



R&D Briefing

Profile of Performance

Trends in regulatory approval times during the 1990s

Median approval times in nine countries
(1990-1995) by year of approval



Figure 1 During the 1990s, on average the UK and France were the fastest authorities to grant marketing authorisations. In 1995 median approval times were lowest in the UK, at 1.1 years closely followed by France at 1.3 years, whilst the USA, Germany, Australia and Spain all had very similar median approval times, of between 1.4 and 1.7 years.

- Regulatory authorities around the world are placing increased emphasis on providing an efficient and high quality approval process. If information on the duration of the review process within different authorities were available, for different compounds, it would be possible to evaluate the effectiveness of performance improvement initiatives.
- Can comparisons be made between authorities with varying review processes? How long are regulatory approval times and have these times altered during the 1990s? Are any trends emerging? Can a baseline be established against which future changes and initiatives can be measured?
- With these questions in mind, and recognising that relevant data in the public domain are limited, CMR International conducted a study of regulatory approval times for new molecular entities in nine major markets. From the results it appears that some of the historical differences between authorities are diminishing and, in the majority of markets, review times are decreasing.

Perspective

The regulatory environment has changed in recent years, largely as a consequence of internal reviews designed to increase the efficiency and quality of the approval process. At the same time relationships have become more open - both those between different national regulatory authorities and those between industry and the agencies. Finally, publication by the European Medicines Evaluation Agency (EMA) of timelines for the review process is expected to have a major impact on approval times in Europe.

Against this backdrop there is a desire to make comparisons and draw conclusions about the performance of different regulatory agencies, particularly now that many authorities have introduced user fees, and essentially simultaneous submissions to a number of agencies make such comparisons possible. The paucity of data in the public domain that will allow such comparisons provides the rationale for a recent CMR International study of regulatory review times from 1990 to 1995 in nine major markets (Australia, Canada, Germany, Spain, France, the UK, Italy, Japan and the USA).

Study Details

Thirty-five pharmaceutical companies in Japan, the USA and Europe provided data on application and approval dates for new molecular entities granted marketing approval in one of the nine markets within the study period. In addition, data were received from five regulatory authorities and, in the case of the USA, obtained from public records.

The data showed a high level of completeness, full information was available for 79% of the 458 compounds marketed during 1990-1995 and for 82% of those approved in that period.

Approval Times Compared

All nine authorities had similar workloads during the 1990s, with the number of compounds approved by each authority estimated to range from 139-184. A direct comparison of mean review times (by year of

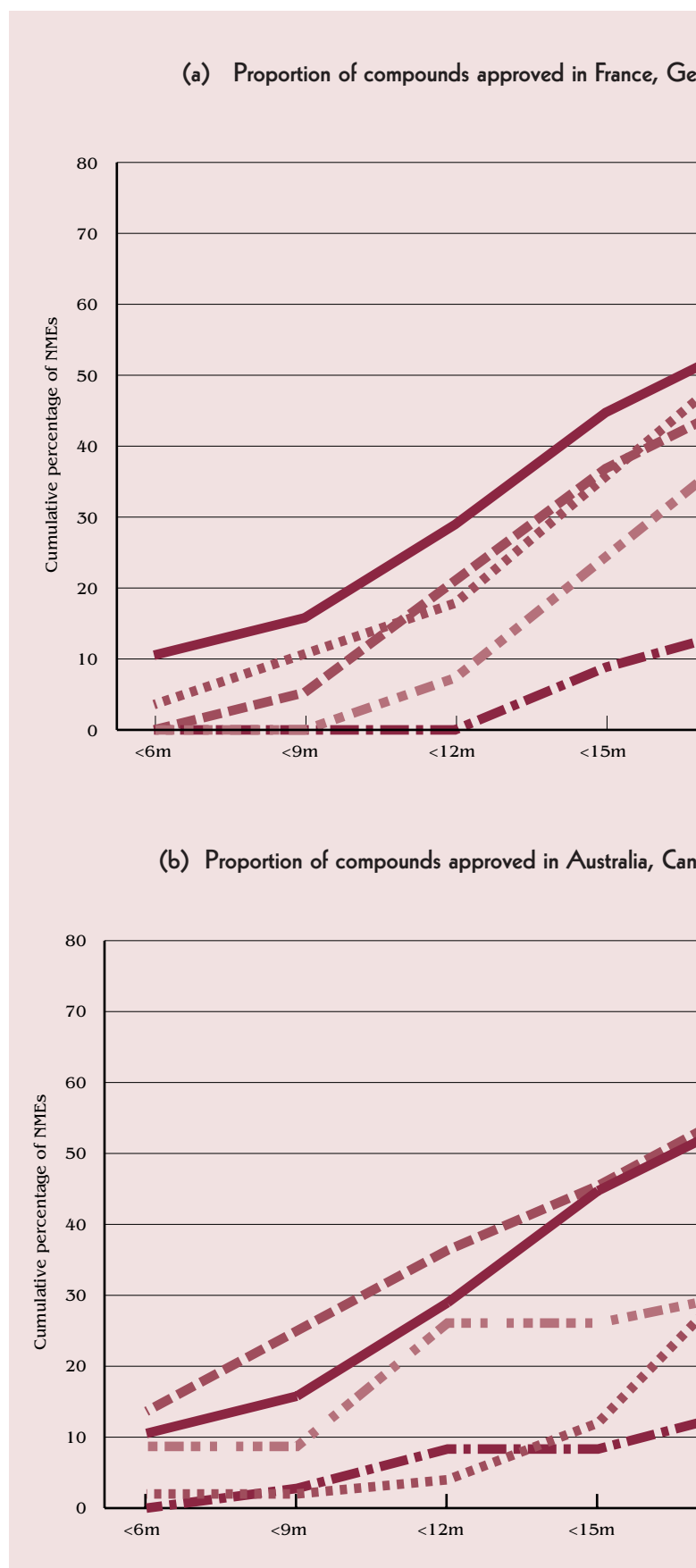
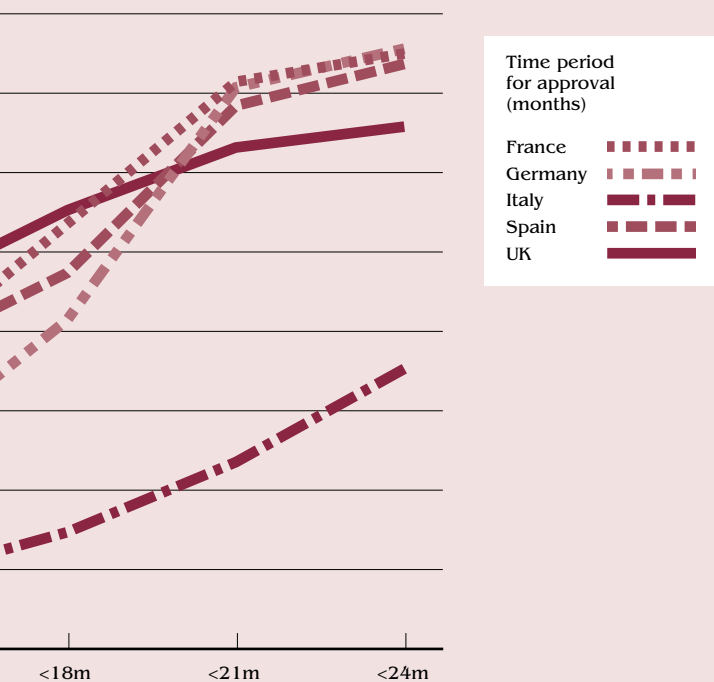
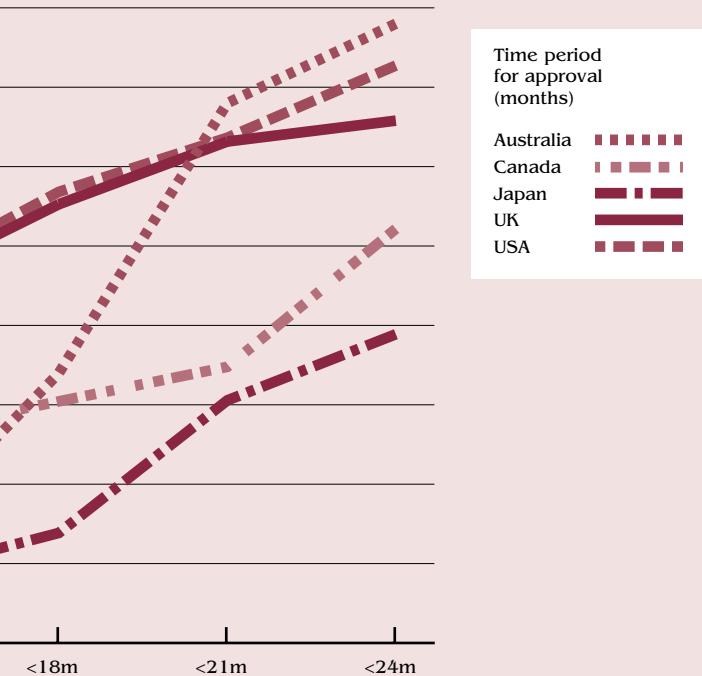


Figure 2 The cumulative percentage of approvals granted within two years in 1994 and 1995 (excluding any compounds approved in 1990-1993) for France, Germany, Australia, and Canada. This compares the "efficiency" across authorities, without taking account of resource

Germany, Italy, Spain and the UK within a two-year period



Canada, Japan, the UK and the USA within a two-year period



...s by each of the regulatory authorities was calculated for
...s submitted before 1990). This provides a measure of relative

es.

approval) reveals a low of 1.3 years for France in 1990 and a high of 4.8 years for Spain in 1991.

To avoid the influence of outliers and skewed distributions, the median review times have been plotted; they show a general decrease with time in five markets and an increase in two (Figure 1). Differences in approval times are less apparent for 1995 than for 1990, the median regulatory review times in 1995 being, with the exceptions of Italy and Japan, two years or less.

Approvals within two years

To obtain a measure of the relative "efficiency" of the different regulatory authorities, the cumulative percentage of approvals granted in 1994 and 1995 was calculated (Figures 2a and 2b). The output of each authority shows some marked differences. Whereas during this period a total of five authorities granted at least one approval within six months, two authorities had approved less than 40% of submissions after two years. For the UK and the USA, over 10% of approvals were granted within six months and over 50% within approximately 16 months.

European versus national approvals

For the European authorities included in this study, a comparison of approval times for national and European review procedures showed little difference in France and the UK. However, on average, national approval times were longer in Germany, Italy and Spain.

Submissions Within a Similar Timeframe

A true comparison of regulatory performance can only be derived from studying the review of simultaneous submissions of identical dossiers to a number of countries; at present this situation applies to very few compounds. It was possible to identify six compounds for which submissions were made to six authorities within six months of each other and to compare approval times.

Some appreciable differences can be seen between approval times in these countries (Figure 3). Reviews of under 12 months have been achieved by a number of authorities for some compounds; however, differences of over two years are apparent between the fastest and slowest approval times for two of the compounds.

Approval times for compounds submitted in Australia, Canada, France, Germany, the UK and the USA within six months of each other

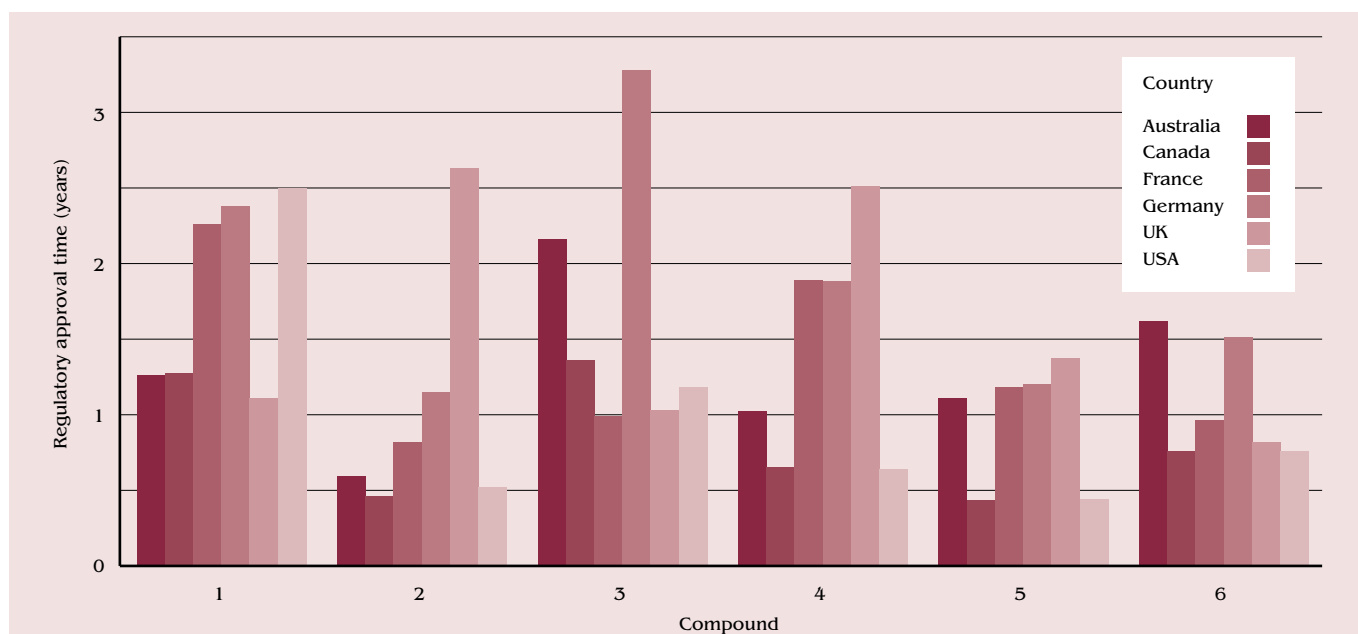


Figure 3 Despite submissions being made within a similar time frame, during which it was assumed that the dossier was unlikely to have changed significantly, there were marked differences in approval times. All six compounds were either assigned a priority or orphan drug status in the USA or were developed as treatment for AIDS or HIV.

Past and Future Trends

Wide differences in average approval times between different regulatory authorities may be a feature of the past. As this study shows, such differences are diminishing, perhaps due to the impact of restructuring and performance improvement initiatives or to the introduction of user fees.

In general, within Europe, approval times show an increasing tendency to converge, and this can be

attributed, at least in part, to the introduction of the new European licensing procedures. It is anticipated that, with adherence to EMEA timelines, European review times will become even more uniform.

The results of this study not only provide a useful indication of the relative performance of regulatory authorities but also establish a baseline against which future changes in the regulatory environment can be evaluated.

This Briefing is based on the paper:

A STUDY OF TRENDS IN PHARMACEUTICAL REGULATORY APPROVAL TIMES FOR 9 MAJOR MARKETS IN THE 1990's.

KE Thomas, JAN McAuslane, C Parkinson, DK Luscombe and SR Walker.

DIA Journal (in press).

September 1997

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