

### ***7.2.1 Principles for Disseminating Research Results***

Physicians have an ethical responsibility to learn from and contribute to the total store of scientific knowledge. When they engage in biomedical or health research, physicians have obligations as scientists, which include disseminating research findings. Prompt presentation to scientific peers and publication of research findings are foundational to good medical care and promote enhanced patient care, early evaluation of clinical innovations, and rapid dissemination of improved techniques.

To fulfill their ethical responsibilities with respect to sharing research findings for the ultimate benefit of patients, physicians should:

- (a) Advocate for timely and transparent dissemination of research data and findings. Physicians should not intentionally withhold information for reasons of personal gain.
- (b) Report the results of research accurately, including subsequent negative findings. This is particularly important where the findings do not support the research hypothesis.
- (c) Maintain a commitment to peer review.
- (d) Disclose sponsorship and conflicts of interest relating to the research, in keeping with ethics guidance.
- (e) Be responsible in their release of research results to the media, ensuring that any information the researcher provides is prompt and accurate and that informed consent to the release of information has been obtained from research participants (or participants' legally authorized representative when the participant lacks decision-making capacity) prior to releasing any identifiable information.

In rare circumstances, the potential for misuse of research results could affect the decision about when and whether to disseminate research findings. Physician-researchers should assess foreseeable ramifications of their research in an effort to balance the promise of benefit against potential harms from corrupt application. Only under rare circumstances should findings be withheld, and then only to the extent required to reasonably protect against misuse.

### ***AMA Principles of Medical Ethics: I,II,III,V,VII***

*Opinion 7.2.1, Principles for Disseminating Research Results, re-organizes content from previous guidance and associated background reports:*

CEJA Report 3-A-16 Modernized *Code of Medical Ethics*

CEJA Report 9-A-04 Guidelines to prevent malevolent use of biomedical research

CEJA Report 1-I-97 Patenting the human genome

CEJA Report 1-A-95 Ethical issues in the patenting of medical procedures

Report of the Judicial Council Dec 1984 New medical procedures

Report of the Judicial Council Jun 1966 Declaration of Helsinki

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To fulfill their ethical responsibilities with respect to sharing research findings for the ultimate benefit of patients, physicians should:

- (a) *Advocate for timely and transparent dissemination of research data and findings.* Physicians should not intentionally withhold information for reasons of personal gain. *[New content sets out key ethical values/concerns explicitly.]*
- (b) Report the results of research accurately, including subsequent negative findings. This is particularly important where the findings do not support the research hypothesis.
- (c) Maintain a commitment to peer review.
- (d) *Disclose sponsorship and conflicts of interest relating to the research, in keeping with ethics guidance.* *[New content addresses gap in current guidance consistent with 7.1.4.]*
- (e) Be responsible in their release of research results to the media, ensuring that any information the researcher provides is prompt and accurate and that informed consent to the release of information has been obtained from research participants (or participants' legally authorized representative when the participant lacks decision-making capacity) prior to releasing any identifiable information.

In rare circumstances, the potential for misuse of research results could affect the decision about when and whether to disseminate research findings. Physician-researchers should assess foreseeable ramifications of their research in an effort to balance the promise of benefit against potential harms from corrupt application. Only under rare circumstances should findings be withheld, and then only to the extent required to reasonably protect against misuse.

***AMA Principles of Medical Ethics: I,II,III,V,VII***

# REPORT OF THE COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS\*

CEJA Report 9 - A-04

Subject: Guidelines to Prevent Malevolent Use of Biomedical Research

Presented by: Michael Goldrich, MD, Chair

Referred to: Reference Committee on Amendments to Constitution and Bylaws  
(Mary W. Geda, MD, Chair)

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## 1 INTRODUCTION

2  
3 In February 1975, a group of leading scientists, physicians, and policymakers convened at  
4 Asilomar, California, to consider the safety of proceeding with recombinant DNA research. The  
5 excitement generated by the promise of this new technology was counterbalanced by concerns  
6 regarding dangers that might arise from it, including the potential for accidental release of  
7 genetically modified organisms into the environment. Guidelines developed at the conference to  
8 direct future research endeavors had several consequences. They permitted research to resume,  
9 bringing to an end the voluntary moratorium that the National Academy of Sciences (NAS) had  
10 instituted several months earlier. They also served to illustrate that the scientific community was  
11 capable of self-governance, thereby securing public trust and persuading Congress not to institute  
12 legislative restrictions.<sup>1</sup> Finally, they underscored the importance of weighing unforeseen risks  
13 inherent in some research against potential benefits that may arise from these same endeavors.

14  
15 In February 2000, a second meeting was held at Asilomar, bringing together members from the  
16 same groups, including some of the original attendees.<sup>2</sup> This meeting was held in honor of the  
17 historic event's 25<sup>th</sup> anniversary and in recognition of the scientific community's increasing  
18 attention to the potentially harmful applications of biotechnology in general – for example, to  
19 facilitate the use of pathogens as deadly weapons.<sup>3</sup> Risk of this latter sort that arises not from  
20 research *per se* but from its intentional misapplication for nefarious purposes constitutes the focus  
21 of this report.

22  
23 The possibility that scientific research may generate knowledge with the potential for harmful as  
24 well as beneficial applications is not new. In recent years, however, it has become imperative to  
25 develop parameters within which to address such research, as heightened concerns have arisen  
26 from the threat of biochemical terrorism and warfare.

## 27 BACKGROUND

28  
29 Physicians' involvement in biomedical research, whether clinical or pre-clinical, traditionally has  
30 been guided by a desire to help alleviate patient morbidity and mortality. In the AMA's *Principles*  
31 *of Medical Ethics*, research activities are grounded in obligations to advance scientific knowledge  
32 and to contribute to the betterment of public health (*Principles V and VII*).<sup>4</sup> The Association's  
33

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\* Reports of the Council on Ethical and Judicial Affairs are assigned to the reference committee on Constitution and Bylaws. They may be adopted, not adopted, or referred. A report may not be amended, except to clarify the meaning of the report and only with the concurrence of the Council.

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1 more recent Declaration of Professional Responsibility, which has been supported by numerous  
2 state and specialty medical societies, further encourages physicians to “work freely with colleagues  
3 to discover, develop, and promote advances in medicine.”<sup>5</sup>

4  
5 Though the fundamental goals of biomedical research may be morally sound, it remains that  
6 researchers sometimes make discoveries that can be put to harmful, as well as beneficial, use.  
7 Despite providing considerable guidance to ensure the ethical conduct of physicians engaged in  
8 human subjects research,<sup>6</sup> the Code of Medical Ethics does not currently address the importance of  
9 physicians playing a proactive role in trying to assess foreseeable consequences of their biomedical  
10 research endeavors, nor does it offer a framework to assist them in doing so.

11  
12 In this, the Code’s research guidelines may reflect the uneven impact of the Nuremberg Code,  
13 which was drafted in response to wartime atrocities that Nazi physicians committed against captive  
14 human subjects, under the guise of biomedical research. To prevent the recurrence of such  
15 blatantly unethical “research,” the Nuremberg Code set out ethical principles intended to guide all  
16 future medical research involving human subjects. It focused largely on the requirement for  
17 informed consent from all research subjects, rather than on possible ramifications of the research;  
18 these were addressed only briefly in a statement that “experiment[s] should be such as to yield  
19 fruitful results for the good of society.”<sup>7</sup> The requirement for consent has remained integral to  
20 modern clinical research in the US. With regard to the latter provision, however, research has been  
21 vetted only to ensure that it produces beneficial results, while neglecting to consider the harmful  
22 ways in which the results could be misapplied. Arguably, this constituted a missed opportunity to  
23 develop normative guidance for the assessment of the goals and potential impact(s) of biomedical  
24 research in general.

#### 25 26 CLASSES OF RESEARCH WITH POTENTIAL FOR MALIGNANT APPLICATION

27  
28 The development, production, stockpiling or use of biological weapons (BW) by any nation is  
29 banned under the 1972 Biological and Toxin Weapons Convention (BTWC),<sup>8</sup> which has been  
30 signed by 167 nations, and ratified by 151.<sup>9</sup> Still, the World Medical Association (WMA) contends  
31 that there remains “a need for the creation of and adherence to a globally accepted ethos that rejects  
32 the development and use of biological weapons.”<sup>10</sup> Moreover, according to the WMA, physicians  
33 are morally obligated to play prominent roles in establishing such an ethos because biological and  
34 toxin weapons (BTW) are intended to incapacitate or kill individuals, outcomes that are antithetical  
35 to the professed duties of physicians. Moreover, as professionals entrusted by society to advance  
36 human welfare, physician-researchers should actively speak out in condemnation of the creation  
37 and use of BTW. As to participation in defensive weapons development, physicians should  
38 consider the potential for offensive application of their research, and carefully weigh the risk of  
39 misapplication against the risks associated with forgoing all weapons research.

40  
41 Additionally, researchers have begun to contend with the possibility that countless areas of  
42 biomedical research can lead to nefarious applications, and inadvertently may aid in the creation of  
43 BW. A recent report from the US National Research Council (NRC), “Biotechnology Research in  
44 an Age of Terrorism: Confronting the Dual-Use Dilemma,”<sup>11</sup> listed seven classes of “experiments  
45 of concern” considered to be especially problematic due to their potential implications for the  
46 creation and use of BW. Specifically, the NRC called attention to experiments that:

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- 1 1. would demonstrate how to render a vaccine ineffective;
- 2 2. would confer resistance to therapeutically useful antibiotics or antiviral agents;
- 3 3. would enhance the virulence of a pathogen or render a non-pathogen virulent;
- 4 4. would increase transmissibility of a pathogen;
- 5 5. would alter the host range of a pathogen;
- 6 6. would enable the evasion of diagnostic/detection modalities;
- 7 7. would enable the weaponization of a biological agent or toxin.

8

9 This list excludes many other areas of research that are less easily distinguished but equally  
10 dangerous if misapplied. For example, researchers have been able to construct functional polio  
11 virus particles *de novo* using relatively standard laboratory techniques and equipment, and freely  
12 available genetic information.<sup>12</sup> Though the potential danger of such an experiment has not been  
13 overlooked,<sup>11</sup> many of the prerequisite experiments that allowed for it, such as the sequencing of  
14 the polio virus genome, certainly could be considered innocuous. Similarly, genome sequencing of  
15 many other pathogens, including those responsible for anthrax, Ebola hemorrhagic fever, and  
16 bubonic plague, would not fall within the NRC's categorization; however, the publication of these  
17 sequences in the open scientific literature,<sup>13</sup> while undeniably important to further understanding of  
18 pathogenicity, could unintentionally facilitate the illegitimate creation and subsequent misuse of  
19 these pathogens.

20

21 Categorical classifications run the risk of being either over- or under-inclusive, as a broad range of  
22 important and seemingly innocuous biomedical research could be used malevolently. This inherent  
23 ambiguity necessitates that *all* biomedical research be ethically assessed.

24

## 25 PROFESSIONAL OBLIGATIONS OF PHYSICIAN-RESEARCHERS

26

27 It has been argued that pure scientific research is morally neutral and thus only its subsequent  
28 application should be subject to ethical scrutiny.<sup>14</sup> Many of the scientists whose discoveries in  
29 atomic energy gave birth to nuclear weapons initially held this position. However, in the wake of  
30 the bombings of Hiroshima and Nagasaki at the end of WWII, some of these same scientists openly  
31 grappled with the possibility that they were ethically responsible in part for the destructive  
32 applications of their findings. As their experience suggests, researchers may be morally  
33 accountable for harms that do not result from their research *per se*, but are borne of its applications.

34

35 Indeed, there is growing acceptance in the scientific community that scientists are obligated to  
36 pursue knowledge both as an end in itself and as a means of improving the world for humankind.  
37 For instance, the preface of the American Society for Biochemistry and Molecular Biology's  
38 (ASBMB's) Code of Ethics states:

39

40 "Members of the ASBMB are engaged in the quest for knowledge in biochemical and  
41 molecular biological sciences with the ultimate goal of advancing human welfare.  
42 Underlying this quest is the fundamental principle of trust. The ASBMB encourages its  
43 members to engage in the responsible practice of research required for such trust by  
44 fulfilling the following obligations:... [including that] investigators [should] promote and  
45 follow practices that enhance public interest or well-being."<sup>15</sup>

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1 Similarly, in its Code of Ethics, the American Society for Microbiology (ASM) states that its  
2 members should “aspire to use their knowledge and skills for the advancement of human  
3 welfare.”<sup>16</sup> With respect to the potential for malign use of research findings, the Council Policy  
4 Committee of the ASM goes further, in stating:

5  
6 “...microbiologists will work for the proper and beneficent application of science and  
7 will call to the attention of the public or the appropriate authorities misuses of  
8 microbiology or of information derived from microbiology. ASM members are obligated  
9 to discourage any use of microbiology contrary to the welfare of human kind.”<sup>17</sup>

10  
11 Unlike the ASBMB and the ASM, however, most scientific societies have not codified this notion  
12 of social responsibility. Nonetheless, the obligation to preserve public trust extends to all  
13 scientists, as a critical element of their collective professional responsibility.

14  
15 Physician-researchers share in this obligation not only by virtue of their membership in the  
16 scientific community, but also because the preservation of public trust is a fundamental aspect of  
17 medical professionalism, the moral duties of which bear upon the whole of their professional  
18 conduct. The WMA has articulated this requirement in its Declaration of Washington on  
19 Biological Weapons, which states that “Physicians who participate in biomedical research have a  
20 moral and ethical obligation to consider the implications of possible malicious use of their  
21 findings.”<sup>6</sup> Though this is an undeniably complicated undertaking, physician-researchers, who  
22 possess profound knowledge of their research and of human health and disease, are arguably in the  
23 best position to assess the potential for and the ramifications of misapplications of their research.

#### 24 25 *Self-regulation*

26  
27 The Code states that “[t]he ultimate responsibility for the ethical conduct of science resides within  
28 the institution (academic, industrial, public, or private) which conducts scientific research *and with*  
29 *the individual scientist* [emphasis added].”<sup>18</sup> In science as in medicine, individual responsibility is  
30 a fundamental aspect of professionalism. To that end, physician-researchers need to understand  
31 research ethics norms, such as scientific responsibility and integrity. Research ethics education,  
32 beginning at the trainee level and extending throughout a career, can sensitize physician-  
33 researchers to the possibility for misapplications of scientific knowledge, and empower them to  
34 make responsible assessments of the research used to generate it. Still, differences in opinion will  
35 continue to arise. It is precisely because no one physician’s ethical judgment is infallible that  
36 human subjects research protocols are vetted by Institutional Review Boards (IRBs). Similarly,  
37 physician-researchers engaged in preclinical biomedical research should peer-review each others’  
38 work.

39  
40 Some experiments present such a degree of potential risk of harmful application that more rigorous  
41 oversight may be warranted. The aforementioned NRC report firmly echoes this notion in its  
42 proposal for a regulatory system that relies on both voluntary self-governance and scientific review  
43 committees to provide oversight for “experiments of concern.”<sup>11</sup> Other proposals have included  
44 establishing registries, perhaps within the Centers for Disease Control and Prevention (CDC), of  
45 researchers who are working with certain pathogens and toxins, and requiring that potentially  
46 dangerous results, including inadvertent discoveries, be reported.<sup>3</sup>

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1 To date, the US Department of Health and Human Services has created the National Science  
2 Advisory Board for Biosecurity (NSABB) which, as part of its mandate, will develop guidelines  
3 regarding appropriate oversight by local Institutional Biosafety Committees or federal officials of  
4 potentially harmful research.<sup>19</sup> Final authority over whether to accept these guidelines, however,  
5 will reside with the federal departments and agencies that support the research. Already, classified  
6 research, presumably for biodefense purposes, has been exempted from any guidelines developed  
7 by the NSABB.

8  
9 With the exception of research involving select agents or toxins identified by the CDC as posing a  
10 severe health threat,<sup>20</sup> formal oversight currently is mandatory only for studies and/or institutions  
11 that receive NIH funding for recombinant DNA research.<sup>21</sup> Though some privately-funded  
12 research organizations voluntarily comply with current NIH research guidelines, and may elect to  
13 comply with NSABB guidelines, they are not required to do so. The NSABB can seek to close the  
14 significant gap in the current regulatory framework by extending the scope of federally regulated  
15 research and encouraging the private sector to adopt the Board's system of oversight. Cooperation  
16 between different countries' research bodies also should be promoted, since research increasingly  
17 is becoming a global enterprise. Physician-researchers will be able to play a leading role in calling  
18 for the creation of and adherence to such global standards for research governance.

19  
20 *Transparency*

21  
22 In some cases, the dangers presented by research either cannot be fully appreciated before it is  
23 conducted, or are the inevitable consequence of research of such importance that it must be allowed  
24 to proceed nevertheless. Such dangers could be addressed by restricting the dissemination of  
25 especially hazardous information. However, such restrictions may be undesirable for a number of  
26 reasons. The Code, for example, emphasizes that timely publication of research is an essential  
27 element in the foundation of good medical care.<sup>22</sup> The elimination of openness in biomedical  
28 research would not only create an aura of secrecy likely to compromise public trust in science, but  
29 also would impede progress and innovation – notably within biodefense research,<sup>23</sup> the  
30 development of vaccines and therapeutics necessary to effectively counter any use of BW.

31  
32 Under exceptional circumstances, it may be appropriate to limit accessibility to the results of  
33 particular experiments. For example, the unexpected discovery of a means by which to engineer a  
34 virus capable of infecting even immunized animals recently prompted a reexamination of openness  
35 in biomedical research,<sup>24</sup> on account of the potential to misuse the research's findings toward the  
36 design of uniquely effective bioweapons. A group including scientist-authors, government  
37 officials, and editors of major scientific journals was convened by the NAS to discuss these  
38 concerns and issued a statement conceding that “there is information that, although we cannot now  
39 capture it with lists or definitions, presents enough risk of use by terrorists that it should not be  
40 published.”<sup>25</sup>

41  
42 Publication restrictions alone would likely prove ineffective, because scientific information is  
43 disseminated not only through mainstream scientific literature, but also through presentations at  
44 scientific meetings and increasingly on the Internet. Hence, it will be essential for members of the  
45 scientific community, including physician-researchers, to consider the implications of presenting  
46 their data in any form. As an additional part of its mandate, the NSABB will be working with  
47 stakeholders, including researchers and editors, to develop guidelines for the communication, in

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1 any form, of potentially harmful research. In the absence of such guidelines, if there is any doubt  
2 as to the propriety of open presentation, researchers would be wise to consult with colleagues in  
3 deciding how to proceed.

4  
5 **CONCLUSION**

6  
7 Biomedical research is essential for providing means by which medicine can continue to advance  
8 human welfare. For it to proceed responsibly, an overall ethical framework must be established  
9 that seeks to balance the ability of biomedical research to generate medical innovations against  
10 harms that may be incurred through its corruption, notably including its application to the  
11 development of biological weapons. As scientists and medical professionals, physician-researchers  
12 should seek to play a major role in the creation of such a framework, and in the execution of any  
13 steps that must be taken to fulfill the obligations it imposes. Chief among these steps is for  
14 physician-researchers to appreciate and advocate the need for diligence and moral fortitude in  
15 assessing the ethical implications and foreseeable consequences of their research and the  
16 dissemination of its findings.

17  
18 **RECOMMENDATIONS**

19  
20 The Council on Ethical and Judicial Affairs proposes that the following recommendations be  
21 adopted and the remainder of this report be filed:

22  
23 Physicians who engage in biomedical research are bound by the ethical obligations of the  
24 medical profession and also are required to meet responsibilities of the scientific  
25 community. Beyond their commitment to the advancement of scientific knowledge and the  
26 betterment of public health, physician-researchers must strive to maintain public trust in  
27 the profession through their commitment to public welfare and safety, as demonstrated  
28 through individual responsibility, commitment to peer review, and transparency in the  
29 design, execution, and reporting of research.

30  
31 Biomedical research may generate knowledge with potential for both beneficial and  
32 harmful application. Before participating in research, physician researchers should assess  
33 foreseeable ramifications of their research in an effort to balance the promise of benefit  
34 from biomedical innovation against potential harms from corrupt application of the  
35 findings.

36  
37 In exceptional cases, assessment of the balance of future harms and benefits of research  
38 may preclude participation in the research; for instance, when the goals of research are  
39 antithetical to the foundations of the medical profession, as with the development of  
40 biological or chemical weapons. Properly designed biomedical research to develop  
41 defenses against such weapons is ethical.

42  
43 The potential harms associated with some research may warrant regulatory oversight.  
44 Physician-researchers have a responsibility not only to adhere to standards for research, but  
45 also to lend their expertise to the development of safeguards and oversight mechanisms,  
46 both nationally and internationally. Oversight mechanisms should balance the need to  
47 advance science with the risk of malevolent application.

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After research has been conducted, consideration should be given to the risk of unrestricted dissemination of the results. Only under rare circumstances should findings be withheld, and then only to the extent required to reasonably protect against dangerous misuse.

These ethical principles should be part of the education and training of all physicians involved in biomedical research.

(New HOD/CEJA Policy)

Fiscal Note: Less than \$500.00

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## CEJA Report 2 – I-97 Patenting the Human Genome

### INTRODUCTION

The Human Genome Project (HGP) is a joint endeavor overseen by the National Institutes of Health (NIH) and the Department of Energy (DOE). International research efforts are coordinated through HUGO (Human Genome Organization). The 15-year HGP began in 1990 and proposes to find the location of 100,000 (or more) human genes, as well as to read the entire genetic script (approximately 3 billion base pairs) by the year 2005. Initial investments focused primarily on developing computerized tools for mapping, sequencing, storing, and handling genes. Despite this, the development of physical and genetic maps has moved forward faster than originally expected. Recently, with the development of new technologies that enable research to proceed more rapidly and efficiently, larger-scale sequencing efforts have begun.

With genetic research moving ahead at light-speed, patenting has become an important issue. Much of the concern in this area has focused on DNA sequences.<sup>1</sup> These sequences may be fragments of a gene (*i.e.*, they code for certain amino acids), or a full gene (*i.e.*, they code for a full protein). Patenting of the former is more controversial, both legally and ethically, than the latter. In this report the Council provides a brief explanation of patent law and its potential application to genomic sequences. After examining some of the ethical concerns regarding patenting human genomic material, it concludes that caution is warranted in this area.

### UNITED STATES PATENT LAW

Patent law is controlled by federal legislation, federal court decisions, and decisions of the Patent and Trademark Office (PTO). The Constitution notes that Congress has the power to “promote the progress of Science and useful Arts, by securing for limited times to Authors and Inventors the exclusive right to their Writings and Discoveries.”<sup>2</sup>

Patent holders do not own an invention—they own merely the patent. A patent then grants the holder the right, for a limited amount of time, to prevent others from commercializing their inventions. In this sense a patent does not confer ownership rights, it confers property rights. This is an important distinction. For example, an easement (another type of property right) granting X access over Y's property to the ocean front does not mean that X owns the property, merely that X has certain rights with respect to the property.

The obverse of patent law is trade secret law. It may be more lucrative to maintain an invention as a trade secret than to disclose it under patenting requirements. For example, Coca Cola originally sought patent protection for Coke, but dropped the application in light of the disclosure requirements. The formula for Coke turned out to be much more valuable as a trade secret than if patented (since the company would have had to disclose how to make it).

Patent law is designed to allow inventors to profit from their inventions, safeguarding intellectual property. At the same time, the patent system is designed to foster information sharing since full disclosure of the invention—enabling another trained in the art to replicate it—is necessary to obtain a patent.<sup>3</sup> One author described a patent as “a contract between its owner and the U.S. government, whereby the owner is given security in exchange for sharing knowledge with the public.”<sup>4</sup> The “contract,” as such, lasts 20 years from the date of filing.

There are two aspects to consider when a patent application is filed: the first is determining whether the thing is an invention, which is potentially patentable, or a discovery, which is not. In some sense, all inventions can be reduced to naturally occurring substances that are merely discoverable. Another way to think about the difference between a discovery and an invention is to consider the distinction between basic and applied research.<sup>5</sup> This distinction, however, is not always clear-cut in the realm of biotechnology. As a result, whether or not to classify a finding as a discovery or an invention often reduces to the requirement of “utility” discussed below. Second, once a finding is classified as an invention and deemed potentially patentable, it must meet the three requirements of novelty, non-obviousness and utility.

### *Novelty*

To meet the novelty requirement, the invention cannot have been known or used by others in this country, or patented or described in a publication in this or a foreign country.<sup>6</sup> In other words, the invention must not have been in the public domain. This issue becomes crucial when an inventor seeks to disseminate his or her invention before issuance of the patent. The United States grants a one year grace period from the time that the invention is disseminated to the time the patent application is filed. In theory this may keep some inventors from disclosing their inventions, or information about them, until they have met the other requirements and thus are ready to file.

### *Non-obviousness*

To be patentable, the invention in question must not have been obvious to one working in the field at the time of the invention.<sup>7</sup> If all of the elements of an invention were described in a single previous publication, even if the invention itself had not been developed, it is considered to be non-obvious. In this sense, what can be patented changes over time. As the state of the art develops, what was once considered non-obvious or novel, may become routine and thus unpatentable.

### *Utility*

Utility requires that the invention must have a practical use beyond merely being a tool for scientific inquiry.<sup>8</sup> The focus here is not on the degree of utility—if an inventor can articulate at least one use for the invention he or she will have met this requirement. This does not mean that if an inventor can articulate the natural function the test has been met—a commercial use (e.g., a therapeutic use) must be identified.

In practice, people can use a patented invention in the absence of a licensing agreement. First, there is an exception that allows the use of a patented invention for research purposes, although if a commercial product arises from the research an agreement must be negotiated between the original patent owner and the researcher. This “research exception” has never been clearly defined and it is uncertain how it would be interpreted if litigated. Second, not all patents are enforced, either because the patent holder does not mind the use or because of the financial cost of enforcement. The patent holder actively must seek either an injunction to prevent use of the patent or the payment of penalties. Third, all patents can be challenged in court, as they often are by companies who have developed the same or similar technology.

## PATENTING DNA

While naturally occurring DNA sequences can only be discovered, and thus are not patentable, sequences that been manipulated or altered are considered inventions and thus

potentially patentable. In 1980, the Supreme Court decided the case of *Diamond v. Chakrabarty* holding that genetically engineered microorganisms are patentable.<sup>9</sup> Moreover, other cases have held that a newly isolated or purified material is patentable (for example, purified: prostaglandins, acetylsalicylic acid, adrenaline composition, and bacterial strains have been granted patent protection).<sup>10</sup> Thus a newly cloned human gene that existed naturally in an impure form in human cells (*i.e.*, it existed only in combination with other DNA), may be patentable. For example, the European Patent Office (EPO) recently allowed a patent for a synthetic gene for H2-relaxin.<sup>11</sup>

DNA sequences may be classified as an invention rather than a discovery, but they must still meet the three requirements of novelty, nonobviousness and utility. Although sequences are potentially novel and non-obvious, they may not remain so.<sup>12</sup> Thus DNA sequences may meet this requirement in the early stages of HUGO, but later developed ones may not since the mechanisms and technology needed to establish new sequences might be obvious from the older sequences. The state of the art might have already progressed beyond the point where DNA sequences are non-obvious. In addition, the utility requirement may cause difficulty. This difficulty is what underlies the controversy between patenting partial and full sequences.<sup>13</sup> While the partial sequence might have some use as a tool for scientific inquiry, in order to satisfy the utility criterion, the inventor might need to articulate the specific function of the full gene or resulting protein. In practice, however, the utility requirement has never posed a significant barrier to obtaining a patent; any proposed use generally is considered sufficient for purposes of the application.

In addition to patents on genetic substances, patents of sequencing processes are also possible. Process patents are often thought to be less economically valuable than substance patents from the standpoint of the patent holder since they do not prevent others from developing the same substance through a different process. In addition to patents on genes and gene sequences, patents may also be sought on genetic therapies or technologies. This report does not address the ethical acceptability of patents on genetic therapies.

## PURPOSE OF PATENTING

Before entering into a discussion of the ethical concerns regarding patenting the human genome, it is useful to identify why patent protection is sought. Large outlays of money are necessary to conduct most biotechnology research. A substantial amount of this money comes from private sources.<sup>14</sup> Given the present state of federal funding for science research, it is unlikely that public money will be able to make up for the loss of private funding. Patenting is thought to encourage private investment into research.<sup>15</sup> Leaving aside for the moment the appropriateness or efficacy of a particular incentive (*e.g.*, patenting) it is important to acknowledge the need for incentives to encourage continued private support of research.

In addition, the patent system is designed to foster information sharing since a patent holder must disclose all of the information regarding his or her invention as part of the patent application. However, it is unclear whether this information sharing actually occurs. Clearly the effect of patent law on private research is different from the effect on academic research, where information sharing is generally the norm. With respect to private research, investigators may be unwilling to share information (or prevented by their company from doing so) until they are prepared to file a patent application. On the other hand, refusing to extend patent protection to DNA sequences will not necessarily result in more information sharing. Industries may choose to keep the sequence information secret until they develop a patentable product.<sup>16</sup> As a result dissemination of information will not only be slowed, as

occurs during the period between patent application and patent approval, but possibly cut off completely.

Biotechnology inventions are more like drug or device patents—there may be no direct benefit to the inventor unless he can market it commercially. This is in contrast to medical procedures, where one can argue that the inventor will still benefit from an invention without patent protection because of increases in the number of patients who come to the inventor for the procedure.<sup>17</sup> Moreover, although physicians may be barred from using a patented medical procedure in the course of their practice because of the potential for financial gain, researchers are not barred from using a patented biotechnology invention in the course of their research (as long as the research is not for financial gain). This is the research exception in patent law. As noted previously, the extent of this protection is unclear. There is some concern that the exception will not hold with the recent proliferation of joint endeavors between biotechnology industries and academic institutions. While a patented material may be used for research purposes, if those research purposes lead to commercial inventions, a license agreement must be negotiated between the original patent holder and the subsequent investigator. As a result, research efforts may be hindered because of high licensing fees.

## ETHICAL CONCERNS

Notwithstanding the uncertainties about the benefits of patent protection, there are ethical concerns with patenting in this context. Most of these concerns focus on the idea that patenting human genomic material results in a harm to human dignity. There are a number of different arguments imbedded in this concept of harm and they will each be addressed in turn.

First, patenting may cause harm because it is equivalent to ownership of human beings.<sup>18</sup> The United States Constitution forbids ownership of people (slavery).<sup>19</sup> However, as stated previously, patents grant property rights rather than ownership rights, although this too may be disturbing. However, the property rights involved here are not rights in a full or complete human being (or even an identifiable human being), but only in parts of human material, separate from any one individual. DNA sequences are not the equivalent of a person, or even a partial person. Moreover, most DNA and even individual genes are not unique to humans—it is the combination that is crucial. Thus patenting a DNA sequence does not seem to grant property rights in another human being. Moreover, it is not clear how DNA is different from proteins or other naturally occurring substances found in human beings that are already patentable—it is just one earlier step on the chain.<sup>20</sup> The Danish Council on Ethics suggests that one concern is the lack of knowledge about DNA. Because it remains unclear where and whether certain attributes that are considered uniquely human are found in the genetic material, it is possible that granting patent rights will result in a violation of human worth.<sup>21</sup> In other words, property rights will be granted in something considered fundamentally “human.” A solution to this may be to ensure that patent descriptions are carefully constructed so as to exclude the naturally occurring form, something that is not always done at this time.

Even if patenting does not confer ownership rights in a human being, there are other ethical concerns. For example, the commodification of human parts is often seen as improper.<sup>22</sup> Even if there is continuity between DNA and patentable proteins, commodification of the former may be more problematic than the latter. For example, the manipulation of core parts, such as germ line therapy, is more ethically controversial than manipulation of somatic cells. Likewise, patenting of proteins may be more acceptable than patenting of earlier, or more fundamental elements that control (to a certain degree) who we are. Furthermore, there may be problems with using market rhetoric.<sup>23</sup> Discussions of patenting presuppose an ability to determine the economic value of the patentable entity. Using

market terminology in relation to DNA may be ethically troubling because it implies that human beings may be broken down into “salable” parts. Recently, a coalition of more than 100 religious leaders issued a statement asking the government to prohibit the patenting of human genes and genetically engineered animals.<sup>24</sup> The coalition, coordinated by biotech adversary Jeremy Rifkin, director of the Foundation of Economic Trends, argued that patenting reduced the history of humanity to a commodity and violates the sanctity of human life. Some commentators have argued that reducing a life form to a composition of matter that is patentable is equivalent to reducing an organism to an object and creates a troubling precedent for ownership of life, including human life.<sup>25</sup> In essence, this argument rests not on the assumption that patenting results in ownership of human beings, but that patenting results in commodification of human beings and the commodification may lead to harm to human dignity.<sup>26</sup>

A final ethical issue focuses on what may be done with patented material. One element of this is a concern that human genes may be altered thus harming human genetic integrity.<sup>27</sup> Refusing patents on altered human genetic material will only indirectly control manipulation of genes—although patenting is designed to encourage investment is it clearly not the only impetus for research. A solution to this would be, instead, to regulate the research and uses of human genetic material. A second element of this concern is a fairness argument. If human genetic material is shared among all humans it should therefore “belong” to all humans. Although genomic research is being conducted on an international level, the resulting therapeutic technologies are not being distributed on a global level. For example, in one case the United States Department of Commerce filed a patent application for a cell line derived from the blood sample of a woman in Panama’s Guyami tribe. No consent had been given for isolation and patenting of the cell line, which was thought to have anti-cancer properties, nor was there any evidence that the woman, or her tribe would gain any benefits from later developed therapies.<sup>28</sup> In a recent California case, a physician-researcher failed to inform a patient that the additional travel to a distant lab and the testing done there were not required for his therapy, but were aimed at isolating a unique cell line that the investigator later sought to patent.<sup>29</sup> Allowing patents on human genetic material gives the patent holder a certain degree of control over the uses of that material. There is no guarantee that the individuals who donate the original genetic material for research will gain any benefit, nor that the resulting therapies will be distributed in a globally just manner.<sup>30</sup> As a result, allowing patent protection for human genomic material may result in greater inequities in the access to beneficial therapies. Patent holders should not be allowed to “sit” on a patent or to grant exclusive licenses to institutions which will not seek to develop the patent. Here too, the solution may be to ensure adequate informed consent or to regulate licensing agreements, not restrict patenting. Nonetheless, greater national attention needs to be paid to the implications of genomic patenting as well as to the international coordination of patenting laws.

## CONCLUSION

While the Council does not feel that patenting of naturally occurring substances is unethical *per se*, it does urge caution in this area. Genetic research holds great potential for the development of new beneficial therapies. However, it is unclear what role patenting may play in ensuring such development. While an outright ban on patenting of genomic material is unlikely and may be unwise, the Council makes the following recommendations:

- 1) Patents on processes—for example, processes used to isolate and purify gene sequences, genes and proteins, or vehicles of gene therapy—do not raise the same ethical problems as patents on the substances themselves and are thus preferable.

- 2) Substance patents on purified proteins present fewer ethical problems than patents on genes or DNA sequences and are thus preferable.
- 3) Patent descriptions should be carefully constructed to ensure that the patent holder does not limit the use of a naturally occurring form of the substance in question. This includes patents on proteins, genes, and genetic sequences.
- 4) One of the goals of genetic research is to achieve better medical treatments and technologies. Granting patent protection should not hinder this goal. Individuals or entities holding patents on genetic material should not allow patents to languish and should negotiate and structure licensing agreements in such a way as to encourage the development of better medical technology.

## REFERENCES

1. For example, Dr. Venter while at NIH filed, but subsequently withdrew, a patent application for a number of cDNA sequences. See, e.g., Paul Riley, Comments: Patenting Dr. Venter's Genetic Findings: Is the national institutes of health creating hurdles or clearing the path for biotechnology's voyage into the twenty-first century? *J. Con. H. L. & Policy* 10:309 (1994).
2. U.S. Const. art. I, 8, cl.8.
3. 35 U.S.C.112 (1988) ("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.").
4. Riley, *supra* note 1.
5. Rebecca Eisenberg, Patents and the Progress of Science: Exclusive rights and Experimental Use, *University of Chicago Law Review* 56:1017-1086 (1989).
6. 35 U.S.C. 102(a)(1988).
7. 35 U.S.C. 103 (1988).
8. 35 U.S.C. 101 (1988). *Brenner v. Manson*, 383 U.S. 519 (1966).
9. 447 U.S. 303 (1990).
10. Rebecca Eisenberg, "Patenting the Human Genome." *Emory Law Journal* 39:721-745, fn. 27, 1990.
11. The Danish Council of Ethics, "Patenting Human Genes," at 16, 1994.
12. Merck recently established a sequence database in the public domain that may make the question of patenting partial sequences moot due to lack of novelty. In addition, there is a federal DNA sequence database available for public use. C. Thomas Caskey, "Gene Patents—A Time to Balance Access and Incentives," *Bioinformatics* 14:298-301, 1996.
13. Karen Lech, "Human Genes Without Functions: Biotechnology Tests the Patent Utility Standard," *Suffolk University Law Review* 27:1631-1660, 1993; George Poste, "The Case for Genomic Patenting" *Nature* 378:534-536, 1995.
14. Rebecca Eisenberg, "Patenting the Human Genome" *Emory Law Journal* 39:721-745, 738, 1990.
15. Reid Adler, "Genome Research: Fulfilling the Public's Expectations for Knowledge and Commercialization," *Science* 257:908-914, 1992.
16. Rebecca Eisenberg, "Intellectual Property Issues in Genomics." *Bioinformatics* 14:302-307, 1996.
17. American Medical Association Council on Ethical and Judicial Affairs, Report 67: "Ethical Issues in the Patenting of Medical Procedures."
18. Baruch Brody, "Protecting human Dignity and the Patenting of Human Genes," Draft Paper Baylor College of Medicine, January 22, 1997 (there are four arguments that patenting human genes harms human dignity: (1) it is equivalent to ownership of humans, (2) it commercializes body parts which should not be commodified, (3) it cheapens that which defines human identity, and (4) it leads to inappropriate modifications in our genetic integrity.).

19. U.S. Const. Amendment 13.
20. There are some opponents of patenting who claim that no naturally occurring substances should be patentable. See, e.g., Kathleen Day, "Church Groups to Fight Patenting of Life Forms," *Washington Post*, Saturday, May 13, 1995.
21. The Danish Council of Ethics, *supra* note 14 at 27.
22. See, e.g., Brody, *supra* note 12.
23. See, e.g. Margaret Radin, *Contested Commodities* (1996).
24. "Religious Leaders Prepare to Fight Patents on Genes." *New York Times*, Saturday, May 13, 1995
25. *Id.*
26. See, e.g., Radin *supra* note 16 and Brody, *supra* note 12.
27. Brody, *supra* note 12.
28. "Life for Sale: Europe says no to patenting life forms, but the US moves ahead." *Utne Reader*, June 1995.
29. *Moore v. Regents of the University of California*, 793 P.2d 479 (Ca. 1990).
30. See, e.g., Bernadine Healy, "Special Report on Gene Patenting," *New England Journal of Medicine*. 327(9):664-668, 1992.

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## Ethical Issues in the Patenting of Medical Procedures

### INTRODUCTION

The patenting of medical procedures has been criticized on general grounds. Commentators have argued that it raises the cost of the patented procedures, thereby limiting patient access to the procedures. In addition, patenting restricts access in the research community, thereby limiting opportunity for peer review and for further research that would build on or use a patented technique. The patenting of medical procedures, although not a new phenomenon, has recently been raised as a concern in relation to litigation in which the holder of a patent on a specific type of ophthalmic surgical incision has sought to enforce the patent.<sup>1,2,4</sup>

In order to avoid any potential confusion, the Council would like to clarify at the outset of this report the terms that will be employed. "Medical process patents" refers to those patents taken out on medical procedures and techniques. According to the statutory language of the United States Code, a patent on a medical procedure is legally characterized as a patent on a medical process. For the purposes of this report, "medical process patent" should be taken as equivalent to "patent on a medical procedure".

### BACKGROUND

The United States Constitution grants Congress the power to make laws "to promote the Progress of Science and useful Arts by securing for limited times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."<sup>5</sup> Accordingly, beginning with the Patent Act of 1790, Congress established a system whereby, in return for full disclosure of a novel, non-obvious and useful invention, an inventor is given broad exclusive rights to the invention for a period of 17 years from the grant of the patent. As a result of a provision in the General Agreement on Tariffs and Trades, effective June 1995, the period of patent protection increased to 20 years from the date that an application is first filed.<sup>7</sup> Patent holders may use the invention themselves or license the invention in exchange for royalties. An unauthorized person, even one with no knowledge of the patent, who "makes, uses or sells any patented invention, within the United States during the term of the patent thereof, infringes the patent."<sup>9</sup> Currently, under legislation passed in 1952, patents are applicable to any new or useful "process, machine, manufacture or composition of matter"<sup>10</sup> where "process" means "process, art or method and includes a new use of a known process, machine, manufacture, composition of matter or material."<sup>11</sup> This definition, while not directly addressing the question of medical procedures, leaves open the possibility of the legitimacy of medical process patents. Furthermore, in a 1980 decision, the Supreme Court granted patent protection to the inventor of an artificial life form on the grounds that "man-made" bacterial plasmids qualify as a new "manufacture" or "composition of matter."<sup>2</sup> This decision to broadly interpret the statutory scope of patentable inventions makes it highly unlikely that medical procedures can be legally excluded from the legal definition of process without additional legislative action.<sup>13</sup> While such a statutory exception has previously been created only for nuclear warfare technologies, legislation was recently proposed to prohibit patents "for any invention or discovery of a technique, method, process for performing a surgical or medical therapy, administering a surgical or medical therapy, or making a medical diagnosis" independent of an otherwise patentable device or pharmaceutical.<sup>14,15,11</sup>

The Patent and Trademark Office (PTO) has approved a number of patents for "pure" process claims as well as the more common claims in which method is combined with some form of novel instrumentation.<sup>11, 17, 18</sup> Throughout the 1980s, these patents tended to be granted to procedures which were rarely used or constituted extraordinary health care.<sup>17,18</sup> However the patenting of medical procedures has recently expanded both in terms of volume of patents issued and the subject matter of the approved process patents. One estimate places the rate of approval of medical process patents at 15 per

week, although this figure does not distinguish between pure process claims and patent claims which involve both a device and a method. In addition, the trend appears to be moving towards the patenting of common and widely used medical procedures, as evidenced by the PTO's decision to grant a patent to a stitch-free incision for cataract removal that is used by an estimated 40% of ophthalmologists.<sup>1,2,4</sup> Equally disturbing is the fact that the patent holder on this procedure has commenced the first infringement litigation involving a physician as co-defendant, defense costs had already reached \$125,000 a year ago and, if the suit is successful up to 2000 surgeons could be subject to similar prosecution.<sup>15</sup> In light of these developments, this report will examine the use of pure medical process patents, including patents for diagnoses, imaging techniques, off-label uses of a pharmaceutical, and methods of administering a biomedical therapy. Medical process patents which involve the patenting of a procedure in conjunction with a device or drug fall outside the scope of this report, as do patents for devices without which a procedure cannot be performed.

## ETHICAL ISSUES

Since the time of Hippocrates, physicians have relied on the open exchange of information without the expectation of financial reward for advancing medical science. The medical profession has a longstanding obligation not to withhold information but rather to share techniques as needed.<sup>19,20,21,22,23</sup> This well-established tradition is in large part reflected in Principle V of the *Principles of Medical Ethics* of the American Medical Association and in Opinion 9.08 of the *Code of Medical Ethics* of the AMA:

V. A physician shall continue to *study, apply and advance scientific know edge, make relevant information available to patients, colleagues, and the public, obtain consultation and use the talents of other health professionals when indicated.* [Emphasis added.]<sup>(p.xiv)</sup>

9.08: New Medical Procedures. In the ethical tradition expressed by Hippocrates and continuously affirmed thereafter, the role of the physician has been that of a healer who serves patients, *a teacher who imparts knowledge of skills and techniques to colleagues*, and a student who constantly seeks to keep abreast of new medical knowledge.

*Physicians have an obligation to share their knowledge and skills and to re- port the results of clinical and laboratory research.* Both positive and negative studies should be included even though they may not support the author's hypothesis. *This tradition enhances patient care, leads to early evaluation of new technologies, and permits the rapid dissemination of improved techniques.*

*The intentional withholding of new medical knowledge, skills and techniques from colleagues for reasons of personal gain is detrimental to the medical profession and to society and is to be condemned.*<sup>p.139</sup>

The impact of Principle V and Opinion 9.08 on the acceptability of medical process patents is unclear. At first glance, they appear to prohibit the patenting of medical processes. On one level, it can be argued that a medical process patent amounts to "the intentional withholding of new medical knowledge. For reasons of personal gain. " However, it can also be argued that medical process patents are consistent with the AMA's *Code of Medical Ethics*. The patent system requires full disclosure of a patented invention and, once a procedure is patented, the patent holder can make it available to other physicians for a reasonable licensing fee. Therefore, it could follow that there need not be any withholding of knowledge.

Yet, even if a convincing argument can be made for the view that patenting does not necessarily entail withholding, Principle V and Opinion 9.08 provide another basis for condemning the patenting of procedures, namely the decrease in professionalism occasioned by physicians who seek and enforce

patents. Physicians who collectively engage in promoting health and patient welfare constitute the medical profession. The patenting of medical procedures, with its emphasis on individual reward, selective sharing and ownership, undermines the coherence of the profession. In addition, a profession is characterized by shared commitment to moral ideals. One of the fundamental principles in medicine is that the health of the patient is a physician's most basic concern. Much of the respect and trust accorded patients arises from the perception that economic concerns do not generally impact medical decisionmaking. In opposition, medical process patents are committed to the primacy of economic benefit and reward. To the extent which economic goals are elevated above those of patient health, the integrity of the profession is severely weakened.

Some commentators have argued that these criticisms of medical process patents are not sufficient justification for a prohibition on patenting medical procedures, that the ethical concerns raised by process patents are also raised by other kinds of health care patents which are well accepted by society as well as by the medical profession.<sup>12, 17, 18,20 (p.140)</sup> For example, pharmaceutical manufacturers patent their drugs, and physicians patent their new devices. Nevertheless, as the remainder of this report demonstrates, there are compelling reasons for distinguishing between patents on medical procedures and patents on drugs and devices.

## PROFESSIONAL AND PATIENT CARE CONCERNS

### *Restricted access to patented procedures*

#### Restricted clinical access

The most compelling argument against medical process patents is grounded in the unacceptable picture of a patented procedure becoming unavailable to patients who require it, particularly when no alternative exists. Once procedures can be patented, physicians will not be able to use a patent procedure without obtaining a license to use the procedure. If the patent holder were to restrict the number of licensees or charge a high price for licensing, then the patent holder would be erecting significant barriers to patient access to a needed treatment.<sup>13,18,24</sup> Such withholding of information to the detriment of patient care is clearly unethical, condemned in texts ranging from the Hippocratic Oath to the AMA's *Code of Medical Ethics*. An additional concern is that the patent process could influence a doctor's medical judgment as to the appropriate treatment.<sup>17,18</sup> In cases in which a patented procedure would be the most advisable therapy, physicians might rationalize the performance of what could be an inferior procedure rather than become a licensee of the patent holder or refer the patient to a licensed physician.

Moreover, the patenting of medical procedures may have a profound chilling effect on the use of any advances in medical procedures. Once patenting is allowed, physicians face a substantial legal risk every time they decide to introduce a new procedure or a modification of an existing procedure into their practice. This is because use of a patented procedure without permission of the patent holder constitutes unlawful infringement of the procedure. While physicians could avoid infringement by obtaining a license, it will often not be clear whether a valid patent exists. There is no obvious way for a physician to know whether a particular procedure has been patented. Even when physicians devise a new procedure or a modification of an existing procedure on their own, they still could be at legal risk if someone else already patented the procedure or the modification. Faced with this uncertainty, physicians may decide that it is safer not to use new procedures or modifications of existing procedures until they can be certain that no patents exist. To achieve such certainty would take considerable time and effort. In the meantime, many patients will not be able to benefit from the procedure or modification. The legal risk from procedure patents exists once patents are permitted even if they are not aggressively enforced. A patent holder is free at any time to seek enforcement of the patent.

The chilling effect of procedure patents distinguishes these patents in an important way from drug or device patents. If a drug or device has been patented, the licensing fee is incorporated into the cost of the drug or device. Accordingly, the physician does not have to worry about inadvertently infringing a drug or device patent, and physicians therefore are not discouraged from using drugs or devices by legal uncertainty about patent infringement.

The concerns about the constraining effects of a patent are especially important in light of the recent shift in patenting from fairly specialized medical procedures to processes of greater applicability, such as detection methods for breast tumors, which increases the number of potential beneficiaries who could be adversely affected by patenting.<sup>17,18,25</sup> It is true that physicians have been able to practice good medicine despite many existing restraints on their autonomy, such as insurance compensation and contractual obligations. However, it does not follow that there should be more restraints.

### Restricted academic access

The prospect of patenting medical procedures raises additional fears in the research community. Patented biomedical procedures may be restricted from peer review because other physicians may not be able to study the procedure without paying a licensing fee.<sup>17,18,26</sup> While the Food and Drug Administration has responsibility for regulating drugs and devices, peer review serves as the primary regulatory mechanism for medical processes.<sup>26</sup> Thus, the potential barriers to peer review from patenting could lead to a decrease in the quality and safety of new procedures. Furthermore, patients who are not knowledgeable about the process of publication and peer review might not realize that patenting does not guarantee scientific merit but might mistakenly think that patenting is a statement of efficacy. As a result, they could subsequently undergo unnecessary or unwarranted procedures. Already, certain techniques have been prominently labeled as "patented" in advertising by physicians even though the techniques have little or no proven scientific merit.

Some concerns about peer review could conceivably be avoided by the application of an expanded form of "the experimental use doctrine" (allowing minimal use of the patented invention which does not interfere with the economic interests of the patent holder) to allow investigational use of patented procedures.<sup>12,18</sup> Patent holders would have incentive to seek peer review, since there is no financial benefit in holding a patent on a useless or dangerous procedure.<sup>27</sup> Yet both the "restricted use" doctrine and the reliance on market forces are limited in their ability to guarantee the timely dissemination of information about the patented technique.<sup>12,18</sup> Disclosure of new procedures would likely take longer in the presence of widespread patenting than when innovation is motivated solely by altruistic or scientific concerns.<sup>23</sup> Physicians seeking patents are frequently admonished by legal counsel not to reveal inventions before filing a patent application.<sup>28</sup> Furthermore, an inventor who is unsure about the patentability of the technique may even defer publication until the patent has been issued, a process that generally takes years.<sup>12</sup> Because a patent is in effect for 20 years, a patented procedure may not be available for use by medical schools in training the next generation of physicians.<sup>29</sup>

Despite the effects of patents on access to new procedures in research and clinical practice, some commentators have argued that patenting may not necessarily entail the withholding of information.<sup>12,17,18,23</sup> As mentioned earlier, the granting of any patent is contingent on the full disclosure of the invention in question. Nevertheless, access to patented procedures is more restricted than it would be if patenting were prohibited.<sup>12,17,18,23</sup> While patenting may provide sufficient access to a description or explanation of a patented technique, it simultaneously creates additional barriers to an individual physician's application of the procedure. Disclosure of the technique without the ability to use the technique does not constitute availability in any substantial sense. Rather, before the information can be considered truly shared the recipient of the information must be able to act on the information. In short, it is difficult to see how the legal requirement to disclose the content of a patent satisfies the ethical

obligation to share information if the actual performance of the disclosed procedure is restricted. While it may be argued that current geographic and financial constraints on patient access to treatment are tolerated by the medical community,<sup>18</sup> it does not follow that the medical profession should erect more such barriers at the expense of the patient and the integrity of the profession. Likewise, while the free flow of information may not be blocked by patenting any more than it is by concerns about dominance in a field, tenure, and prestige,<sup>18,23</sup> the fact that there are such barriers to data sharing does not mean that they should exist and proliferate.

### *Increased Financial Burdens*

An ancillary argument against medical process patents is that patenting of medical procedures may lead to an increase in the cost of health care via licensing fees or the costs of infringement litigation. While royalty fees may be "nominal" from a percentage perspective, these small percentages over a great number of procedures can substantially increase the cost of health care, especially with the widespread proliferation of patents.<sup>3, 4, 19, 29</sup> In addition, it is necessary to consider the additional costs of infringement litigation as patent-holders attempt to collect on their promised monopoly. Legal costs associated with patenting and licensing are already quite high, with a recent survey showing that universities spent \$52.8 million on such fees, litigation and associated costs in 1992 alone. It is likely that an increase in these kinds of expenses resulting from biomedical process patents expenses will be carried by the patient population via an increase in the cost to the consumer undergoing the procedure. This is unacceptable; physicians have an ethical obligation not to place additional financial burdens on their patients. While in certain cases patenting may be fiscally neutral or actually economically benefit patients by leading to a decrease in the cost of treatment as new, less expensive procedures replace older ones,<sup>2,3</sup> it is not clear to what extent this line of reasoning is generalizable, and there is little supporting empirical data from which to draw conclusions.

### *Enforcement and patient confidentiality*

A final ethical concern involves the way in which patent claims could be enforced. While it is easy to track the sales of a device or pharmaceutical, it may be significantly more difficult to monitor a physician's use of a patented technique.<sup>29, 31</sup> In addition, the monitoring of medical procedures could potentially compromise the privacy of both patients and physicians.<sup>17,26,29</sup>

It may be possible to conduct enforcement in such a way as to be both effective and confidential, for example by charging doctors, insurers, group practices or health maintenance organizations fees based on yearly numbers of patients seen rather than on a case-by-case basis.<sup>31</sup> However it is not clear how to ensure accuracy of reporting by these groups without compromising confidentiality in some manner.

## INCENTIVE TO INNOVATE

Despite the aforementioned concerns about the potential consequence of patenting medical procedures and techniques, proponents argue that these costs are outweighed by the main benefit of patenting, namely that the procedure might not have been available at all in the absence of the patent system.<sup>12,17,18,23,32</sup> It is senseless to fault patenting for restricting access to medical procedures if the procedures would not have been developed otherwise. For, although patents provide for individual benefit to inventors, either economically or in terms of recognition and respect for their discoveries, it may be argued that this is not the primary purpose of the patent system.<sup>17,18,32</sup> Rather, patent policy is predicated on securing the invention for public benefit by offering a reward as an incentive to innovate and disclose, and individual reward considered in itself is a secondary concern.

Not all procedures require extensive research and development; however, some do. These procedures may never be made available to the public at all without the possibility of patent protection. For example, estimates of the total costs incurred in the development of the patented technique of Surrogate Embryo Transfer (SET) range from \$500,000<sup>24</sup> to \$1.25 million.<sup>29</sup> Furthermore, complex medical procedures are developed in an academic world in which government funding is often insufficient and the distinction between for-profit and non-profit academic research is becoming blurred.<sup>12</sup> Often, in order for new products to come into existence at all, there must be private funding of developmental research.<sup>21</sup> Private companies may be unwilling to provide capital for research and development if they cannot expect to see an economic return on their investment.<sup>17, 18, 32</sup> It may be argued that patenting, by offering broad exclusive rights, provides precisely that incentive. In addition, once a process is patented and licensed by an academic institution, it is possible that the royalty fees can be used to support the hospital and its investigators in further research.<sup>4</sup>

An ancillary argument for the patenting of medical procedures is that, for innovative physicians who wish to protect their interests, the alternative to patenting is non-disclosure.<sup>23</sup> With patenting, the physician is guaranteed some kind of reward for making the procedure public knowledge. Without such a guarantee, those physicians who wish to protect their discoveries may keep them secret, thereby hindering the dissemination of knowledge.<sup>17, 18, 23</sup> While uncommon in the medical community, such non-disclosure has occurred historically (most notoriously, the refusal of four generations of the Chamberlen family to reveal their discovery of the obstetrics forceps<sup>5</sup>) and continues in more subtle forms today.<sup>22</sup>

The argument that patents are needed to ensure disclosure is not adequate to justify patenting medical procedures. Given the aforementioned strong ethical prohibitions on withholding information, patenting is being inappropriately promoted to solve a dilemma that clearly should not exist. While those who violate disclosure requirements may respond to economic incentives rather than principles, it is inappropriate to reward their unethical behavior by providing an economic benefit to disclosure. Rather patenting can be ethically defensible only if it performs a function beyond merely rewarding violators for something they should have done in the first place.

While the argument that the patenting of medical processes is necessary to enable and promote procedural advances seems strong initially, there is no evidence of the argument's empirical soundness. Medical process patents have been possible since the early 1950's but were rarely issued until recently. The fact that medicine advanced rapidly from World War II to the late 1970's despite the absence of medical process patents undermines the central claim that economic incentive is needed to induce innovation in the realm of medical procedures. In addition, although patents can provide economic benefits to inventors, the medical field has, over the years, established its own internal system of rewards, including recognition and respect for discoveries through the publication of findings in respected medical journals and other media. While proponents of patenting might point out that the ophthalmologist involved in the aforementioned patent infringement suit initially attempted to publish his work, only to be rebuffed by a peer-reviewed journal, the important point is that the prospect of publication provided sufficient incentive for the ophthalmologist to develop his new procedure.

This type of appeal to non-financial incentives does not entirely address the issue of incentive for innovation, for internal recognition and respect do not necessarily generate the money to enable the creation of new procedures in the first place. The patent system provides incentive for investors as well as individual physician-inventors and the investors are neither recipients of nor concerned with internal prestige as much as financial reward. Yet this defense of medical process patents is ultimately unconvincing. While there is no substantive empirical data about the level of incentive needed to promote

innovation and disclosure in the biomedical sciences,<sup>17, 18, 32</sup> it is reasonable to claim that this level would be significantly lower for procedures than it would be for devices and pharmaceuticals. Unlike the development of innovative medical instruments or pharmaceuticals, the development of medical processes usually relies on intellectual curiosity and creativity rather than the availability of capital for research and development. Especially in the case of pure medical process patents, the innovative step tends to be a novel mental step rather than the creation of a new physical entity. While this does not mean that this type of innovation is any less worthy of reward, it does imply that the need for outside funding costs that might require later recovery is generally less pressing than in the case of devices or pharmaceuticals. SET is one obvious counterexample, yet this alone does not undermine a prohibition on patenting of medical procedures as we do not, in any context, require general rules to meet the impossible condition of working faultlessly.

## REGULATION VS. PROHIBITION

It may be argued that the distinction between product patents and process patents does not arise from some feature unique to medical process patents but rather results from the comparison of inappropriate medical process patents with appropriate patents on devices and pharmaceuticals. If the comparison were drawn instead between a procedure such as SET, an appropriate candidate for patenting, and a corresponding device or pharmaceutical, then the troublesome discrepancy in the strength of the incentive-to-innovate justification would likely evaporate. SET likely would not have been developed in the absence of patent protection, so the benefits occasioned by patenting are tangible and comparable to that occasioned by other kinds of acceptable patents. In addition, the costs are no more than other medical patents since SET, as a rare procedure, has relatively little impact on physician autonomy, and the scarcity of potential beneficiaries makes the potential decrease in accessibility even less than that tolerated in the case of many devices and pharmaceuticals. Because some process patents may be as justifiable as drug or device patents, it is often argued that process patents should be regulated rather than prohibited.<sup>17, 18</sup> Ethical codes, according to this line of reasoning, should distinguish between inappropriate and appropriate patents.

The basis on which to draw a distinction between appropriate and inappropriate patents can be found in the fundamental tenet of the patent system that a patented invention be both "novel" and "non-obvious". While the novelty condition requiring that the patented invention be new is likely too broad to discourage the patenting of procedures such as the cataract incision, the requirement that the patented invention be non-obvious may be significantly more useful. In order for a procedure to qualify as non-obvious, it must represent a substantial advance over the state of the prior art, one which could neither have been easily deduced from the background of medical knowledge at the time of the generation of the procedure,<sup>12</sup> nor have been readily obvious to a skilled worker in the field.<sup>36</sup> While this condition is met by procedures such as SET, other patented procedures such as the diagnosis of chronic fatigue syndrome<sup>37</sup> and the use of vasodilators for treatment of male impotence<sup>1</sup> fall short of this standard. Indeed rigorous application of the standard would not only remove the procedures which are currently causing an uproar in the medical community from patent protection but would ensure that procedures worthy of patent protection could come into existence. It seems reasonable to assert that generally the procedures which were non-obvious would be the ones that required additional incentives and economic investment.

Nevertheless, the option of regulation is not tenable. Unfortunately, as supported by the recent furor of the patenting of medical procedures, there is a significant gap between a strict interpretation of novel and non-obvious and the way that these terms are currently applied in assessing patent applications. As in the case of biotechnology generally, the Patent and Trademark Office (PTO) has applied the statutory rules too broadly, resulting in unduly expansive patenting decisions.<sup>35</sup> Often the PTO relies on subsequent litigation challenging the validity of issued patents to weed out those patents which are not truly novel

and non-obvious. The trend in recent years toward the widespread patenting of common medical procedures undermines the essential distinction between appropriate and inappropriate medical process patents. While inappropriate medical process patents may be particularly vulnerable to court challenge,<sup>18</sup> this is not an acceptable solution, for it leaves unaddressed the additional costs incurred by litigation as well as the inaccessibility and professional compromises that may occur while the application and subsequent litigation are pursued. In short, while the ethical problems with patenting might be solved in theory by drawing a distinction between inappropriate and appropriate medical process patents, such a solution is not useful in practice.

## CONCLUSION

A physician has the ethical responsibility not only to learn from but also to contribute to the total store of scientific knowledge when possible. Physicians should strive to advance medical science and make their advances known to patients, colleagues and the public. This obligation provides not merely incentive but imperative to innovate and share the ensuing advances. The patenting of medical procedures poses substantial risks to the effective practice of medicine by limiting the availability of new procedures to patients and should be condemned on this basis. Accordingly, the Council believes that it is unethical for physicians to seek, secure or enforce patents on medical procedures.

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Report of the Judicial Council  
December 1984

**NEW MEDICAL PROCEDURES.** In the ethical tradition expressed by Hippocrates and continuously affirmed thereafter, the role of the physician has been that of a healer who serves patients, a teacher who imparts knowledge of skills and techniques to colleagues, and a student who constantly seeks to keep abreast of new medical knowledge.

Physicians have an obligation to share their knowledge and skills and to report the results of clinical and laboratory research. This tradition enhances patient care, leads to the early evaluation of new technologies, and permits the rapid dissemination of improved techniques.

The intentional withholding of new medical knowledge, skills and techniques from colleagues for reasons of personal gain is detrimental to the medical profession and to society and is to be condemned.

Prompt presentation before scientific organizations and timely publication of clinical and laboratory research in scientific journals is an essential element of good medical care.

## REPORTS OF STANDING COMMITTEES OF THE HOUSE OF DELEGATES

### JUDICIAL COUNCIL

The following reports (A, C, D) were presented by Dr. E. G. Shelley, *Vice Chairman*. Report B, "Eulogy for James H. Berge, MD," appears on page 12. Report E, "Nominations for Affiliate Membership in the American Medical Association" appears on page 163.

#### A. Declaration of Helsinki

During the past several years, the American Medical Association has given much attention to the subject of ethical guidelines for clinical medical investigation. A number of meetings have been held at which representatives of the Association and other organizations such as the American Federation for Clinical Research, the American Society for Clinical Investigation, the Central Society for Clinical Research, and the American College of Physicians, have discussed the desirability of adopting guidelines or standards or rules for clinical medical investigation. It is the consensus of knowledgeable individuals in this field that guidelines for medical clinical investigation should be developed and promulgated. It is the further thinking of these individuals, and the Judicial Council concurs in this thinking, that the Declaration of Helsinki adopted by the World Medical Association in 1954 is the expression of basic principles to which all honorable physicians and investigators can subscribe and may be accepted as guides to ethical conduct in medical investigation.

The Judicial Council has reviewed the Declaration of Helsinki and is of the opinion that it is in accord with the *Principles of Medical Ethics* of the American Medical Association. The Judicial Council, therefore, submits this Declaration to the House of Delegates with the recommendation that the House of Delegates endorse the Declaration of Helsinki as a guide to those who are engaged in clinical medical investigation.

#### DECLARATION OF HELSINKI RECOMMENDATIONS GUIDING DOCTORS IN CLINICAL RESEARCH

It is the mission of the doctor to safeguard the health of the people. His knowledge and conscience are dedicated to the fulfillment of this mission. The Declaration of Geneva of the World Medical Association binds the doctor with the words: "The health of my patient will be my first consideration" and the International Code of Medical Ethics declares that "Any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest." Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to suffering humanity, the World Medical Association has prepared the following recommendations as a guide to each doctor in clinical research. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Doctors are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and the clinical research, the essential object of which is purely scientific and without therapeutic value to the person subjected to the research.

##### I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.
2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.
3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.
5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

##### II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in his judgment it offers hope of saving life, re-establishing health, or alleviating suffering. If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity, the permission of the legal guardian replaces that of the patient.
2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient.

### III. Non-Therapeutic Clinical Research

1. In the purely scientific application of clinical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom clinical research is being carried out.
2. The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.
- 3a. Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.
- 3b. The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully his power of choice.
- 3c. Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.
- 4a. The investigator must respect the right of each individual to safeguard his personal integrity, especially if the subject is in a dependent relationship to the investigator.
- 4b. At any time during the course of clinical research the subject or his guardian should be free to withdraw permission for research to be continued. The investigator or the investigating team should discontinue the research if, in his or their judgment, it may, if continued, be harmful to the individual.

REPORT OF REFERENCE COMMITTEE ON AMENDMENTS TO CONSTITUTION AND BYLAWS: On recommendation of the Reference Committee, the House voted to adopt Report A of the Judicial Council and Report M (p. 51) of the Board of Trustees and urged publication of the Declaration of Helsinki in state and local journals for the information of all physicians.

The following report was presented by Dr. Philip H. Jones, *Chairman*:

Report A of the Judicial Council and Report M (p. 51) of the Board of Trustees urge that the Declaration of Helsinki, already adopted by the World Medical Association, be endorsed by the House of Delegates as a guide to those who are engaged in clinical medical investigation. The Judicial Council report further indicates that the Declaration of Helsinki is in accord with the *Principles of Medical Ethics* of the American Medical Association.

#### C. Special Report Concerning Unethical Hospital Assessments

At the Clinical Convention of the AMA House of Delegates in November 1965, the Pennsylvania delegation introduced resolution no. 13. The resolution reads as follows:

WHEREAS, A 'bed tax' has been imposed on doctors serving on the medical staffs of hospitals under the guise of voluntary contributions to intern and resident educational programs; and  
 WHEREAS, Physicians have lost their hospital privileges as a result of refusing to pay such 'contributions';  
 and  
 WHEREAS, Such taxes have been declared in violation of the *Principles of Medical Ethics* of the American Medical Association; Section 7, paragraph 9, which reads as follows;

"Compulsory Assessments, that is, assessments which, if not paid, would automatically cause doctors to lose staff membership, are not in the best traditions of ethical practice. It is not proper to condition medical staff membership on compulsory assessments for any purpose." (Judicial Council, 1962);

therefore be it

*Resolved*, That it is hereby declared to be a violation of the *Principles of Medical Ethics* of the American Medical Association for a physician, group or organization of physicians to take any action that imposes payment by physicians to a hospital for any purpose when such payment or nonpayment will, in any way, affect the granting or retention of hospital privileges to any physician.

The Reference Committee on Insurance and Medical Service, believing that the *Resolved* clause of resolution no. 13 broadens the area of previous Judicial Council opinions, recommended that resolution no. 13 be referred to the Judicial Council for consideration and such action as it deems necessary.

In 1952 the Judicial Council called attention to proposals whereby some hospitals suggested that physicians who utilize the hospital facilities pay to the hospital a percentage of the fees which they receive from their patients while being cared for in the hospital. The Council expressed its opinion that this was a form of fee splitting or sharing of professional fees with a lay organization which should not render professional services in the first place, but which in addition, has already levied its regular bill for the services which it legitimately rendered.

At the June 1958 Annual Convention of the Association, resolution no. 55 asked that the House of Delegates reiterate its position with regard to condemning compulsory assessments of members of medical staffs for building funds and the practice of required audits of staff members' financial records as a requisite for continued staff appointment. The Reference Committee on Medical Education and Hospitals recommended