THE HARVARD MOUSE AND ALL THAT: LIFE PATENTS IN CANADA

CELA Publication #454
ISBN #1-894158-98-9

Michelle Swenarchuk
Director of International Programmes

October 2003

CANADIAN ENVIRONMENTAL LAW ASSOCIATION
L'ASSOCIATION CANADIENNE DU DROIT DE L'ENVIRONNEMENT

130 SPADINA AVENUE • SUITE 301 • TORONTO, ONTARIO • M5V 2L4
TEL: 416/960-2284 • FAX 416/960-9392 • WEB SITE: www.cela.ca

TABLE OF CONTENTS

INTRODUCTION

On December 5, 2002, the Supreme Court of Canada released its decision that a higher life form, a genetically–engineered mouse, developed at Harvard University for use in cancer research was not patentable.[1] The case had been extensively covered in the media, bringing to public attention the little-known practice of granting patents on living things. Harvard had argued that Canada needed to follow the patent practice in the United States, where the mouse and other animals are patentable. In declining to do so, the Court opened the door to a wide debate on the role of life patents in public policy, and the value of a distinct Canadian path.

What is a patent?

A patent is a form of intellectual property, a "category of intangible rights protecting commercially valuable products of the human intellect" which includes trademarks, copyright and trade-secret rights. (Black's 1999) These forms of property essentially compensate thinkers for their work and contribution to society.

In contemporary law, patents are available to those who create new inventions, defined as:

> any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter.[2]

Patentability requires that something be new, inventive (not obvious), and useful. Historically, patents were available for objects and processes (widgets and chemical reactions) that were invented by humans, but not for something that occurred in nature (an element on the periodic table). Patent law represents a social contract: an inventor gets an exclusionary right to use and control an invention for twenty years in return for

disclosure, describing how he/she made the invention in the application so someone else, "skilled in the art" can do the same thing eventually. This bargain was intended to provide public benefits by encouraging inventors to disclose inventions rather than assert other forms of property rights, such as trade secrets, which would preclude any use by others.

Life patents

In 1980, in a 5-4 decision, the US Supreme Court granted a patent on a micro-organism, a bacteria used in treating oil pollution[3], opening the door to the patenting of living things. Since then, thousands of patents on micro-organisms, plants, animals, genes, and cells have been granted in the US, Europe and Japan. The US standard for patentability is now commonly described as "anything under the sun made by the hand of man." The World Trade Organization Agreement on Trade-Related Intellectual Property (TRIPs), concluded in 1994, has been the basis for requiring the approximately 150 WTO member countries to adopt patent regimes consistent with those of the OECD countries, engendering serious controversy in many developing countries.

The Canadian Intellectual Property Office (CIPO) decided to grant patents on single-celled life forms. According to spokesman Michael Gillen, senior biotechnology examiner, "We're not questioning whether genes should be patented because US courts have ruled that they can."[4] Canada now patents proteins, genes, and cells from plants, animals, and humans, and human and animal diagnostics performed on the human or animal body, but not outside the body. Patents are not granted on whole plants, plant

varieties, human and animal organs, or human and animal therapies (including gene therapies) performed on the human or animal body. (Canada 2002)

The Harvard Oncomouse in Canada

In 1985, Harvard University applied for a Canadian patent on a transgenic mouse developed by scientists by the insertion of a foreign gene into the mouse, disposing it to develop tumours for use in cancer research. This was the precedent claim on a “higher life form” a multicellular, complex mammal. The Commissioner of Patents refused the claim, which included "all (similar transgenic) non-human mammals", and the decision went to the Supreme Court of Canada. Justice Bastarache, writing for the majority of the Court, held that

> the unique concerns and issues raised by the patentability of plants and animals necessitate a parliamentary response. Only Parliament has the institutional competence to extend patent rights or another form of intellectual property protection to plants and animals and to attach appropriate conditions to the right that is granted. [5]

THE LIFE PATENTS DEBATE

Harvard University argued that patents are necessary to enable biotechnology companies to raise money from investors for research and innovation. Further, transgenic animals are human inventions, since every cell in the body is changed, and Canada needs to patent life because the US and Europe do so, and Canada will lose private investment funds if the policy differs in Canada.[6]

ARUGMENTS AGAINST PATENTS ON LIFE

The question of invention

Patents are available by law for inventions. A fundamental dispute related to patents on life forms is whether humans can be considered to have invented them, or whether they are phenomena of nature which humans are only able to discover. Dr John Sulston, winner of the 2002 Nobel Prize in Physiology or Medicine argues:

> The genome sequence is a discovery, not an invention. Like a mountain or a river, the genome is a natural phenomenon …. Inventing human genes is impossible. So every discovery relating to genes - their sequence, functions and everything else - should be placed in the pre-competitive arena… We should not be patenting whole life forms, such as transgenic mice or cotton plants … we did not invent these organisms, only the specific modification that made the mice susceptible to cancer or the cotton resistant to pests. (Sulston 2002)

Nor does he accept the rationale commonly advanced by patent officials for granting patents on genes if they can be isolated or replicated outside the body:

> This argument has always seemed absurd to me. The essence of a gene is the information it provides - the sequence. Copying it into another format makes no difference. It is like taking a hardback book written by someone else, publishing it in paperback and then claiming authorship because the binding is different.

An animal such as a transgenic mouse has been changed from its natural progenitors by human intervention, but the mouse into which a novel gene has been introduced, with its complexity and myriad natural qualities, is a product of nature. Scientists are entitled to obtain patents on the processes by which the mouse is modified, as Harvard did, enabling them to obtain economic returns from that work. It is difficult to see how isolating a gene or replicating it turns it from a natural phenomenon into a human invention. Rather, it is illogical and contrary to human and evolutionary history to hold that the cells and genes

whose evolution over millennia made humanoids into *homo sapiens* were invented in the past three decades by humans. The distinction between discoveries of nature and human invention has been largely erased in patent law, leaving an edifice of life patents whose foundation is a legal fiction.

Patents reward inventors for the application of knowledge to practical uses. However, as Dr. Sulston argues, the essence of genes is the information, the knowledge, that they contain. Hence, to patent genes is to patent knowledge itself, depriving society as a whole of the time for dissemination and exploration of a new type of knowledge in order to maximize its social benefits[7]. "We no longer have a patent system that rewards inventors for their creativity but one that essentially rewards investors for their investment", argues Deryck Beyleveld, Director of the Sheffield Institute of Biotechnological Law and Ethics in the UK. (Adam 2002)

EQUITABLE ACCESS TO THE BENEFITS OF BIODIVERSITY

The patenting of life forms impedes equitable access to the benefits of biodiversity as patents on the genes of crops and livestock concentrate economic power in large agricultural businesses, and facilitate appropriation by them of genetic resources and knowledge developed over millennia by indigenous and local communities in developing countries. This exploitation of indigenous peoples' knowledge is a growing global concern. Applicants for patents need not identify the geographic origin of genetic materials claimed, nor whether the purported invention was developed using the knowledge of indigenous peoples. This results in a risk of misappropriation of indigenous knowledge, through patenting, without the consent of the peoples whose knowledge has been used and without appropriate compensation to them. (Canadian Environmental Law Association: 2001)

The United Kingdom Commission on Intellectual Property Rights has concluded that an expansion of intellectual property rights is unlikely to benefit developing countries, and is likely to lead to higher-priced medicines and seeds, making poverty reduction more difficult. (Mayer 2002)

IMPACTS OF PATENTS ON THE ADVANCEMENT OF SCIENCE

Debates in the scientific and legal literature demonstrate that patents on life forms are having harmful effects on the advancement of science, by making research tools (transgenic animals, markers, assays, laboratory reagents) expensive or unavailable; preventing "downstream" research on genes; preventing development of new drugs and diagnostic tests; reducing or delaying the publication of research results; and reducing the information that would otherwise be freely available to scientists.

The proliferation of patenting has

> changed the conduct of biomedical research in some ways that are not always consistent with the best interests of science...It has encouraged some companies to make protected materials and methods available to investigators under terms that seem unduly onerous. In a few well-publicized cases, and likely in many more undocumented ones, it has fostered policies that have inhibited the use of new scientific findings, even in the not-for-profit sectors, and has reduced open exchange of ideas and materials among academic scientists. (US 2000)

Transgenic mice as research tools: the US experience with the Harvard mouse

Patenting of life forms has resulted in inaccessibility and high cost of research tools, including transgenic mice. Approximately twenty five million mice were used worldwide in research in 2000, constituting 90% of all animals used in research. Scores

have been patented in the US subsequent to the US patenting of the Harvard mammals. (Malakoff 2000,)

The patent led to a well-publicized controversy. Harvard granted DuPont Corporation an exclusive license to distribute the mice, but some scientists objected to the terms of DuPont's distribution licenses. Dupont placed limits on breeding or redistributing the animals, and imposed a "reach through" clause requiring anyone who developed a product through the use of the mouse, or any derivative strain, to pay royalties to DuPont.

Dr Harold Varmus, then Director of the National Institutes of Health (NIH), initiated a four year process of negotiation with DuPont to make the mice broadly available to non-profit researchers. Ultimately, NIH and Dupont signed a Memorandum of Understanding providing that the Public Health Service and its grantees (non-profit academic researchers) may use the patented mice without cost for biomedical research purposes. NIH has subsequently contributed funding to a mouse breeding facility to make unpatented mice available to academic researchers**.** (Smaglik: 2000b) In effect, senior research scientists have been impelled to reverse the impact of the patents on transgenic mice in order to spur innovation in non-profit medical research.

Human cells and genes

The patenting of single cell life forms, cells and genes, has widespread impacts on science and healthcare. The number of gene patents granted is rising at an accelerating rate. In 2001, the US Patent Office granted over 5000 DNA patents. Of the 9456 patents claiming "nucleic acid" it has granted, 8334 of them were granted since 1996. The European Patent Offices has granted several thousand patents on genetic inventions and in Japan, the number is over five thousand. (OECD 2002)

One controversy concerns the patenting by Human Genome Sciences Inc. of a protein, CCR5, required for HIV infection. The patent application covered the gene, its protein, the fragments of DNA used to locate the gene, details related to the chemical components of the gene, and potential applications of this knowledge. Despite the fact that independent researchers at the NIH in the US **subsequently** discovered that the gene facilitates the entry of HIV into the human body, the patent was granted to Human Genome Sciences. This patent covered use of the gene for any purpose, allowing HGS to profit from the later discovery. The patent has resulted in considerable commercial control over the development of a new class of AIDS drugs, even though HGS did not know of the role of CCR5 in HIV infection when it filed for the patent. (Smaglik 2000a, Marshall 2000)

THE MYRIAD CANCER GENE PATENTS

MYRIAD CLAIMS

Genetics is a factor in approximately 5 to 10% of breast cancers, and mutations on genes called BRCA1 and BRCA2 cause 80% of these cancers. They are common but not exclusive to Jews of Ashkenazi descent. By the age of 70, most women carrying these genes will have breast cancer. Women who have the BRCA2 gene are also at high risk for ovarian cancer. In 2001, 1200 Ontario women were tested for these genes, and almost 4000 people received counselling for the possibility of carrying the disease. (Macdonald 2002, Hurst 2001)

Myriad Genetics Inc. of Utah has obtained a series of patents in Canada, the US and Europe on the BRCA1 and BRCA2 genes, giving Myriad control over both the genes and

the specific test the company has developed for the gene. Myriad essentially claims a monopoly on the entire genes, any information relating to or derived from them, and all methods developed to diagnose and treat hereditary breast cancer and ovarian cancer, including therapies for cancers from genetic mutation, screening of drugs for cancer therapy, and screening for the genes in women. Myriad also claims that its patents give it the right to store all new information about these genes in its own labs, building up the only source of this genetic data in the world, and through the DNA samples in its labs, control over the "raw material" of this gene worldwide. In Europe, the Myriad claims have been described as "a monopoly on all genetic work associated with the breast and ovarian cancer predisposition gene brca1" (Lecubrier 2002) and as **"**an unwarranted and novel restriction on medical practice." (Wadman 2001)

Canadian reactions to the patents

In July 2001, Myriad told Canadian provincial governments to stop using any tests other than its own test to detect the genes, or face a lawsuit. The Myriad test costs about $3,850, while Canadian tests cost $1,300, and in the opinion of experts, are equally reliable. Counselling is an important part of the testing procedure since tests may lead to difficult decisions, including prophylactic mastectomies or drugs, questions about whether to inform family members, and the risk of discrimination from employers and insurers. The government of British Columbia stopped funding the testing after the Myriad threats, so BC women must pay Myriad for the tests themselves, but do not have the counselling that accompanies it in provincial health programs.

The governments of Ontario, Manitoba, Quebec and Alberta decided to contest the Myriad claims, and to continue using the Canadian test. Tony Clement, Ontario Minister of Health and Long Term Care explained:

> How can publicly-funded healthcare and equitable coverage be sustained when we add to the existing financial pressures on our health system the potential monopoly pricing of a whole new category of diagnostics over which Ontario - and indeed Canada's other provincial and territorial jurisdictions – have little or no control over approval or pricing…. We are therefore forced to ask ourselves the much larger question: Is the entire fruit of human genome project research and the mapping of the human gene going to come down to a series of monopolies setting exclusive prices for tests which most of Canada – indeed most of the world, especially the poorer countries – cannot afford?
>
> Patent claims on a gene sequence that cover uses for all diagnostic innovations in the future are not in the public interest or in the interests of the promotion of a competitive market in diagnostic testing.[8]

In January 2003, Clement, joined by BC health minister Colin Hansen called the patenting of genes "abhorrent" and again called on the federal government to prevent it. Dr. Josef Penninger, Toronto geneticist, noted that a Myriad legal victory in Canada

> could ruin the health care system….(since) in 10 years, we will probably know 50 genetic defects that predispose us to strokes, heart disease, cancer, diabetes, etc., and of course people will want to know. But no health care system in the world will have enough money to do this if profit is involved and only a few people will have the money to afford it.

The Canadian Cancer Society also expressed concern at the breadth of the patents and called on the federal government to take action to ensure that the patents don't interfere with Canadian women's access to testing, accompanied by appropriate counselling and the timely development of knowledge of the relationships of genes to health. Further, the Society advocated that provincial governments challenge the breadth of claims and Myriad's administration of them. (Canadian Cancer Society 2003-3)

Reaction to the Myriad patents in Europe

Despite the granting of patents to Myriad in Europe, seventeen European laboratories do diagnostic tests on the BRCA1 using other tests. Officials of the Institut Curie in France consider that the direct sequencing technology used by Myriad and its approach of focusing on the detection of point or small sized genetic abnormalities fails to detect 10 to 20% of expected mutations. Europeans also expressed concern that a Myriad monopoly on this technology would cause Europeans to lose expertise in the field, prevent their improving or developing diagnostic tests, and increase costs of screening. Further, concerns were expressed that the Myriad requirements conflict with a holistic approach to public health, by separating biological research and clinical investigation from patient care.

In 2001, a challenge to the Myriad patents was launched in the European Patent Office by the Insitut Curie, almost all European genetics societies, many scientific institutions, the governments of Holland and Austria, and the Swiss Social Democrat Party. The opponents argue that since the gene sequence was available in data bases, the patents should be revoked on grounds of lack of priority, novelty, and inventiveness, and insufficient description of future therapeutic uses. The institutions began the challenge to two patents and subsequently added the third. The challenge is necessary, in the view of Gert Matthijs of the Belgian Centres for Human Genetics, since

> It is not only about breast cancer but about hundreds of gene patent applications. If nothing is done, it will be almost impossible to practice genetic analyses properly in the future.[9]

Current status

To date, Myriad has not followed through on its threats to sue Canadian provinces for their continuing use of Canadian tests for BRCA1 and 2, and the European challenges to the patents are in process. French officials have stated that if the challenges are unsuccessful, France may opt for "licence d'office," allowing override of drug patents if contrary to the public interest. The ministers of health and research have expressed support for extending the licence system to genetic diagnosis. Patents have been granted in many countries on genes implicated in numerous diseases, including Alzheimers, HIV/AIDs, and cancer, but these Myriad cancer gene patents are the most notorious in the literature, having provoked opposition from governments and scientists across Canada and Europe. Whether or not Myriad is successful in enforcing these patents will be indicative of whether public interest arguments will be effective in limiting the negative impacts of diverse life patents.

Stem Cell patents

Human stem cells have the potential to develop into many types of tissues and organs, and therefore have extraordinary importance for healthcare. The Wisconsin Alumni Research Foundation has patents on five of the 72 stem cell lines used in US federally funded research, and has an licensing agreement with Geron Corporation granting the company exclusive rights to develop products from stem cells derived from nerve, heart and pancreas cells, and non-exclusive rights to the use of blood, cartilage and bone cells. Geron has also developed heart, nerve, pancreas, bone, liver and blood cells from the stem cells and has filed for patents on the methods used. Patents on stem cells may impede research in this field and mean royalty fees will have to paid for future

development of replacement human organs and tissues. (Ontario 2002, "WARF Geron" 2002)

Diagnostic tools and tests

Over 400 clinical genetic tests were available by 2001, and hundreds more are being developed. (OECD 2002) Biomedical patents have been criticized for interfering in the availability of diagnostic tools and tests.

A survey of US laboratories showed that some labs have refrained from offering genetic testing services for haematochromatosis, a progressive iron-overload disease, because of patents granted on tests for the disease. Scientists had begun genetic testing before the patents were awarded, but 30% of those surveyed reported discontinuing or not developing genetic testing after the grant of the exclusive licence on the patents. Limited clinical testing may inhibit further discoveries regarding the gene which causes the disease. The study also showed a delay in publication of data regarding cloning the HFE for a year after the patent application was filed. (Merz 2002)

Impacts of patents on the dissemination of scientific results

The commercialization of science, including through biomedical patents, has contributed to delay in the publication of scientific results. A survey of life scientists found that 19.8% of those questioned said their publication results had been delayed by more than 6 months at least once, considerably longer than the 60 days considered acceptable by the National Institutes of Health. Of those, 46% reported delays to allow time for patent applications; 33% to protect the proprietary value of research results by means other than patent applications…26% to allow time to negotiate license agreements; and 17% to resolve disputes over intellectual property. Further, 34% of faculty have been denied

access to research results suggesting that data withholding has affected many life-science faculty. (Blumenthal et al 1997)

Unfettered and timely sharing of research results is a fundamental requirement for scientific advance.

> Openness in the sharing of research results is a powerful ideal in modern science ….communalism, the shared ownership and free exchange of research results and approaches, is a fundamental norm underlying the social structure of science. Such sharing is critical to the advancement of science…External pressures (for breaching the ideal of openness) include…processes and procedures related to the commercialization of university research. (Blumenthal et al 1997, p.1)

The commercialization of science, including through patenting of results, may be undermining the integrity of scientific publications.

> Commercial considerations may also lead to a culture of secrecy, including delays in publication while patents are filed…The most serious concern, however…is that conflicts of interest may affect what gets published. (Nature Neuroscience 2000)

The editors of the journal cited studies showing that studies of drugs and cancer treatments supported by manufacturers have been found more likely to find results favourable to the companies' products than studies not funded by commercial interests.

Nature instituted a new policy in August 2001 due to “suggestive evidence” that publication practices in biomedical research have been influenced by the commercial interests of writers and general concern among researchers and others about the possible undermining of the integrity of scientific research by increasing commercial links and consequent influences. Authors are "invited" to disclose competing financial interests including funding, employment, personal financial interests and “patents or patent applications whose value may be affected by publication.” Those authors who decline to

provide the information may still publish, but their refusal to provide disclosure is reported. (Campbell 2001)

ROLE OF PATENTS IN PROMOTING MARKET-FOCUSED RESEARCH

Patents on genes, an aspect of the commercialization of research, may contribute to companies' placing a disproportionate focus on discoveries that maximize profits to the private sector by targeting large, potentially lucrative markets rather than those which might most benefit public health. This exacerbates disparities of treatment between rich and poor populations and between industrialized and developing countries. It also emphasizes research that doesn't focus on major public health benefits, such as obesity, smoking, and inactivity, with their known impacts on heart disease, stroke and diabetes. (Willison and MacLeod: 2002)

Summary of life patent impacts

In summary, patents on life forms provoke many concerns regarding the advancement of science and the provision of medical diagnosis and treatment including:

- patent holders are being allowed to patent a part of nature, a basic constituent of life;
- inappropriate rewards are gained by using patents on DNA fragments whose purpose is not known to patent the entire gene from which the fragments originate;
- impediments to development of diagnostics and therapeutics due to costs of patented research data;
- patent stacking (several different ways of patenting a genomic sequence) which discourages product development due to high royalty costs payable to all patent owners;

- secrecy of patent applications resulting in scientists finding, late, that patents have already been granted related to work they are doing, leading to unexpected licensing costs and patent infringement penalties;
- private biotechnology patent holders can monopolize certain gene test markets;
- patent filings are replacing journal articles as places for public disclosure, reducing the body of knowledge in the literature;
- patents may contribute to a focus on research leading to lucrative market gains rather than subject areas of greatest benefit to public health; and
- clinical practice is harmed by limits on the types of tests that can be preformed with patented genes. (Human Genome Project 2001 and Ontario 2002)

In promoting these results, life patents may conflict with three fundamental purposes of the patent system. Rather than rewarding human invention, they allow the private appropriation of natural phenomena.. Instead of fostering disclosure of new scientific discoveries, they may reduce the disclosure that would otherwise occur through the culture of science. Rather than fostering innovation, they may deter it.

LIFE PATENT REFORM PROPOSALS

The confluence of international concern with the impacts of TRIPs and observed impacts of patenting on science and medicine in OECD countries has generated a spectrum of reform proposals, from bans on life patents to changed patent administration to procedures for ethical screens.

Patent exceptions

No patents on life

The *Harvard Oncomouse* case concerned “higher” life forms, and though interveners did not concede that the decision to patent single cell life forms in Canada was properly made, the Court considered only higher, complex life forms. Internationally, numerous governments and citizens’ organizations have expressed opposition to patents on all life forms (Africa Group undated; Greenpeace1999)

Avoiding patents: keeping information in the public domain

Despite the proliferation of life patents, the question remains whether the results of research in the public sector, or funded by public monies, should be placed in the public domain rather than being patented. Important examples of use this strategy exist. On March 14, 2000, President Clinton and Prime Minister Blair issued a joint statement in support of keeping "raw fundamental data on the human genome, including the human DNA sequence and its variations...freely available to scientists everywhere." The SNP Consortium, comprised of ten large pharmaceutical companies and the UK Wellcome Trust has established a non-profit foundation to find and map 300,000 SNPs, (single nucleotide polymorphisms, common minute variations in human DNA) and make the information available to the public. (Ontario 2002) In April 2003, scientists at the Michael Smith Genome Sciences Centre in British Columbia were the first in the world to sequence the SARS coronavirus, and they immediately posted the data on the Centre's website, to make it available to researchers worldwide. (BC Cancer Society 2003)

No patents on human materials

In Canada, the federal Standing Committee on Health of the House of Commons recommended in 2001 that humans and "any human materials" not be patentable, commenting:

> The Committee is seriously concerned about the patentability of human material. We are deeply disturbed that the *Patent Act* does not specifically disallow patenting with respect to human genes, DNA sequences, and cell lines. Treating human biological components as patentable property is repugnant to many of us. It entails their commodification and paves the way for their commercialization. Given the importance that this Committee attaches to the respect of human dignity and integrity, we urge that patents be denied in relation to human material. (Canada 2001)

In contrast, Canadian Biotechnology Advisory Committee called for a more narrow ban on patents "on human bodies at any stage of development" intended to apply only to "entire human bodies from the zygote to an adult body" but allowing patenting of DNA sequences, gametes (sperm and ova), stem and other cells and organs. The CBAC wording, echoing the European Directive, is unclear and untested, but invites extraordinary impacts on healthcare and human values from the breadth of its acceptance of human patents, including whole organs and sex cells.

No patents that conflict with "ordre public or morality"

Although Canada and the US do not include this limitation to patenting, the TRIPs and European law permit an exception to patentability for inventions whose commercial exploitation should be prevented

> to protect *ordre public* or morality including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by law[10].

Public order has been given an narrow interpretation in international patent tribunals, being limited to the protection of public security, the physical integrity of individuals as part of society, and the protection of the environment. (Gold 2001) However, the EC Directive also excludes patents on processes to clone humans and to modify germ line identity of humans, the use of human embryos commercially, and modification of genes of animals causing suffering without substantial medical benefit on this basis[11]. Ontario has suggested that "As stem cell research develops we must ask whether a monopoly on the method to create a new human liver or other organ would not be an affront to Canadian values and morality." (Ontario 2002, p.46)

Ontario recommended inclusion of "ordre public" in Canadian law, with unspecified criteria for its application, but as a basis for challenge to a patent, not as a basis for examiners to refuse a patent application. The process would be administered by a body separate from the patent examiners and comprised of experts in science, ethics and competition. Interveners in the *Harvard Oncomouse* case proposed an assessment of environmental and human health risks as an element of decision-making regarding patenting of plants and animals, without specifying a decision-making body. (Canadian Environmental Law Association2001)

Tighten utility requirements and limit the scope of patents on genetic materials

Numerous governmental and scientific bodies have proposed changes to patent laws and administration to limit the negative impacts of life patents, particularly for genes and stem cells. Early gene patents were granted on genes and gene fragments, (ESTs, expressed sequence tags and SNPs, single nucleotide polymorphisms) without

identification of the corresponding gene, protein, biological function, or potential commercial product, such as therapeutic proteins and genetic diagnostic tests. Recent proposals for change concern the application of the basic patent requirements of inventiveness and utility, and limits on the scope (breadth) of patent claims.

The Nuffield Council on Bioethics in the UK argues that with patents on DNA, "the patent system is in danger of not achieving its main goal: to stimulate innovation for the public good" and that thousands of recent patents on DNA sequences are of "doubtful validity," since merely using computers to identify genes and then patent them by sifting published sequences does not involve inventiveness. (Adam: 2002) Sandy Thomas, director of the council claims the council is "talking about a reassessment of the system, not just a little bit of tightening here and there."

In response to criticism of its patenting practices, the US patent office has tightened requirements for utility in patents, and now requires that patents claimants demonstrate a "specific and substantial utility" (US 2001)

Ontario recommends changes in Canadian patent law and administration. First, it proposes using the utility requirements to restrict patents on fundamental genomic concepts and genetic research tools, so that patents are only granted for specified uses and narrow applications. This approach would provide a partial limit on the problem of "patent stacking" and appropriation by a patent holder of scientific work done by others after the grant of the patent. It would also prevent genetic patent claims covering all

future diagnostic uses of a gene. Further, Ontario calls for amendments to the *Patent Act* to limit the scope of gene patents so that use of the information in a gene is not restricted, though making, using, selling and importing the chemical material it in an industrial setting would be precluded. Reproduction of the patented material for healthcare use of an individual should be permissible.

Ontario expressed concern regarding the implications of patents on stem cells while the Nuffield Council proposed limiting patents on stem cell lines to "precisely described industrial applications" and requiring that the patents identify the source of the cells used, whether adult, fetal or embryonic. The European Commission is also considering changes to its previous practice of granting wide-ranging patents on human DNA sequences, due to pressure from scientists and the public.

Protection from patent infringement lawsuits for scientists and health professionals.

Most countries allow use of patented inventions for research and experimentation, but legally the "research exemption" is narrow:

> …to be precise, the research exemption holds that a product or process covered by a patent may be freely made, or used to test whether the patent description is sufficient to enable one to replicate what the inventor has done and whether the product or process performs as stated in the patent. (OECD 2002, p.58)

In effect, the exemption does not facilitate further research on the patented invention, but only verification of patent claims. At issue is its applicability to further scientific research or experiments using the patented materials, including research tools. In Europe, acts "done privately and for purposes which are not commercial" and "acts done for experimental purposes relating to the subject matter of the invention" are permitted,

but "privately" has not been defined judicially[12]. The British Royal Society has called for clarification of the definitions in the exception.

In the US, the scope of the exemption is narrow and contested. It includes research for "philosophical curiosity" and the pursuit of pure knowledge or only where there's no institutional or commercial purpose, and therefore does not apply to most biotechnological research. (Gold 2001)

The Canadian exception is vague. It dates from a 1971 decision of the Supreme Court of Canada[13] regarding research aimed at sustaining a compulsory licence but the licence provisions have been eliminated. The *Patent Act* permits generic drug makers to use patented products to conduct research and improve them in order to satisfy regulatory requirements regarding pharmaceuticals.[14]

For policy makers studying the impacts of life patents, an exception for researchers is a priority. Ontario calls for clarification of the current Canadian law, and broadening of the exceptions to ensure that researchers will not be sued for research which may ultimately lead to commercial products, including genetic diagnostic and screening tests. Specifically, it calls for an amendment to the *Patent Act*:

> …that protects private or non-commercial study on a patented invention, or research on the patented subject mater to investigate its properties, to improve upon it, or to create a new product or process. This amendment should also be extended to non-commercial clinical use. (Ontario 2001, p.50)

Although Canada currently does not patent methods of medical treatments, the exemption only applies to treatments performed inside the body, but not to devices or treatments used outside the body. This distinction is impractical in modern medicine since many medical processes occur both inside and outside the body. Concerned with access to genetic technologies for the purposes of healthcare, Ontario proposed that the current medical treatment exemption be replaced by protection from patent infringement actions for "medical practitioners providing medical services, including both treatment and diagnosis, to patients" (Ontario 2001, p.51). This protection should extend to all health care practitioners (not only doctors) and medical facilities. It would permit patenting of genetic technologies but allow unlimited use of the technologies in clinical care. The report does not discuss the implications of removing the current exception for medical treatments, which could presumably create new barriers to use of these technologies.

Licensing strategies

Many important life patents are subject to licensing agreements, and a survey of the licensing of patents regarding diagnosis of genetic disorders showed that almost all the patents were being licensed exclusively. (OECD 2002)

The US National Institutes of Health has developed a "strategic licensing policy" on patents "to promote public health and dissemination of research results while encouraging market competition and attempting to obtain appropriate financial returns" (OECD 2002, p.54) It grants mostly non-exclusive licences, and retains the right to use

inventions for non-commercial research and to ensure broad dissemination of research results.

Canada's *Patent Act* permits the Canadian government to use a patented invention, on approval by the Commissioner of Patents, with payment of compensation to the patent holder, or without the Commissioner's consent in "cases of national emergency or extreme urgency…[or for] "a public non-commercial use[15]." In October 2001, the Canadian federal government was prepared to over-ride Bayer's patent on Cipro should it become necessary to treat Canadians due to attacks using anthrax. The WTO ministerial declaration in Doha in November 2001, provides that governments have the right to take measures "to protect public health and, in particular, to promote access to medicines for all" including through the use of compulsory licences for drugs. Ottawa is now considering how to amend the *Patent Act* to facilitate the production of generic drugs for export to developing countries.

Ontario argues that to prevent the Doha statement from being a "hollow right," access to medicines must include access to diagnostic procedures to determine which medicines to provide, and the *Patent Act* should be amended to allow compulsory licenses of patents for genetic diagnostic and screening tests, on payment of a reasonable royalty. The British Royal Society supports use of compulsory licences and competition law where patents "unreasonably affect use and development of inventions." (Royal Society 2002 p. 10)

Opposition procedure

It is possible to request a re-examination of a patent in Canada on narrow grounds, or to apply to the Federal Court to challenge a patent, an expensive and slow process. In Europe, any person opposed to the grant of a patent may request an administrative review of the patent on any ground within nine months of its issuance. Ontario proposes that a similar process be made available in Canada, to provide greater transparency, rigour and public confidence in the patent process. The CBAC recommends that Canada introduce an opposition procedure permitting a challenge to a patent on grounds that it is "invalid or void" but does not specify what the grounds should be for such a finding. It proposes a six month time limit for initiation of the challenge, and completion of the process within eighteen months.

Specialized bodies for patent reviews

Currently, in Canada, the jurisdiction over patent cases is dispersed amongst federal and provincial courts for patent infringement and validity cases, while the statutory right of appeal from decisions of the Patent Office is to the Federal Court alone. Ontario proposes that the federal government create a specialized court, a group of judges with expertise in technology and patent law, to hear patent law disputes.

Gold and Caulfield have proposed an independent panel of experts in ethics, social policy and science, with powers to suspend the enforcement of a patent until any ethical concerns have been met as part of "a flexible system of addressing ethical concerns until

governments are able to formulate and implement adequate regulatory processes." The proposal is oriented to patenting by medical professionals of donated biological materials to identify genes without consent from the donors or sharing of benefits with them. The Board would have clear guidelines on types of concerns that could be raised by patent examiners or interested third parties. (Gold and Caulfield: 2002)

Using Canadian Medicare listing of covered services to promote ethical patenting

Medical necesssity is the standard for listing of services including tests and drugs for coverage under Medicare, but Richard Gold proposes that a broader test be used regarding tests, services and medications based on use of biomedical materials, namely, that they "only be listed if the person having patent rights to the biomedical material demonstrates that ethical concerns have been appropriately dealt with" including conduct of the research leading to the product, availability of the patented materials to other researchers on an equitable basis, and ethical marketing and distribution of the product. Use of the broad policy umbrella of the medicare system would mean that a broader range of ethical concerns could be addressed than under the patent law system alone. (Gold 2000)

CONCLUSION

The decisions that led to the proliferation of single cell life patents in Canada occurred without public scrutiny or involvement. Few Canadians have ever heard of the *Chakrabarty* case in the US Supreme Court, or the uncritical thinking in the Canadian patent office that led to its emulation in Canada. The *Harvard Mouse* case was the first life patent case to attract wide media coverage, and anecdotal evidence suggests that most

Canadians are shocked to learn that a private company may have effective ownership rights to genes and cells that exist in their bodies. The OECD noted that while international experts attending the January 2002 workshop were unanimous in accepting patents on genes, a gap exists between their thinking and that of the public. The terms "repugnant" from the Canadian federal Health Committee and "abhorrent" from former Ontario Health Minister Tony Clement, suggest that at least some Canadian legislators would support restraints on life patents. The dizzying pace of life patent applications is a serious problem now, but since the genetic revolution has only begun, the pace will accelerate further, rapidly closing doors to policies to protect the public interest in human values, the advancement of science, and healthcare.

Canada urgently needs now what should have occurred before life patents were approved twenty years ago, a full public debate, not only amongst governments and legal, scientific and ethical experts, but with appropriate consultation with all Canadians. The debate should include a credible examination of the totality of impacts of life patents and result in law reform that re-balances the law to better accord with the original social purpose of the patent system and contemporary Canadian values. The current state of the law is aptly described by the sixteenth century English proverb:

> The law doth punish man or woman
> Who steals the goose from off the commons,
> But lets the greater felon loose
> Who steals the commons from the goose.

ENDNOTES

[1] Commissioner of Patents v. President and Fellow of Harvard College and the Canadian Council of Churches, Evangelical Fellowship of Canada, Canadian Environmental Law Association, Greenpeace Canada, Canadian Association of Physicians for the Environment, Action Group on Erosion, Technology and Concentration, Canadian Institute for Environmental Law and Policy, Sierra Club of Canada, Animal Alliance of Canada, International Fund for Animal Welfare Inc. and Zoocheck Canada Inc., 2002 SCC 76, and at www.lexum.umontreal.ca.

[2] *Patent Act*, .R.S.C, c.P-4, s.2

[3] *Diamond v.Chakrabarty*, 447 U.S. 303 (1980)

[4] quoted in Hurst, L. Hurst, L. (2001) Utah patent-holder claims exclusive right to diagnose cancer gene. Democratic Underground, 11 August 2001, www.democraticunderground.com, accessed 21/10/03.

[5] op.cit. para 199.

[6] Commissioner of Patents v. Harvard College, Respondent's Factum, Smart & Biggar, Barristers and Solicitors, Ottawa, 19 February 2002.

[7] Dr Ursula Franklin, personal communication, January 17, 2003.

[8]Clement: (2001)

[9] quoted in (2002) EMBO Reports 3: 1120-1122.

[10] World Trade Organization, Agreement on Trade-Related Intellectual Property, Article 27(2)

[11] EU Directive on the legal protection of biotechnological inventions 98/44, Article 6.

[12] Community Patent Convention 1975, Art 31(a & b) p11, para 3.23

[13] Micro Chemicals Ltd.v.Smith Kline & French Inter-American Corp. (1971) 2 CPR (2d) SCC.

[14] *Patent Act*, R.S.C. c P-4, s.55.2

[15] ibid. Section 19

REFERENCES

Adam, D. 2002. Bioethics council demands tighter rules on gene patents. 418 *Nature*:356

Africa Group: undated Taking Forward the Review of Article 17.3B of the TRIPs Agreement, www.tradeobservatory.org, accessed 8/07/03.

Balter, M. 2001. Cancer Research: Transatlantic War Over BRCA1 Patent *Science* 292: No. 5523 p.1818

Black's Law Dictionary, 7th edition, West Group, St. Paul, Minnesota, 1999.

Blumenthal *et al*. 1997. Withholding Research Results in Academic Life Science, Evidence from a national survey of Faculty. 277 *Journal of American Medical Association 1224* -1228.

Butler, D. & Goodman S. 2001. French researchers take a stand against cancer gene patent. *Nature* 413:95

British Columbia Cancer Society 2003. 2003/04/12:Genome Sciences Centre sequences SARS associated corona virus, www.bccancer.bc.ca, accessed 10/6/03.

Campbell, Philip. 2001. Declaration of financial interests. *Nature* 412:751.

Canada. 2001. Report of the Standing Committee on Health, House of Commons, Assisted Human Reproduction: Building Families, Dec.2001, http://www.parl.gc.ca/InfoComDoc/37/1/HEAL/Studies/Reports/healrp01-e.htm

Canada 2002. Patenting of Higher Life Forms and Related Issues, Report to the Government of Canada Biotechnology Ministerial Coordinating Committee, Canadian Biotechnology Advisory Committee, June 2002.

Canadian Cancer Society. 2002-2003 The Patenting of BRCA1 and 2 genes, www.cancer.ca

Canadian Environmental Law Association. 2001 *Memorandum of Fact and Law, Commissioner of Patents v. Harvard College*, www.cela.ca

Editors 2000. Financial conflicts in biomedical research. *Nature Neuroscience* 3:299

Clement, T. 2001 Speech RE: Myriad Gene Patent Issue, September 19,2001. www.health.gov.on.ca. Accessed 4/7/03.

Gold, E.R. 2000. Biomedical Patents and Ethics: A Canadian Solution, (2000) *McGill Law Journal/Revue de droit de McGil*l: 45, 413-435.

Gold, E. R. 2001. Patenting Life Forms: An International Comparison, prepared for the Canadian Biotechnology Advisory Committee, February 2001, www.cbac-cccb.ca.

Gold, E.R. and Caulfield, T. A.. 2002. The moral tollbooth: a method that makes use of the patent system to address ethical concerns in biotechnology. *The Lancet* 359: 2268-70.

Greenpeace. 1999. No patents on life - Greenpeace protests at the Eruopean (sic) Patent Office in Munich., 31 August 1999. http://archive.greenpeace.org, accessed 10/21/03

Human Genome Project Information online 2002. Genetics and Patenting: www.ornl.gov/hgmis/elsi/patents.html, accessed 1/11/02

Hurst, L. 2001. Utah patent-holder claims exclusive right to diagnose cancer gene. Democratic Underground, 11 August 2001, www.democraticunderground.com, accessed 21/10/03.

Lecubrier, A. 2002. Patents and Public Health, European Molecular Biology Organization, *EMBO Reports* 3: 1120-1122, www.nature.com, accessed 4/7/03

Macdonald, L. 2002. Gene Patenting: Is It too Late to Stop it? Canadian Breast Cancer Network, www.cbcn.ca/english/adv_db.php?show&43, accessed 4/7/03)

Malakoff, D. 2000. Suppliers: The Rise of the Mouse, Biomedicine's Model Mammal. *Science* 288: 248-253.

Marshall, E, 2000. Gene patents: Patent on HIV Receptor Provokes an Outcry" *Science* 287: 1375 -1377.

Mayer, S . 2002. Are Gene Patents in the Public Interest? *Bio-IT World*, www.bio-itworld.com/archive/111202/insights_public.html , accessed 4/7/03)

Merz J. F. *et al*. 2002. Diagnostic testing fails the test. *Nature* 415:577- 579

Ontario. 2002. *Genetics, Testing & Gene Patenting: Charting New Territory in Healthcare,* Toronto

OECD. 2002. *Genetic Inventions, Intellectual Property Rights and Licensing Practices - Evidence and Practices.* Paris: Organization of Economic Cooperation and Development

The Royal Society. 2002. *Keeping science open: the effects of intellectual property policy on the conduct of science,* www.royalsoc.ac.uk/files/statfiles/document-221.pdf accessed July 8, 2003

Schmidt, S. 2003. Ottawa pressured to outlaw gene patents: Myriad genetics case: Provinces back Ontario in defying U.S. firm's threats. 2003 *National Post*, 08 January 2003 p.A12

Smaglik, P. 2000a. Could AIDS treatments slip through patents loophole? *Nature 404:* 322

Smaglik, P 2000b. NIH cancer researchers to get free access to 'OncoMouse.' *Nature* 403:350.

Sulston, John. 2002. Heritage of Humanity, *Le Monde Diplomatique*, December 2002.

US 2000. "Testimony of Harold Varmus, Hearing on Gene Patents and Other Genomic Inventions" (The House Judiciary Subcommittee on Courts and Intellectual Property), 13 July 2000, online: http://www.house.gov/judiciary/varm0713.htm (date accessed: 15 March 2002)

US 2001.USPTO Utility Examination Guidelines, 66 fed.Reg.1092 (2001)
US and UK, 2000. (Joint Statement by President Clinton and Prime Minster Tony Blair of the UK) , www.geneticalliance.org/geneticissues/clintonblair.html, accessed 9/29/03.

Wadman,M. Testing time for gene patent as Europe rebels. *Nature* 413:443.

"WARF, Geron reach agreement on stem cells" 2002. *The MilwaukeeBusiness Journal*, Janary 9, www.bizjournals.com/milwaukee/stories/2002/01/07/daily22.html?t, accessed 9/30/30.

Willison, D. and MacLead, S. 2002. Patenting of genetic material: Are the benefits to society being realized? *Canadian Medical Association Journal* 167(3), www.cmaj.ca, accessed 4/7/03