14 Block Me Not: Genes as Essential Facilities?

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Disease gene patents are a serious and sensitive issue. Policy in this area has to be very carefully deliberated upon-as any mistake could have severe consequences for biomedical drug discovery and human health. Literature is replete with concerns that patents over gene sequences would 'block' biomedical drug development. However as Walsh and others warn, before seeking solutions to this blocking impasse, we need to ask ourselves if there is such 'blocking' in the first place.

My paper seeks to demonstrate that antitrust can offer us a good framework to study the blocking issue. By applying the essential facilities doctrine to individual cases where access to a gene patent has been denied, one can assess the existence and maybe extent of blocking in this industry. This data could then be used to assess as to whether the blocking is of such a widespread nature as would warrant a substantial legal and/or institutional response.

With the IMS Health case before the ECJ, the essential facilities doctrine has taken centre stage in Europe. A recent report by the JFTC seems to suggest that Japan is serious about invoking this doctrine. However the parameters of this doctrine are far from settled. Antitrust authorities do not enough guidance on issues such as determining appropriate license fees for access, optimal number of licensees etc. In keeping with my focus on blocking and disease gene patents, I have dealt mainly with one aspect of this doctrine-namely the question of "essentiality". Essentiality would in most cases help in a determination of 'blocking' i.e. if the facility is a non-essential one, then there can possibly be no blocking. However the converse need not always be true-i.e. if the facility is an essential one, but is widely licensed, then it is quite possible that there would be no blocking.

Introduction

The phrase 'block me not' is a play on the name of a highly sensitive plant, the 'Touch Me Not'. Known scientifically as 'Mimosa Pudica', this plant, found mainly in some pacific islands literally shrinks/folds up upon any kind of touch-hence the name. In much the same way as this plant, 'gene patents' and in particular disease gene patents are a highly sensitive issue and unless handled with the appropriate amount of delicacy, could have fatal ramifications for biomedical drug discovery.

By disease genes, I mean not only diseases that have their bases in genetic disorders but also diseases that though 'non-genetic' in origin, could still have gene-based cures. As is the case with HIV/AIDS, some of these diseases are fatal-unless we find a cure for them quick enough, we are likely to witness an increasing number of deaths each year.

The change of 'touch' to 'block' in the topic is reflective of the 'blocking' problems inherent in the biomedical industry. To explain further, the biomedical industry is characterized by the "cumulative innovation" paradigm, wherein the discovery of a gene sequence is only the first step; vast amounts of additional time effort and money will have to be spent turning such sequence information into viable products, tests and cures for genetic conditions and diseases. Nonetheless, those who patent such 'raw data' will find themselves in a strong bargaining position and will undoubtedly be able to secure for themselves significant financial return, quite often at the cost of holding up further downstream research. This potential "blocking" or 'lack of access" problem could adversely impact upon drug discovery, as many diseases today are known to be gene based.

In contrast to the prospect of an anticommons as envisaged by Heller and Eisenberg, the "blocking" or "access" issue is not a problem of accessing multiple rights but one of accessing relatively few (or perhaps even one) patents on a key upstream invention. This paper will concern itself with only the "blocking" or "access" issue.

1. Unblocking Gene Patents: If It Aint Broke, Don't Fix It

The biomedical industry seems an ideal target for blocking problems to occur, given the fact that:

i) Patents were granted at the initial stages on mere DNA sequences, with no other known function than their mere use as probes. This has the potential of limiting the freedom of other researchers, particularly those in the pharmaceutical industry from developing further downstream products based on these gene sequences.
ii) Genes are finite in number. It is also extremely

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difficult to invent around gene patents.

iii) A single gene may have more than one function-with the result that a patent on the gene could cover all its potential uses.

Two of the most controversial gene patents that have raised concerns of blocking in a stark manner are the patents on the CCR5 gene and the BRCA genes. In 2000, the USPTO granted a patent to Human Genome Sciences (HGS) covering the nucleotide sequence of CCR5. The utility of the invention was defined, among other things, as a tool for screening for receptor agonists and antagonists, and as a diagnostic tool for detecting mutations in the gene itself. A utility in HIV/AIDS research was not mentioned- as admitted by HGS, no such utility was contemplated at the time. Other researchers subsequently discovered that the CCR5 receptor was the "docking receptor" used by the HIV virus to infect a cell-consequently the gene could have tremendous implications in AIDS research and the possibility of a cure. However, the patent grant meant that HGS could exclude all such researchers from using the CCR5 gene in their research. It was feared that this patent would have a "blocking" effect on AIDS research.

In much the same way, Myriad has been accused of stifling research because it has been unwilling to widely license the diagnostic use of its patents on the breast cancer genes, BRCA1 and 2 (and their mutations). Myriad's exorbitant demands for royalties put its test out of the reach of clinics and hospitals (involved in research that requires the test results). Consequently, it was feared that clinical research would be impeded, yielding long-term social costs. Myriad's actions could have the effect of preventing the emergence of new and improved tests.

Various solutions have been proposed to tackle the blocking issue. Some have recommended patent law reform, such as ensuring that only 'use patents' are granted for genetic inventions. Some others have sought to redress this through administrative regulation such as antitrust and some others have even sought to address this through health related regulation. However before weighing up the pros and cons of such proposals, one has to take a step backward and ask the question: "Is there a 'blocking' in the biomedical industry in the first place?

Despite initial concerns echoed by many that the biomedical industry would be characterised by a severe 'blocking' issue, till date, there has been little concrete evidence that this has in fact occurred. For example, in 2001, Walsh et al (*1) in a report indicated that the theoretical possibility of such blocking concerns may have been offset by certain 'working solutions' adopted by the industry.

These working solutions combine taking licenses, inventing around patents, infringement (often informally invoking a research exemption), going offshore, developing and using public tools, and challenging patents in court.

One has however to bear in mind that notwithstanding the general finding that there is no evidence of systematic or large scale blocking in this industry, one-off instances do exist. Myriad's licensing practices could perhaps be considered a good example in this regard. Maybe there will arise more such instances in future. It is therefore important that we constantly monitor this industry and assess individual blocking situations as they arise to determine the need for a broader and more systematic response to concerns of blocking.

It is in this regard that antitrust offers a good structural framework to help us determine the existence and extent of blocking in each individual case. I will show in this paper how the doctrine of essential facilities (EFD) helps us achieve this. Paradoxically, the very application of an antitrust remedy would help us determine if there is a "blocking" in the first place.

2. The Essential Facilities Doctrine

The "essential facility doctrine", is designed to deal with the danger that a monopolist in control of a scarce resource will extend its monopoly power vertically from one level of production to another. The "scarce resource", which may range from a physical bottleneck (such as a telecommunication network or a port) to an Intellectual Property Right, would qualify here as the "essential facility". A denial of access to this facility would then qualify as an abuse of dominant market power, and the dominant undertaking would be forced to grant 'access' on fair and reasonable terms. The essential facilities doctrine has its origins in the US (*2) and has been most widely applied in regulating access to physical infrastructure such as transport facilities (notably, ports) or utility networks (e.g. pipelines, energy networks).

EC position:

The concept of essential facilities (EF) becomes relevant within Art. 82 of the EC-Treaty which prohibits the abuse of a dominant position.

Although the parameters of the 'essential facilities' doctrine has still not been worked out fully in the EU, some broad conclusions can be

(*1) J. Walsh, A. Arora and W. Cohen 'Effects of Research Tool Patenting and Licensing on Biomedical Innovation' in W.M. Cohen and S.A. Merrill (eds.), *Patents in the Knowledge-Based Economy* (Washington: National Academies Press, 2003) at 287

(*2) United States v. Terminal Railroad Association, 224 U.S. 383 (1912).

drawn from case-law.

1. In order to arrive at a finding that a dominant position relating to the ownership of an intellectual property right has been abused, there has to be exceptional circumstances, beyond a mere refusal to license. Although the nature of such exceptional circumstances has not been clearly articulated, they can be broadly culled out from case law such as Magill and IMS.
2. The three criteria developed in *Magill* (*3), *Bronner* (*4) and *IMS* (*5) to determine whether a refusal to license or supply constitutes an abuse may serve as a starting point:
   a. the refusal to access the facility is likely to eliminate all competition in the relevant market and/or prevent the emergence of a new product for which there is potential consumer demand;
   b. the facility itself is indispensable to carrying on business, inasmuch as there is no actual or potential substitute in existence for that facility, and
   c. such refusal is not capable of being objectively justified (justifications being such of lack of creditworthiness or capacity constraints).

Of all these factors, the one that will be focussed upon in this paper is "essentiality". Needless this say, this factor underpins the very essence of the EFD i.e. if the facility is non-essential, then presumably, a competitor need have no access to it in order to compete effectively.

The question of essentiality becomes relevant at two stages of the application of the essential facilities doctrine:

1. When determining the issue of dominance; and
2. When determining the issue of abuse.

To explain further:

One has to bear in mind the fact that the EFD is not a stand-alone concept. Rather it is a subset of the wider mandate to not abuse a dominant position. As stressed upon earlier in this chapter, before arriving at a finding that there has been an abuse of a dominant position, one has to determine that the undertaking in question occupies a position of 'dominance' in the market. In most cases, market power (determined in turn by factors such as market share) will determine dominance. Market power will in turn significantly hinge upon how "essential" the facility itself is.

The doctrine becomes important at the stage of determining abuse as well. One of the three criteria developed in *Magill*, *Bronner* and *IMS* to determine whether a refusal to license or supply constitutes an abuse is that the facility is indispensable to carrying on business, inasmuch as there is no actual or potential substitute in existence for that facility.

Japanese position:

Unlike the EU, neither the antimonopoly law of Japan nor any of the JFTC decisions seem to clearly articulate a doctrine of essential facilities. However a recent study group report by the Japan Fair Trade Commission (JFTC)(*6) seems to suggest that the JFTC is now recommending the application of the Essential Facilities Doctrine (EFD) in a more extensive manner.

The report however does not delineate the specifics of the doctrine and how it would be applied. All it does is to draw out a very broad framework

3. Essentiality and Inventing Around: Get Creative!!

As has been stressed in the earlier chapter, one of the essential prerequisites for an application of EFD is a determination that the facility is in fact an essential one. The question of "essentiality" would in large part turn upon the availability of substitutes available for inventing around the patent. In the case of patents on human genes, substitutes do exist, at least theoretically. Let's explore some of them:

Animal genes:

Since animal genomes share a striking similarity to the human genome, it may be theoretically possible to substitute an animal gene for a human one. In a recent BBC report (*7) it was stated that scientists discovered a gene, in the nematode worm, that was quite similar to the human breast and ovarian cancer gene BRCA1. It was hoped that this gene could offer some clues for the development of breast and ovarian cancer. Given Myriads heavy-handedness in enforcing its patents on the BRCA 1 and 2 genes, researchers keen on working on these genes without paying the exorbitant royalties demanded by Myriad could consider using the nematode gene instead.

(*3) RTE v. Magill [1995] ECR 743

(*4) Oscar Bronner v Media Print [1999] 4 CMLR 112

(*5) IMS Health GmbH & Co OHG v NDC Health GmbH & Co KG (C418/01)

(*6) Report of the Study Group on the Antimonopoly Act October 28, 2003. The Study Group on the Antimonopoly Act was chaired by Kenichi Miyazawa, Honorary Professor, Hitotsubashi University) and held a series of meetings since October 2002.

(*7) See 'Primitive Worm Gives Cancer Clue' (http://news.bbc.co.uk/1/hi/health/3368685.stm)

Muteins:

Another interesting area that could throw up potential substitutes is protein engineering-this involves the artificial modification of genes to yield new proteins or 'muteins'. Examples of successful muteins include Betaseron, an analog of human beta interferon differing from the natural sequence by only a single amino acid.

Unnatural Base Pairs:

The revolutionary concept of 'unnatural base pairs' is quite similar to the concept of 'muteins' but goes one step further. As the name itself suggests, 'artificial' base pairs or 'unnatural' base pairs are added on to the natural base pairs (AT-GC) in a DNA sequence. The design of such novel base pairs is being exploited to add functionality to the nucleic acid and is only limited by the creativity of the chemist.

However the above 'substitution' possibilities are easier said than done. What one has to bear in mind that it is not a mere theoretical possibility that would qualify something as a substitute. Rather, the concerned substitute has to be a viable alternative-technologically, financially and legally. Technologically, an assessment has to be made as to whether one could expect broadly similar/accurate results when researching on the substitute (be it an animal gene, a mutein or an unnatural base pair) as opposed to patented human gene.

Given the fact that this paper focuses on a highly sensitive area such as human disease genes, one has to bear in mind that a slight difference in genetic structures could result in fundamental alteration in function. Consequently, one would need to seriously question as to whether research on an animal gene could yield similar results.

One would also have to assess whether such research would be financially viable one, given the high R&D costs inherent in any biomedical research. In terms of legal feasibility, the doctrine of equivalents could kick in to prevent research on an animal gene (or any substitute) that is similar to the patented human gene in question.

However, at the same time, it has also to be borne in mind that a 'mere competitive disadvantage' would not suffice to invoke this doctrine. Rather it has to be shown that 'duplication' of the facility is impossible or extremely difficult owing to physical, geographical or legal constraints.

Offshore Research:

Another strategy that is increasingly coming to be deployed in the biomedical industry today is to conduct research involving patented products/processes in offshore jurisdictions where the patentee has failed to procure a patent registration. This strategy received a boost with the recent ruling in *Bayer AG v Housey Pharmaceuticals* that stated that if the results of research using 'patented products/processes' is 'information' and not a 'product', then importing such information to the US would not amount to a patent infringement.

To illustrate this point, consider the example of NimbleGen, which uses the patented processes of Affymatrix to produces custom microarrays from a facility in Iceland. Since Affymatrix has failed to patent its technology in Iceland, NimbleGen can conduct its research unhindered in this jurisdiction. NimbleGen conducts research on behalf of select customers and then ships the resulting data back to those customers in areas where the technology in question is patent protected. Under the *Bayer* ruling, since the result of this patented process is 'information' rather than a physical product, it would not tantamount to patent infringement.

As suggested earlier, one of the key dilemmas in applying the EFD to intellectual property is the fact that blocking is the very essence of an intellectual property grant. This has been reiterated in almost all the 'essential facility' cases, beginning with *Volvo vs Veng*. (*8) Consequently, one has to be extremely cautious about over-extending the application of this doctrine in a manner that would destroy the incentive to create the essential facility in the first place.

Further an extensive application of EFD may not only destroy the incentive to create for the prospective patentee, it may also do so for a competitor. To elaborate, a liberal application of the EFD would translate to easy access to the patented technology for the competitor-this in turn would mean a reduction in the incentive to 'invent around'. The necessity to 'invent around' the patent is often the mother of future inventions.

4. Essentiality- A Sliding Scale

Underlying the very essence of the "Essential Facilities Doctrine' is the concept of 'essentiality'. However this concept is not a uniform one-rather, it is a variable one, depending on several factors. I will focus on two of these factors, namely the level of technological sophistication ('technology') and the extent of legal protection ('law'). I call this the 'techno-legal lever'. To explain further, consider the following:

- The level of technological sophistication is high in the United States. Consequently, it could be argued that it may be comparatively easier to invent around in the US than it would be in a relatively less technologically

(*8) Case 238/87, 1988 ECR 6211

sophisticated country such as India. Therefore a patent may be more of an essential facility in India than it is in the United States.

- Essentiality would also depend on the legal regime and the extent of patent protection conferred on an invention in such jurisdiction. Thus for example, the Indian patent regime protects inventions to a far lesser degree than the regimes in the United States or even Japan. In fact, as of today, the Indian patent regime does not grant product patents for genetic inventions-rather one can only avail of a process patent here.
- Similarly, the doctrine of equivalents is not as well developed in India as it is in the US or Japan. Consequently, an invention may be less essential in India than it is in the US-as the legal regime offers considerably more flexibility to invent around.
- In much the same way, if the patent grant is a narrow one, the scope for inventing around is far greater. Indeed in some cases, a strict application of patenting pre-requisites could result in the patent not being granted at all. This is what happened in the case of the patent application by HGS claiming the CCR5 receptor gene. Although this patent was granted by the USPTO (*9) the JPO rejected this patent on the ground that it lacked utility and inventiveness. (*10) As noted earlier, the grant of this patent by the USPTO was severely criticised as the utility cited was a highly speculative one (HGS had freely admitted that it did not know the gene's role in the HIV virus at the time it filed its patent application). The rejection by the JPO seems therefore to reflect better patent policy. Consequently, one could surmise that it may be easier to invent around in Japan than it is in the US as the patent grant is a stricter one.

Conclusion

Disease gene patents are a serious and sensitive issue. Policy in this area has to be very carefully deliberated upon-as any mistake could have severe consequences for biomedical drug discovery and human health. Academic literature is replete with concerns that patents over gene sequences would 'block' biomedical drug development. However as Walsh and others warn, before seeking solutions to this blocking impasse, we need to ask ourselves if there is such 'blocking' in the first place.

I have sought to demonstrate in this paper that antitrust can offer us a good framework to study the blocking issue. By applying the essential facilities doctrine to individual cases where access to a gene patent has been denied, one can assess the existence and maybe extent of blocking in this industry. This data could then be used to assess as to whether the blocking is of such a widespread nature as would warrant a substantial legal and/or institutional response.

I suspect that one of the main obstacles hampering a full-fledged analysis of the biomedical industry as would enable one to assess 'blocking' in a more comprehensive manner is the lack of information (pertaining to issues such as licensing). For example, some licensing agreements may even prohibit the disclosure of the very existence of the license. This need for more data could perhaps offer one of the strongest justifications for antitrust intervention. Antitrust authorities have greater powers to call for information in comparison to their counterparts from other institutions such as the patent office.

With the *IMS Health case* before the ECJ, the Essential Facilities Doctrine (EFD) has taken centre stage in Europe. A recent report by the JFTC seems to suggest that Japan is serious about invoking this doctrine. However the parameters of this doctrine are far from settled. Antitrust authorities do not have enough guidance on issues such as determining appropriate license fees for access, optimal number of licensees etc. In keeping with my focus on blocking and disease gene patents, I have dealt mainly with one aspect of this doctrine-namely the question of "essentiality". Essentiality would in most cases help in a determination of 'blocking' i.e. if the facility is a non-essential one, then there can possibly be no blocking. However the converse need not always be true-i.e. if the facility is an essential one, but is widely licensed, then it is quite possible that there would be no blocking.

I have also sought to demonstrate that essentiality is a local concept and not a universal one; thus it would depend on factors such as the level of technological sophistication and the extent of patent protection in the concerned jurisdiction.

It is impossible to predict at this stage whether the working solutions referred to by Walsh would continue to offset a blocking impasse. As a wise man once said "We tend to overestimate what would happen in a year and underestimate what can happen in 10 years." Therefore the need for constant vigil over this industry cannot be overstated.

(*9) U.S. Patent No. 6,025,154 (2000).
(*10) The application filed in Japan was rejected in October 2003 (See Application Number 2000-171338)


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