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COMPUTER-AIDED DRUG DESIGN USING PATENTED COMPOUNDS: INFRINGEMENT IN CYBERSPACE?

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INTRODUCTION

Suppose you are a research chemist[1] who specializes in the synthesis of organic compounds.[2] You have created such a compound and obtained a United States patent to protect your rights in it.[3] Your goal is to perform experiments to determine what

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* J.D. Candidate, June 2002. This Comment is dedicated to my daughter, Ella Kathryn Field, whose life began in 2000. Thank you to Professor Janice Mueller for suggesting this topic.

1. Chemistry is "[t]he science of the composition, structure, properties, and reactions of matter, especially of atomic and molecular systems." THE AMERICAN HERITAGE DICTIONARY OF THE ENGLISH LANGUAGE 328 (3d ed. 1996) [hereinafter AMERICAN HERITAGE DICTIONARY].

2. A compound is a "substance consisting of atoms . . . of two or more different elements in definite proportions that cannot be separated by physical means." AMERICAN HERITAGE DICTIONARY, *supra* note 1, at 388. An organic compound is a compound containing carbon atoms. ROBERT THORNTON MORRISON & ROBERT NEILSON BOYD, ORGANIC CHEMISTRY 1 (6th ed. 1992). Living organisms produce organic compounds. *Id.* The synthesis of organic compounds involves using simple compounds as "building blocks" to make "larger and more complicated compounds." *Id.*

3. A United States patent gives an inventor "the right to exclude others from making, using, offering for sale, or selling the [patented] invention throughout the United States." 35 U.S.C. § 154(a)(1) (1994). *Accord* Prima Tek II, L.L.C. v. A-Roo Co., 222 F.3d 1372, 1379 (Fed. Cir. 2000). This protection lasts for a term of twenty years from the application date. 35 U.S.C. § 154(a)(2).

To qualify for U.S. patent protection, an invention must fall into one of four categories: (1) "process"; (2) "machine"; (3) "manufacture"; or (4) "composition of matter." 35 U.S.C. § 101 (1994). A chemical compound falls into the composition-of-matter category. *See In re* Kirchner, 305 F.2d 897, 903 (C.C.P.A. 1962) (noting that a chemical compound is a "'composition of matter' within the contemplation of" 35 U.S.C. § 101). An invention also must be useful, novel, and non-obvious. 35 U.S.C. §§ 101-103 (1994 & Supp. 1999).

A patent is set forth in a "specification." 35 U.S.C. § 112 (1994). The specification must include claims that "particularly point[] out and distinctly claim[] the subject matter" of the invention. *Id.* It is these claims that actually "define[] the scope of the protected invention." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 619 (Fed. Cir.

other compounds will react with your patented compound.[4] You hope that these experiments will lead you to the discovery of a new drug.[5]

Meanwhile, a second chemical researcher has pulled a copy of the patent of your compound off the Internet.[6] The patent describes your compound in great detail,[7] including the spatial coordinates for each of the thousands of atoms of which a molecule of your compound is composed.[8] She plugs these coordinates into a computer program designed to create models of molecules such as yours.[9] Her goal, like yours, is to determine what other compounds will react with your patented compound, and she likewise hopes that her efforts will lead to the discovery of a new drug.

However, unlike you, the second researcher is not performing any experiments using your real compound. She is using a computer simulation of your patented compound. Doing so, the second researcher discovers what other compounds will react with your compound and quickly hones in on the most promising possibility.[10] She now goes to the lab, synthesizes the actual compound she discovered using her computer, and verifies that it works as the computer predicted it would.[11] The second researcher applies for a patent on the drug she has just discovered–the one you wanted to find. However, she discovered the drug by using *your* patented compound in cyberspace.

1995) (citing Yale Lock Mfg. Co. v. Greenleaf, 117 U.S. 554, 559 (1886)).

4. A chemical reaction is "[a] change or transformation in which a substance decomposes, combines with other substances, or interchanges constituents with other substances." AMERICAN HERITAGE DICTIONARY, *supra* note 1, at 1503.

5. *See* discussion *infra* pp. 1006-07 (discussing traditional methods of drug discovery).

6. The U.S. Patent and Trademark Office (USPTO) web site features a searchable database of patents. *Databases: Patent Full-Text and Bibliographic*, *at* http://www.uspto.gov/patft/index.html (last modified Jan. 16, 2001). The database's coverage ranges from the first patent issued in 1790 to the most current patents. *Id.*

7. A patent must contain a written description of the invention in "full, clear, concise, and exact terms." 35 U.S.C. § 112. This written description must describe how to make and use the invention "as to enable any person skilled in the art to which it pertains . . . to make and use" it. *Id.*

8. *Cf., e.g.*, U.S. Patent No. 5,942,428, at cols. 22-146 (issued Aug. 24, 1999) (listing spatial coordinates for each of the 3,471 atoms comprising a molecule of the one of the patent's subject compounds).

9. One definition of a model is a "set of mathematical equations which are capable of representing accurately the chemical phenomenon under study." ALAN HINCHLIFFE, MODELING MOLECULAR STRUCTURES 9 (1996).

10. *See* discussion *infra* Part I Section B. pp. 1006-10 (discussing how researchers identify candidate drug molecules using molecular modeling in structure-based drug design).

11. *See* discussion *infra* Part I Section B pp. 1006-10 (discussing how researchers evaluate candidate drug molecules using structure-based drug design methods).

You believe that the second researcher infringed your patent by making and using your compound to discover her drug.[12] You quickly place a call to your friendly neighborhood patent lawyer, and you tell him of your plight. He tells you that he believes that under the current state of the law, the second researcher did not infringe your patent.[13] He says that the patent on your chemical compound covers the actual compound only, and not the spatial coordinates of the compound that the second researcher used in her computer model.[14] He offers to do some further research, perhaps hoping to find a useful law review comment directly on point. However, he believes that you are out of luck in your infringement claim.

This Comment addresses the issue of whether such unauthorized cyberspace use of a chemical compound is or should be infringement. Part I provides background information on the science that underlies the legal issues. Part II analyzes whether the unauthorized making or using of a patented compound in cyberspace is infringement under existing law. Finally, Part III contends that making or using a patented compound in cyberspace should be infringement for a variety of policy reasons and also proposes two possible solutions.

To fully appreciate the legal issues involved, the reader must first be familiar with underlying scientific principles.

I. PROTEINS, ENZYMES, AND DRUG DESIGN

This Part provides background information on the underlying scientific principles involved in the issue of whether making and using a compound in cyberspace is or should be infringement. Section A discusses proteins and enzymes. Then Section B discusses

12. *See* 35 U.S.C. § 271 (Supp. 1999) (stating that "whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States . . . infringes the patent"). If every limitation of the patent claim is found in the allegedly infringing invention, then a court will find literal infringement. *See, e.g.*, Tate Access Floors, Inc. v. Maxcess Techs., Inc., 222 F.3d 958, 964 (Fed. Cir. 2000) (stating that "[l]iteral infringement requires that every limitation of the patent claim can be found in the accused device"). Even if an accused invention "does not literally infringe a claim, [it] may still infringe under the doctrine of equivalents." *Id.* The basic issue under the doctrine of equivalents is whether the differences between the patented invention and allegedly infringing invention are "insubstantial." Kemco Sales, Inc. v. Control Papers Co., 208 F.3d 1352, 1364 n.6 (Fed. Cir. 2000). The traditional three-part test for determining equivalence is whether the inventions "perform substantially the same function, in substantially the same way, to achieve substantially the same result." *Id.* at 1364.

13. *See* discussion *infra* Section II pp. 1010-19 (analyzing whether making or using a patented chemical compound in cyberspace is infringement under existing law).

14. *See In re* Papesch, 315 F.2d 381, 391 (C.C.P.A. 1963) (holding that "the thing that is patented is not the formula but the compound identified by it").

traditional and modern approaches to drug design.

A. Proteins and Enzymes

Proteins are the primary molecules of interest in designing drugs because they are involved in almost all essential life processes.[15] Proteins are composed of chains of amino acids.[16] A short chain of amino acids is a peptide, while a longer chain is a polypeptide.[17] When a polypeptide chain contains more than approximately fifty amino acids, the chain is then called a protein.[18] Of particular importance is that enzymes are a type of protein.[19] Enzymes are catalysts[20] that allow essential chemical reactions to occur in cells.[21] Without enzymes, cellular reactions would not be

15. DOROTHY E. SCHUMM, ESSENTIALS OF BIOCHEMISTRY 107 (2d ed. 1995); SPENCER L. SEAGER & MICHAEL R. SLABAUGH, ORGANIC AND BIOCHEMISTRY FOR TODAY 239 (2d ed. 1994). Drug design also involves types of molecules other than proteins, such as DNA and RNA. Charles E. Bugg et al., *Drugs by Design*, SCI. AM., Dec. 1993, at 92, 93.

The human body contains a tremendously large number of proteins. *See* SCHUMM, *supra*, at 240-41 (describing "that a typical human cell contains 9000 different proteins and that a human body contains about 100,000 different proteins"). In fact, half the dry weight of the human body is protein. George D. Rose, *No Assembly Required*, SCIENCES, Jan.-Feb. 1996, at 26, 27.

16. SCHUMM, *supra* note 15, at 107; SEAGER & SLABAUGH, *supra* note 15, at 230. An amino acid is a type of organic acid. *Id.* An amino acid incorporated into the chain of a protein is called an amino acid residue. *Id.* at 235.

Although hundreds of amino acids exist, there are only twenty different amino acids that make up naturally occurring proteins. *Id.* at 233. Ten of these amino acids are called "essential amino acids" because the human body is incapable of producing them itself. JOHN MCMURRY, FUNDAMENTALS OF ORGANIC CHEMISTRY 456-57 (2d ed. 1990). Humans must obtain these essential amino acids by eating food that contains protein. *Id.*

Proteins are generally very large molecules. SEAGER & SLABAUGH, *supra* note 15, at 238. For example, the molecular weight of glucose, a sugar, is 180 atomic mass units ("amu"). *Id.* In contrast, even a small protein such as hemoglobin has a molecular weight of 65,000 amu. *Id.*

17. SEAGER & SLABAUGH, *supra* note 15, at 235. The bonds that hold amino acids together in a chain are called peptide bonds. SCHUMM, *supra* note 15, at 110.

18. SEAGER & SLABAUGH, *supra* note 15, at 235. Scientists frequently use the terms polypeptide and protein interchangeably. *Id.*

19. SCHUMM, *supra* note 15, at 117; SEAGER & SLABAUGH, *supra* note 15, at 257.

20. A catalyst is a compound that speeds up a chemical reaction without itself being used up in the reaction. SEAGER & SLABAUGH, *supra* note 15, at 258. Enzymes are very efficient catalysts, some of which can increase the speed of a reaction by a factor of 10^{20}. *Id.* at 257. Also, enzymes are often very specific in the types of reactions that they catalyze. *Id.* at 258. Another important property of enzymes is that cells can control and regulate the catalytic behavior of enzymes. *Id.* at 259.

21. *Id.* For example, an enzyme called DNA ligase is necessary for DNA synthesis in cells. SCHUMM, *supra* note 15, at 118-19.

An everyday example of an enzyme in action is the discoloration of fruits and vegetables. SEAGER & SLABAUGH, *supra* note 15, at 266. The en-

fast enough to support life.[22]

Proteins can function in many different ways[23] in biological systems due to their structural complexity.[24] The chains of amino acids that make up protein molecules are often "twisted and folded into a complex three-dimensional structure."[25] Figure 1, below, shows a schematic drawing of the three-dimensional structure of a protein molecule.

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zyme polyphenoloxidase catalyzes a chemical reaction that converts certain compounds in the tissue cells of the fruit or vegetable into brown-colored products. *Id.*

Defective enzymes often cause hereditary diseases. *Id.* at 260. For example, albinism, Niemann-Pick disease, phenylketonuria, and Tay-Sachs disease are all caused by enzyme defects. *Id.*

22. SEAGER & SLABAUGH, *supra* note 15, at 257.

23. For example, proteins are responsible for the metabolism of food, defining the skeleton and skin, transporting oxygen, regulating respiration, immune system response, DNA replication, "and serv[ing] as both signal and sensor for the network of chemical messages that interconnects . . . organs." Rose, *supra* note 15, at 27.

24. SEAGER & SLABAUGH, *supra* note 15, at 242.

25. *Id.* This "looping and coiling" of a protein molecule is not random. MORRISON & BOYD, *supra* note 2, at 1235. Instead, forces between the molecules that make up the protein interact to give the protein its natural, most stable structure. *Id*

The structure of a protein has four levels: primary, secondary, tertiary, and quaternary. SCHUMM, *supra* note 15, at 110-13; SEAGER & SLABAUGH, *supra* note 15, at 242.

The primary structure of a protein is "[t]he linear sequence of amino acid residues" in the chain. *Id. Accord* SCHUMM, *supra* note 15, at 110. Genetics determines the primary structure of a protein molecule. MORRISON & BOYD, *supra* note 2, at 1235. The primary structure of a protein then determines its secondary structure. SCHUMM, *supra* note 15, at 111. The secondary structure refers to how a protein chain is arranged into patterns. *Id.*; SEAGER & SLABAUGH, *supra* note 15, at 242. An example of secondary structure is the spring-like shape of the alpha-helix, the familiar shape of a DNA strand. SCHUMM, *supra* note 15, at 111; SEAGER & SLABAUGH, *supra* note 15, at 243.

A protein's "tertiary structure is the configuration that the protein takes in space." SCHUMM, *supra* note 15, at 112. The "bending and folding of a protein into a specific three-dimensional shape" is its tertiary structure. SEAGER & SLABAUGH, *supra* note 15, at 245.

The quaternary structure of a protein involves the arrangement of a protein molecule with other protein molecules. SCHUMM, *supra* note 15, at 113. *See infra* note 26 and accompanying figure (depicting the quaternary structure of a protein). Quaternary structure involves the combination of individual protein chains, called subunits. SCHUMM, *supra* note 15, at 113; SEAGER & SLABAUGH, *supra* note 15, at 248. For example, the well-known hemoglobin molecule is an almost round protein molecule whose quaternary structure consists of four subunits held together. *Id.* at 248-49.

The use of modern technology, including high-speed computers and nuclear magnetic resonance imaging, tremendously simplifies the process of determining the atom-by-atom structure of a protein molecule. Rose, *supra* note 15, at 28.

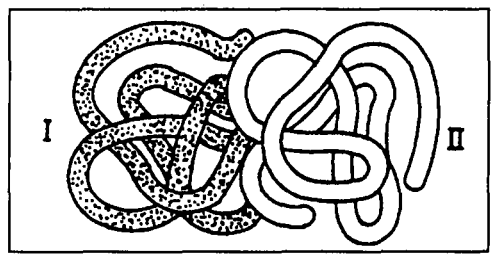

Fig. 1[26]

It is this shape of an enzyme molecule that largely determines its function.[27] Enzymes function by reacting with other molecules called substrates.[28] At a particular place on the enzyme molecule, "there is a site of a size, shape, and chemical nature just right to hold the" substrate.[29] This location is called the active site.[30] For the enzyme to function properly, the enzyme and substrate "must fit together like a lock and key."[31] Thus, when chemists set out to design a new drug, they look for an appropriately shaped molecule so that the drug molecule binds to the active site of a particular enzyme.[32] The drug molecule thus impairs the enzyme's activity.[33]

Scientists use these principles of protein and enzyme chemistry in their approaches to designing new drugs.

B. Traditional and Modern Approaches to Drug Design

Drug design using traditional methods is a slow process.[34]

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26. U.S. Patent No. 5,331,573, fig. 3C (issued July 19, 1994). This drawing represents a quaternary structure of a protein containing two subunits, labeled "I" and "II." *Id.* at col. 5, ll. 39-43.

27. Rose, *supra* note 15, at 26.

28. MORRISON & BOYD, *supra* note 2, at 1112. A substrate is a "substance that undergoes a chemical change catalyzed by an enzyme." SEAGER & SLABAUGH, *supra* note 15, at 259.

29. *See* MORRISON & BOYD, *supra* note 2, at 1112 (discussing the binding of an enzyme with a molecule of acetaldehyde as the substrate).

30. SEAGER & SLABAUGH, *supra* note 15, at 262.

31. *Id.* This lock-and-key analogy is attributable to Emil Fischer (1852-1919), a German chemist who was an early pioneer in protein research. *Id.*; The Nobel Foundation, *Biography of Hermann Emil Fischer*, *at* http://www.nobel.se/chemistry/laureates/1902/fischer-bio.html (last modified June 16, 2000). Fischer was awarded the Nobel Prize in Chemistry in 1902. The Nobel Foundation, *Chemistry 1902*, *at* http://www.nobel.se/chemistry/laureates/1902/index.html (last modified June 16, 2000).

32. Bugg et al., *supra* note 15, at 93.

33. *Id.*

34. *See id.* at 92 (comparing slow, traditional methods of drug design with modern structure-based design); Matthew J. Plunkett & Jonathan A. Ellman,

Researchers have discovered many of the drugs currently marketed today either by "chance observation or by systematic screening of large numbers of natural and synthetic substances."[35] In the traditional method of designing drugs, a researcher first identifies a substance that shows promise as the starting point for a new drug.[36] This substance is known as a lead compound.[37] The researcher must then make numerous individual modifications to the structure of the lead compound.[38] After each and every modification, the researcher performs experiments to determine how these changes to the lead compound's structure affect the compound's properties.[39] Even after the researcher obtains a lead compound that has the desired effect, the researcher often must continue to modify the compound to attempt to increase its potency or reduce its toxicity.[40] Eventually, the researcher may develop a compound that is both potent and safe.[41]

However, drawbacks exist with this traditional method of drug design.[42] With the traditional method, for every one drug that ends up on the market, researchers probably experimented with and rejected thousands of other compounds along the way.[43] Therefore, this method is inefficient, time-consuming, and costly.[44] The traditional approach to drug design is like "making and testing many keys in order to find one that happens to fit a lock of un-

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Combinatorial Chemistry and New Drugs, SCI. AM., Apr. 1997, at 68, 69 (comparing traditional drug design with modern techniques of combinatorial chemistry).

35. Bugg et al., *supra* note 15, at 92. Researchers typically look for signs of the activity they are seeking wherever they can find it, including in "diverse collections of synthetic compounds or of chemicals derived from bacteria, plants[,] or other natural sources." Plunkett & Ellman, *supra* note 34, at 69.

36. Plunkett & Ellman, *supra* note 34, at 69.

37. *Id.*

38. *Id.*

39. *Id.* After each modification, the researcher must test both the chemical and biological properties of the lead compound. *Id.*

40. Bugg et al., *supra* note 15, at 92.

41. Plunkett & Ellman, *supra* note 34, at 69. In spite of the apparent inefficiency of the traditional approach to drug design, it has "provided treatments for everything from minor aches to life-threatening illnesses." Bugg et al., *supra* note 15, at 92.

42. Bugg et al., *supra* note 15, at 92; Plunkett & Ellman, *supra* note 34, at 69.

43. Plunkett & Ellman, *supra* note 34, at 69.

44. Bugg et al., *supra* note 15, at 92; Plunkett & Ellman, *supra* note 34, at 69. *See also* Manuel A. Navia, *New Tactics Available to Better Fight Diseases of the Poor*, KNIGHT-RIDDER TRIB. BUS. NEWS: BRIDGE NEWS—NEW YORK, Feb. 1, 2000, *available in* 2000 WL 10329134 (discussing how drug companies cannot sustain their current high levels of research-and-development spending, so they must develop more efficient methods of drug development to better provide drugs for the poor). Advancing from a lead compound to an actual drug for sale in pharmacies can take "many years and hundreds of millions of dollars" using the traditional method of drug design. *Id.*

known shape."[45]

Scientists needed to improve the efficiency of drug design by "moving away from expensive trial-and-error methods."[46] Fortunately, modern technology has come to the rescue.[47] Advances in the power of computer hardware and software have made possible the process of "rational drug design."[48] Rational drug design involves the use of molecular modeling computer software that simulates in cyberspace the structure and reactivity of molecules of interest in designing drugs.[49] While the traditional approach to drug design is similar to "making and testing many keys in order to find one that happens to fit a lock of unknown shape," the rational drug design approach involves "prior study of the shape and arrangement of tumblers in a lock [to] lead to rapid design of an effective key."[50]

Such computer modeling of molecules developed throughout the twentieth century.[51] A model is "a replica or facsimile of a real object."[52] Long before scientists used computers for modeling, chemists created physical representations of the structure of molecules.[53] In 1929, Paul Dirac[54] made this famous statement: "[T]he underlying physical laws necessary for the mathematical theory

45. Bugg et al., *supra* note 15, at 92.

46. Navia, *supra* note 44. *Accord* T.L. Graybill et al., *Enhancing the Drug Discovery Process by Integration of High-Throughput Chemistry and Structure-Based Drug Design*, *in* MOLECULAR DIVERSITY AND COMBINATORIAL CHEMISTRY: LIBRARIES AND DRUG DISCOVERY 16 (Irwin M. Chaiken & Kim D. Janda eds., 1996) (stating that "[a]n imperative across the drug industry is to accelerate the drug discovery process").

47. *See generally* Bruce R. Gelin, *Current Approaches in Computer-Aided Molecular Design*, *in* COMPUTER-AIDED MOLECULAR DESIGN: APPLICATIONS IN AGROCHEMICALS, MATERIALS AND PHARMACEUTICALS 1 (Charles H. Reynolds et al. eds., 1995) (discussing the history of computer simulation methods in chemistry, giving an overview of common techniques and applications, and examining trends and future prospects); Bugg et al., *supra* note 15 (discussing how structure-based design has succeeded in developing new drugs); Plunkett & Ellman, *supra* note 34 (describing how technology has allowed the creation of combinatorial chemistry techniques to greatly speed the process of drug development).

48. Gelin, *supra* note 47, at 1-2 & 5.

49. *Id.* at 5. A researcher who creates a particular system of rational drug design can even obtain patent protection for it. *See* U.S. Patent No. 5,331,573 (issued July 19, 1994) (describing a "method of design of compounds that mimic conformational features of selected peptides").

50. Bugg et al., *supra* note 15, at 92.

51. Gelin, *supra* note 47, at 1-3.

52. *Id.* at 3.

53. *Id.*

54. Paul Adrien Maurice Dirac (1902-84) helped found the study of quantum mechanics. *P.A.M. Dirac*, *at* http://hussle.harvard.edu/~clevy/dirac.html (last modified Aug. 4, 1996). Dirac won the Nobel Prize for Physics in 1933. The Nobel Foundation, *Physics 1933*, *at* http://www.nobel.se/physics/laureates/1933/index.html (last modified June 16, 2000).

of . . . the whole of chemistry are . . . completely known."[55] However, chemists continued to develop new methods of using mathematical theories to describe real molecules.[56] In the early 1960s, a researcher first used a computer to perform calculations necessary to model several different molecules.[57] The increase in power of computer hardware and knowledge from previous simulations allowed researchers to create greatly improved software for molecular modeling.[58]

One method of rational drug design is called structure-based design.[59] Unlike the traditional approach to drug design, the starting point in structure-based design is not the drug.[60] Instead, it is the drug's "molecular target in the body."[61] After the researcher identifies this target molecule, she next must determine its three-dimensional structure—particularly the structure of the molecule's active site.[62] The researcher then uses a molecular modeling computer program to test candidate drug molecules to see how well they fit into the active site.[63] Next, the researcher actually makes the compounds that the computer simulation indicated are promising.[64] She then experiments with the actual drug candidate and the target molecule to determine whether the computer model was accurate.[65] After determining why the candidate either succeeded or failed, the researcher can then return to the computer and test modifications that may prove to be more successful.[66]

Molecular modeling software is not perfect, however.[67] Programs cannot exactly predict a target molecule's structure or the fit of a candidate molecule within the target's active site.[68] How-

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55. Gelin, *supra* note 47, at 1.

56. *Id.*

57. *Id.* The researcher was J.B. Hendrickson, who used a computer to calculate the molecular energies of the molecules cyclopentane, cyclohexane, and cycloheptane. *Id.* at 1 & 10 n.8.

58. *Id.* Creators of such molecular modeling software can obtain patent protection for the software. *See* U.S. Patent No. 5,742,290 (issued Apr. 21, 1998) (describing a "molecular orbital modeling system with an improved function processor").

59. Bugg et al., *supra* note 15, at 92.

60. *Id.*

61. *Id.*

62. *Id.* at 94.

63. *Id.* This fit must be tight to ensure that the drug will be both potent and specific. *Id.* If the drug remains attached to the target for a long time, then the required dosage of the drug can be lower. *Id.* If the drug fits perfectly into the target molecule's active site, then it is less likely to react with other molecules to cause side effects. *Id.*

64. Bugg et al., *supra* note 15, at 94

65. *Id.* Modeling software is not perfect, so some of the compounds fail these experiments. *Id.*

66. *Id.*

67. *Id.* at 98.

68. *Id.*

ever, the ability of these programs to make such predictions is improving as researchers learn more about the underlying theory of the software.[69] The ideal computer simulation would lead a researcher immediately to a drug's best composition, so that the researcher would not have to make and experiment on less-effective candidates.[70]

The use of molecular modeling software to assist in rational drug design has become quite common.[71] There is reason to believe that such software will continue to improve.[72] Thus, the use of molecular modeling software in rational drug design will likely become even more important in the future.[73] Therefore, the issue of whether making or using a patented compound in cyberspace is infringement can only increase in importance.

II. INFRINGEMENT IN CYBERSPACE UNDER EXISTING LAW

This Part analyzes whether making or using a patented compound in cyberspace is infringement under existing law. Section A defines the issue, establishes an example patent for analysis, and discusses the general principles of patent infringement analysis. Next, Section B considers claim construction of the example patent. Then, Section C analyzes whether making or using a patented compound in cyberspace is literal infringement under existing law. Finally, Section D analyzes whether making or using a patented compound in cyberspace is infringement under the doctrine of equivalents.

A. The Issue

The Introduction section above describes the situation at is-

69. Bugg et al., *supra* note 15, at 98.

70. *Id.* This technique is at its best when a researcher can "make the best drug on the first try." *Id.*

71. *See* Gelin, *supra* note 47, at 5 (stating that "[a]mong the life sciences perhaps the leading application [of molecular modeling], in terms of use and investment in equipment, people, and software, has been rational drug design.") (emphasis omitted). *Cf.* Guan-seng Khoo & Thiam-seng Koh, *Using Visualization and Simulation Tools in Tertiary Science Education*, 17 J. COMPUTERS MATHEMATICS & SCI. TEACHING 5, 5 (1998) (describing the widespread use of computer-assisted molecular modeling and advocating for using such techniques in college-level science education); Teresa Ortega, *Pushing the Parameters in Computational Chemistry*, CHEMICAL MARKET REP., Mar. 9, 1998, at FR19, FR19 (characterizing "the market for molecular modeling software programs [as] quite mature"); Marvin R. Rich, *The Art of Molecular Modeling*, 55 ART J. 40, 40-41 (1996) (describing the author's incorporation of computer simulations of molecules into his artwork).

72. Bugg et al., *supra* note 15, at 98.

73. *See* John Rennie, *The Elite Inventions*, SCI. AM., Mar. 1999, at 8 ("The computer . . . was suggested as the most important invention of the past two millennia. Given another few years, who's to say that . . . rational drug design wouldn't be, too?").

sue here.[74] A researcher obtains a patent on a protein crystal, which the researcher plans to use in designing a new drug. The patent describes the spatial coordinates of the atoms of the compound in detail. A competitor uses these coordinates in a molecular-modeling computer program, quickly discovers candidate drug compounds, and soon synthesizes and patents the desired drug.

As an example, suppose that our hypothetical researcher obtained United States Patent Number 5,942,428, entitled "Crystals of the Tyrosine Kinase Domain of Non-Insulin Receptor Tyrosine Kinases" ("the '428 patent").[75] Tyrosine kinases are enzymes that, among other things, signal processes in immune-system cells.[76] When this signaling becomes out of control, inflammatory responses and diseases can occur.[77] Thus, an inhibitor compound that blocks the effect of tyrosine kinases may be the basis for drug design.[78] The '428 patent has four claims.[79] Claims one and two describe crystals of a particular tyrosine kinase of a specified size.[80] Claims three and four describe the same tyrosine kinase but define the molecule by its three-dimensional atomic coordinates.[81]

In our example, assume that our hypothetical competitor used the atomic spatial coordinates from claim three of the '428 patent in a molecular-modeling computer program.[82] Therefore, the issue is whether, by making and using the patented compound from the '428 patent in cyberspace, the competitor infringed the researcher's patent.

The United States Patent Act[83] provides that patent infringement occurs when anyone "without authority makes, uses, offers to sell, or sells any patented invention, within the United States . . . during the term of the patent therefor."[84] In determining infringement, a court must consider the patent's claims, which actually "define[] the scope of the protected invention."[85]

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74. *See* discussion *supra* Introduction pp. 1001-03 (describing a hypothetical situation in which a competing researcher develops a new drug using data from the patent on a researcher's compound).

75. U.S. Patent No. 5,942,428 (issued Aug. 24, 1999).

76. Alexander Levitzki & Aviv Gazit, *Tyrosine Kinase Inhibition: An Approach to Drug Development*, 267 SCI. 1782, 1782 (1995).

77. *Id.* These diseases include cancer, arteriosclerosis, and psoriasis. *Id.*

78. *Id.* From 1985 to at least 1995, many researchers began projects geared towards synthesizing compounds that can inhibit the activity of the "signaling pathways" that tyrosine kinases trigger. *Id.*

79. U.S. Patent No. 5,942,428, at cols. 349-50.

80. *Id.* at col. 349.

81. *Id.* at cols. 349-50.

82. *See id.* at cols. 22-273 (listing spatial coordinates for each atom of the compounds from claims three and four).

83. 35 U.S.C. §§ 1-376 (1994 & Supp. 1999).

84. 35 U.S.C. § 271(a) (Supp. 1999).

85. Bell Communications Research, Inc. v. Vitalink Communications Corp.,

A court determining infringement employs a two-step analysis.[86] In the first step, the court construes the claim in question "to determine its scope and meaning."[87] In the second step, the fact finder compares the construed claim to the invention accused of infringement.[88] If the fact finder determines that each and every element of the claim is present in the accused invention, then this accused invention literally infringes the patent claim.[89] Even if the accused invention "does not literally infringe [the] claim [, it] may still infringe under the doctrine of equivalents."[90] Infringement under the doctrine of equivalents occurs if every claim element is present in the accused invention "either literally or equivalently."[91]

B. Claim Construction

The first step in a patent infringement analysis is claim construction, in which a court interprets the "scope and meaning" of the claims in question.[92] When a court construes a claim, it first considers intrinsic evidence.[93] Intrinsic evidence includes the specification[94] of the patent at issue and its prosecution history, if the history is in evidence.[95] Normally, a court can successfully

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55 F.3d 615, 619 (Fed. Cir. 1995) (citing Yale Lock Mfg. Co. v. Greenleaf, 117 U.S. 554, 559 (1886)). *See also supra* note 3 (discussing the requirement that patents include claims).

86. *See, e.g.*, Tate Access Floors, Inc. v. Maxcess Techs., Inc., 222 F.3d 958, 964 (Fed. Cir. 2000) (stating that "[a] determination of infringement requires a two-step analysis").

87. *Id.* A jury does not construe claims. Markman v. Westview Instruments, Inc., 517 U.S. 370, 372 (1996). Instead, the court must interpret a patent's claims as a matter of law. *Id.*

88. *See, e.g.*, *Tate Access Floors*, 222 F.3d at 964 (stating that "[s]econd, the claim as properly construed must be compared to the accused device or process").

89. *See, e.g., id.* (stating that "[l]iteral infringement requires that every limitation of the patent claim be found in the accused device" and that "[d]etermination of infringement . . . is a question of fact").

90. *Id. See generally* CHISUM ON PATENTS §§ 18.02-18.04 (2000) [hereinafter CHISUM] (providing an overview of the doctrine of equivalents).

91. *Tate Access Floors*, 222 F.3d at 964. *See* discussion *infra* Part II Section D pp. 1015-19 (discussing what the law considers to be "equivalent").

92. *Tate Access Floors*, 222 F.3d at 964.

93. *See, e.g.*, Optical Disc Corp. v. Del Mar Avionics, 208 F.3d 1324, 1334 (Fed. Cir. 2000) (stating that when "interpreting an asserted claim, we look first to the intrinsic evidence of record" (citing Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)).

94. A patent's specification includes both "a written description of the invention" and the invention's claims. 35 U.S.C. § 112.

95. *See, e.g.*, *Optical Disc*, 208 F.3d at 1334 (defining "intrinsic evidence" as "the patent itself, including the claims, the specification and, if in evidence, the prosecution history"). Patent "prosecution" is "[t]he process of obtaining a patent from the Patent Office." ROBERT PATRICK MERGES, PATENT LAW AND POLICY: CASES AND MATERIALS 35 (2d ed. 1997). "Prosecution history" refers to the "arguments and claim amendments made during prosecution to obtain

construe a claim using only intrinsic evidence.[96] However, if the intrinsic evidence by itself is insufficient, then the court may also consider extrinsic evidence.[97]

A court begins its analysis of the intrinsic evidence by examining the words that make up the claim itself.[98] The court normally gives claim terms their ordinary meanings.[99] The court may use the dictionary definition of a term to determine its ordinary meaning.[100] However, if the patent's specification shows that the patentee intended to give a "novel meaning to a claim term," then the court uses that meaning rather than the term's ordinary meaning.[101]

A court construing claim three of our example '428 patent would first examine the words of the claim. At issue here is the word "crystal." Claim three reads: "A *crystal* of the catalytic domain of FGF-R tyrosine kinase, wherein said catalytic domain has a three-dimensional structure characterized by the atomic structure coordinates of Table 3."[102] The dictionary definition of the term "crystal," which the court may use to determine the term's ordinary meaning,[103] is "[a] homogenous solid formed by a repeating, three-dimensional pattern of atoms, ions, or molecules and having fixed distances between constituent parts."[104] However, the specification of the patent defines "crystal" as "a polypeptide in crystalline form."[105] The dictionary definition here does not contradict the definition from the specification,[106] so the court would

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allowance of the patent." BLACK'S LAW DICTIONARY 1221 (6th ed. 1990) (defining "prosecution history estoppel").

96. *Optical Disc*, 208 F.3d at 1334.

97. *See, e.g., id.* (stating that "extrinsic evidence may be considered if needed to assist in determining the meaning or scope of technical terms in the claims"). "Extrinsic evidence" is external to the patent and prosecution history, "such as expert testimony, inventor testimony, dictionaries, and technical treatises and articles." *Vitronics Corp.*, 90 F.3d at 1584.

98. *Optical Disc*, 208 F.3d at 1334.

99. *Id.*

100. *Id.* at 1335. Dictionaries are technically extrinsic evidence, because they are not "part of an integrated patent document." *Vitronics*, 90 F.3d at 1584 n.6. However, the Court of Appeals for the Federal Circuit has stated that dictionaries "are worthy of special note." *Id.* A dictionary definition may allow a judge "to better understand the [claim's] underlying technology." *Id.* Thus, the court may use a dictionary definition in the "intrinsic evidence" stage of claim construction, provided that "the dictionary definition does not contradict any definition found in . . . the patent documents." *Id.*

101. *Optical Disc*, 208 F.3d at 1334-35.

102. U.S. Patent No. 5,942,428, at cols. 349-50 (issued Aug. 24, 1999) (emphasis added).

103. *Optical Disc*, 208 F.3d at 1335.

104. AMERICAN HERITAGE DICTIONARY, *supra* note 1, at 451.

105. U.S. Patent No. 5,942,428, col. 3, ll. 58-59.

106. In fact, the specification's definition is circular. Therefore, the dictionary definition of "crystal" is necessary to interpret the word "crystalline" in the

conclude that the patentee did not intend "crystal" to mean something out of the ordinary. Therefore, the court can use the dictionary definition of "crystal" in its construction of the claim.[107] Having completed claim construction, the first step in infringement analysis, the court can now move on to the second step.

C. Literal Infringement

As the second step in a patent infringement analysis, a jury[108] compares the construed claim to the invention accused of infringement.[109] For the accused invention to literally infringe a patent claim, the jury must find "every limitation of the patent claim . . . in the accused device."[110] In our hypothetical example, assume that the court has construed the word "crystal" to mean a homogenous *solid* having certain characteristics.[111]

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specification.

107. *Cf. Optical Disc*, 208 F.3d at 1334-35 (stating that "[w]ithout evidence in the patent specification of an express intent to impart a novel meaning to a claim term, the term takes on its ordinary meaning"). This Comment's hypothetical example assumes that the prosecution history is not relevant to the claim construction analysis. If it were, the court would have to consider the prosecution history before being able to conclude that the dictionary definition of "crystal" applied. *Cf. id.* (stating that the court considers the prosecution history "if [it is] in evidence").

An example similar to this Comment's hypothetical example occurred when a district court construed a chemical composition claim involving the term "oligomer." Abbott Lab. v. Alra Lab., Inc., No. 92-C-5806, 1997 WL 667796, at *2-*5 (N.D. Ill. Oct. 24, 1997). The relevant claim at issue "recites . . . four features: (i) An *oligomer*; (ii) having a 1:1 molar ratio of sodium valproate and valproic acid; (iii) of the unit formula, $(CH_3CH_2CH_2)_2CHCO_2Na/(CH_3CH_2CH_2)_2CHCO_2H$, and; (iv) containing about four such units." *Id.* at *2 (emphasis added). The court first examined the claims and found that none of the claims defined the term "oligomer." *Id.* at *3. The court then considered that "[t]he generally accepted definition of oligomer . . . is a composition made up of a relatively small number of identical repeating units joined end to end." *Id.* (citing MAITLAND JONES, JR., ORGANIC CHEMISTRY 821 (1997)). The court next examined the wording and diagrams of the specification to determine whether the patentee intended to alter that definition. *Id.* at *3-*4. The court found that the specification was consistent with the ordinary definition. *Id.* at *4. The court then turned to the prosecution history, and it determined that the patentee did not surrender the ordinary meaning of the word during prosecution. *Id.* at *5. Consequently, the court concluded that "[t]here is no question that the basic definition of an oligomer applies here." *Id.* at *4.

108. Although claim construction is an issue of law, "[d]etermination of infringement is a question of fact." Tate Access Floors, Inc. v. Maxcess Techs., Inc., 222 F.3d 958, 964 (Fed. Cir. 2000). This Comment's hypothetical example assumes that the fact finder is a jury.

109. *See, e.g., id.* (stating that "[s]econd, the claim as properly construed must be compared to the accused device").

110. *Id.*

111. *See* discussion *supra* Part II pp. 1013-14 (construing the word "crystal" in claim three of the example '428 patent).

A jury would likely find that making and using a computer model of the compound recited in claim three of the '428 patent is not literal infringement.[112] The accused infringer did not make a "crystal," as required by the claim. The court in our example construed "crystal" as being a solid. However, the accused infringer did not make or use an actual *solid*, but rather a *representation* of that solid using the patented compound's spatial coordinates as data.[113] The Court of Customs and Patent Appeals[114] held in *In re Papesch*[115] that a patent on a compound protects only the actual compound, and not a representation of that compound.[116] Therefore, the accused product does not contain every element of the claim and does not literally infringe the patent.

D. Infringement Under the Doctrine of Equivalents

Even if the accused invention "does not literally infringe [the] claim[, it] may still infringe under the doctrine of equivalents."[117] Courts developed the doctrine of equivalents to protect a patentee against an infringer who makes only insubstantial changes in the patented invention.[118] The doctrine dates back to cases from the

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112. The issue would likely not even get to a jury. The court would likely grant summary judgment of non-infringement, which the court does if no reasonable jury could find infringement. Caterpillar Inc. v. Deere & Co., 224 F.3d 1374, 1379 (Fed. Cir. 2000).

113. *See* discussion *supra* Part I Section B pp. 1006-10 (discussing computer modeling of molecules).

114. Holdings of the Court of Customs and Patent Appeals from before September 30, 1982, are binding precedent on the Court of Appeals for the Federal Circuit. South Corp. v. United States, 690 F.2d 1368, 1369 (Fed. Cir. 1982) (en banc). The Federal Circuit has exclusive appellate jurisdiction over cases involving patent law. 28 U.S.C. §§ 1295(a)(1), 1338(a) (1994 & Supp. 1999). Congress established the Federal Circuit on October 1, 1982. CHISUM, *supra* note 90, at app. 21, ch. 450. Congress merged the Court of Customs and Patent Appeals and the Court of Claims into the Federal Circuit. S. REP. NO. 97-275, at 2 (1981), *reprinted in* 1982 U.S.C.C.A.N. 11, 12. Congress established the Federal Circuit to improve the administration of several areas of law, including patent law. CHISUM, *supra* note 90, at app. 21, ch. 450.

115. 315 F.2d 381 (C.C.P.A. 1963).

116. *Id.* at 391. In *Papesch*, Judge Rich wrote that:

> From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae [and] the chemical nomenclature . . . are mere symbols by which compounds can be identified, classified, and compared. But a *formula is not a compound* and while it may serve in a claim to identify what is being patented, as the metes and bounds of a deed identify a plot of land, the thing that is patented is *not the formula* but *the compound identified by it*.

Id. (emphasis added).

117. Tate Access Floors, Inc. v. Maxcess Techs., Inc., 222 F.3d 958, 964 (Fed. Cir. 2000).

118. Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 607 (1950).

early-nineteenth century.[119] By 1853, the principle was well established that a copy of a patented invention could infringe the patent even if it differs in form from the claimed invention.[120]

In 1950, the Supreme Court discussed the purpose of the doctrine of equivalents in *Graver Tank & Manufacturing Co. v. Linde Air Products Co.*[121] The Court noted that

> to permit imitation of a patented invention which does not copy every literal detail would be to convert the protection of the patent grant into a hollow and useless thing. . . . Outright and forthright duplication is a dull and very rare type of infringement. To prohibit no other would place the inventor at the mercy of verbalism and would be subordinating substance to form. It would deprive him of the benefit of his invention. . . .[122]

In 1997, in *Warner-Jenkinson Co. v. Hilton Davis Chemical Co.*,[123] the U.S. Supreme Court upheld the validity of the doctrine of equivalents and attempted to clarify the doctrine's correct scope.[124] The Court held that "the doctrine of equivalents must be applied to individual elements of the claim, not to the invention as a whole."[125]

The Court in *Warner-Jenkinson* then discussed the proper test to determine equivalence.[126] It considered the two existing tests--the "triple identity" test and the "insubstantial differences"

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119. *See* Gray v. James, 10 F. Cas. 1015, 1016 (C.C.D. Pa. 1817) (No. 5,718) (requiring for infringement that "where the machines are substantially the same, and operate in the same manner, to produce the same result, they must be in principle the same"); Odiorne v. Winkley, 18 F. Cas. 581, 582 (C.C.D. Mass. 1814) (No. 10,432) (stating that "[m]ere colorable differences, or slight improvements, cannot shake the right of the original inventor"); Park v. Little, 18 F. Cas. 1107, 1108 (C.C.D. Pa. 1813) (No. 10,715) (instructing the jury that an improvement in only the "form" of an invention, rather than the "principle," is infringement).

120. *See* Winans v. Adam, 56 U.S. (15 How.) 330, 342 (1853) (stating that "it is a familiar rule that, to copy the principle or mode of operation described, is an infringement, although such copy should be totally unlike the original in form or proportions").

121. 339 U.S. 605 (1950).

122. *Id.* at 607.

123. 520 U.S. 17 (1997).

124. *Id.* at 21.

125. *Id.* at 29. In so holding, the Court attempted to strike a balance between (1) the public's interest in "the definitional and public-notice functions of" patent claims and (2) the inventor's interest. *Id.* The Court reasoned that as long as courts consider equivalence on an element-by-element basis, "the doctrine will not vitiate the central functions of the patent claims themselves." *Id.* at 29-30.

This element-by-element approach differs from that in *Graver Tank*, in which the Court defined the test for equivalence as comparing the devices as a whole. Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 608 (1950).

126. Warner-Jenkinson Co. v. Hilton Davis Chemical Co., 520 U.S. 17, 39-40 (1997).

test.[127] The "triple identity" test looks at whether elements "do the same work in substantially the same way, and accomplish substantially the same result."[128] On the other hand, the "insubstantial differences" test asks if there was "only an 'insubstantial change'" in the element.[129] The Court concluded that either of these tests might be appropriate in particular cases, and that the "essential inquiry" is whether "the accused product or process contain[s] elements identical or equivalent to each claimed element of the patented invention."[130] The Court also noted that there is no infringement if "a theory of equivalence would entirely vitiate a particular claim element."[131]

The patentee in our example can argue that the competitor's use of the patented compound's spatial coordinates in a molecular modeling program is infringement under the doctrine of equivalents. The patentee can maintain that this cyberspace use in-

127. *Id.* at 39.

128. *Graver Tank*, 339 U.S. at 608. This test is also known as the "function/way/result" test. *Speech of the Honorable Paul R. Michel Given to the New Jersey Intellectual Property Law Association*, *in* 9 FED. CIR. B.J. 139, 143 (1999) [hereinafter *Michel Speech*].

129. *Michel Speech*, *supra* note 128, at 143. Federal Circuit Judge Michel commented that using the insubstantial differences test rather than the function/way/result test reduces predictability. *Id.*

130. *Warner-Jenkinson*, 520 U.S. at 40. Well-established limits exist on the doctrine of equivalents, such as prosecution history estoppel and the limitations of prior art. *See id.* at 30-33 (holding that in prosecution history estoppel, a patentee is estopped from asserting equivalence if the patentee amended a claim during prosecution to avoid prior art); Wilson Sporting Goods Co. v. David Geoffrey & Assocs., 904 F.2d 677, 683 (Fed. Cir. 1990) (holding that "there can be no infringement if the asserted scope of equivalency . . . would encompass the prior art"). Prosecution history estoppel and the effect of prior art are irrelevant to this Comment's hypothetical example, so the Comment does not further discuss these doctrines.

The Court of Appeals for the Federal Circuit recently issued an en banc decision that severely limited the availability of the doctrine of equivalents to patentees. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 566-69 (Fed. Cir. 2000) (en banc) (holding that a complete bar exists to the application of the doctrine of equivalents where the patentee made any narrowing amendment for any reason, voluntary or otherwise), *cert. granted*, 121 S. Ct. 2519 (2001). If the Supreme Court does not overrule *Festo*, then the doctrine of equivalents will be unavailable to most patentees, because "[t]he vast majority of patent applications contain claims that are initially rejected in view of the prior art, and are only allowed after being amended." *Id.* at 618 (Michel, J., concurring-in-part, dissenting-in-part). This Comment's hypothetical example assumes that the patent applicant made no narrowing amendments during prosecution, so *Festo* does not apply.

131. *Warner-Jenkinson*, 520 U.S. at 39 n.8. However, the Court did not explain the meaning of "vitiate," which has created confusion. *See generally* Craig Y. Allison, *What it Means to "Entirely Vitiate" a Claim Element in Light of Warner-Jenkinson*, 82 J. PAT. & TRADEMARK OFF. SOC'Y 563 (2000) (discussing how the Federal Circuit has attempted to define "entirely vitiate" on a case-by-case basis).

volves the equivalent of each element of the patent claim. The elements of claim three are a crystal of a particular compound, with each atom having spatial coordinates as specified.[132] Using the triple identity test, the patentee can argue that the computer representation contains the equivalent of each atom of the crystal. Each atom does the same thing (interacts with the atoms of candidate drug molecules), the same way (by following the laws of chemistry and physics for such interactions), to achieve the same result (to determine how candidate drug molecules will react with the patented compound).[133]

The patentee can also argue that this cyberspace use is analogous to decisions in which courts found infringement under the doctrine of equivalents where the accused infringers substituted digital computers for the analog means claimed in the patent.[134] Furthermore, the patentee can contend that it would be unjust to allow a competitor to "exploit the . . . significant efforts and costs incurred by a patentee in identifying, isolating, and effectively producing a protein,"[135] and that the doctrine of equivalents should prevent this injustice.

However, a court is likely to hold that using computer representations of atoms is not equivalent to using the patented compound itself, because a computer representation of a molecule is substantially different from the actual molecule itself.[136] Each cyberspace atom does not do the same thing the same way as each real atom.[137] The "atoms" in the molecular modeling program do not interact with each other following the laws of chemistry and physics—they interact according to imperfect models of chemical and physical laws.[138] It is not enough that they achieve the same

132. U.S. Patent No. 5,942,428, at cols. 349-50 (issued Aug. 24, 1999).

133. *Cf. Graver Tank*, 339 U.S. at 608 (employing the triple identity test).

134. *See* Hughes Aircraft Co. v. United States, 717 F.2d 1351, 1363-66 (Fed. Cir. 1983) (finding equivalence where the accused infringer substituted an onboard computer to control the position of a satellite in place of the claimed means for transmitting and receiving analog signals from ground control), *overruled on other grounds by Festo*, 234 F.3d at 574-75; Decca Ltd. v. United States, 544 F.2d 1070, 1080 (Ct. Cl. 1976) (stating that "infringement is not avoided by showing that digital instead of analog techniques are used in the accused system").

135. Jeffrey P. Kushan, Comment, *Protein Patents and the Doctrine of Equivalents: Limits on the Expansion of Patent Rights*, 6 HIGH TECH. L.J. 109, 111 (1991).

136. *Cf. Warner-Jenkinson*, 520 U.S. at 39-40 (allowing the use of the "insubstantial differences" test for determining equivalence).

137. *Cf.* Gelin, *supra* note 47, at 3 (defining a model as a "replica or facsimile of a real object" (emphasis omitted)).

138. *Cf.* Bugg et al., *supra* note 15, at 98 (stating that "the predictive ability of computer programs leaves something to be desired, both for solving the structure of a molecular target and for assessing the fit and attraction between a proposed drug and its target").

result of determining how candidate drug molecules will react with the patented compound.[139] The claim at issue requires an actual crystal composed of actual atoms.[140] Finding representations of these atoms to be equivalent would completely vitiate these claim elements. Therefore, the accused use does not contain every element of the claim or its equivalent. Consequently, a court would likely hold that the cyberspace use of the patented compound is not infringement under the doctrine of equivalents.

Thus, under existing law, a competitor's making and using of a patented compound in cyberspace likely does not infringe, either literally or under the doctrine of equivalents. However, policy-based reasons exist that support the notion that the making and using of a patented compound in cyberspace should be infringement.

III. THE UNAUTHORIZED CYBERSPACE USE OF A PATENTED COMPOUND SHOULD BE INFRINGEMENT

This Part proposes that the unauthorized making or using of a patented compound in cyberspace should be infringement. Section A discusses the classical underlying policies of patent law and how these policies support the proposal that cyberspace use of a patented compound should be considered infringement. Then, Section B considers two possible solutions.

A. The Underlying Policies of Patent Law

The broad goal of the United States patent system is "to provide an economic incentive for technological advancement and investment in scientific research."[141] The system also allows the dissemination of information important to spurring future technological innovation by requiring patent applicants to fully disclose their subject matter.[142] "The patent system encourages both invention and investment" and provides society with the benefits of "wealth and information."[143]

A number of economic policy justifications for patent law exist.[144] Four of such justifications are: (1) "natural law"; (2) "re-

139. *Cf.* Texas Instruments, Inc. v. United States Int'l Trade Comm'n, 805 F.2d 1558, 1571 (Fed. Cir. 1986) (holding that "[e]quivalence . . . is not established by showing only accomplishment of the same result").

140. U.S. Patent No. 5,942,428, at cols. 349-50 (issued Aug. 24, 1999).

141. Timothy J. Douros, *Lending the Federal Circuit a Hand: An Economic Interpretation of the Doctrine of Equivalents*, 10 HIGH TECH. L.J. 321, 325 (1995).

142. *Id.*

143. *Id.*

144. *See generally* Fritz Machlup, *An Economic Review of the Patent System*, *in* SUBCOMM. ON PATENTS, TRADEMARKS, AND COPYRIGHTS OF THE COMM. ON THE JUDICIARY, U.S. SENATE, 85TH CONG., 2D SESSION, STUDY NO. 15 (1958) (evaluating the economics of the United States patent system and discussing

ward-by-monopoly"; (3) "monopoly-profit-incentive"; and (4) "exchange for secrets."[145] These theories all support that the cyberspace use of a patented compound should be infringement.

The "natural-law" theory is that a person has a natural, exclusive "property right in his own ideas."[146] If someone else uses that person's ideas without authorization, then society must consider this to be stealing.[147] A rival should not be able to benefit from that person's intellectual efforts "without expending any energy or costs."[148] Therefore, this theory morally obligates society to protect a person's intellectual property rights through a patent system.[149]

The natural-law theory clearly supports that cyberspace use of a patented compound should be infringement.[150] Under this the-

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the four traditional justifications for patent protection); Steve P. Calandrillo, *An Economic Analysis of Intellectual Property Rights: Justifications and Problems of Exclusive Rights, Incentives to Generate Information, and the Alternative of a Government-Run Reward System*, 9 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 301 (1998) (discussing economic and non-economic justifications for awarding intellectual property rights and proposing a government-run alternative to existing systems); Seth A. Cohen, *To Innovate or Not to Innovate, That Is the Question: The Functions, Failures, and Foibles of the Reward Function Theory of Patent Law in Relation to Computer Software Platforms*, 5 MICH. TELECOMM. & TECH. L. REV. 1 (1998-99) (discussing the reward function and prospect function theories of patent law, particularly as applied to computer software); Douros, *supra* note 141 (discussing the purposes of patent law and the doctrine of equivalents, and proposing the application of Judge Learned Hand's negligence formula to the doctrine of equivalents); Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 VA. L. REV. 305 (1992) (applying the economic theory of rent dissipation to patent law); Edmund Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265 (1977) (introducing the prospect theory of patent rights, likening patents to mining claims); Robert B. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839 (1990) (applying various theories of patent law justification to how courts should interpret the scope of patent claims); A. Samuel Oddi, *Un-Unified Economic Theories of Patents—The Not-Quite-Holy Grail*, 71 NOTRE DAME L. REV. 267 (1996) (discussing classical and post-classical theories that justify patent law and concluding that there is no "unifying" theory).

145. Machlup, *supra* note 144, at 21. Several "post-classical" theories also exist. Oddi, *supra* note 144, at 281-85. One of these theories is the prospect theory. *See generally* Kitch, *supra* note 144 (introducing the prospect theory of patent rights, likening patents to mining claims). Another post-classical theory is the rent-dissipation theory. *See generally* Grady & Alexander, *supra* note 144 (applying the economic theory of rent dissipation to patent law).

146. Machlup, *supra* note 144, at 21. John Locke and Adam Smith both espoused this philosophy. Calandrillo, *supra* note 144, at 314-15.

147. Machlup, *supra* note 144, at 21.

148. Calandrillo, *supra* note 144, at 303.

149. Machlup, *supra* note 144, at 21. Common sense also dictates that inventors should be compensated for their efforts and should, therefore, have a property right in the inventions that these efforts generate. Calandrillo, *supra* note 144, at 315.

150. *But cf.* Calandrillo, *supra* note 144, at 310 (discrediting the natural-law

ory, a researcher who develops and obtains a patent on a protein crystal for use in designing new drugs should have an exclusive "property right in his own ideas."[151] A competitor should not be able to profit from the researcher's efforts and bypass the researcher's development costs just because the competitor uses the patented compound in a new, virtual way rather than an old, real-world way.[152] Therefore, natural-law theory morally obligates society to allow such patent protection.[153]

Another classical justification for the patent system is the "reward-by-monopoly" theory, which states that an inventor is entitled to a reward for her services "in proportion to their usefulness to society."[154] Because inventors provide useful services to society, society should reward inventors with patent protection.[155] This theory also supports that the cyberspace use of a patented compound should be infringement.[156] The useful service here that the patentee provides to society is a compound that may lead to the discovery of new drugs. This service is no less useful simply because the competitor uses the compound in cyberspace.

A third classical theory justifying the patent system is the "monopoly-profit-incentive" theory.[157] This theory assumes that inventions are necessary for industrial progress.[158] Inventors and investors will not sufficiently create and exploit inventions without the incentive of the monopoly granted by patents.[159] Without this monopoly, inventors and investors would be limited only to a competitive level of profits, which may be too low to make invention

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theory as an actual justification for the United States patent system); Oddi, *supra* note 144, at 274 (noting that the natural-law "theory has not received much attention in the modern era, because, perhaps, of the relative demise of natural law jurisprudence"). The Constitution grants power to Congress to create a patent system "[t]o promote the [p]rogress of [the] useful [a]rts." U.S. CONST. art. I, § 8, cl. 8. Thus, the Constitution grants a legislated right, not a natural right, to patent protection. Calandrillo, *supra* note 144, at 310. Therefore, an inventor does not have "an inherent right to his creation." *Id.*

151. Machlup, *supra* note 144, at 21.

152. *Cf.* Calandrillo, *supra* note 144, at 303 (stating that without patent protection, "rivals may profit from another's intellectual efforts without expending any energy or costs other than the relatively minor costs required to duplicate the socially valuable creation").

153. *Cf.* Machlup, *supra* note 144, at 21 (stating that "[s]ociety is morally obligated to . . . protect [an inventor's] property right").

154. *Id. Accord* Oddi, *supra* note 144, at 274. This theory is the "earliest and most widely accepted theory related to the patent system." Cohen, *supra* note 144, at 3-4.

155. Machlup, *supra* note 144, at 21; Oddi, *supra* note 144, at 274.

156. *But cf.* Machlup, *supra* note 144, at 54 (noting that a flaw in the reward-by-monopoly theory is that the reward an inventor receives through a patent is not necessarily proportional to its "social usefulness").

157. *Id.* at 21.

158. *Id.*

159. *Id.*

and investment worthwhile.[160]

The monopoly-profit-incentive theory also supports infringement for the cyberspace use of patented compounds.[161] A monopoly incentive to research and development is particularly important in a field such as drug development, where "often the innovator will expend hundreds of millions of dollars on research and development before a commercially viable product can be developed and marketed."[162] Without patent protection, many companies would not invest in research and development that might not prove to be economically worthwhile.[163] Therefore, as computer-assisted drug design becomes more important,[164] protecting patented compounds from cyberspace infringement is necessary to continue to encourage drug companies to invest the huge sums of money needed for drug-design research.

Finally, the fourth classical theory is the "exchange-for-secrets" theory.[165] This theory is that the patent system induces inventors to publicly disclose information about their inventions instead of keeping this information secret.[166] This incentive to disclose involves a "bargain between [an] inventor and society," where the inventor gives up secret knowledge to society in exchange for patent protection.[167] Industrial progress will slow down if inventors maintain their inventions as secret.[168] This theory also supports prohibiting the unauthorized use of patented compounds in cyberspace.[169] A researcher who discovers a promising target compound will likely keep its formula secret if patent protection will not guard against its use in cyberspace.[170]

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160. *Id.*

161. *But cf.* Machlup, *supra* note 144 at 50 (noting that a weakness of the monopoly-profit-incentive theory is that in addition to encouraging productive research, patent monopolies also encourage potentially wasteful research by forcing competitors to seek substitute inventions).

162. Calandrillo, *supra* note 144, at 303 n.2.

163. *Id. Cf. In re* Hogan, 559 F.2d 595, 606 (C.C.P.A. 1977) (stating that restricting the scope of a composition-of-matter claim to only the form that existed when the inventor filed a patent application "would be a poor way to stimulate invention").

164. *See* Rennie, *supra* note 73, at 8 (suggesting that rational drug design may turn out to be one of "the most important invention[s] of the past two millennia").

165. Machlup, *supra* note 144, at 21.

166. Cohen, *supra* note 144, at 4; Oddi, *supra* note 144, at 274-75.

167. Machlup, *supra* note 144, at 21.

168. *Id.*

169. *But cf. id.* at 52-53 (noting that a weakness of the exchange-for-secrets theory is that because several inventors often have the same idea at around the same time, it is not likely that all these inventors will keep the idea secret).

170. *Cf. Hogan*, 559 F.2d at 606 (stating that restricting the scope of a composition-of-matter claim to only the form that existed when the inventor filed a patent application "would be a poor way to . . . encourage its early disclosure").

Therefore, all four of these classical policy justifications for patent protection support that the unauthorized making or use of a patented compound in cyberspace should be infringement. A problem exists, though, because this conduct is not likely infringement under current law.[171] However, at least two possible solutions to this problem exist.

B. Possible Solutions

This Section proposes two possible solutions that will protect patentees of chemical compounds against their unauthorized cyberspace use. These solutions include: (1) inventors can apply for method claims in addition to composition-of-matter claims; and (2) courts can extend the doctrine of equivalents.

One possible solution is for an inventor to apply for method claims,[172] in addition to composition-of-matter claims, for a compound that is a promising target for use in computer-aided drug design. These method claims can describe the actual process for using the patented compound in computer-aided drug design.[173] Then, if a competitor does use the compound in cyberspace, he will

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171. *See* discussion *supra* Part II Section D p. 1018 (concluding that making or using a patented chemical compound in cyberspace without authority is not likely infringement under existing law).

172. *See* 35 U.S.C. § 101 (allowing an inventor to receive a patent on "any new and useful process"). The Court of Appeals for the Federal Circuit broadly upholds method claims. *Cf.* State St. Bank & Trust Co. v. Signature Fin. Group, Inc., 149 F.3d 1368, 1375-77 (Fed. Cir. 1998) (allowing business method patents).

173. *See* U.S. Patent No. 6,083,711, at cols. 61-66 (issued July 4, 2000) (claiming a method for using the patentees' previously patented herpes protease compound in computer-aided drug design of possible herpes protease inhibitors). Claim one, the only independent claim, reads:

> 1. A method of identifying a candidate inhibitor compound capable of binding to, and inhibiting the proteolytic activity of, an alpha, or beta herpes protease, said method comprising:
>
> a) introducing into a computer program information derived from atomic coordinate [sic] defining an active site conformation of a herpes protease molecule based upon three-dimensional structure determination . . . , wherein said program utilizes or displays the three-dimensional structure thereof;
>
> b) generating a three dimensional representation of the active site cavity of said protease in said computer program;
>
> c) superimposing a model of the inhibitor test compound on the model of said active site of said protease;
>
> d) assessing whether said test compound model fits spatially into the active site of said protease;
>
> e) incorporating said test compound in a protease activity assay . . . ; and
>
> f) determining whether said test compound inhibits proteolytic activity, or the herpes virus in said assay.

Id. at col. 61.

be liable for literal infringement of the method claims.[174] Thus, the composition-of-matter claims will protect the inventor from the unauthorized *actual* use of his compound, while the method claims will protect him from the unauthorized *virtual* use of his compound. An advantage of this solution is that an inventor can specifically obtain protection against cyberspace use of a compound regardless of whether the law recognizes cyberspace use as infringement of a composition-of-matter claim. A disadvantage of this solution is that it cannot retrospectively protect inventors who have already obtained patents on compositions of matter but not methods of drug design.[175]

Another possible solution is for courts to extend the doctrine of equivalents[176] so that the scope of a composition-of-matter claim would include a competitor's cyberspace use in addition to real use. A competitor infringes under the doctrine of equivalents if the compound he uses "contain[s] elements identical or equivalent to each claimed element of the patented" compound.[177] Elements are equivalent if they "do the same work in substantially the same way, and accomplish substantially the same result."[178] A court could extend the scope of a composition-of-matter claim by broadly interpreting the atoms of a cyberspace representation of a compound as doing the same thing (interacting with the atoms of candidate drug molecules), the same way (by following the laws of chemistry and physics), and reaching the same result (determining how candidate drug molecules interact with the patented compound) as the atoms of the real compound.[179]

This solution has advantages and disadvantages. One advantage of this solution is that it logically extends an existing doctrine, instead of either judicially or legislatively creating a new

174. *See* discussion *supra* Part II Section C pp. 1014-15 (discussing literal infringement).

175. A patentee can apply for the reissue of an existing patent if the patentee "claim[ed] more or less than he had a right to claim." 35 U.S.C. § 251 (1994 & Supp. 1999). However, a patentee may not enlarge the scope of a claim after "two years from the grant of the original patent." *Id.* Also, the patentee cannot introduce any "new matter" into a reissue application. *Id.* Thus, reissue provides a remedy only in a narrow set of circumstances.

176. *See* discussion Part II Section D *supra* pp. 1015-18 (discussing infringement under the doctrine of equivalents).

177. Warner-Jenkinson Co. v. Hilton Davis Chemical Co., 520 U.S. 17, 40 (1997).

178. Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 608 (1950).

179. *Cf. id.* (employing the triple identity test). *But see* Merges & Nelson, *supra* note 144, at 883 (asserting that overly broadening the scope of a chemical patent claim can have a potentially negative economic effect). However, licensing and cross-licensing tend to lessen the potential negative effect of broad patents. *Id.* Licensing and cross-licensing are common practices in the chemical industries. *Id.*

doctrine. A major disadvantage of this solution is that the Court of Appeals for the Federal Circuit would not likely be inclined to expand the scope of the doctrine of equivalents at all, considering that the court recently severely limited the availability of the doctrine of equivalents to patentees.[180]

CONCLUSION

Computer-aided drug design is important today and will become more important in the future. Researchers can now evaluate how candidate drug molecules will react with target molecules by using computer modeling. This process speeds up drug design and dramatically reduces its cost.

Owners of patents on protein molecules potentially useful in drug design are at risk, however. Competitors can take the information published in such patents and use it to simulate these patented molecules in cyberspace. Under existing law, this is not infringement, either literally or under the doctrine of equivalents.

Underlying patent-law policy supports that this cyberspace use should be infringement. Fortunately, possible solutions to the problem do exist. One solution is that when researchers apply for composition-of-matter claims on potential target compounds, they should also apply for method claims describing the process of using their compounds in computer-aided drug design. Another possible solution is for courts to extend the doctrine equivalents to cover the cyberspace use of a patented compound.

As computer-aided drug design becomes even more important, recognizing the cyberspace use of patented compounds as infringement will increase researchers' incentive to discover such compounds, and researchers will be less likely to keep information about these compounds secret.

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180. *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 566-69 (en banc) (Michel, J., concurring-in-part, dissenting-in-part) (holding that a complete bar exists to the application of the doctrine of equivalents where the patentee made any narrowing amendment for any reason, voluntary or otherwise), *cert. granted*, 121 S. Ct. 2519 (2001). *See also supra* note 130 (discussing the ramifications of *Festo*). Unless the Supreme Court overrules *Festo*, competitors will be able to copy patents and avoid liability in many technological fields. *Festo*, 234 F.3d at 617. Patents on protein molecules will be "particularly harmed." *Id.* A competitor can now avoid infringement of a protein patent by substituting just one insignificant amino acid at one position, without changing the protein's function. *Id.* Thus, even if the court extended the doctrine of equivalents to cover the use of a patented compound in cyberspace, a patentee would still not receive much protection. A competitor could simply substitute an insignificant amino acid at one position within the computer model to avoid infringement.