

Emerging Markets: Latin America

Development and Submission strategies for pharmaceutical registration

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

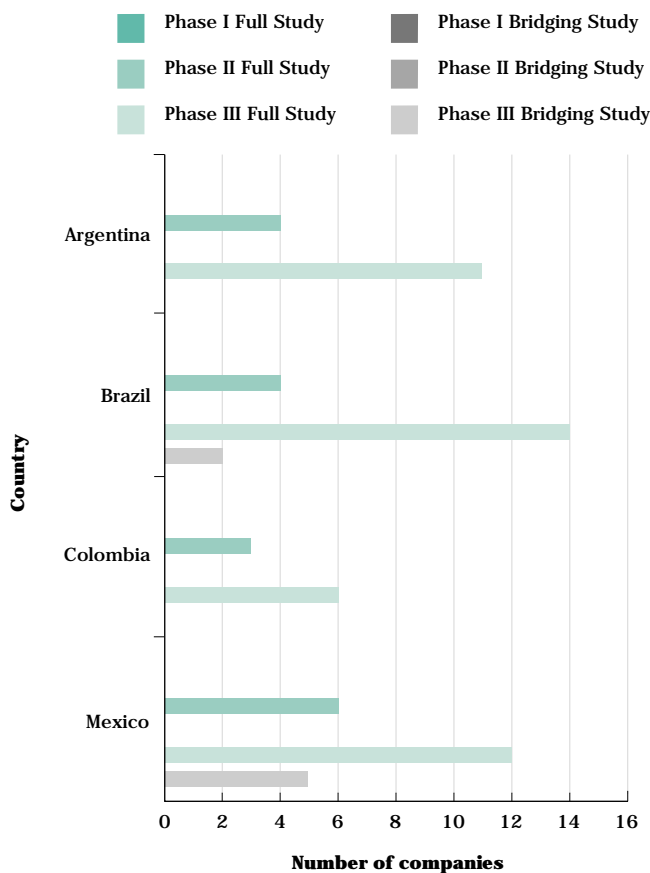


Figure 1 **Markets where clinical development is conducted prior to submission.** Countries in which responding companies conduct clinical trials in each of the four Latin American countries studied, separated by phase and type of clinical study. Most companies will wait until Phase III to conduct studies in these markets, which will often be pivotal studies, forming part of the company's global development programme. As such, where clinical trials are conducted in these markets, they will generally be full, rather than bridging studies.

- ❑ *The emerging markets of Latin America 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 may emanate from the need for local clinical trials or the requirement for a Certificate of Free Sale. Lack of transparency in the review process and difficulties in ensuring confidentiality of the data submitted 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 Latin America (Argentina, Brazil, Colombia and Mexico) gained from questionnaires returned by 27 of the 48 companies approached.

Clinical development

The profile for clinical development was similar in all four Latin American markets (*Figure 1*) with the majority of respondents waiting until Phase III to conduct clinical trials. Often these studies are pivotal to the company's global development plan and as such reflect the quality of clinical research conducted in the region.

Generally, however, trials in these markets are initiated to take advantage of local expertise in the clinical discipline concerned or to provide local physicians with experience of the product before marketing (*Figure 2*). Additionally, at the time of this study, the completion of a local clinical trial was a prerequisite for marketing authorisation in Mexico.

Submission strategies

A single strategy for simultaneous submission to all major markets in the region is the current approach of 12 companies, while some have separate strategies for each market and yet others adopt case-by-case or non-standard approaches. The majority favour a single

Development strategies in Latin America – reasons for conducting trials in local markets

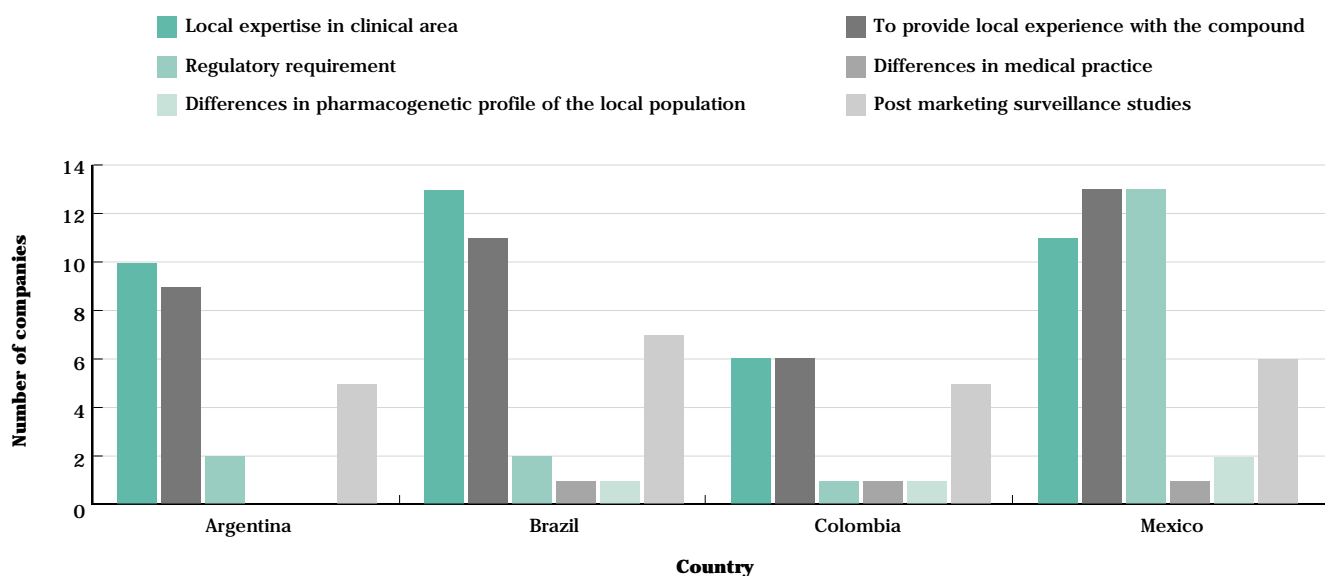


Figure 2 Reasons for conducting trials in local markets. Respondents were able to choose as many of the 6 given reasons as they believed to be applicable to the rationale behind their clinical development strategy. In most cases, companies will conduct trials to make use of local expertise in a given discipline, or to provide local physicians with pre-launch experience of the compound.

Submission strategies in Latin America – timing of requirement for CFS in local market

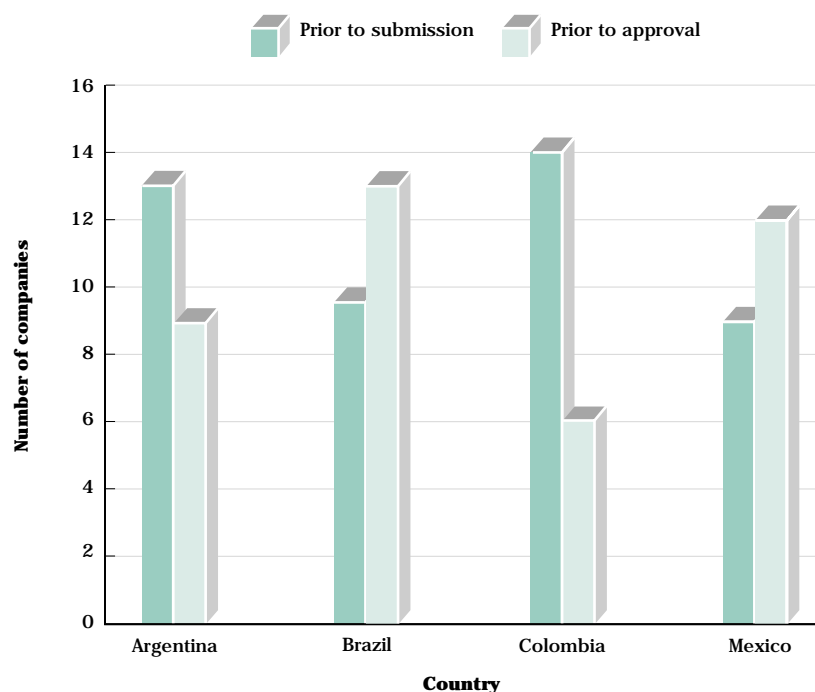


Figure 3 **Timing of the requirement for a certificate of free sale (CFS).** Respondents indicated whether they had generally been required to produce a CFS at the time of submission to each market, or whether they have been able to submit an application without the CFS being available, i.e. with the production of the CFS being delayed until the final approval. The study showed that it is more likely that a company will be able to delay submission of a CFS in Brazil and Mexico, with the authorities in Argentina and Colombia appearing to be more strict in their requirements for a CFS at submission.

strategy for the future; current initiatives to harmonise regulatory requirements between key countries will aid this objective.

Prior to submission in Latin America the majority of companies have already submitted the dossier in the EU, and 65% have also submitted in the USA. Even so, a Certificate of Free Sale (CFS), normally a requirement for submission in emerging markets, is generally not available at that time. To avoid delays some companies, with the regulatory authority's agreement, have postponed providing the CFS until immediately prior to approval (*Figure 3*). It appears that Argentina and Colombia remain more strict in their requirement for a CFS at submission.

A number of companies managed to make submissions in Latin America within 12 months of a submission to an ICH (International Conference on Harmonisation) country, suggesting that the emerging markets of Latin America are being incorporated into companies' core development programmes.

Local experience

The regulatory authorities in the four surveyed markets appear to be working efficiently in terms of granting marketing approvals, with a relatively small backlog of compounds. However, companies still experience a number of difficulties which can become barriers to rapid registration (*Figure 4*). The requirement by these less experienced regulatory authorities to see a Certificate of Free Sale pre-submission is a major issue of concern; similarly, the request by some authorities for peer reviewed articles in support of a submission is yet another hurdle to be overcome. The success of some companies in negotiating a delay in the provision of a CFS (*see Figure 3*) suggests a potential starting point for changes in this area.

Lack of transparency during the review process, often a function of limited resources, is perceived as a barrier to registration in this region, although recent investment in technology and personnel by the Argentinean regulatory authority has improved review times and transparency in that country. Intellectual property and

Experience with MAAs in Latin America

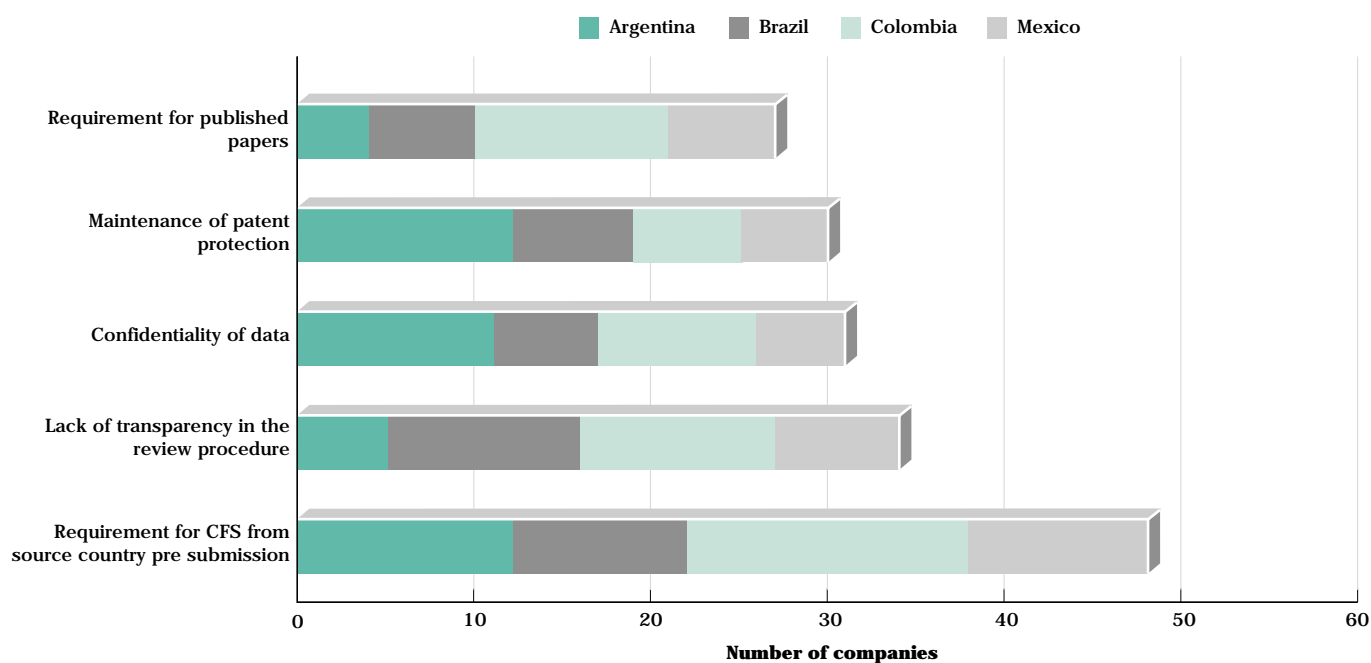


Figure 4 **Major barriers to rapid registration.** Participants were asked to identify, from a list of factors, which caused them problems when registering new drugs in Latin America. The requirement for a certificate of free sale to be submitted prior to submission was the most common problem experienced across the region, along with a lack transparency in the review procedure and difficulties in ensuring confidentiality of the data submitted.

data protection legislation differ considerably between the Latin America markets, causing further concerns to the industry.

- better understanding of the basis for regulatory requirements, and
- increased communication between industry and the regulatory authorities

Steps for the future

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

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.

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