400
300
200
100

Diversification Delivers

Peter Steele of Thomson routes out the fuel that is firing the growth in drug discovery technologies, and explains how to keep the supply protected

Peter Steele studied Chemistry at Durham University, and subsequently Information Science at The City University in London. Throughout his career he has worked with patent literature, primarily in the pharmaceutical industry, including 16 years as Head of the Patent Information Unit attached to the intellectual property function of Glaxo Holdings. A period of IP consultancy in the 1990s yielded many publications based on analysis of pharmaceutical patents, including a series of company profiles in Current Opinion on Therapeutic Patents, and in-depth reports under the Inframonitor imprint. Peter founded Current Patents Ltd in 1998 to develop Dolphin, the database of all pharmaceutical inventions, acquired in 2002 by Thomson Scientific.

Blockbuster drugs tend to grab headlines but, arguably, it is the technologies used to identify these high-revenue pharmaceuticals that are more important in the long term. During the 1970s, innovation in the pharmaceutical field averaged around 3.5 per cent of all innovation, as measured by the subject breakdown of patent specifications published across all technologies and all major countries – steady growth since then has brought the current level to around seven per cent. It is interesting to consider what has caused this growth and what its effects have been on the industry.

INTERNATIONAL PATENTING – THE PCT ROUTE

Adoption of the Patent Cooperation Treaty (PCT) by the drug industry is perhaps the single most important factor in the growth we have observed over the past decade. Strictly speaking, it is almost 30 years since the PCT came into effect but the drug industry, more so than most others, was very slow to begin using it on a large scale. In Table 1, we see year-on-year growth in the use of the PCT generally. Quite understandably, drug companies were at first not prepared to risk using this new, untried route when seeking protection for their latest inventions, which they naturally hoped would turn out to be blockbusters. However, use of the PCT system grew with familiarity, helped by a change in the early 1990s where the decision as to whether to pursue a particular patent application could be delayed by up to 30 months from its original filing date. This 'thinking time' was critical for drug companies as they undertook preclinical testing of their most promising candidates.

Table 1:

	1980	1985	1990	1995	2000	2005
All PCTs	2,895	5,743	16,103	35,636	79,858	125,194
Pharma PCTS	124	420	1,765	5,193	10,666	13,985
%	4%	7%	11%	15%	13%	11%

Source: Esp@cenet

Table 2:

A New compounds
B New uses, formulations of known compounds
C Chemical processes (including combinatorial technology)
D Biotechnology
E Devices

CPG section	1999	2000	2001	2002	2003	2004	2005	2006
A	30	29	35	44	50	65	72	73
B	94	108	127	168	149	117	122	138
C	22	24	27	36	34	33	31	33
D	80	92	126	140	170	165	175	159
E	17	22	28	34	42	39	39	39
Total	243	275	343	422	445	419	439	442

As a result, we see inventions classed as 'medicinal preparations' contributing as much as 15 per cent to the total output of PCT applications by the mid-1990s. But since then there seems, by this criterion at least, to have been a slackening in the growth rate for pharmaceuticals. Growth has

continued – there are now almost 300 medicinal PCTs published each week, which represents a hundred-fold increase from 1980 – but patenting across all technologies is growing even faster.

BROADENING THE TECHNOLOGY BASE

In order to explain this apparent downturn, it may be useful to look at some data drawn from the Current Patents Gazette (CPG). This weekly alerting publication began during 1998 and aims to cover not only drugs but also the supporting technologies used by drug companies and their collaborators in the discovery process. For the purposes of CPG, inventions are classified intellectually into one of five sections, depending on what is being claimed (see Table 2).

Based on these figures, the past decade has certainly seen continuing growth in the sector's innovation, though possibly reaching a plateau around 2003. There is no sign of the downturn which was evident when only medicines were taken into account. More importantly, coinciding with the peak of activity occurring in 2003, there is a switch of innovative resources into the field of biotechnology. Whereas patenting of new uses and formulations was the single most important element of CPG during its first four years, the focus is now on biotech, which accounts for more than 150 inventions in an average week. Incidentally, the growth in biotech is matched by new compound patenting, which has more than doubled over this period.

DRUG DISCOVERY TECHNOLOGY

The challenge then is to find what is fuelling the industry's continuing innovative growth, given that patenting of actual medicinal preparations is in decline. A good place to start looking is in the technical field of microbiology – an area in which patent examiners have been placing a lot of the gene technology that forms the basis for many modern drug discoveries. Thomson Pharma shows some 9,000 inventions filed during 2004/5 which have been classified as microbiology, with around four per cent of them associated with a specific product. In contrast, the 15,000 medicinal inventions yield 22 per cent of drug linkages. Clearly the gene technologies are in general more remote from identifiable commercial products, though that is not to say

Table 3:

Technology	Drug links %	Third party links %
Medicine	22	10
Microbiology	4	15
Proteins and nucleic acids	8	17
Physics	2	9

that they will not turn out to be ultimately useful in the cause of identifying such products.

Interestingly, the microbiology patenting has more than 15 per cent linkage to other companies, whereas for medicines generally the figure is barely 10 per cent. This indicates that even though the technology is remote from marketed products, it is nevertheless a hive of third party activity. The intelligence gathered for Thomson Pharma includes collaborative patent filing, patent disputes, and licensing, and clearly there is substantially more of this type of activity associated with the infrastructure patenting, even at this early stage of its existence.

The more established fields of nucleic acid and protein chemistry occupy an intermediate position with respect to product linkage (about eight per cent), but show an even higher third party involvement figure (almost 17 per cent). It seems that emerging technologies are more likely than others to require the intervention of other companies or institutions when it comes to acquiring intellectual property (see Table 3).

Table 4:

Patentee	Number of patents
IBM	115
GSK	85
Pfizer	83
Affymetrix	83
University of California	74
Hitachi	66
J&J	63
Siemens	61
Roche	60
Medtronic	58
Philips	53
Bayer	48
GE	45
Merck & Co	44
Agilent	43
Applera	42
Fujitsu	39
US Government	32
MicroSoft	31
Novartis	30

PHYSICS IN DRUG DISCOVERY?

It may not be immediately obvious why inventions of interest to the drug industry should be classified as physics, but the fact is that there are now almost 10,000 inventions each year that fall into that category. The majority of these relate to the measurement of light, principally in the context of fluorescence-based immunoassays, but there is a substantial and growing sub-set concerned with computerisation. The extremely low figure of two per cent drug linkage comes as no surprise for these subjects, and the mid-range figure of nine per cent for third party interactions is close to that for the industry's overall innovation profile. Looking specifically at the inventions classed as computing, several recurring themes may be identified:

- Pharma-informatics (monitoring drug delivery)
- Predictive modelling of drug regimes
- Stock control and prescription management
- Rule-based DNA analysis
- Metabonomics
- Binding site identification
- Protein array analysis in diagnosis
- Drug delivery devices (pumps, and so on)
- Molecular modelling

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This list could be much longer, but hopefully serves to demonstrate the diversity of the innovation that now supports the drug industry. Some of these themes are ones which simply did not exist a decade ago, and some might well fall broadly within the field known as 'business methods', which in most jurisdictions are regarded as unpatentable.

DIVERSIFICATION LEADERS

A 'top 20' ranking of this physic-based innovation makes for interesting reading, being an eclectic mix of well-known big pharma names with niche companies and giants from the electronics and software sectors. The 'outsiders' are led by IBM, supported by Hitachi, Siemens, Philips and General Electric. Affymetrix and Medtronic are niche operators, while Microsoft, Applera and Agilent represent the software industry (see Table 4).

If the field is restricted to patent applications that have been researched in depth by the Thomson Pharma analysts, this has the effect of elevating Pfizer to the leading position, which they occupy principally on the strength of a diverse programme of crystal structure determinations.

CONCLUSION – A CHANGING LANDSCAPE

From the perspective of classic medicinal chemistry, drug industry innovation might well seem to have reached a plateau, or even to be in decline. But that conclusion ignores the diversification that has occurred over the past decade, which has brought 'alien' disciplines, such as computing, into the drug discovery infrastructure. A holistic view of the subject takes in this multidisciplinary innovation and results in a picture now dominated by biotechnology rather than medicinal chemistry. This change of emphasis in patenting mirrors a shift of emphasis at the commercial end of the business, where biopharmaceuticals are a major target for big pharma, while generic manufacturers are increasingly turning their attention to bioequivalents. ◆

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