

# The changing regulatory environment in Latin America

## Focus on good review practices

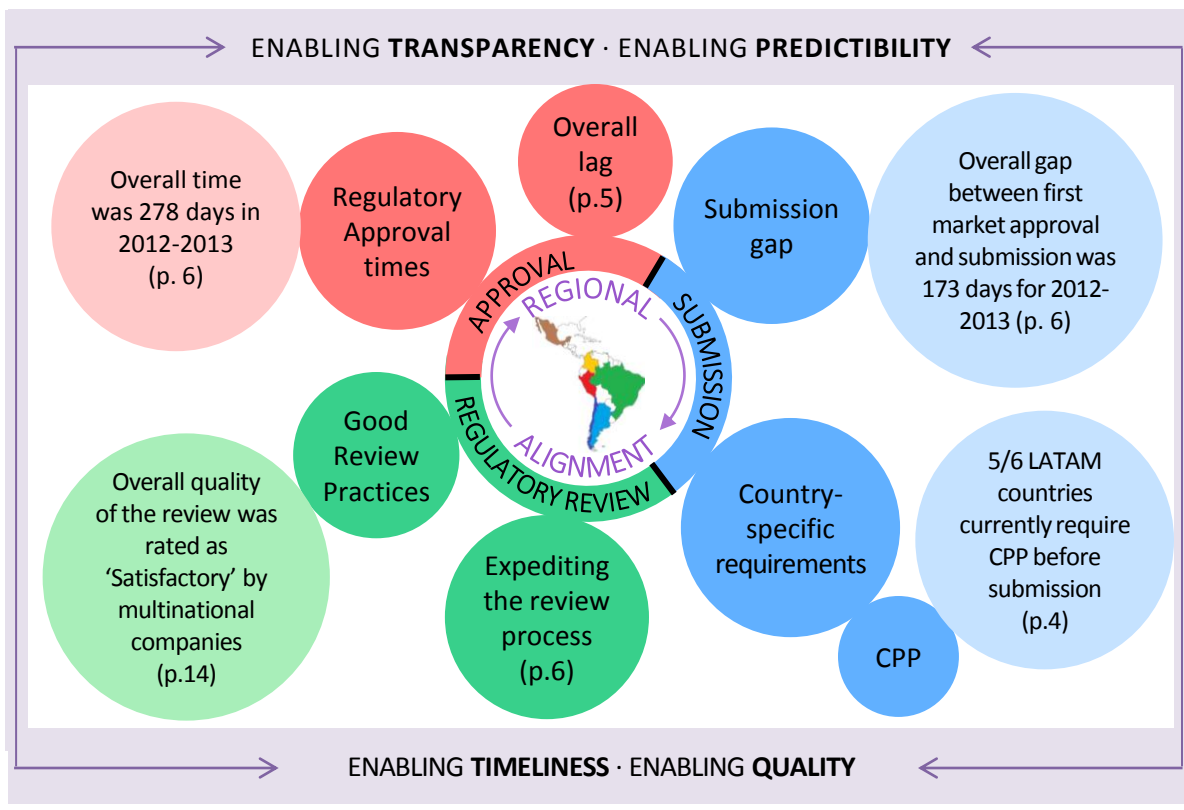
### Key points

The emerging markets of Latin America (LATAM) are becoming increasingly important to pharmaceutical companies in their strategies for global registration of new medicines and making them available to patients.

**Regional alignment:** Country-specific challenges to pharmaceutical companies looking to enter the LATAM region remain and many of these stem from a wide spectrum of regulatory philosophies, review practices and other policies as well as procedural issues. Building trust and confidence should be encouraged and LATAM countries should continue aligning their activities regionally and reinforcing harmonisation initiatives.

**Facilitating the review:** Factors such as better communication and increased agency-industry interactions and collaborations will result in increased knowledge, capacity and expertise and could lead to a more efficient and timely review process.

**Elements of good-quality review:** As agencies in LATAM develop their processes and practises, it is important that they also build quality into the process and continue to embed widely documented good review practices (GRevP). Within the agencies, these practices will promote not just timeliness, but also process predictability, consistency, transparency and high quality across both the review and management of the process.



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### A new regulatory landscape in Latin America

Today, the emerging markets of Latin America (LATAM) offer considerable potential for pharmaceutical investment and growth. Nevertheless, challenges remain for agencies to build quality review systems into their submission and review guidelines and practices and for companies to meet diverse agency requirements and expectations. This Briefing follows the decade-long journey LATAM agencies have undertaken to address these challenges.

### Studies to examine the evolving environment in LATAM

In 2004, the Centre for Innovation in Regulatory Science (CIRS) started an initiative to look at regulatory practices beyond the three major markets of the EU, USA and Japan. This initiative has examined the regulatory environment in the emerging markets to assess whether medicines are becoming available to patients in a timely and efficient manner with appropriate safeguards for the public health. With this goal in mind, a number of CIRS studies in the emerging markets, including countries in the LATAM region, have been undertaken since 2004 (Appendix).

### Stakeholder discussions on regulatory review in LATAM

A decade later, in 2014, CIRS held an International Workshop in Lima, Peru, “Focus on Latin America: Building quality submission and review processes and practices – Overcoming challenges and meeting expectations”. The intent was to discuss:

- how agencies are building quality into their review process
- what the challenges are to moving from a guidance document to the use of good review practice in the daily workings of an agency
- how this can underpin good regulatory decisions, performance measurement and quality

### Recent interactions with agencies and pharmaceutical companies in LATAM

The majority of the results presented in this report are from studies conducted by CIRS between 2011- 2013. Recognising that most agencies have made revisions to their practices since then, in 2015 CIRS contacted all the agencies discussed in this Briefing in order to obtain insights into the changes in their jurisdictions. Additionally, CIRS visited agencies and local pharmaceutical companies in Colombia, Brazil and Mexico in September 2015, in order to obtain further updates and information on agency practices and process modifications. This Briefing reflects those most recent interactions.

### Briefing objectives

The aim of this Briefing is to review and summarise the findings from the major studies and interactions carried out by CIRS in LATAM in the last decade in order to describe the changes to the regulatory landscape, focusing on the following topics:

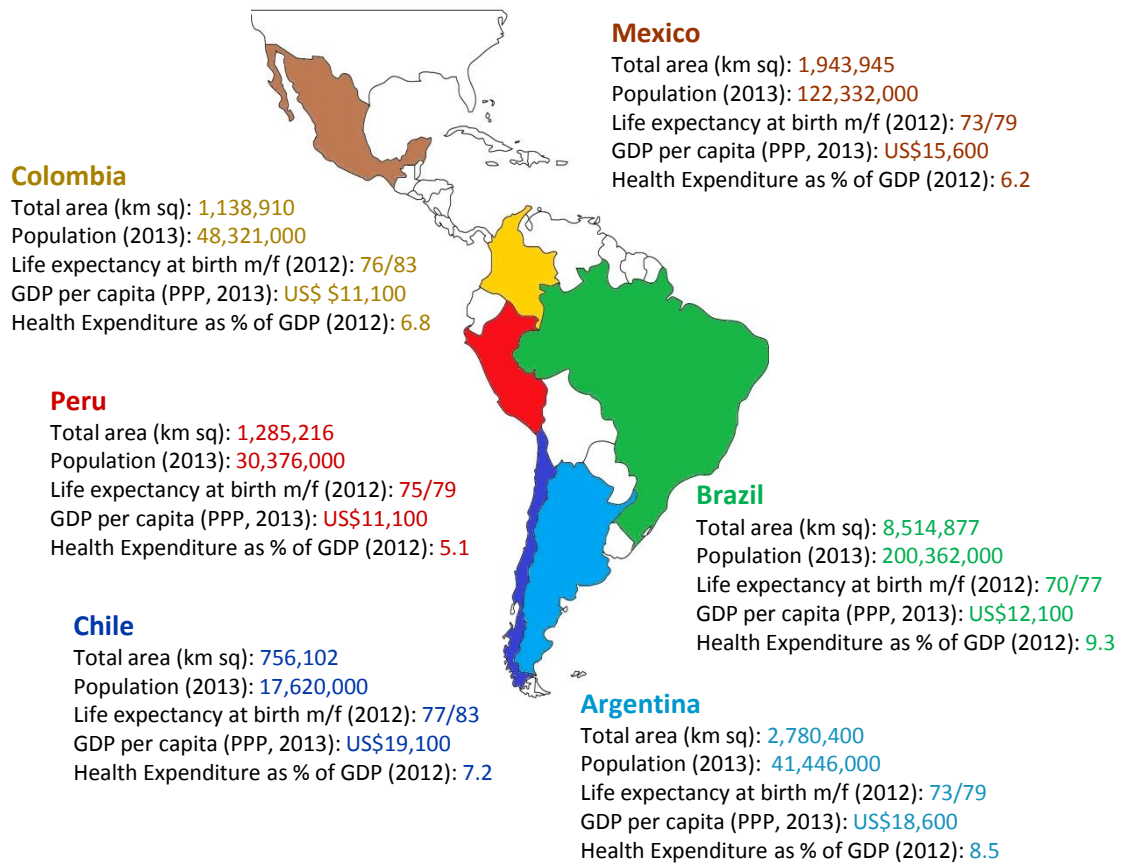
- The alignment of regulatory procedures in the region of Latin America
- Changes in regulatory review times
- The extent to which good review practices are embedded in the agencies
- Recommendations and learnings from the 2014 CIRS Workshop in Lima
- Recent observations and insights from agencies and companies based in Colombia, Brazil and Mexico

This Briefing is intended as a background document to encourage discussion among and between regulatory agencies and companies of the outlined key issues, and to promote further improvements to the LATAM regulatory landscape.

### A region of cultural, political, and economical diversity

The countries described in this Briefing, (Argentina, Brazil, Chile, Colombia, Mexico and Peru), make up a large part of Latin America and they were selected based on their perceived importance as “emerging market” countries. Although these six countries share some cultural commonalities, they have diverse demographic and economic characteristics as illustrated in Figure 1.

**Figure 1:** Characteristics of the countries included in the study with regards to total area, population size, life expectancy at birth, Gross Domestic Product (GDP) per capita and health expenditure as a % of GDP



Source: CIA Factbook, WHO. 2015

### Road to cross-agency recognition

The regulatory burden on agencies and pharmaceutical companies will continue to grow in the future, and both stakeholders will need to continue building trust and confidence within and across the two groups, in order to facilitate cooperation, sharing of information and alignment.

Although the LATAM region does not have a centralised or harmonised procedure for drug registration, efforts have been made to adopt or adapt the guidelines from the ICH countries in order to help harmonise the requirements for the development and approval of new medicines. The LATAM countries have also been aligning their activities regionally and reinforcing harmonisation, mainly through the initiative of the Pan American Health Organization (PAHO) via the Pan American Network for Drug Regulatory Harmonization (PANDRH). Moreover, four out of the six countries have been recognised by PAHO as **Level 4** national regulatory authorities for their competent and efficient performance - Mexico (2012), Brazil (2010), Colombia (2010) and Argentina (2009). The key topics for alignment have included sharing safety data, developing a common pharmacopeia, and recognising reciprocal acknowledgement of clinical site and GMP inspections.

### Benefits and barriers to alignment

Both the agencies and companies may benefit from regulatory alignment through increased opportunities for participation in the development of shared standards, practices and data package requirements. This would allow agencies to better focus limited resources on the most important parts of the dossier for review and companies to decrease time required to respond to questions from agencies.

Despite these motivating factors, country-specific challenges remain to pharmaceutical companies looking to enter the LATAM region, and many of these stem from a wide spectrum of regulatory philosophies, review practice, policies and procedural issues as outlined in Figure 2.

**Figure 2: Key procedural aspects for LATAM countries (as of 2014).**

|  | Argentina | Brazil | Chile | Colombia | Mexico | Peru |
|--|-----------|--------|-------|----------|--------|------|
| <b>Review process and data requirements</b>              |           |        |       |          |        |      |
| ICH electronic Common Technical Document (eCTD) accepted |           |        |       |          |        |      |
| All ICH guidelines are followed                          |           |        |       |          |        |      |
| Selected ICH guidelines only are followed                |           |        |       |          |        |      |
| Local clinical testing required                          |           |        |       |          |        |      |
| <b>Certificate of a Pharmaceutical Product (CPP)</b>     |           |        |       |          |        |      |
| CPP is required for application                          |           |        |       | a        | a      |      |
| CPP required after application but prior to approval     |           |        |       |          |        |      |
| Legislation of CPP required by Embassy                   |           |        |       |          |        |      |
| <b>Other policy and procedural issues</b>                |           |        |       |          |        |      |
| IP protection laws implemented                           |           |        |       |          |        |      |
| Pricing is part of approval                              |           |        |       |          |        |      |
| Health Technology Assessment agency in place             |           |        |       |          |        |      |

Where:  Yes  No     a = CPP timing can be negotiated to allow more flexibility for the application

### Key recommendations for the future

Further steps (Figure 3) will need to be taken at country and regional levels to engage both regulators and industry in order to improve the review procedures, promote alignment and further develop an environment that will encourage pharmaceutical companies to include LATAM countries in plans for developing new medicines available to patients globally.

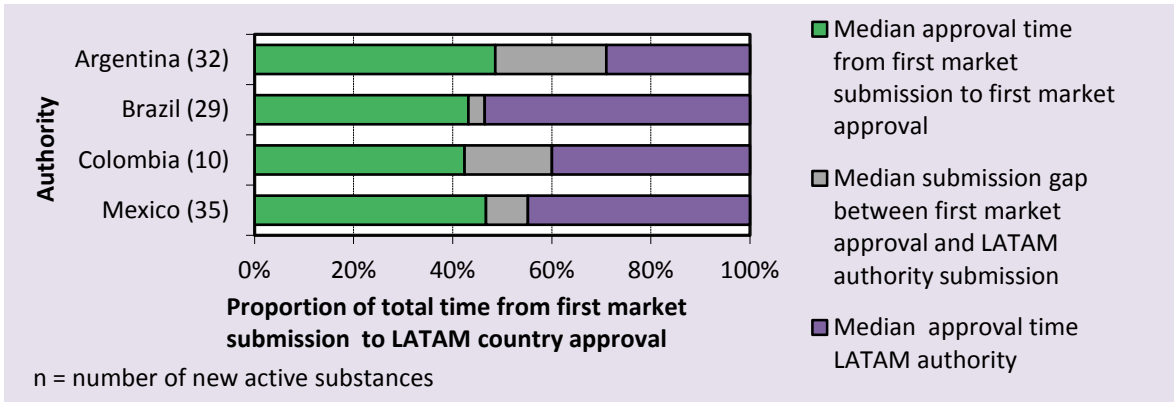
**Figure 3: Recommendations developed during the 2014 CIRS International Workshops in Lima to benefit regional alignment**

| Challenge                     | Recommendation for agencies  |
|-------------------------------|--|
| Mutual recognition            | Create more opportunities for regulatory agencies to understand each other's systems, strengths and challenges through international collaborations  |
| Alignment of agency processes | Target sub-regional country alignments based on strengths, weaknesses and common objectives; consider leveraging the PAHO tiering system   |
| Communication                 | Increase the interaction and cross-agency training of reviewers  |
| Sharing of information        | Build on some of the progress related to good manufacturing practice (GMP) inspections such as medical devices inspection; use the WHO prequalification to expedite reviews; share inspection information and reduce the burden to produce GMP certificates. |
| Sharing of review practices   | Consider alignment on a common review template.; survey the use of submission formats in the region; encourage the use of the CTD format.  |

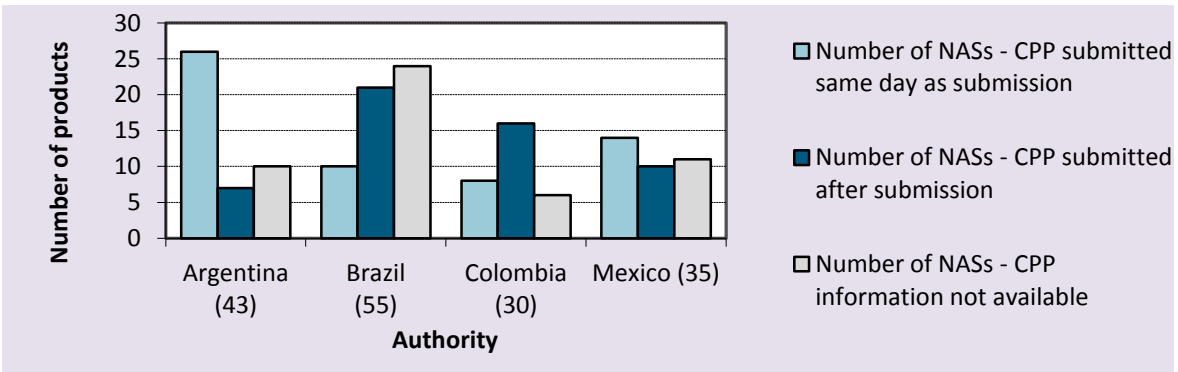
**Regulatory review processes and timelines**

The time to bring a new active substance (NAS) to emerging market countries can be measured by the submission gap (time between first market approval and submission to the particular authority) and time needed for the agency approval process. Both factors are a complex mix of company strategy, such as market or product importance; the local regulatory environment, such as the timing of the CPP, local clinical trial requirements or the type of the review process. Figures 4, 5 and 6 illustrate these aspects for Argentina, Brazil, Colombia and Mexico, based on results from the annual CIRS Emerging Markets Industry Benchmarking study (Appendix for details).

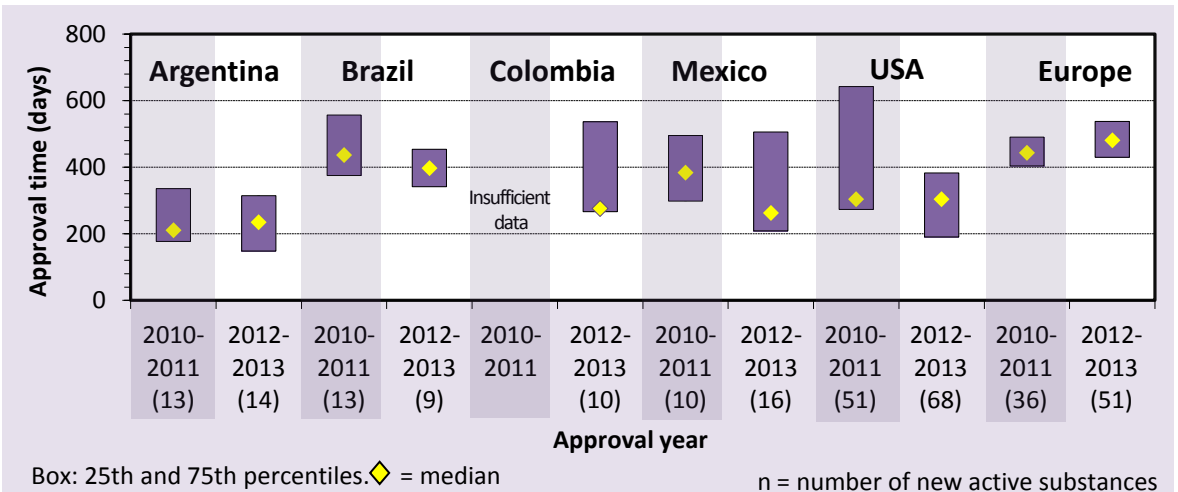
**Figure 4: Overall lag time to LATAM countries for NASs approved 2009-2013**



**Figure 5: Number of products and timing of CPP submission for NASs submitted 2009-2013**



**Figure 6: Regulatory approval times for NASs approved 2010-2011 and 2012-2013**



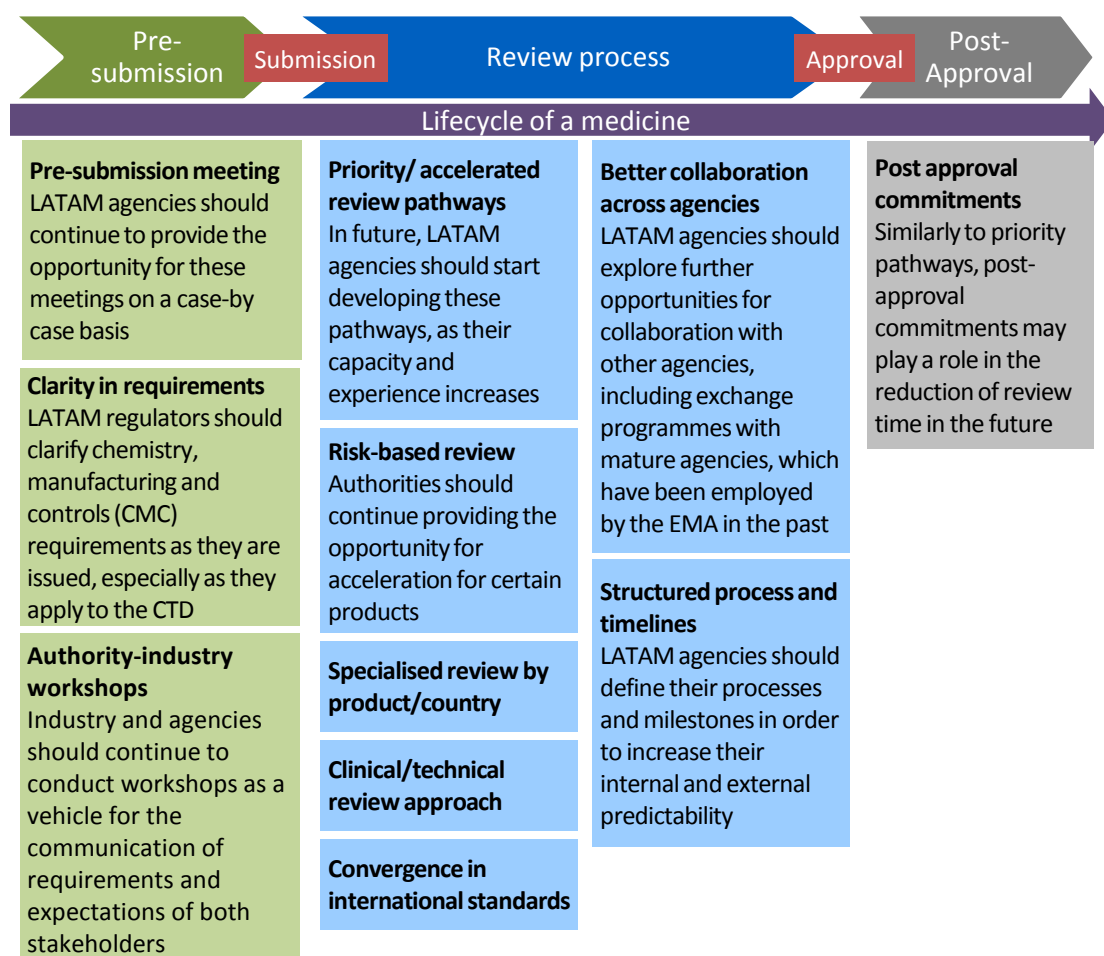
The overall lag time to a country is made up in varying proportions of the submission gap and approval timing (Figure 4). The submission gap for LATAM agencies was a median 162 days for 2011-2012 and 173 days for 2012-2013. The gap differed across the countries; for example, the gap was shorter for Brazil than Argentina due to the fact that it is possible to submit a dossier to Brazil prior to obtaining the CPP (Figure 5), whereas early submissions to Mexico may be due to the availability of the three risk-based submission routes, including the equivalence agreement, as well as the influences of company strategy.

Approval times (Figure 4 and 6) can be used as indicators of the regulatory environment, though a clear understanding of differences between country processes is needed. For example, although approval time for Argentina was twice as fast as for Brazil, this is likely due to the fact that Argentina uses a verification approval route whereas Brazil typically conducts a full dossier review. The overall median approval time for Argentina, Brazil, Colombia and Mexico was 372 days in 2010-2011 and 278 days in 2012-2013. A number of these agencies have currently been undergoing improvement initiatives that appear to have had a positive effect on regulatory review times.

### Expediting the review process

In order to further shorten the regulatory review approval time at LATAM agencies, the medicine review process should be considered as a continuum and crucial events that occur before and after the actual review need to be considered (Figure 7). Factors such as better communication and increased agency-industry interactions and collaborations will result in increased knowledge, capacity and expertise and could lead to a more efficient and timely review process.

**Figure 7: Opportunities and recommendations developed during the 2014 CIRS International Workshop in Lima to expedite the review process during the lifecycle of a medicine**



## Beyond timelines - looking at quality of the review process

Although a speedy review is vital to ensure that medicines become available to patients in a timely manner, the quality of the review process is also important for agencies to ensure that review decisions are scientifically sound and consequently only safe and effective medicines reach the market.

As agencies in LATAM develop their processes and practises, it is important that they also build quality into the process and continue to embed widely followed documented good review practices (GRevP). Within agencies, these practices will promote not just timeliness but also process predictability, consistency, transparency and high-quality decisions across both the review and management of the process.

**Figure 8: Attributes that enable a good regulatory review**



CIRS has carried out a number of studies to measure the GRevP that LATAM and other emerging market agencies have in place and how well these are embedded into their practices. An example is the CIRS study entitled “Understanding the enablers of good regulatory process and decision making - What are the features that enable a transparent, timely, predictable and good-quality review?”

For this study, which was conducted in emerging countries including Brazil, Mexico and Peru, 12 multinational companies rated the agencies’ overall performance related to the key attributes (transparency, timeliness, predictability, and quality) that make up a good review (Figure 9). It is important to note that this study was conducted in 2011 and that many of the recommendations noted have been initiated or adopted by these agencies through process and organisational changes. Consequently, this study should be regarded as a reflection on how agencies can measure the quality of their processes and decision making and has served to stimulate improvements within these agencies.

**Figure 9: Results of the 2011 “Enabler study”: overall company ratings and recommendations for LATAM agencies with regard to predictability, transparency, quality and timeliness**

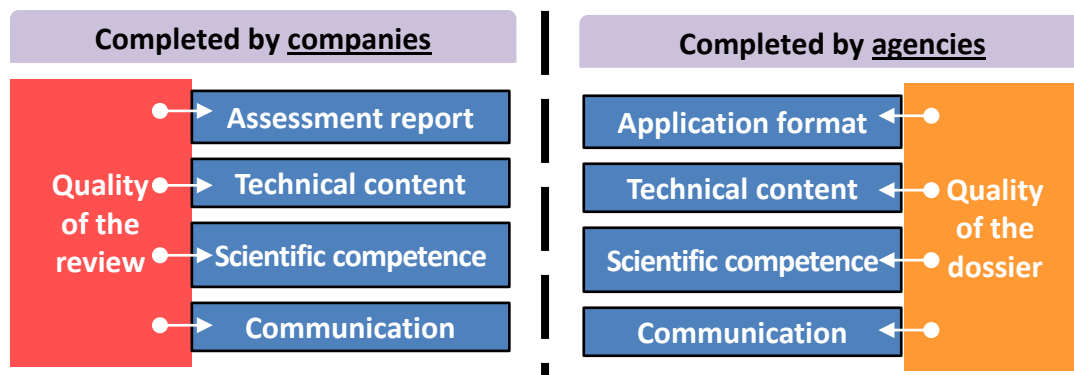
| Agency | Predictability | Transparency | Quality | Timeliness | Element in which the agency excels  | Recommendation for the agency’s improvement  |
|--------|----------------|--------------|---------|------------|---|--|
| Brazil | Yellow         | Yellow       | Green   | Orange     | Quality, independence, well resourced<br>GMP inspections<br>The electronic queue system                                 | Better harmonisation with ICH guidelines<br>Increase dialogue with companies<br>Improved timelines   |
| Mexico | Yellow         | Yellow       | Yellow  | Orange     | Initiated open meetings via video links<br>Pre-NDA consultation<br>More initiatives to align with FDA and Health Canada | More communication during review process<br>More resource needed for renewals and to support GMP inspections/recognition<br>Work on achieving target timelines |
| Peru   | Orange         | Yellow       | Orange  | Orange     | Published draft regulations for public feedback   | Be open to external training, by experts<br>More reliance on using other agencies feedback<br>More training on technical information and knowledge             |

Rating scale of agencies by companies: Unsatisfactory Poor Satisfactory Good Excellent

## Measuring quality of the review process using a Quality Scorecard

Measuring quality of the review is important as it increases trust amongst stakeholders and achieves a broader acceptability of the review conducted. Although it is very difficult to measure quality per se, it is possible to instead measure the different activities that are believed to make up a quality review. Consequently, in 2004, CIRS developed the concept of using a Quality Scorecard to get feedback from companies on the agencies' review and from agencies on the company submission with regards to specific parts of the review/dossier (Figure 10).

**Figure 10: Improving predictability and regulatory decision making using mirroring quality scorecards for agencies and companies**



## Quality Scorecard results

In 2013, CIRS used the validated scorecard to conduct a study of six multinational companies regarding their perception of the quality of the review in LATAM agencies based on the assessment of 16 products. The results for a selected number of questions (out of a total of 45 questions) were mapped out in the form of aggregated scorecards (Figures 12-15) to build a picture of areas (Figure 11) in which an agency works well as well those that could be improved, and to enable cross-agency comparisons. The overall aim of these scorecards is to provide standardised, systematic feedback regarding efforts to help enable, enhance and embed the elements of GRevP (transparency, predictability, quality and timeliness) into the agency's review.

**Figure 11: Checklist for a scorecard on agency performance**

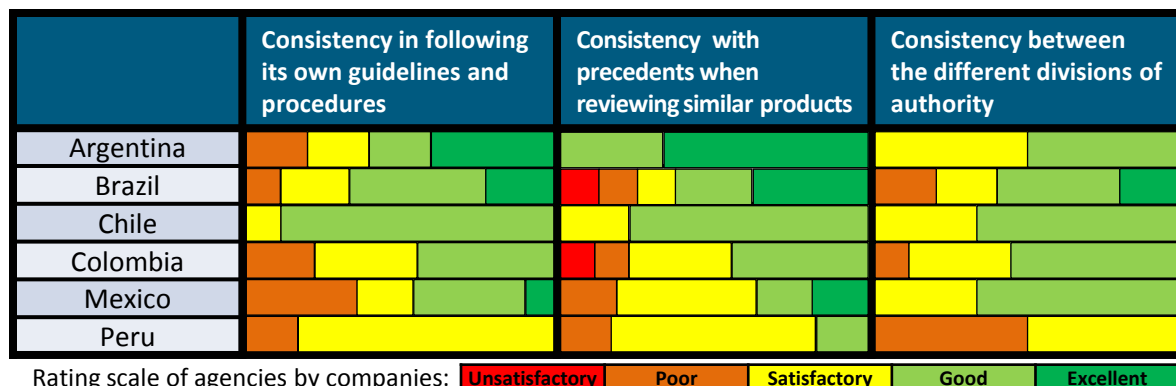
Completed by Companies

- ✓ **Scientific Advice:** The extent of interaction between the agency and the applicant throughout the development process
- ✓ **Communication:** How appropriate the agency's communication and responsiveness were during the review process
- ✓ **Consistency:** Whether the agency followed its own guidelines and precedents when assessing the product; How consistent the advice was in relation to previous experiences and precedents
- ✓ **Professional/scientific competence:** Whether the agency experts had the appropriate knowledge and experience for the product under consideration
- ✓ **Procedures:** How rigorously the agreed review procedures for applications had been followed
- ✓ **Questions:** The usefulness and relevance of the questions asked during the review process and whether these highlighted valid issues or were they based on a misunderstanding or misinterpretation of the dossier
- ✓ **Product information:** Whether final Summary of Product Characteristics/Product labeling was arrived at fairly and openly with requests for changes driven by science
- ✓ **Overall satisfaction:** Whether the result of the review arrived at the outcome that the applicant had expected or whether there was a fundamental difference between the expectations and the conclusions of the agency



## Predictability

**Figure 12: 2013 Aggregated scorecard results based on how six multinational companies rated the review of their dossier by each agency. Each bar shows the proportion of dossiers (16 in total) that were given the specific rating by companies. Selected questions on enabling a predictable review are shown.**



### Predictability: Comments from industry regarding the 2013 scorecard study

#### Areas where review **excelled**:

Argentina: “Follows the process”; Brazil: “Stability requirements according to local guideline”, “Labelling requirements in line with ref agency”; Mexico: “Consistent guidelines usage”



#### Areas where review could **improve**:

Brazil: “To not introduce new requirements for pending applications” Colombia: “To improve consistency in review process between therapy areas”; Mexico: “To improve alignment between reviewers”; Peru: “To adhere to the structure of an international CTD”



### Predictability: Observations from agencies and companies following interactions in 2015

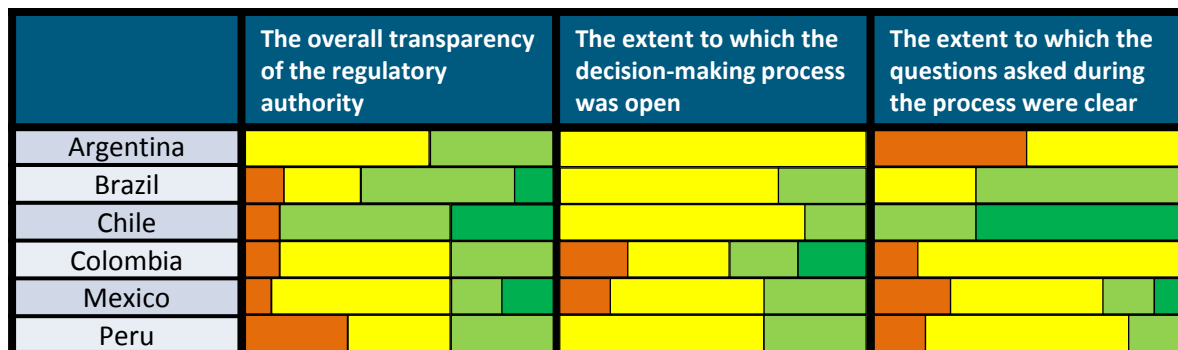
Brazil: The agency’s recent steps to improve predictability have been met with positive response from companies. For example, the agency has been submitting its guidelines for public consultation before finalising them and publishing on the agency website. Additionally, the requirements are continuously reviewed by the agency in order to harmonise them with international standards. With regard to clinical trial applications, the industry noted that there has been good movement. The pre-review validation queue time has been long but the agency is developing a submission guideline based on ICH to reduce discrepancies and improve first cycle review times.

Colombia: Colombia’s recent changes to its review process and guidelines have not been welcomed by some companies. Industry highlighted that although they agree that the agency should have tailored approaches to regulation, it is crucial that these are aligned with international guidelines. Companies noted that there is currently little predictability in the review times, and review and advisory committee timelines have slowed, which may relate to the fact that the agency appears to be moving from abridged reviews back to carrying out full assessments.

Mexico: Since 2011, Mexico has put in place strategic actions to reduce review backlog, such as removal of certain barriers to market entry (e.g., CPP), harmonisation with international practices and administrative modernisation. The agency has also introduced a risk-based approach (i.e., equivalence route) as well as an Authorised Third Party (ATP) process which involves dossier pre-evaluation by an independent company in order to reduce agency review times. Nevertheless, although the equivalence route target time is 60 days, and the ATP route has been shown to reduce the review time by about two years for new drugs (from 30 to 4.5 months), these reductions are somewhat variable. Additionally, companies are unsure whether the total time has been reduced due to long queue times to obtain a pre-submission meeting with the New Molecular Committee (NMC). Consequently this requirement for an NMC meeting in case of an equivalence route is now being questioned by some companies.

Transparency

Figure 13: 2013 Aggregated scorecard results based on how six multinational companies rated the review of their dossier by each agency. Each bar shows the proportion of dossiers (16 in total) that were given the specific rating by companies. Selected questions on enabling a transparent review are shown.



Rating scale of agencies by companies: **Unsatisfactory** **Poor** **Satisfactory** **Good** **Excellent**

Transparency: Comments from industry regarding the 2013 scorecard study



Areas where review **excelled**:

Brazil: “Good quality of questions”, “Good communication”; Chile: “Dossier status can be monitored online”, “Clear questions”; “Assessor can be contacted directly”; Mexico: “Pre-submission enables technical issues to be resolved”; Peru: “Open dialogue with reviewer”



Areas where review could **improve**:

Argentina: “Improve communication and admin flow between departments”, “To provide clear information of review status”; Brazil: “To send questions in batches”; Chile: “More open and direct communication with professionals regarding review”; Mexico: “Better communication with sponsor”

Transparency: Observations from agencies and companies following interactions in 2015

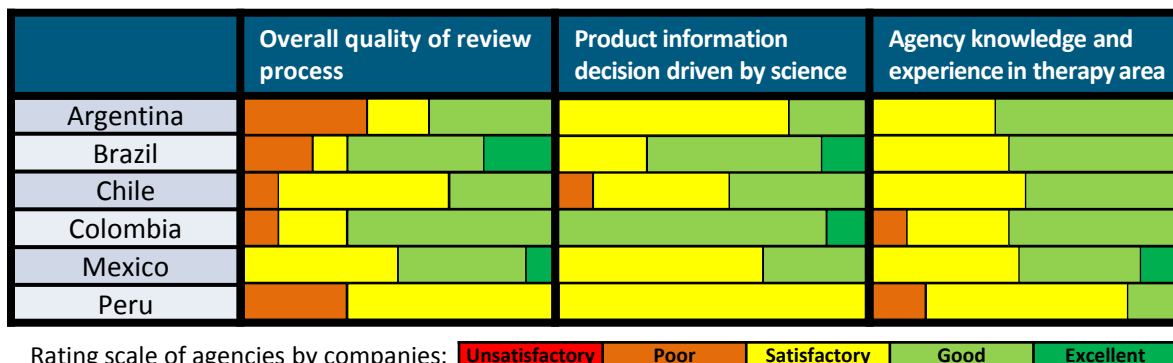
Brazil: The agency has noted that it has recently put more emphasis on pre-submission meetings, which has been recognised by the industry. Companies agree that the meetings have become more common, of good quality and productive; a guidance is also available. The agency has also indicated that it has been increasing its transparency by introducing a ‘Contact Us’ system to answer queries as well as by publishing the summary basis of approval and an analysis on its current queue time.

Colombia: Companies have noted that they have been recently receiving many questions from reviewers which appear irrelevant, and there are inconsistencies around the interpretation of requirements; this has had particular impact on oncology submission. On the other hand, because of complicated interpretations of data exclusivity requirements for clinical studies, the industry is supplying the agency with large amounts of clinical data, which may be slowing the review process. The agency suggested that a checklist could be developed which will contain the specific items needed for the review and that there should be a maximum size limit imposed on the dossier. Additionally, companies have suggested the agency create a set of clear guidelines on data protection.

Mexico: Companies have noted that the agency has been inconsistent with regards to approval criteria and requirements, and often asks for more data than other agencies. The pre-submission meeting with the NMC occasionally results in unaligned requirements. Moreover, the equivalence process is further complicated as, although the agency has replaced the need for a CPP with a requirement for clinical data in a Mexican population, companies noted that the lack of clear guidelines on trial data and the percentage of required population forces them back to using a CPP. The agency has undertaken to establish more consistent review and approval criteria.

Quality

Figure 14: 2013 Aggregated scorecard results based on how six multinational companies rated the review of their dossier by each agency. Each bar shows the proportion of dossiers (16 in total) that were given the specific rating by companies. Selected questions on enabling a quality review are shown.



Quality: Comments from industry regarding the 2013 scorecard study

Areas where review excelled:

Brazil: “Expert staff”

Areas where review could improve:

Argentina: “Where there are divergences not to rely just on the reference agency opinions, but use a systematic scientific assessment”; Chile: “To develop competence and therapeutic knowledge of the reviewers”; Mexico: “Alignment between reviewers”; Peru: “Understand structure of ICH CTD”



Quality: Observations from agencies and companies following interactions in 2015

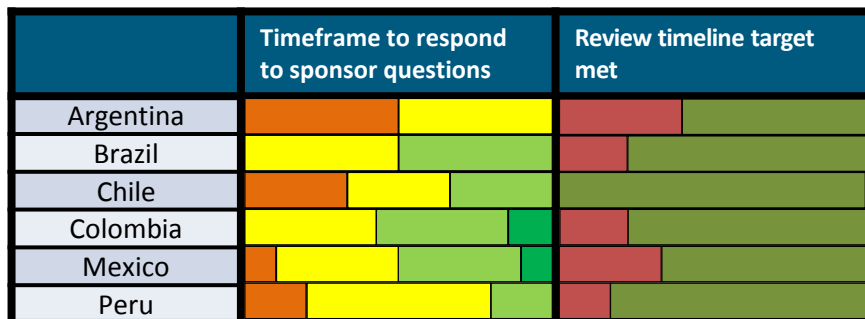
Brazil: The local company affiliates have noted that the agency has been only slowly building expertise in many technical areas, and this may be related to a lot of resource to resolve the large backlog in biologic submissions. The agency has been mitigating this by restructuring the review process, and increasing the number of reviewers as well as by involving the reviewers in capacity building and in attending training programmes and international scientific meetings. Brazil has also placed more emphasis on increasing its interactions as well as in cooperation agreements with other regulatory agencies through WHO and PAHO, for example.

Colombia: Companies have suggested that an emphasis on increasing staff numbers as well as the continuous training of reviewers will increase the agency expertise and ultimately will have a positive impact on the review process. Revision of the review process and better alignment with international practices has also been highlighted as a priority.

Mexico: The agency has taken steps to increase the quality of their review by training its staff. Nevertheless, challenges remain as companies would like to see better alignment between reviewers. In recent years, the agency has acted to promote pharmacovigilance (PV) activities by putting more PV systems in place and aligning them better with good PV practice guidelines issued by PAHO.

## Timeliness

**Figure 15: 2013 Aggregated scorecard results based on how six multinational companies rated the review of their dossier by each agency. Each bar shows the proportion of dossiers (16 in total) that were given the specific rating by companies. Selected questions on enabling a timely review are shown.**



Rating scale of agencies by companies:

### Timeliness: Comments from industry regarding the 2013 scorecard study

#### Areas where review **excelled**:

Argentina: “Timelines are good”; Brazil: “Expedited review time met”; Colombia: “Adherence to timelines”; Mexico: “Fast timelines”, “CPP post submission allows faster submission time”



#### Areas where review could **improve**:

Argentina: “Timelines for Risk Management Plan evaluation”; Brazil: “Decrease the queue for review”; Chile: “To reduce time, if review is based on existing approval in reference agency”, “Extend timeframe for questions”; Colombia: “To reduce review timelines”; Mexico: “To improve commitment to give responses in a timely manner”; Peru: “To adhere to official timelines”



### Timeliness: Observations from agencies and companies following interactions in 2015

Brazil: Companies have observed that that due to the fact that the agency is focusing more on reviewing new drugs, new indications and label changes are lagging. Additionally, the current submission queue time is very long but the agency has been working on reducing this from >100 to 60 days. Brazil has also created a measure by which dossiers with deficiencies do not return to the start of the queue but the review resumes straight away (target time of 30 days). The agency has also put a priority system in place that uses a checklist to determine product inclusion; nevertheless, companies noted that better guidelines are needed in order to truly address accelerated reviews for unmet medical need.

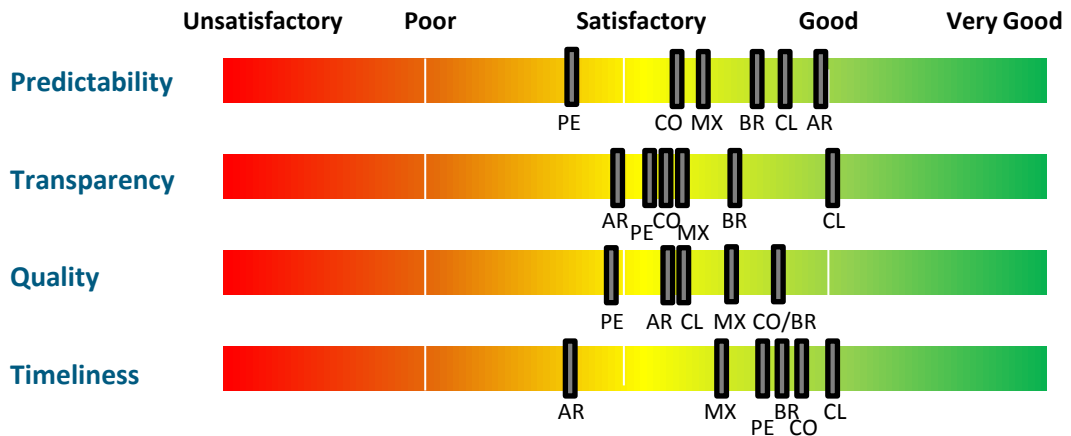
Colombia: Companies highlighted that the review process time may be increasing and the timelines are long and unpredictable even when there are prior approvals in reference agencies; this may relate to the agency’s movement to carry out full assessments rather than abridged reviews. The increasing timelines may also relate to the fact that the industry is supplying the agency with potentially too much data due to complexities in data exclusivity issues. By creating a better communication platform between the agency and the industry, it will be possible for the stakeholders to work together on clearer guidelines and process changes.

Mexico: The agency has improved its review timelines in recent years through the introduction of risk-based approaches, thereby avoiding duplication of effort. Additionally, submissions are expedited if multinational trials include at least 8% of relevant populations. The backlog has also been successfully reduced, as pre-verification administrative procedure time has been shortened from one year to three working days. Nevertheless, companies have noted that certain process changes, such as the requirement for an NMC meeting and the need for a risk management plan for PV before approval, have added to the overall time, despite a decrease in the agency review time.

**Quality Scorecard 2013 Study - Conclusion**

Overall, agencies were mostly scored by companies as ‘satisfactory’ in the areas of predictability, transparency, quality and timeliness. Agency averages are shown below on a sliding scale (Figure 16).

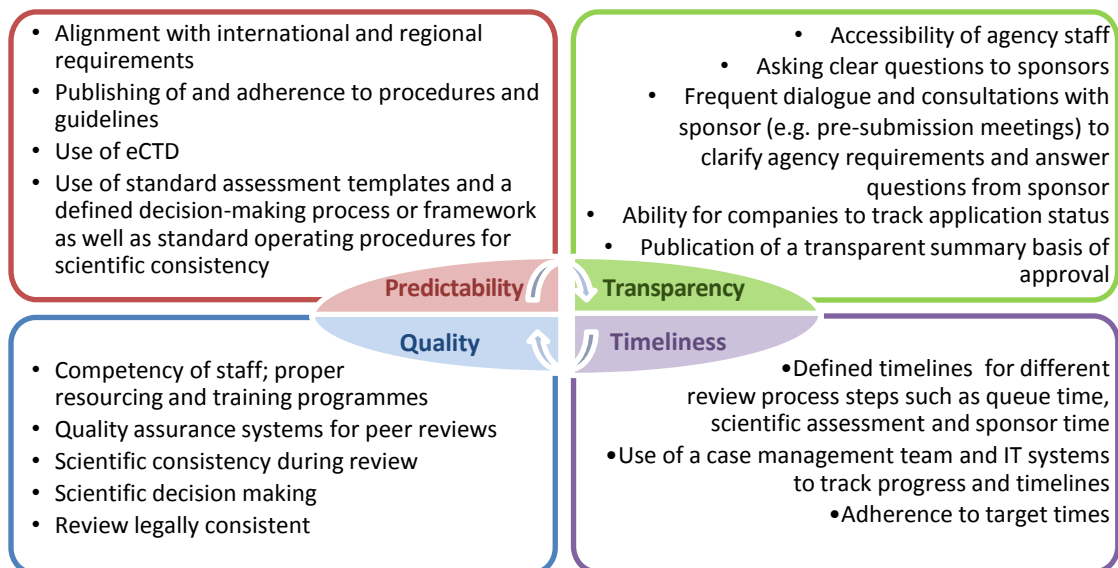
**Figure 16: Average results of each set of questions from Figures 12-15 on enabling predictability, transparency, quality and timeliness. Each agency average is shown as a slider on the scale, where AR = Argentina, BR= Brazil, CL = Chile, CO = Colombia, MX = Mexico, PE = Peru**



**The way forward**

Although most agencies received a ‘satisfactory’ rating, room for improvement remains to ensure a better quality review and improved decision making. Nevertheless, as this study was carried out in 2013, changes have taken place which have been reflected in this report through more recent insights. Going forward, agencies should measure the quality of their review on a regular basis in order to see whether process and system changes are successfully promoting the attributes of predictability, transparency, quality and timeliness into the review practices of an agency. Recommendations on how to enable a good quality review process are itemised below (Figure 17).

**Figure 17: Practices to enable a good review and promote predictability, transparency, quality and timeliness**



It is important to note that the overall lessons learned in this report can be applied to other agencies in the emerging markets beyond Latin America. Finally, although it is essential that emerging market countries establish tailored approaches to regulation that effectively use their resources, it is crucial that these also are aligned with widely followed international guidelines and GRevPs.

### Approval time

Time calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.

### Certificate of Pharmaceutical Product (CPP)

A certificate issued in the format recommended by the World Health Organization (WHO), which establishes the status of the pharmaceutical product

### Good review practices (GRevP)

Documented best practices related to the process, format, content, and/or management of a review, with the goal of promoting timeliness, predictability, consistency, transparency and high quality of the content and the management of reviews. This is achieved through the use of review tools such as standard operating procedures and templates and reviewer learning activities such as training and mentoring.

### New active substances (NASs)

A chemical, biological, biotechnology or radiopharmaceutical substance that has not been previously available for therapeutic use in humans and is destined to be made available as a 'prescription only medicine', to be used for the cure, alleviation, treatment, prevention or in vivo diagnosis of diseases in humans. The term NAS also includes:

- An isomer, mixture of isomers, a complex or derivative or salt of a chemical substance previously available as a medicinal product but differing in properties with regard to safety and efficacy from that substance previously available
- A biological or biotech substance previously available as a medicinal product, but differing in molecular structure, nature of source material or manufacturing process and which will require clinical investigation.

- A radiopharmaceutical substance that is a radionuclide or a ligand not previously available as a medicinal product. Alternatively, the coupling mechanism linking the molecule and the radionuclide has not been previously available.

Applications that are excluded from the study

- Vaccines
- Any other application, where new clinical data were submitted.
- Generic applications.
- Those applications where a completely new dossier was submitted from a new company for the same indications as already approved for another company.
- Applications for a new or additional name, or a change of name, for an existing compound (i.e. a 'cloned' application).

### Overall lag

Date of submission at the first regulatory agency to the date of regulatory approval at the target agency

Liberti L, McAuslane N, Patel P, Breckenridge A., Eichler HG, Peterspm R. 2013. Regulatory review: how do agencies ensure the quality of decision making? *Clin Pharmacol Ther.* 13: 305-308.

McAuslane N, Cone M, Collins J. 2006. *R&D Briefing: A cross-regional comparison of the regulatory environment in emerging markets.* CMR International Institute for Regulatory Science. Available at: <http://cirsci.org/sites/default/files/RD%2050%20Feb06%20EM%20Cross%20Regional%20Compar.pdf>

McAuslane N, Cone M. 2006. *R&D Briefing: Building Quality into Regulatory Activities: What does it mean?* CMR International Institute for Regulatory Science. Available at: <http://cirsci.org/sites/default/files/RD46.pdf>

McAuslane N, Patel P, Liberti L, Connelly P. 2012. *Workshop report: Evolving the Regulatory Review Process What are the features which enable a transparent, timely, predictable and good quality review; Centre for Innovation in Regulatory Science.* Available at: [http://cirsci.org/sites/default/files/CIRS\\_December\\_2011\\_WS\\_Report.pdf](http://cirsci.org/sites/default/files/CIRS_December_2011_WS_Report.pdf)

Pan American Health Organization, PAHO-PANDRH website. [http://new.paho.org/hq/index.php?option=com\\_content&view=category&layout=blog&id=1156&Itemid=3865&lang=en](http://new.paho.org/hq/index.php?option=com_content&view=category&layout=blog&id=1156&Itemid=3865&lang=en)

Patel P, McAuslane N, Liberti L, Connelly P. 2014. *Workshop report: Focus on Latin America; Building quality submission and review processes and practices – Overcoming challenges and meeting expectations.* Centre for Innovation in Regulatory Science. Available at : [http://cirsci.org/sites/default/files/CIRS\\_January\\_2014\\_Workshop\\_Report.pdf](http://cirsci.org/sites/default/files/CIRS_January_2014_Workshop_Report.pdf)

Prat AG. 2013. A practical overview of requirements for drug registration in Latin America. *TOPRA Rapporteur.* 13:5-10.

The World Health Organization. 2015. *Countries.* Available at <http://www.who.int/countries/en/>

US Central Intelligence Agency. 2015. *The World Factbook.* Available at: <https://www.cia.gov/library/publications/the-world-factbook/>

A list of CIRS studies in the area of emerging markets, including countries in the LATAM:

| Pilot CIRS Studies  |
|---|
| <p><b><i>Emerging market agency benchmarking study</i></b></p> <ul style="list-style-type: none"> <li>• <b>Pilot initiated in 2015</b></li> <li>• <b>Intent:</b> To assess time taken to approve medicines and analyse influencers of submission and approval time from an agency perspective, using agency-supplied metrics</li> </ul>   |
| Ongoing CIRS studies  |
| <p><b><i>Emerging markets industry benchmarking study (annual) - 2006-present</i></b></p> <ul style="list-style-type: none"> <li>• <b>Intent:</b> To benchmark time taken to approve medicines and analyse influences of submission and approval time from an industry perspective</li> <li>• <b>Outcome:</b> Annual report based on Emerging Markets Regulatory review Times (EMaRReT) database updated by participating companies</li> </ul>  |
| Completed CIRS studies  |
| <p><b><i>Identifying Good Review Practices Through the Use of the Quality Scorecard Programme: Scorecard on the Latin American Regulatory Authorities</i></b></p> <p>- Study conducted in 2013 (concept developed in 2004)</p> <ul style="list-style-type: none"> <li>• <b>Intent:</b> To provide standardised, routine feedback regarding efforts to enhance the quality, predictability, transparency and timeliness of an agency's review and submission practices</li> <li>• <b>Outcome:</b> Scorecards based on feedback collected from companies following the review of a major new application</li> </ul> |
| <p><b><i>Understanding the enablers of good regulatory process and decision making What are the features that enable a transparent, timely, predictable and good-quality review?</i></b></p> <p>- Study conducted in 2011</p> <ul style="list-style-type: none"> <li>• <b>Intent:</b> To review the enablers of good review process and decision making and to uncover the features that enable a transparent, timely, predictable and good-quality review</li> <li>• <b>Outcome:</b> Results from a survey completed by agencies and companies</li> </ul>  |
| <p><b><i>A Cross-regional Comparison of the Regulatory Environment in Emerging Markets</i></b></p> <p>- Study conducted in 2006</p> <ul style="list-style-type: none"> <li>• <b>Intent:</b> To identify barriers to the timely authorisation of safe and effective medicines in the region</li> <li>• <b>Outcome:</b> Briefing based on data collected from companies, and a survey and face-to-face interviews with the agencies</li> </ul>  |



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