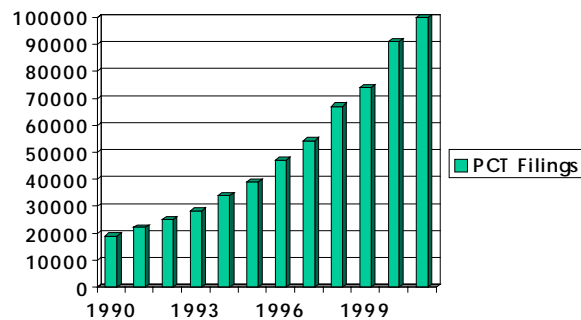


How Real are Patent Thickets, reach-through Rights, Royalty Stacking and Dependency, and Freedom-to-Operate Restrictions?

Philip Grubb
Novartis International AG

How Thick is the Thicket?

- The annual number of patent filings has been increasing exponentially.
- In 2001 over 100,000 PCT filings were made – over 5 times the number in 1990.



How Thick is the Thicket?

- This means that more and more patents and applications need to be considered when determining whether or not one is free to operate.
- This is particularly true for gene and research tool patents.



Opportunities - and Problems

- The availability of patent protection for genes and research tools constitutes a great opportunity for small biotech companies. They can use such patent rights to make money from useful inventions without having to develop drug products themselves.
- For pharmaceutical companies, this creates some problems, since they may have to pay to use tools which earlier might have been published and freely available.
- The problem hardly exists for academic research. In Europe, non-commercial research on a patented invention may not amount to patent infringement. Patent holders will usually try to enforce their rights against infringers with money – companies, not universities.



Are these Problems New?

- No. Problems of dependency have been with us for a long time. To take a simple example, a new drug may fall under a broad claim of an earlier patent, or licenses may be required for certain uses.
- Such situations can in almost all cases be regulated by licensing (including cross-licensing) under free market conditions.



Royalty Stacking – How high is the Stack?

- For a biotech drug product (protein, Mab, etc.), royalties could be owed to, for example:
- An academic institution with which the company entered into a research collaboration agreement resulting in the product.
- A biotech firm owning a broad patent to the class of product (e.g. humanized MAbs),
- A university with a patented production process,
- Another company with a patent to a specific indication for this class of product.



Royalty Stacking – How high is the Stack?

- Royalties in this situation could easily exceed 10%, even without any reach-through royalties for research tool patents. The total cost of goods should not be much above 20% if the product is going to be economically viable.
- One solution is to negotiate a reduction in the royalty rate in the event that other royalty-bearing licenses are needed. Typically reductions of 25 – 50% may be achieved.
- It is not to the advantage of any licensor if the total royalty burden is too high – then no-one will get anything.



Research Tools – what are they?

- A research tool is a composition of matter or a process which is used primarily in the research laboratory.

In the context of pharmaceuticals, it is either

- a material (biological or otherwise) used in the selection or testing of a drug candidate, rather than a component of a medicament; or
- A process of screening or testing, rather than of manufacturing or using a drug.
- Examples – markers, assays, receptors, enzymes, trans-genic animals, etc.



Are Genes Research Tools?

- They may be, for example if the gene is associated with a disease state and a compound acting upon the gene or its expression product may be a therapeutic candidate.
- Genes may also have utility as diagnostics or even directly as therapeutic materials (gene therapy).
- In transgenic plants, the marketed product (seed) will itself contain the transgene.



Patents for Research Tools

- It is sometimes said that research, particularly academic research, cannot constitute patent infringement because of the so-called "research exemption". This is not correct.
- In the USA, there is effectively no such exemption.
- In Europe, it is generally not infringement to experiment with an invention with the object of studying how it works, or improving upon it. But when a patented invention is used for its normal purpose without consent, that use is infringement, even if the use is within the laboratory.
- The inventor of a research tool is entitled to a fair return upon his investment, and fair compensation for the use of his patent.



What is Fair Compensation?

- The holder of a patent for a research tool may for example
 - charge a monopoly price for the tool itself (reagent, kit)
 - require a fixed annual fee for the use of the tool
 - charge a fee based on the amount of use (number of assays run, etc.)
- What he is not entitled to do is to demand a royalty based on sales of a drug product found with the help of the tool.
- If I patent an improved bunsen burner, I do not expect to get a royalty on everything that it heats up.



Why Downstream Royalties are not Appropriate

- In the normal situation, a research tool patent does not contain claims to products found by using the tool (reach-through claims, RTC)
- In the absence of RTC, there is no legal basis to require a royalty on something not covered by the patent. In the USA, this is arguably patent misuse (Bayer v. Housey, 2001).
- There are often many different tests and assays which may be used in the selection of a drug. If royalty is charged for all of these, on top of royalties which may be required for patents which would actually be infringed, the royalty stack will certainly get too high.
- Companies may be tempted to agree for short-term reasons.



NIH Guidelines

- In the USA, the NIH, which provides most of the funding for academic research, has taken the clear position that imposition of downstream royalties is not appropriate for recipients of NIH funding (Fed. Reg. 64, 248, 23 Dec. 1999).
- The NIH hopes that "other not-for-profit and for-profit organizations will adopt similar policies and refrain from seeking unreasonable restrictions or conditions when sharing materials."



How Far can I Reach?

- For the reasons just given, most inventors of research tools now try to obtain RTCs which would on their face cover the end-product as sold.
- A simple RTC of the type "A compound testing positive in the assay of Claim 1" would almost certainly lack novelty.
- A more limited claim would be "A compound identified according to the method of Claim 1" Scope?
- The chance of inherent lack of novelty is reduced by limiting the claim to a medical use.
- Such claims, particularly if coupled to an excessively broad main claim, could be very dangerous if valid.



Example – EP 287 653 B 1

16. The use of a compound as identified in the screening assay of claim 15 for the preparation of a pharmaceutical suitable in the treatment of hypertension, said compound being different from aldosterone.



Example – EP 724 637 B 1

35. A CRF₂ receptor antagonist for use in therapy, wherein said CRF₂ receptor is encoded by a nucleic acid sequence according to claim 1.

37. Use of a CRF₂ receptor antagonist for the manufacture of a medicament for treating cerebrovascular disorders, wherein said CRF₂ receptor encoded by a nucleic acid sequence according to claim 1.



Example – EP 680 517 B 1 (1)

- A method for determining the toxicity of a compound comprising the steps of
 - a) separately culturing one or more eukaryotic cells which, in toto, are characterized by:
 - i) at least one promoter or response element which responds to redox stress
 - ii)DNA stress, iii)protein stress, iv).....energy/Ionic stress,each of which said promoters or response elements being operatively linked to a gene which encodes a detectable product;
 - b) exposing each of said one or more cultures of cells to said compound;
 - c) quantifying the detectable product in each of said cultures; and
 - d) creating a stress-induction profile for said compound.



Example – EP 680 517 B 1 (2)

- A method of decreasing the toxicity of a drug, comprising the steps of:
 - a) determining the type of stresses caused by said drug using the methods according to any one of claims 5 – 27; and
 - b) modifying said drug to alter or eliminate the portion thereof causing said determined stresses.
- A modified drug produced by the method according to claim 29 or 30.

In other words – use a cellular assay to check if a drug is toxic, and if it is, change it until it isn't – and then I'll claim it. A classic example of what in the UK would be called a "free beer claim".
In opposition proceedings before the EPO, claims 29 – 30 were deleted.



Example – USP 6,048,850

- A method for selectively inhibiting PGHS -2 activity in a human host, comprising administering a non-steroidal compound that selectively inhibits activity of the PGHS -2 gene product to a human host in need of such treatment.
- This is the famous COX-2 patent of Rochester University, who are in litigation with Pharmacia. The validity of this patent is being contested, and probably it will not be upheld by the courts.



Should the Law be Changed?

- There are suggestions that patents for genes, which are required by the Biotechnology Patenting Directive, should be use-limited, to avoid undue dependency problems.
- This would be contrary to Art 27.1 of the TRIPs Agreement.
- Genes are no more than chemical compounds. When product per se protection for chemicals was introduced in Germany in the 1970's there were gloomy predictions of serious dependency problems and calls to make the claims use-limited. The problems did not happen; use limitations were not needed then and are not needed now.
- Problems can be dealt with by the courts applying existing law in a sensible way.



Freedom to Operate

- To ensure freedom to operate, companies must increasingly engage in defensive patenting.
- Having an early filing date in the USA is the best protection against being blocked by the patenting activities of a subsequent inventor. Publication alone may not be enough.
- Research departments need to ensure that they are not infringing valid patents of other parties.

- HOWEVER --



Are you really dependent?

- If you see a published PCT application claiming what is being done in your research laboratory –

DON'T PANIC

- Remember that only a granted patent gives enforceable rights.
- Check the Register and the file history
- Your research program may have finished before any patent is granted

