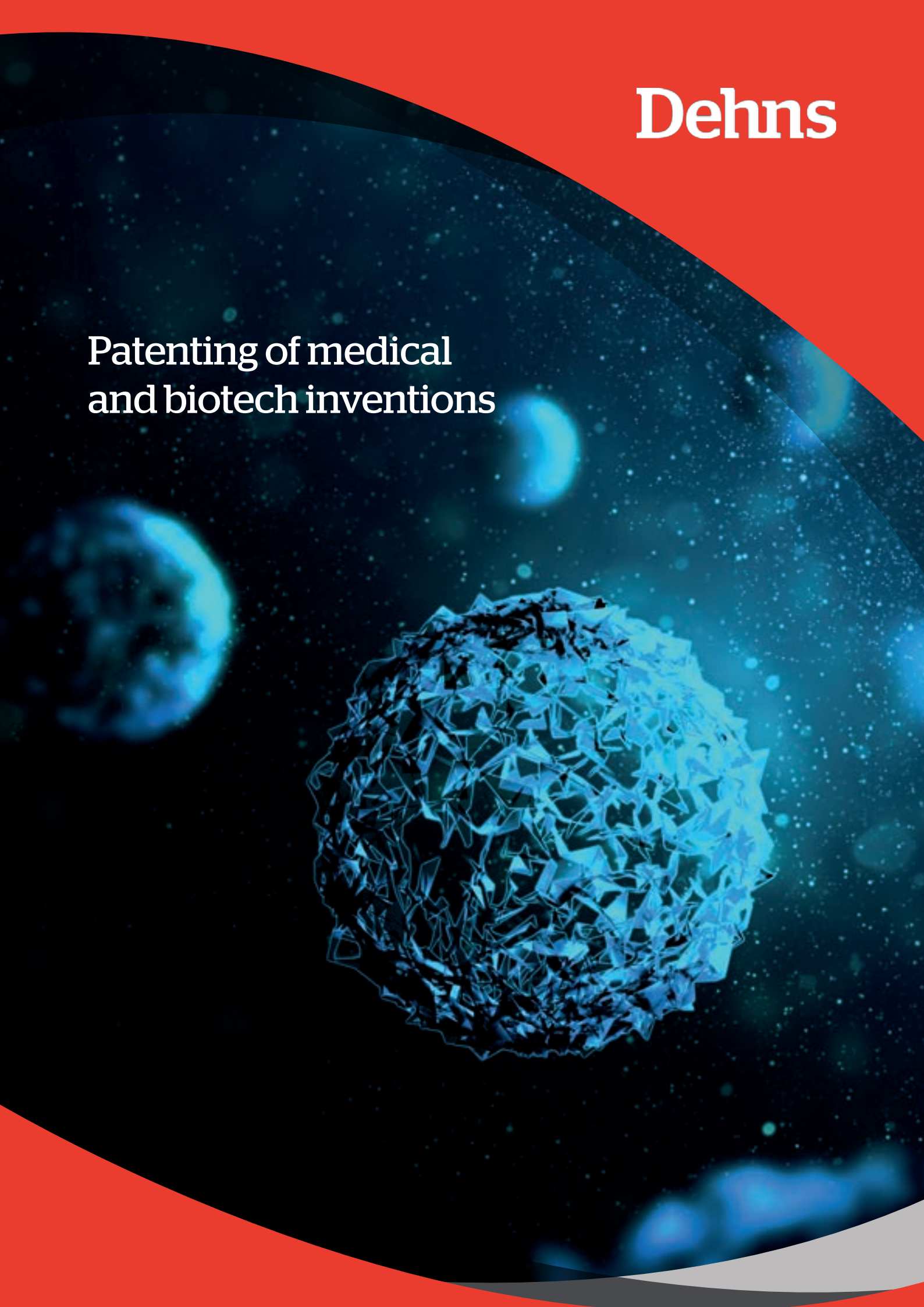
Dehns

Patenting of medical and biotech inventions



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Introduction

The patent system rewards inventors who produce useful new inventions by granting them the right to stop others from copying their invention for up to 20 years. This time allows inventors to recoup their research and development costs. Patents are vitally important for the pharmaceutical industry because it can take up to US$1 billion to bring a new therapeutic drug onto the market. Without the patent system to protect such investments, there would be no new medicines! Patents and patent applications are also particularly important to small biotech companies because they are often some of the few valuable assets that biotech companies can present to potential investors when seeking investment.

In our "Dehns Guide – The Patent System" (see www.dehns.com), we have given details of the patent examination process and some information on related issues such as determining ownership of an invention and freedom to operate considerations. Whilst these general issues apply to all inventions, there are a number of issues which only apply to inventions in the medical and biotech fields.

Particular issues which apply to medical and biotechnological inventions include the following:

- How are DNA and protein sequences claimed in patent applications?
- How can you claim new methods of therapeutic treatment?
- How much experimental data do you need to support a therapeutic invention?
- Can you claim new micro-organisms?
- Is the morality of the invention relevant to its patentability?

The aim of this booklet is to provide inventors and those applying for patents with more information on what can be patented in the medical and biotech fields, and details of some of the special requirements and rules which apply in these fields.

For those who are not very familiar with the language of patents, a Glossary of useful terms and abbreviations is included at the end of this guide.

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General issues

What is a patent application?

A patent application is essentially a 20-50 page book which describes an invention in a combination of legal and scientific language. After the patent application has been filed, examined and, if necessary amended, the text of the granted patent will be based on the text of the patent application. All patent applications around the world have the same basic format and they are usually made up of the following sections (in this order).

Field of the invention

The patent application usually starts with a single paragraph which gives a very brief summary of what the invention relates to.

Background

The next section describes the background to the invention. Usually, there will be a discussion of the field of technology that the invention relates to, details of the problem that the invention addresses and information on how people have previously tried to solve that problem. The aim of this section is to educate the Patent Office Examiners about the field of the invention, and (hopefully) to enable the Examiners to appreciate the merits of the new invention.

Statements of Invention

The Statements of Invention are concise definitions of the invention; they will correspond to the main claims (see below). These Statements are normally followed by details of examples of the key features of the invention and which examples are most preferred.

Examples

The Examples section serves two main functions:

i. To provide details of how to put the invention into practice, and
ii. To justify the breadth of the claims.

This section is written in standard scientific language, in the same level of detail as that which would be included in a scientific paper.

Claims

The most important section of the patent application is the claims section.

The claims are short sentences or paragraphs which provide concise definitions of the invention in words (not pictures or other diagrams). The claims usually have a cascading structure with claim 1 being the broadest claim (i.e. of widest scope), with subsequent claims adding further features to the invention, thus narrowing the scope of the claims.

The claims will usually cover more than what the inventor has made. In particular, simple modifications and variants of the invention should be covered by the claims in order to ensure that a competitor cannot get easily round the granted patent by making such modifications/variants.

During the examination of the patent application, it is primarily the scope of the claims which will be considered by the Patent Office Examiners (i.e. to see whether what is being claimed is novel and inventive). After the grant of the patent, it is the claims that will define the scope of the acts that the Applicant can stop others from doing.

Figures

Any graphs (for example, illustrating experimental data from the Examples) and technical drawings are included at the end of the patent application in the Figures section. However, the legends to the Figures are usually placed just before the Examples.

Criteria for patentability

In order to be patentable, the invention (as described in the patent application) must satisfy certain criteria. These criteria are basically the same in all countries around the world, although there are some important exceptions.

The main criteria – which are examined by the Patent Office Examiners – are summarised as follows.

Novelty

The invention (as defined in the claims) must be new over everything that is in the public domain anywhere in the world before the date that the patent application is filed at the Patent Office. (Such public information is often referred to by Patent Attorneys as the 'prior art'.)

For example, the previous publication of scientific papers or conference abstracts, oral or poster presentations relating to the invention, non-confidential information about the invention given to potential buyers and public demonstrations of the invention can all destroy the novelty of the invention. This is why it is vitally important to keep all details of the invention confidential until a patent application has been filed.

(One important exception to this rule is in the US, where inventions can – under certain circumstances – still be considered to be novel if the US patent application is filed within one year of a public disclosure of the invention.)

For novelty to be destroyed, the prior art must disclose every feature of the claimed invention. Novelty is a black/white issue: if there is at least one difference between what is being claimed and what has previously been disclosed, then the claimed invention is novel.

For example:

Prior art		Invention	
PCR primer	CGTTATGCG	CGTTATGC**T**	Novel
Peptide	MALGDGG	MAL**A**DGG	Novel

Inventive step

The invention (as defined in the claims) must also be inventive, that is, it must not be obvious, bearing in mind what is in the public domain before the filing date of the patent application. If the invention gives an unexpected advantage or a surprising result, this is often a good indication that the invention is not obvious.

Obviousness must be judged through the eyes of a person (also known as 'the skilled person') who is familiar with all general techniques in the area of technology of the invention but who is incapable of any spark of inventive thought. Whether an invention is obvious or not is often the subject of much argument between Patent Attorneys (on behalf of their clients) and Patent Office Examiners.

One test for inventive step which is often used by Patent Office Examiners (especially in Europe) is whether the invention is obvious to try with a reasonable expectation of success.

Considering the above 'novelty' examples further, if the change of one nucleotide leads to a PCR primer with a greatly-increased half-life, then such a primer might be considered to be inventive. Similarly, if the change of one amino acid in a peptide leads to an unexpectedly large increase in the activity of that peptide, then the inventiveness of that peptide might be acknowledged. Hence even small changes can potentially be patentable.

Clarity

The language that is used in the claims to define the invention must be clear enough so that a person who is familiar with the general area of technology of the invention (i.e. the 'skilled person') can readily understand what is being protected in the patent application and what is not.

Enablement

After reading the patent application, and taking into account common general knowledge at the filing date of the patent application, the skilled person must be able to put all aspects of the claimed invention into practice.

Support

The claims of the patent application will usually cover more than merely what the inventor has made. In particular, simple modifications and variants of the invention will also be claimed. Although it is not necessary to show in the patent application that examples of every modification and variant have been made, the Examples section should include a range of examples which show that such modifications/variants can be made and would be expected to work. (Further information on this point is given below.)

How much data do you need in the patent application?

The Examples section of medical and biotech patent applications is particularly important. There are specific requirements which apply to this section. This is one of the reasons that medical and biotech patent applications are often a lot longer and more complex than patent applications in other areas of technology.

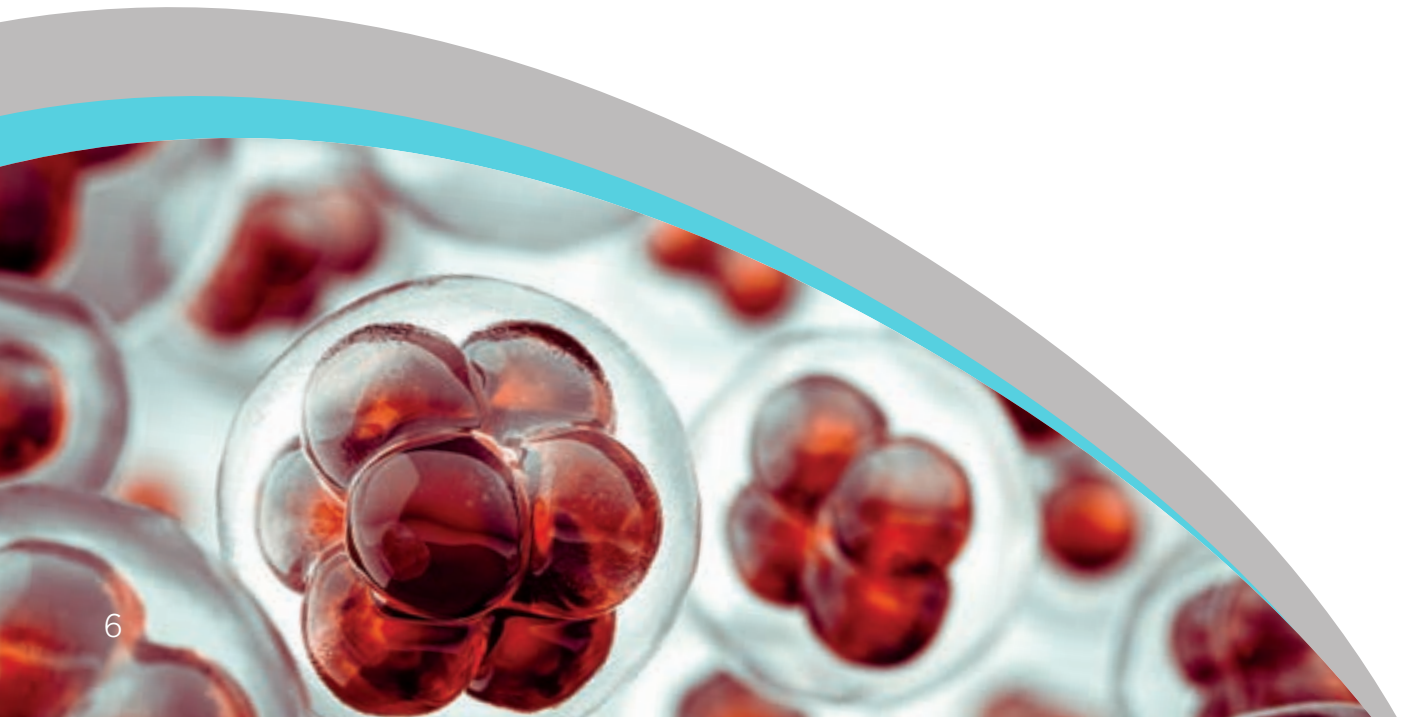
Essential criteria

The Examples section of the patent application must provide the following information:

i. It must provide details of how to put the claimed invention into practice, i.e. it must satisfy the 'enablement' requirement. For example, if the claims relate to the use of a complex chemical structure, then the Examples section must show how that chemical structure can be made.

ii. For inventions which relate to new uses of known medicaments, the Examples section must demonstrate that the medicament is efficacious for that new use. For example, if methods of treating cancer with a particular drug are already known, and methods of treating diabetes with the drug are now being claimed, then the patent application must demonstrate that the drug can be used to treat diabetes. (See below for the level of information that is required.)

Details of (i) and (ii) must be included in the patent application when it is filed.



Other criteria

It is often also useful to include data in the Examples section on the following:

iii. Data to justify the breadth of the claims in order to satisfy the 'support' requirement. For example, if the invention is based on the elucidation of a novel biochemical pathway in mice, it would be useful to include data to show that the same biochemical pathway is present in humans.

iv. Comparative data showing results obtained with the invention compared to results obtained using a previously-known example which is close to the invention (preferably against the **closest** previously-known example). Such data can be used to highlight the inventive step of the invention. Ideally, the results obtained with the invention are shown to be particularly advantageous or unexpectedly efficacious.

What level of data is needed?

Patent applications are generally filed at an early stage in the development of the product, method or process (primarily to ensure that the invention is still novel at that time). For example, patent applications for new drugs are generally filed during the drug development stage, i.e. well before clinical trials in humans have started and possibly even before the lead compound has been identified.

The level of data that Patent Offices expect to see in patent applications is therefore relatively low. It may, for example, be *in vitro* data based on a key biochemical pathway which the new drug or antibody blocks, or basic *in vivo* data produced in animal models. It must be reasonable (or plausible), however, for the person of average skill in the relevant area of technology to expect that the invention will work based on the information contained in the patent application.

When to file the patent application?

In general, it is important to file one's patent application as early as possible in order to obtain an early filing date. However, for inventions in the medical and biotech fields, the requirement to include an appropriate level of data in the patent application is equally important, if not more so. The competing requirements of getting an early filing date and obtaining an adequate level of data have to be balanced in each case. For inventions made in academia, the pressure to publish also has to be considered.

Morality issues

Most countries have patent laws which prohibit – directly or indirectly – the patenting of immoral inventions. However, the concept of morality is difficult to define: attitudes to morality vary widely between different countries and different religions, and they also change over time.

The notion that patents should not be granted for immoral inventions is based on the generally-accepted view that the patent system should not condone the production of immoral inventions. One example which is often quoted is that it would be inappropriate to grant a patent on a letter-bomb.

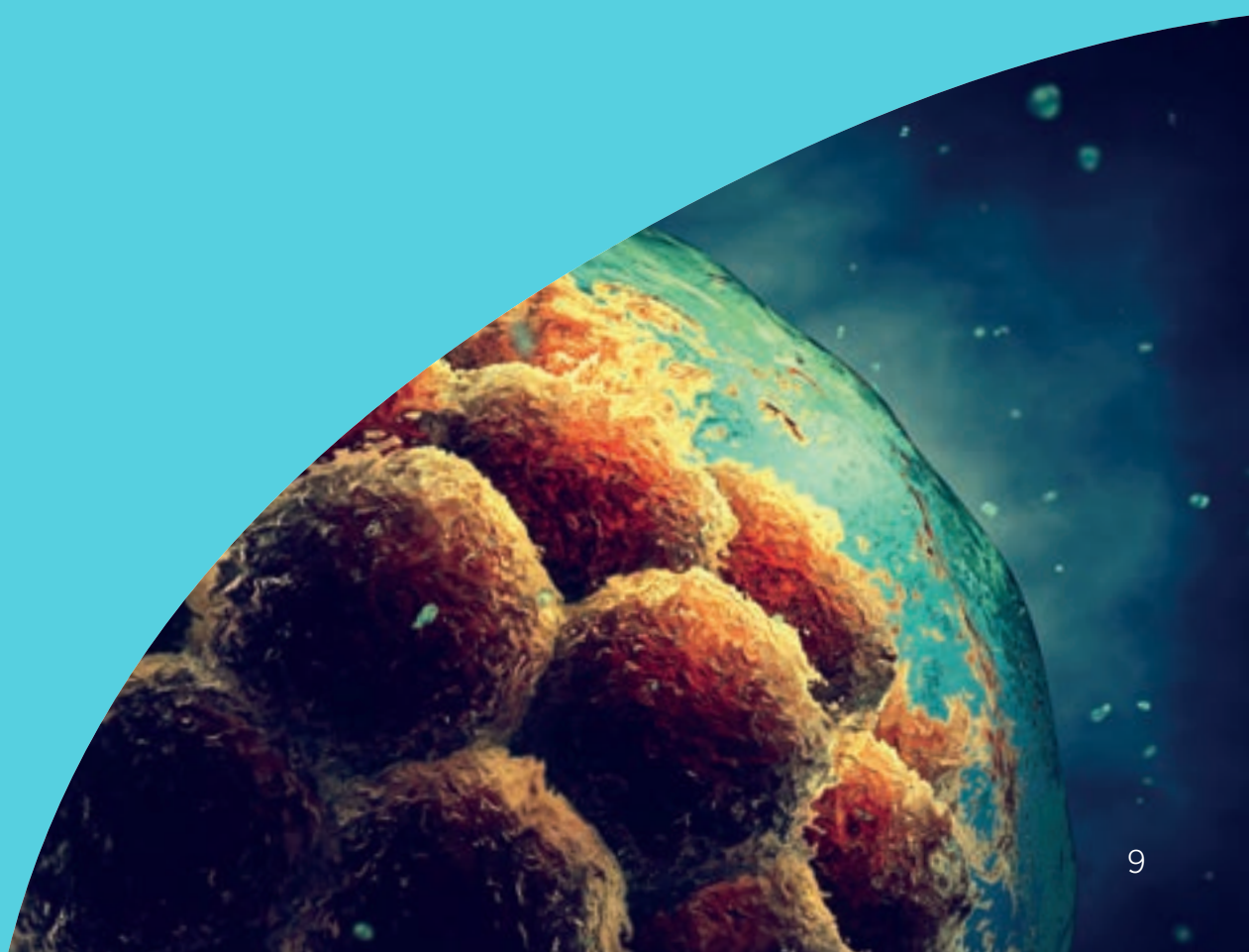
Over the past few decades, the Patent Offices have had to address the morality of patenting proteins, genes and transgenic plants; and the Patent Offices have not accepted arguments that it is immoral to patent these products. As for transgenic animals, the European legislators have developed a balancing test: does the benefit to mankind from the use of the transgenic animal outweigh any suffering caused to the transgenic animal? On the other hand, the European legislators have used a 'red-line' test for the patenting of human embryonic stem cells: if such cells can only be obtained by killing a human embryo, then inventions based on such cells are considered to be immoral and hence not patentable (irrespective of any potential beneficial uses that such cells could have). The human body, and the various stages of its development (e.g. blastula, embryo, foetus), are also not patentable.

Since the concept of morality varies over time (*in vitro* fertilisation and heart transplants were initially considered to be immoral by some when they were first developed), the patent courts try to maintain a flexible approach to this issue.

Disclosure of origin of biological material

A number of countries have introduced a requirement into their patent laws that states that the ‘origin’ or ‘source’ of all biological or genetic material referred to in patent applications filed in those countries must be identified in those patent applications.

This requirement is likely to be introduced soon on an international level, but the precise details of how such a system is to be implemented have not yet been resolved. Until that time, it is prudent to include details in patent applications of where the biological or genetic material was obtained, and to ensure that prior informed consent for the use of that material has been obtained from the appropriate party or authority.



Search and examination of patent applications

The following is a simple summary of how a patent is obtained in a single country.

Filing the patent application

Once the text of the patent application has been finalised between the inventors and their Patent Attorney, it is filed at a Patent Office (e.g. at the UK IPO) and it will then be assigned to a Patent Examiner. Like Patent Attorneys, Patent Examiners have scientific backgrounds and are experts in patent law.

Search report

In order to assess the novelty and inventive step of the claimed invention, the Patent Examiner will first carry out a search to determine what was in the public domain before the date that the patent application was filed. Such searches often include scientific journals, trade journals and published patent applications.

The Patent Examiner will then produce a Search Report which lists the documents which have been found. This is then sent to the Patent Attorney, usually together with copies of the cited documents.

Examination report

The Search Report is often accompanied by an Examination Report from the Patent Examiner giving his written opinion on the novelty and inventive step of the claimed invention, the clarity of the language used in the claims, and on whether or not the level of data included in the patent application is adequate. (If the Search and Examination Reports are not issued together, then the Examination Report will issue later.)

These Reports often raise a complex mixture of technical and legal objections which, at first sight, can look quite daunting. However, with appropriate guidance from a Patent Attorney, ways of dealing with the objections raised can usually be found.

A written reply to the Examiner's Examination Report must be filed (usually within a set deadline); this reply will generally be a mixture of arguments against the Examiner's objections and amendments/ restrictions to the patent claims. One or more Reports and replies thereto might be necessary before all of the Patent Examiner's objections are overcome (assuming that they can be), and the patent is granted.

Grant

Once the patent application has been granted, the text of the patent application (which will probably have been amended during the examination process) then becomes the text of the granted patent.

After grant (and not before), the Applicant is given the right to stop others from making, using or selling the invention – as defined in the patent claims – but only in the countries where patents have been granted. Such rights have to be enforced by the Applicant in the courts.

Patenting of chemical and biotech products

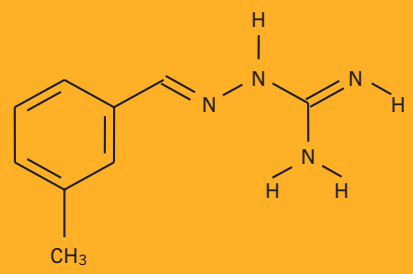
Medicines

Medicines can be patented in the same way as any chemical product, that is, by reference to the chemical name or structural formula. As with all inventions, it is also important to capture variants and modifications of the new medicine in order to ensure that competitors cannot easily get around the patent.

Novel medicaments

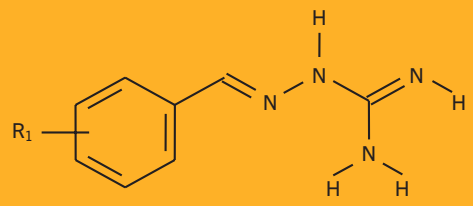
New chemical entities are generally claimed by reference to a core structural formula and variants of that formula.

For example, consider a new lead compound which has the following structure:



If the CH3 group can in fact be placed at any point around the phenyl ring and it does not have to be CH3, then it would be appropriate to claim the compound as follows:

1. A compound of Formula I:



wherein R1 is a C1-20 alkyl group or amino, or a pharmaceutically-acceptable salt thereof.

It should be noted that the above claim relates not only to the lead compound, but to a family of compounds in an attempt to claim all related compounds which have the same desired effect. If all such related compounds (e.g. variants, derivatives, salts, isomers, etc.) are not claimed, then it may be very easy for a competitor to get around the scope of any resulting patent.

The Examples of the patent application would need to demonstrate how the above class of compounds can be made. Furthermore, some data would need to be included to show that the claimed compounds have efficacy in the treatment of the disease for which the compounds are to be used (e.g. efficacy data on a selection of compounds which are representative of the family of claimed compounds; you do not have to test them all).

In a patent application which claims a new medicament, it is common practice also to claim methods of treatment using the new medicament and possibly also processes of making the medicament. As long as all of these claims are based around the new medicament, then it is generally possible to include all such claims in a single patent application.

DNA and proteins

DNA and proteins are treated by the Patent Offices as chemical entities.

If they are claimed in isolated or purified form, then that form will be novel over the forms that are present in the organism from which they are obtained. Patents may also be granted for artificial DNA constructs such as cDNA and genetically-engineered proteins. The patent application must give details of the use of the new gene or protein.

Sequence Listings

If the patent application mentions DNA/RNA sequences of 10 or more nucleotides or polypeptide sequences of 4 or more amino acids (whether or not such sequences are claimed in the claims section), then the patent application must be accompanied by a "Sequence Listing", which lists the sequences in a defined format and gives them Sequence Identifier Numbers (SEQ ID NOs). The Sequence Listing must be filed in electronic format so that the Patent Offices can readily compare the sequences in the Sequence Listing against those in its databases.

If such sequences are referred to in the patent claims, then the SEQ ID NOs should be used (instead of reciting the full sequences in the claims).

DNA sequences

Examples of claims to DNA sequences include the following:

1. An isolated nucleic acid molecule having a sequence identity of at least 90% with SEQ ID NO: 1 and which encodes a melanocortin receptor.
2. An isolated nucleic acid molecule which codes for a polypeptide of SEQ ID NO: 2.

Claim 1 above covers not only a DNA or RNA sequence of SEQ ID NO: 1, but also variants of that sequence which encode the specified receptor. (It is necessary to include a functional definition of the nucleic acid molecule (e.g. "which encodes a melanocortin receptor") in order to exclude molecules which are non-functional.)

Polypeptide and peptide sequences

Examples of claims to polypeptide and peptide sequences include the following:

3. A purified polypeptide comprising an amino acid sequence having at least 95% sequence identity with SEQ ID NO: 2 and which binds FSH with a K_i of less than 10 nM.
4. A peptide of formula X1-X2-A-G-C-X3-L-V-F-X4, wherein
   X1 is acetyl or is absent;
   X2 is L or I;
   X3 is F or W; and
   X4 is amide or is absent.

Claims to vectors and host cells

If the invention is based on the identification of a new gene or polypeptide, then patent claims to vectors or plasmids comprising the claimed genes and host cells comprising such vectors/plasmids will generally be allowed in the same patent application.

Genomic DNA patents in the US

In 2013, the US Supreme Court ruled that US patents could not be granted for genomic DNA because such genomic DNA was considered to be a "product of nature". Since that time, the USPTO has extended this principle to reject patent applications on any product of nature (e.g. a new drug isolated from a plant).

It is important to note that this ruling only applies to US patents; it does not affect the patentability of genomic sequences or other natural products in other countries. Furthermore, the ruling does not affect the patentability of artificial DNA constructs (such as cDNA or of expression vectors comprising genomic DNA), or of patent claims to methods of using genomic DNA.

Antibodies

There are several ways to claim antibodies in patent applications: these range from purely functional definitions based on the antibody's binding affinity, through to defining the complete heavy and light chain amino acid sequences of the antibodies. Increasingly, the Patent Offices are requiring more structural (i.e. sequence) information in the patent claims as it becomes more recognised that small changes to the antibody's sequence can have profound effects on its properties.

Antibodies defined by antigens

Traditionally, the European Patent Office (EPO) has granted claims of the following format, particularly if the protein antigen itself satisfies the criteria for patentability:

1. An antibody which binds specifically to protein X.

In such claims, the antibody is being defined indirectly, that is, by reference to the antigen to which it binds. Care needs to be taken, however, to ensure that such claims do not inherently cover known antibodies, particularly if the protein is part of a family of well-known proteins (e.g. GPCRs) and antibodies against other proteins are already known. In such circumstances, a claim of the following format should be considered:

2. An antibody which binds to protein X, but not to protein Y.

   (where protein X is the novel protein and protein Y is a known one having epitopes in common with the novel protein.)

Antibodies defined by epitopes

In cases where the antigen to which the antibody binds is already known and some antibodies which bind to that antigen have already been publicly disclosed, a general claim to all antibodies to that antigen will lack novelty. However, broad claims to antibodies that are directed to specific epitopes on that antigen might still be possible (assuming that the known antibodies are not directed to those epitopes).

Epitopes may be defined by reference to a specific monoclonal antibody which binds to that epitope or by reference to the continuous or discontinuous amino acid sequence of the epitope in the antigen.

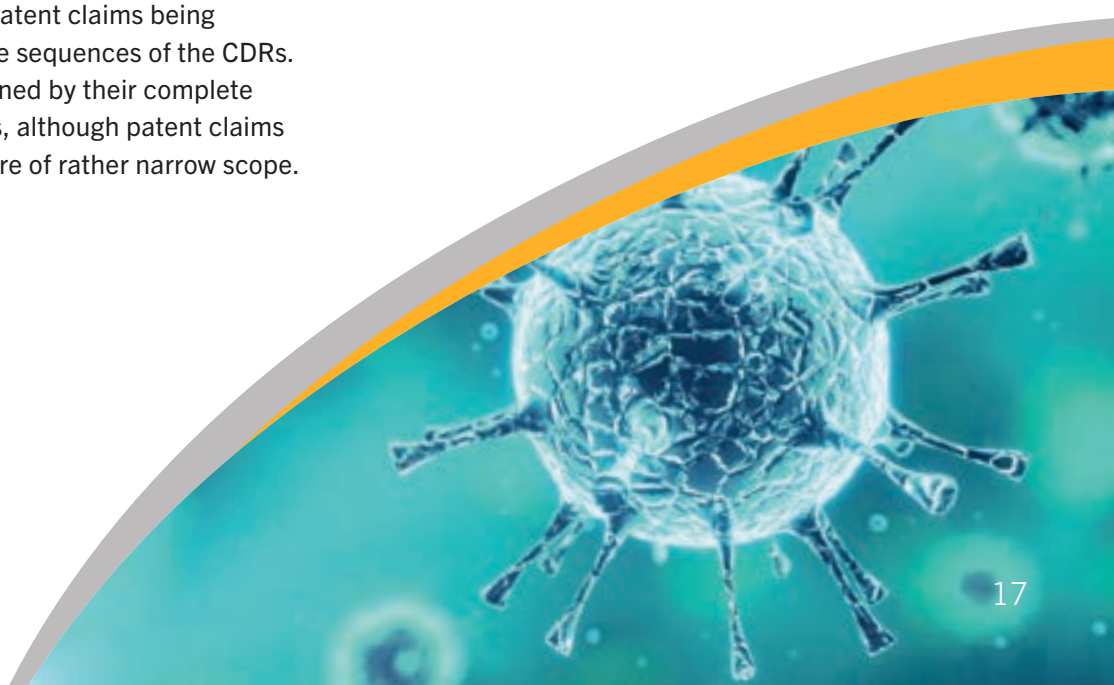
Antibodies defined by sequence

With the advent of phage-display libraries and readily-available DNA sequencing methods, antibodies are now often defined by reference to specific amino acid or nucleic acid sequences of one or more of the CDRs which form the antigen-binding sites of the antibody. If sufficient supporting data is available, variants of the CDRs may also be claimed in order to try to avoid the patent claims being limited merely to the precise sequences of the CDRs. Antibodies may also be defined by their complete VH and VL chain sequences, although patent claims based on such sequences are of rather narrow scope.

It should be noted, however, that if an antibody is known (for example, an antibody that is produced by a known hybridoma), then merely determining the sequence of that antibody will not render that antibody new – it is still the same chemical entity. However, specific fragments of that known antibody might still be patentable.

Claiming antibodies in the form of an antibody-drug conjugate (ADC) is an additional way to achieve novelty over a previously-known (non-conjugated) antibody.

Antibody patent applications will often also include claims to expression vectors comprising nucleic acid molecules which encode the new antibodies and host cells which produce such antibodies.



Target patents and reach-through claims

It is often the case that an inventor identifies a new biochemical target and obtains knock-out/knock-down data to demonstrate the target's involvement in a metabolic pathway. From a scientific perspective, such a discovery could be highly significant; but from a patent perspective, consideration needs to be given to what will eventually be commercialised – because the patents will need to cover such commercial products or methods.

It must first be recognised that the main commercial interest in such inventions is unlikely to be the target – it will be the compounds (e.g. agonists or antagonists) which bind to the target. Ultimately, it will be those compounds which are sold as medicaments.

In terms of patenting such inventions, there are two main strategies, depending on whether the invention has been made in a commercial or an academic context.

Inventions made by commercial companies

If the invention has been made by a commercial company, the general strategy is to keep all information about the target **confidential** and only to patent the compounds which interact with the target. Keeping the target as a trade secret provides the company with a commercial advantage – no one else knows what their compounds are interacting with. (This can be done because the patent system requires the identification of the compounds and some evidence that they are efficacious, but it is does not require the target to be identified.) Therefore, for as long as the target remains out of the public domain, the company can continue to benefit from this commercial advantage.

Inventions made by academics

If the invention has been made by an academic, then keeping the target confidential for any length of time is unlikely to be an option; there will probably be a strong pressure to publish details of the invention. Under such circumstances, it is generally recommended to direct the patent application to all new compounds which have been found to bind to that target, and to antibodies; uses of those compounds/antibodies (and ones which are known to bind to that target) can also be claimed for the treatment of diseases associated with that target.

Even after publication of the identity of the target, it will still generally be possible to obtain patent protection to new compounds which bind to that target (unless the identification of the target makes all such compounds obvious); but this option will be open to all parties after the publication of the target.

Screening method claims

It might also be possible to obtain patent protection for methods of screening for agonists/antagonists which bind to the target, but such claims can be of limited value due to the difficulty of enforcing them (i.e. how do you find evidence of people using such methods?).

Reach-through claims

As mentioned above, the commercial aim of such 'target' inventions is to find compounds which bind to the target and which can block or enhance its activity. Therefore, claims of the following scope are highly desirable:

1. An agonist or antagonist which binds to [target X].

Unfortunately, such claims are generally not obtainable, primarily because the claim does not adequately identify the agonists/antagonists (and hence how can the Patent Examiners determine whether such claims are novel or inventive?).

On the other hand, claims of the following format might be allowable in some countries, if sufficient agonists/antagonists are known or described in the patent application:

2. Use of an agonist/antagonist of [target X] for the treatment of [disease/disorder associated with target X].

Micro-organisms and human cells

The general criteria for the patenting of micro-organisms are the same as for all other inventions: is the micro-organism novel and inventive? Here, it must be remembered that the 'novelty' criterion for patentability does not mean "is it new?" in terms of "did it previously exist?"; it means "has it previously been made available to the public?" Hence newly-discovered bacteria and genetically-modified bacteria are both potentially patentable.

Novelty of inventions based on newly-discovered micro-organisms

As mentioned above, in patent terms, 'novel' means not previously 'made available to the public'. So, the first person to find and isolate a new bacterium from a soil sample, for example, might have made a novel (and potentially patentable) invention.

If the bacterium is claimed in the patent application in an 'isolated' form, that form will be novel over the previously-known mixture of that bacterium with numerous other micro-organisms in the soil. If the bacterium is shown to have some practical use and is sufficiently different from other bacteria which have previously been known for that use, then the use and inventive step hurdles may be overcome.

Micro-organisms which are derived from known micro-organisms

In order to satisfy the enablement requirement, the patent application must contain sufficient information on how to put the invention into practice.

If the new micro-organism is derived from a known one (for example, a plant gene has been inserted into a known *E. coli* bacterium), then a method of making the new micro-organism can probably adequately be described – in words – in the patent application.

An example of a claim to such a bacterium is the following:

1. An *E. coli* mutant which contains genes encoding proteins [X and Y], wherein the mutant is capable of producing ethanol.

Enablement of newly-discovered micro-organisms

If the micro-organism is not previously known (for example, a newly-identified bacterium or fungus), then it will not be possible to describe how to make such a micro-organism in words in the patent application.

In such cases, a sample of the micro-organism may need to be deposited under the 'Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure' with an International Depository Authority (IDA). Under this Treaty, if a sample of the micro-organism is deposited with one IDA, the enablement requirement is deemed to be satisfied in all of the (approximately 80) countries that have signed the Treaty. The Treaty's rules allow access to the deposit by third parties under defined conditions.

Using this or similar procedures, samples of new bacteria, phages, viruses, cell lines, fungi and seeds can be deposited in order to satisfy the enablement requirement.

Human cells

The same issues apply to human cells. For example, the first person to isolate and purify a particularly advantageous human cell line may be entitled to a patent on that cell line.

Following the discovery of stem cells, numerous patent applications have been filed to such cells. In particular, numerous patent applications have been filed towards induced pluripotent stem (iPS) cell lines and methods of inducing iPS cells to form specific cell types.

Transgenic plants and animals

The Patent Offices treat transgenic plants and transgenic animals as complex chemical compositions. For example, if the insertion of a foreign gene into a known organism produces a novel and non-obvious transgenic organism, then that organism is potentially patentable.

Transgenic plants

The development of plants with increased drought or salt tolerance, or plants with enhanced nutrient contents, are important goals for the agro-biotech industries. The production of crops with such features may help to feed the Earth's ever-increasing population.

Patent claims often refer to plants having genes which code for desirable traits, where the genes have been isolated from a first plant and inserted into a second plant in order to confer those traits on that second plant. For example:

1. A transgenic rice plant which comprises a gene encoding [foreign protein] stably integrated into its genome.

Transgenic animals

Transgenic animals are generally claimed in the same way as transgenic plants, that is by reference to a parent animal and the new gene which has been inserted into it. For example:

2. A transgenic cow comprising a nucleotide sequence encoding human insulin, wherein the nucleotide sequence is inserted into the cow's genome in such a way that human insulin is secreted into the cow's milk.

However, most Patent Offices do not allow claims to cover humans (on morality grounds). Hence any patent claims covering transgenic animals or transgenic mammals need to exclude humans, e.g. by claiming "a non-human transgenic animal" or "a non-human transgenic mammal".

Medical devices

Biotech inventions are often incorporated into medical devices and hence, if appropriate, it is important to include a claim to such a device in the patent application.

Examples of medical devices

Common examples of biotech-based medical devices include devices which test blood or urine for the presence of sugars or hormones (e.g. glucose monitors and pregnancy dip-strips), implantable devices (e.g. taxol-coated stents and synthetic grafts) and injectables (e.g. insulin and adrenalin pens).

Disposables

In addition to the device, it is often useful to be able to sell a disposable accessory for the device, such as cartridge or dip-strip. (The sale of such accessories also provides an additional revenue stream.)
Hence patent claims should be tailored to such accessories also.

For example, a patent application which relates to a new antibody against a peanut allergen might include all of the following claims:

1. An antibody against the peanut allergen, wherein the CDR sequences...
2. A device for detecting peanut allergens, comprising the antibody of claim 1.
3. A cartridge for use in a peanut allergen detecting device, comprising...
4. A method for detecting peanut allergens, comprising the steps...

Patenting of biotech methods

Methods and processes

In addition to granting patents on products such as drugs, DNA and antibodies, the Patent Offices will also grant patents to methods of doing things and processes for making things. The claims of these patents will reflect the steps which are to be taken in the invention's method or process.

Action patents

New ways of doing things or new ways of using known products can be patented by referring to the new actions which make up the invention, for example:

1. A method of reducing the rodent population in an area, the method comprising baiting the area with a rodenticide comprising digitoxin and banana extract.

Process patents

New processes are generally claimed by referring to the essential steps in the new process. For example:

2. A process for the preparation of an antibody-toxin conjugate, the process comprising the steps:

    i. Reacting an antibody with a conjugating reagent to form an antibody-conjugating reagent moiety; and

    ii. Reacting the antibody-conjugating reagent moiety with a toxin to form an antibody-conjugate-toxin complex, wherein the conjugating reagent is...

Diagnostic assays

Whilst methods of diagnosis are patentable in most countries, the wording of the patent claims often has to be chosen very carefully in order to avoid exclusions which are present in many patent laws.

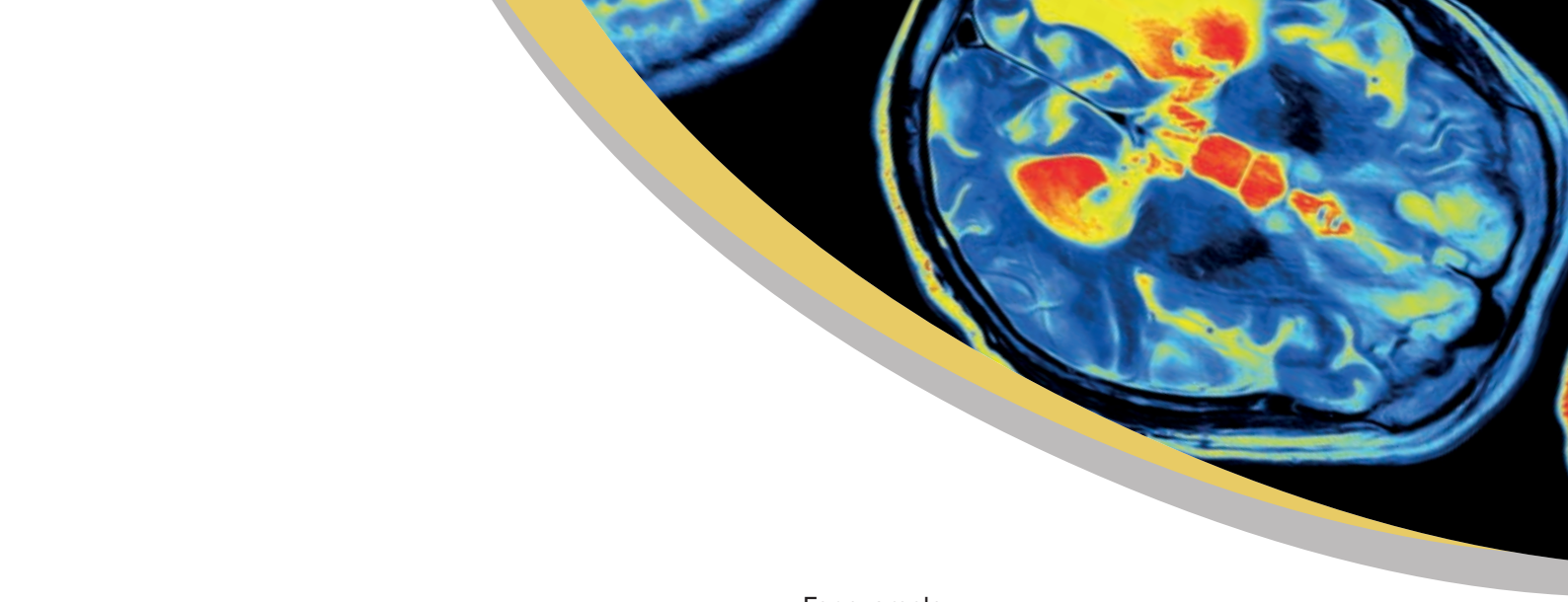
Examples of method of diagnosis claims

Diagnostic assays are generally claimed as methods which refer to the key steps which are involved to obtain the diagnosis, for example:

1. A method of diagnosing Alzheimer's disease, the method comprising the steps:

    i. Isolating blood cells from a blood sample obtained from a patient; and

    ii. Determining the presence or absence of BLA4 protein in the isolated blood cells, wherein the presence of BLA4 protein in the total protein is indicative of Alzheimer's disease in the patient.



Medical imaging

Patents on medical imaging techniques (e.g. magnetic resonance imaging) usually refer to the data-acquisition and data-processing steps, but often do not refer to the final diagnostic step (in order to avoid the exclusions mentioned above).

For example:

1. A method of imaging an artery in a region of interest in a patient using magnetic resonance imaging, the method containing the steps of:

    i. Injecting a magnetic resonance contrast agent into a vein remote from the artery;
    ii. Monitoring the region of interest by using a series of magnetic resonance radio frequency pulses...
    iii. Generating an imaging initiation signal after detecting the arrival of the contrast agent in the region of interest;
    iv. Collecting magnetic resonance image data in a magnetic resonance imaging sequence...; and
    v. Constructing an image of said artery, using the magnetic resonance image data, wherein the artery appears distinct from the adjacent veins and background tissue.

Method of diagnosis patents in the US

In 2012, the US Supreme Court ruled that patents which were based on a correlation between a biomarker and a disease were not allowed because they were attempting to monopolise a 'law of nature'. The US district/appeal courts and the USPTO are still trying to resolve how the Supreme Court's decision should be applied in practice, but the decision has already had a significant impact in some areas (e.g. preventing the patenting of some pre-natal diagnostic methods). This decision only applies to US patents.

Maximising patent protection for pharmaceutical products

Although the maximum life of a patent is usually 20 years, there are a number of actions that companies can take in order to extend the patent protection for their new drugs – whether the drugs are standard chemical entities or biologics. These actions include filing new patent applications which claim additional uses for the drugs or new formulations for the drugs. Of course, it is not only the original developer of such drugs that can file such patent applications.

These new patent applications will still have to satisfy the general criteria for patentability, including ensuring that the new claims are both novel and inventive over the publication of the parent patent applications.

First medical use

If a new medical use is found for a compound which has not previously been used in any therapeutic or diagnostic context, then the EPO (and a few other countries) will allow a broad claim of the format:

EPO	Compound X for use as a medicament or for use in therapy

Second or further medical indications

Patent applications may also be based on new uses (e.g. repurposing) for previously-known medicines. For example, aspirin is well known for the treatment of headaches. If it was now found that it could be used to treat colon cancer, then a new patent application could be filed which claimed uses of aspirin to treat colon cancer.

Inventions based on the discovery of such new uses are claimed in different formats depending on the country where the patent application is filed. (The main reason for this is that most countries do not allow methods of treatments to be claimed directly, the most notable exception to this being the US.)

Examples of allowable formats include the following:

US	A method of treating colon cancer, comprising administering an effective amount of aspirin to a patient in need thereof
EPO	Aspirin for use in a method of treating colon cancer
Canada	Use of aspirin in the manufacture of a medicament for the treatment of colon cancer

Specific treatments

Even if the medicament is already known for the treatment of a particular disease, it may still be possible to obtain patent protection in the following areas:

i. A specific treatment regimen (e.g. a weekly dose of 1mg drug/kg body weight).
ii. A new mode of administration (e.g. intra-muscularly).
iii. Administration of the medicament to a defined group of patients (e.g. HIV+ patients).

However, justifying the non-obviousness of the above inventions can often be difficult; and proving infringement can also be a significant issue.

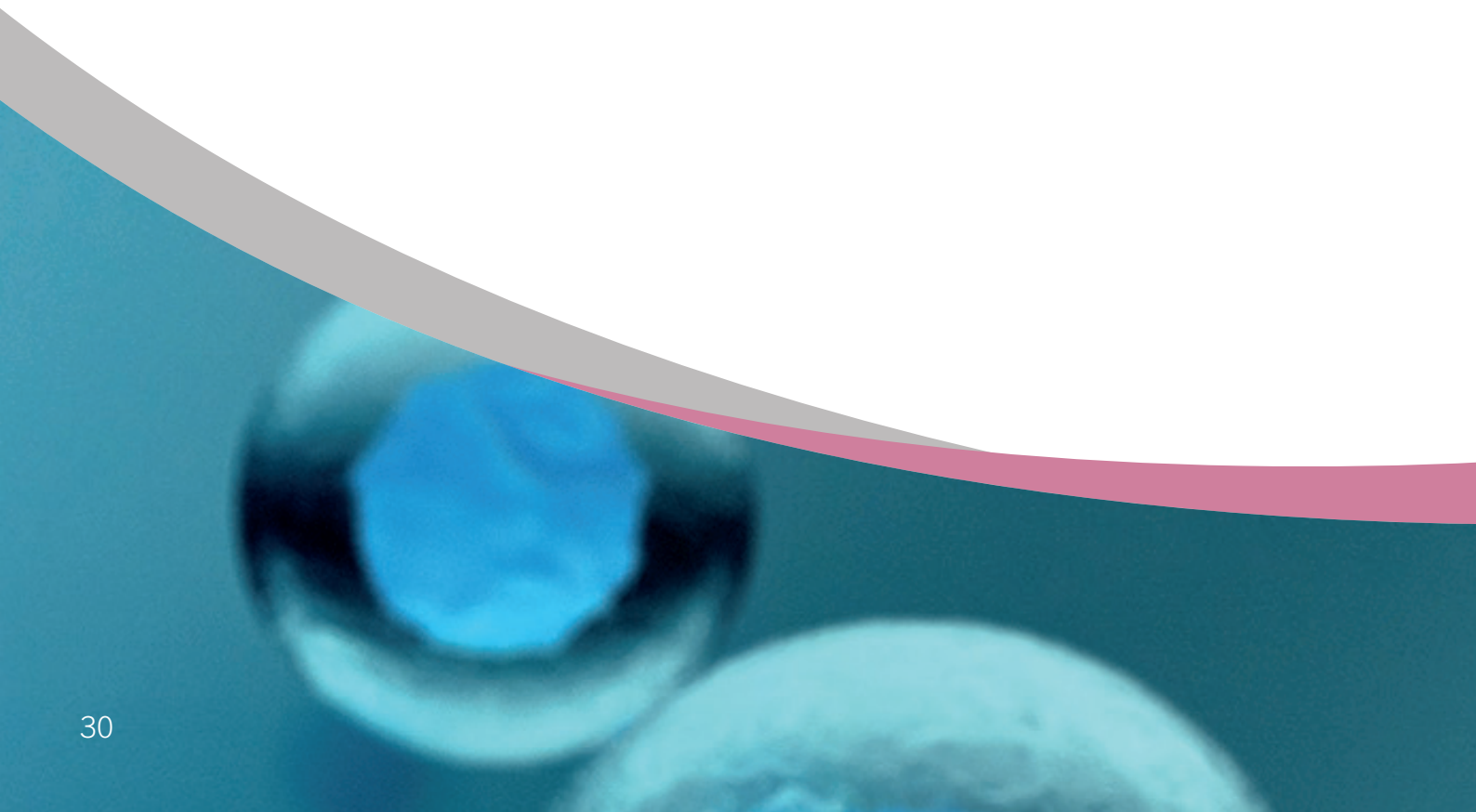
Formulations and combinations

Patent applications are often filed for new formulations of known medicaments, for new combinations of active ingredients and new dosages of known medicaments, for example:

i. A pharmaceutical tablet comprising aspirin, trehalose and 2.5mM – 5.0mM sodium chloride.
ii. A pharmaceutical composition comprising ibuprofen and an antibody against TNF-α for simultaneous, sequential or separate use in the treatment of inflammation.
iii. A pharmaceutical composition comprising 2.75mM – 3.35mM salbutamol.

Obtaining a marketing authorisation (MA) for a drug

Before a company is allowed to sell a new drug, the quality, efficacy and safety of that drug must first be investigated in clinical studies in humans. Once it has been approved, a marketing authorisation (MA) (also known as a product license, PL) is granted for that drug.



Supplementary Protection Certificates (SPCs)

It can often be 10-15 years between the date that a patent application for a new drug is filed and the date that the marketing authorisation (MA) for that drug is granted. This means that a company may only have 5-10 years of patent life within which to recoup the development costs for that drug.

This issue is recognised in many countries by extending either the life of the patent or the specific product for which MA has been granted. For example, in the EU, an SPC may be granted which extends patent protection for the product for which MA has been granted for up to five years; this may be extended a further six months if paediatric investigations have also been carried out.

Similar laws apply in other countries, although the period and scope of additional protection varies.

Regulatory Data Exclusivity (RDE)

Regulatory data laws may be used to prevent third parties from using a company's clinical trial data. (For example, if Company A wished to make use of Company B's data in support of Company A's application for marketing authorisation of their drug.) These regulatory laws are independent of the patent laws.

Biosimilars and biobetters

After a biotherapeutic product has been placed on the market, competitors will often try to develop 'biosimilar' products and be ready to market them once the patents on the original biotherapeutic product have expired. They might also try to develop 'biobetter' therapeutic products, which might be structurally or functionally different from the original biotherapeutic product. The patenting issues that apply to biosimilars are different from those that apply to biobetters.

Patenting of biosimilars

A biosimilar may be defined as "a biotherapeutic product which is similar in terms of quality, safety and efficacy to an already-licensed reference biotherapeutic product" (World Health Organisation). The reference biotherapeutic product will be one which has already passed the relevant clinical trials and a marketing authorisation will have been granted for it. After the patents on the original biotherapeutic product have expired, other drug companies will often try to produce such biosimilars in order to exploit the market for that biotherapeutic product.

From a patenting perspective, the biosimilar product is likely to be structurally identical (or at least very similar) to the reference biotherapeutic product. Hence any patent claims to the biosimilar product are likely to lack novelty over the (known) reference biotherapeutic product.

However, it might still be possible to patent the following:

i. New formulations comprising the biotherapeutic product.
ii. New combinations comprising the biotherapeutic product and other active agents.
iii. New dosage regimes using the biotherapeutic product.
iv. New processes to make the biotherapeutic product.

Patenting of biobetters

In order to be patentable, any patent claims to biobetters will have to satisfy the standard criteria for patentability: the claimed biobetter will have to be novel and inventive over everything in the public domain at the filing date of the patent application to the biobetter, including everything which is in the public domain at that time about the reference product and any biosimilars.

By definition, biobetters will be structurally different from the reference biotherapeutic product and hence they might well be novel for this reason alone. For example, compared to the reference biotherapeutic product, the biobetter might:

i. Have a different amino acid sequence.
ii. Be a fragment of the reference product or a chimeric product.
iii. Have a different glycosylation pattern.
iv. Have different attachments, such as PEGylation.

The inventive step of the biobetter is likely to be judged on whether or not the differences (such as the above) over the reference product are not obvious, and whether the biobetter has surprising or unexpected properties compared to the reference product. Examples of such properties could, for example, be that the biobetter has a significantly longer half-life, an unexpectedly higher enzyme activity or surprisingly better efficacy.

Glossary of terms

Budapest Treaty
Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (1977) (an international treaty on the depositing of micro-organisms to address the enablement requirement).

CIPA
Chartered Institute of Patent Attorneys (the body which regulates UK patent attorneys).

CJEU
Court of Justice of the European Union (formerly called the European Court of Justice, ECJ).

EP
European patent or patent application.

EPC
European Patent Convention (the law which governs the examination and grant of European patents).

EPO
European Patent Office (the Patent Office which examines and grants European patents).

FTO
Freedom to Operate (whether there are any third-party patents which might be used to prevent a company from commercialising their product, method or process).

IP
Intellectual Property (a general term which covers patents, trademarks, copyright and design rights).

IPRP
International Preliminary Report on Patentability (the Examination Report which issues on a PCT application).

ISR
International Search Report (the Search Report which issues on a PCT application).

MA
Marketing Authorisation (also known as a Product License).

Official Action
Official Action, Office Action and Official Letter are all synonyms for the examination reports produced by Patent Office Examiners.

PCT
Patent Co-operation Treaty (the treaty under which international patent applications are filed).

Prior art
All documents which were in the public domain before the filing/priority date of the patent application.

Priority year
The 12 months after the filing of the earliest priority patent application.

RDE
Regulatory Data Exclusivity (a form of protection obtainable for clinical trials data). The RDE laws are separate to patent laws.

Skilled person
A person who is skilled in the area of technology of the patent but who is incapable of inventive thought.

SPC
Supplementary Protection Certificate (an extension of up to five years of patent protection but which only covers a product having a Marketing Authorisation).

UKIPO
UK Intellectual Property Office (the trading name of the UK Patent Office).

USPTO
US Patent & Trade Mark Office (the body which grants US patents).

WIPO
World Intellectual Property Organisation (the body which oversees the Patent Cooperation Treaty and other international IP treaties).

Written Opinion
A preliminary report on the patentability of an invention which is issued on an International (PCT) patent application. It subsequently forms the IPRP.

This booklet is based partly on information which was first published by the author in the following articles:

- "Patenting of micro-organisms" Webber, P.M., Nature Reviews Drug Discovery 5, 13 (January 2006)
- "Patenting antibodies" Webber, P.M., Nature Reviews Drug Discovery 5, 97 (February 2006)

It must be emphasised that the information given in this booklet should be seen merely as providing guidance on the general principles of patenting medical and biotechnological inventions. There are numerous exceptions to the general principles discussed herein and patenting practice varies from country to country. Consequently, it is recommended that professional advice be sought for any specific matter.

About Dehns

Dehns is one of the leading European firms of specialist patent and trade mark attorneys, with 6 offices and more than 200 people. Consistently top-tier ranked by all major legal and IP directories, our core business for almost 100 years has been to obtain and defend Intellectual Property Rights for local and international clients, including start-ups and university spin-outs, SMEs and multinational corporations.

Life sciences and biotechnology

Dehns' life sciences and biotechnology team consists of 15 qualified and trainee patent attorneys. Of the 10 qualified patent attorneys, 8 have been awarded PhDs for their research on a variety of topics and, as a result, routinely handle patents in fields such as immunology, antibodies, genomics, proteomics, microbiology, peptides, biotherapeutics, diagnostic assays, recombinant protein production, nutraceuticals, biofuel production, and cosmetics, to name but a few.

All our attorneys provide a wide range of patent services including patentability assessments, writing patent applications, obtaining granted patents, defending and opposing granted patents and providing advice on aspects such as Freedom to Operate, due diligence, infringement and validity.

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