

Patenting the tools of drug discovery

Many patents containing claims on drug discovery tools have been issued or are pending, including patents on: 1) cDNA fragments; 2) Crystallised receptors, especially their use in software related rational drug design methods; and 3) Target genes/proteins and their uses in screening and in mechanistic therapeutic applications. This article discusses these patents, the US PTO's views on the utility of their claims and their potential court interpretation.

During the first decade and a half of biotechnology, roughly until the mid 1990s, patent attorneys, corporate licensing officers, research directors, the US Patent and Trademark Office (PTO) and the courts struggled to solve the primary questions of patent protection and enforcement in the young field: are living things patentable? (Yes); are naturally occurring genes or proteins patentable? (Yes, in isolated form); does an applicant need to demonstrate clinical effectiveness to fulfil the 'utility' requirements of the patent law for a new therapeutic agent? (No); does a patent claim to, say, 'TPA' cover a subsequent generation 'TPA'? (No); does a claim to insulin cover insulin from all animal species (No); is the sequence of a gene obvious from knowledge of the protein it encodes? (No); is the use of a patented drug in clinical research an infringement? (No). Some degree of predictability, statute by statute, regulation by regulation, and case by case, found its way into US patent law.

With the arrival of massive sequencing capacity, intellectual property (IP) questions have multiplied and become more complicated. The experience gained from regulations and decisional case law is of limited use in answering the new IP issues of the genomic and postgenomic era. For example, is there a way to extract IP value from the crystallisation of a previously known receptor? How best to protect computer-based, rational drug design methods? Can one obtain patent protection for all leads and/or drugs found by screening libraries with a newly isolated target? Will it be an infringement under US law

to import data gathered abroad using a screening process patented in the US? Does the use of a target in the secrecy of one's lab for 'research purposes' subject the surreptitious user to damages based on the sales of a successful drug developed with that target?

It may well be another 15 years before we know the answers to most of these questions, or until we achieve some measure of predictability. In an exercise of unlawyerly incaution, however, I will venture some answers here or at least provide a framework for analysis. I will first give a few examples of patent filings on drug discovery tools. Then I will deal with some of the common perceptions of patents on research tools, and finally I will ask the question: what are these patents worth?

Let me dispel a common misconception before we start. There is nothing inherently improper or misguided about obtaining and asserting a patent against someone who is 'just doing research' with a patented drug discovery tool, such as an isolated target or receptor. Certainly, one person's research tool is another person's commercial product. In that sense, a patented target used for screening is no different than a patented spectrophotometer used for the same purpose. No one will seriously argue that spectrophotometers are not patentable because their use is in research. It is clear that when the use of the patented material or instrument is with commercial purposes, US law recognises a cause of action for patent infringement. Perhaps a limited academic use for purposes of investigating the structure of the receptor might be exempt from a

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Figure 1 Receptor DNA claim in Human Genome Sciences's US Patent 6,025,154

- 1 An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:**
- (a) a polynucleotide encoding amino acids 1 to 352 of SEQ ID NO:2
 - (b) a polynucleotide encoding amino acids 2 to 352 of SEQ ID NO:3
 - (c) a polynucleotide encoding a polypeptide having the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 97183
 - (d) the complement of (a); the complement of (b); and the complement of (c)
- 8 An isolated nucleic acid molecule comprising a polynucleotide encoding at least 50 contiguous amino acids of SEQ ID NO:2**

claim of patent infringement. At present in the US, that is about the scope of the so called 'experimental use' exemption. All other uses are actionable.

Examples of patent filings on drug discovery tools

Complete receptors and their uses

Figure 1 shows claims 1 and 8 of Human Genome Sciences's (HGS) patent on the isolated polynucleotides of the originally called HDGNR10 Receptor¹. This receptor is described in the patent as being a G-protein chemokine receptor and useful, among other things, in screening for compounds which can be used to treat chemokine mediated conditions such as T-cell mediated autoimmune diseases including allergies, arthritis, etc.

The claims dominate anyone who would make, use, sell or import the polynucleotides involved in the coding of this receptor. The claims will dominate the manufacture of the receptor by recombinant means regardless of the ultimate use of the receptor. Such ultimate uses may even be some that were not known on the filing date of the patent application.

Indeed, after the filing date of the HGS application it was discovered by others that this HDGNR10 is the very receptor involved in the entry of HIV into T cells, the so called CCR5 Receptor. The value of this isolated receptor for use in screening for anti-AIDS drugs became quickly apparent to the scientific community and a great deal of misinformed controversy arose in the non-legal press about the unfairness of allowing the discoverer of the receptor DNA (by whatever name) to dominate subsequent uses which were not envisioned by him. There is nothing unprecedented in such a situation, however. It is one that is well

known to all pharmaceutical research companies and that has a firm place in the annals of chemical patent law throughout the world. The inventor of a new composition of matter who provides at least one real use for it has always been entitled to dominate all future uses, even those she did not or could not have envisioned on her filing date. In fact, the discoverer of any novel and non-obvious subsequent use may be entitled to his own patent and both sides will then block each other for the subsequent use, necessitating a cross licence.

Now I want to ask a different question: is the discoverer of a receptor and its relation to a disease entitled to a patent for treating the disease using drugs which operate through the receptor *in vivo*? A first answer is that a patent claim like the one in Figure 1 to 'isolated polynucleotides' does not dominate the polynucleotides when these are in their natural context, that is, when they are not in 'isolated' form but are part of the human body where they have been since evolution put them there. Thus, treatment with a drug that binds to the receptor in the body will not infringe a patent claim to an 'isolated' receptor polypeptide.

Secondly, once the receptor is isolated, one can obtain a patent claim drawn to a high throughput screening method using isolated receptor X to discover drugs (for example, a method of screening for compounds that bind to receptor X). It is essentially impossible, however, to obtain a composition of matter claim to any and all future compounds to be discovered with the screen (for example, a compound that binds to receptor X or a compound obtained from screening receptor X for those compounds that bind to it). Such composition of matter claims are difficult to obtain because of the very stringent written description requirements of US patent law, as presently interpreted by the PTO. These would require an applicant to include a substantial amount of structural description of such compounds, including formulae and methods of preparation. Since one does not know what compounds will bind one cannot readily meet this requirement.

While administration of an individual drug discovered by the screening method may well be the basis of a relatively narrow method of use patent claim (for example, a method of treating HIV-AIDS by administering an effective dose of 'ZT') a broader claim drawn to administration of any and all antagonists that bind to the new receptor would be much more desirable. Such a broader claim is very hard to obtain because, in most instances, there will have already been in the prior art at least one drug to treat the disease and which inherently acted through the receptor, even though the mechanism

had not been fully understood. An old principle of pharmaceutical patent law says that discovery of the underlying mechanism of action of an old drug does not entitle the discoverer to a new patent that would dominate the administration of the old drug.

Does that leave the discoverer of the receptor and its relation to disease no hope for a broad claim commensurate with her contribution? There is one set of circumstances in which such an inventor may be able to obtain and enforce a mechanism-based claim. **Figure 2** shows an example of a patent issued to Cortex Pharmaceuticals Inc which, if the constellation of facts is just right, might represent such a situation.

The Cortex claim is to a method of treating psoriasis by any antagonist which binds to angiotensin II. If Cortex's scientists were the first to discover that angiotensin II is involved in the mechanism for psoriasis, and none of the prior drugs used or published as useful for psoriasis inherently operated through such mechanism, then a broad claim such as that in **Figure 2**, not limited to any chemical structure or formula, might well be available and might survive an invalidity attack. If old anti-psoriatic drugs inherently operated through angiotensin II then such a claim might not be novel and might be invalidated in a court challenge.

Crystallised receptors

Let us now examine another increasingly common scenario, in which a scientist, after laborious efforts, succeeds for the first time in crystallising a previously known target and obtains the Cartesian co-ordinates for a high-resolution three-dimension-

Figure 2 Mechanism-based method of use claim in Cortex's US Patent No 5,104,877

A method for treating psoriasis comprising administering to a human in need of such treatment a therapeutically effective amount of an angiotensin II antagonist

al picture of the molecule. This picture of the molecule can be displayed on a computer screen and used for designing ligands which bind to the active site of the target. In other words, the resulting data and its use for rational drug design are valuable drug discovery tools. Can this invention be patented? Indeed it can.

According to the PTO's Examination Guidelines for Computer-Related Inventions (CR Guidelines), data *per se* is not patentable subject matter. Thus, while it may not be possible to obtain a claim to the crystallographic data *per se* (even though they may well be novel and non-obvious), a method of using such data, such as in rational drug design, may overcome the reluctance represented by the CR Guidelines, and be allowable.

One allowable set of patent claims are those drawn to a method of designing drugs on a computer screen. One such example is shown in **Figure 3**. This software patent claim, to a virtual design method of inhibitors using the 3D picture of a herpes protease, will be infringed by anyone

Figure 3 Drug design claim using a virtual receptor in SKB's US Patent 6,083,711

A method of identifying a candidate inhibitor compound capable of binding to, and inhibiting the proteolytic activity of, an alpha, or beta herpes protease, said method comprising:

- (a) introducing into a computer program information derived from atomic coordinate defining an active site conformation of a herpes protease molecule based upon three-dimensional structure determination comprising a catalytically active site formed by at least the interaction of three amino acids Serine, Histidine and Histidine, wherein said program utilises or displays the three-dimensional structure thereof
- (b) generating a three-dimensional representation of the active site cavity of said protease in said computer program
- (c) superimposing a model of the inhibitor test compound on the model of said active site of said protease
- (d) assessing whether said test compound model fits spatially into the active site of said protease
- (e) incorporating said test compound in a protease activity assay for a protease characterised by said active site of said protease, or an antiviral assay for an alpha or beta herpes virus
- (f) determining whether said test compound inhibits proteolytic activity, or the herpes virus in said assay

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Figure 4 Organic chemical claimed by reference to its receptor in Vertex's US Patent 5,756,466

An ICE inhibitor comprising:

(a) a first and second hydrogen binding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide -NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339

1) the distance from the centre of mass of the moderately hydrophobic moiety [of the inhibitor] in the P2 binding pocket to the carbonyl oxygen of Arg-341 of ICE is between about 7.1 Å and about 12.5 Å.; 2) the distance from the centre of mass of the moderately hydrophobic moiety [of the inhibitor] in the P2 binding pocket to the amide nitrogen of Arg-341 of ICE is between about 6.0 Å and about 12 Å.; etc

who carries out drug design on a computer screen. Note that this is not a high throughput screening claim in the 'wet chemistry' meaning of the term. This patent protects *in silico* design in a virtual environment. Note also that this claim is not limited by any mention of Cartesian co-ordinates, thus allowing the patent holder to claim infringement of those who might obtain a different crystalline form of the protease.

Another way to exploit the information gained from newly crystallising a receptor is represented by US Patent 5,756,466 owned by Vertex, and shown in Figure 4. This patent claim (which is shown only partially because of its length), claims not the receptor, but compounds which have been designed utilising the three-dimensional picture of the receptor. Note for example the reference to the formation of hydrogen bonds between certain backbone atoms of ICE and hydrogen bonding moieties of the putative inhibitor, as well as the distances in Angstroms between certain portions of the inhibitor and certain atoms of ICE.

Such claims are difficult to obtain and are vulnerable in that they may, because of their breadth, improperly cover prior art compounds that have been used for the same purpose and which inherently have the same three-dimensional arrangements as the ones falling under the claims. The PTO is not equipped to examine prior art compounds in order to estimate their co-ordinates in Angstroms. Most of the chemical literature moreover does not include compound co-ordinates and this also severely limits a thorough examination of such a claim. Conversely, it may not be readily

apparent if a compound evaluated for commercialisation by a third party against the patent claim infringes or not. Nevertheless, when the factual circumstances are just right, a claim as the one shown in Figure 4 can obviously be very valuable to the patent holder.

Enforcement issues with patents on drug discovery tools

As evidenced by the claims shown in Figures 1, 2 and 3, the PTO has shown no reluctance in granting patents on such drug discovery tools as the DNA and protein sequences of complete receptors, methods of screening for leads and drugs, methods of computer-assisted drug design, and on occasion, receptor-based method of therapy claims. The PTO examines such claims under well-established principles in evaluating the utility novelty, non-obviousness and enablement of the underlying invention.

Obtaining a patent on a drug discovery tool such as a receptor or a piece of software is, of course, only part of the story. A more complex and perhaps more uncertain part follows the issuance of the patent. It is at this point that the patent owner must confront the questions which most commonly come up in discussing these types of patents: how does one police them? How does one know if one's competitors are using them? What if a competitor has already used the receptor while the patent was pending and stops now that it has issued? What if a competitor goes abroad and imports the data developed with the tool? Figure 5 lists a few of the more common critiques of research tool patents. Let us now discuss these briefly.

Pre issuance use. Under all major patent systems of the world, including since March 2001 under the United States system, a patent application is published 18 months from its first filing date. This means that the specifications, including the DNA and protein sequences, all software flowcharts and all screening methods, become part of the public domain at that time. Since it normally takes upwards of three years to obtain an issued patent in the US, and longer in other countries, there is a lengthy period of time during which a copier can freely and legally use the research tool and not be enjoined from doing so until the patent is actually granted. Given the possibility of using a discovery tool in order to generate drug leads, copiers may be tempted to take advantage of the interim period after publication and before issuance to use the invention with commercial purposes. One possible ameliorative remedy is the provision under US and European law that such a user, while not subject to injunction until patent issuance, may still be liable

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for ‘reasonable royalties’ based on pre-issuance use, provided such use infringes a claim that issues in substantially unchanged way from the way it published. The question of what is a ‘reasonable royalty’ in these kinds of patent rights is discussed below.

Policing. A drug discovery tool such as a piece of software is, by its very nature, used in the darkened computer rooms of one’s competition. It is impossible to ascertain from the eventual sale of an approved drug whether one’s patented software was used in the discovery process. It is therefore very hard to police infringing uses. Luckily, the courts in the US are not unaware of the complications of establishing infringement of patented inventions which are used in the secrecy of a competitor’s plant. Recent decisions from the CAFC have led to an understanding that it is possible to initiate litigation in a Federal District Court based on a previous request for information from the potential defendant. This request can be accompanied by a well drafted and fair confidentiality agreement, so as to assure the recipient that the information received will only be used for evaluation purposes. If, as is often the case, the potential defendant refuses to disclose information, a Court presented with such evidence of attempt and refusal may allow the initiation of litigation and with it the full use of discovery processes.

Use abroad. It is an infringement in the United States to import a product made by a process patented in the US, as long as the product made abroad has not been materially changed or does not end up becoming a trivial and non-essential component of another product. Thus, a US process patent can block importation of a drug made by the process. It is unclear as of this writing, however, whether a process claim which covers the

screening of drug leads against a receptor would be infringed by importation of the data resulting from the screening process. In other words: is data a ‘product’ encompassed by the importation statute? The legal analysis required to approach this issue is beyond the scope of this paper, and it involves – among other things – a close study of the legislative history of the importation statute. There is a case pending in Federal Court in California, Synaptic Pharmaceuticals v MDS Panlabs, Inc where the issue may be addressed and resolved. The facts are similar to the ones we have discussed here so if the case goes to full decision we may have an answer in the next few years.

Clinical use. There is in the United States an immunity from infringement for anyone who carries out infringing activities with a ‘patented invention’ in pursuit of regulatory approval for a drug². Thus, the making, using or selling of a generic version of a patented drug, so long as it is with an eye towards obtaining FDA approval for the generic version can be carried out during the life of the patent on the drug. The unresolved question is whether a patented receptor or patented software used in the pursuit of regulatory approval for a drug, would be immune under this so called ‘clinical research’ exemption. The issue in such case would be that the material for which approval is sought (the drug), is not the ‘patented invention’ for which the immunity is sought (the target or software). How far would one take this exemption if that were to be the case? Would use of a patented instrument used during clinical trials on a candidate drug be exempt from infringement? Common sense may say to us that the answer is ‘no’. However, the statute is drafted quite broadly, and does not limit the exemption to the candidate ‘drug’, but apparently extends it to any ‘invention’, including research tools.

Preclinical use. Even if the ‘clinical research exemption’ applied broadly to the use of targets or software in pursuit of clinical approval for drugs, we now ask: would this exemption extend to the preclinical use of the software or receptor? In other words, would a company’s use of a patented target to discover drug leads be covered by the ‘clinical research’ exemption? One side of the argument would be that if such is the case then patents on targets used in drug discovery are without any value whatsoever. The other side of the argument is that since no drug can be sold without FDA approval in the US – so that even the act of discovery or lead improvement is ultimately in pursuit of regulatory approval – the clinical research exemption applies to such early activities. The

Figure 5 Common critiques of drug discovery tool patents

- 1 They might be used before the patent issues
- 2 Their use is hard to police
- 3 They might be used abroad and a non-infringing product imported.
- 4 Their clinical use may be exempt from infringement
- 5 There is uncertainty as to whether their preclinical use is exempt.
- 6 The statute of limitations (6 years) may be too short for realistic infringement damages

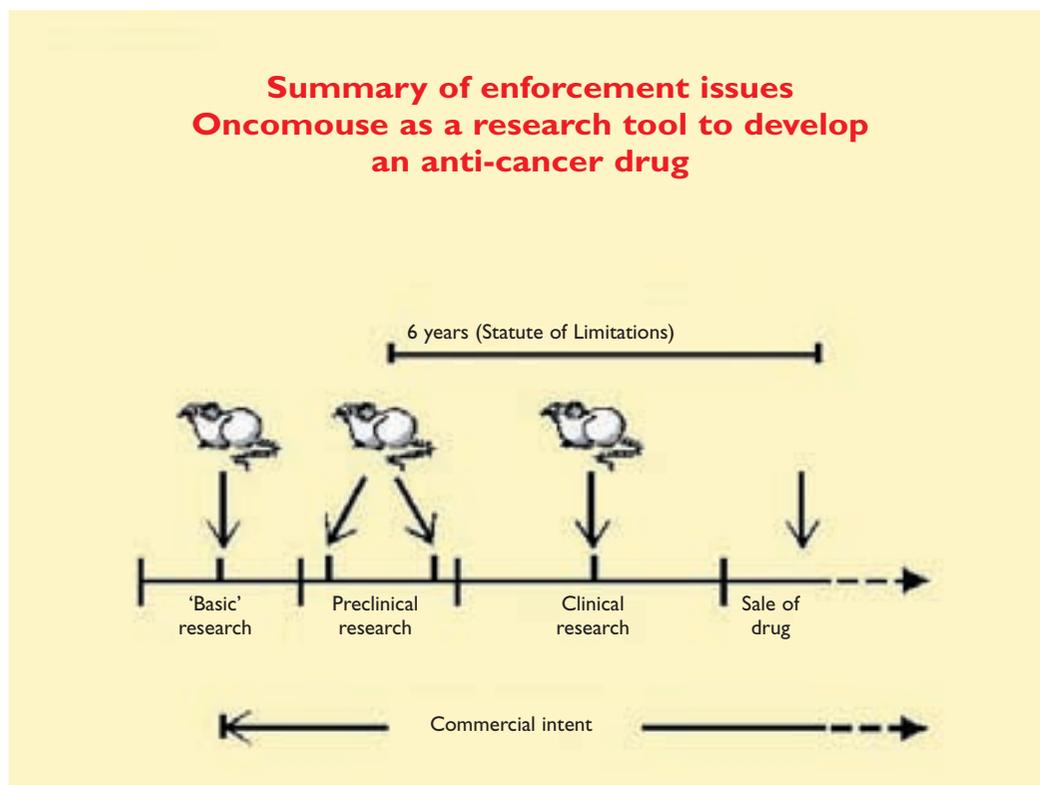


Figure 6

reach of the exemption will therefore have to be refined in the next few years.

Statute of limitations. There is in the United States a statute of limitations of six years for recovery of damages for past infringement³. In other words, if use of a patented drug discovery tool occurred more than six years ago and never again since then, those acts of infringement are no longer actionable. Only use of the tool within the last six years would be actionable. Whatever the measure of damages for the use (see below) it must have occurred relatively recently. Given the long periods of time involved in drug discovery and lead improvements, six years may not be a very long period of time. However, if the patented software or target are claimed narrowly, and intervening improvements have rendered the original material obsolete – and thus it is no longer used after six years – the patentee may have no remedy for the earlier acts of infringement.

Figure 6 shows a summary of our discussion, using as an example a knock out mouse as a drug discovery tool. The figure shows a line which spans from the time when the mouse is used in 'basic' research without commercial intent, to sale of a drug discovered with the mouse. In principle, actionable events are those that fall under the time when there is commercial intent. In addition, if the lawsuit is filed at the

point of the arrow, then any use of the mouse more than six years before the date of the suit is no longer actionable due to the statute of limitations on damages. As we discussed, the courts have still to decide if the infringing use of the mouse during clinical trials of the drug is exempt or not. Assuming that it is exempt and also assuming that preclinical use is not exempt, then the only period during which a non-exempt use of the patented mouse occurred in Figure 6 is the one event of preclinical research inside the six year statute. After that the mouse was no longer used in an actionable manner.

What, then, is a single use of a drug discovery tool worth? This question takes us finally to an analysis of the measure of damages for infringing uses of drug discovery tools.

The monetary value of patents on drug discovery tools

What is the measure of damages for the infringing use of a drug discovery tool? Is it reasonable to include the actual discovery of a drug and the value it has conferred on the patented tool's early use? What happens if the drug has not yet been discovered? Is it reasonable to speculate that the use of the tool might eventually result in such a discovery? These are very complex questions and the courts have only recently started grappling with them.

The US patent statute on damages has been interpreted to mean that a patentee is entitled to her lost profits but, if such cannot be shown (for example because the patentee is not manufacturing or selling and therefore has no profits in the first place), then she is entitled to at least a ‘reasonable royalty’⁴. There is a well-established case on damages in US patent law, known as *Georgia-Pacific Corp v United States Plywood Corp* (1970)⁵ which sets forth a long list of factors a court should use when deciding what is a ‘reasonable royalty’ as a measure of infringement damages. The court should place itself in the place of a ‘willing licensor’ and ‘willing licensee’ who are negotiating a licence at arm’s length, and then try to ascertain the value of the licence to either party. Among the considerations to be taken into account by the court are such factors as to whether there is an established royalty (for example, if a patentee has licensed his patent to others already), what type of licence it would be (exclusive vs non-exclusive, territorial vs worldwide, etc), rates for comparable patents, competitive relationship between the parties, etc.

One of the important considerations in all of these factors is the so-called ‘custom of the industry’. How does the drug discovery industry generally license these types of patent claims? Do they charge a one time fee? Do they charge a fee plus milestones? Do they charge a royalty based on the

sale of eventual drugs discovered with their tools? The latter is known as a ‘reach through royalty’ and is illustrated in **Figure 7**. This figure shows our oncomouse being licensed by the patent owner, Company X, to a Company Y which will do drug discovery with the mouse. Y is assumed to be able to invent a drug using this mouse and, therefore, Company X negotiates for a share of the profits made by the sale of the ultimate drug.

In *Rite-Hite Corp v Kelley Co, Inc* (1995)⁶ the CAFC stated that a patent holder is entitled to ‘any damages which are reasonably foreseeable’. An argument can therefore be made in litigation that reach through royalties are reasonably foreseeable for drug discovery tools and should be the measure of damages in the appropriate case. There is also support in US case law for the proposition that the royalty base does not have to be calculated from the direct sale or use of the actual patented product. It is customary, for example, to ascertain the measure of damages upon infringement of a claim to a process of manufacture by referring to the sales of the product produced by the patented process, even if the product is not patented. After all, it is more convenient to measure the sales of a tangible product than to count the number of ‘times’ a process for its manufacture has been used.

All of this leads to the conclusion that the courts in the US are quite liberal in their determination of

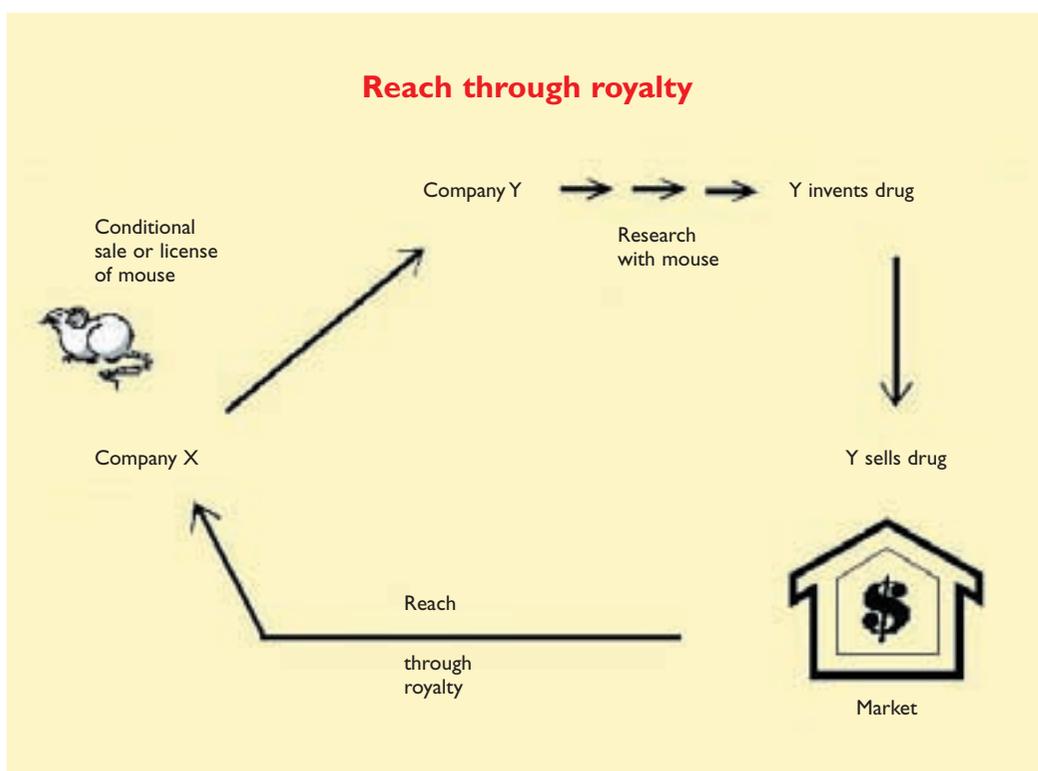


Figure 7

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References

- 1 The author's law firm is outside counsel for HGS.
- 2 35 USC Section 271(e)(1).
- 3 35 USC Section 286.
- 4 35 USC Section 284.
- 5 *Georgia-Pacific Corp v United States Plywood Corp* 166 USPQ 235 (DCt SDNY, 1970).
- 6 *Rite-Hite Corp et al v Kelley Co, Inc* 35 USPQ 2d 1065 (Fed Cir 1995).
- 7 *Sibia Neurosciences Inc v Cadus Pharmaceutical Corporation* 55 USPQ 2d 1927 (Fed Cir 2000).
- 8 Mueller, J. No Dilettante Affair: Rethinking the Experimental Use Exception to Patent Infringement for Biotech Research Tools. 76 *Washington Law Review* (January 2001).

the measure of damages, and in their definition of what is a 'reasonable royalty'. In an appropriate case, then, a court may decide that a reach through royalty tied to the sales of a drug is an appropriate measure of damages for the infringement of a patented drug discovery tool used at some earlier point in the discovery of the drug. It is unlikely that such a result would result from a purely speculative exercise, based on hypothetical future discoveries of drugs not yet in existence. However, in a case where there are actual sales of a drug discovered with the patented tool, the court might be more inclined to award reach through damages.

Conclusions

As we explained at the beginning of this paper, many questions remain before a measure of predictability will find its way into commercial and legal opinions on the value of patents on drug discovery tools. As happens in many other areas of the law, the process by which we will get there is slow and will develop case by case, statute by statute.

Litigation has already started in the lower courts. Chiron has sued Vertex on its patents on HCV receptor-based screens. The patents involved were sent back to the PTO for re-examination, and the case is presently stayed. In contrast, when Chiron sued Gilead on the same patents the case settled. Integra sued Merck on its patents on a cell adhesion receptor and a jury found on behalf of Integra for \$15 million. Scriptgen sued 3-Dimensional Pharmaceuticals on its patents on drug screening by thermal unfolding of proteins. The case settled. We already discussed Synaptic v MDS PanLabs on the importation of data. Lower court cases, however, especially if they settle provide little if any guidance or precedent.

The one case on a drug discovery tool patent that has reached the CAFC is *Sibia v Cadus* (2000)⁷ which involved a patent of Sibia on a cell-based screening method for the identification of compounds that exhibit activity with respect to particular cell surface proteins. Reversing a jury finding on behalf of Sibia for \$18 million, the Court of Appeals held the Sibia patent invalid for obviousness. The closest prior art was a paper which showed the precise assay of the Sibia patent, although not for use in screening unknown compounds. The court of appeals, holding that such an extension would have been obvious, stated that 'the express teachings in the art provide the motivation and suggestion to modify [the paper] such that the recombinant cells described therein should be used with compounds not previously known to interact with them for purposes of drug screening'.

While the case teaches us something about obviousness of screening methods, it is unfortunately not very instructive on the several issues we have addressed in this paper. We will need more such appellate cases, especially in the areas of scope of the clinical research exemption, on the measure of damages or on the importation of data, before we in the legal community will be able to advise our clients with confidence based on weight of authority rather than only reasoning based on assumptions.

Aware of the level of uncertainty in the field, commentators have started suggesting statutory remedies. Professor Janice Mueller of the John Marshall Law School has suggested a possible statutory scheme where the public would be allowed the freedom to use research tool patents for discovery of new technology with a post facto reach through royalty⁸. To the extent this is seen as a compulsory licensing regime, many in the industry may recoil and reject it off hand, ignoring the valuable merits of her proposal.

Regardless of the outcome of litigation or legislation, it is clear that patents on the tools of discovery are at the very core of the endeavours of the specialised drug discovery industry. Patents protect the products of their work and their investments, and it is unlikely that we will see a decrease in filings on these inventions any time soon. Parties confronting these patents, either in their own portfolios or in the portfolios of the competition, may choose to respect them or to ignore them at their own risk. Such parties, by their licensing efforts or by their learned ignorance, will continue creating the 'custom of the industry' in the way such patents are valued and exploited. And the 'custom of the industry' will, for better or worse, end up determining the measure of their worth. **DDW**

Dr Jorge Goldstein holds a PhD from Harvard University, and has done post-doctoral work research at the Massachusetts Institute of Technology. Dr Goldstein is a founding director of the biotechnology group of the intellectual property law firm, Sterne Kessler Goldstein and Fox, PLLC. His intellectual property law experience has been principally in areas such as genomics, bioinformatics, drug discovery, molecular and cell biology, recombinant DNA technology, immunology, transgenics and therapeutic methods. He has lectured internationally on multiple topics relating to his work. Dr Goldstein would like to acknowledge members of his law firm with whom he has had many discussion on the topic of drug discovery tools and their patents. Special mention goes to Robert Esmond, Larry Bugaisky and Don Featherstone.