



R&D Briefing

Strategic Statistics (2)

Pharmaceutical investment and output in major markets

Percentage change in R&D expenditure (1997 - 1998e)

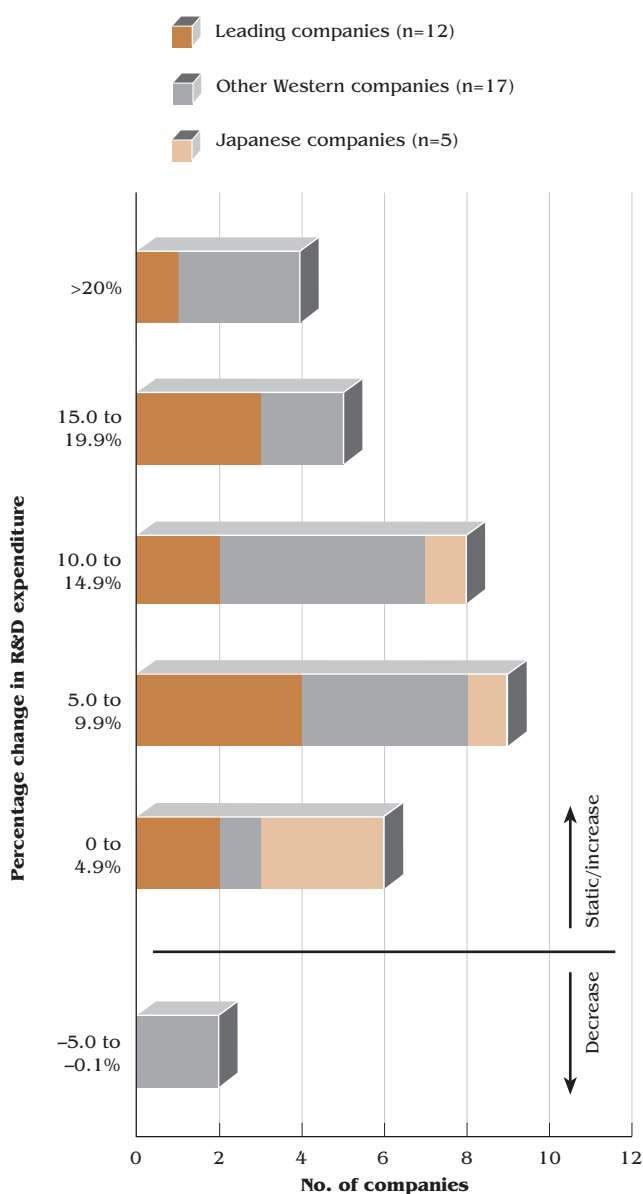


Figure 1 The mean increase in R&D expenditure between 1997 and 1998 was estimated to be 11% for the 34 respondent companies.

- Staying ahead in a complex, global industry requires knowing the answers to a constant stream of questions. As the pharmaceutical industry continues to face exacting times, the need for up-to-date information is vital to companies for effective strategic planning.
- What is the current level of R&D expenditure? Is this being supported by adequate sales? Are sufficient compounds emerging from the clinical pipeline to sustain such investment in R&D? Indeed, what is the likelihood of a new active substance reaching the market? Where are the most marketing authorisations granted?
- Answers to such questions reveal industry trends, that in turn allow individual companies to put their own statistics in perspective. To this end, the first CMR International survey of pharmaceutical investment and output received enthusiastic support, and it is now repeated annually.
- The recent round of data collection on activities of 42 companies in 1997 showed continued investment in R&D, albeit with a lower overall rate of increase, coupled with a rise in the annual output of new products.

Perspective

Widespread interest in the findings from the 1997 CMR International survey of pharmaceutical investment and output (R&D Briefing No.15) was expressed at a meeting for representatives of those companies that had contributed data. It was therefore decided to repeat the survey in 1998 for activities completed in 1997, with the inclusion of some extra information. Separate questionnaires were used to address three key areas:

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

Data were collected from 42 companies, including 34 of the top 50 by R&D expenditure in 1996, and 14 of the leading 15 by R&D expenditure. Seven of the companies were Japanese and two were biotech companies.

R&D Expenditure and Sales

The pharmaceutical industry is continuing its investment in the research and development of new active substances (NASs). This message is reflected in the global pharmaceutical R&D expenditure, estimated to be US\$ 37bn in 1997 and US\$ 40bn in 1998. The 37 companies that provided information on R&D expenditure in this survey were responsible for 63% of that projected expenditure.

These figures have been calculated from data previously collected by CMR International, and are based on company estimates for 1998. Experience shows that companies are able to predict their R&D expenditure with an accuracy of $\pm 5\%$.

The level of R&D expenditure is expected to increase overall by a mean of 11% between 1997 and 1998 for 34 companies providing relevant information. Two of these anticipated a decrease and one expected R&D expenditure to remain static over this period (*Figure 1*).

Ratio of R&D expenditure to sales in 1996, 1997 and 1998e

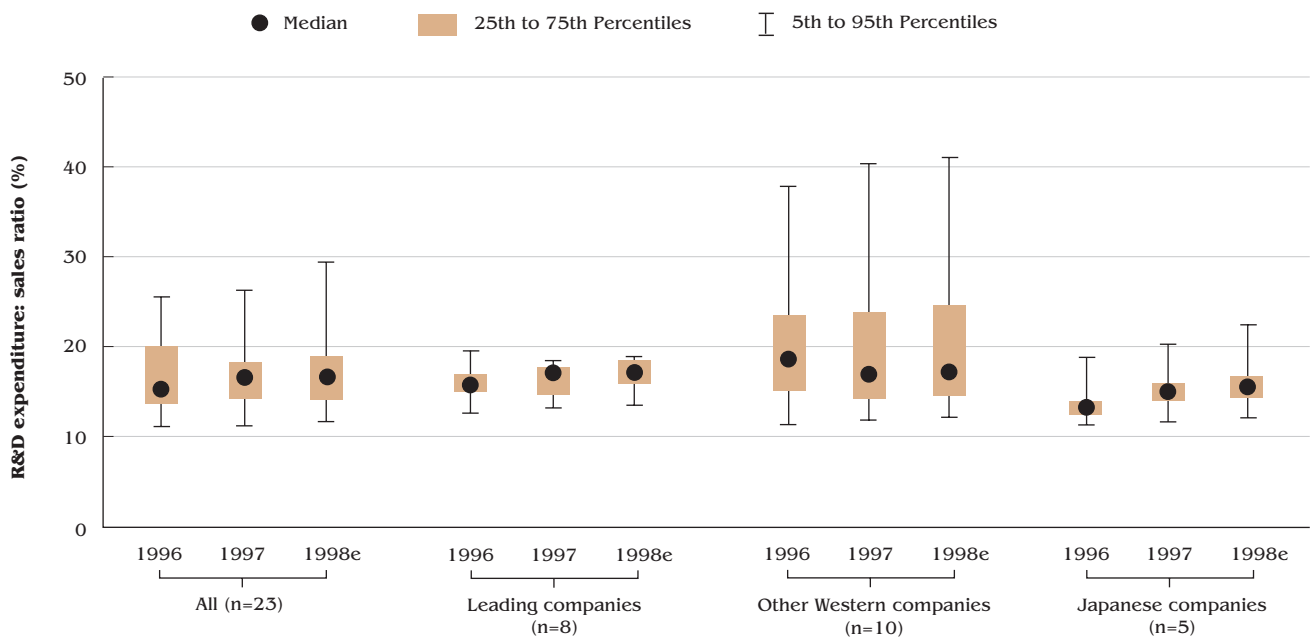


Figure 2 The median R&D expenditure to sales ratio for the 23 respondents as a whole has increased slightly over the period (15.7, 16.6 and 16.5 for 1996, 1997 and 1998e respectively).

The rate of increase may, however, be falling. Between 1996 and 1997, the overall rate of increase in R&D expenditure was 6.0%, just over half the mean yearly rate of increase for the years 1990 to 1996.

Where does the investment go?

The percentage of R&D expenditure allocated to line extensions was determined for the first time in the 1998 survey. This revealed that leading companies allocate a mean of 26% of their pharmaceutical R&D expenditure to researching and developing line extensions; the figure for other Western companies was 19%.

As expected, investment in new active substances predominates, accounting for a mean of 72% of pharmaceutical industry expenditure.

Another new feature of this recent survey was investigating the proportion of R&D expenditure being

made outside the company in the form of research contracts with academia and external commercial organisations. This revealed that in 1997, US\$ 2.6bn (17% of R&D expenditure) was allocated to external commercial R&D contracts by the 23 participating companies that provided this information; this figure is estimated to increase by 15% in 1998. Likewise an increase of 18% is anticipated for research contracts with academia; in 1997 the level of support through such contracts was US\$ 686m (3.8% of R&D expenditure).

Is investment sustained by sales?

The mean percentage increase in sales between 1997 and 1998 was estimated at 6.9%; for Japanese companies a mean decrease (-1%) was anticipated. Despite this, the mean R&D expenditure to sales ratio has increased slightly over the period 1996-1998, and is expected to be 18.8% overall in 1998 for 23 respondent companies (Figure 2). For the five Japanese companies

Percentage of NASs in active clinical development at the end of 1997 by therapeutic area

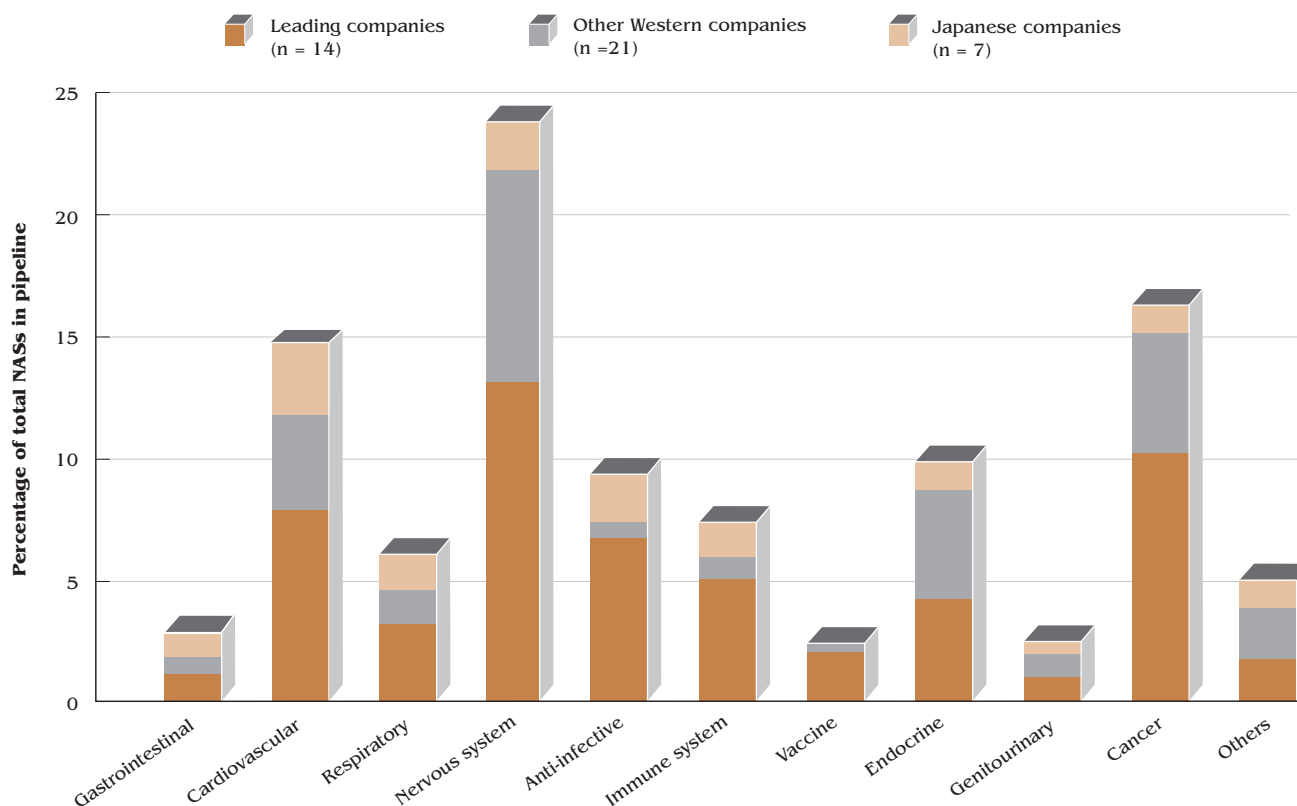
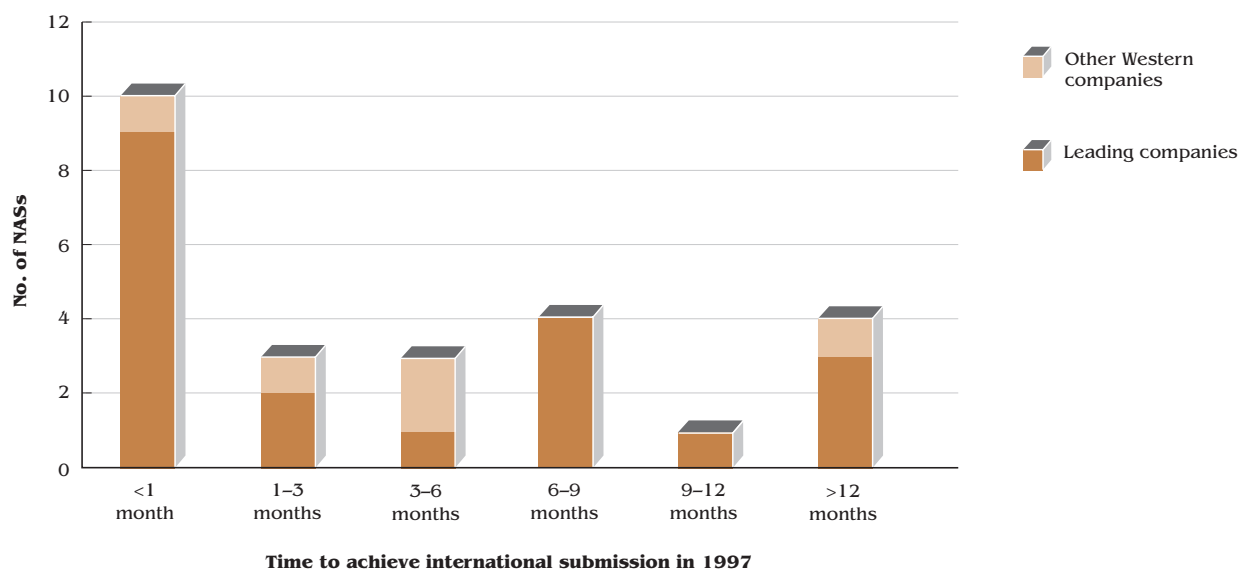


Figure 3 Nervous system, cancer and cardiovascular areas continue to attract most clinical development. However, leading companies decreased development of cardiovascular NASs by 20% between 1996 and 1997, whilst development of cancer therapies increased by 11%.

Time for the submission of an NAS to achieve international status in 1997



The time between the first and last submission necessary for an NAS to achieve international status in 1997 is shown. It should be noted that the first submission may have been prior to 1997. For the submission of an NAS to have achieved international status, a dossier must have been submitted to regulatory authorities in two of the three ICH regions of Japan, Europe (defined as three from the UK, Germany, France, Italy and Spain) and USA.

Figure 4 Twenty-five NASs, submitted by 15 companies, achieved international submission in 1997; for 21 NASs the time between the first and last submission necessary to achieve international status was less than one year.

that supplied data, the increase in this ratio is more marked, from a mean of 14.1% in 1996 to an estimated 16.4% in 1998.

Clinical Development Pipeline

Information on 488 new active substances that were in active clinical development at the end of 1997 was provided by 42 companies, 31 of which had participated in the previous survey. Leading companies are more active in this field, developing, on average, almost 20 NASs per company, compared with around 10 for Japanese and less than 7 for other Western companies. More particularly, the NASs in development by leading companies are expected, on average, to achieve higher peak sales than those of other companies.

As previously, the highest proportion (over 70%) of NASs were in Phases I or II of clinical development, with Japanese companies having relatively few compounds

in Phase I. Phase III accounted for 18% of NASs while the remaining 10% were the subject of, or pending, a submission for marketing authorisation. Only a small proportion of NASs (6%) were designated as back-up compounds, and the majority of these were within Phase I.

The therapeutic areas where the most clinical development is directed remain the nervous system, cancer and cardiovascular diseases (Figure 3). However, some changes had occurred since 1996. Leading companies decreased development of cardiovascular NASs by 20% and endocrine NASs by 25%, while their activity in the areas of respiratory and cancer treatments increased by 33% and 11%, respectively.

Marketing probability

For the first time, the survey sought success rates currently used by companies to assess marketing probability, for each phase of clinical development, from the decision to start preclinical development to

Time taken from regulatory approval to launch for the EU and six other major markets in 1997

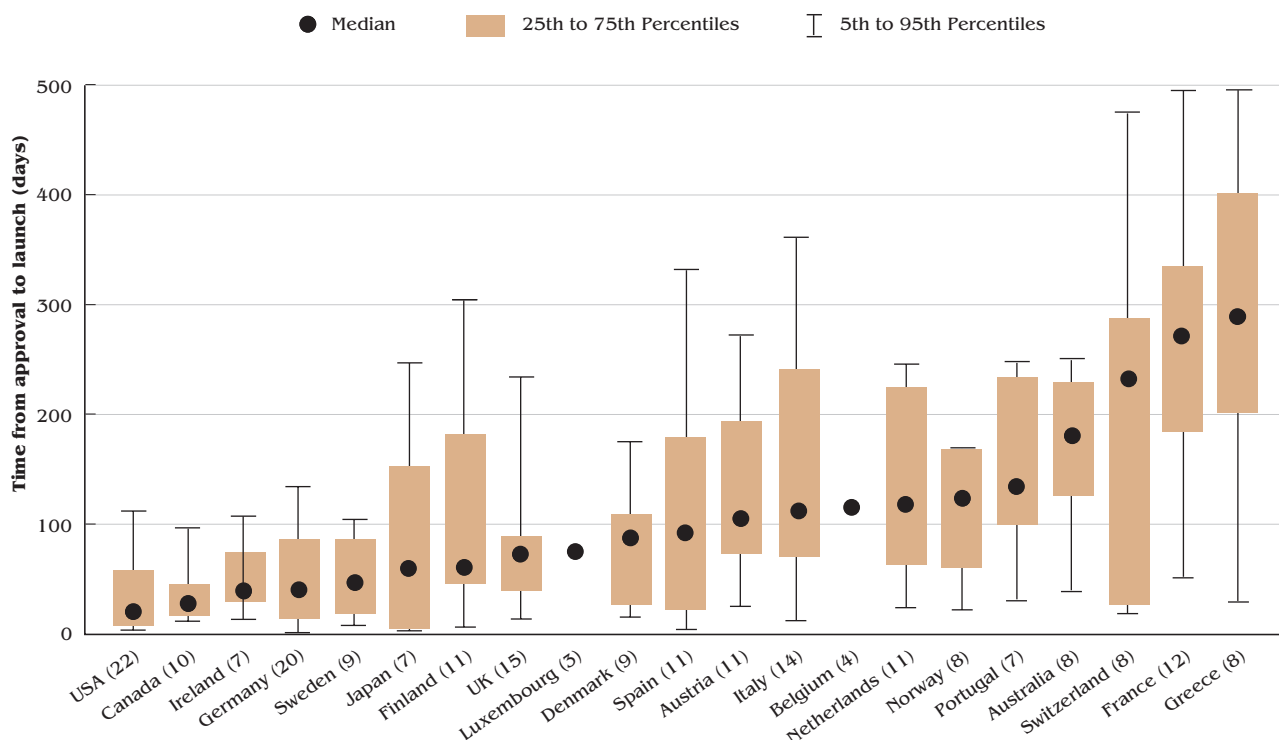


Figure 5 The mean and median delay from approval to launch in the Member States of the EU and six other major markets was 115 days and 81 days respectively.

() = number of NAs for which marketing delay could be calculated for each market

support administration to humans. There is little difference in the mean success rates between leading, other Western and Japanese companies. Assuming constant success rates across therapeutic areas, the 14 leading companies surveyed are likely to market an average of 1.6 NAs per company per year for the next five years, a 60% increase in the rate of the last five years.

During 1997, 19% of compounds in the clinical pipeline were terminated, generally during early development. Surprisingly however, 9% of all terminations occurred during Phase III and a further 3% after submission.

Regulatory and Marketing Activities

A profile of regulatory submissions and marketing authorisations within the EU countries and six other major markets was supplied by 39 companies. Of the 327 submissions in 1997, relating to 66 new active substances, the individual country receiving the most was Canada.

The increasing drive towards international submissions was apparent in the 1997 data. Thus, 21 NAs were the subject of international submissions (that is, submission of the dossier to regulatory authorities in two of the three ICH regions of Europe, USA and Japan) within 12 months, over 60% more than in the previous year's survey (Figure 4).

World marketing

During 1997, 322 marketing authorisations, relating to 83 different NAs, were granted to 28 companies. As previously, the USA was the leading market in terms of authorisations granted.

The time taken between regulatory approval and launch reflects a potentially costly delay to marketing. The mean and median delays, over all companies, were 115 days and 81 days, respectively (Figure 5). The longest delays were experienced in France, Greece and Switzerland, where the median was over 230 days.

Number of NMEs marketed for the first time in the world (1988-1998e)

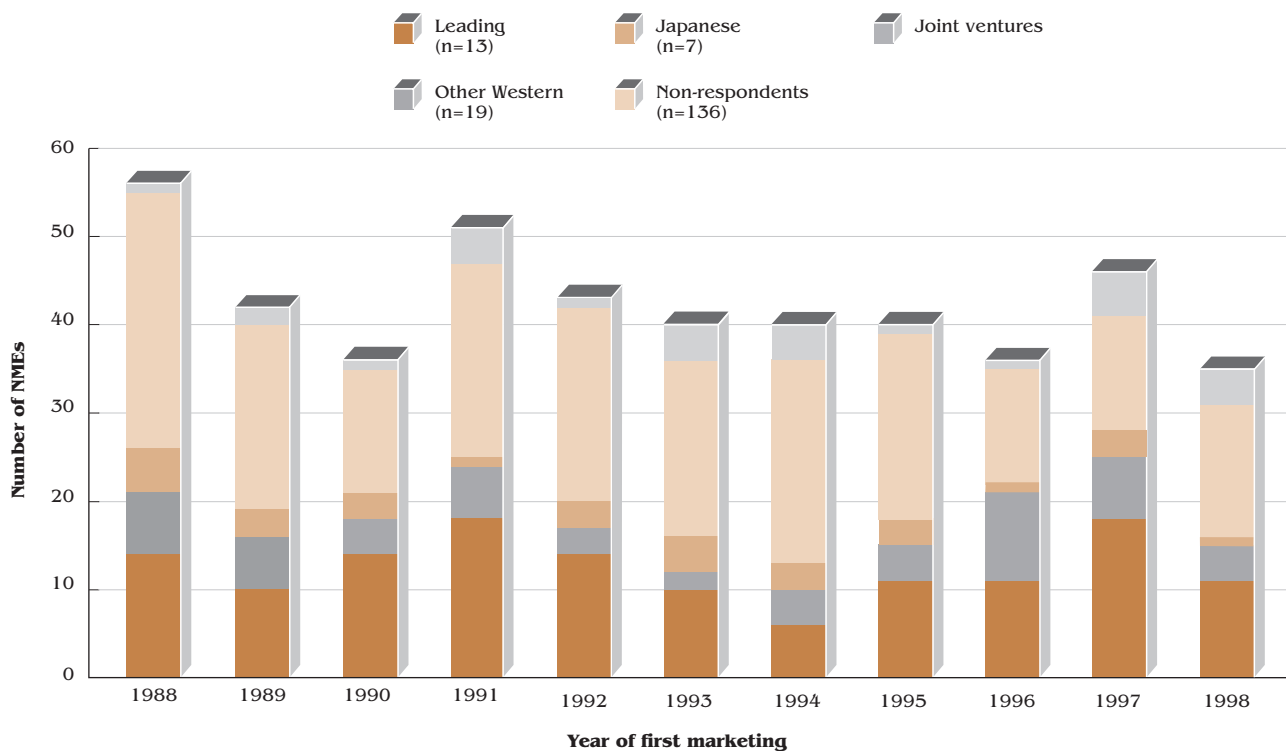


Figure 6 1997 stands out as an exceptional year in terms of NME output, with 46 NMEs being introduced on to the world market.

A rise in the annual number of new molecular entities (NMEs) introduced on to a world market occurred in 1997, the first increase in six years (*Figure 6*). Of the 46 NMEs appearing as marketed products in 1997, 72% were introduced by respondent companies. Figures for 1998 suggest that 1997 will stand out as an exceptionally successful year in terms of NME output, against a continuing downward trend.

Adding Value

With each annual round of data collection, the value of this investment and output survey increases markedly. The identification of trends, or aberrations, through the monitoring and timely reporting of up-to-date activities in drug development enables CMR International to be forward looking in the realm of marketed medicines.

A copy of this R&D Briefing is available on the CMR International web site.

Copies of the full report, "Activities of the International Pharmaceutical Industry in 1997: Pharmaceutical Investment and Output", which contains 97 pages, 48 figures and tables and 7 appendices, are available **free of charge to CMR International sponsoring companies**. The report can be ordered quoting reference number CMR98-104R2.

Copies of the full report are also available to sponsoring companies only on the CMR International web site.

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