

PATENTS AND TECHNOLOGY TRANSFERS IN A BIOTECHNOLOGY CONTEXT

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This paper aims first to give an overview of patent practice as it relates to biotechnology and pharmaceuticals. It does not aim to be exhaustive but to provide a general outline of patent practice with a particular emphasis on biotechnology and related fields. Such knowledge is important for it should be noted that while science and technology rapidly advance so to do the various governmental directives and policies on the subject. There exists no well established and accepted body of jurisprudence relating to biotechnology. Much like the subject matter it covers, the jurisprudence continues to evolve and grow rapidly. Secondly, an overview of issues relating to the transfer of such technology is provided.

PART ONE

1.0 Introduction

The comments that follow refer not only to Canadian practice but also aim to provide an overview of practice throughout the world and, as such, also includes an emphasis on American and European policies and practices. Such an approach is justified when one considers that both the U.S (USPTO) and European Patent Offices (EPO) are generally the first to encounter the particular problems and issues associated with the patentability of biotechnology inventions. Given their economic importance, the relative speed at which they process applications, and their thoroughness, the positions of these two particular offices provide guidelines and also serve to influence the policy of the Offices of other countries such as Canada.

2.0 General Principles With Respect to Patentability

2.1 Underlying Purpose

The purposes underlying patent legislation are based partly on the interest of the State to promote disclosure and access to innovations and partly to promote the interests of individuals by granting a monopoly over their inventive work. The holder of a patent is granted a right to prevent others from using in a commercial manner the invention as described in the patent during its term. It should, however, be noted that in most countries, including Canada, the commercialisation of medicines is not dependent on the granting of a patent but rather upon the receipt of a *Notice of Compliance* from the federal government.

For a business a patent is a means to protect the investment made in R&D programs. It is a negative right in that it does not provide the right to do something (ex. market a pharmaceutical product or new weapon), instead it provides the right to prevent others from manufacturing, selling or using the invention protected by the patent.

The principal exception to this right is the exemption that exists for experimental purposes. The fact that one is the owner of a patent does not allow one to prevent others from experimenting with the patented object or using it for experimental purposes without commercial gain. In essence the State, in exchange for granting the monopoly, obtains disclosure of the essential elements of an invention so as to allow the public the benefit of using the elements of the disclosure to further the advancement of science and technology. Thus the manner in which the invention is described and claimed is of the utmost importance since this will determine the outer parameters of the protection sought.

From a procedural viewpoint a patent is delivered by the appropriate authority of a country, for that country and usually for a period of 20 years

from the date of the filing of the patent application. An application must be filed by either the inventors or their assignees. In the field of research, employers are generally regarded as the owners of the patent when the employee's main function is to invent. However, it is advisable to clearly state in a contract of employment that the employer owns the inventions of the employee to avoid any uncertainty, since such uncertainty will harm the potential of the invention.

In the United States, exceptionally, even if the inventors have assigned their invention only the inventors may sign the declaration that accompanies the application for a patent. If they refuse to sign the declaration the application may be deemed to have been abandoned.

2.2 Subject Matter of Invention

For a patent application to be granted it is necessary that its subject matter be :

- an invention
- demonstrating utility
- showing novelty
- demonstrating some inventive activity
- and be sufficiently described

One of the bases for the refusal of a patent application or the invalidation of a patent after grant is an insufficient description. The description may be considered insufficient if it does not sufficiently describe the object of the invention, the process of its manufacture or, most particularly in the U.S., its use. The description must be sufficiently clear and precise to inform others skilled in the relevant art how to create and use the invention without having to resort to excessive experimentation or trial and error, when the patent expires.

2.3 Making One's Bed

It should not be forgotten that once a patent application is filed it is no longer possible to either modify or to add any details to its description. Thus, it is necessary to take the time to assemble the greatest amount possible of information prior to filing the patent application. The exception being in the United States where it is possible to better define the object of the protection sought through the filing of a "continuation in part". However, a "continuation in part" does not afford the inventor the right to remedy substantive defects in the original application.

2.4 Public Disclosure Fatal

It should also be noted that the application should be filed **before** any public disclosure of the invention is made since this will constitute an insurmountable barrier to obtaining a patent in most of the world, with the notable exceptions being Canada and the United States which still provide for a twelve (12) month "grace" period.

3.0 What is an Invention in Patent Terms

3.1 The Definition Contained in the Patent Act

The Canadian Patent Act states that:

Invention means any new and useful art, process, machine, manufacture, composition of matter, or any new and useful improvement in any art, process, machine, manufacture, composition of matter (Section 2)

As patentable material microorganisms, viruses, nucleotides, proteins, etc. fall under the classification of "composition of matter". They are also referred to, so as to distinguish them from chemical products as, "biologically active composition of matter" or BACoM.

3.2 Novelty

Regardless of the nature of the invention it must be novel. That is, prior to the filing of the patent application, it must not have been made publically available by any person by any means anywhere in the world. Forms of disclosure include published documents, public use of the invention, sales or, as a general rule, any communication to a third party that is not governed by a confidentiality agreement (written or tacit).

3.2.1 Grace periods (United States and Canada)

Canada and the United States are countries that grant grace periods to inventors who have publicly disclosed their inventions prior to having filed for a patent. The grace period is one year from the date of the first public disclosure. However, a patent application made in the United States or Canada on the basis of this grace period may not form the basis of an application in countries with an absolute novelty rule.

3.2.2 The European Model, Absolute Novelty

In Europe, Japan and in most, if not all, other countries, the novelty requirement is absolute. If the invention has been made accessible to the public prior to the date of filing of the patent application then no patent may be obtained, even if the disclosure arose from the inventors themselves. One of the worst scenarios arises when the inventors have published details of the invention in scientific journals.

To the extent that protection is sought only in North America the grace periods are highly advantageous. However, they are also a trap when one seeks to extend the protection elsewhere.

3.2.3. Natural or preexisting BACoM: One Cannot Patent a Discovery

Because the object of a patent must be "novel", that is to say not previously available or described prior to the filing of the patent application, it becomes apparent that substances already existing in a natural state do not fulfill the criterion of "novelty". One cannot patent a discovery. However, while these substances, in their natural state, may not be patentable *per se* they can, under certain circumstances, benefit from protection if they have some distinguishing features. Thus, it is possible to patent recombinant plasmids containing portions of cDNA, or substances with a high degree of purity that have not been previously achieved. Specific uses of these natural substances may also be the subject of a patent.

3.3 Utility

An invention is above all a thing having some utility. At first glance this condition might appear redundant but it has permitted the resolution of certain fundamental problems associated with patents in the field of biotechnology. In a well known American case the object of the invention was a sequence of nucleotides from the human genome that had no known particular utility at the date of the filing. The U.S. Patent Office ruled that their use as genetic markers did not fulfill the criteria of utility and rejected the application.

It is frequently necessary to convince U.S. patent examiners of the utility of an invention by furnishing them with exhaustive tests. In the case of pharmaceuticals, examiners have even occasionally demanded testing on humans to show utility. To counter this zeal and do away with this testing requirement the U.S. Patent Office has produced new guidelines. However, it

should be noted that while such testing might not be officially required some U.S. patent examiners still have a skeptical attitude relative to the utility of such applications and it is best to provide them with more than just suppositions as to the utility of an invention.

It should be noted that in Europe a showing of utility must be disclosed but not necessarily proven. It is simply necessary to show that the object of the invention has either industrial or quasi-industrial applications.

3.4 Inventive Activity: Obviousness

3.4.1 According to Whom?

For an invention to be patentable it must show more than utility and novelty. The invention must not be obvious but must show evidence of some inventive activity. This criterion does not appear in the Canadian Patent Act but has been elaborated by Canadian courts who found the requirement to exist within the term "invention" itself.

The issue as to obviousness is determined by the use of a fictitious person. In patent law this elusive creature is a person "skilled in the art" who possesses the technical knowledge associated with each particular technique contained in the invention. This fictitious person is presumed to have access to whatever documentation existed prior to the filing of the application. This person determines whether the invention is either described or suggested in the art in such a manner that its creation would be obvious. Absolute predicability is not necessary, a reasonable expectation of success may render the object of the invention obvious.

3.4.2 Nucleotide Sequences, Monoclonal Antibodies and Obviousness

The question of obviousness is particularly relevant to certain nucleotide sequences. Especially when the protein coded by this nucleotide sequence has been previously known. Thus, when the protein itself is already known, the application for the nucleotide sequence itself is generally rejected on the basis of obviousness.

In a similar fashion the question of obviousness frequently arises in the case of new monoclonal antibodies whose existence may be empirically predicted from the knowledge of the antigenic properties of a known substance. In such cases the Patent Office has rejected the application.

Also the European Patent Office and the Board of Appeals of the US Patent Office (which constitutes the jurisdiction of appeal of the U.S. Patent Office) have shown a tendency to contest the inventive activity of applications where the product claimed was empirically known, where the incentive to manufacture and/or isolate was obvious or where the technique was considered routine.

However, if a nucleotide sequence or an antibody shows unexpected improved properties and unforeseen difficulties during their isolation are overcome then, since such unforeseeable characteristics have arisen, this particular sequence or antibody may be patentable.

3.4.3 Selection Patents

It may unexpectedly be determined that a particular substance belonging to a larger family of substances produces superior results to those obtained using other members of the group. This type of innovation may be patentable even though the group of substances and its properties were well known in the past if the particularly effective substance was not clearly identified. This is termed a non-obvious selection.

4.0 Types of Claims That May Be Made in Patent Applications

4.1 Products

The product may be claimed by its structure or, if the structure is unknown, by the process of its manufacture: (product X obtained by process Y). It should be noted that a composition, an association of at least two different components, may be patentable even if individually the components are known. The criterion of novelty applies to the object of the invention which is a composition. It should however be emphasized that the composition should not be obvious but that it show an unexpected and particular utility.

One might envisage product X whose chemical formula is well known and which is used as a herbicide. If one discovers certain pharmaceutical properties associated with X that would allow one to cure a disease or diseases then one may attempt to obtain a patent not on the product *per se* but rather on a pharmaceutical composition including X and an acceptable pharmaceutical excipient. One might also protect one's innovation by means of other claims (see below).

4.2 Process or Method

A process or method is also patentable. It is claimed by detailing the essential steps to follow in order to obtain the desired result. It might be a new process for manufacturing or a new use. American patent law was amended in November of 1995 to permit claims for biotechnological processes where at least one of the starting materials or end products are novel and nonobvious.

An important exception to this rule of patentability in Canada and in Europe are medical and veterinary treatments. Such treatments are not patentable *per se* but in certain cases may be claimed as pharmaceutical uses.

4.3 New Uses of Known Products

New uses for a product that is otherwise known may also be patentable. This is particularly the case when a product or its composites are well known. Such claims are labelled "Use of the product X for doing Y.. "

A particular type of use claim are claims for a second pharmaceutical use. It is not rare to discover a new use for a medicine that has been used for some time. For example a new use for aspirin for the treatment of bunions (unexpected and non-foreseeable use) might be patentable. This type of claim, however, offers protection that might be difficult to benefit from as infringement might be difficult to prove.

4.4 Notable Exceptions to the Right to Patent of BIACoM

Relative to BIACoM the following exclusions should be noted:

In Canada, higher life forms including plants and animals, are not patentable. However microorganisms may be patented if they meet all the patentability requirements including utility and reproducibility. This position, derived from jurisprudence, was reiterated by the Patent Office of Canada which recently rejected an application relating to the famous Harvard transgenic mouse. In Europe, despite the European Patent Convention prohibiting the patenting of animal and plant varieties, genetically modified animals have been recognized as patentable because they were not found to constitute an animal "variety" but merely a new animal.

In Canada and Europe methods detailing a medical treatment are prohibited. In the United States "use" related claims are forbidden. However, in the U.S., patent protection may be obtained with respect to claims as to medical treatment and claims related to a specific composition.

5.0 Canada: New Rules

As of October 1, 1996 new rules relative to the application of the Patent Act will go into effect. The changes that relate to biotechnology are as follows:

5.1 Deposit of Microorganisms

The most important change arises from Canada signing the *Treaty of Budapest* and the recognition of the use of international depositories for microorganisms. The net effect is that frequently to satisfy the requirement relating to sufficiency of description it is necessary to deposit the microorganism that one seeks to protect, particularly more so when the invention may not be reproduced without the benefit of such a deposit because the invention itself or certain starting materials are unavailable to the public. That would be the case, for example, for naturally occurring microorganisms claimed in the form of a purified culture.

Deposits for such patents must be made, at the latest, the day of filing of the patent and the deposit number must be communicated without delay to the Commissioner of Patents. Deposits made in conformity with the prescribed norms will be kept secret for 18 months and shall then be made available to the public or independent experts. It is very important to consider these delays when contemplating making such a deposit with a foreign organization such as the *American Type Culture Collection (ATCC)*.

For Canadian applications filed prior to October 1, 1996 it should be noted that the applicant has one year, from October 1, 1996, to file or transfer their deposits to an organization recognized by the *Treaty of Budapest*.

5.2 Deposit of Amino Acid Sequences and Nucleotide Listings

Another new requirement contained in these new Rules provides for the deposit of computerized listings when the invention relates to nucleotides or amino acids sequences said to be new. The purpose of this requirement is to allow for the comparison between sequences alleged to be new and existing sequences so as to determine whether the alleged new sequences are really new.

These deposits must be effected using special software, such as PatentIn, which is available from the USPTO and the EPO.

6.0 Provisional Patent Applications: Patenting Strategy

A relatively new rule in the United States allows for the filing of provisional applications. The advantage of such applications is that they are not required to be accompanied by claims but only with a description of what is considered to be the invention. Once a provisional application has been filed the inventor has one year to convert the provisional application into a regular application.

Aimed particularly at small inventors the provisional application is nonetheless useful to inventors who need to act quickly as their results have been published (press releases, articles, conferences, etc.). Use of this procedure is advised only in cases of extreme urgency and where strategically useful.

7.0 Patenting Medicines

In the field of pharmaceutical products the State has provided certain supplementary rules relative to both patentability and marketing. As we have seen while seeking to promote research and development the State also wishes to ensure that the public shall benefit from inventions in this field, that they will not be toxic and that they will be available at an affordable price.

7.1 Origins of Medicines

Medicines are chemical products. They may be of mineral, vegetative, or animal origin. However the question remains as to whether products derived from human beings, such as blood and its derivatives, mother's milk, organs or portions of organs may be considered as medicines. These products, once removed from donors, may often undergo costly and elaborate transformations prior to being administered to patients to either treat, mitigate or prevent disease.

More and more frequently medicines are being developed from biotechnology. These products have the benefit of being free from contamination, are less costly, and less toxic to human beings. Examples of some of the products derived from biotechnology include: human insulin used during the treatment of diabetes, alpha interferon used as an antiviral and anticancer agent and human growth hormone used to treat dwarfism .

7.2 Bringing a Medicine to Market

When a new molecule is found and appears to have therapeutic effects in laboratory tests the substance may not immediately be placed upon the market. The manufacturer is obliged to respect the regulatory conditions to market the new medicine. The company must obtain the necessary authorisations and submit to the control of the Director General of Health and Welfare Canada (D.G.H.W.). They are obliged to prove the effectiveness of the pharmaceutical product through successive clinical trials (phase 1, phase 2, phase 3).

During the clinical trial period the objective of the manufacturer is to obtain permission to place the product on the market, the permission is contained in a *Notice of Conformity*. This *Notice* confirms that the medicine respects the norms prescribed by Health and Welfare Canada for human or veterinary use and that its sale is authorised for the Canadian market. The authorisation, while granted for an indefinite period, may be suspended or revoked in the interest of protecting public health.

It is important to note that to obtain a patent an inventor is not obliged to have completed the clinical trials required by the DGHW. As with other inventions the examiner adopts the working hypothesis that the product will eventually be used for its purposes as a medicine.

We have seen that patents do not provide the right to make and sell one's invention, only to stop others from doing so. This means that the regulatory process is essential to the marketing of many pharmaceutical inventions. The time delays are extremely long, up to ten years. These delays should be seriously considered when devising a patent strategy for patents in this field.

7.3 Decision to Patent Drugs/Medicines

Pharmaceutical laboratories involved in research invest considerable sums of money in hopes of finding the particular molecule that will ensure their success.

To recover the costs associated with research and development these companies, when placing the product on the market, they may attempt to protect their invention by obtaining a monopoly on exploitation. However not all medicines developed are necessarily patentable. Like any other invention they must fulfill the criteria of patentability contained in the law and in the jurisprudence which we have already reviewed. The same rules apply to drugs and medicines that result from biotechnology. Certain human proteins obtained by genetic engineering, such as human insulin, erythropoietin, interferon alpha-2b have been patented and are currently marketed.

7.4 Intermediate Products

As we have just seen a medicine actually administered to the patient may be protected by a patent. The question remains, however, as to whether the intermediate products are patentable. The intermediate products that might be claimed are the precursors to the final product. They represent an indispensable and necessary step towards the final preparation of drugs. It would appear that such intermediate products may be patentable in Canada in the same application as the final products where there is sufficient structural similarity with or if it was used to prepare the final products. If it has a use in addition to the final product, it may be subject to another patent application.

7.5 Aspects of the Effect of a Patent for a Second Therapeutic Use

The grant of a patent for a second therapeutic use limits the patentee to exploiting the particular claims of the new patent. This should be contrasted with the monopoly granted the patentee for the pharmaceutical product itself. In such a situation the first patentee enjoys exclusivity for the first use and all subsequent uses derived from the drug but he will not be able to exploit the second use without the permission of the holder of the second patent. Relative to the holder of the second patent, he is obliged to obtain the permission of the first patentee, if the first patent is still valid, to market the drug for its new use. Obviously when the first patent expires the first invention may be copied by any person including the owner of the second patent.

7.6 Patent Status of BACoMs

To conclude this part we provide the following table which briefly summarizes the types of claims that have or have not been allowed in Canada, Europe and the U.S. with respect to subject matter relevant to this paper.

Table 1 - Status of BACoM Claims Canada, Europe and the United States

Object of the invention	Patentable subject matter ¹	Example of typical claims
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		CANA DA	EURO PE	UNITE D- STATE S	
living matte r ge net ic ally mo difi ed	ani mal	NO	YES, but under oppo sition	YES	A transgenic non-human mammal all of whose germ cells and somatic cells contain a recombinant activated oncogene sequence.
	micr oorg a nism cell, etc	YES	YES	YES	The hybrid cell line ECACC 87#050801. CA 1,337,717
ge net ic ally un mo di fie d livi ng matte r	ani mal	NO	NO	NO	-

	microorganism, cell etc.	YES	YES	YES	A biologically pure culture of <i>Bacillus megaterium</i> ATCC strain 55000, or mutants thereof, wherein said mutants are capable of controlling the soybean pathogen <i>R.Solani</i> without phytotoxic effect on the soybean plant. US 5,393,729
	polypeptide	YES	YES	YES	An isolated peptide of SEQ ID No:7. US 5,519,118.
	Nucleotide sequence	YES	YES, except if the coded protein is known.	YES	A DNA replication sequence adapted to couple to the 3' end of a DNA strand wherein said DNA strand wherein said DNA strand is not natively coupled to the DNA replication sequence having a DNA sequence selected from the group selecting of SEQ ID No, SEQ ID No 86, SEQ ID No 87 and SEQ ID No 89. US 5,389,531.
	Composition	YES	YES	YES	An insecticidal composition comprising the <i>Bacillus sotiradisum</i> bacterium of claim X, and an agriculturally adjuvant.

method in biotechnology	YES	YES	YES	<p>Method of producing a polypeptide having the sequence shown in SEQ ID No:6, comprising the step of:</p> <p>a) culturing an host cell which has been transformed with the DNA sequence of claim X under conditions which permit the expression of the polypeptide ; and</p> <p>b)harvesting the polypeptide.</p> <p>US No 5,479,122.</p>
Method of medical or veterinary treatment	NO	NO	YES	<p>A method for the treatment of a behavioural disorder with change of mood comprising administrating to a mammal in need thereof selected from dogs and cats, an active ingredient selected from selegiline, its racemate, the laevorotatory isomer, mixtures thereof in any proportions , and pharmaceutically acceptable salts thereof, in association with a pharmaceutically acceptable carrier. US No 5,547,995</p>

Use	YES	YES, but in case of drug by using the wordi ng used below .	NO	Use of <i>compound X</i> for the treatment of the Y.
2nd use	YES	YES	NO	Use of a (known) compound X for the manufacture of a medication for the (new) therapeutic treatment of Y.

1. Once the requirements of novelty, non-obviousness and utility have been complied with.

PART TWO

1.0 Transferring Biotechnology and Related Matter

As we know biotechnology encompasses a large and various group of possible products. Biotechnology has been broadly defined as including: "any technique that uses living organisms or parts of organisms" to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses. Biotechnology extends over most of the area of the life sciences.

We also know that biotechnology and pharmaceutical companies, universities and research centres are all involved in the various activities relevant to the life sciences from initial fundamental research, subsequent development phases of research and finally the creation of new products subject to commercial use.

It is important to keep in mind therefore that each stage in the process of going from research to final products may be subject to different considerations when it comes time to discuss the transfer of technology in this field at any particular stage of development.

2.0 Importance of Confirming Transfers in Writing

In our opinion being aware and understanding the importance of protecting technology transfers by contract and having knowledge of the ideal contents of such contracts is not necessarily guarantee the consistent use of such agreement in the field of the life sciences. The most important advice therefore that one may provide in this respect is that any entity, large or small, owning or wishing to purchase technology should have in place a licensing or technology transfer program which is well defined understood by all working within its parameters, and applied consistently.

There is a tendency in the biotechnology field in particular to transfer technology or vital information relating to technology without first entering into some of the agreements we will discuss later in this paper.

This reticence is partly explained by the principle of the free movement and exchange of ideas common in the field of scientific research which run contrary to the element of distrust imposed by legal advisors.

We shall not endeavour to provide every single type of contract or the ideal contents such contracts since the literature abounds on this subject. Our experience is not to the effect that the inadequacies of technology transfer agreements or poor patenting strategy are the sole source of problems for those involved in this field. The worst problems arise when the parties to a transfer do not, as a matter of course and a matter of practice automatically proceed to a written exchange on the various elements of the transfer. Such oversights can become very costly and jeopardize years of hard work and even ultimately cost society to lose the benefits of the practical application of the technology involved or at least slow down such advances. These comments are especially true in the trans-national context.

3.0 More than Two Parties to the Agreement

It is not uncommon in the biotechnology field that a transfer which commenced between only two parties evolves to include several participants. This situation can arise in the trans-national context as well.

We know that biotechnology is derived from research efforts in universities, the life sciences industry (biotechnology, pharmaceutical, medical, etc.), government sponsored or private research centres and so on. Some of these parties to research efforts find themselves in the position of having to license

out technology while others find themselves on the other side of the bargaining table.

Because of this interaction of several players at any given time along the evolutionary road of a particular product it is important that all players abide by the same set of rules. It is important that the owner of the technology retain full control over the fruits of its labour. You have probably already been advised of the importance of foreseeing in such transfers the inclusion of clauses relating to alternative dispute resolution systems, legal forum for disputes, applicable law for dispute resolution clauses and so on.

3.1 Investors and Financing Entities

The same comments can be made for entities that are in the business of financing research efforts. Often the entity that is loaning money to the owner of a technology, or taking a position in it, must play the same role as the technology owner especially when the entity that is to be financed has little or no other assets of any value.

4.0 Form of Protection of the Object of Transfer

4.1 Do Not Concentrate Only on Licences and Patented Technology

There are several ways by which technology may be transferred. We have seen that biotechnology and pharmaceutical inventions can be subject to patent protection. Such technology may also be protected without recourse to patenting. In fact the practice of focusing only on patent rights in a technology transfer context and evaluating only the patent rights being transferred should not be blindly followed. Furthermore licence agreements are not the only manner by which technology can be transferred. Confidential information relating to processes, know-how and trade secrets all form part of the patrimony of a company in the same way that a patented invention does.

4.2 Publication of Applications by Patent Office: Effect on Strategy

It must be kept in mind that in most countries, except the United States for the time being, patent applications are made available to the public eighteen (18) months after they are filed. Even a United States patent filed in accordance with the Patent Cooperation Treaty will be made public prior to grant.

This public disclosure means that anyone interested may consult the Patent Office where protection is sought and literally review the patent application and obtain a description of the invention. There are therefore situations where it is strategically unnecessary/unadvisable to file for a patent.

4.3 Alternatives to Standard Licences

In the biotechnology field transfers are often made at a point in time when patent protection is not even available given the rudimentary stage of the research involved or the lack of a practical application for it. In law, secret undisclosed information which has not become part of the public domain consists of an intangible asset. This means that the transfer can take place without a licence and with respect to unpatented matter. These agreements can take the form of confidentiality agreements, know-how agreements, turn key agreements and even joint venture agreements amongst others.

Prudence dictates that, depending on the technology involved and the degree to which it has evolved, it is always advisable to consider the advantages of contractual technology transfer over that of simple licensing. The choice of the proper vehicle should be pegged to the state of development of the technology and the goals and strategy of the parties involved.

4.4 Trade Secrets and Know-How

4.4.1 Definition

A trade secret can be defined as information, including, but not limited to, a formula, pattern, compilation, program, method, technique or process, or information contained or embodied in a product, device or mechanism which:

- is or may be used in a trade or business;
- is not generally known in a trade or business;
- has economic value from not being generally known; and
- is subject of efforts to maintain its relative secrecy that are reasonable in the circumstances.

One of the main advantages of a trade secret, compared to a patent, is relatively apparent from its definition. Where patent law requires that the patentee disclose to the public its invention in such a way that the invention can be reproduced by others, as we saw in PART ONE, the very essence of a trade secret is that it is not disclosed to the public. A trade secret loses all of its

value once it is publicly disclosed, where as a patent cannot be obtained unless full and adequate disclosure is made. Trade secrets can extend the life of an eventual patented invention.

4.4.2 Protecting the Secret

There are, many steps which can be taken in controlling trade secrets to ensure against their misappropriation and disclosure to the public by the members of an organisation, they include:

- developing secured areas in research and manufacturing areas;
- only certain employees are made aware of trade secret and are bound to secrecy by appropriate agreements;
- all publications by persons aware of the trade secret are reviewed before release to ensure that the company's proprietary information is not disclosed;
- all trade secrets must be committed to print;
- all documented trade secrets must be stored in a safe place;
- all plant visits by outsiders must be documented and such visits must always be conducted under escort;
- all licensees of relevant technology must be required to maintain the confidentiality of trade secrets.

Trade secret protection is not limited to the patentable subject matter we have reviewed in the first part of this paper. As a result, such things as know-how, compilation of information, and other business information, which are not protectable by patents, may be protected as a trade secret. A trade secret does not have to be inventive, it is sufficient that there is enough originality to distinguish a trade secret from every day knowledge in the business. Therefore, the potential subject matter of a trade secret encompasses and exceeds that which can be the subject matter of a patent. Trade secrets may be used in respect of biotechnology in cases where patent protection, or any other form of industrial property protection rights, is not available to protect the particular subject matter.

When it is expected that the biotechnology life span will be equal to, or longer than the time of protection secured by a patent and when the secret cannot be discovered by reverse engineering, trade secret protection will be an effective form of protection for biotechnology.

5.0 Practical Aspects of Technology Transfer

5.1 Choice of Licensee or Licensor

It is important that the parties to a technology transfer carefully choose their co-contracting party. This is especially true for a licensor who wishes to grant an exclusive licence to a licensee for any significant period of time. There are few worse situations than being tied in with a business partner who may be able to meet the minimum obligations of the licence arrangement but unable to make the agreement a mutually beneficial endeavour for both parties.

5.2 Due Diligence

It is important that the licensee, prior to contracting, carry out a due diligence evaluation of the technology offered by the licensor. We do not use the term "due diligence" lightly. Every aspect of the technology to be licensed must be examined to ensure everything from the proper chain of the title of the licensor in the technology, the right to license itself, the validity of the patent in the event patented technology is being licensed and the extent of protection afforded by the patent as expressed by the specification and the claims of the patent, the likelihood that a patent application will be granted and the protection likely to be granted by the patent office in the event the technology transfer consists of a patent application, and all other factors important to the peaceful enjoyment of the licence by the licensee.

These comments are also relevant to the behaviour of a party which finances or invests in the licensor. Before financing or investing in a company which represents that it has a technology to license one must carry out a due diligence verification of the technology owner's contentions. The investor or financing party must also ensure that the conditions of the licence accepted by the licensor are optimal so that the licensor fully benefits from the technology it owns thus making it more capable of repaying its creditor or increasing profits for the party that has taken a "position" in the licensor's business.

5.3 Time of Transfer

There is no set strategy that may be dictated with respect to the optimal point in time when one must transfer or receive technology. It is based on the particular business needs of the parties to the contract at any given time. It may also depend on the relative financial strength of the parties. A licensor might license earlier than it would ideally wish to in the event it requires cash in the short term for further development and wishes to accelerate its arrival to the market place.

The value of an invention normally increases as the development stage of the final product advances. This can mean, therefore, that the licensor obtains less for a licence if he licenses early. This will provide an opportunity to a licensee who may or may not wish to contribute to the further development process, to obtain technology at a lower initial price and then retain some control over the further development of the technology and perhaps even foresee a reimbursement schedule for part of the additional investment.

5.4 Confidentiality and Proper Use of Materials Remitted

Whether one proceeds contractually or through a licence agreement and whether the technology is patented or not, it is always vital that the parties have a clear understanding of what the technology is that it is being transferred. Licensor should be very careful to maintain the confidentiality of the information and biological material that will be released to another party. The biological material to be transferred should be sufficiently described to ensure that there is a clear understanding between the parties as to exactly what materials are being investigated. Licensor should make sure that the confidentiality of the information disclosed will be kept absolutely confidential and that the potential licensee will not use the information transferred for its personal profit until a licensing agreement is concluded.

Another consideration is the concern that health regulators have with regard to improper use of biological materials or inappropriate handling. It is important to ensure that the group receiving the biological material agree to use the material in compliance with all laws and regulations of their country. Furthermore, the group receiving the biological material should agree to save and hold harmless the transferor of the material in the event of improper use of the receiving group. It is also usually stipulated that the recipient will use the materials in accordance with local laws and regulations relating to such materials.

6. Disclosure and the Absolute Novelty Rule

We have already seen that the absolute novelty rule regarding the public disclosure of patents applies in most countries. In said countries an invention cannot under any circumstances be disclosed before the filing date of the application. We have also seen that in Canada and in the United States there is a twelve month grace period for such disclosure. The disclosure of invention in accordance with a signed confidentiality agreement is in principle not considered to be a public disclosure. As such the technology transfer agreement or confidentiality agreement is not normally considered to be a

public disclosure. Where one is certain that the market for the invention exceeds Canada and the United States it is recommended to apply for patent protection as soon as there is a risk of public disclosure especially considering that for a disclosure to become a bar to patent registration it can occur in Canada for example and operate as a bar to filing in another country..

7. Issues in Licensing Biotechnology

7.1 Introduction

The present section discusses a few of the issues that potential licensors and licensees should consider in negotiating and drafting biotech licence agreements such as determining who owns the biological materials licensed, defining the rights to be licensed, selecting grant clauses, the field of use and territorial restrictions, determining licensing fees and royalties, and preparing provisions maintaining confidentiality.

7.2 Definitions

The clarity of any licence agreement, whether in respect of biotechnology or not, depends on the terminology used in the agreement is clearly defined and whether the definitions used have been fully considered and carefully drafted. One must accurately define the product to be conveyed. An accurate definition should include both what product is conveyed and what form that product may take. In addition to defining what is conveyed, it is crucial for the rights holder to make clear the rights of the parties's in derivatives, spin-offs or improvements of the invention transferred. It is recommended that clear and separate definitions be used to distinguish the different aspects of a technology being licensed where a different royalty base will exist depending upon how the licence subject matter is utilized by the licensee. Definitions for "Licensed Biological Materials", "Licensed sale lines", "Licensed microorganisms", and "Licensed product" can be included to distinguish different aspects of the technology.

Making separate definitions is useful when it comes time to grant different rights in respect of different aspects of the technology that is transferred.

7.3 Ownership, Right of Transfer

A licensor must ensure that his title in a technology and any tangible biological materials involved is clear and he must ensure that the licensee

recognizes that the licensor enjoys such title. Due diligence on the part of the licensee of course will ensure that the licensor has a clear title in the property being transferred.

It often happens that the technology being licensed was developed in whole or in part by a governmental agency. Restrictions may be placed on a transfer of such technology as a result of the contractual arrangement between the agency and the party offering to transfer the technology. Limitations may include the duration of licences that may be granted and the right to grant exclusivity. As such, the licensee should always ensure that the licence agreement contains warranties to the effect that the licensor is entitled to transfer the rights of the technology being licensed and ideally take steps necessary to ensure that such warranties representations are true.

7.4 Exclusive or Non-Exclusive Grant

The type of grant will depend primarily on the type of technology being offered. If it is a fundamental discovery from which developments will follow, (pioneer technology), it is to the benefit of the licensor to grant the technology on a non-exclusive basis. On the other hand, with an improvement technology, it will often be necessary to grant an exclusive licence in order to attract a worthwhile licensee.

7.5 Extent of Transfer

7.5.1 Derivatives

Given the nature of the technology transferred in the biotechnology, medical or pharmaceutical contexts it is important to foresee in a technology transfer agreement the rights the parties will have in the event the materials transferred undergo random mutations having an effect on the licence rights transferred. It will be important therefore to provide definitions in such agreements as to what is understood by the term derivative in this context.

We take the liberty of proposing two definitions which have been suggested by the *Biotechnology Committee of the Licensing Executives Society* of which our firm is a member:

"Derivative" means progeny, clones, sub-clones or products of parent wherein such progeny and sub-clones include non-identical progeny and sub-clones of parent and such progeny includes progeny which would not have been made but for the parent.

"Derivative" means any progeny and any genetically engineered modification wherein such progeny and genetically engineered modification is based on and incorporates all of the essential features of the parent. The genetic material is substantially unchanged. The genetic material is substantially based on an incorporates an essential element of the parent and is verifiably distinct from the parent. The structural and/or functional characteristics are identical to or are predictable, expected result of genetically engineered modifications of the parent. The genetic material is substantially similar to the material from which it is derived in having a substantial portion of the characteristics of the parent genetic material, or any genetically engineered modification which is substantially based on and incorporates an essential element of the parent without a substantial change in phenotypic expression.

From the licensor's stand point, the definition of derivatives will enable the licensor to cover all changes to the biological material which function in essentially the same way as the material originally transferred. Once the derivatives are defined, the parties must determine who will have rights in those derivatives.

7.5.2 Improvements and Rights to Income from Spin-Offs

In addition to natural changes in the technology that is transferred, changes can occur in a technology as a result of the efforts of the licensee or even of the licensor. A licensee may for example develop a new use for the technology which the licensor had never even contemplated in the first place. Licensors will often contend that the improvement falls within the licence agreement while the licensee who may have devoted a great deal of money of research that led to the improvement will argue that the improved products or uses for that matter are outside of the original grant so that no royalties are due. There may also be a dispute as to whether the improvements are so detached from the initial material transferred that one or the other of the parties has the right to apply for patent protection.

This situation is avoided by defining and negotiating the rights to improvements and spin-offs in advance.

7.5.3 Field of Use and Territorial Restrictions

The consideration in deciding upon the field of use depends on whether or not the technology to be licensed is of a pioneer or improvement nature. Pioneer technologies normally have a variety of commercial applications. A licensor who grants exclusive licences for different fields of application can maximize the royalty return. For example, a licensor could grant an exclusive licence of a product in the field of therapeutic use and another exclusive licence in the field of diagnostics.

In the case of improvement inventions, normally the technology is licensed in the sole area in which the improvement is useful.

Territorial restrictions can be set up to enhance royalty return. The technology can be licensed country by country to different companies providing they are identifiable market in each country. This can be broken down further to identifiable regions within a country. However, if the potential licensee is clearly able to properly exploit the technology on an international basis, licensor could then grant a worldwide licence into the transferred technology.

7.5.4 Royalties

In view of the varied uses of biotechnology and the manner in which ensuing products can be sold, it is important to use ingenuity in developing royalty rates. It is, however, extremely difficult for the parties to decide on what is fair market value to charge for the use of the licensed technology. Royalties need not be only form of payment in licences. Other forms of remuneration may include licensing fees, minimum annual payments to reflect performance, and single lump-sum payments.

Licensing allows the owner of the technology to recover expenses incurred in developing an invention. The cost incurred in protection the invention by patents can be recovered by licence fees associated with the signing-up of each licensee. Initial licence fees are usually not creditable towards royalties.

The Biotechnology Transfer Committee of the Licensing Executive Society USA/Canada has published the following suggested royalty rates in the field of biotechnology:

Table 2 - Suggested Royalty Rates

PRODUCT	ROYALTY RATE
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Research Reagents (e.g. expression vector, cell culture, media supplements)	In the range of 1% to 5% of net sales
<u>Diagnostic products (e.g. monoclonal antibodies, DNA probes)</u>	In the range of 1% to 5% of net sales
<u>Therapeutic products (e.g. monoclonal antibodies, cloned factors)</u>	In the range of 5% to 10% of net sales
<u>Vaccines</u>	In the range of 5% to 10% of net sales
<u>Animal health products</u>	In the range of 3% to 6% of net sales
<u>Plant/agriculture products</u>	In the range of 3% to 5% of net sales

Notwithstanding the foregoing table, the setting of royalty rates is determined on a case by case basis and will be influenced by various factors such as the economic benefit to be derived by the licensee, exclusivity versus non-exclusive grant, extent of the field of use, extent of territorial restriction and all other relevant factors.

ROBIC + LAW
+ BUSINESS
+ SCIENCE
+ ART

ROBIC + DROIT
+ AFFAIRES
+ SCIENCES
+ ARTS

