Biotech briefing note

HL's guide to making your biotech IP investable

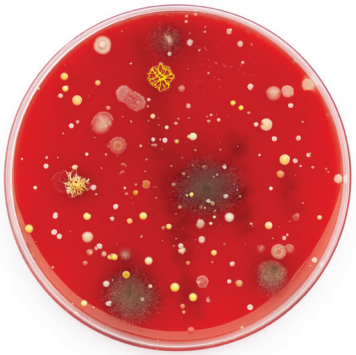
At the core of any biotech company is an innovative piece of science which is believed will lead to new and beneficial healthcare products. The company's Directors and advisors use their scientific insight and business acumen to push these new healthcare products along the road towards market. Often the innovation has provided one or more new drug candidates which the biotech company moves along the stages of R&D towards (hopefully) having a new blockbuster drug on the market, or is aimed at earlier or better detection of disease and the biotech company works to validate and refine the sensitivity and selectivity of the diagnostic tests.

To make it worthwhile spending time and money developing a new healthcare product, there needs to be an exclusive market, at least for a few years, during which the product can be sold at a price which enables re-couping the investment and making a profit. Therefore, aside from the company's key individuals, the core of any biotech company is the innovative piece of science and the intellectual property (IP) – usually patents – protecting it.

In this comprehensive guide, we will provide useful tips for creating and maintaining a patent portfolio that genuinely provides a biotech company with the hoped-for IP position and helps makes it an attractive choice for investors.

The guide covers the key aspects of making your biotech IP investable:

- Building a robust and investable patent portfolio
- Ensuring your IP is ready for due diligence
- The impact of other people's IP on you
- Patenting problems specific to the biotech and healthcare sector



Building a robust and investable patent portfolio

When are you ready to file a new patent application?

This is a difficult balancing act between, on the one hand, ensuring you file before any competitors working in the same space as you so you get the earliest priority date, and on the other hand, waiting until such time as there's enough evidence available to put into the new patent specification to show that the new healthcare product really works as claimed. Waiting too long means a competitor can get in before you and take the lead or exclude you from that technology space. However, filing too soon could mean there's not enough evidence to confirm that the new healthcare product actually works, or actually works for all of the applications claimed, which could be a problem.

Clearly a patent application for a new drug is filed years before clinical trials are performed, which are the true test of whether the drug works. Therefore a key test is whether it is plausible that the new drug works and whether it is plausible that the new drug works in all of the ways claimed. What might be "enough" evidence depends on both the nature of the invention and the scope of claims to be pursued. As an example, this was one of the issues grappled with in the recent high profile dispute between Actavis and Warner-Lambert relating to the drug pregabalin. The patent in question claimed treating neuropathic pain generally which was construed to encompass all types of neuropathic pain. Whereas, the patent specification was found to have evidence which only confirmed the usefulness of pregabalin for treating peripheral neuropathic pain, and not central neuropathic pain and therefore this was not evidence for treating (all types of) neuropathic pain.

What should your patent filing and prosecution strategy be?

A standard approach is to file the first patent application wherever the inventors are based, followed within 12 months by a priority claiming international (PCT) patent application.

Then wait until the end of the international phase before seeking patent protection in the countries/regions of interest. This standard approach can provide what's required, but there's no need to follow this exact route if you can achieve a better position by doing something different. Identifying the best strategy will involve an awareness of what's helpful at different stages for the business and an awareness of what's possible before different patent offices.

Some patent offices, like the United States Patent and Trademark Office (USPTO), may do very little with a new patent application within the first year of filing, whilst others offer more information. The UK Intellectual Property Office (UKIPO), for example, can provide a search and initial examination report well within the 12 month priority period. Analysis of this information can help shape subsequent patent prosecution strategy such as modification of the claim structure or description of the application and give some understanding of the likely final patent scope. Therefore, filing first, or early, with the UKIPO might be useful regardless of where inventors or a company is based. As a note of caution, however, it is necessary to take into account any national patent laws dictating that inventions made in that country and/or by citizens with that nationality must be first filed with their national patent office or that a foreign filing licence is obtained. Since biotech and healthcare inventions often result from international collaboration, the interplay of these provisions needs to be built into the first filing decision.

Once a new patent application is filed, how should you run patent prosecution?

This depends on when you need granted patents and/or when you need a strong indication that patent protection will be obtained and what the scope of that protection might be. If you need to maintain exclusivity by having or enforcing IP, then granted patents are key and many patent offices offer mechanisms for accelerating patent prosecution. Whilst the requirements, costs and effectiveness of these different mechanisms varies, it could be valuable for core patents. Conversely, there can be reasons to want to slow down patent prosecution or delay certain stages. Such reasons include insufficient information to make certain decisions or a need to defer certain costs. However, such delay means third parties like potential investors don't have the comfort of knowing the technology is patented. A good solution can involve blending together patent prosecution options, for example, to get rapid grant of a patent in one country – confirming patentability and achievable scope of protection, whilst the corresponding patents in other countries progress more slowly. Alternatively, you could take steps to get an early official indication from a patent office that the technology is patentable in the form of a positive opinion on an international patent application.

As you can see it is possible to drive your patenting strategy in a variety of ways depending on requirements and there is no such thing as a one size fits all solution.

Is your IP ready for due diligence?

Now we understand the basics of building a robust patent portfolio, so it is important to consider how to make your patent portfolio ready for external review or due diligence. The rigour and detail of IP due diligence varies across the life of a biotech company, varying with the size of investment sought (and IP awareness of the investigator), culminating in detailed considerations when assets are to be bought by "big pharma" – who are very IP savvy.

Nevertheless common themes run across all due diligence exercises. It is worth being mindful of getting and keeping your IP portfolio in good order from the outset, even if the due diligence to be performed is minimal, because in my experience any "issues" tend to magnify and become more costly to fix with the passage of time. To get a patent portfolio that is valuable, it needs to be grown and adapted in a way that aligns with the business plan.

Do your patents actually cover your healthcare product?

When prosecuting or critically reviewing a family of patents and patent applications, the first and most important question to consider is whether or not those patents cover the product or method they are supposed to cover. This might sound obvious, but often a patent application is drafted and first filed at the start of an R&D project and it may be several years later that a lead drug candidate is identified and optimised or a diagnostic test is validated. Furthermore, pre-grant interaction between a patent examiner and a biotech company's patent attorney can take a few years.

Good communication between those managing the IP and the R&D team should prevent divergence and help keep the patent protection aligned with the drug development. Furthermore, that good communication should help spot when the drug development programme has produced a refinement or incremental step which is itself a patentable invention. This could create a new layer of patent protection to strengthen a patent portfolio and, as such a new patent filing occurs later in time, potentially extend the duration of patent coverage.

As an early biotech company is often many years away from obtaining marketing approval for a new healthcare product, the issue of Supplementary Protection Certificates (SPCs) in Europe (or Patent Term Extensions (PTEs) for the US) can be forgotten about. However, it is best not to completely ignore this issue since such extension of exclusivity will become important later on and to review the claim structure with a view to SPC requirements.

Where do you have patent protection?

There's no such thing as a world patent. Patents are territorial meaning they provide rights in a specific geographical area which is often just one country. Since patents are territorial rights, another consideration for a biotech company's patent portfolio is where to seek patent protection. This means determining issues including the geographical prevalence of a particular disease and the willingness of healthcare systems to pay for the healthcare product being developed and where potential generic competitors have manufacturing plants.

Whilst there are mechanisms to delay final decisions and costs associated with filing patent applications in all countries of interest, due to the nature of the healthcare industry, decisions about where to seek patent protection often need to be taken years before a product is ready for market. It is wise to keep your options open (assuming budgets allow) if a final decision cannot be made because you can't go back and "add a country" to a patent family at a late stage.

Clearly, your patent protection for a new healthcare product should at least cover all the major markets. Consequently, there could be country selection differences between different patent filing programmes for different types of healthcare products. Having articulated reasons for the selection of territorial scope of patent protection in each patent family helps decision making internally and provides ready answers to any questions on this topic.

What is the likelihood that patents will be granted?

Seeking patent protection takes time. Therefore, due diligence associated with initial funding rounds on an early stage biotech company might be performed before any patents are granted. The question then becomes what reassurance can be offered to show that granted patents can be expected?

In most situations, it is worth anticipating this question so that a positive answer is readily available. A good solution is to accelerate the prosecution of at least one patent before a well-respected patent office that performs substantive search and examination to achieve a granted patent. This will give a good idea of the scope of patent protection that might be expected. A number of patent offices offer accelerated prosecution programmes and the UK Intellectual property office (UKIPO) can offer a relatively low cost, rapid and high quality service. If that patent portfolio is at an earlier stage, obtaining a positive opinion on your international patent application can be useful.

Who owns your IP?

In most cases the lack of clarity of who owns the IP comes from not completing all paperwork because it was considered a low priority compared with the myriad of other pulls on time and resources. However, since you can be sure that ownership will be examined, to be ready for due diligence, the chain of title for each patent family of your patent portfolio should be clearly documented all the way from the original inventors to your company. Trying to fill in gaps in a chain of title during a due diligence process can cause delays since key individuals may have moved on and could be harder to contact and/or they may now see an opportunity to make money, if significant investment is being considered.

As well as having a completely documented chain of title, the correct ownership of each patent or patent application should be recorded with the relevant national patent offices.

There are two good reasons for doing this. Firstly, any independent due diligence checks made using patent database information available online will show the same information you are presenting. Secondly, failure to do this in a timely fashion can negatively affect your rights.

What's it for?

Whilst the cost of maintaining a patent portfolio is minor in comparison with clinical trials, there is still a cost associated with growing, maintaining and defending patents. Knowing the purpose for having each piece of IP will show that your IP is actively managed and no unnecessary costs are incurred. Regular reviews of your IP schedule are useful to identify if any IP is no longer required and can be divested or allowed to lapse.

As you can see there are a number of considerations to build into your IP management which can make due diligence on your IP a more straightforward prospect.

The impact of other people's IP on you

As we noted at the start of this guide, the core of a biotech company is an innovative piece of science which it is hoped will lead to a new and beneficial healthcare product. A biotech company ought to be building a robust and defensible patent portfolio that helps provide market exclusivity and commercial advantage. However, it should be borne in mind that other people's IP can affect your ability to go ahead and commercialise your new healthcare product.

Many technological developments build on and refine earlier work. This earlier work might have been patented in such a way that the scope of protection embraces your new development or refinement of the technology. Consequently, permission to use that earlier patented technology would be required. This concept often uncovers a frequently held misconception about the patent system.

Having a granted patent does not provide a legal right to go ahead and commercialise the patented invention ignoring other IP rights. A patent is not a permissive right, but a negative right – it is a tool to use to stop someone else commercialising your invention. When patents are understood in this way, it can be seen that a patent protecting a new area of technology could embrace later developments and refinements of that technology.

Additionally in many areas, such as where there is a large, unmet clinical need, it is highly likely that competitors around the world will be working on creating solutions which will have similarities to your new healthcare product. Patents held by such competitors can also have an impact on your commercialisation plans.

What to do about third party (i.e. other people's) IP?

If the new healthcare product is a further development of earlier research, it is likely that the scientists involved are well acquainted with that earlier research. The key then becomes analysing whether that earlier research was patented and who owns those patent rights because it may be appropriate to either licence or acquire those rights. An example of the above situation is when a biotech company is created as a spin-out from an academic institution. The new biotech company would need to ensure they obtain all the necessary rights or licences to use the technologies proposed.

The timing for dealing with this type of third party IP should be as early as possible as the situation is readily identifiable. Delaying would be unwise since it could make the company less attractive to investors or be more difficult to resolve with passing time as individuals move on or want more from the agreements.

In certain technical fields it may be clear who the competitors are. Analysis of competitor IP can be performed by searching patent databases using applicant or inventor names.

A more complete freedom to operate analysis usually involves extensive searching through patent databases using key words or classification codes to identify any potentially relevant third party IP.

In both of the above situations, the identified patents and patent applications need to be carefully analysed to determine whether it creates a bar to commercialisation and, if so, what can be done about that identified problematic IP.

What to do when an IP problem is identified?

One route would be to take a licence, if needed, to certain patents. But what happens between competitors who are unwilling to grant such licences? Also, you may not want to take a licence under a competitor's patent which you believe isn't claiming something new and so ought not to have been granted.

Patent systems provide a number of mechanisms to "attack" third party IP and each of these mechanisms might have a role to play in ensuring a clear path to commercialisation.

Before a patent is granted, the claims are generally amended during prosecution. A pending patent application that initially seems to be an issue, might not be after further prosecution. Therefore, it is worth monitoring such patent applications. You may also want to affect the course of patent prosecution to increase the chances that the patent application will be amended away from being a problem to you. It is possible in some jurisdictions to submit third party observations during patent prosecution, which can be anonymous, providing pertinent information to the patent Examiner. There are no limits on the number of times third party observations can be submitted, but the Examiner has discretion over how much action is to be taken in view of them.

After a patent is granted there are options for more active and extensive involvement in arguing the case for a patent to be revoked. A number of jurisdictions allow for opposition proceedings, usually before a patent office, just before or after patent grant. It is possible to oppose a European patent within nine months from grant attacking it for a range of issues. Opposition proceedings can be very effective to have a patent narrowed or revoked since only about a third of European patents which are opposed survive completely unscathed. Additionally, most countries provide a system for invalidation proceedings before a court to attack a granted patent and push for it to be revoked.

When is the correct time to perform a freedom-to-operate analysis or competitor analysis?

Clearly, it is wise to do the analysis prior to product launch and to perform the analysis in each, or at least a representative sample of, the countries where the product is to be launched. However, there are a number of factors that indicate that such analyses should be performed much sooner in the R&D process. The extensive cost, time and effort of clinical trials directs that you would want some certainty about having a clear path to ultimate commercialisation before embarking on clinical trials. If problematic European patents are identified, there is only a nine month window in which an opposition can be filed. Furthermore, if the best course of action to deal with third party patents involves an opposition, with possible subsequent appeal proceedings, or a revocation action, the timescales involved can be several years.

The patent landscape is continually shifting, and this is particularly so in crowded technology areas. Patent applications remain unpublished for the first 18 months so scouring a patents database at one time point may not pick up something identifiable as a potential issue later. Consequently, any analysis may need to be repeated at intervals. Your IP strategy should include building an awareness of other people's IP and taking the required steps to ensure that it does not thwart the progress of new and much needed beneficial healthcare products.

Patenting problems specific to the biotech and healthcare sector

As we've mentioned, one of a biotech company's key assets is the patent protection they can get for their new therapeutic or diagnostic. However, patent law has evolved in such a way that certain types of subject matter are not considered "inventions", or are specifically excluded from being awarded patent protection. The field of biotechnology, in particular, has a number of such obstacles littering the way for a biotech company which vary from jurisdiction to jurisdiction, meaning that something which may be patentable in the US may be more difficult to get patented in Europe and vice versa. Clearly if useful patent protection is to be obtained in a biotech company's target markets, the patenting strategy must include ways to manoeuvre around those obstacles. Even when looking at already granted patents, there can be cause for concern about the patentability (also called patent eligibility) of the subject matter involved if leading case law on that topic has changed over time.

Can you secure patent protection for new methods of treatment for diseases?

One example of these obstacles is the question of whether you can get patent protection for new methods of treatment for diseases – this is important as a key goal of the biotech and healthcare sector is the development of new treatments for disease.

US and Australian patent practice allow claims directed to a method of treating a disease by administering a specific new drug to treat that disease. However, for public policy reasons, a number of jurisdictions do not allow patents for methods of treatment as it is believed that doctors should not be hindered by patents when looking after their patients. Such jurisdictions include the important markets of Europe, Japan, China, Korea and India. Fortunately, in most jurisdictions with such exclusions, it is possible to obtain patent protection for the new chemical compound, or for a new pharmaceutical composition containing that chemical compound. Also, other approaches are often allowed to secure the required patent protection. In Europe, for example, it is possible to obtain patent protection in the guise of a 'purpose limited product claim' for the first medical use of a new compound and for subsequent uses of that compound in new and inventive treatments.

Can you get patent protection for methods of diagnosing disease?

Another example of such obstacles is the question of whether you can get patent protection for methods of diagnosing disease and for personalised medicine. Again, this is important as other key goals of the biotech and healthcare sector are early stage disease detection, the accurate differentiation between conditions with similar symptoms but different underlying causes, and personalising medicine to ensure a patient gets the correct treatment.

Following a US Supreme Court ruling in 2012, it has become difficult to obtain patent protection for diagnostic methods in the US. The Court presided over a patent case involving a method, which included giving a drug to a patient, measuring the metabolites of that drug and comparing to known effective threshold amounts, prior to determining whether to increase or decrease the dosage of the drug for that patient (Mayo v Prometheus). The Court determined this method was not patent eligible subject matter because the relationship between the naturally-produced metabolites and therapeutic efficacy and toxicity was considered to be a natural phenomenon;

other steps of the method did not constitute a patentable invention. The situation then became more challenging in 2015 when the US Court of Appeals considered another diagnostic method based on the finding that cell-free fetal DNA could be detected in maternal plasma or serum (Ariosa v Sequenom). The method required amplifying a paternally inherited nucleic acid from the maternal plasma or serum sample and then detecting the paternally inherited nucleic acid of fetal origin. The court determined that the presence of the cell-free fetal DNA in maternal plasma or serum is a natural phenomenon and that the remaining steps of amplifying and detecting DNA were standard at the time of the invention.

The United States Patent and Trademark Office (USPTO) has issued guidelines intended to clarify what is patentable, offering examples of strategies that could be employed to get patent protection in this area. However, there have subsequently been several cases suggesting that the Patent Trial and Appeal Board, part of the USPTO, is not following those guidelines. Some commentators have even suggested these cases also bring some of the doubts towards methods of treatment. It appears that the situation is still evolving and that for the time being getting patent protection for diagnostic methods and certain personalised medicines in the US may be difficult or at least require additional considerations. In July 2017, the USPTO acknowledged there is discontent with the situation so perhaps beneficial developments will soon be forthcoming.

In Europe, diagnostic methods practiced on the human or animal body are explicitly excluded from patent protection. Nevertheless, there are ways to secure valuable patent protection associated with diagnosis and correlations between a biomarker and a disease. Methods that give interesting results, but don't allow a final diagnosis on which action can be taken, are not excluded as diagnostic methods. Also, methods involving steps of a technical nature that are performed *in vitro* on biological samples previously taken from the body do not fall under this exclusion.

So the situation is currently easier for patentees of diagnostic innovations in Europe than in the US.

Therefore, your patent strategy should incorporate, from the outset, approaches to deal with the various obstacles to patentability affecting biotech and healthcare innovation. Additionally, when reviewing granted patent rights, whether for possible acquisitions or investment, there may now be reasons for doubting the validity of those existing rights and so giving good reason to take extra steps to secure the IP position.

In conclusion

Having robust IP protection is critical for a new healthcare product, as it is one of the key foundations on which a biotech company is built. Over the course of this guide, we have shared our key tips for creating and maintaining a patent portfolio that genuinely provides a biotech company with the hoped-for IP position and makes it an attractive choice for investors.

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