mice line, while deriving a similar genome, does not result in an identical genome.[127] Nevertheless, the cloned organism patents are analogous to the transgenic mice patents that are supposedly under review by the Patent and Trademark Office.[128] Accordingly, when interpreting the statutory provisions of patent law as applied to the cloned organism patents, the transgenic animal patents will provide dispositive pedagogy.

C. ENABLEMENT

One of the difficulties in grasping the unique issues surrounding the patentability of a cloned organism lies in the enabling aspects of claim interpretation.[129] The patent application must include a "written de-

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from cDNA libraries. *See id.* The special segments of cDNA, known as "expressed sequence tags" or ESTs, were very short (only 200 - 500 base pairs in length) and the NIH had not demonstrated that the ESTs coded for anything. *See id.* However, the NIH proceeded under the guise that it was more likely than not that the ESTs were of a significant length to be unique enough to belong to only one gene. *See id.* However, while the sequences were new and presumably not obvious, their utility was nondemonstrable and the utility argument could not be rebutted. *Id.* at 236. Accordingly, the applications were withdrawn, but that has not stopped a flood of similar applications from entering through the private sector. *See id.* One estimate is that it will require eight years of review before these applications are processed. *See id.*

127. *See* Marsha L. Montgomery, *Building a Better Mouse—and Patenting It: Altering the Patent Law to Accommodate Multicellular Organisms*, 41 CASE W. RES. L. REV. 231, 238 (1990).

128. *See generally* U.S. Patents cited *supra* note 94.

129. *See* TITLE I-BIOTECHNOLOGICAL MATERIAL PATENTS, 103rd Cong., 1st Sess., 1993 [hereinafter TITLE I]. The House of Representatives and the Senate are currently attempting to resolve issues surrounding the Biotechnology Patent Protection Act of 1993. *See id.* The Bill passed by the Senate, S. 298, [hereinafter S-298] seeks to amend 35 U.S.C.A. § 103 (1994) by adding the following subsections:

> (c) Notwithstanding any other provisions of this section, a claimed process of making or using a medicine, manufature, or composition of matter is not obvious under this section if -
>
> (1) the machine, manufacture, or composition of matter is novel under Section 102 of this title and nonobvious under this section;
>
> (2) the claimed process is a biotechnical process as defined in subsection (d); and
>
> (3)(A) the machine, manufacture, or composition of matter, and the claimed process invention at the time it was made, were owned by the same person or subject to an obligation of assignment to the same person; and
>
> (3)(B) claims to the process and to the machine, manufacture, or composition of matter-(I) are enentitled to the same effect filing date; and
>
> (ii) appear in the same patent application, different patent applications, or patent which is owned by the same person and which expire or is set to expire on the same date.
>
> (d) For the purposes of this section, the term 'biological process' means any method of making or using living organisms, or parts thereof, for the purposes of making or modifying products. Such term includes recombinant DNA, recombinant RNA, and other processes involving site specific manipulation of genetic material.

scription of the invention" disclosing enough information to enable one skilled in the relevant art to make and use the invention.[130] The shear magnitude of a genomic region makes it impossible to identify every detail of the invention, and therefore makes it rather difficult to assert the validity of a patent to a patent examiner or over the arguments posed by a prospective infringer.[131]

Accordingly, an inventor has two choices: 1) either describe the invention in limited detail and expose the patent to loss of property rights to inventions that are "neither described nor enabled"; or 2) describe the invention from a variety of perspectives and run the risk of a narrow interpretation of the claims.[132]

Section 112 of Title 35 requires that:

> "the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."[133]

Id.

Additionally, S-298 proposes to amend 35 U.S.C.A. § 282 (1988) through the addition of the following:

> A claim issued under the provisions of Section 103(c) of this title on a process of making or using a machine, manufacture, or composition of matter shall not be held invalid under Section 103 of this title solely because the machine, manufacture, or composition of matter is described to lack novelty under Section 102 of this title or to be obvious under Section 103 of this title.

Id.

130. *See* 37 C.F.R. § 1.101 (1995); MPEP § 702, 706 (6th ed. 1995).

131. *See* LEWIN, *supra* note 18, at 499. The compression of DNA is characterized by the packing ratio. *See id.* The smallest human chromosome contains 4.6 X 10^7 base pairs of DNA, which is equivalent to 1.4 cm of extended DNA. *Id.* at 500.

132. *See* 35 U.S.C.A. § 112 (1994). Para. 1 provides that "[t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same . . . . " *Id.*

133. *See* 35 U.S.C.A. § 112 (1994). *See also* Seymour v. Osborne, 78 U.S. (11 Wall.) 516, 555 (1871). Interestingly, a very similar issue was the subject of the Supreme Court's decision over one-hundred and twenty-five years ago. *See id.* "Whatever may be the particular circumstances under which the publication takes place, the account published, to be of any effect to support such a defense, must be an account of a complete and operative invention capable of being put into practical operation." *Id. See also* Cohn v. United States Corset Co., 93 U.S. 366, 370 (1876). "[U]nless the . . . description does exhibit the invention in such a full and intelligible manner as to enable persons skilled in the art . . . to comprehend it without assistance from the patent, or to make it, or repeat the process claimed, it is insufficient to invalidate the patent." *Id. See also* WILLIAM H. FRANCIS, PATENT LAW 193 (4th ed. 1995). "Whether a particular prior art patent or publication contains an 'enabling' invention disclosure or description of an invention and thus negates novelty or demonstrates obviousness must be determined in the particular factual context of each case." *Id.*

To satisfy the Section 112 requirements, three distinct provisions are mandated: 1) a written description of the invention; 2) an enabling disclosure; and 3) disclosure of the best mode of practicing the invention.[134]

In the course of biotechnology patent prosecution, many times the main issue is whether the disclosure would require "undue experimentation" to be enabling.[135] Issues surrounding the predictability of the art and the scope of claims are among the most hotly contested sources of litigation in the field of biotechnology.[136]

However, one mechanism to satisfy the enabling requirement of Section 112 is to deposit a sample of the subject matter of the patent application (i.e. a strain of cells, bastulla cell from which clones are derived, etc.) with the Patent and Trademark Office, thereby guaranteeing accessibility to the public.[137] But, as the Court pointed out in *Hybritech, Inc. v. Abbott Laboratories*, "It is well settled . . . that biological materials need not be deposited when the invention can be practiced without undue experimentation from biological materials available in the prior art."[138] Effectively, this is the same as giving possession of the invention to the public.[139]

Following the precedent established with the transgenic mice patents,[140] and considering it in the context of the now abandoned copy DNA ("cDNA") sequence patents prosecuted by the National Institutes of Health ("NIH"), it is apparent that cloned organisms are much more closely related to the transgenic animals, in terms of patentability and invention, as opposed to fragments of cDNA.[141] Surely, when compared the NIH applications for cDNA, any potential cloned organism inventor will have no trouble showing utility.[142] Manipulation through cloning of dairy cows to improve milk output characteristics is undoubtedly useful

134. *See* North Am. Vaccine, Inc. v. Am. Cyanamid Co., 7 F.3d 1571, 1577 (Fed. Cir. 1993). It is the patent applicants' responsibility to disclose their inventions adequately. *Id.* at 1577.

135. *See* 35 U.S.C.A. § 112 (1994).

136. *See* Brian P. O'Shaughnessy, *The False Inventive Genius: Developing a New Approach for Analyzing the Sufficiency of Patent Disclosure Within the Unpredictable Arts*, 7 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 147, 166 (1996).

137. *See* Matthew B. Tropper, *Patentability of Genetically Engineered Life-Forms: Legal Issues and Solutions*, 25 J. MARSHALL L. REV. 119, 134-135 (1991).

138. *See* Hybritech, Inc. v. Abbott Lab., 4 U.S.P.Q.2d 1001, 1011 (C.D. Cal. 1947), aff'd, 7 U.S.P.Q.2d. 1191 (Fed. Cir. 1988).

139. *See Ex parte Goeddel*, 5 U.S.P.Q.2d 1449 (Bd. Pat. App. & Int'f. 1985).

140. *See generally* Patents cited *supra* note 94.

141. *See* Scott A. Chambers, *Comments on the Patentability of Certain Inventions Associated with the Identification of Partial cDNA Sequences*, 23 AIPLA Q.J. 53, 57 (1995).

142. *See id.*

to society.[143]

The problem lies in the enablement.[144] By depositing a sample of the blastullar cells giving rise to the cloned progeny, an applicant could satisfy the requirements of Section 112.[145] Presumably, this would only serve to allow others to attempt to determine what genetic modifications had been made, but this is analogous to searching for a penny in an ocean.[146]

Uniqueness issues could be satisfied in the same manner in which medical doctors administer paternity suits.[147] These tests are qualitative and quantitative while providing a very high statistical standard.[148]

Issues surrounding the patentability of cloned organisms may be the subject of congressional inquiry and congress may opt to adopt legislation as discussed supra.[149] Nevertheless, from this analysis of the similarities between cloned organisms and transgenic animals, it is clear that, absent a few bumps in the road, cloned organisms are as patentable as genetically engineered mice or pigs.[150]

IV. CONCLUSION

Biotechnology patent law is progressing through its late teens, having successfully survived the adolescent years.[151] The question of the

143. *See Bovine Cloning to Benefit Human and Animal Heath Care Fields* (visited Sept. 3, 1997) <http://www.infigen.com/tech-cloning.html>.

144. *See* O'Shaughnessy, *supra* note 136, at 182.

145. *See* Tropper, *supra* note 137, at 134-35.

146. *See id.*

147. *See* Diana Sheiness, *Patenting Gene Sequences*, 78 J. PAT. & TRADEMARK OFF. SOC'Y 121, 122 (1996).

148. *See* DRYER & LATA, *supra* note 114, at 249. Each enzyme must be characterized on an individual basis; nevertheless, these enzymes are of immeasurable value in probing (mapping) the sequences of DNA derived from phages, plasmids, and other genomic structures. *See id.* Through their successful utilization, it is also possible to make deliberate modifications of DNA at known sites, enabling the observation of the modifing effect on protein translation. *See id.*

149. *See* TITLE I, *supra* note 129.

150. *See* LEWIN, *supra* note 18, at 635. While Courts have held that cDNA sequences are patentable, it is unclear whether a patent will issue for an entire genome, or even a significant portion of it. *See id.* cDNA is a single-stranded DNA complementary to an RNA, synthesized from it by reverse transcription in vitro. *Id.* at 736. Wholesale gentic cloning is most closely characterizable with the patent issed for the transgenic mouse. *See id.* Transgenic animals are created by introducing exogenous (foreign) DNA sequaences (plasmids) into the germ line via addition to the egg. *See id.*

151. *See Hearing on the Competitveness of U.S. Biotechnology Industry Before the Subcomm. on Science, Technology, and Space of the Senate Comm. on Commerce, Science, and Transportation*, 103rd Cong., 2d Session, 18, 29 (1994) [hereinafter *U.S. Biotech Industry*]. Since its genesis, the United States biotechnology industry has released to the public 23 new pharmaceutical compounds and holds nearly 300 other compounds awaiting FDA approval. *See id. See also* Biotech's Latest Wrinkle (visited Oct. 13, 1997) <http:/bi-

patentability of genetically engineered animals is answered by the numerous examples of transgenic animal patents issued by the Patent and Trademark Office.[152]

Hesitantly at first, the Patent and Trademark Office followed the lead of the Supreme Court's decision in *Chakrabarty*,[153] and further defined the question of patenting living organisms in the Board of Patent Appeals and Interferences' nonobvious rejection in *Ex parte Allen*.[154] While *Allen* exposed the failure of the altered oysters to meet Section 103's nonobvious requirement,[155] the man-made mollusk satisfied the subject matter and utility requirements of Section 101.[156]

The acceptance of cloned organisms as patentable inventions by the Patent and Trademark Office is imminent. Undisputedly, patents have issued for a variety of transgenic animals, thereby showing that a genetically altered non-human organism can satisfy the requirements of patentability. No reason exists to suggest that the same process will not occur for cloned organisms or the precursors to cloned organisms. Patents have issued for unnatural, transgenically created animals.[157] A patented invention is presumed valid until proven otherwise.[158] Since naturally propagated offspring of unnaturally occurring (transgenic) animals are patentable, then it follows that unnaturally propagated (cloned) offspring of unnaturally occurring (transgenic) animals are patentable as

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otech.nature.com/cgibin/wilma.cgi-/v15n3.862430-442.html> [hereinafter *Biotech*]. A total twenty-seven Initial Public Offerings and forty-seven follow-on offerings during 1996 raised $5.4 billion in equity capital, bringing the combined market cap for all biotech companies to $205 million. *See id.* This is due, in part, to the increasing number of publically traded biotechnology companies operating in the United States competing for investor dollars. *See id.* The number of biotechnology companies in the United States increased from fewer than 100 before 1970 to around 1,330 in 1994. *See id.* Global sales of biotechnology derived products grew from zero to $5.9 billion in the period from 1980 to 1992, increasing to $7.0 billion by 1993. *See Hearings, supra* note 151.

152. Patent '385; Patent '384; Patent '742; Patent '340; Patent '669; Patent '309; Patent '126; Patent '407; Patent '597; Patent '550; and Patent' 482, *supra* note 94.

153. *See* Diamond v. Chakrabarty, 447 U.S. 303, 308 (1980). The Supreme Court held that "a genetically engineered bacterium designed for the bioremediative purpose of scavenging oils was patentable due to the significant alterations made to naturally occurring bacteriam via multiple cDNA transfection." *See id.* Because the genetically engineered bacterium was significantly different that that occurring naturally, it was deemed man-made for the purposes of patentability. *See id.*

154. *See Ex parte Allen*, 2 U.S.P.Q.2d 1425, 1427 (P.T.O. Bd. Pat. App. & Int. 1987).

155. *See* 35 U.S.C.A. § 103 (1994).

156. *See* 35 U.S.C.A. § 101 (1994). Section 101 establishes a standard of utility for a patent to issue for an invention. *See id.*

157. *See generally* Patents cited *supra* notes 94, 96-98.

158. *See* 35 U.S.C.A. § 282 (1994). *See also* Roper Corp. v. Litton Systems, Inc., 757 F.2d 1266, 1270 (Fed. Cir. 1985). "A patent is born valid. It remains valid until a challenger proves it was stillborn or had birth defects, or it is no longer viable as an enforceable right." *Id.* at 1270.

well. Looking to the precedent established by the transgenic patents, a patent for a cloned non-human organism is more than likely under review at this time.

The moratorium on human cloning[159] will allow for a thoughtful resolution of the deeply entrenched ethical issues that surround human cloning. Imagining twenty identical copies of a human will remain the fodder of science fiction screenwriters and novelists.[160] But keep looking to the pastures and the hillsides for herds of identical cattle and sheep grazing the countryside. A closer look may reveal the mark *patent pending*.

Timothy G. Hofmeyer

159. *See* Ted C. Fishman, *You've Nothing to Fear from My Clone and Me*, U.S.A. TODAY, Aug. 4, 1997, at 13A. In June of 1997, the Nat'l Bioethics Advisory Comm'n established the parameters of cloning research and recommended a ban on human cloning. *See id.*

160. *See* ORWELL, *supra* note 2.