Patent Focus

Researched and written by Genericsweb

Genericsweb is a provider of information products and services to the generic pharmaceutical industry. Its flagship product, Pipeline Patent Intelligence is the industry leader in providing comprehensive research and analysis of patents protecting pharmaceutical products worldwide.

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The changing face of patents in generic pharmaceutical development: Facts and figures

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Anyone who has been involved in development of generic pharmaceuticals over the past 10–15 years will be well aware of the increase in importance of patents over that period. It may seem clear to those heavily involved in investigating the patent landscape and forming corresponding development strategies that their role has become more complex. But it is possible that the overwhelming amount of patent-related issues faced by such executives prevents them from understanding exactly what is changing and why.

Based on the analysis of comprehensive patent data relating specifically to generic pharmaceutical development, this paper takes a step back and draws insight from two distinct groups of products, those first authorised in the EU in 1987 and the others in 1997 (Table 1). The aim is to identify how the patent landscape has changed in the bigger picture and to suggest how this could affect the manner in which generic pharmaceutical companies determine their strategy, and structure their organisations in the future.

Of course one could benefit in drawing insight from a similar study of a greater number of drugs; however such quantitative analysis is not the intent of this paper. Greater insight may also be gained from studying drugs authorised more recently; however, the delayed nature of patent publications combined with a need for identification of long-term trends precludes such analysis at this time. The trends noted for products launched in 1987 may be affected by the longer periods of patent filings available for analysis compared with those launched in 1997; however, this is considered to reinforce the results rather than skew them in any direction.

WHAT HAS CHANGED?

First, the nature of the patent filings will be addressed. Patent applications for single-active, small-molecule pharmaceutical products can fall in one of four broad categories: molecule, process, formulation and use. The nature of these filings indicates the technological area where the innovator has concentrated on any lifecycle management and dictates the necessary capabilities required to develop non-infringing generic products. Such trends are generally compounded by resultant patent filings by generic competitors seeking to protect their R&D efforts to circumvent the innovator patents.

Looking first at the patent category distribution for the products launched in 1987 (Figure 1), it is clear that, in general, much emphasis was placed on the use of formulation patents by the innovator to extend the life of their products in the face of generic competition. Comparing this with a similar distribution for products launched in 1997 (Figure 2), it can be seen that innovators are now using patent systems around the world to protect a much broader range of

aspects of their product beyond active pharmaceutical ingredient (API) expiry, than they were 10 years earlier. The distribution does not necessarily show that the number of formulation patents filed is any less than ten years previous, but it does show that formulation expertise is no longer the only prerequisite to successful generic product development. With a greater relative importance on molecule and process patents across most products, API development has become a significant challenge in avoiding patent infringement when developing generics over the past ten years. The increase in use of patents for lifecycle management has, in the most part, been negated by clarification of regulatory guidelines in most major territories; however, this may again become significant with the introduction of 8 + 2 + 1 data exclusivity in Europe at the end of 2005.

Table 1: Drugs analysed and compared in this paper

First EU Authorisation 1987	First EU Authorisation 1997
Cabergoline (caberg)	Montelukast (montel)
Ciprofloxacin (cipro)	Pramipexole (pram)
Loratadine (lorat)	Quetipaine (quet)
Cyclosporine (cyclo)	Rivastigmine (rivas)
Omeprazole (omep)	Valsartan (valsar)

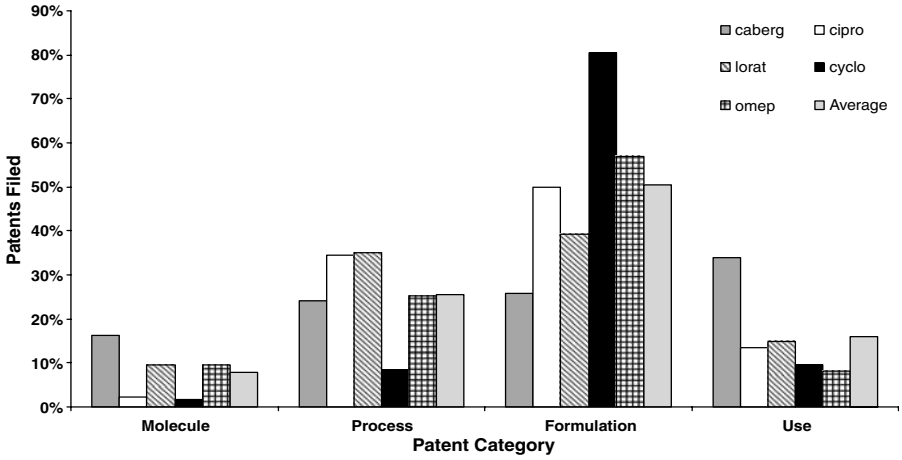

Figure 1: Patent category distribution (1987 launch)

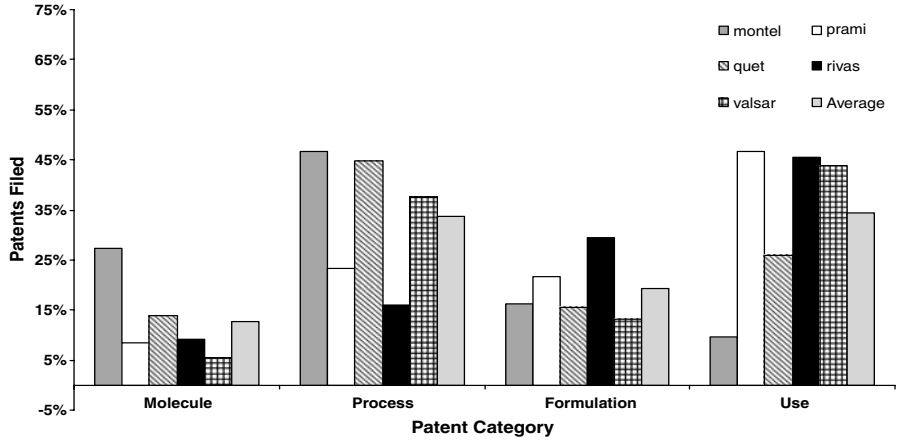

Figure 2: Patent category distribution (1997 launch)

The interdependent nature of molecular form and formulation in achieving bioequivalence, combined with increasing activity in these categories, is suggested to be at least partly responsible for the more recent consolidation of API manufacturers with formulators around the world.

HOW HAS THE GENERICS INDUSTRY RESPONDED?

Based on this apparent increase in patent complexity, it would make sense that companies seeking to develop non-infringing generics would start the process earlier in the life of the drug. This would improve the chances of successful development both by reducing the number of patents to circumvent at that time and by improving the chances of successfully protecting any innovative methods of doing so, on the basis of there being much less published prior art.

Looking at the percentage of patent filings over the three-year period prior to launch through to eight years subsequent to launch for each group of molecules (Figure 3), two very different trends are seen. For those drugs launched in 1987 a steady increase in patent filings is seen following launch; however, for those launched in 1997 a significant rise in patent filings from year six onwards is evident, suggesting that certain players in the generics industry have recognised the change in the patent environment and sought advantage in early development strategies. Evidence can be found to suggest that this generic 'lag' time is getting shorter; however, this data is not presented here.

Finally, an analysis has been conducted of the relative contribution different countries' generic pharmaceutical industries have made to the patent landscape for each group of molecules (Figure 4). While the effects of the innovator's country filings have been reduced to a certain extent for this analysis, they have not been removed completely. This shows several changes over the decade between the drugs analysed. First, India, as a patenting nation, is applying for a larger proportion of patents, taking its share from traditionally strong developing nations such as Germany and the USA, although these still remain among the strongest. Secondly, the industry in countries such as China, Korea and Taiwan do not appear to be proactively responding to the challenges presented by increased patent complexity. With such lack of focus on what is perhaps the most significant constraint in generic pharmaceutical development, it may be some time before these players catch up with those

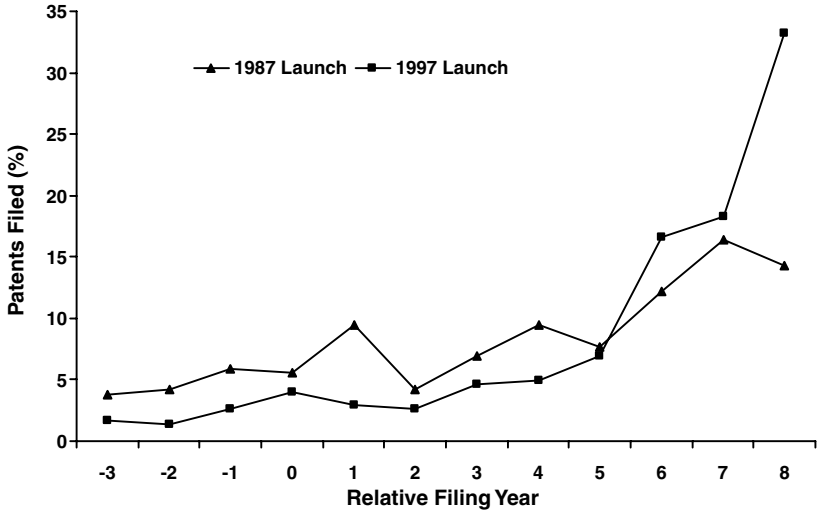

Figure 3: Post-launch patent filing trends

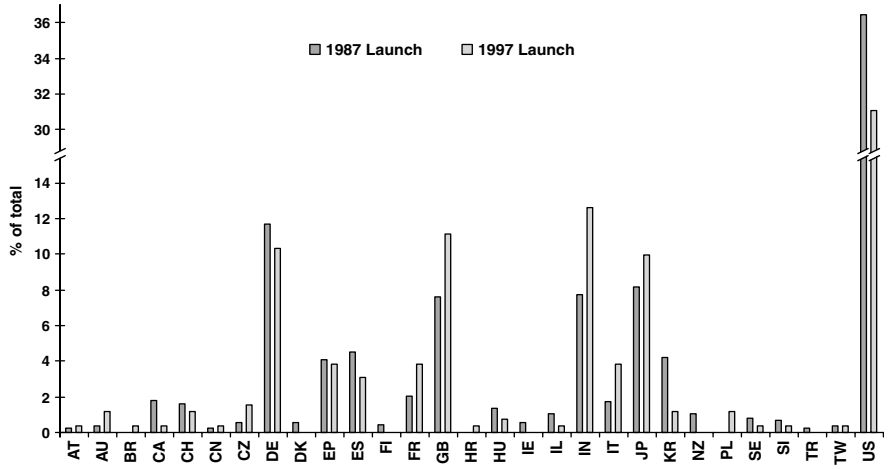

Figure 4: Patent filings by country (1987 and 1997). Abbreviations: AT, Austria; AU, Australia; BR, Brazil; CA, Canada; CH, Switzerland; CN, China; CZ, Czech Republic; DE, Germany; DK, Denmark; EP, European Patent Office; ES, Spain; FI, Finland; FR, France; GB, United Kingdom; HR, Croatia; HU, Hungary; IE, Ireland; IL, Israel; IN, India; IT, Italy; JP, Japan; KR, Republic of Korea; NZ, New Zealand; PL, Poland; SE, Sweden; SI, Slovenia; TR, Turkey; TW, Taiwan; US, United States

in more proactive countries to compete in developed markets, despite their significant domestic capabilities.

WHAT'S NEXT?

The face of patents in pharmaceutical development is changing as innovators employ more challenging lifecycle management techniques. This is placing an increased importance on understanding and monitoring the patent landscape across all divisions of generic companies from a very early stage in the lifecycle of the drug, to ensure maximum success of developing a non-infringing product and to perhaps secure some patent protection to limit competition. As companies increasingly seek development partners in countries that have not adapted to the need to proactively address patent issues they will need to ensure that partners are flexible enough to change processes and formulations as required by the ever-changing patent landscape, or they may need to sit back and wait while the more proactive developers take their share of the early generic market.