

Emerging Markets: Asia

Development and Submission strategies for pharmaceutical registration

Development strategies in Asia – markets where clinical development is conducted prior to submission

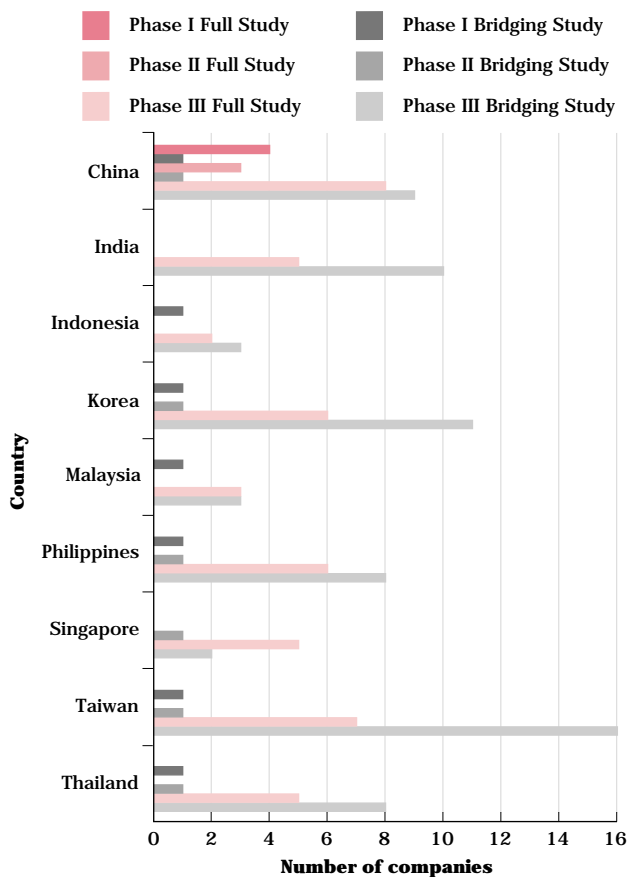


Figure 1 Markets where clinical development is conducted prior to submission. Clinical development in Asia does not generally occur until Phase III clinical trials. At this stage, companies will either carry out full or bridging studies, with the majority of studies being conducted in the commercially most important markets of China, Korea, India and Taiwan. Currently clinical studies conducted in Asia do not generally become part of a pivotal clinical development package for submission in other markets.

□ *The emerging markets of Asia offer considerable potential for pharmaceutical investment and growth. However, diverse regulatory systems and requirements between these markets can create significant obstacles to efficient development and registration of new medicines.*

□ *Considerable delays to submission emanate from the requirement for a Certificate of Free Sale, generated in the source country, and the need for local clinical trials. Lengthy review times and lack of transparency in the review process are further barriers to rapid registration.*

□ *These problems, coupled with the lack of regulatory harmonisation between markets in the region, are among the major issues of concern to the pharmaceutical industry.*

□ *Based on these findings, generated in a questionnaire based survey in 1998 among 25 companies, CMR International advocate building a better understanding of regulatory requirements across the region and increased communication between industry and regulatory authorities.*

□ *Since this survey was carried out, a number of regulatory authorities have begun to address some of these issues.*

Perspective

Increasingly, the emerging markets of Central and Eastern Europe, Latin America and Asia offer enormous potential for growth in pharmaceutical sales. These markets are of critical importance to the future success of pharmaceutical companies and yet considerable hurdles must be overcome before a new medicine achieves marketing approval.

To gain insight into the difficulties encountered within these three regions, CMR International conducted a survey in 1998 to identify:

- Companies' current strategies for registration, and development, of new active substances in these markets;
- Factors inhibiting timely and successful registration.

This R&D Briefing presents data for major markets in Asia (China, India, Indonesia, South Korea, Malaysia, the Philippines, Singapore, Taiwan and Thailand) gained from questionnaires returned by 28 of the 48 companies approached.

Clinical development

Clinical trials are carried out in all markets of the region (Figure 1), particularly those of greatest commercial importance. Most clinical development occurs during Phase III, with companies being divided in their choice of full or bridging studies. A bridging trial facilitates extrapolation of foreign clinical data to the new region.

There is little evidence that studies carried out in Asia are pivotal to the company's global development plan for submission in other world markets.

The majority of clinical trials from the region are conducted to meet local regulatory requirements (Figure 2); this is not surprising as China, South Korea, Taiwan and India all require some locally generated clinical trial data for registration. Generally, trials are to be completed prior to approval being granted, although occasionally the data are required to be part of the submission. Studies are also initiated to provide local physicians with experience of the product before marketing.

Development strategies in Asia – reasons for conducting trials in local markets

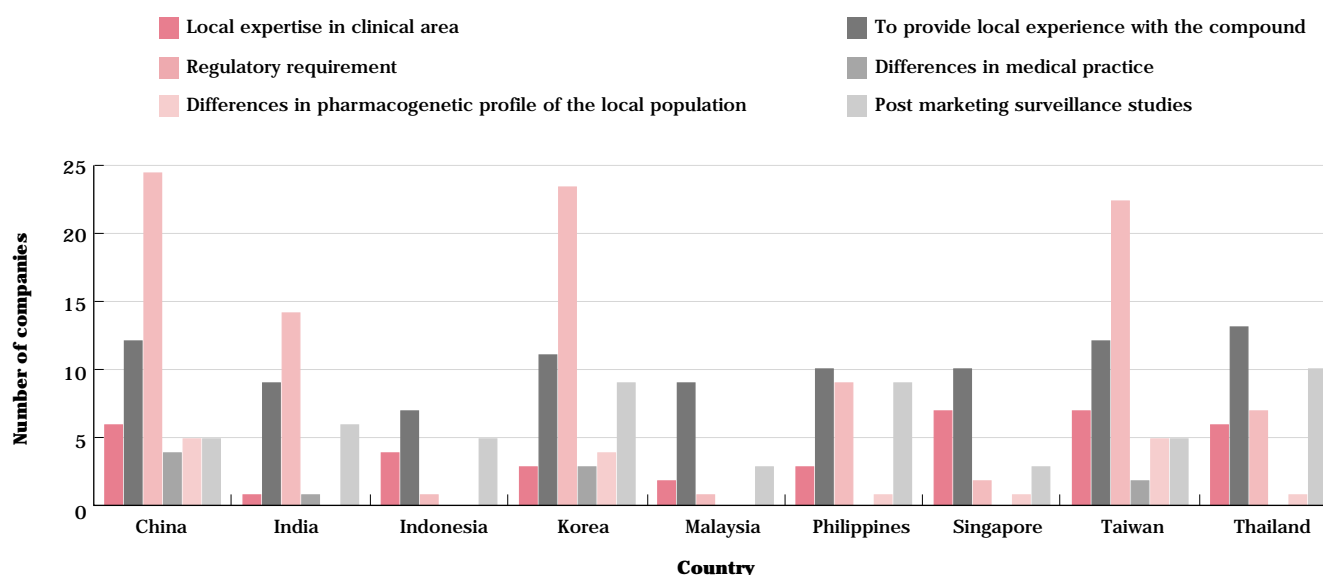


Figure 2 Reasons for conducting trials in local markets. Studies are usually conducted in order to meet local regulatory requirements. However, companies will also conduct trials in these markets to make use of local expertise and to provide local physicians with experience of the compound.

Submission strategies in Asia – timing of requirement for CFS in local market



Figure 3 Timing of the requirement for a certificate of free sale (CFS). The study showed that it was rare for a company to be able to delay the submission of the CFS until just prior to approval, with most being required to provide the CFS at submission to all authorities.

Submission strategies

The current strategy for submission in this region varied between companies; many use separate strategies for each market while others adopt a case-by-case approach. This situation probably reflects the marked lack of regulatory harmonisation across the region. However, most companies are aiming to develop a single strategy for simultaneous submission to all major markets in the future.

In nearly all cases, submissions in Asia occur after the dossier has been submitted in the EU (European Union) and, to a lesser extent, in the USA. One or two companies will also have prior submission in Japan. Even so, the requirement by many of the major countries of the region, namely China, the Philippines, Indonesia, Thailand and Taiwan, for a Certificate of Free Sale (CFS) to be included in the marketing authorisation dossier can cause considerable delays. Companies have had little success in overcoming this problem through

being able to postpone the provision of the CFS until just prior to approval (Figure 3). The estimated delays to marketing authorisation applications in these markets range from 9-12 months on average.

Local experience

Not surprisingly, this requirement for a CFS from the source country prior to submission is seen as the major barrier to registration in Asia (Figure 4). In addition, companies have to contend with long review times, possibly due to lack of efficiency and resources within the regulatory authorities. Only Thailand and the Philippines managed to approve more than 60% of the compounds submitted to them by respondent companies within the last three years. Lack of transparency during the review process further compounds the difficulties in achieving rapid marketing authorisation.

Experience with MAAs in Asia

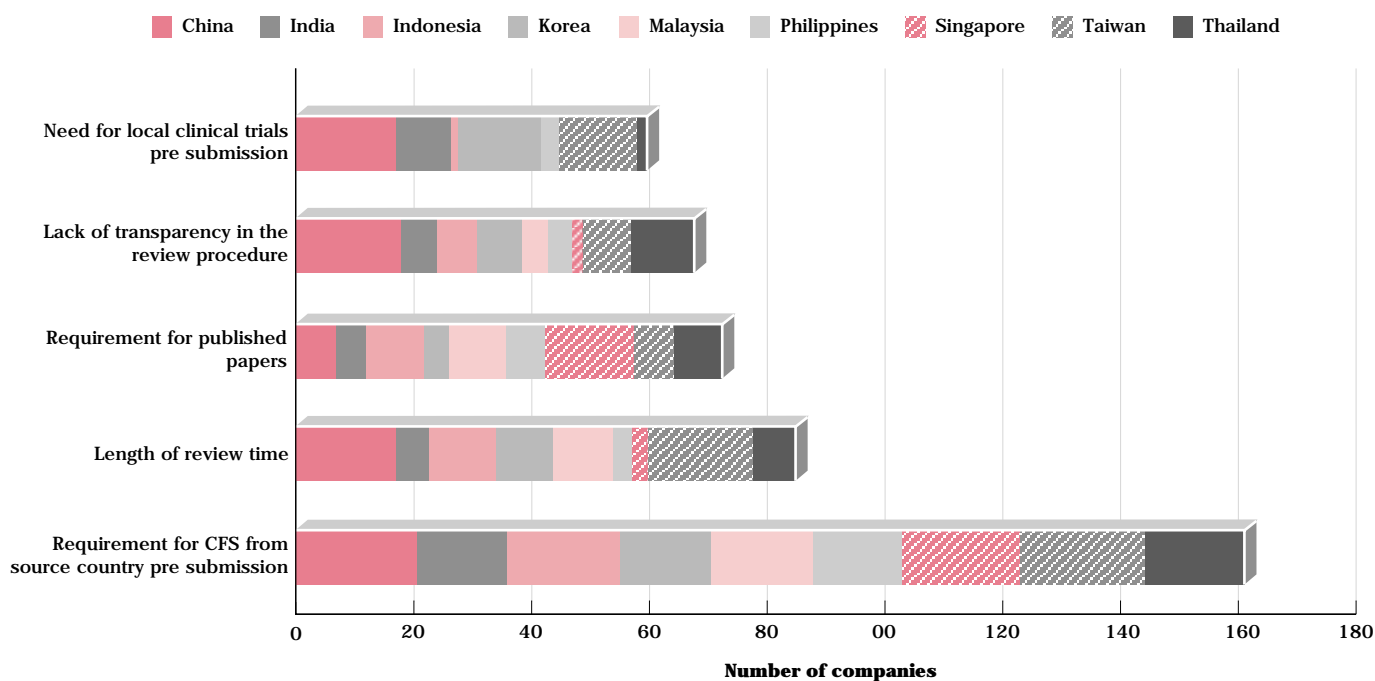


Figure 4 **Major barriers to rapid registration.** Participants were asked to identify, from a list of factors, which caused them problems when registering new drugs in Asia. The requirement for a certificate of free sale to be produced prior to submission was by far the most common problem experienced overall, followed by the length of the regulatory review time.

Steps for the future

For pharmaceutical investment and development in the emerging markets of Asia to continue and grow, a number of issues must be addressed. To this end, it is recommended that:

- better understanding of the basis for regulatory requirements, and
 - increased communication between industry and the regulatory authorities
- will facilitate a trend towards more efficient and consistent regulatory reviews. These in turn will assist the industry in harnessing the potential of the region.

Copies of R&D Briefings are available on the CMR International web site.

This Briefing on the Emerging Markets is part of a series of three briefings on Asia (No 24A), Central and Eastern Europe (No 24B) and Latin America (No 24C).

Copies of the full report on Emerging Markets, "The Registration of Pharmaceuticals in Emerging Markets: Submission Strategies and issues of concern in Asia, South America and Central and Eastern Europe", which contains 131 pages, 70 figures and 2 appendices, are available free of charge to CMR International sponsoring companies. The report can be ordered quoting reference number CMR99-108R.

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

November 1999

R&D Briefing 24A



CMR International

Novellus Court, 61 South Street, Epsom, Surrey KT18 7PX

Tel: +44(0)1372 846100 Fax: +44(0)1372 846101 E-mail: cmr@cmr.org Web Site: <http://www.cmr.org>