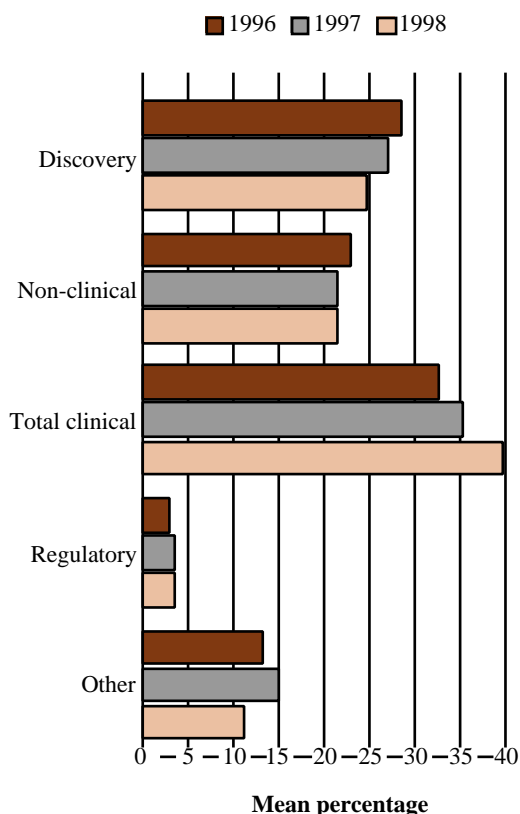


STRATEGIC STATISTICS (3): PHARMACEUTICAL INVESTMENT AND OUTPUT IN 1998

Figure 1 *R&D expenditure by functional activity 1996-1998; Major companies*

There has been a considerable increase in the proportion of R&D expenditure allocated to clinical studies between 1996 and 1998 (from 32.5 to 39.5%, respectively).



Economic pressures to increase output while containing growth in R&D expenditure, coupled with unprecedented opportunity in the form of emerging discovery technologies are among the factors putting pressure on companies to re-examine their strategic direction. The annual survey of investment and output by CMR International, relating to three areas of pharmaceutical R&D activity, provides vital support for effective strategic planning.

Key findings from the fourth survey:

- Clinical studies consume an ever increasing proportion of R&D expenditure despite unchanging numbers of new active substances in the clinical development pipeline.
- Regulatory submissions and market launches both fell substantially in 1998.
- Major companies look set to increase their annual output of novel medicines over the next five years.

Further annual surveys will reveal whether these trends remain the same in the next decade. Further annual surveys will reveal whether these trends remain the same in the next decade.

Following the successful format of previous years (R&D Briefings No. 15 and 22), the fourth annual survey of pharmaceutical investment and output sought information on three activities in 1998 comprising:

- International pharmaceutical R&D expenditure and sales;
- Products in the clinical development pipeline;
- New active substance (NAS) activity; submission, authorisation and marketing.

Fifty-one companies responded to at least one of three questionnaires used in this survey; they included 43 of the top 50 companies by R&D expenditure in 1997.

In a move away from previous geographical analyses, companies were grouped according to their R&D expenditure on ethical (prescription only) pharmaceuticals in 1998:

Major = >\$1bn; Medium = \$0.4-\$1bn; Other = < \$0.4bn.

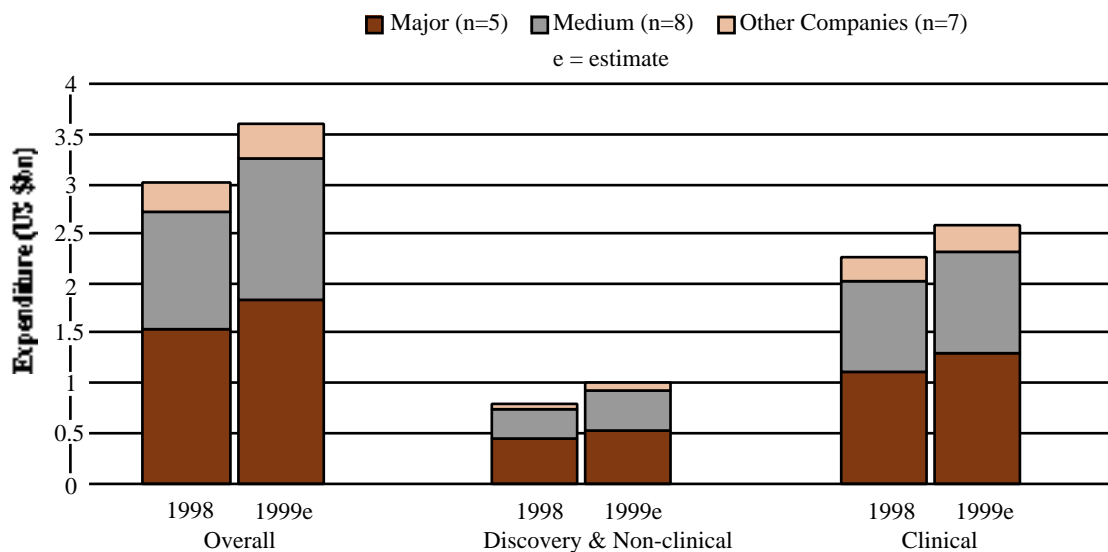
Despite the focus on cost containment and efficiency, the global pharmaceutical industry continues to increase its yearly investment in research and development.

In 1998 this was projected to be US\$ 39bn, up from US\$ 37bn in 1997. Sixty-four percent of that expenditure is attributed to the 37 companies providing data for this part of the survey.

In previous years there has been concern that the mean increase in yearly R&D expenditure has been faster than the average sales growth rate. This situation remains for the pharmaceutical industry as a whole, but some companies are starting to contain R&D expenditure as a proportion of sales. For a group of 16 companies (8 Major, 4 Medium, 4 Other) able to supply annual global sales figures for 1990-1998, the rate of growth in global sales between 1997 and 1998 was 11% while the growth in R&D expenditure was only 8%. However, predictions for 1999 suggest the growth in both parameters will be equal, at 11%.

Figure 2 R&D expenditure allocated to commercial contracts in 1998, with estimates for 1999

Respondent companies anticipate that the proportion of R&D expenditure allocated to commercial outsourcing contracts will rise to 22.1% of R&D expenditure in 1999, compared with 20.4% of their combined R&D expenditure in 1998.



The focus of investment

Novel products remain the focus for investment, with 72% of all R&D expenditure being allocated to new active substances (NASs).

The pattern of R&D expenditure might be changing, however. Between 1996 and 1998 there was a considerable increase in the proportion of R&D expenditure allocated to clinical studies by the major companies (Figure 1). While investment in discovery research declined over the three year period, clinical evaluation expenditure increased from 32.5% to 39.5%. In real terms this equates to a rise in expenditure from US\$ 3.9bn in 1996 to US\$ 5.3 bn in 1998.

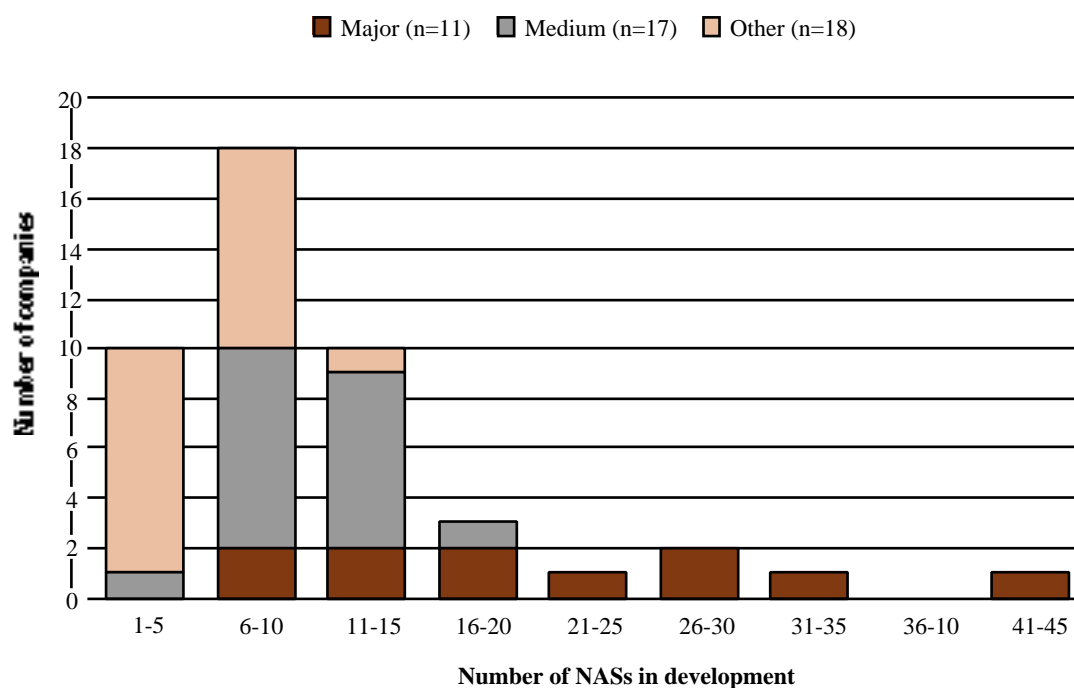
The shift in R&D functional expenditure to clinical research, as shown in Figure 1, may be a reflection of the number or position of compounds within the clinical development pipeline. However, there has been little

change in the total number of NASs in clinical development between 1996 and 1998 and the average number in Phase III, the most expensive stage of clinical development, has not changed considerably. This implies that the cost of clinical evaluation is increasing.

In their bid to curtail costs, access expertise and increase speed in clinical development, companies are making greater use of contract research organisations. In 1998 the investment in commercial contracts for clinical research was almost three times higher than the amount spent on discovery and non-clinical commercial contracts (Figure 2). By 1999 it is estimated, by a group of 20 companies, that the cost of outsourcing clinical studies will exceed US\$ 2.5bn. Overall, there is expected to be a year on year increase in all R&D commercial outsourcing expenditure.

Figure 3 *New active substances in clinical development in 1998; number per company*

On average, Major companies had 21 NASs in clinical development at the end of 1998, compared with 10 and six for Medium and Other companies, respectively). There has been little change in the total number of NASs in clinical development between 1996 and 1998.



A healthy pipeline?

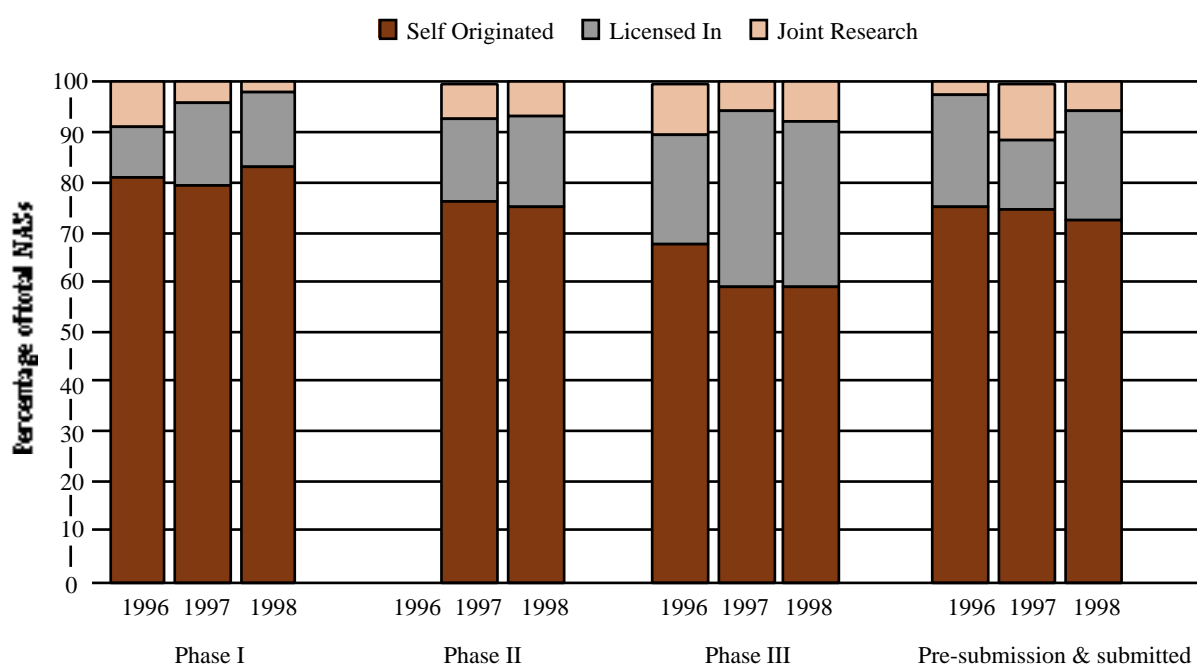
Major companies, as expected, have on average more NASs per company (21) in their clinical development pipeline (Figure 3) than either Medium (10) or Other companies (6). The overall average for 1998 of 13.7 NASs per company can be compared with 1996 and 1997 figures of 13.9 and 15.0, respectively, for 27 participants that provided relevant information. As in previous years, nervous system, cancer and cardiovascular conditions head the list of therapeutic areas for which NASs are being developed.

Looking externally for compounds to supplement the internal development portfolio remains an important strategy, and licensed-in products represent 20% of the total clinical development pipeline. The proportion of new active substances that are licensed-in from external organisations increases through the phases of clinical

research (Figure 4). There has been a marked increase over the past two years in the proportion of compounds undergoing Phase III investigation that are licensed-in (from 22% in 1996 to 33% in 1998).

Figure 4 Origin of new active substances within each phase of clinical development 1996-1998

The proportion of compounds undergoing Phase III clinical investigation that have been licensed in has increased from 22% in 1996 to 33% in 1998.



Clearing the regulatory and marketing hurdles

Twenty-one companies (8 Major, 8 Medium and 5 Other companies) have provided information on their regulatory and marketing activities over the past three years (Figure 5). These data reveal a substantial decrease in the number of submissions made to regulatory authorities in 1998, the total being less than half the number filed in the previous year. Likewise, there was a marked fall in the number of marketing authorisations received in 1998, and in the number of new active substances to which these authorisations related.

The number of new molecular entities (NMEs) first launched on to the world market was also down in 1998. Only 35 NMEs were introduced on to any one of the world markets, being the lowest annual output of NMEs in the last two decades.

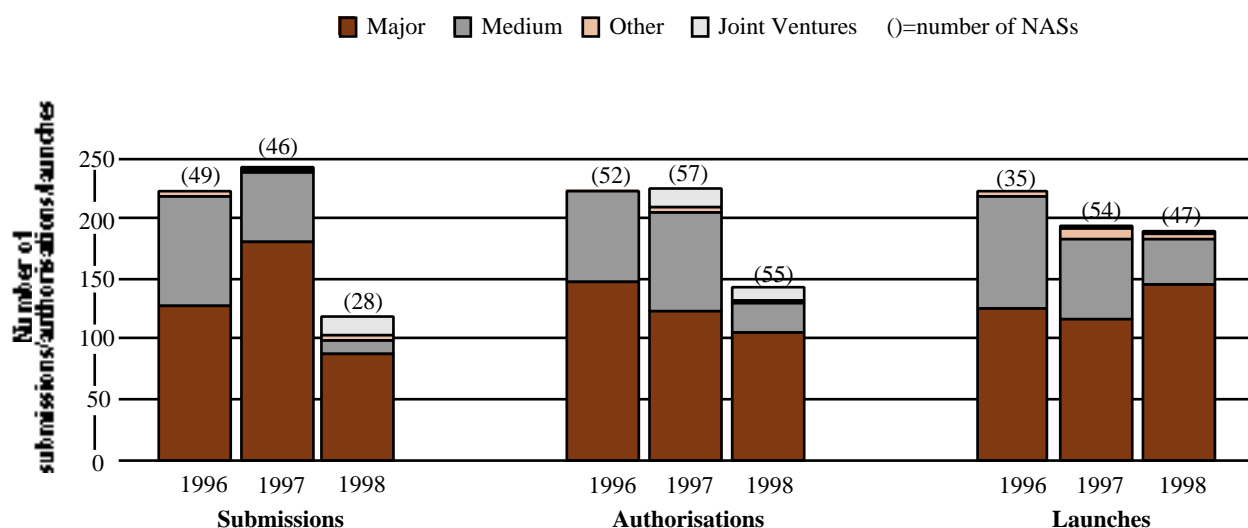
These figures do not provide a favourable forecast for increased output in the next few years. However, by using information on products in the pipeline and

applying success rates obtained from companies in 1998, there is some room for optimism. It is estimated that major companies will launch 1.8 NASs per company per year over the next five years; this represents increasing output by, on average, 60%.

Speeding up the development process remains a key objective. The mean development times for NMEs first marketed anywhere in the world in 1998 (Figure 6) show that major companies were considerably faster (mean 10.9 years; median 9.0 years) than the industry average (mean 13.5 years; median 13.4 years). Overall, however, the industry has yet to show an improvement in development times over those observed in the early 1990s.

Figure 5 Regulatory and marketing activities 1996-1998

The number of regulatory submissions, marketing authorisations and launches of new active substances within the EU, Australia, Canada, Japan, Norway, Switzerland and the USA are presented for 21 respondent companies. The number of NASs for which one or more submissions were made fell by 39% between 1997 and 1998.



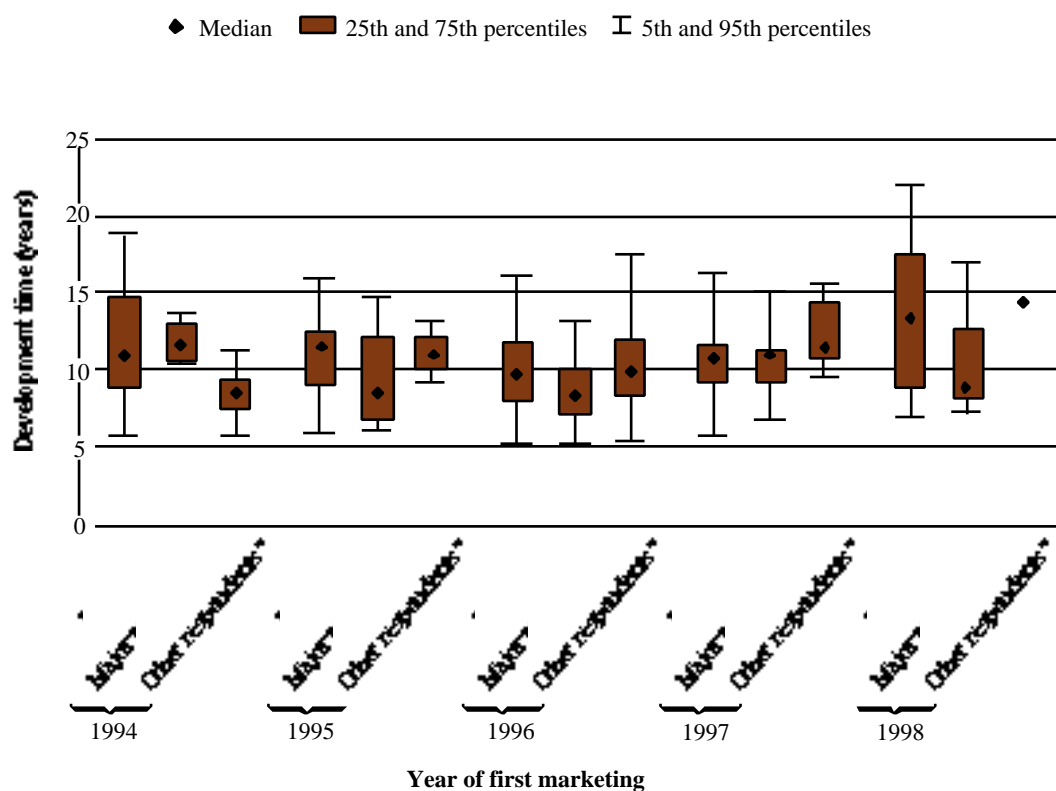
A valuable resource

This R&D Briefing reflects but a few statistics from the wealth of data that is now generated by these annual surveys of pharmaceutical investment and output which are contained within the full report. With the

completion of each successive round of data collection, CMR International is creating an invaluable R&D resource for the global pharmaceutical industry.

Figure 6 *Development times for new molecular entities first marketed 1994-1998*

The average development time for NMEs first marketed in 1998 by Major respondent companies (mean 10.9; median 9.0 years) was considerably faster than the industry average (mean 13.5; median 13.4 years). "Industry" includes NMEs marketed by companies that did not respond to this survey.



* Medium and Other Respondents



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Copies of the full report "Activities of the International Pharmaceutical Industry in 1998: Pharmaceutical Investment and Output", which contains 100 pages, 53 figures and 8 appendices, are available free of charge to CMR International sponsoring companies. The report can be ordered quoting reference number CMR99-126R.

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