Expert Opinion on Therapeutic Patents

ISSN: 1354-3776 (Print) 1744-7674 (Online) Journal homepage: informahealthcare.com/journals/ietp20

Drug patenting in 2001

Peter Steele

To cite this article: Peter Steele (2002) Drug patenting in 2001, Expert Opinion on Therapeutic Patents, 12:1, 3-10, DOI: 10.1517/13543776.12.1.3

To link to this article: https://doi.org/10.1517/13543776.12.1.3

Expert Opinion

Ashley Publications
www.ashley-pub.com

Drug patenting in 2001

Peter Steele
Current Patents Ltd., Middlesex House, 34-42 Cleveland Street, London W1T 4LB, UK

Statistical analysis of the pharmaceutical patent literature is described, with examples drawn from existing and forthcoming compilations. A six year ranking of key therapeutic innovators places GlaxoSmithKline clearly in the lead, followed by Merck & Co. and Aventis. When platform technologies are also included there are some dramatic changes, including entry of the US Government and the University of California into the top ten. Country of origin, subject matter and collaborations are also considered. Factorial maps resulting from correspondence analysis are explained.

Expert Opin. Ther. Patents (2002) 12(1):3-10

1. Introduction

This overview is based on material assembled for *Drug Patents 2001*, a reference book [1] covering pharmaceutical and biotech patenting from 1995 through to mid-2001, a total of almost 49,000 inventions. The book serves in part to update an in-depth analysis of therapeutic innovation from 1994 to 1998 [2], itself updated a year later in the series *Current Trends in Pharmaceutical Discovery* [3]. However, in this latest version some additional material is included, effectively extending the analysis into areas of platform technology not covered previously.

The base material for the 1994 - 2000 analyses is derived from *Patent fast-alert*, a weekly abstracting and indexing service focusing on patents from major authorities which have clear, stated therapeutic utility. The particular advantage of using this focused source of therapeutic patents is that the documents are indexed using a strictly hierarchical scheme, which in turn permits specific diseases and pharmacological mechanisms to be mapped to the correct higher level terms in preparation for analysis. Without this facility to group related diseases and mechanisms, stable correspondence analysis, one of the most powerful tools available, would be impossible.

The directly therapeutic innovation referred to accounts for some 150 new patent documents each week, whereas roughly three times this quantity falls within the broader definition employed by *Current Patents Gazette*. This weekly publication has competitive intelligence as its focus and seeks to include all subject matter which might be of interest to the pharmaceutical and supporting industries. The additional material is in fields such as diagnostics, process and formulation technology, packs and dispensing devices, gene manipulation, microfluidics, electrotherapy and so on. The *Gazette* does not have systematic indexing and in any case many of these infrastructure inventions have neither a medical indication nor a mechanism of action even indirectly associated with them. However, this broader content arguably gives a more accurate picture of innovative effort in the industry and so some of the statistics and graphs below make use of *Gazette* material from the first 20 weeks of 2001.

2. Key players - the leading innovators

Table 1 is a listing of companies and other institutions active in therapeutic patenting over the past six years, ranked according to number of qualifying patent documents. Within the commercial sector there have of course been many mergers and acquisitions during that period, so that virtually all of the companies named there have changed in size and nature since 1995.

Table 1. Top applicants of 2001.

Rank	Applicant Name	Total patents	%	Patents in 1995	Patents in 1996	Patents in 1997	Patents in 1998	Patents in 1999	Patents in 2000	Rank in 2001
1	GlaxoSmithKline	1911	4.51	234	193	294	353	454	383	1
2	Merck & Co.	1364	3.22	231	238	261	235	222	177	2
3	Aventis	1211	2.86	280	217	207	162	145	200	4
4	Pfizer	1049	2.48	148	168	167	153	195	218	3
5	Eli Lilly	1048	2.47	163	237	171	220	136	121	10
6	Roche	762	1.80	121	112	126	126	143	134	7
7	AHP	733	1.73	126	120	80	141	142	124	37
8	Pharmacia	707	1.67	158	135	109	108	106	91	6
9	AstraZeneca	593	1.40	64	81	83	92	132	141	9
10	Novartis	484	1.14	94	92	114	64	53	67	21
11	Univ. California	479	1.13	70	76	99	103	86	45	8
12	US Government	471	1.11	84	85	72	74	67	89	5
13	Incyte	466	1.10	2	11	26	187	127	113	21
14	Takeda	439	1.04	95	90	66	70	49	69	14
15	BMS	429	1.01	96	83	59	76	57	58	64
16	Novo Nordisk	401	0.95	44	71	70	71	78	67	52
17	J&J	380	0.90	58	67	57	56	57	85	111
18	Bayer	367	0.87	52	75	67	50	57	66	10
19	HGS	353	0.83	18	76	53	79	51	76	15
20	Sanofi	336	0.79	64	53	49	71	40	59	29

AHP: American Home Products; BMS: Bristol-Myers Squibb; J&J: Johnson & Johnson; HGS: Human Genome Sciences

That being so, it is perhaps surprising to see such stability in Figure 1, where the six-year ranking is compared with that for the early part of 2001. The ranks for 2001 are included in the final column of Table 1 but it must be borne in mind that these are based on all pharma/biotech patenting, rather than the explicitly therapeutic innovation shown elsewhere in that tabulation. Despite the general upheaval (and the different selection rules), it is only Eli Lilly (down from 5th to 10th), Novartis (10th to 21st) and AHP (7th to 37th) that have moved by more than a couple of positions over six years. Significantly perhaps, the two resulting top ten vacancies have been occupied by the US Government (including the NIH) and the University of California, non-corporates with more than the usual amount of platform technology in their portfolios (Figure 1).

The case of Eli Lilly is rather special, since the company has not been involved in a major merger and its mid-1990s patenting was dominated by a huge volume of raloxifene patenting, now a past phenomenon. Patenting by Novartis and AHP also appears to have declined rapidly but it may simply be that these innovators have especially pure portfolios, with a high proportion of therapeutic patents and relatively little platform technology.

Some other interesting movements in the rakings are highlighted in Figure 2, where steady declines in the outputs of Pharmacia and BMS are juxtaposed with quite rapid growth from Millennium and Isis. Incyte Genomics, ranked 13th overall, temporarily leapt to 4th position in 1998 on the strength of some vigorous gene patenting, but has now subsided to 21st. It is not until these data are expressed graphically that some of these changes and trends become apparent.

3. Collaborations and alliances

The same observation applies to the networks formed by jointly filed patent applications, namely that the interrelationships can be seen clearly only when displayed in two dimensions. Some of the joint filings from 2001, of which there were almost 400 in the first 20 weeks, are shown in a tree structure in Figure 3. The entire map includes more than 50 simple pairs (not shown here) indicating a single collaborative filing, but even in a sample as small as this, roughly two-thirds of the patents are grouped in clusters with four or more nodes. There are mini-clusters with five and six nodes, respectively, focused on Pharma Mar and the University of Texas System, while Schering AG and Merck & Co. fall within less focused small clusters.

However, most striking are two large clusters showing many interwoven connections. The French cluster has CNRS as its principal focus, with INSERM and Institut Pasteur as second-

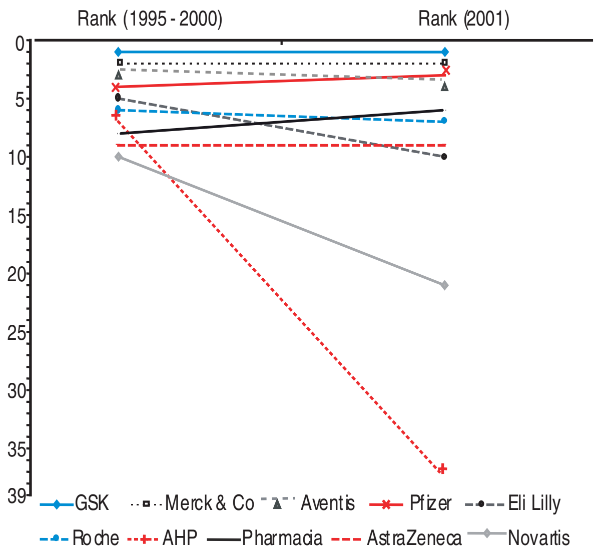

Figure 1. Comparison of the top ten applicants (1995 - 2000) with their current 2001 standings.

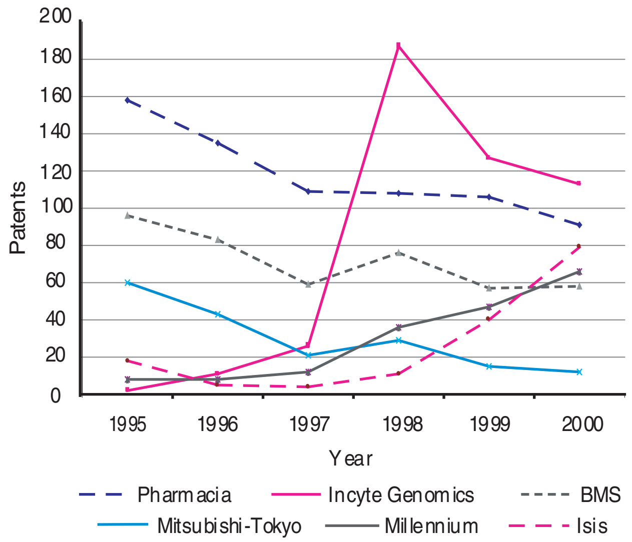

Figure 2. An examination of the fortunes of other interesting companies between 1995 and 2000.

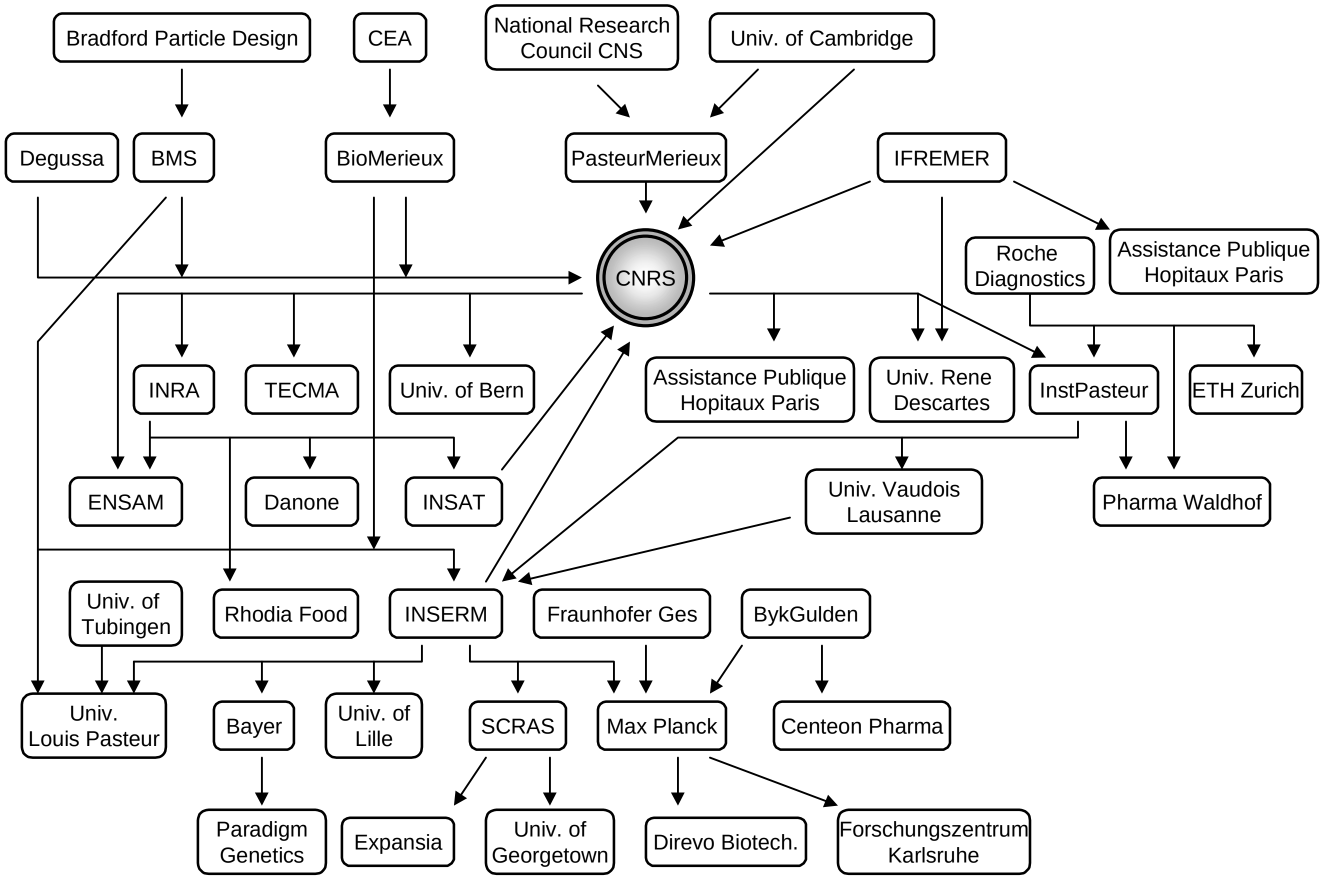

Figure 3. Network of joint patenting in 2001.

Table 2: Origin of inventions in 2001.

		Out of 7305	%
US	USA	3272	44.8%
JP	Japan	716	9.8%
DE	Germany	707	9.7%
GB	United Kingdom	530	7.3%
FR	France	398	5.4%
CA	Canada	222	3.0%
CH	Switzerland	160	2.2%
IT	Italy	139	1.9%
NL	Netherlands	123	1.7%
SE	Sweden	120	1.6%
AU	Australia	97	1.3%
IL	Israel	95	1.3%
BE	Belgium	90	1.2%
KR	Korea	87	1.2%
DK	Denmark	77	1.1%
ES	Spain	69	0.9%
AT	Austria	41	0.6%
IN	India	40	0.5%
CN	China	38	0.5%
FI	Finland	36	0.5%
RU	Russia	32	0.4%
NO	Norway	25	0.3%
HU	Hungary	24	0.3%
IE	Ireland	22	0.3%
NZ	New Zealand	19	0.3%
ZA	South Africa	12	0.2%
TW	Taiwan	11	0.2%
BR	Brazil	10	0.1%
GR	Greece	9	0.1%
IS	Iceland	9	0.1%
SG	Singapore	9	0.1%
PL	Poland	7	0.1%
CZ	Czech Republic	6	0.1%
	Others	53	0.7%

ary foci; UK and German universities form part of this mainly non-industrial network. Roche and BASF fall towards the edge of the cluster while Bayer and, surprisingly, BMS are more deeply involved. The other rather more extensive cluster is clearly US-based, oriented around the University of California and the US Government. Linked indirectly to these, however, is GSK as a secondary focus.

The value of this type of analysis becomes apparent when it is necessary to link a particular product or technology to the patents which protect it, for example in a competitive intelligence database like DOLPHIN [4]. On the majority of occasions when a collaboration is announced, in a press release for example, the true originator of the intellectual property rights is not identified. Typically a commercial enterprise has licensed rights from a non-industrial partner but does not mention that partnership. By reference to a tree structure of joint patent applications it may be possible to infer true ownership. Using a conventional patents database it may be possible to identify the jointly assigned patent property of two parties, but for a given assignee it is not generally possible to identify joint applications and collaborators.

Table 3: *Gazette* classification.

Section	Nature of claim
A	New compounds
B	New formulations & uses
C	Chemical process & combinatorial technology
D	Biotechnology
E	Devices & equipment
F	Electrotherapy & other non-chemical treatments

4. Origin of inventions

In performing analysis for *Current Patents Gazette*, analysts note the street addresses of the inventors, in order to give the most accurate possible view of where the research was conducted. Again, in a conventional database this would often not be possible; alternative data elements such as assignee address or priority country are likely to be misleading. From Table 2 it is clear that the US currently accounts for almost half of all pharma/ biotech innovation, judged on inventor locations, followed by Japan and Germany with 10% each. Approximately 10% of inventions name inventors from two or more countries.

Year-on-year, changes in this ranking will of course occur only slowly, but it will be interesting to watch the emergence of new countries. Cuba, for example, does not feature at present but is known to have an active biotechnology research community which is beginning to file patent applications internationally. The economic G7 countries, with the intervention of Switzerland, occupy the top eight positions. Other European countries and the countries of the broader G20 grouping account for most of the remainder of Table 2, exceptions being Israel, Hungary, New Zealand, Taiwan and Singapore.

5. Subject matter

For *Gazette* purposes again, inventions are broadly classified into six Sections (A - F) according to the nature of the novelty claimed (Table 3).

This classification is crude, but when expressed graphically it can help to distinguish the strategies of patent applicants. The radar charts in Figure 4 summarise the patenting of the 12 most prolific patentees from early 2001 in this field. Straight away it

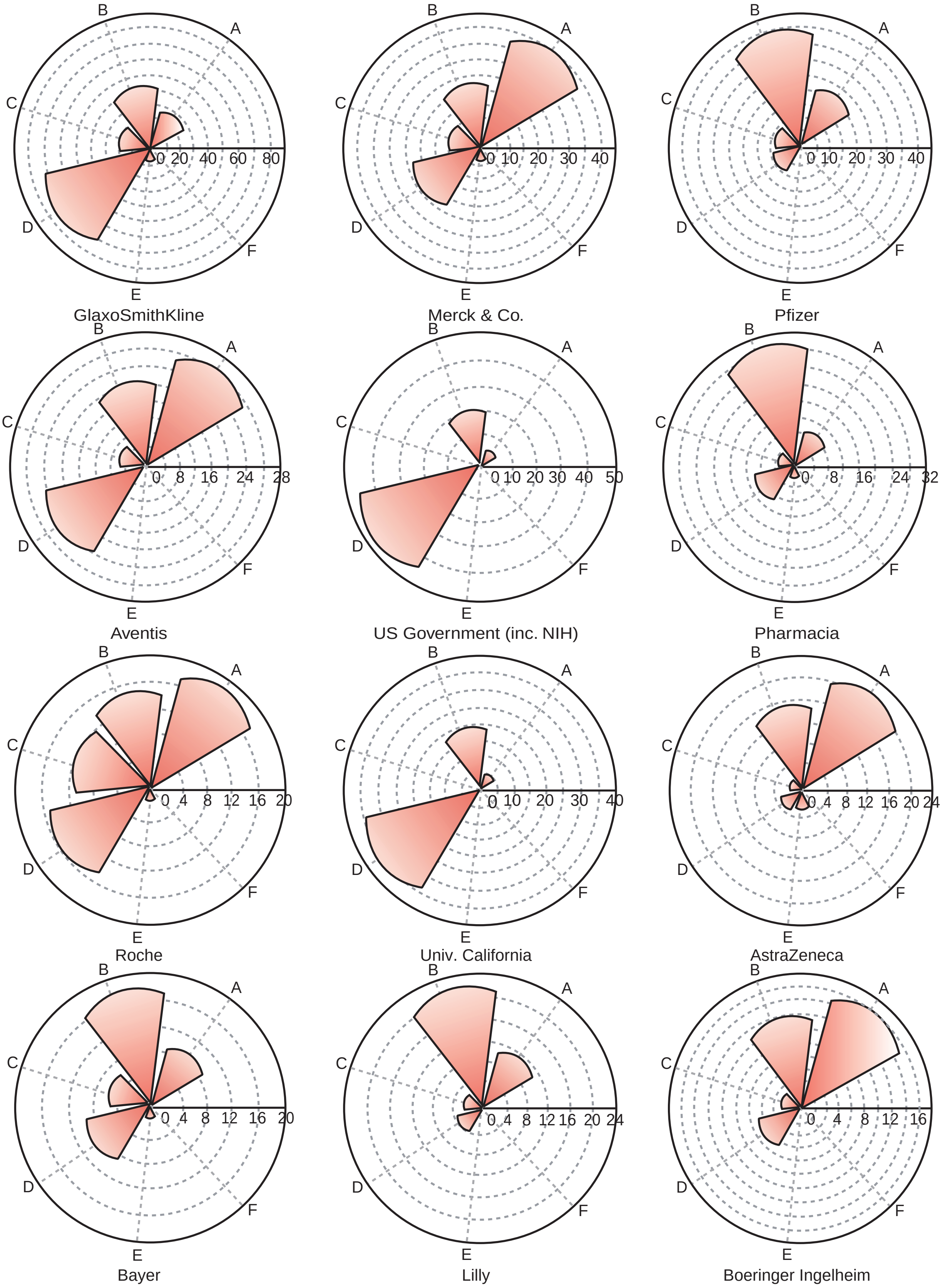

Figure 4. Twelve most prolific patentees from early 2001.

Table 4. Most common main IPCs used in 2001.

		Out of 5003	%
A61K	Medicinal preparations	1386	27.70
C12N	Microorganisms and enzymes	892	17.83
C07D	Heterocyclic compounds	564	11.27
C07K	Peptides	422	8.43
C12Q	Control of microbiological processes	346	6.92
G01N	Analysis, chemical and physical	292	5.84
A61M	Drug administration devices	187	3.74
C07H	Nucleosides and nucleic acids	150	3.00
C07C	Acyclic and carbocyclic compounds	149	2.98
A61N	Electrotherapy and radiotherapy	111	2.22
A61B	Diagnosis and surgery	57	1.14
C12P	Fermentation to produce chemicals	56	1.12
A01N	Pesticides and agrochemicals	47	0.94
A01K	Animal husbandry and transgenics	31	0.62
A23L	Foods and nutrition	29	0.58
A61F	Prostheses and dressings	29	0.58
C07J	Steroids	29	0.58
A61L	Sterilizing and disinfection	26	0.52
C07F	Compounds containing phosphorus, silicon etc.	23	0.46
G06F	Digital data processing	18	0.36
A61J	Containers for pharmaceuticals	13	0.26
B01L	Chemical laboratory apparatus	13	0.26
B01D	Separation of materials	9	0.18
B65D	Containers and packaging	9	0.18
C07B	Organic chemistry methods and apparatus	9	0.18
C08F	Macromolecular compounds	9	0.18
C12M	Apparatus for microbiology	9	0.18
B01J	Chemical processes, colloids and catalysts	8	0.16
C08B	Polysaccharides	6	0.12
A61H	Physical therapy	5	0.10
A61P	Therapeutic activity of chemical compounds	5	0.10

is apparent that the US Government and the University of California have atypical but near-identical profiles and it is no coincidence that the two organisations were linked in the tree structure discussed previously. The two leaders, GSK and Merck, differ principally in their relative emphasis on biotech and new compounds respectively; it is the SmithKline Beecham component of the GSK portfolio which is responsible for the excess of biotech. Aventis and Roche also have similar profiles, the latter with rather more emphasis on process chemistry. Pharmacia and Pfizer form a near-identical pairing, sharing a focus on the use and formulation of known compounds, but AstraZeneca alone displays a clear focus on new compounds.

Table 5. Breakdown of IPC C12Q 1/68.

C12Q 1/68	
Section C	Chemistry
Class 12	Biochemistry - Genetic engineering
Subclass Q	Measuring or testing, process control
Group 001	Measuring or testing microbiological processes
Subgroup 68	Involving nucleic acids

An alternative and more detailed view of subject matter comes from analysis of International Patent Classifications (IPCs), the hierarchical subject codes applied to applications by patent offices. As indicated in Table 4, more than 30 main IPCs (at sub-class level) are needed to classify the range of subject matter covered by *Current Patents Gazette*. It is not too surprising to find A61k (medicinal preparations), A61m (drug administration devices) and C07d (heterocycles) near the top of the ranking, but many of the other subclasses are concerned with fundamental biotechnology and would have been far less prominent in the corresponding ranking ten or even five years ago; likewise A01k, the sub-class concerned with transgenics.

It is perhaps rather unexpected to see Section G (physics) used for more than 6% of the patents, but this is largely explained by the classification of many gene manipulation inventions under techniques for analysing biological material (sub-groups of G01n-33). Combinatorial chemistry also leads to some distant classifications, such as G06f (computing) and B01j/l (chemical processes and apparatus). Significantly, in this age of genomics, the single most common full (sub-group level) IPC is C12q-001/68, for which the full meaning is given in Table 5.

6. Correspondence analysis

The IPCs, useful though they are for distinguishing broad areas of technology, are insufficiently detailed to allow meaningful analysis of therapeutic targets. Indeed an indexing sub-class for recording therapeutic uses, A61p, was introduced only in the most recent (seventh) edition of the IPC; it came into use at the beginning of 2000 but is still by no means universally applied to pharmaceutical patents and applications. This is regrettable because correspondence analysis based on therapeutic categories and pharmacological mechanisms has been found to be one of the most effective and unbiased ways of expressing the information diversity of a set of pharmaceutical patents.

However, as indicated previously, the hierarchical indexing applied to therapeutic patents in *Patent fast-alert* is suitable for this purpose. As an illustration of the factorial maps which can be created in this way, that for plane 1/2 is shown (Figure 5). Along dimension 1, pain and neurological disor-

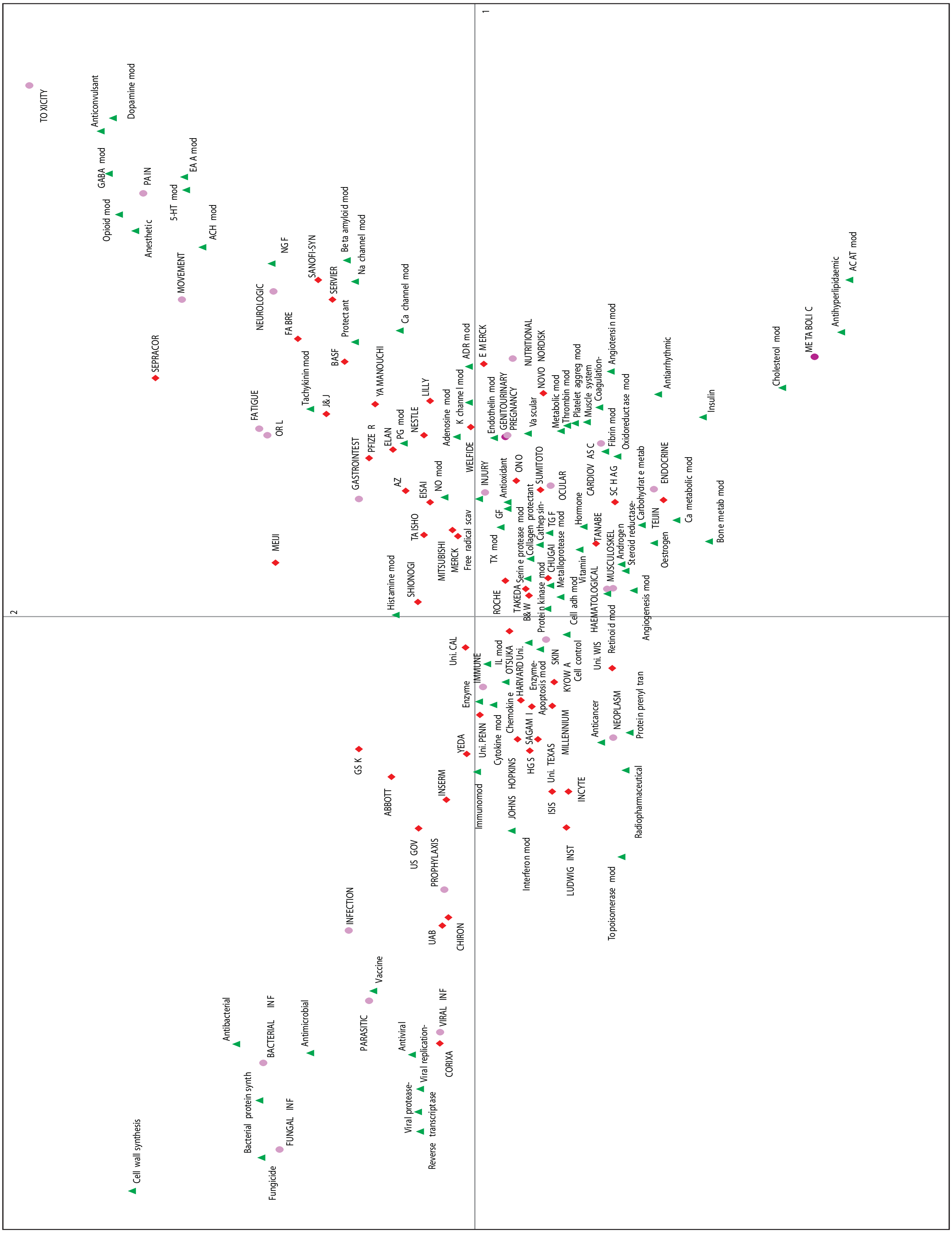

Figure 5. Plane 1/2 factorial.

ders (associated with excitatory amino acid and neurotransmitter mechanisms) and cardiovascular disease, occupying positive positions, are contrasted with fungal, viral and bacterial infections and the associated mechanisms. But on dimension 2 it is CNS and microbial topics that are associated with the positive axis, in contrast with the metabolic and cancer topics on the negative axis. These two principal dimensions together express ~ 50% of the total information content of this very large data set. When they are intersected at right-angles, the resulting plane has the therapeutic and pharmacological points (circles and triangles respectively) laid out in two dimensions in such a way as to indicate intuitively their similarity or dissimilarity. This factorial map is vectorial, in that points lying along a particular straight line from the origin tend to be associated. Their distance from the origin indicates how distinctive they are; a point near the periphery is atypical and/or of low weight.

When companies' patent portfolios are projected onto this plane, their positioning is determined by their therapeutic and pharmacological make-up. For example, companies such as Sanofi-Synthélabo and Servier, positioned on the upper right diagonal of plane 1/2, are likely to have portfolios quite skewed towards neurologicals. Merck lies in the same direction but much closer to the origin, indicating more normal or average activity; possibly this is a so-called barycenter effect, innovations in the upper right quadrant being balanced by others in the lower left. There is a vast amount of detail in these maps and their value lies in the fact that they are unbiased, being based on a statistically rigorous manipulation of independently assigned index terms.

7. Expert opinion

The statistical evaluation of pharmaceutical patenting reviewed here represents the culmination of almost a decade's innovation analysis. The sources referred to, including the forthcoming reference annual and database, are intended as an addition to the sources available to competitive intelligence professionals in the industry.

Bibliography

1. Drug Patents 2001. Matthew Sparrowhawk (Ed.) Current Patents Ltd.
2. Five years of drug patenting. N Grandjean, PR Steele (Eds.) *Curr. Trends Pharm. Dis.* (1999) 2:(1&2).
3. Drug patenting in 1999 - an update. N Grandjean and PR Steele (Eds.) *Curr. Trends Pharm. Dis.* (2000) 3(2):85-111.
4. DOLPHIN: Database of all Pharmaceutical Inventions, Current Patents Ltd.

Affiliation

Peter Steele
Managing Director, Current Patents Ltd
Middlesex House, 34-42 Cleveland Street
London W1T 4LB, UK
Tel.: 020 7323 0323;
Fax: 020 7631 9927;
E-mail: peter@current-patents.com