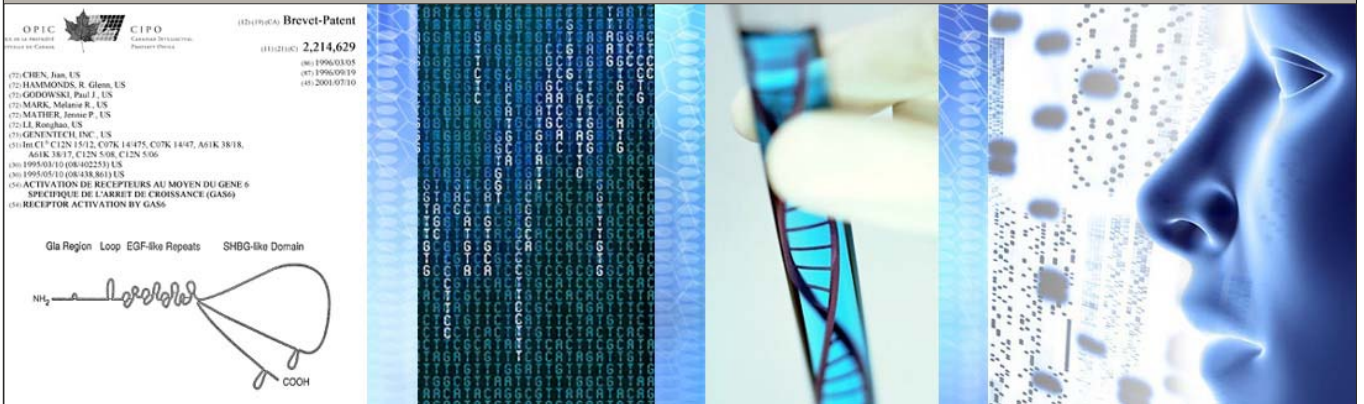


Science Matrix

Final Report

July 2005



Study on the breadth of human gene patents granted by the Canadian Intellectual Property Office (CIPO), the European Patent Office (EPO) and the United States Patent and Trademark Office (USPTO)

Prepared for the Canadian Biotechnology Advisory Committee

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Aussi disponible en français sous le titre, Étude de la portée des brevets liés à des gènes humains octroyés par l'Office de la propriété intellectuelle du Canada (OPIC), l'Office européen des brevets (OEB), et l'United States Patent and Trademark Office (USPTO).

Science-Metrix

Final Report

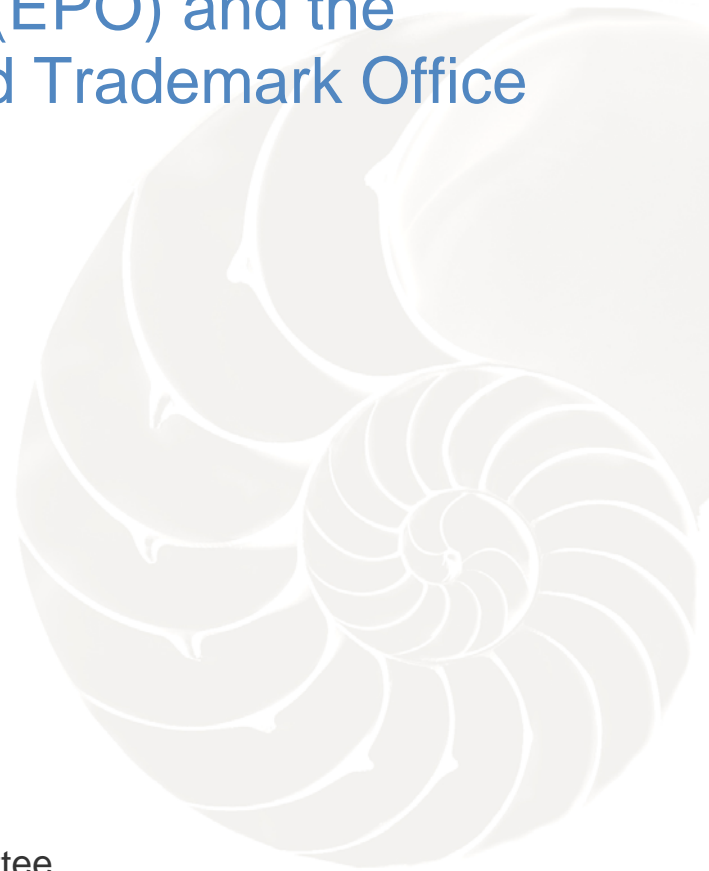
Study on the breadth of human gene patents granted by the Canadian Intellectual Property Office (CIPO), the European Patent Office (EPO) and the United States Patent and Trademark Office (USPTO)

July 2005

David Campbell, M.Sc. and
Stéphane Bergeron, Ph.D.

Prepared for the
Canadian Biotechnology Advisory Committee

Science-Metrix specializes in the measurement and evaluation of science, technology and innovation. Our data collection and assessment methods include bibliometrics, scientometrics, technometrics, surveys and interviews, environmental scans, monitoring and intelligence gathering. We perform program and policy evaluations, benchmarking and sector analyses, market studies and strategic planning. Science-Metrix has a robust knowledge of life and environmental sciences.



Breadth of human gene patents across patent offices

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Breadth of human gene patents across patent offices

Executive Summary

Patenting of human genes is a highly complex and sensitive issue. All countries that have a system of intellectual property (IP) and are facing the challenges brought by biotechnology need to adapt their patent systems. This could however result in divergences among the practices of patent offices in different countries and produce varying levels of protection for patented inventions. Having become increasingly concerned by the issue of human gene patenting, the Canadian Biotechnology Secretariat (CBSec), on behalf of the Canadian Biotechnology Advisory Committee (CBAC), mandated Science-Metrix to evaluate whether existing differences among the practices of the Canadian Intellectual Property Office (CIPO), the United States Patent and Trademark Office (USPTO), and the European Patent Office (EPO) lead to human gene patents of varying scope.

To make this evaluation, a comparative analysis of the claims in human genes patents granted by the three patent offices based on the same application filed under the Patent Cooperation Treaty (PCT) was conducted. In several instances, methodological barriers impeded proper comparison of claims between patent offices. For many patent families, the U.S. equivalent of the Canadian and European patents was fragmented in a complex sequence of divisional, continuation and/or continuation-in-part (CIP) patents making it difficult to compare claims among patent offices with confidence. In these instances, and in other cases where attorneys specialized in biotechnology patenting were not able to explain the differences in the language used in the claims, no conclusions were drawn. However, there were several key findings from the patent analysis.

Based on a literal interpretation of claims, U.S. patents often appear to provide a narrower scope of protection than is provided by European and Canadian patents, which are generally comparable in terms of their protection, although Canadian patents tend to be slightly broader in scope. Canadian patents are often the most similar to the PCT application suggesting Canadian examiners had requested fewer changes than the U.S. and European examiners. This could perhaps be explained by the fact that restriction requirements to limit the examination of an application to a single invention, which result in the abandonment of claims or in divisional patents, are far more common in the U.S. and Europe than in Canada. However, this finding must be interpreted with caution since the sample size of the present study is small (i.e. 24 human gene patent families). In addition, many experts in biotechnology patenting were surprised by this finding; one of them could not recall any occasion when he had not been requested by the examiner to amend the claims in the PCT application for the eventual Canadian patent.

In general, U.S. examiners appear to be stricter regarding claims on nucleic and amino acid sequences, being more reluctant than Canadian and European examiners to issue “reach-through” claims for mutants, derivatives, analogues, and homologues of the claimed sequences. However, an expert in biotechnology patenting pointed out that Canadian examiners are becoming more and more like their peers in the U.S. in this respect.

In some instances, European or Canadian examiners were the most stringent, issuing the narrowest claims. European claims sometimes provide more specifications of a method or the characteristics of a protein (e.g. molecular weight, isoelectric point), thereby reducing their breadth. In some areas Canadian practices are the most restrictive, for instance, claiming of transgenic animals, which is allowed by the USPTO and the EPO, is forbidden in Canada.

The legal interpretation of claims, which varies from one country to another, also has an impact on patent scope. In Canada, where the concept of purposive construction prevails, claims are interpreted more stringently than in the U.S. where the doctrine of equivalents provides a little more flexibility to the claim language, buffering literal differences in patent scope. In Europe, the situation is more complex as each member state applies its own national laws. For example, practices in the UK, which applies the concept of purposive construction, are stricter than in France and Germany, which apply the concept of sympathetic construction which gives the most flexible interpretation of claims. However, unique to the EPO is the morality or “ordre public” clause, which can radically reduce the scope of a patent.

Finally, according to experts in biotechnology patenting, as the field of biotechnology has matured, patent offices have become much stricter with regard to the application of patentability criteria. The USPTO in 2001 published new guidelines with respect to utility and written description and U.S. examiners are nowadays the most likely to reject applications on the grounds of utility and enablement criteria. In 1999, the EPO implemented the European Union Directive on the Legal Protection of Biotechnological Inventions and European examiners are now the strictest over non obviousness. In Canada, examiners are becoming stricter, and their practices are becoming more and more similar to that of U.S. examiners.

1 Introduction

Patents are granted by governments and provide the patent owner exclusive rights to use, make, sell or import an invention for a specified period of time. In exchange for this protection, the patent holder must make complete disclosure of all the details of the invention and best practice in order to inform the public about the current “state of the art”, and to enable its use by others upon release into the public domain, generally 20 years following the original filing of the patent.

The origins of the patenting system are unclear. The British claim to have the oldest patent system in the world with origins that can be traced back to the 15th century when the Crown granted specific privileges to manufacturers and traders. In Canada, the Patent Act was officially introduced in 1869 under Federal jurisdiction and was modeled on the first U.S. Patent Act of 1790. Since then, the Canadian Patent Act has been amended several times in order to tailor it to an ever evolving society and to take account of technological and scientific change. These amendments have mainly been influenced by the U.K. and U.S. patent acts, and more recently by the European Patent Convention (EPC) (Duy, 2001). During the 1990s, Canada signed up to four international treaties including the classification of patents, the international recognition of microorganism deposits, the international norms for the protection of new plant varieties, and the Patent Cooperation Treaty (PCT) which covers international procedures allowing the granting of a patent in more than 100 member countries.

The Canadian Patent Act and its equivalent in the U.S. and Europe were established both to protect inventions and to ensure that they were properly patented. According to these laws, to be eligible to be patented, an invention must satisfy three specific criteria: it must have utility, novelty and non-obviousness. The utility requirement means that the claimed invention must have a credible and substantial utility that is either asserted in the specification or is well-established. An invention will fail the novelty requirement if some public disclosure of the invention has been made before the patenting application. Finally, the non-obviousness requires that no prior art or previous work exists that suggests or reveals the invention as whole. In other words, in the light of the existing knowledge, the invention must be inventive (see chapter 15 in the Canadian Manual of Patent Office Practice).

Nevertheless, many applications for gene patents have been granted although these three criteria were not always met. In particular, several irregularities have been reported in relation to patents on human genes. A study that analysed 74 U.S. issued patents for human genes revealed that 38% of claims were problematic (Paradise, 2005). The most common problem was that the patents claimed far more than was actually discovered by the individual inventor. For instance, some applicants have taken advantage of the redundancy of the genetic code by claiming every potential sequence relating to the claimed protein without any description of those sequences. Other examples include protection for any future related genes (e.g. isoforms or mutated forms) without giving specific descriptions of those genes or claimed gene polymorphism associated with different conditions or diseases without any scientific correlations (Paradise, 2005).

Similarly, a study conducted jointly by the Japanese Patent Office (JPO), the European Patent Office (EPO) and the United States Patent and Trademark Office (USPTO) identified a recent trend in the area of biotechnology patenting consisting of applications containing claims relating to future inventions based on currently disclosed inventions. For instance, some applications claim all possible pharmaceutical candidate compounds and methods of using such candidates which might be considered to be beyond the scope of the invention (Trilateral Project, 2000). This phenomenon refers to “reach-through” claims. In general, these types of claims attempt to capture the value of a discovery before it has evolved into a full invention. In 2004, the U.S. Court of the Federal Circuit, ruling on the Rochester case, declared the “reach-through” claims as invalid (University of Rochester, 2004). According to experts, this decision will have repercussions on claim drafting, freedom-to-operate and even the wording of many licensing agreements (Silva, 2004).

Thus, there are complex questions in relation to genetics and human gene patents, concerning which matter and which applications can be patented, which open the door to public debate and generate controversy. Several experts have suggested that Intellectual Property (IP) in these areas could impair scientific progress and access to medical care (Merz, 2002; Paradise, 2005). Indeed, because of the limitations they impose, patents, when granted overly broad protection, could affect the development of treatments or diagnostic tools based on related matter (Lecrubier, 2002; Cyranoski, 2004). The case of Myriad Genetics is probably one of the most famous examples of the complexity of DNA gene patenting and related issues.

Myriad Genetics holds a set of patents that give very wide protection for *BRCA1* and *BRCA2* genes, which appear to be the cause of many breast and ovarian cancers (PHGU, 2004). Therefore, Myriad has a virtual monopoly over the development of diagnostic tools based on these genes, which was keeping the costs of cancer tests at high levels and thus became the source of huge controversy in the public health care sector. The first patent concerning the *BRCA1* gene was revoked in May 2004, and the European Patent Office has recently rejected the essential points of a second patent concerning *BRCA1* (Institut Curie et al. 2005).

Concerned by this situation, Industry Canada and Health Canada asked the Canadian Biotechnology Advisory Committee (CBAC) to examine the IP regime as it relates to human genetic materials and their potential implications for the health sector.

This complex situation is also likely to lead to the adoption, by different countries, of amendments to national patent laws and regulations to tailor IP systems in relation to gene patenting. This could result in wide divergences in the practices employed by the patent offices of different countries, and affect the scope of any granted patents.

Canada has obligations under international treaties, agreements and conventions that may constrain changes to its domestic IP regime. Thus, before embarking on any changes, and particularly in relation to patenting human genes, it is important for Canada to know where it stands in terms of key international organizations and trading partners. As part of its program of work, the CBAC requires

comparative information on the practices of the Canadian Intellectual Property Office (CIPO), the USPTO and the EPO as it relates to the patenting of human genes. Thus, the Canadian Biotechnology Secretariat (CBSec), which is collaborating with the CBAC, mandated Science-Metrix to conduct a study to evaluate whether practices in different patent offices produces patents that vary in breadth.

Section 2 briefly describes the method used for the comparative analysis of human gene patents granted by the CIPO, the USPTO and the EPO from the same PCT application. Section 3 presents the major differences found in the breadth of coverage of Canadian, European and U.S. patents. These differences are discussed from both a literal and legal perspective. The report concludes with a summary of some of the general trends arising from the analysis.

2 Methods

The aim of this study is to compare the scope of the human gene patents granted by the Canadian Intellectual Property Office (CIPO), the United States Patent and Trademark Office (USPTO), and the European Patent Office (EPO) with the goal of determining whether the CIPO's examination processes are more or less restrictive than those of the USPTO and EPO in relation to patent applications in this area. In order to allow comparison of the breadth of patent claims, patents analyzed must have been granted by all three patent offices, based on the same application. To sample these patents, a search was made for patents obtained through an international application under the Patent Cooperation Treaty (PCT). This treaty enables patent protection to be sought simultaneously in several countries from the filing of a single application.

2.1 Building the patent dataset

To build a relevant patent dataset, Canadian gene-based patents were retrieved from the CIPO database using keywords-in-title and keywords-in-abstract searches, but limiting these searches to patents granted between 1990 and 2004, and to patents obtained through applications under the PCT. The search query keywords used were: allele, cdna, chromosome, dna, exon, expressed sequence, gene, genetic, genomic, genotype, haplotype, intron, linkage map, loci, locus, microsatellite, minisatellite, mtdna, mutation, nucleic acid, nucleoside, nucleotide, physical map, plasmid, promoter, radiation hybrid map, rna, rnai, rnam, rnat, and rnarm which identify gene related patents. This search retrieved 1,059 gene-based patents resulting from a PCT application that had been granted in Canada over the 15 year period considered.

Next, data on patent families were retrieved for each of the Canadian patents sampled using their assigned numbers to build batch queries in Synopsis, an Open Patent Service (OPS) Client Software produced by Entory. Synopsis accesses data on patent families through the EPO's OPS, which in turn provides access to the EPO's INPADOC database. The INPADOC database claims to cover 95% of all patents published worldwide since 1973, and clusters patents by families based on their priority numbers¹. Since every patent obtained through application under the PCT is assigned a priority number by the PCT, all patents derived from the same international application will fall within the same patent family. Thus, once data on patent families were obtained for the above sampled patents, it was possible to search for families where the international application led to a patent award in all three regions (Canada, the U.S., and Europe) using country/region codes (i.e. CA for Canada, U.S. for the United States, and EP for Europe), which constitute a portion of the patent numbers. Since Synopsis does not allow retention of only those patent families that contain patents issued in all three regions, a computer application was developed to read and perform searches on the family data retrieved using Synopsis (e.g. ca* AND us* AND ep* in "patent families"). This procedure resulted in 760 from the original 1,059 gene related patents granted in Canada through the PCT, whose families included at least one granted patent in the U.S. and Europe.

¹ http://www.european-patent-office.org/inpadoc/pfs_index.htm, visited May 2005.

Because human gene patents cannot be efficiently identified using keywords-in-title and keywords-in-abstract searches, and because claimed sequences often lack information on the source organism (scientific name and common name), the 760 gene patent families were screened individually to identify those related to human genes and which included Canadian, U.S. and European patents derived from the same international application. The resulting dataset included 24 human gene patent families where an international application led to a patent being granted in Canada, the U.S. and Europe (see Appendix A). The patents thus obtained are suitable for comparing the breadth of claims across patent offices.

2.2 Patent analysis

Although the rules in all three patent offices state that a patent shall be granted for only one invention, the use of restriction requirements that limit the scope of patents irrespective of the field of the invention is more common in the USPTO. Restriction requirements are used by patent examiners as discretionary tools to limit the examination of a patent to a single invention when an application actually covers at least two independent or distinct inventions (e.g. an application claiming the DNA sequence of a gene, and the antibody directed against the protein coded by that gene for use in a diagnostic kit) rendering the proper examination of the application difficult. Following a requirement for restriction, the applicant must elect which of these inventions the claims (and, hence, examination) will be restricted to. The remaining claim(s) can be made the subject of divisional applications which will retain the filing date of the original applications. Consequently, multiple U.S. patents often match up to a single patent in the CIPO or EPO where such restriction requirements are less frequent.

Another situation that may result in multiple U.S. patents, but only a single patent in the CIPO or EPO is where an applicant makes use of continuation or continuation-in-part (CIP) applications. Patent law prohibits double patenting, that is patenting of claims from two separate applications relating to the same invention. However, in order to allow inventors to improve on their inventions and patent these improved products, the USPTO allows submission of what is known as a CIP application, i.e. a new application filed during the lifetime of an earlier non-provisional application, repeating a substantial portion, or all of the earlier non-provisional application and adding matter (not disclosed in the earlier non-provisional application) in order to improve on the initial application.

The main advantage of CIP applications is that the examiner cannot rely upon the pending parent patent application to render the improved invention unpatentable. The claims in the CIP application may focus either solely on the new matter, in which case a separate patent issued for the new applications, or they may include those of the parent application, in which case the original application is subsequently abandoned. The former approach is often preferred even though additional issue and maintenance fees will be incurred in cases where substantial effort has already been invested in arguing the case for the parent application. The reason for this is that the CIP application might not be assigned to the examiner of the parent application, and thus the applicant might have to justify again the claims made in the original application to have them allowed.

When applicants are at the beginning of a new research project, they often protect initial art (e.g. mutations in the DNA sequence of a gene underlying a disease) only in the U.S., the largest market worldwide. This is most likely because the costs incurred in protecting an invention at a very early stage

in several countries cannot be justified. Over the course of their research, the applicants can chain CIP applications to protect new matters related to the initial art (e.g. development of diagnostic tools to identify carriers of said mutations underlying said genetic disease), although the chain must not be broken. At some point, the applicants will seek protection in other countries for the whole spectrum of their invention and will thus file an international application by pooling the claims of all patents in the CIP sequence. If the PCT application includes claims that were not the subject of the previous CIP applications, then this application will be considered a new CIP application in the U.S. and only the new claim will be awarded protection. It is also possible that the patent issued from the PCT application will be followed by continuation or CIP patents. As a result, the U.S. patent derived from the PCT application will represent only a fragment of the claims covered by the corresponding Canadian or European patent.

In comparing the breadth of claims for patents granted by the three patent offices, it is therefore important that both the claims of Canadian, U.S. and European patents derived from a single PCT application, and also the claims of divisional or CIP patents associated with any of these three patents are analysed. Information on divisional or CIP patents should be available from data on patent families.

For 12 of the selected 24 human gene patent families, the international application originated in the U.S. For many of these families, the U.S. equivalent of the Canadian and European patents is fragmented in a complex sequence of divisional, continuation and/or CIP patents making it difficult to compare claims among patent offices with confidence (see Appendix A). However, for the 12 human gene patent families for which the international application originated from countries other than the U.S., most had no continuation or CIP patents in the U.S., rendering comparison more straightforward (see Appendix A). For two of these families, a requirement for restriction resulted in the segmentation of the PCT application in the U.S. and since in both cases only one divisional patent was created, the impact on the analysis of claims is limited.

Two additional factors make comparison difficult. The first is voluntary amendments by the applicant to claims of an international application on entry into the national phase, which can lead to differences in the submitted applications among patent offices prior to examination. The second is issue date variation among patent offices for patents obtained from the same PCT application. For example, the PCT application FR9100269 led to a U.S. patent in 1995, to a European patent in 1997 and to a Canadian patent only in 2003 (see Appendix A). Differences in the claims of these patents might therefore be due to the timing of practices rather than to differences in the practices of the three patent offices.

Therefore, in order to discriminate among the multiple sources of variations that might affect the breadth of patents among patent offices, a detailed history of the process of entry of international applications in the national phase for patents in Canada, the U.S. and Europe is needed for some of the 24 selected families. This information was obtained through a series of telephone interviews with applicants, patent lawyers (or patent agents), and patent examiners with experience of the three patent offices.

The conclusions drawn from observed differences in the claims of Canadian, European and U.S. patents are based on a qualitative analysis of claim language by two biologists with expertise and hands-on experience in molecular biology, who cross-verified their analyses. To support the literal analysis of

claims, interviews with applicants, patent examiners, patent agents and patent attorneys were conducted to establish how observed differences in the breadth of claims would likely be interpreted in terms by a court. Detailed patent analyses for the 24 human gene patent families are presented in Appendix B.

3 Comparative analysis of patent breadth

A comparative analysis of patent coverage granted within the 24 human gene patent families revealed various differences, which fall into one of two broad categories:

- differences between patent offices that do not affect patent breadth;
- differences between patent offices that do affect patent breadth.

Sections 4.1 and 4.2 examine both categories in light of observations made in the comparative analysis of patents granted by the Canadian Intellectual Property Office (CIPO), the United States Patent and Trademark Office (USPTO), and the European Patent Office (EPO) from the same Patent Cooperation Treaty (PCT) application.

3.1 Differences that do not affect patent breadth

Two main differences that do not affect patent breadth were observed. The first relates to medicines and is not specific to gene-based patents. In Canada and Europe, claims relating to medicines are “use claims”, whereas in the U.S. they are “method claims”. The following is an example of their drafting by the different jurisdictions:

Use of an effective amount of **a substance** that activates the CNTF (ciliary neurotrophic factor) receptor **for treating** obesity and diseases associated therewith in a patient. (Claim 1 of Canadian patent in family WO9822128)

The **use of a substance** that activates the CNTF (ciliary neurotrophic factor) receptor **for the manufacture** of a medicament for treating obesity and diseases associated therewith. (Claim 1 of European patent in family WO9822128)

A method of treating obesity and diseases associated therewith in a patient **comprising the step of administering** to said patient an effective amount of **a substance** that activates the CNTF (ciliary neurotrophic factor) receptor. (Claim 1 of U.S. patent in family WO9822128)

In Canada, claims focus on the use of compound X for treating disease Y; in Europe they focus on the use of compound X for the manufacture of a medicament for treating disease Y; and in the U.S. they focus on a method of treating disease Y comprising the step of administering compound X. The difference in the language used in the Canadian and European patents is subtle and implies that in Canada, a patient using the drug could be infringing the patent, while in Europe it would be the manufacturer selling the drug that would be the infringer. However, in practice, in Canada it is also the manufacturer selling the drug that is deemed to be infringing the patent; thus, despite the wording, both patents provide more or less equivalent protection in their respective jurisdictions (telephone interviews).

In the U.S., however, the difference is more significant since physicians using protected “methods of medical treatment” to treat patients could be sued by the patent holders, thereby seriously impeding their day to day work. This is the main reason why “methods of medical treatment” are not patentable under

the European Patent Convention (Article 52(4) of EPC) and the Canadian Patent Act (Section 2 of the Patent Act; see the Manual of Patent Office Practice Chapter 12.04.02). However, according to these two documents, this prohibition does not apply to products, and particularly substances or compositions, used in any of these methods.

Although “methods of medical treatment” are patentable under the U.S. Patent Act (35 U.S.C.), the impact of this difference on patent scope must be interpreted with caution. It has been established in the U.S. courts that the patent holder cannot sue the users of a method if the patented “method of medical treatment” is a technique and does not involve pharmaceuticals.² In these circumstances, none of the differences highlighted above regarding protection of medicines would result in patents of different scope. This underlines the importance of considering differences in the wording of the claim from both a literal and a legal perspective in estimating their impact on patent breadth (telephone interviews).

Another frequent difference that does not impact on patent scope relates to the form of the disclosed gene or protein (see Sections B.1.2 and B.2.1). When nucleic or amino acid sequences are involved, U.S. claims often state that the molecule must either be isolated, synthetic or recombinant, while Canadian and European claims are generally not so specific. An example of this is given below:

An isolated, synthetic or recombinant DNA molecule comprising a nucleotide sequence encoding...
(Claim 1 of U.S. patent in family WO9107492)

A DNA sequence encoding the CDR1, CDR2 and CDR3 regions... (Claim 1 of Canadian patent in family WO9107492)

A DNA sequence encoding the CDR1, CDR2 and CDR3 regions... (Claim 1 of European patent in family WO9107492)

In the U.S., the Canadian and European versions of the claim would be interpreted as not involving the hand of man, in that the claimed DNA is not distinguished from its natural state and would therefore not meet the statutory requirements under 35 U.S.C. 101 (telephone interviews). However, in Canada and Europe the “isolated” specification is implicit (telephone interviews). Indeed, sequences in their natural state lack novelty under the patent law in all three jurisdictions, and are therefore unpatentable subject matter (Gold, 2003). The specification of “synthetic” or “recombinant” does not confer a difference on the DNA molecule since production by a new process does not render a product novel (telephone interviews).

3.2 Differences affecting patent breadth

Section 4.2.1 presents some general trends in the differences in the breadth of patents based on a literal interpretation of the claims. To support the literal analysis of claims, these general trends are balanced

² <http://cbac-cccb.ca/epic/internet/incbac-cccb.nsf/fr/ah00403f.html>, Visited June 2005.

with a summary of the legal interpretation of the language used (Section 4.2.2). Finally, insights gleaned from interviews with experts in biotechnology patenting regarding the evolution of examination practice in the three patent offices are summarized in Section 4.2.3.

3.2.1 Literal interpretation of claim differences

Analysis of the 24 human gene patent families allowed identification of some general trends regarding differences in the breadth of patents granted by the CIPO, the EPO and the USPTO. The language used in U.S. patents is usually more restrictive than that in European and Canadian patents. As such, the protection afforded by U.S. patents is often narrower than that provided by European and Canadian patents, which are generally comparable in terms of their protection, although Canadian patents tend to be slightly broader in scope.

There are three main procedures that can result in patents of different scope between patent offices: voluntary amendments made by the applicant; restriction requirements imposed by the patent examiner; and formal rejections by the examiner based on patentability issues. The latter two procedures are the result of the examination process itself and generally reflect differences in the practices of the three patent offices.

When a patent application covers at least two independent or distinct inventions (e.g. diagnostic kit, pharmaceutical, antibody, DNA molecule, protein), the patent examiners in all three patent offices have the discretion to apply restriction requirements to limit the examination of a patent to a single invention. Following imposition of a restriction requirement, the applicant must decide which claims the invention (and, hence, the examination) will be restricted to. The remaining claim(s) can be made the subject of divisional applications, or simply abandoned. If only one patent office makes a restriction requirement on a PCT application and, the applicant decides to abandon some claims, the resulting patent will be narrower in scope than the patents derived from the same PCT application granted by the other two patent offices. The rules in all three patent offices state that a patent shall be granted for only one invention (Canadian Patent Act, EPC, and 35 U.S.C.). However, the use of restriction requirements to limit the scope of patents, irrespective of their field of invention, is more common in the USPTO (telephone interviews). Of the 24 patent families analyzed in the current study, 11 contain divisional patents in the USPTO, compared to only one in the EPO and none in the CIPO.

For many patent families where the scope of protection appeared more restrictive in the U.S., the U.S. patent derived from the PCT application lacked numerous of the claims included in the Canadian and European patents suggesting imposition of a restriction requirement by the U.S. examiner (see Sections B.1.1, B.1.2, B.1.3, B.1.5, B.1.10, B.2.1, B.2.3, B.2.7, B.2.10, and B.2.13). Using the search methodology developed for this study, and additional searches using keywords targeting the subject and authors of these inventions in the USPTO database, no divisional patents or pending divisional patents covering these missing claims were found for any of these patent families. It is unlikely that divisional patents could have been overlooked, unless they were filed prior to 2001 since before this date the

USPTO was not allowed to publish pending patents. As most U.S. patents resulting from international applications in the families studied were issued prior to 2001 (see Appendix A), this might have been the reason. However, this would imply that missed divisional patents would still be pending as of 2004, a less likely scenario considering the speed of examination in the U.S.

In these cases, it would appear that the applicants probably chose not to file divisional applications in the U.S. either because the U.S. was not the home market of the applicants (for 7 out of 10 of these patent families the PCT application originated from countries other than the U.S.) or because the applicants felt that the granted claims provided them with sufficient protection in the U.S. (telephone interviews). However, for most patent families it was not possible to completely rule out the possibility of divisional U.S. patents covering the details covered in the Canadian and European patents. If divisional U.S. patents did exist, then the U.S. patents would be less restrictive, although often still much more restrictive than corresponding Canadian and European patents.

On the other hand, the absence of some claims, in a U.S. patent for instance, might be the result of a rejection by the examiner based on patentability issues (novelty, non-obviousness, utility, disclosure) or a voluntary amendment by the applicant to add these claims to the PCT application for consideration by the Canadian and European examiners only. However, as applicants usually seek the same protection in all patent offices this latter hypothesis is unlikely.

Differences also exist in the formulation of claims. These differences cannot be the result of restriction requirements, but may very well be the result of rejections by examiners or voluntary amendments in only one or two of the three patent offices. Again the latter hypothesis is less likely, but cannot be ruled out (telephone interviews). Though, if this was to be the case, observed differences would not be a reflection of different practices in the patent offices.

One of the most significant differences in the formulation of claims can be seen in multiple patent families (see Sections B.1.5, B.1.10, and B.2.1) and relates to nucleic and amino acid sequences. For example, comparative analysis of the claims in patent family WO9709348 (see Section B.1.10) revealed that the PCT application was broader than any of the patents finally granted for amino acid and DNA sequences, which suggests action by all three patent offices to limit the breadth of cover originally applied for. However, the extent of limitation varies among patent offices. The most restrictive is the U.S. patent, which covers only sequences (DNA or amino acid) described within the body of the patent. The European patent is slightly less restrictive in covering, sequences with 89% or 95% identity (depending on the sequence in question) with the described sequences. The Canadian patent is the broadest claiming any sequences having substantially the same sequences as described within the patent. However, if the Canadian claim was to be invalidated by a court, a more restrictive dependent claim would apply, requiring that the sequence should share at least 95% identity with the described sequence.

Attorneys specialized in biotechnology patenting told Science-Metrix that the USPTO is now being “very picky” about what is described in the claims; in other words it requires that the invention should be commensurate with the scope of enablement provided by the application disclosure and that the

applicant should be in possession of the full scope of the claimed invention. They are disinclined to allow “reach through” claims of the type – “any sequence having some percent of identity with the described sequence” or “a functionally equivalent sequence” or “a sequence substantially the same as the described sequence”. In fact, U.S. examiners are unlikely to allow claims for mutants, derivatives, analogues, or homologues unless the applicant clearly describes each claimed variant in the disclosure, such that any one skilled in the art could replicate the invention commensurate with the scope of the claims being made, which is rarely the case (failure to meet the enablement requirement of 35 U.S.C. § 112). In addition:

Under 35 U.S.C. § 102(g), conception of a gene, it is not sufficient to define a gene solely by its principal biological property (e.g. biological function) because a conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Conception has not been achieved until reduction to practice has occurred, i.e. until after the gene has been isolated. (Pierce 2005, p. 446)

At best, the USPTO might allow a claim of the type “or any equivalent sequence by virtue of the degeneracy of the genetic code”. The opinion of an expert in biotechnology patenting, was that the CIPO is becoming closer to the U.S. in this regard, but is slightly more flexible on claimed DNA sequences (telephone interviews).

As mentioned previously, Canadian patents are, generally, the broadest; in 7 out of 24 patent families (see Sections B.1.5, B.1.6, B.1.10, B.2.3, B.2.4, B.2.9, and B.2.12). In all seven patent families, the Canadian patent was the most similar to the PCT application suggesting that the Canadian examiner had requested fewer changes than the European and U.S. examiners. Many experts in biotechnology patenting were surprised by this finding. Most agreed that, typically, applicants first file for a patent in the U.S., and then file a PCT application. Consequently, the claims are likely to be framed in a way that will make them acceptable in the U.S., and thus it would be assumed that U.S. patents would be more similar to the PCT application. In addition, one of the experts interviewed could not recall any occasion when he had not been requested by the examiner to amend the claims in the PCT application for the eventual Canadian patent. However, in only three out of seven patent families had the PCT application originated in the U.S., which is contrary to their expectations.

In one of the seven patent families, the PCT application had originated in Canada which could explain the similarity between the Canadian patent and the PCT application. One possible explanation for the other patent families could be that U.S. patents are often issued first (see Appendix A). In Canada, quite frequently, applicants modify their claims based on the already issued U.S. patent. Historically, this has been one way to advance the prosecution of Canadian patents because Canadian examiners like to see claims in conformity with U.S. claims (telephone interviews).

Another expert in biotechnology patenting suggested that Canadian examiners might not apply the requirement for unity of invention in the same way as U.S. and European examiners. According to this expert, applicants are often required to make some restrictions and limit their PCT applications to a

specific group of claims in the U.S. in particular, but also in Europe, whereas in Canada this is less usual. This hypothesis is supported by the present dataset (i.e. the 24 human gene patent families), which shows numerous divisional patents in the U.S., one divisional patent and a few pending divisional patents in Europe, and none in Canada.

Despite European and Canadian patents generally being broader in scope than U.S. patents, European and Canadian practices were in some instances stricter. Practices in the EPO appear to have led, in some instances, to claims that include more detail about the product and/or the method of the invention. According to a biotechnology patent attorney, this reflects a general tendency at the EPO:

The EPO has become very strict on what we would call a supporting disclosure. At the EPO, in order to achieve a very broad scope of protection you need to have a consistently broad supporting disclosure. If a method is described in the examples with a single set of specific conditions, the chances are that the EPO is not going to allow you to have a broad claim which applies your method generally. The rule is if you are claiming an invention as a broad range, you must have examples in the description that work across the whole range. You cannot only have one example at the one end of the range, and then extrapolate over the whole range. (telephone interview)

For example, in patent family WO9201053 (see Section B.1.4), the patents granted by the USPTO and the CIPO are almost identical, while claims 4 and 6 of the European patent differ significantly from their equivalents in Canada and the U.S. These claims in the EPO patent include specific and very detailed information, such as the name of the vector used, and the physicochemical properties of produced TCF-II (molecular weight, isoelectric point, protein stability, biological function description and the amino acid composition). This renders the European patent more restrictive. For instance, in the advent of a discovery by another group of a variant of the claimed TCF-II, a court might consider infringed Canadian and U.S. patents if this new protein had a similar function and high level of homology with the claimed protein. However, in the case of a European patent which specified the exact amino acid sequence and other characteristics of the claimed protein, a court might find that the new protein was not an infringement (telephone interviews).

Clearly, the more details that are included in a claim, the easier it is for a competitor to bypass the claim by modifying the invention (e.g. finding variants of a protein), but the easier it is for the applicant to prove infringement of the claim if the competitor exposes himself to liability. On the other hand, the less detailed the claim, the harder it is for a competitor to bypass it by modifying the invention, but the easier it is for him to invalidate the claim in court. Generally speaking, applicants seek claims that provide a good balance between the quality and the scope of protection. A practice often adopted by applicants to find a balance between quality of protection and scope of protection is to draft claims of different scope relating to the same matter, using one broad independent claim and additional dependent claims each adding details to the parent claim (telephone interviews). This allows the applicant to get a good scope of protection while ensuring that its preferred production method or “best mode” remains protected in the

case where its broad claim would be invalidated in court. However, in the above example, the European patent includes all the specifications in a single narrow claim.

Another strategy that is used by applicants when dealing with a gene-based or protein-based invention is to claim as many different aspects of the invention as possible, including DNA sequences, amino acid sequences, vectors, and host cells, even when these aspects have already been described in a related method claim. For example, in patent family WO9524480 (see Section B.1.9), the analysis revealed that the U.S. and Canadian patents were almost identical, while the European patent differed slightly. The three patents have one common claim (claim 4 in the European patent; claim 2 in the U.S. and Canadian patents) related to the method of producing recombinant FK506 binding protein. The claim specifies the use of an expression vector to transform a host cell and the recovery of the recombinant protein produced by culturing the transformant. In addition, the U.S. and Canadian patents have three more dependent claims (claims 3, 4 and 5) on components of the method claim, namely the expression vector, the host cell and the recombinant protein.

There are two main reasons for drafting patents in this way. First of all, product claims (e.g. vector, host cell, recombinant protein) usually provide better protection than method claims (e.g. production method of a recombinant protein) since it is easier to prove infringement of the former. For example, if a claim on a product exists, then any manufacture, use or sale of this product is illegal, and it is fairly easy for an applicant to prove that the composition of the product (e.g. a drug) is the same as that of the patented product. However, in the case that the claim applies only to the production method, it is difficult (without access to his laboratory or factory) to prove that a competitor is replicating each step of the process (telephone interviews). Secondly, it is important to have claims that cover each component of an invention in order to prevent competitors from performing steps along the whole chain of possible activities (telephone interviews). In the case that a patent holder tried to sue a competitor over production of the vector, for instance, a court would conclude that the U.S. and Canadian patents were being infringed, but not the European patent unless the DNA sequence itself (or the protein) were claimed. In this case, the DNA sequence encoding the protein was claimed in the European patent such that its breath is not seriously affected. Establishing multiple claims relating to the same matter is also useful in the case that one of the claims, for example the method claim, is invalidated in court. An applicant in Canada and the U.S. could still rely upon the remaining claims to protect the invention in these countries, but not in Europe.

The main aspect on which Canadian practice is more stringent leading to claims of reduced scope in comparison to U.S. and European patents, pertains to protection of transgenic animals. In 2002, the Supreme Court of Canada determined that a transgenic mouse, with cells genetically altered by a cancer-promoting gene (oncogene), was not patentable subject matter in Canada.³ An attorney specialized in biotechnology patenting told us in interview that:

³ <http://www.cba.org/CBA/newsletters/ip-2003/ip2.aspx>, Visited June 2005.

The question in Canada is now about what the scope and language of your claims are going to be so that you have some form of equivalent protection to the transgenic animal complementary to what you could get in the U.S. and Europe where transgenic animals are patentable. For example, someone could seek protection for a modified cell. The issue is then going to be the position of the CIPO on what such a claim actually cover. Is it just the cell or will it include the cell as it may exist in the tissue of the transgenic animal. If it is just the isolated cell it is limiting, whereas if it includes the cell as it may exist in the transgenic animal, it provides an equivalent protection provided someone who would manufacture, use or sell the transgenic animal would expose himself to liability. (telephone interviews)

The same year the Supreme Court of Canada announced its decision in the Harvard Mouse case, a PCT application with a claim pertaining to a transgenic animal with induced cystic fibrosis led to a patent being granted in Canada (Section B.2.3). The claim on the transgenic animal had been reformulated in the Canadian patent to include a heterologous cell system in which cystic fibrosis has been induced by incorporating the recombinant cloning vector into the cells, while the European patent included a claim on the transgenic animal itself. Although in this case, the Canadian claim is more restrictive given the claim does not include the cell as it may exist in the transgenic animal, the number of similar cases is not sufficient to be able to clearly establish where CIPO practice is heading in this area (telephone interviews). In fact, in a patent issued in 2004 (CA2219629), protection for a transgenic non-human mammalian cell (i.e. a murine cell) comprising human DNA, and a method comprising the step of generating the transgenic non-human mammal was granted by the CIPO.

The EPO is unique in including a clause on morality that forbids the granting of patents that threaten “ordre public” and hinder scientific progress. For example, the EPO initially granted the Harvard mouse patent for a transgenic animal, as in the U.S. patent. However, it was challenged on the grounds that it was contrary to the provision on morality and the wording of the patent was changed to read “a rodent” instead of “an animal”. More recently, there was a further challenge and the claim was revised again to restrain the rodent to a mouse. Thus, in Europe there is a somewhat unpredictable morality restriction that can lead to narrower patents than those issued by the Canadian and U.S. patent offices (Cyranski, 2004; telephone interviews).

3.2.2 Legal interpretation of claim differences

In order to establish the real impact of the differences in the breadth of patents granted by the CIPO, the EPO and the USPTO resulting from the same PCT application, it is essential to understand how these differences are likely to be interpreted from a legal perspective in each of the three jurisdictions.

The rules of interpretation of patent claims vary in the three countries. In the U.S., the court analyzes a patent on a claim-by-claim basis and interprets each claim by analyzing each of its constituent components independently. If there has been a literal infringement on all components, the new invention is deemed to infringe the claim. An infringement of a single claim is judged to be an infringement of the

patent (Wagner, 2005). Furthermore, U.S. patents can be interpreted under the doctrine of equivalents which originates from a U.S. Supreme Court opinion enunciated in *Graver Tank and Mfg. Co.*, 1950).

This doctrine is also applied in Japan and China and gives a little more flexibility in the interpretation of the language of claims (Wagner, 2005). The court decides a literal interpretation of each component in a claim and then examines whether the invention under investigation accomplishes substantially the same function in substantially the same way to obtain substantially the same result as the prior art (CIPP, 2005; Wagner, 2005). If it does for all components, the invention is judged to infringe the claim. Therefore, an invention that might appear to be different from a literal perspective could be judged to infringe the patent on prior art. However, the doctrine of equivalents only applies where the applicant was not forced to abandon a broader claim in the patent prosecution process.

Patents are also analyzed on a claim-by-claim basis in Canada, but they are not broken down into their constituent components and are interpreted by applying the concept of purposive construction (CIPP, 2005). This concept was laid down by Lord Diplock and applied for the first time in Canada in 1989 in the *O'Hara* case (Sotiriadis, 1996). The notion of purposive construction rests on the court reading the claims through the eyes of a skilled person, with that person's understanding in the context of the invention described as a whole in the patent application. Nevertheless, the courts will limit the scope of the invention to the language used in the claims, but if some specifications restrict the scope and do not appear in the opinion of the skilled person to be essential for performance of the invention, these specifications will not be considered by the court (Sotiriadis, 1996).

In Europe, the situation is more complex given that member states apply different national laws and interpret claims differently. For example, in France and Germany, claims are interpreted under the concept of sympathetic construction. The court is sympathetic to the inventor and interprets patent claims in order to confer on the inventor what has actually been invented. In contrast to the doctrine of equivalents and the concept of purposive construction, this legal interpretation is not based on a strict reading of the claims (CIPP, 2005). Since the UK applies the concept of purposive construction, a court in Germany or France is more likely to find infringement of a patent than a court in the UK even though all these courts would have considered the same claim wording.

Generally speaking, the rules of interpretation are stricter in Canada and the UK followed by the U.S., and then Germany and France. Thus, the legal interpretation of claims in the different jurisdictions might balance out literal differences in scope. Canadian patents are the broadest, but their legal interpretation is the most severe. U.S. patents are the narrowest, but their interpretation is more flexible. European patents fall in the middle in terms of breadth, and their interpretation varies from being strict to being accommodating. However, European patents are also liable to be subjected to the EPO's clause on morality.

3.2.3 Temporal differences in the practices of patent offices

From a temporal perspective, the practices of patent offices with respect to examination of biotechnology-based patent applications, including human gene inventions, have gradually evolved to become more stringent:

As with any newly developing technology, the patent examination practice in biotechnology evolves over time. As the technology matures, the office must continually evaluate the state of the art and the effects the state of the art has on examination decisions. Revision of examination guidelines, coupled with the ever-changing state of the art, will naturally result in modification of examination practice. (telephone interviews)

The patent law, our understanding of biology, and our understanding of what the patent office is going to be able to do changes over the years. Therefore, it is hard to imagine that the answer to the question “Did the practices of patent offices change over time regarding patenting of human genes?” could be anything but yes. (telephone interviews)

The practice of patent offices has changed over time, and in particular in the USPTO. This has an impact in Canada since it influences the way we (patent attorneys) view and draft patent applications. (telephone interviews)

In the early days of biotechnology patenting (i.e. the early 1990s), examination guidelines were less strict and examiners were granting overly broad claims (telephone interviews). As biotechnology matured, and with the advent of automated sequencing and the Human Genome Project, it has become routine to isolate and sequence DNA. Patenting requirements have become correspondingly more stringent. The European Union Directive 98/44/EC on the Legal Protection of Biotechnological Inventions, implemented by the EPO in 1999 and applicable to all EU states from 2000, introduced some specific requirements for the granting of patents for human gene sequences. Whereas in the past the isolation of a gene sequence was often difficult and involved inventive skills, this is rarely the case today. At the EPO, in order for it to be patentable, a non-obvious function or activity over the prior art normally has to be established for the DNA or the protein it encodes. This must have been elucidated by the applicant by the filing date, although additional supporting data may be filed later (telephone interviews). Similarly in the U.S., it has become more and more difficult to establish claims on DNA sequences for which the function of the claimed gene had not been recognized or has been recognized based on homology searches (i.e. without being tested and confirmed). The examining practice of the EPO, the USPTO and the JPO (Japanese Patent Office) regarding the patenting of nucleic acid molecule whose functions are inferred based on homology searches are described in a Trilateral Study (Trilateral Project, 2000).

However, it appears that the EPO is the most severe in applying the non-obviousness patentability criteria for DNA sequences, and the USPTO the least strict (CIPP, 2005). The EPO is more likely than the USPTO to reject a claim on a gene, for example a human gene encoding insulin, if another gene

(prior art) with similar functions has been recognized, for example a swine gene encoding insulin, on the basis that it takes no inventive steps to isolate another gene (i.e. a homologue) with similar characteristics (telephone interviews). In fact, very minor nucleotide changes are now patentable in the U.S. (telephone interviews).

On the other hand, since the release of guidelines on utility and written description in 2001, the USPTO has increased its requirements regarding enablement and utility patentability criteria, and is the strictest of all patent offices in this respect (CIPP, 2005; telephone interviews). This has resulted in the USPTO being less inclined to give a broad scope of protection, particularly for claims relating to mutants, derivatives, analogues and homologues of described DNA sequences. Nowadays, U.S. examiners want to insure that what is claimed has industrial applicability and that the description in the disclosure is adequate to allow one skilled in the art to perform the invention over its entire scope (telephone interviews).

Thus, whereas U.S. examiners are unwilling to grant reach-through claims to cover mutants, derivatives, analogues and homologues of described DNA sequences, they allow patenting of such variants over the prior art. In Europe, the reverse holds, and in Canada, CIPO examiners are starting to be stricter, emulating the U.S. examiners (telephone interviews).

4 Conclusion

The present study aims to evaluate whether existing differences among the practices of the CIPO, the USPTO, and the EPO lead to human gene patents of varying scope. To achieve this objective, a comparative analysis of the claims in human genes patents granted by the three patent offices based on the same application filed under the PCT was conducted.

In summary, differences observed between human gene patents granted by the CIPO, the EPO and the USPTO can be classified in two categories. The first category includes differences in the claim language that do not affect patent breadth such as differences related to the protection of “methods of medical treatment” (see Section 3.1). The second category consists in differences that affect patent breadth. In order to conclude on the impact of these differences on the scope of protection provided by patents, they must be interpreted from both a literal and legal perspective (see Section 3.2).

Overall, the literal interpretation of observed differences in the claims granted by the three patent offices suggests that U.S. patents are usually more restrictive than Canadian and European patents, which are generally comparable in terms of their protection, although Canadian patents tend to be slightly broader in scope.

For many patent families where the scope of protection appeared more restrictive in the U.S., the U.S. patent derived from the PCT application lacked numerous of the claims included in the Canadian and European patents suggesting imposition of a restriction requirement by the U.S. examiner. No divisional patents or pending divisional patents covering these missing claims were found for any of these patent families. In these cases, it would appear that the applicants probably chose not to file divisional applications in the U.S. However, for most patent families it was not possible to completely rule out the possibility of divisional U.S. patents covering the details covered in the Canadian and European patents. If divisional U.S. patents did exist, then the U.S. patents would be less restrictive, although often still much more restrictive than corresponding Canadian and European patents.

On the other hand, the absence of some claims, in a U.S. patent for instance, might be the result of a rejection by the examiner based on patentability issues (novelty, non-obviousness, utility, disclosure) or a voluntary amendment by the applicant to add these claims to the PCT application for consideration by the Canadian and European examiners only. However, as applicants usually seek the same protection in all patent offices this latter hypothesis is unlikely.

Differences also exist in the formulation of claims. These differences cannot be the result of restriction requirements, but may very well be the result of rejections by examiners or voluntary amendments in only one or two of the three patent offices. Again the latter hypothesis is less likely, but cannot be ruled out. Though, if this was to be the case, observed differences would not be a reflection of different practices in the patent offices.

In general, U.S. examiners appear to be stricter regarding claims on nucleic and amino acid sequences, being more reluctant than Canadian and European examiners to issue “reach-through” claims for mutants, derivatives, analogues, and homologues of the claimed sequences. However, an expert in biotechnology patenting pointed out that Canadian examiners are becoming more and more like their peers in the U.S. in this respect.

Often, Canadian patents are the broadest, and in these cases they are the most similar to the PCT application suggesting Canadian examiners had requested fewer changes than the U.S. and European examiners. This could perhaps be explained by the fact that restriction requirements to limit the examination of an application to a single invention, which result in the abandonment of claims or in divisional patents, are far more common in the U.S. and Europe than in Canada. However, this finding must be interpreted with caution since the sample size of the present study is small (i.e. 24 human gene patent families). In addition, many experts in biotechnology patenting were surprised by this finding; one of them could not recall any occasion when he had not been requested by the examiner to amend the claims in the PCT application for the eventual Canadian patent.

In some instances, European or Canadian examiners were the most stringent, issuing the narrowest claims. European claims sometimes provide more specifications of a method or the characteristics of a protein (e.g. molecular weight, isoelectric point), thereby reducing their breadth. In some areas Canadian practices are the most restrictive, for instance, claiming of transgenic animals, which is allowed by the USPTO and the EPO, is forbidden in Canada.

The legal interpretation of claims, which varies from one country to another, also has an impact on patent scope. In Canada, where the concept of purposive construction prevails, claims are interpreted more stringently than in the U.S. where the doctrine of equivalents provides a little more flexibility to the claim language, buffering literal differences in patent scope. In Europe, the situation is more complex as each member state applies its own national laws. For example, practices in the UK, which applies the concept of purposive construction, are stricter than in France and Germany, which apply the concept of sympathetic construction which gives the most flexible interpretation of claims. However, unique to the EPO is the morality or “ordre public” clause, which can radically reduce the scope of a patent.

Finally, according to experts in biotechnology patenting, as the field of biotechnology has matured, patent offices have become much stricter with regard to the application of patentability criteria. The USPTO in 2001 published new guidelines with respect to utility and written description and U.S. examiners are nowadays the most likely to reject applications on the grounds of utility and enablement criteria. In 1999, the EPO implemented the European Union Directive on the Legal Protection of Biotechnological Inventions and European examiners are now the strictest over non-obviousness. In Canada, examiners are becoming stricter, and their practices are becoming more and more similar to that of U.S. examiners.

The present study highlights some trends in the evolution of patent office practice regarding the patenting of human genes. However, these trends are based only on insights gleaned from telephone

interviews with experts in biotechnology patenting. It would be very interesting to conduct a study that examined the differences in the scope of human gene patents granted over different periods of time to test the hypothesis that the scope of patents granted in a particular field narrows as the field matures. It was not possible to prove or discount this in the current study due to the small size of the population of PCT applications on human genes that actually led to a granted patent in the CIPO, the USPTO, and the EPO. Also, not enough patents that were granted in the early years of biotechnology (i.e. in the early 1990s) were included in the analysis. A future study should analyse the human gene patents from a single database, for example the USPTO, in order to get a sufficiently large sample size to adequately cover different periods of time.

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Appendix A - Sample of human gene patent families

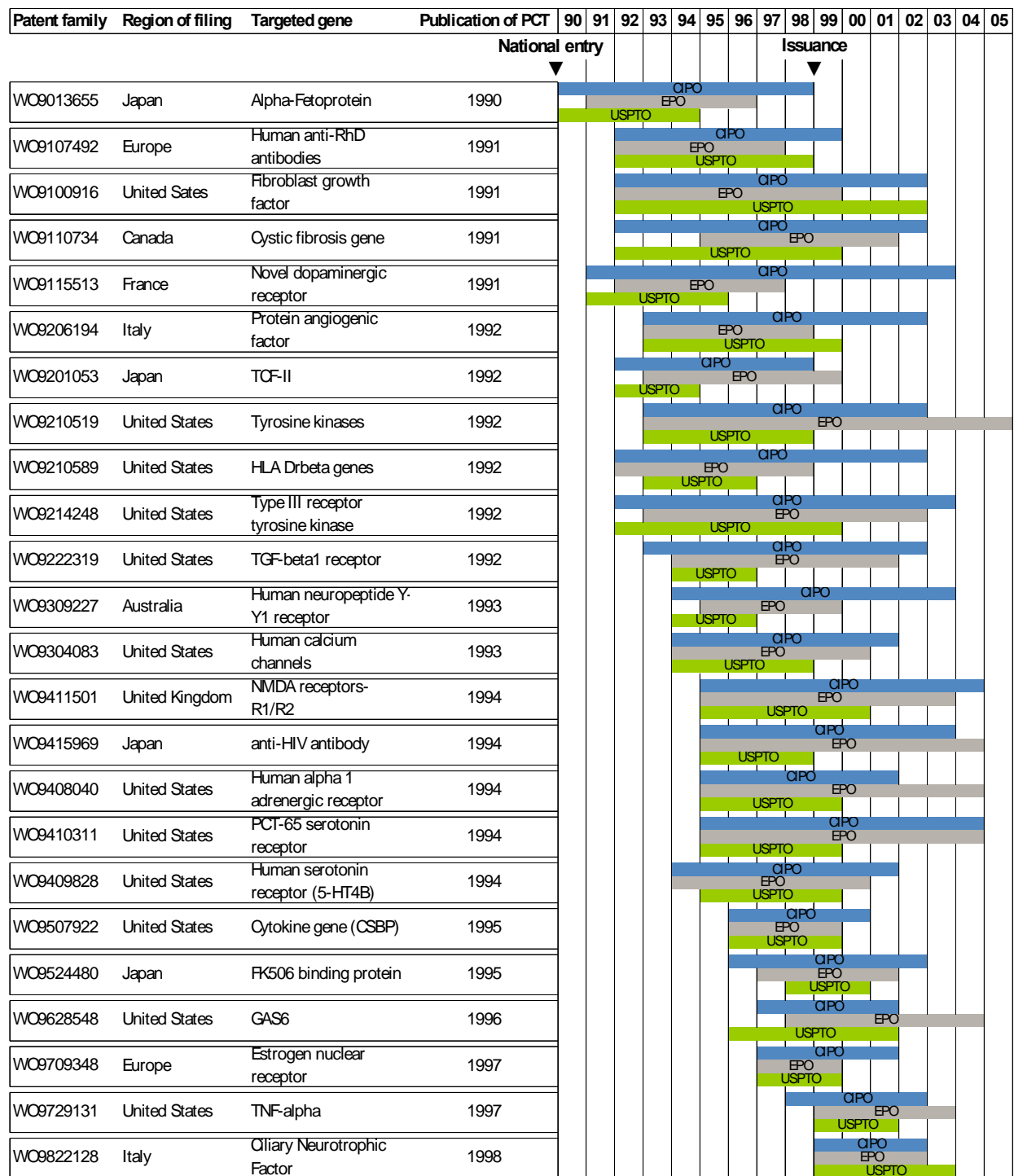


Figure 1 Selected human gene patent families for comparison of the breadth of claims among patent offices

Source: Compiled by Science-Metrix

Appendix B - Patent analysis

This section provides a comparative analysis of the breadth of patent claims granted by the CIPO, the USPTO and the EPO for 24 human gene patent families. As already mentioned, divisional, continuation and/or CIP applications are more common in the U.S. such that a Canadian or European patent may be fragmented into multiple patents in the U.S. Fragmentation makes it more difficult to compare claims among patent offices with confidence; therefore, patent families where this has occurred (see Section B.2) will be treated separately from patent families in which there is a single patent in each patent office (see Section B.1).

B.1 Simple cases: a single patent in each patent office

Section B.1 presents patent families in which the international application was not subjected to divisional, continuation and/or CIP procedures at the national phase in any of the three patent offices. Thus, these patent families include a single patent from each patent office, allowing direct comparison of claims between Canadian, European and U.S. patents (Figure 2). Most international applications within these families originated from countries other than the U.S. (10 out of 11 families).

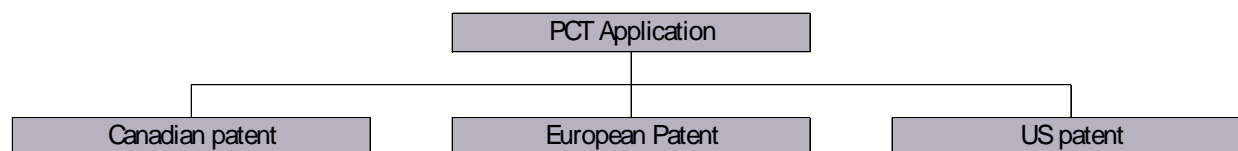


Figure 2 Phylogeny of a simple patent family where no divisional, continuation and/or continuation-in-part procedures led to fragmentation of patents at the national level

Source: Science-Metrix

B.1.1 Patent WO9013655: Protein binding the α -fetoprotein gene

This invention relates to DNA coding for a protein which specifically binds to the enhancer of α -fetoprotein gene, promoting the gene transcription. Since the protein is involved in transcription, this DNA could be used for the creation of a highly efficient gene expression system using animal cells. The PCT application was filed in Japan (JP9000557) and led to a single patent in all three patent offices (CA2032167/EP427863/US5302698).

In this patent family, the U.S. patent shows striking differences from the Canadian and European patents, which are identical. The US patent has three claims protecting only the sequence of the protein. Although the equivalent patents from the CIPO and EPO include claims for sequence of the protein, they are broader in scope and include claims on the methodology which is described in great detail. These additional claims list and explain all the steps involved in the process, and provide the name and a description of the cell line, of the vector and of restriction enzymes used in the process. If all these

details are included in a single independent claim, this narrows the breadth of the patent. Nevertheless, an applicant might want to include these details because this may be its preferred production method (telephone interviews). In addition, such specifications often accompany one broad independent claim in the form of dependent claims each giving details additional to the parent claim, thereby reducing the impact on the breadth of the patent. This is the approach used by the applicant in drafting the Canadian and European patents.

Given that the Canadian and European patents both cover the same matter as the US patent, namely the sequence of the protein, but that supplementary claims in the Canadian and European patents provide protection for items not covered by the US patent, namely the methods and tools of the present invention, the scope of the Canadian and European patents is broader.

This conclusion is based on the fact that the three patents originated from the same international application and are thus homologues. However, the significant dissimilarities observed in the US patent suggest that the PCT application might have been subjected to a restriction requirement in the US national phase. If so, it could be that the applicant filed a divisional application to cover the matter missing from the granted patent. Using the search methodology developed for this study and an additional search using keywords targeting the subject and authors of the present invention in the USPTO database, no divisional patent nor pending patent were found. It is unlikely that a divisional patent could have been overlooked, unless it was filed prior to 2001 since the USPTO was not allowed to publish pending patents prior to this date. Given that the US patent was issued in 1994, this is very unlikely. It could simply be that the applicant chose not to file a divisional application in the US because it was not his home market and he felt that the granted claims provided him sufficient protection. However, it is not possible to rule out the possibility of a second US patent covering the details covered in the Canadian and European patents.

On the other hand, the absence of method claims in the US patent might be the result of a rejection by the US examiner based on patentability issues (disclosure not supporting method claims, lack of inventive steps, etc.) or of voluntary amendments by the applicant upon entry in the national phase in Canada and Europe to add these claims to the PCT application. Given the absence of a rationale to justify such amendments, this hypothesis is very unlikely. However, it cannot be completely discounted because the PCT application being written in Japanese meant that it was impossible for us to determine whether the supplementary matter in the Canadian and European patents was included in the international application.

Regardless which of these hypotheses is true, differences between the US patent and the Canadian and European patents do exist. They render the US patent more restrictive, and mean that the European and Canadian patents provide better protection to the applicant. However, this situation might be balanced by the existence of a divisional US patent. In this case, the observed differences might disappear and make this statement invalid.

B.1.2 Patent family WO9115513: Polypeptides having a dopaminergic receptor activity

The invention in question is directed to novel polypeptides having dopaminergic receptor activity and nucleic acid sequences encoding these novel polypeptides. The novel polypeptides can be used as drugs, and in the screening of drugs that affect dopaminergic receptors. The PCT application was filed in France in 1991 and led to a patent in the US (US5407823), in Europe (EP474846), and in Canada (CA2060325). A divisional application of EP474846 was filed in Europe (EP783037). However, this application has only two claims, and even if they were granted, the scope of the European patent would not be affected. Thus, the current analysis will ignore this application.

Within this patent family, there is a considerable variation in the number of claims among patent offices. The PCT application has 24 claims, the US patent has 12 claims, the European patent has 22 claims and the Canadian patent has 40 claims. Thus, not all patents cover the same extent of matter. The most striking difference is that the US patent lacks claims pertaining to antibodies for the novel polypeptides, to processes for detecting ligands of the novel polypeptides and studying its affinity with the said ligands, to diagnostic methods for detection of genetic anomalies, of punctual mutations and of pathologic expression of the novel polypeptides, and to a medicament comprising an active substance over the novel polypeptides. The Canadian patent also lacks the medicament claim.

When a patent application covers such a wide array of applications (e.g. diagnostic kit, medicament, antibody, DNA molecule, protein), USPTO examiners often use restriction requirements on the basis of lack of unity of invention to reduce the scope of the patent. This most likely occurred in this case. However, the applicant has not made asserted his right to file divisional applications to protect these missing components in the US, unless divisional patents or pending applications would have been missed in our searches. One possible explanation for this is that since the US is not the home market of the applicant, he felt it was not worth the additional effort of protecting all aspects of his invention in the US given the degree of protection provided by the granted claims. These claims cover the polypeptides and DNA sequences encoding of the proteins, which are the foundations for all remaining claims. An alternative explanation would be that the US examiner, after revising the application, considered that the invention was not sufficiently disclosed over the entire scope of the claims, and therefore did not grant claims pertaining to those aspects lacking demonstration.

All three patents cover the novel polypeptides, the DNA sequences encoding these polypeptides, recombinant vectors comprising any of the DNA molecules described, host cells transformed with the recombinant vectors, and nucleotide probes derived from claimed DNA molecules. The Canadian and European patents, as in the PCT application, claim two polypeptides as having the amino acid sequences described in the patent, or a fragment of any of these sequences such that when exposed to the surface of a cell: they can link dopamine to its agonists and antagonists, it can be recognized by antibodies that also recognize the claimed sequences, but not by antibodies for dopaminergic receptors D-1 and D-2, and it can be used to produce specific antibodies recognizing the claimed sequences, but not the dopaminergic

receptors D-1 and D-2. The US patent claims the same two amino acid sequences. However, it does not claim the fragment of any of these amino acid sequences based on its recognition by antibodies since the claims on antibodies are not included in the US patent. Instead, the patent claims any polypeptide whose corresponding nucleic acid molecule hybridizes to a probe complementary to the DNA sequences encoding the two amino acid sequences described in the patent. This difference may or may not have an impact on the breadth of the patent depending on the specificity of the recognition by the antibodies and of the hybridization with selected DNA probes.

In addition, the US patent specifies that the polypeptides and DNA molecules must be isolated while the Canadian and European patents do not include any restriction regarding the source of the claimed polypeptides and DNA molecules. However, this does not render the US patent stricter since all sequences are implicitly considered to be isolated from their natural sources by the CIPO and EPO (telephone interviews). Indeed, sequences in their natural sources lack novelty under the patent law in each jurisdiction considered, and are therefore unpatentable (Gold, 2003).

The first 22 claims of the Canadian patent are almost identical to the 22 claims of the European patent, although the claims of the European patent are slightly more detailed methodologically and include type of recombinant vectors, and host cells used. In this particular case, it appears that the Canadian examiner who issued the patent in 2003 made decisions based on the European patent, which was granted in 1997. Indeed, the Canadian patent includes the methodological details in the European claims, in the form of additional dependent claims, which accounts for the Canadian patent having 18 more claims than the European patent.

For this family, the examination appears to have been stricter in the US, but the main reductions in the scope of the patent might be due to a restriction requirement or to the claims not meeting patentability requirements (novelty, non-obviousness, utility, and disclosure) rather than to practices specific to gene patents. The Canadian patent, in this case, is more restrictive than the European patent, the claim pertaining to the medicament being absent from the former. Given that the US patent was issued first, in 1995, it is unlikely that the observed differences are the result of the differences in timing. Although the Canadian and European patents were issued, respectively, eight and two years after the US patent, the European is the broadest of the three while it is generally recognized that the examination process of patent offices became more restrictive over time (telephone interviews).

B.1.3 Patent WO9206194: Human protein with angiogenesis properties

This invention relates to nucleotide sequence coding for a human protein with angiogenesis regulative properties. This patent family also refers to vectors containing this sequence, to molecular characterization of the gene and to the production of corresponding polyclonal and/or monoclonal antibodies. The PCT application was filed in Italy in 1991 and led to a single patent in all three patent offices (CA2092533/EP550519/US5919899).

Surprisingly, the US patent only has one claim on the sequence of the protein and its function as an angiogenic factor, while the Canadian and European patents each have 45 claims, which differ only slightly. Similarly, the international application covers the matter in the Canadian and European patents with 51 claims, which suggests that the US patent examiner drastically eliminated claims from the PCT application during the examination process. However, the huge differences between the US patent and those granted by the CIPO and the EPO indicate the possible existence of divisional US patents covering the matter originally included in the PCT application. To explore this hypothesis, additional searches in the USPTO database were performed using keywords related to this invention, the applicant's name and the inventors' names. An environmental scan was also conducted on the applicant's portfolio. These additional searches did not lead to the identification of related patents either issued or pending. Perhaps the applicant did not choose to protect the matter covered by the removed claims in the US given that it was not its home market. In addition, the applicant, the Italian National Research Council, is a government organization, and compared with large biotechnological firms such organizations often do not have the budget to maintain multiple patents for a single invention.

An alternative explanation could be that the US examiner withdrew 50 out of the 51 claims in the PCT application on the grounds of patentability. However, given that most of these claims were not found to be unpatentable in Canada and Europe, this is unlikely. No matter which of these hypotheses is true, the scope of the US patent has been significantly narrowed in comparison to the Canadian and European patents.

Although the claims of the patents granted by the EPO and the CIPO were overall very similar, slight differences that affect patent breadth were observed in claims 6, 16 and 27. For these claims, the European patent specifies that one or more amino acids have been substituted without affecting the angiogenic activity of the protein, whereas the Canadian patent specifies that up to 22% of amino acids were deleted from amino acids 1 to 31 without affecting the angiogenic activity of the protein. In the PCT application, there are four corresponding claims for each of claims 6, 16 and 27 of the Canadian and European patents, and these provide protections for mutants that alter angiogenic activity rather than retaining the angiogenic activity of the claimed protein. Thus, both the Canadian and European examiners limited the breadth of the claims in the original international application, but in different ways.

It is somewhat surprising that the Canadian and European patents do not claim the same types of mutations. The Canadian patent claims deletions, while the European patent claims substitutions. This difference has a significant impact since these mutations do not have the same effect on a sequence. A deletion involves the elimination of an amino acid producing a shorter sequence, whereas a substitution consists of the replacement of one amino acid by another, the sequence remaining the same length. Since both types of mutations were claimed in the PCT, it is difficult to understand why two examiners from different countries did not retain the same type of mutations or both types of mutations. Nevertheless, the European patent is broader since it does not limit the invention; it protects amino acid modifications at any position regardless of their number.

Thus, the US patent is the most restrictive of the three followed by the Canadian patent.

B.1.4 Patent WO9201053: Production of active TCF-II

The present patent family provides a plasmid containing DNA encoding the amino acid sequence of a novel glycoprotein derived from human fibroblasts designated as TCF-II. The cells transformed with the plasmid and a production method for a biologically active substance using the transformed cells was also claimed. According to the inventors, TCF-II could be used in pharmaceutical products such as a hepatocyte growth factor, a tumor cytotoxic factor, and a biochemical or pharmacological reagent. The PCT application was filed in Japan in 1991 and led to a single patent in the CIPO, the EPO and the USPTO (CA2066618/EP539590/US5328836).

The patents granted by the USPTO and the CIPO are almost identical. The European patent has some differences, the most important being in claims 4 and 6. These claims in the EPO patent include specific and very detailed information such as the name of the vector used and the physicochemical properties of produced TCF-II (molecular weight, isoelectric point, protein stability (pH and temperature), biological function description (growth inhibitor and cytotoxicity effect) and the amino acid composition). This makes the European patent more restrictive. For instance, in the advent of the discovery, by another group, of a variant of the claimed TCF-II, the court might consider that this infringed Canadian and US patents if the new protein had a similar function and high level of homology with the claimed protein. However, since the European patent specifies the exact amino acid sequence and other characteristics of the claimed protein, a court might find that the new protein would not be an infringement.

Clearly, the more details that are included in a claim, the easier it is for a competitor to bypass the claim by modifying the invention (e.g. finding variants of a protein), but the easier it is for the applicant to prove infringement of the claim if the competitor exposes himself to liability. On the other hand, the less detailed the claim, the harder it is for a competitor to bypass it by modifying the invention, but the easier it is for him to invalidate the claim in court. Generally speaking, applicants seek claims that provide a good balance between the quality and the scope of protection. A practice often adopted by applicants to combine quality of protection with scope of protection is to draft claims of different scope relating to the same matter, using one broad independent claim and additional dependent claims each adding details to the parent claim (telephone interviews). However, in this case the European patent includes all the specifications in a single narrow claim.

Since the PCT application was written in Japanese, it was impossible for us to determine if the specifications in the European patent were an addition requested by the European examiner or if they had been part of the international application and had been excluded by the Canadian and US examiners. However, based on the view provided by the analysis of the 24 patent families, the former hypothesis appears more likely as European patents tend to provide more details in their claims.

For this patent family, the European patent is narrower than the Canadian and US patents, which are similar in the scope of their protection.

B.1.5 Patent family WO9309227: Human neuropeptide Y-Y1 receptor

The invention relates to a cDNA sequence and a genomic DNA sequence, which encode the human neuropeptide Y-Y1 receptor. These DNA sequences can be used to express the NPY-Y1 receptor in cells and can be used to screen compounds for neuropeptide Y agonist and antagonist activity. The PCT application was filed in Australia in 1992 and led to a single patent in all three patent offices (US5571695/CA2123108/EP668910).

The PCT application and the Canadian patent each count 13 claims, the European patent counts 12 claims and the US patent counts 10 claims. The first and second claims of all the patents and the PCT application apply to the cDNA molecule and the genomic DNA molecule encoding the receptor. These two claims in the PCT application are broader than in the three patents protecting a DNA molecule having a sequence substantially the same as the sequence described for each molecule, or a functionally equivalent sequence. In the Canadian patent, the phrase “or a functionally equivalent sequence” was removed from both claims, whereas in the European patent the phrase “a sequence substantially the same as” was removed from both claims. In the US patent, both phrases were removed. Usually, a sequence functionally equivalent to another sequence is a more restrictive wording than a sequence substantially the same as another sequence. For example, a DNA sequence having a mutation at a single nucleotide will be considered substantially the same, but may well code a protein with a different function, whereas a sequence coding a protein with an equivalent function is more likely than not to be substantially the same as the claimed sequence. Thus, the USPTO examiner was the most severe in this case followed by the EPO, and then the CIPO.

The US patent also lacks four claims pertaining to a method of screening compounds for NPY agonist or antagonist activity. This can either be explained by the decision of the US examiner to reject those claims, or by a restriction requirement imposed by the examiner to split the patent. Even though no divisional patent was found, a pending patent might have been overloaded; thus it is not possible to rule out this later hypothesis. The Canadian patent is the only one in which the claim on the neuropeptide Y-Y1 receptor was in a substantially pure form from the PCT application.

Overall, it can be concluded that the Canadian patent is the broadest of the three followed by the European and the US. The Canadian patent is the most similar to the PCT application. The differences in the breadth of these patents are not likely to be due to issue dates which vary from 1996 for the US, 1999 for Europe, and 2003 for Canada. If differences had been due to changes in patent office practices between 1996 and 2003, then it would be expected that the US patent would be the broadest followed by the Canadian and then the European patents. It can therefore be fairly safely assumed that it was different practices among patent offices that produced these differences.

B.1.6 Patent family WO9411501: Human NMDA receptor

The patent family in question concerns a transfected cell line that expresses a human NMDA receptor. The cell line can be used to design and develop NMDA receptor subtype-selective compounds for use as

therapeutic agents. The PCT application was filed in the UK in 1993 and led to a single patent in all three patent offices (US6130058/CA2148599/EP672140).

All three patents present some variation from the international application, with the Canadian patent being the closest to it. The PCT application counts 17 claims, the Canadian patent 15, the European patent 7 and the US patent only 4 claims. The basis of these patents is the transfected cell line capable of expressing an NMDA receptor. The Canadian patent specifies that the cell line is a eukaryotic cell line in the first claim and that the NMDA receptor to be expressed is of human origin in a second dependent claim, while both these statements are fused in a single claim in the European patent, thereby reducing its scope to the human receptor. The US claim relating to the recombinant cell line is broader than the corresponding Canadian and European claims regarding the type of cell line used for expression of the receptor, but stricter regarding the DNA sequences used in the transfection. Indeed, the US claim allows the use of any cell line, but limits the set of DNA molecules to transform the host cell to those encoding claimed human NMDA receptor subunit isoforms (R1a, R1d, R1e and R2A) while the broadest claim of the European and Canadian patents allows transformation with any R1 and/or R2 subunit isoform. The US patent restriction on DNA sequences is more significant than that imposed by the Canadian and European patents which can therefore be considered broader.

The three patents claim an expression vector. The European claim is of the same breadth as in the PCT application and covers an expression vector comprising any human NMDA R1 and/or R2 subunit isoform. The Canadian and US claims are stricter being limited to an expression vector comprising any of the claimed human NMDA receptor subunit isoforms (R1a, R1d, R1e and R2A).

The Canadian and European patents both claim a process for the preparation of the transfected cell line. The Canadian patent describes the process and specifies the cell line to be used in a single claim, whereas the European patent specifies the cell line in a second dependent claim. In addition, the cell line specified in the Canadian patent, a mouse Ltk⁻ host cell, is more precise than that specified in the European patent, a rodent fibroblast cell. Thus, with respect to the process, the European patent is broader than the Canadian patent, and the scope of the US patent is reduced since the process is not claimed.

Regarding DNA sequences, the Canadian and US patents claim the same NMDA receptor subunit isoforms (R1a, R1d, R1e, and R2A), while the European patent has no claims pertaining to the DNA molecules. This is a significant restriction in the European patent since claims on DNA molecules usually provide a backup protection for any other claim that might be invalidated in court. Indeed, DNA molecules are the basis of any claims in a gene-based patent. In this case, the scope of the European patent is clearly limited since in the absence of protection over the DNA sequences themselves, a receptor could be produced in a different cell line to the one claimed (e.g. a prokaryotic cell line) without infringing the patent.

The European patent also lacks claims covering the recombinant NMDA receptor subunits, which the Canadian and US patents include. This again is a significant difference since in order to demonstrate

infringement or the European patent, the applicant would have to prove that an individual in possession of a recombinant receptor subunit had produced it using the claimed transfected cell lines.

Finally, both the Canadian and European patents claim the use of the transfected cell line for screening and designing medicaments which act upon the human NMDA receptor. The fact that this is absent from the US patent limits the rights of the applicant in the US on a drug that eventually might be discovered using the claimed cell line. The absence of this claim in the US patent might be due to a restriction requirement imposed by the examiner, in which case the claim might be covered by a divisional U.S. patent that was missed because it was pending.

Globally, the Canadian patent appears to be the broadest followed by the US, and then the European patent. The reduction in the breadth of the European and US patents relative to the international application might be the result of the examination, but it could also be the result of a reformulation of claims by the applicant to reduce their number and concomitantly minimize filing fees (telephone interviews). Additional fees are payable per claim in excess of 10 claims at the EPO, and at the USPTO additional fees are payable for multiple dependent claims, for individual claims in excess of three, and for claims (dependent or independent) in excess of 20; the CIPO demands no such claim fees. If the significant reductions in the breadth of the European patent are really due to the examination, then given that the patent was issued in 2003, this might reflect recent changes at the EPO designed to make the examination of gene patents stricter (telephone interview). The US and Canadian patents were granted in 2000 and 2004 respectively.

B.1.7 Patent WO9415969: Chimeric antibody against HIV

This particular patent family provides an invention related to a chimeric human-mouse gene fragment which codes for the variable regions of an antibody that act on neutralizing human immunodeficiency virus (HIV). Using this gene to produce the recombinant antibody could help to treat and prevent AIDS. The PCT application was filed in Japan (JP9300039) and led to a single patent in all three patent offices (CA2153165/EP678523/US5773247).

Comparison of the patents granted by the CIPO, the USPTO and the EPO shows that claims in the three patents are, overall, very similar. However, the wording and the structure of the claims in the European patent differ slightly from the other two, although providing an equivalent coverage. These claims essentially relate to the sequence of the chimeric antibody and to the function of the encoded antibody.

A more significant difference is that the Canadian and US patents lack five of the EPO claims (claim 6 to 10). One of these explains the approach used to produce the recombinant antibody from the chimeric DNA fragment. The others mention the utilization of a vector comprising the DNA fragment, and the utilization of a host cell transformed with the vector, and specify that the recombinant antibody could be used as a diagnostic and pharmaceutical tool.

Unfortunately, since the PCT application was written in Japanese, it was impossible for us to determine if these additional claims were in the international application been examined by all three countries. Consequently, it was impossible to judge whether these differences were the result of a restriction requirement or a rejection by the Canadian and US examiners, or of voluntary amendments by the applicant to add these claims for Europe only. The first hypothesis seems more likely since any voluntary amendments made by the applicant to broaden patent coverage would logically be done in the three patent offices to seek the same protection in all countries. However, the latter hypothesis cannot be completely ruled out.

Considering that claims concerning the utilization of the recombinant antibody as a diagnostic and pharmaceutical tool are not covered by the Canadian and US patents, the CIPO and the USPTO patents can be seen as being more restrictive. However, it could be that divisional patents, pending or not, covering this aspect of the invention were overlooked.

B.1.8 Patent WO9410311: Cloning of the PCT-65 receptor

This invention relates to the cloning and characterization of the PCT-65 serotonin receptor protein. In addition, patents within this family encompass interspecific variations of the PCT-65 receptor and a method for screening drugs targeting central nervous system activity. The PCT application was filed in the US in 1993 and led to a single patent in all three patent offices (CA2147838/EP666915/US5914236).

Searches in patent databases did not reveal additional pending patents, divisional, continuation and/or CIP patents for this patent family other than the patents obtained directly from the PCT application. Therefore, we can make stronger assumptions about the reasons for differences between patent offices.

The patents granted by the CIPO and EPO are almost identical and any differences too minor to affect the breadth of these patents. Consequently, for this patent family, the practices employed by the CIPO and EPO would appear to be very similar. On the other hand, the US patent differs in many ways. Only those differences that impact on patent breadth are described.

The broadest claim (claim 2) of the Canadian and European patents specifies that the PCT-65 sequence encodes for a vertebrate serotonin receptor, having a homology equal to or greater than 90% with the sequence described in the patent. In the US patent, the broadest claim refers to a mammalian (e.g. claim 1 in the US patent) rather than a vertebrate receptor, but does not specify the sequence or the level of homology required for a sequence to be protected.

Considering the source organism referenced in the claims, the European and Canadian patents are broader in encompassing all vertebrate species including mammals, while the US patent is limited to mammals. On the other hand, the US patent does not limit its broadest claim strictly to the described sequence, leaving the door open for protection of sequences that would share less than the 90% homology required by the Canadian and European patents. When combining both criteria (i.e. the source organism and the level of homology) in interpreting the breadth of claims, it might be concluded that all

three patents are equivalent. Indeed, a mammalian sequence might be the only one to meet the “at least 90% of homology” criteria among vertebrates.

In this case, there are two possible scenarios. In the first, a competitor discovering a new mammalian receptor whose DNA sequence had 88% homology with the described sequence would not be liable in using the receptor in Canada or Europe. However, a legal action against the competitor could be instigated in the US since the scope of the US patent is not delimited with a specific homology criteria or described sequence. Based on telephone interviews with lawyers expert in biotechnology patenting, a court would be unlikely to find that the competitor was infringing the patent. In fact, a single nucleotide or amino acid polymorphism is patentable in the US (telephone interviews) and the USPTO is reluctant to allow protection of variants based on homology or identity criteria. However, under the doctrine of equivalents which prevails in the US, a court might find the competitor was infringing the patent if the function of the new receptor were identical to the claimed receptor, and if the owner of the patent did not relinquish a broader claim against its patent. In these circumstances, the US claim does not appear to be narrower than in the PCT application. Thus, in some instances, the US patent could be broader than the Canadian and European patents.

In the second scenario, a competitor who discovered a new mammalian receptor whose DNA sequence had at least 90% homology with the patented sequence would infringe the Canadian and European patents, but not necessarily in the US where no specification regarding homology is included. Any decision therefore would again rest on the application by the court of the doctrine of equivalents. If the receptor has 91% homology with the nucleotide sequence encoding the claimed receptor, but has a different function, it is highly likely that the competitor would be judged not to be infringing the US patent. In this case, therefore, the US patent can be considered to be narrower than the Canadian and European patents. Overall, the protection provided by the three patents is fairly similar.

B.1.9 Patent WO9524480: FK506 binding protein gene

This patent family provides the sequence of the FK506 binding protein gene and a method of producing a recombinant FK506 binding protein. The use of the gene enables FK506 binding protein expression, and could be used to facilitate the mechanism of immunosuppression, or to screen therapeutics for autoimmune diseases. The PCT was filed in Japan in 1995 and led to a single patent in all three patent offices (CA2185098/EP754754/US6136584).

Analysis of this set of patents revealed that the US and Canadian patents were almost identical, while the European patent differed slightly. The three patents have one common claim (claim 4 in the European patent; claim 2 in the US and Canadian patents) related to the method of producing recombinant FK506 binding protein. The claim specifies the use of an expression vector to transform a host cell and the recovery of the recombinant protein produced by culturing the transformant. In addition, the US and Canadian patents have three more dependent claims (claims 3, 4 and 5) on components of the previous claim, namely the expression vector, the host cell and the recombinant protein.

The additional claims in the Canadian and US patents exemplify a strategy often used by applicants when dealing with a gene-based or protein-based invention. The general approach consists of claiming as many different aspects of the invention as possible, including DNA sequences, amino acid sequences, vectors, and host cells even though these aspects are already described in the method claim. There are two main reasons for drafting patents in this way. First of all, product claims (e.g. vector, host cell, recombinant protein) usually provide better protection than method claims (e.g. production method of a recombinant protein) since it is easier to prove infringement of the former. For example, if a claim on a product exists, then any manufacture, use or sale of this product is illegal, and it is fairly easy for an applicant to prove that the composition of the product (e.g. a drug) is the same as that of the patented product. However, in the case that the claim applies only to the production method, it is difficult (without access to his laboratory or factory) to prove that a competitor is replicating each step of the process (telephone interviews). Secondly, it is important to have claims covering each component of an invention in order to prevent competitors from performing steps along the whole chain of possible activities (telephone interviews). In the case that the patent holder tried to sue a competitor for production of the vector, for instance, a court would conclude that the US and Canadian patents were being infringed, but not necessarily in EPO patent. Having multiple claims relating to the same matter is also useful in the case that one of the claims, for example the method claim, is invalidated in court. The applicant can still rely upon the remaining claims to protect the invention.

Thus, it can be seen that the breadth of the three patents would seem to be very similar, but when legalities are taken into account, it can be seen that the European patent is narrower in scope and provides less protection. There is no clear reason in this case for the difference since the types of claims omitted from this European patent, are otherwise generally permitted by the EPO. Many of the experts interviewed were surprised that this difference existed.

B.1.10 Patent family WO9709348: Orphan receptor

This patent family relates to a DNA sequence encoding a novel human estrogen nuclear receptor (ER β), to its amino acid sequence, and to its use in isolating therapeutics and testing the hormonal effects of other molecules. The PCT application was filed in Europe in 1996 and led to a patent in the US and Europe in 1999 (US5958710/EP792292) and in Canada in 2001 (CA2201098). A divisional application of EP792292 was published by the EPO in 1999 and the patent (EP935000) is pending. However, this divisional application is identical to the PCT application initially submitted to the EPO and thus has no impact on the current analysis. The use of divisional applications in Europe is discussed in section 4 Discussion and Conclusions.

Comparative analysis of the claims in the PCT application (12 claims) and in the patents granted by the CIPO (12 claims), the USPTO (7 claims), and the EPO (17 claims) revealed some interesting differences regarding their breadth. The PCT application is broader than any of the patents in relation to the claims on amino acid and DNA sequences, which suggests action by all three patent offices to limit the breadth of the claims. However, the extent of limitation varies among patent offices. The most restrictive is the

US patent in claiming only sequences (DNA or amino acid) described within the body of the patent. Attorneys in biotechnology patenting told us that the USPTO was very strict in protection of DNA sequences and were generally disinclined to allow claims of the type “any sequence having some percent of identity with the described sequence” (telephone interviews). The European patent is slightly less restrictive, claiming sequences, depending on the sequence in reference, with 89% or 95% identity with described sequences. The Canadian patent is the broadest claiming any sequences having substantially the same sequences as described within the patent. However, if this claim was to be invalidated in court, a more restrictive dependent claim would apply which requires that the sequence should share at least 95% identity with described sequences.

The European patent in two additional ways claims DNA sequences based on hybridization under stringent conditions to probes derived from described sequences. These two additional claims may or may not give broader protection to DNA sequences encoding ER β than the European patent, depending on the level of identity that is required for hybridization under described conditions. Nevertheless, the Canadian patent is still the broadest.

In the case that claims requiring a minimal identity with sequences are considered by a court to be too wide and are withdrawn from the European and Canadian patents, more restrictive dependent claims can be applied specifying the source organism. In this way, the European patent can be seen to be less strict in adding two claims; one requires that the receptor be derived from mammalian cells and the other requires that the receptor be derived from rat or human cells. The Canadian patent, on the other hand, has only one additional dependent claim stating that the receptor has to be derived from rat or human cells. Interestingly, the US patent protects the receptor whether it is derived from mouse, rat or human. Thus, the US patent would be broader than the Canadian and European patents, in the case that the broader Canadian and European claims were invalidated in law.

All three patents include a claim regarding the identification of molecules which bind ER β , but the US patent is more precise, and thus stricter, regarding the method used to identify such molecules. In addition, the US patent omits four claims included in the original PCT application and in the Canadian and European patents. These claims relate to the use of ER β in determining molecules for use in the treatment of diverse diseases or conditions (prostate or ovarian cancer, benign prostatic hyperplasia, diseases of the central nervous system, osteoporosis, cardiovascular disease, or ER β or ER α specific diseases or conditions), in the development of a drug design method, and in the testing of estrogenic or other hormonal effects of a substance. Even if a divisional US patent covering those four claims was missed because it was pending, the US patent still remains the strictest.

Given that the US and European patents were both issued in 1999 and that the Canadian patent was issued in 2001, it is unlikely that observed differences would be due to changes in the practices of patent offices. In any case, the Canadian patent which was issued two years after the U.S. and European patents, is the broadest of the three, while it is generally recognized that the practices of patent offices became stricter over time (telephone interviews). Consequently, the examination for this PCT

application can be assumed to have been stricter in the US. The Canadian and European patents are similar in scope, although the Canadian patent is slightly broader than the European one. Overall, the Canadian patent is the most similar to the PCT application.

B.1.11 Patent WO9822128: hCNTF to treat obesity and related diseases

The subject of the invention is the use of molecules such as human ciliary neurotrophic factor (hCNTF) or mutants of hCNTF, which activate the CNTF receptor as active principles in the formulation of pharmaceutical compositions suitable for the treatment of obesity and related diseases. The PCT application was filed in Italy in 1997 and led to a single patent in the CIPO, the EPO and the USPTO (CA2271781/EP946189/US6565869) as illustrated in Figure 2.

Comparison of patents within this family revealed a tendency that observed in the case of two other patent families (see Sections B.1.7 and B.1.9). Once again, claims were similar, with the US and Canadian patents were almost identical in breadth, and the European patent differing slightly.

The first claim in all three patents is very broad covering the use of CNTF in the treatment of obesity and any associated diseases in a patient. All also have a dependent claim reducing the breadth of the first claim to the treatment of diabetes associated with obesity. However, the European patent also restricts the claim to the treatment of hyperglycemia or hyperinsulinemia associated with obesity in the form of a dependent claim (claim 6). Because claims would be analyzed one by one in a court, the EPO patent provides better protection in the case that the broad parent claim (the first claim of all patents) was invalidated. If this were to happen, the European patent would still protect the use of CNTF for the treatment of diabetes, hyperglycemia or hyperinsulinemia associated with obesity, while the Canadian and US patents would only protect the use of CNTF in the treatment of diabetes associated with obesity. Thus, the European patent is broadest, but only if the broad parent claim has been invalidated.

Since the additional claim in the European patent was not included in the original PCT application, an amendment either at the request of the European examiner or from the applicant has likely been made. Given that the supplementary claim in the EPO provides better protection, a voluntary amendment made by the applicant seems the more likely scenario. It is impossible to determine if the amendment was requested at all three patent offices (and Canadian and US examiners rejected the modification), or only the EPO. In the opinion of the experts in the field that were interviewed, there would seem to be no justification for such a rejection by the examiners considering that a broader claim was granted in all three jurisdictions.

As in the PCT application, the European patent claims the use of DNA encoding hCNTF, or a mutant hCNTF, for the manufacture of a medicament for gene therapy of obesity and associated diseases, while the Canadian and US patents claim the use of DNA encoding hCNTF, or a mutant hCNTF, for treating obesity and associated diseases, but without specifying that it is gene therapy. Although this is not likely to have an impact on the breadth of the European patent relative to the Canadian and US patents, as “gene therapy” implicitly covers any kind of “gene therapy” (i.e. the introduction of the DNA into a cell

by any known means), it is likely that the Canadian and US examiners requested this change in the formulation of the claim (telephone interviews), but merely as a formality.

For this particular patent family, differences in the language used in the patents granted by the three patent offices do not have a profound impact on the breadth of the claims and all three are similar in scope.

B.2 Complex cases: multiple patents in at least one patent office

This section analyzes patent families where the international application was subject to divisional, continuation and/or CIP procedures at the national phase. In most cases (11 out of 13 families), the international application originated in the US. These procedures, which mainly affected US patents in the families sampled, resulted in a complex sequence of up to 18 related US patents for one equivalent patent in Canada and Europe. In these cases, comparison of patent scope between the different offices is seriously hindered. For example, if some claims are present in the Canadian and/or European patents, but absent in the corresponding US patents, it could be that either the Canadian and/or European patents have a wider scope, or that a related US patent was missed because it was pending. On the other hand, if related US patents cover more subject matter than the corresponding patent in Canada and/or Europe, it could be that the US patents have greater scope, or that additional corresponding Canadian and/or European patents have been missed because they are pending from a second international application, or because there was a restriction requirement on the international application.

B.2.1 Patent family WO9107492: Human anti-RhD antibodies

The present patent family includes patents for an invention providing DNA sequences encoding complementary determining regions of variable domains of human anti-RhD antibodies and their use in the production of recombinant chimeric antibody molecules. The PCT application was filed in Europe in 1990 and led to a single patent in Canada (CA2068222) and Europe (EP500659), but to two patents (US5831063 and its divisional US5919910) in the US (Figure 3).

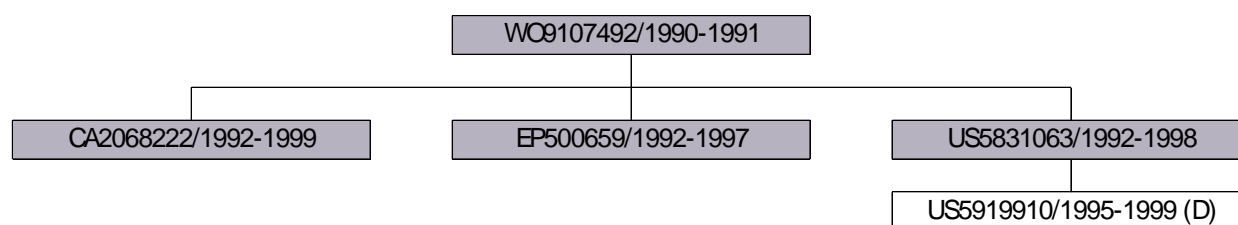


Figure 3 Phylogeny of patent family WO9107492

Source: Science-Metrix

Together, the two US patents have a total of 54 claims while the PCT application has only 20 claims and the Canadian and European patents only 14 claims. The Canadian and European patents are identical. There are two reasons for the numerous claims in the US. Firstly, the invention touches upon both the

V_H and V_L domains of the anti-RhD antibodies and the US patent treats each domain in separate claims. However, this does not have a tangible impact on the breadth of the US patent.

Secondly, both the V_H and V_L domains comprise a CDR1, CDR2 and CDR3 region, and the invention covers, for each region in a domain, a series of alternative DNA sequences. The US patent claims specific combinations of CDR1, CDR2 and CDR3 DNA sequences, and each combination is the subject of an independent claim. The Canadian and European patents, on the other hand, present all DNA sequences for all three regions of both the V_H and V_L domains in a single claim, and allow for any combination of CDR1, CDR2 and CDR3 DNA sequences. Therefore, the US patent is much more restrictive allowing only specific combinations of CDR1, CDR2 and CDR3 DNA sequences.

The US patent is more restrictive on a number of other points. The Canadian and European patents claim functional equivalents of the claimed sequences, whereas the US patent is strictly limited to sequences described within the disclosure. The US patent also lacks one, two and three DNA variants of, respectively, the CDR1, CDR2 and CDR3 region of the V_H domain, and one DNA variant of both the CDR1 and CDR2 regions of the V_L domain. In claiming DNA sequences, the US patent specifies that the molecule must be either isolated, synthetic or recombinant. Although the lack of the “isolated” specification would imply that a gene in the natural organism would be protected in the US, this is not the case in Canada and Europe where the specification is implicit. The specifications for “synthetic” and “recombinant” do not confer a difference on the DNA molecule since a product made by a new process is not rendered novel by the process (telephone interviews).

Regarding the vector used to express the V_H and V_L domains, the US is more precise specifying that the vector is a pSV2gpt vector. However, this specification is added in a dependent claim to a broader claim for which there is an equivalent in Canada and Europe. Therefore, the US patent would only be stricter with respect to the vector if the broader claim were to be invalidated in the US, but not in Canada and Europe. The US patent also has no claims pertaining to the polypeptides and to the method of Rh-typing.

The divisional US patent covers the Canadian and European claims on chimeric antibodies and on pharmaceutical compositions.

In this case, the US patent is clearly more restrictive than the Canadian and European patents, and this conclusion is still true if divisional patents, pending or not, on the polypeptides and the method of Rh-typing were missed.

B.2.2 Patent WO9100916: The Fibroblast growth factor receptor gene

The present invention concerns the isolation of different forms of the fibroblast growth factor receptor (FGFR) including truncated forms, which inhibit the ligand (FGF) function. It also provides details on production methods and antibodies against these receptors. The PCT application was filed in the US in 1990 and led to a single patent in the CIPO and the EPO (CA2063431/

EP481000) and to multiple patents in the USPTO (US6384191/US6355440/US6350593/US5707632) as illustrated in Figure 4.

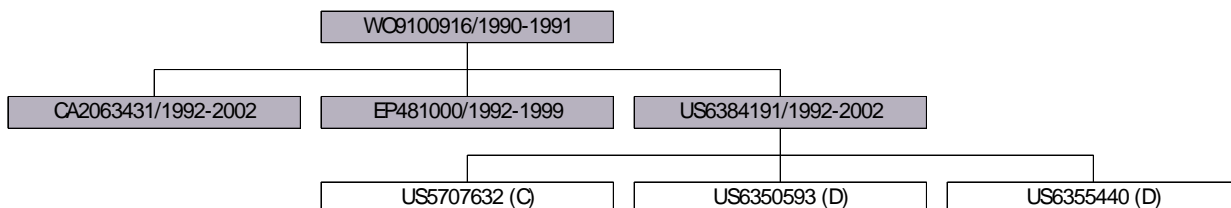


Figure 4 Phylogeny of patent family WO9100916

Source: Science-Metrix

Analysis of this patent family revealed several differences in the formulation of claims between patent offices. However, given the nature of these differences it was not possible to provide conclusions regarding their impact on patent scope.

B.2.3 Patent family WO9110734: Cystic fibrosis gene

In this invention, the cystic fibrosis gene and its gene product are described for mutant forms. The genetic and protein information is used in developing DNA diagnosis, protein diagnosis, carrier and patient screening, cloning of the gene and manufacture of the protein, and development of cystic fibrosis affected animals. The PCT application was filed in Canada in 1991 and led to a single patent in Canada (CA2073441) and Europe (EP667900), but to two patents (US6001588 and its divisional US5981178) in the US (Figure 5).

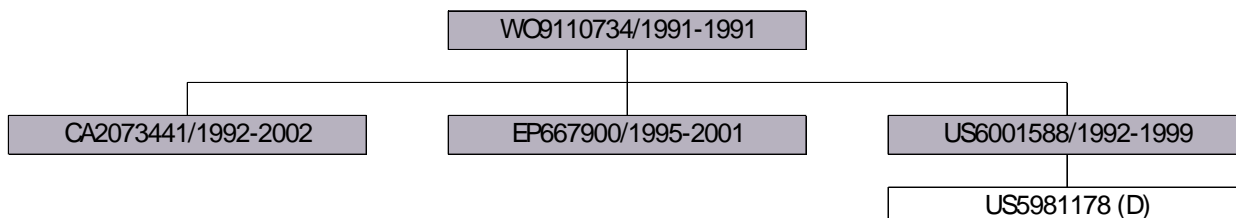


Figure 5 Phylogeny of patent family WO9110734

Source: Science-Metrix

The Canadian patent is the most similar to the PCT application with the exception of one claim pertaining to a transgenic animal (see below), both documents having 47 claims. The similarity between the two documents might result from the fact that the PCT application originated in Canada, and thus the applicant is likely to have drafted the PCT application in conformance with Canadian standards (telephone interviews). Although the European patent has fewer claims (12), it is drafted in such a way as to cover almost the same components as the Canadian patent. The two US patents together have 24 claims, but do not cover all the components found in the Canadian and European patents.

A striking difference between the Canadian, European and US patents lies in the claimed variants of the DNA molecule encoding the CFTR polypeptide. The Canadian patent claims DNA molecules characterized by nucleotide variants at 6 nucleotide positions (129, 556, 621+1, 711+1, 1717-1, and 3659) and of DNA variants resulting in deletion of or alteration to amino acids in the CFTR polypeptide at 14 residue positions (85, 148, 455, 178, 493, 507, 542, 549, 551, 560, 563, 574, 1077, and 1092). The corresponding US claims lack one nucleotide mutation (129) and five amino acid mutations (148, 551, 563, 574, and 1077), and the European claims lack one amino acid mutation (551). However, all the mutations claimed in the Canadian patents are fully described in the disclosure of both the US and European patents. It is therefore difficult to conjecture what was the rationale behind the US and European examiners rejections, which result in the breadth of their respective patents being narrower than the Canadian patent.

A recombinant cloning vector and a host cell transformed with the vector are claimed in all three patents. However, the Canadian and US patents are broader than the European patent and allow for human host cells. The Canadian patent has a broad claim allowing the use of almost any host cells, and a more specific claim stating that the host must consist of human epithelial cells. All patents describe a method of producing a mutant CFTR polypeptide, but only the Canadian and European patents claim a purified mutant CFTR polypeptide.

The three patents claim DNA sequences corresponding to fragments of the CFTR gene for use as probes in diagnostic kits. The US and European patents specify that these fragments should contain at least one of the claimed mutations. Although the Canadian patent is, from a literal perspective, broader than the other two patents protecting fragments whether or not they include one of the claimed mutations, only those fragments containing one such mutation will actually be useful in diagnostic kits.

The Canadian patent claims a method for diagnosing a cystic fibrosis (CF) patient or carrier based on hybridization with a labeled DNA probe and on an immunological assay with antibodies specific to mutant CFTR polypeptides; a process of detection of CF patient or carrier based on the hybridization assay and the immunological assay; and an immunoassay kit and a hybridization kit. The US divisional patent claims all three components, the method, the process and the kit, but only for the hybridization assay. It might be that the components relating to the immunological assay are the subject of another divisional patent that might have been missed because it was pending, or that the claimed invention was not commensurate with the scope of enablement provided by the application disclosure regarding the immunological assay, or that the applicant was not in possession of the full scope (the antibodies) of the claimed invention. Since both US patents were issued in 1999, it is unlikely that, as of 2005, a pending patent would have been missed. However, based on the findings in the current study, a restriction requirement seems likely given that antibodies are often considered as an invention distinct from the DNA sequences and the proteins at the USPTO. Thus, the applicant might have decided not to pursue a divisional patent following a restriction requirement. Nevertheless, the examination practices at the USPTO are likely to be the source of this difference. The European patent covers both diagnostic methods, but not the components relating to the process and the kit. However, the impact on the breadth

of the European patent is limited since the process and the kit are to a degree protected by the claims relating to the diagnostic methods.

A significant and very interesting difference from the claim in the original PCT application is related to a cystic fibrosis affected animal. In the US patent, despite the fact that the USPTO allows patenting of transgenic animals, the claim has simply been omitted, perhaps for one of the aforementioned reasons. In Europe, the claim is very similar to that in the PCT application and relates to a non-human animal comprising a heterologous cell system transformed with a recombinant cloning vector expressing a human mutant CFTR polypeptide, which induces cystic fibrosis in the animal. In Canada, the patent was issued in 2002, the year that the supreme court of Canada made its decision in the Harvard mouse case, banning the patenting of transgenic animals in Canada. Therefore, the claim language in the Canadian patent has been reformulated to provide a reasonably equivalent, but more limited protection for a heterologous cell system comprised of mouse cells in which cystic fibrosis has been induced by incorporating the recombinant cloning vector. Thus, the transgenic animal itself is not claimed in the Canadian patent which is therefore stricter.

Overall, the US patent is the strictest followed by the European patent and the Canadian patent which is similar in breadth to the European patent.

B.2.4 Patent family WO9210519: Novel tyrosine kinases JAK1 and JAK2

This patent family relates to novel tyrosine kinases comprising multiple protein kinase catalytic domains, and to DNA sequences encoding these proteins. Two such kinases are described and designated JAK1 and JAK2. The PCT application was filed in the US in 1991 and led to a single patent in Canada (CA2097200). In Europe, the application led to a granted patent (EP560890) and a divisional application (EP1482049). In the US, a restriction requirement on the PCT application led to a first patent (US5852184) and to 4 subsequent divisional patents (US5716818, US5658791, US5821069, US5910426) (Figure 6).

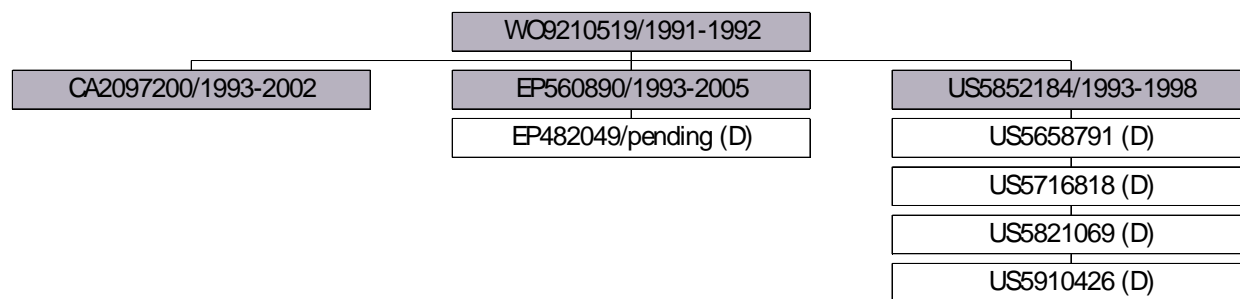


Figure 6 Phylogeny of patent family WO9210519

Source: Science-Metrix

Patents in the three countries cover two protein tyrosine kinases (JAK1 and JAK2) and the DNA encoding these proteins. However, there are some differences in the claims. The Canadian patent, which

was issued in 2002, is the most similar to the international application, and the minor changes in this patent appear to have been copied from the US patent US5852184, which was issued in 1998.

For example, the US (claim 1, Table I) and the Canadian (claim 11, Table I) patents added to the claim in the PCT application (claim 11, Table I) specifications such as “purified isolated” to qualify the DNA molecule, and claimed a specific DNA molecule. The US patent is strictly limited to the DNA sequence of SEQ ID No. 1 (claim 1 and 2, Table I), which is the sequence of JAK1, as is claim 11 in the Canadian patent. However, the Canadian patent and the PCT application establish that the nucleic acid molecule of claim 11 is either JAK1 or JAK2 in claims 17 and 18 (Table I). Therefore, claim 11 in the Canadian patent should have been written so as to include a DNA molecule with the sequence as defined in SEQ ID No. 1 (JAK1) or SEQ ID No. 2 (JAK2), similar to the European patent which was granted in 2005 (claims 5 and 6, Table I). Unfortunately, this error in the Canadian patent was repeated in the claim for the proteins (i.e. the Canadian patent only refers to SEQ ID No. 1), whereas the US divisional patent (US5716818) covering the proteins, and the European patent both refer to SEQ ID No. 1 or SEQ ID No. 2. However, these differences are not likely to have a profound impact as anyone with expertise would consider the disclosure in interpreting the claims.

Table I Difference in the language of claims pertaining to DNA encoding JAK1 and JAK2 between patents

Patent	Claim	Claim language
WO9210519	11	A nucleic acid molecule comprising a nucleotide sequence encoding an animal protein tyrosine-like molecule comprising a polypeptide having multiple catalytic domains but no SH2 domains.
	17	The nucleic acid molecule according to claim 11 wherein the PTK-like molecule is JAK1.
	18	The nucleic acid molecule according to claim 11 wherein the PTK-like molecule is JAK2.
CA2097200	11	A purified isolated nucleic acid molecule which codes for an animal protein tyrosine kinase comprising multiple protein kinase catalytic domains but no SH2 domain, the complementary sequence of which hybridizes to the nucleotide sequence set forth in SEQ ID No: 1 at the following conditions: 65°C, 6XSSC, 1% SDS with a final wash of 0.2XSSC, 0.1% SDS, at 65°C.
	17	The nucleic acid molecule according to claim 11 wherein the PTK is JAK1.
	18	The nucleic acid molecule according to claim 11 wherein the PTK is JAK2.
US5852184	1	A purified isolated nucleic acid molecule which codes for a human protein tyrosine kinase like molecule which has multiple protein kinase catalytic domains, but no SH2 domain, the complementary sequence of which hybridizes to the nucleotide sequence set forth in SEQ ID No: 1 at the following conditions: 65°C, 6XSSC, 1% SDS with a final wash of 0.2XSSC, 0.1% SDS, at 65°C.
	2	The isolated nucleic acid molecule, consisting of the nucleotide sequence set forth in SEQ ID No: 1.
EP560890	5	A nucleic acid molecule having the nucleotide sequence shown in Figure 2.
	6	A nucleic acid molecule having the nucleotide sequence shown in Figure 8.

Source: Compiled by Science-Metrix from patents published by the CIPO, USPTO and EPO.

Nevertheless, the Canadian patent is broader than the US and EP patents for DNA sequences. The Canadian patent claims any DNA molecule encoding JAK1 or JAK2 isolated from any animal which hybridizes with the nucleic acid sequence referred to under specified conditions. Thus any production of a mutant, derivative, analog or homologue hybridizing with the particular nucleic acid sequence under specified conditions would infringe the Canadian patent. The US patent on the other hand is limited to a

protein of human origin that would hybridize to the sequence in reference, and the European patent is strictly limited to sequences (of human origin) described in the disclosure.

Regarding the first claim relating to the proteins themselves, the Canadian patent is broader encompassing any protein, from any animal, the DNA sequence of which hybridizes with the nucleic acid sequence in reference under specified conditions. In comparison to the Canadian patent, the claim in the US patent only covers animal proteins of mammalian origin. In Europe, the animal protein must be isolated from a human or a mouse and must also include two protein kinase catalytic domains. On the other hand, the US and European patents claim additional proteins comprising fragments of JAK1 and JAK2, such that they protect mutants, derivatives, analogues, and homologues. The US patent protects a broader range of such proteins than the European patents. Considering that the claims in the US and European patents are of a more recent date, it is difficult to establish whether the Canadian patent is broader or stricter with regard to the claimed proteins. However, if the pending European patent were to be granted by the examiner in its current form, the protection over DNA molecules and proteins would be broader in Europe. Indeed, the divisional application covers fragments of an animal protein tyrosine kinase having one or more catalytic domains, but no SH2 domain, and nucleic acid molecules encoding these fragments. Given that the examination of the divisional application will be assigned to the examiner of the parent patent, and that the scope of claims on DNA molecules and proteins was restricted in the latter, it is unlikely that claims in the divisional application will be granted without limitations being imposed (telephone interviews).

The European and US patents lack three claims that are included in the Canadian patent and the PCT application, in relation to a method of identifying agonists or antagonists of the protein, and to the agonists and antagonists themselves. However, agonists and antagonists are included in the divisional application in Europe. Therefore, it is likely that they will be granted in the future. There might also be a pending divisional application in the US that was missed. It might also be the case that the applicant chose not to apply for a divisional patent following a restriction requirement, or that the US examiner considered the scope of the claimed invention was not commensurate with the scope of enablement provided by the application disclosure, or that the applicant was not in possession of the full scope of the claimed invention.

In the US, there is a divisional patent on a method of detecting protein tyrosine kinase molecules in a sample using an antibody. The antibody is claimed in all three patents and in the PCT application, but no detection method is included in the Canadian and European patents or the PCT application. This is likely due to a decision by the US applicant (i.e. voluntary amendment) to broaden its protection in its own market.

Overall, the European patent appears to be the most restrictive followed by the US patent, and then the Canadian patent.

B.2.5 Patent family WO9210589: HLA DRbeta DNA typing

The invention in the present patent family provides primers for the amplification of specific nucleic acid sequences of the second exon of HLA DRbeta genes and probes for identifying polymorphic sequences contained in the amplified DNA. The PCT application was filed in the US in 1991 and led to a single patent in Canada (CA2075037) and Europe (EP514534). In the US, the patent derived from the PCT application (US5567809) is related to 17 US patents through divisional, continuation and/or CIP procedures. Given the complexity of relationships between US patents, we do not depict the phylogeny of patent family WO9210589.

Of the 18 US patents, 11 are related to the Polymerase Chain Reaction (PCR) developed by Kary Mullis who was awarded the Nobel Prize in 1993 for his invention. The remaining 7 patents are the only ones closely related to the invention claimed in the PCT application. It is therefore possible to compare the breadth in the US, Canadian and European patents by focusing on the US patents only (US5310893, US5468613, US5541065, US5567809, US5604099, US5665548 and US6194561).

The PCT application has 30 claims and presents a method and kit to detect allelic variants of DRbeta genes, and specify the complete set of primers and probes that may be used in the kit. The European patent, which was issued in 1998, reduced this number to 16 claims. The Canadian patent, which was granted in 2002, is almost identical to the European patent with the exception that it has a supplementary claim, which is also present in the PCT application, covering two additional probes. Nevertheless, both patents provide a similar scope of protection over the invention. The US patent obtained from the PCT application (US5567809) covers the two supplementary probes in the Canadian patent and the international application, but overall protects fewer probes and primers. However, two related US patents (US5468613 and US5604099) obtained in 1995 and 1997 are very broad, and encompass the detection method for a variety of genes, including DRbeta genes, using any primers and/or probes.

In this case, the US equivalent is broader than the Canadian and European patents. However, it should be noted that these US patents are related to the PCR invention (they are in the same patent family) that opened up a new era in biotechnology with diverse applications such as the genotyping of organisms (i.e. detecting specific genetic polymorphisms in the DNA of organisms). Given that in general, the scope of an invention is commensurate with the contribution made by the applicant over and above the prior art (telephone interviews), it is not surprising that the USPTO awarded broad patents to the inventors of the PCR, an invention that opened up a new field (i.e. distant prior art), for genotyping applications of their invention. Because of their broad scope, the US patents (US5468613 and US5604099) are more likely to be easily contestable in court. If they are eventually invalidated, then the scope of protection in the US will be reduced to what is claimed in the US patent, obtained directly from the PCT application (US5567809), and the protection in the US will be narrower. This is not beyond the realms of possibility since the Cetus Corporation, the original owner of the PCR patent, has been subject to numerous legal attacks over patents within this patent family.

B.2.6 Patent WO9214248: A novel human receptor tyrosine kinase gene

This patent family encompasses a DNA sequence encoding a novel human growth factor receptor described as a type III receptor tyrosine kinase that binds specifically to the vascular endothelial cell growth factor. The PCT application was filed in the US in 1992 and led to a single patent in the CIPO and the EPO (CA2083401/EP536350) and to multiple patents in the USPTO (US5861301/US5766860) as shown in Figure 7.

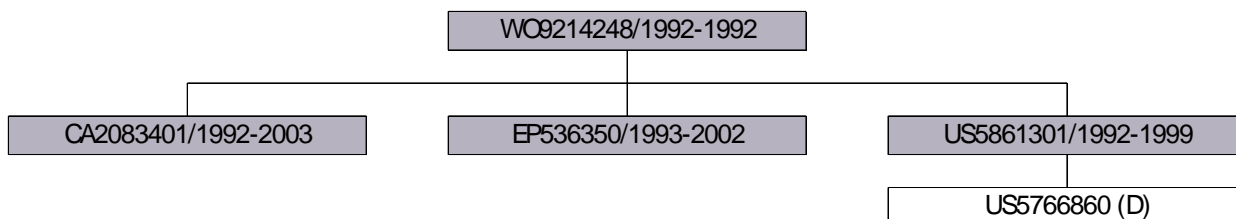


Figure 7 Phylogeny of patent family WO9214248

Source: Science-Metrix

In this patent family, the PCT application has 17 claims, the Canadian patent 18, the European patent 12 and the US patents cover 10 claims. The first claim in all three patents, derived directly from the PCT application, relates to a recombinant DNA molecule encoding human type III receptor tyrosine kinase. This claim is broader in the European patent since it covers any corresponding nucleotide sequence by virtue of the redundancy of the genetic code. Since this specification was not in the PCT application, it is likely that the applicant made a voluntary amendment to the original claim. However, it is not possible to determine whether the amendment was submitted to the EPO only, or to all three patent offices. If the former, then it is not possible to draw any conclusions about the practices of patent offices; if the latter is the case then it can be concluded that the USPTO and the CIPO were stricter than the EPO.

There is a second difference that negatively affects the scope of the Canadian and US patents. All three patents claim a screening method to identify active compounds that could be used as pharmaceuticals to affect the interaction of vascular endothelial cell growth factors (VEFG) on type III receptor tyrosine kinase. However, the Canadian and US patents claim the method for screening only VEGF antagonists, while the European patent includes both agonists and antagonists. Rather surprisingly, the PCT application did not include the method so it may be assumed that a voluntary amendment was made by the applicant to all three jurisdictions and that the USPTO and CIPO were stricter than the EPO.

Overall, for this patent family, the European patent is broader than the Canadian and US patents which are similar in scope.

B.2.7 Patent family WO9222319: Receptor like TGF- β 1 binding molecules

The following patents relate to a family of substantially pure, receptor like TGF- β 1 binding glycoproteins and their encoding DNA molecules. These molecules are characterized by their ability to

bind the TGF- β 1 molecule. Consequently, this family of molecules is useful for identifying and/or quantifying TGF- β 1 in a sample, as well as inhibiting its effect on cells. The PCT application was filed in the US in 1992 and led to a single patent in Canada (CA2111853) and Europe (EP590071). In the US, a restriction requirement on the PCT application led to two patents (US5578703 and its divisional US5731200) which are both CIP of a previous US patent (US5229495) (Figure 8).

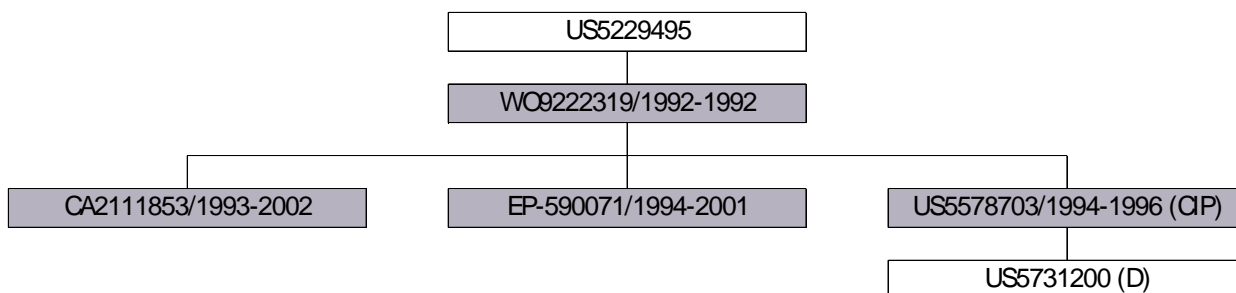


Figure 8 Phylogeny of patent family WO9222319

Source: Science-Metrix

The PCT application has 23 claims, the Canadian patent 14 claims, and the European patent 10 claims. The three US patents together have 15 claims. The Canadian patent and the US divisional patent cover nucleotide sequences encoding a membrane derived receptor-like TGF- β 1 binding protein. Both patents cover isolated cDNA and mRNA molecules; the US patent also covers isolated genomic DNA molecules. The two patents also claim host cells, in particular COS cells, transformed with nucleotide sequences encoding the binding protein. The first claim in both patents is very broad providing protection for any probes that might be derived from the claimed DNA sequence, thereby potentially hindering the search for homologues of the binding protein that might potentially lead to a therapeutic against cancer caused by TGF- β 1. In Europe, none of the claims pertaining to DNA molecules encoding the binding protein were granted.

In each patent, three binding proteins with molecular weights of 35-40kD, 70-80 kD (a dimer of the 35-40 kD protein), and 160 kD are claimed. The Canadian patent is the only one to claim proteins with whole amino acid sequences in reference. The European patent specifies only two segments of the sequence that must be in the proteins allowing for mutations in the remaining portions of the sequence. The US patents' claims on the proteins are even broad and provide no information on the amino acid sequences. In subsequent dependent claims, the US patent (US5229495) provides some information on segments of the sequence that should be in the protein, as in the European patent. Contrary to what is normally observed, in the PCT application, the scope of these claims is narrower than in some of its derived patents (i.e. the European and US patents). Consequently, it is difficult to conclude whether or the breadth of these claims between the three jurisdictions differs, given that the same amino acid sequence appears in the disclosure of all patents.

For all three countries, there is a claim on a method for identifying TGF- β 1 in a sample. However, unlike the PCT application, and the Canadian and European patents, which claim the use of all three

binding proteins in the method, the US patents only claim the use of the binding protein with a molecular weight of 35-40kD upwards. Although the US claim may seem more restrictive, the difference is likely the result of the fragmentation of the application in the US, and not of a rejection by the examiner. Therefore, it appears safe to assume that the court would interpret the language of the claims as giving the inventor rights over the entire scope of it's the invention (i.e. including the use of all three proteins).

The US patents have no claims pertaining to the use of claimed binding proteins to inhibit the effect of TGF- β 1 on a cell (e.g. medicament), to peptide fragments of claimed binding proteins, or to antibodies directed against claimed binding proteins. The PCT application, and the Canadian and European patents, do include these aspects of the invention. However, the European patent limits the use of the binding proteins to inhibit the effect of TGF- β 1 on a cell to therapeutic use, and does not claim as many peptide fragments as the Canadian patent.

From the literal reading of the claims, the Canadian patent appears broader and touches on all aspects of the invention found in the PCT application, whereas the European and US patents both lack claims on important aspects of the invention; no divisional patents appear to have been missed in either patent office.

B.2.8 Patent family WO9304083: Human calcium channels

The invention covers isolated DNA encoding each of human calcium channels alpha1, alpha2, beta and gamma subunits, including subunits that arise as spliced variants of primary transcripts. Cells and vectors containing the DNA and methods for identifying compounds that modulate the activity of human calcium channels are also described. The PCT application was filed in the US in 1992 and led to a single patent in Canada (CA2113203). In Europe, the PCT application led to a first patent (EP598840), a divisional patent (EP992585), and a pending patent (EP469074) of a second divisional application. In the US, the patent derived from the PCT application (US5846757) is within a chain of continuation, CIP and divisional patents. In total, there are 17 related US patents in the chain and one pending patent for which no documentation is available because it dates back to 1995 and the USPTO only started to publish pending patents in 2001 (Figure 9).

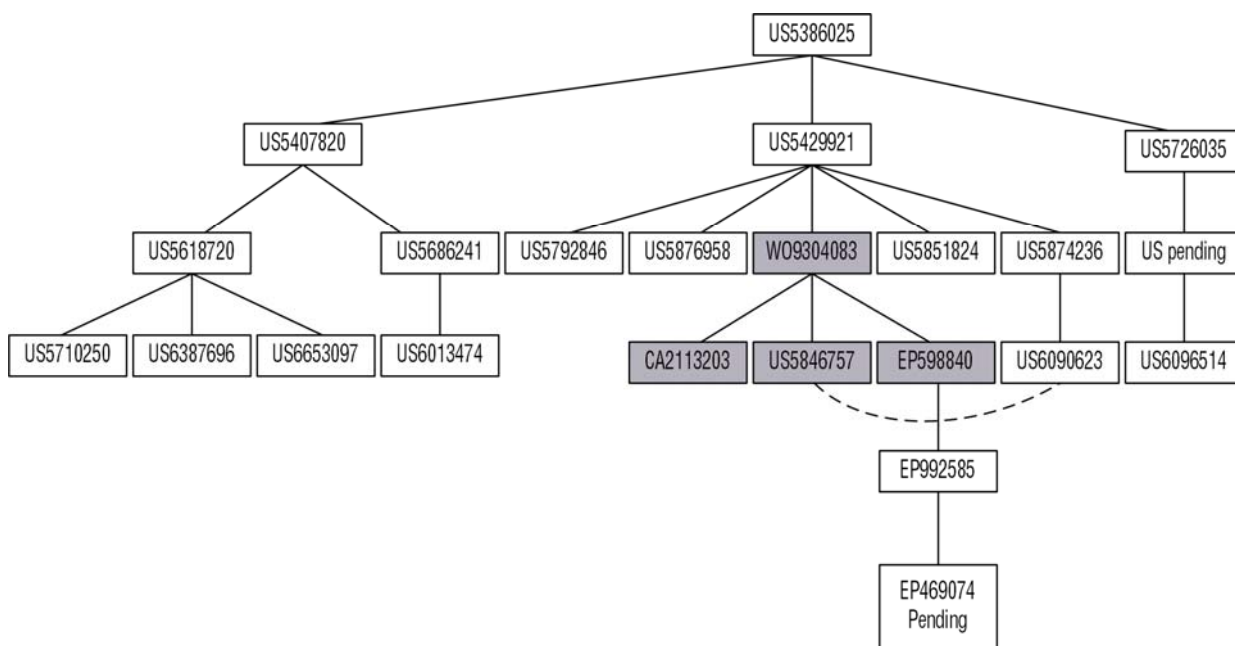


Figure 9 Phylogeny of patent family WO9304083

Source: Science-Metrix

Because of the complexity of the US chain of patents, it is impractical to compare the breadth of protection in Canada and Europe with that in the US. Indeed, it is impossible to define with certainty which US patents should be included in a comparison due to the presence of horizontal and vertical relationships (parent/child relationships), between US patents. For example, the US patent derived from the PCT application is related to US patent number 6090623, while not being directly connected with it through a divisional, continuation or CIP procedure (Figure 9). Also, if all US patents were to taken into account in a comparison, the US protection would be of greater scope, but this difference could not be interpreted in terms of examination practices.

The PCT application has 39 claims, the Canadian patent has 149 claims, and the European patents, excluding the pending patent, have 23 claims. Overall, the Canadian patent covers the same material as the PCT application, but with more detail in relation to the disclosed sequences. The European patents (including the pending patent) protect only the alpha1 and alpha2 subunits in the claim for DNA sequences and only the alpha2 subunits in the claim for substantially pure subunits. Such significant differences are difficult to explain. However, it could be that additional divisional pending patents were missed in Europe. Nevertheless, the Canadian patent is broader than the European one, being almost identical to the PCT application.

B.2.9 Patent WO9408040: Human alpha 1 adrenergic receptors

This patent family is related to the isolation and characterization of human α_1 adrenergic receptors. The invention provides methods for different applications related to these receptors. The PCT application was filed in the US in 1993 and led to a single patent in the CIPO and the EPO (CA2145182/EP663014)

and to multiple patents in the USPTO (US5861309/US6083705/US6156518/US6448011) as illustrated in Figure 10. In addition, the European patent has two divisional patents that are pending.

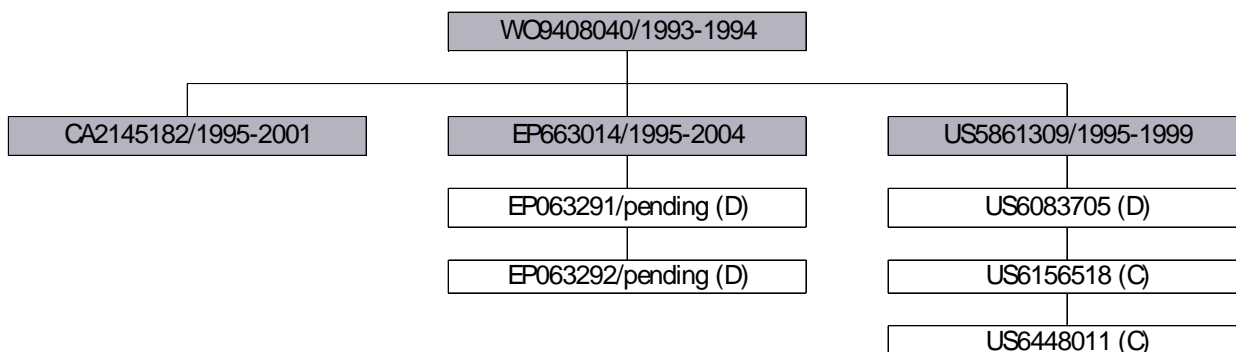


Figure 10 Phylogeny of patent family WO9408040

Source: Science-Metrix

To ensure unbiased comparison of scope across patent offices, all patents, including divisional, continuation and/or CIP patents, and divisional applications were considered. It was found that coverage was very similar in all patent offices, and in the case of minor differences these had little or no impact on patent scope. The analysis of this patent family revealed a close resemblance between the Canadian patent and the PCT application. The PCT application and the Canadian patent claim matter related to three variants of the human α_1 adrenergic receptor gene, namely α_{1a} , α_{1b} and α_{1c} . The four granted US patents together cover material related to the three variants of the gene. The European patent covers only the human α_{1c} adrenergic receptor. However, similar to the US patents, when the divisional applications are considered, all claims related to the three variants are covered. Since it is impossible to determine in which form the claims related to the α_{1a} and α_{1b} receptors will be granted in Europe, the comparison of patents was limited to claims related to the human α_{1c} adrenergic receptor.

The analysis revealed that several claims in the PCT application and the Canadian patent related to the human α_{1c} adrenergic receptor were not included in the patents granted by the USPTO and the EPO, or the two pending European applications. The missing claims relate to antisense oligonucleotides targeting the receptor, to probes of 15 nucleotides in length interacting with the receptor, and to pharmaceutical compositions and therapeutic agents based on antisense oligonucleotides to reduce the expression of the receptor. These observations suggest either a restriction requirement or a formal rejection of some claims by the European and US examiners. In the first case, the missing claims might be the subject of additional divisional patents that were overlooked because they were pending, or they might simply have been abandoned by the applicant. In the second case, the European and US examiners might have rejected these claims on the basis that the claimed invention was not commensurate with the scope of enablement provided by the application disclosure, or that the applicant was not in possession of the full scope of the claimed invention.

Whatever the reason for these differences, there is no doubt that the decisions taken by the US and European examiners led to patents of narrower scope in the US and Europe.

B.2.10 Patent WO9409828: Cloning of 5-HT4B receptor and related utilization

This patent family is related to the isolation and characterization of the 5-HT4B receptor. The invention provides methods using antibodies, probes and antisense oligonucleotides in targeting the 5-HT4B receptor. These methods are useful tools for detecting the receptor, and for screening drugs and therapeutics. The PCT application was filed in the US in 1993 and led to a single patent in the CIPO and the EPO (CA2127117/EP624100), and to multiple patents in the USPTO (US5985585/US6300087/US6432655) (Figure 11).

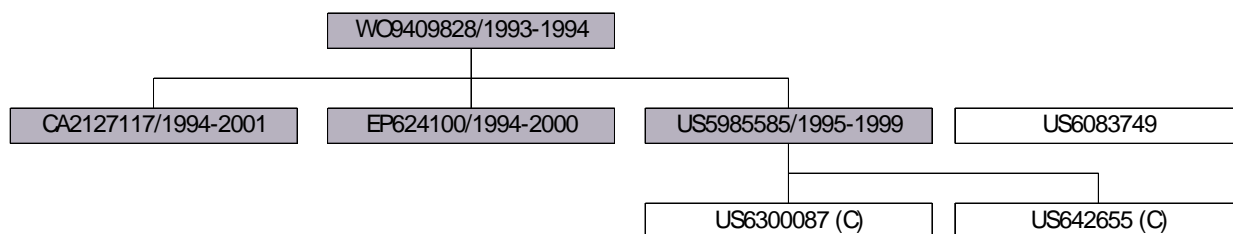


Figure 11 Phylogeny of patent family WO9409828

Source: Science-Metrix

The analysis of this patent family revealed interesting differences that might affect the breadth of patents among patent offices. The PCT application and the European and Canadian patents, claim a nucleic acid probe which is at least 15 nucleotides in length and which is capable of specifically hybridizing with a sequence encoding a human 5-HT4B receptor. However, only the European patent claims the use of this probe to screen a gene library and to isolate any gene with which the probe hybridizes. Although this claim might appear to increase the breadth of the European patent, this is not the case. Indeed, anybody who manufactured, used or sold the probe, no matter for what purpose, would infringe not only the European patent, but also the Canadian patent on the basis of the probe claim. In this case, the additional claim in the EPO patent provides only an additional protection. For example, the owner of the patent could demonstrate either that a competitor was using the probe (method claim) or that he was in possession of the probe (product claim) to prove infringement (telephone interviews). Furthermore, in the case that one of these claims was invalidated by the court, the applicant would still have some protection. Since the method claim (i.e. the use of the probe) was not included in the PCT application, this modification (i.e. amendment to the patent) might have been made on a voluntary basis or at the request of the European examiner. No matter which, the breadth of both patents remains the same, but it is important to note that the US patents cover neither of these claims.

Another major difference between the European and the other patents lay in 4 claims (claims 34 to 37) related to a monoclonal antibody binding the 5-HT4B receptor. These claims protect matters not covered by the Canadian and US patents, making the European patent broader. Because these claims were

included in the PCT application, the differences suggest either a restriction requirement or a formal rejection of some claims by the Canadian and US examiners. In the former case, the missing claims might be the subject of additional divisional patents that were missed because they were pending, or perhaps were simply abandoned by the applicant. In the latter case, the Canadian and US examiners would have rejected these claims on the basis that the claimed invention was not commensurate with the scope of enablement provided by the application disclosure, or that the applicant was not in possession of the full scope of the claimed invention.

Patents from all three patent offices include claims on a pharmaceutical composition or a method to treat abnormalities related to the expression level of 5-HT₄B receptor. However, the European patent, and the PCT application, has a supplementary claim in this area. This claim (claim 38) is the first in the group of claims on pharmaceutical composition in the European patent; and it is fairly broad and protects any type of molecule (e.g. antibodies, antisense RNA, chemical compounds) affecting the expression of this receptor. The subsequent claims in the European patents are more specific about the molecule to be used as a pharmaceutical composition, and the claims in the Canadian and US patents are almost identical to the corresponding European claims. Therefore, it appears that the European examiner granted broader claim than his opposite numbers in Canada and the US.

The US patents omit several of the claims in the Canadian and European patents. These relate to diagnostic and detection methods, processes employing antibodies, methods used to isolate the receptor, and probes specific to the receptor. The US patents focus on pharmaceutical and drug screening applications. A restriction requirement would be a likely explanation for these claims not being included in the US patents. However, no additional divisional patents, pending or otherwise, were found. It might therefore simply be that the applicant did not choose to file divisional applications for these aspects. Even if divisional patents in the US have been overlooked, the US patent still remains narrower than the European patent in terms of common claims among patent offices.

In this patent family it is clear that the EPO was less severe in granting the patent, with the CIPO ranked next, followed by the USPTO.

B.2.11 Patent WO9507922: Cytokine suppressive anti-inflammatory drug binding protein gene

The invention concerns the identification of a cytokine suppressive anti-inflammatory drug binding protein gene and describes methods and assays related to the protein encoded by this gene to screen and identify new drugs. The PCT application for this patent family was filed in the US in 1994 and led to a single patent in the CIPO and the EPO (CA2171982/EP724588), and to multiple patents in the USPTO (US5783664/US5777097/US5869043/US6033873/US5871934/US5955366/US6361773) as illustrated in Figure 12.

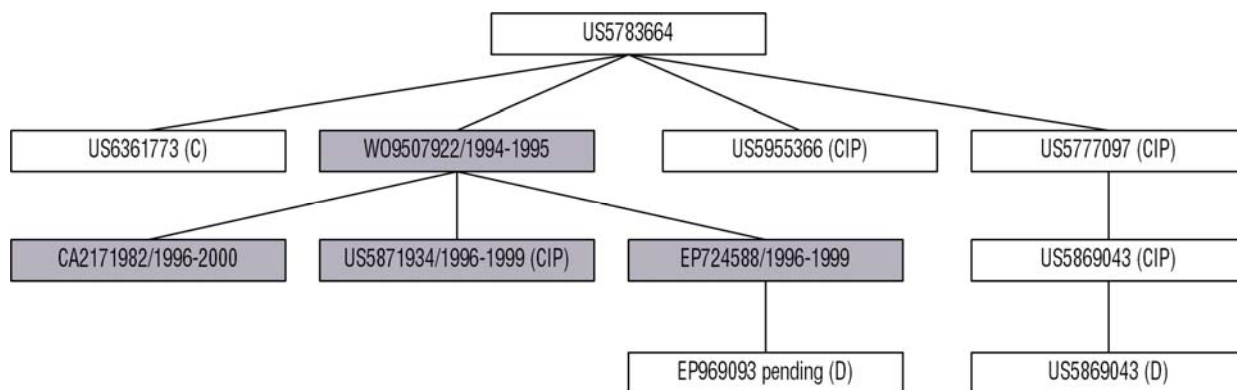


Figure 12 Phylogeny of patent family WO9507922

Source: Science-Metrix

In addition, the EPO patent has a divisional application. Obviously, this application cannot be used in order to compare the breadth of patents among patent offices since it has yet to be reviewed by a European examiner, i.e. it is pending. However, even if this patent were issued, its impact on the current analysis would be negligible, its claims being either very similar to the claims already granted in Europe, or simply non-existent in the international application. These later claims cannot be considered since they have not been assessed in all three patent offices. Thus, regardless of the European examiner's decision on the pending patent, the conclusions of the current analysis will be unchanged.

There are major differences between the PCT application and patents granted by the CIPO, the USPTO and the EPO. For instance, claim 29 of the PCT application, which describes the utilization of a transgenic animal, does not appear in any of the patents issued in this family. This suggests that patent examiners from all three countries considered that the applicant had not sufficiently described the invention over its entire scope, and particularly with regard to the transgenic animal, or that the applicant was not in possession and control of the transgenic animal at the time of examination.

In addition, all patents include three claims not found in the PCT application. Thus, the applicant has likely made voluntary amendments in all jurisdictions, all of which were accepted by the relevant examiner. These claims protect any amino acid sequence with at least 85% identity (first claim), at least 90% identity (second claim) and at least 95% identity (third claim) with the sequence provided in the written description. At first glance, these three claims may seem redundant since sequences with at least 90% or 95% identity with the described sequence are captured by the claim requiring at least 85% identity. However, these claims offer greater protection to the applicant. According to patent attorneys in the field of biotechnology, it is a common and a good practice to get claims of different scope because an applicant can be sued in order to invalidate its patent. In such a case, the court will investigate on a claim by claim basis and if it finds the broader claims to be invalid, in this case the claims requiring at least 85% and 90% identity, the narrower claim will persist, in this case the claim requiring 95% identity, and the applicant will still have some degree of protection.

Besides differences between the granted patents and the PCT application, mostly minor differences were observed between the Canadian, the European and the US patents. One difference, however, is significant and relates to a method for the identification of a compound that interacts with the cytokine suppressive anti-inflammatory drug binding protein (CSBP). The PCT application, the European patent and the US patent present a method based on physical interaction between a candidate compound and the CSBP and a method based on the biological effect of the test compound on the CSBP as detection tools to validate the potential of the compound as a drug. The Canadian patent covers only the method based on the enzymatic assay (i.e. the biological effect).

In claiming these methods, the US patent specifies that the protein to be used in the assay can be any conservative substitution variants or natural allelic variants of the claimed protein. Similarly, the European claim, and the PCT application, do not specify any threshold regarding a level of identity for determining which protein variants can be used in the assay. Thus, the European patent covers the use of any protein so long as it is a CSBP (e.g. conservative substitution variants or natural allelic variants) while the Canadian patent claims the use of any protein with a sequence sharing at least 85% identity with the claimed protein.

At first glance, the Canadian claim appears stricter and more specific than the US and European claims, which cover any sequence related to the claimed sequence without specifying a minimum degree of identity between the two, although it is difficult to compare the criteria of 85% identity in the Canadian patent with the criteria of any CSBP, conservative substitution variants or natural allelic variants of the European and US patents. Indeed, the formulation in the US and European patents leaves room for a subjective interpretation of the claims by the court. For example, a person skilled in the art might find a sequence sharing 80% identity with the claimed sequence to fall within the scope of the invention, while another person skilled in the art might find a sequence sharing 90% identity with the claimed sequence to be invalid (telephone interviews). Furthermore, courts in different countries apply different national laws such that the interpretation of could vary among countries (telephone interviews). Based on the opinion of experts interviewed, no conclusions could be drawn about this difference or to infer any implication for the breadth of the patents.

Therefore, the Canadian, European and US patents all contain modifications, relative to the PCT application, in two areas, a transgenic animal, and levels of identity when claiming the CSBP. It can be seen then, that the examiners in the three patent offices examined the application in similar ways although the Canadian examiner applied greater stringency regarding methods of identifying active drugs on the CSBP.

B.2.12 Patent WO9628548: Receptor activation by gas6

The present invention relates to the identification and characterization of growth arrest-specific gene 6 (gas6), which is an activator of Rse and Mer receptor tyrosine kinase. Thus, gas6 polypeptides could be used to enhance proliferation, differentiation or cell survival. In addition, the invention provides kits and

articles of manufacture including gas6 polypeptide to treat different types of cells. The PCT application for this patent family was filed in the US in 1996 and led to a single patent in the CIPO and the EPO (CA2214629/EP815224) and to multiple patents in the USPTO (US6169070/US5580984/US5142056/US5892052/US6150530/US6531610/US6667404) (Figure 13).

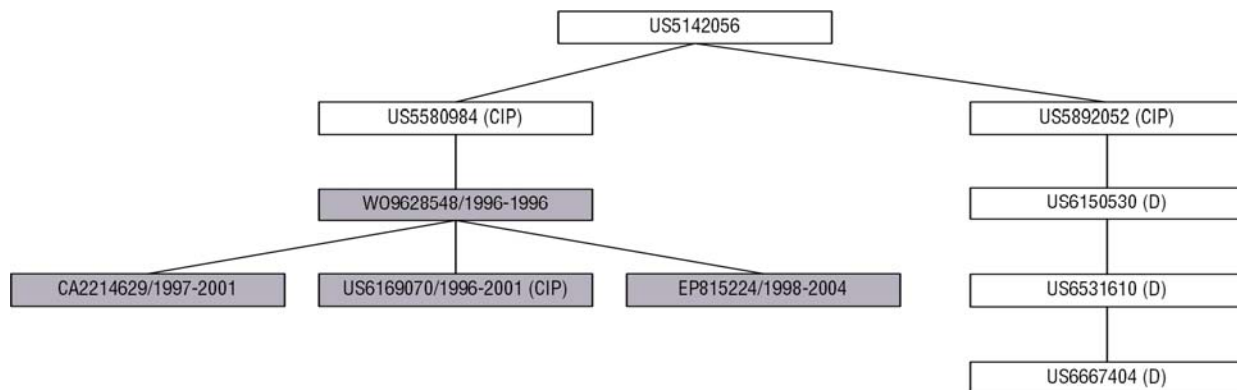


Figure 13 Phylogeny of patent family WO9628548

Source: Science-Metrix

Comparison of US patents with the patents granted by the CIPO and the EPO was difficult. The claims in the seven US patents taken together were very different from those in the PCT application and in the Canadian and European patents. The majority of US patents claim chemical formula and enumerate all potential variants of the molecule structure in terms of chemical groups. Since these claims were unique to the US patents no comparison could be made with either the Canadian or European patents. Further searches in the USPTO database were conducted and two additional US patents (US6255068/US6211142) were found. These two US patents contain claims that are in part very similar to those in the PCT application and in the Canadian and European patents, but also contain unrelated claims. Unfortunately, these two patents were not linked (by divisional, continuation and/or CIP procedures) to the US patent derived from the PCT application (US6169070). Since the method developed by Science-Metrix is based on analysis of patents belonging to the same family and relating to the same PCT application, the two independent US patents could not be considered. Given the complex situation in the US, the analysis focused on the differences that existed between the Canadian and European patents.

Analysis of the first claim in the Canadian and European patents revealed an important difference affecting patent scope. The Canadian claim, which is identical to the PCT application, protects variant gas6 polypeptides lacking one or more glutamic acid residues from the A domain of native gas6. In the European patent, the claim covers a variant, as does the Canadian claim, but also a fragment of gas6, wherein the variant or fragment must share at least 75% sequence identity with native gas6 with the amino acid sequence described in the disclosure.

Thus, the European claim protects the matter as claimed in the Canadian claim, but in addition covers any sequence sharing at least 75% identity with the gas6 protein. Since the additional matter covered in the European patent was not part of the PCT application, an amendment to the claim, whether voluntary or at the request of the European examiner, must have been made by the applicant at the national phase. Given that the amendment resulted in the widening of the European patent, it is unlikely that the examiner would have requested such a modification. If the amendment was made on a voluntary basis by the applicant only in Europe, then the difference between the Canadian and European patents cannot be assessed on the basis of different patent offices' practices. However, if the voluntary amendment was made in each region, then it would appear that the European examiner was more flexible than the Canadian examiner, thereby leading to a patent of greater scope in Europe. This latter hypothesis seems more likely considering that an applicant usually seeks the same scope of protection across the countries where he submits its application. Although no conclusion will be drawn regarding what happened in the US, it is of interest to note that the additional matter covered by the European patent did not appear in any of the 9 US patents, or the two unrelated patents.

Minor differences were also observed. For instance, claim 12 in the Canadian patent, and the PCT application, specify that the method used to produce recombinant gas6 variants is to be carried out in the absence of Vitamin K; the claim describing the production method in the European patent is not accompanied by any such dependent claim. However, whatever its reason, this difference has little or no impact on patent scope given that the specification regarding Vitamin K is in a claim depending on a more general parent claim.

Another difference relates to a methodological detail regarding the use of a gas6 variant as a medicament for different types of cells. The patents granted by the EPO and CIPO claim the use of a variant gas6 polypeptide as a medicament for activating the Rse or Mer receptor of a cell. Both patents have a set of independent claims covering this, in which the type of cell to be treated is left open. However, in subsequent dependent claims, the European patent specify that the cells to be treated include glial cells, neural cells, hematopoietic cells, mononuclear cells and cells of the testes, ovary, prostate, lung or kidney, while the Canadian patent focus on mononuclear cells only. Therefore, in the event that the broader independent claims in the Canadian and European patent would be invalidated in court, the remaining European dependent claim would provide broader protection than the corresponding dependent claim in Canada.

Based on the differences identified, the European examiner appears to have been more flexible than the Canadian examiner in issuing a broader patent. However, it could be that the major difference observed in the first claim was the result of a voluntary amendment by the applicant only in Europe, in which case the European patent would be only slightly broader than the Canadian patent.

B.2.13 Patent WO9729131: Human antibodies against TNF- α

This patent family focuses on methods of synthesizing recombinant human antibodies binding human TNF- α , and on characterization of such antibodies. These antibodies are useful for the detection and inhibition of TNF- α and they could be used as therapeutic agents. The PCT application was filed in the US in 1997 and led to a single patent in the CIPO and the EPO (CA2243459/EP929578), and to multiple patents in the USPTO (US6258562/US6090382/US6509015) as illustrated in Figure 14.

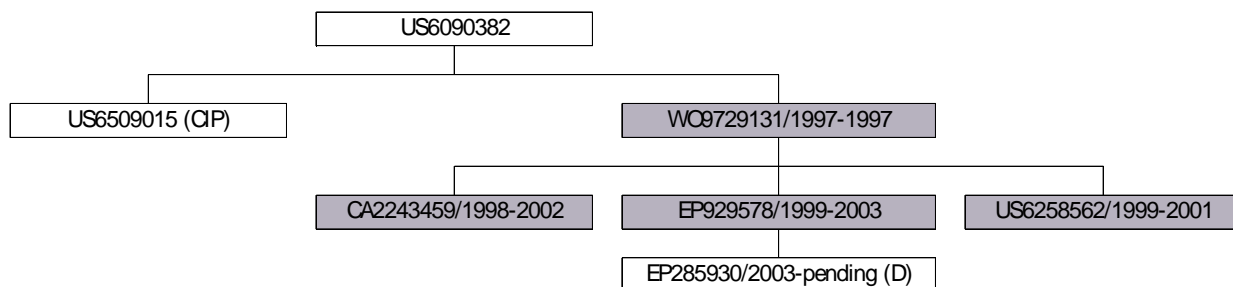


Figure 14 Phylogeny of patent family WO9729131

Source: Science-Metrix

Furthermore, there is a divisional application for the European patent which is pending and thus cannot be used in order to compare the breadth of patents among patent offices since it has not yet passed through the examination process. However, in the event of this patent being granted, its impact on the current analysis would be negligible as considering its claims are either very similar to the claims already granted in Europe or simply are not in the international application. These claims cannot be considered since they have not been assessed in all three patent offices. Thus, regardless of the European examiner's decision on the pending patent, the conclusions of the current analysis are unchanged. It should be noted that all related US patents are considered as a single patent in the current analysis.

Although the Canadian and European patents were very similar, there is a significant difference between the two relating to a claimed recombinant human antibody, or antigen binding portion thereof, for use in neutralizing the activity of human TNF- α , but not human TNF- β . The Canadian claim uses a fairly broad interpretation providing protection for any recombinant human antibody, or antigen binding portion thereof, which has the capacity to neutralize human TNF- α , but not human TNF- β (claim 21). In contrast, the European claim provides a specific description of the recombinant human antibody, or antigen binding portion thereof, to be used in neutralizing human TNF- α , but not human TNF- β . Indeed, the European claim states:

A recombinant human antibody, or antigen binding portion thereof, that neutralizes the activity of human TNF- α but not human TNF- β and has the identifying characteristics of an antibody as defined in any one of claims 1 to 18. (EP929578, claim 19)

Within each of the first 18 claims of the European patents, the antibody is characterized by information on, for example, its sequences, dissociation values, isotypes, and function. Although the first 20 claims in the Canadian patent provide similar information on the antibody, claim 21 of the Canadian patent does not refer to them in claiming the antibody. Thus, the European claim offers a narrower protection to the applicant relative to the Canadian claim. Since the Canadian patent is identical to the PCT application with respect to this claim, it is likely that the European examiner imposed this reduction in breadth, mirroring the stricter practices in the EPO. However, as mentioned earlier, narrower claims are more difficult to invalidate, and as such the protection afforded by the European claim is more solid. No equivalent claim was found in any of the three US patents. Therefore, a divisional US patent, maybe a pending one, might have been missed.

The most striking difference between the group of US patents and the corresponding patents in Canada and Europe consists in the absence in the US patents, of the claim on the use of the recombinant antibody, in combination with a long list of drugs for the treatment of diverse diseases. The US patents only claims the use of the antibody to treat disease, as a standalone product not to be used in combination with other drugs. This is an interesting difference since it is likely to be the result of a rejection by the US examiner on the basis that the claim, as found in the Canadian and European patents, was not commensurate with the scope of enablement provided by the application disclosure. Indeed, the applicant most likely provided sufficient information on how to use the antibody in combination with the hundred of drugs listed, to allow a skilled individual to perform the invention in treating patients. However, it is not possible to completely rule out the possibility that the US examiner would have made a restriction requirement, thereby forcing the applicant to either eliminate this portion of the claim or file a divisional application. Since, the portion removed from the US claim does not, in our view, represent an invention distinct from the remaining portion of the claim, this latter hypothesis is not very likely.

Therefore, the Canadian patent is the broadest followed by the European patent. The US patents would be stricter unless some divisional patents have been missed.