



Bulletin of the Observatory — PRAIS



Year 1, No. 1, March 2014. Basic medicines regulatory capacity in the Americas

**PRAIS — Regional Platform on
Access and Innovation for
Health Technologies**



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The Bulletin of the Observatory — PRAIS is a digital publication produced by the [Medicines and Health Technology Unit](#) of the Pan American Health Organization (PAHO) whose periodicity depends on the availability of updated country data within the Observatory at the Regional Platform on Access and Innovation for Health Technologies (PRAIS).

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1. Introduction and general considerations

Strengthening medicines regulatory capacity requires us to analyze the existing strengths and opportunities for improvement in our region. This first issue of the bulletin presents an overview of the development of medicines regulation in the Region of the Americas by analyzing the “basic regulatory profile” based on 20 “basic medicines regulatory indicators.” This sample represents 25 countries or approximately 71.4% of the total number of Member States at Pan American Health Organization (PAHO). All countries were given a random country code for the presentation of results.

The information presented here does not constitute an in-depth evaluation of their specific

strengths and opportunities for improvement.

The data were collected using different methodologies, such as: consultant interviews (The Pharmaceutical Sector Country Profile process); on site evaluations (National Regulatory Authority functionality assessment); and self-report with follow-up by PAHO (PAHO representative national assisted evaluation).

However, it provides an initial look at regulatory capacities in the countries and in the region as a whole, both in general and in the different areas of regulatory activity linked to the indicators. This analysis will also serve as an introduction to a more detailed evaluation of specific regulatory capacity to be presented in subsequent issues of the Bulletin.

2. Achievement characterization of the regional basic medicines regulatory capacity

- The basic indicators provide the minimum information needed for a simple understanding of the capacity and functions that correspond to a regulatory profile. The indicators were selected to provide a quick, direct analysis and the responses were given in qualitative binary (yes/no) format. The indicators are presented in the Observatory — PRAIS Bulletin with achievement

percentages and data visualization format followed by an descriptive analysis.

- On average, the data (Figure 1) shows that the participating countries successfully met 68.8% of the requirements as indicated by the basic indicators (“yes” responses), but did not achieve 31.2% of them.
- The evaluated data indicate different levels of achievement of the set of indicators in the different countries (Figure 2):

Figure 1. Profile of basic medicines regulatory capacity in the Region of the Americas: achievement average of 20 basic indicators in 25 evaluated countries

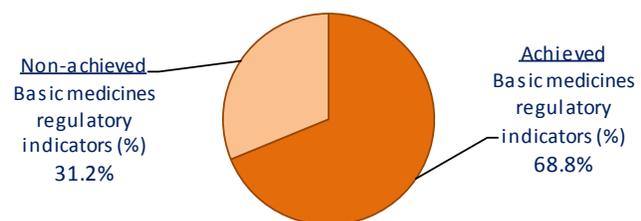
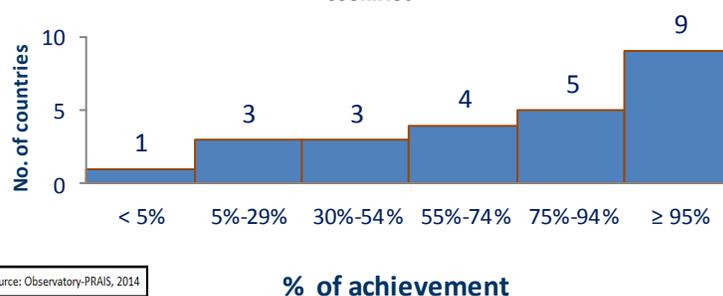


Figure 2. Distribution of countries by degree of basic medicines regulatory capacity in the Region of the Americas: achievement average of 20 basic indicators in 25 evaluated countries



Source: Observatory-PRAIS, 2014

- Nine countries have achieved “greater than or equal to 95%” of the indicators (36% of the countries);
- One country is in the category of having achieved “less than 5%”; and
- While 15 countries (60% of total countries) have met between 5% and 94% of the basic indicators.

3. Characterization of the level of achievement by indicator

- The basic medicines regulatory indicators were selected from “the Pharmaceutical Sector Country Profile data collection tool,” WHO document. The 20 indicators represent a view to providing the basic information necessary for a general understanding of a country’s performance.
- Table 1 lists all the basic indicators along with the number of countries and percentage (based on the frequency of yes/no responses) that have attained each of them (based on 25 Member States of PAHO). All basic indicators were given a code.
- Indicator #0902 has the highest achievement rate with 24 out of 25 (96%) countries participating in harmonization initiatives or collaborating with national regulatory authorities.
- This is followed by four other top performing indicators: #0907 (inspections), #0909 (authorization to import medicines), #0911 (licensing of manufacturers), and #0910 (sampling for lab testing).

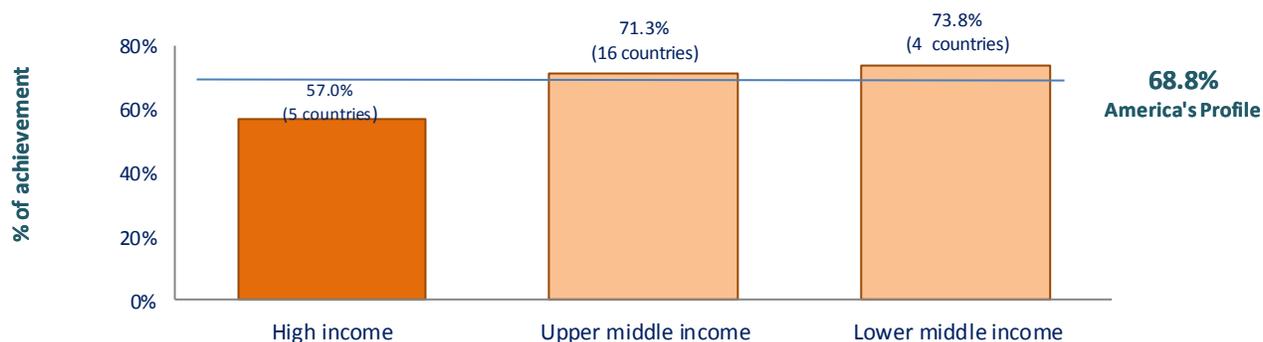
Table 1. Achievement of the basic medicines regulatory indicators in the 25 countries evaluated — March 2014	Number of countries (%)
0902 - Does the national medicines regulatory authority (NMRA) participate in harmonization or collaboration initiatives?	24 (96%)
0907 - Are there legal provisions that exist permitting inspectors to inspect premises where pharmaceutical activities are performed?	23 (92%)
0909 - Are there legal provisions that exist requiring authorization to import medicines?	22 (88%)
0911 - Are there legal provisions that exist requiring manufacturers to be licensed? If yes, please attach the appropriate document or provide the URL.	22 (88%)
0910 - Are there legal provisions that exist allowing the sampling of imported products for testing?	21 (84%)
0900 - Are legal provisions that establish the functions and responsibilities of the NMRA in place?	20 (80%)
0904 - Does the NMRA have a legal provision that requires a marketing authorization (registration) for all pharmaceutical products on the market?	20 (80%)
0912 - Are there legal provisions for quality control of the pharmaceutical market?	19 (76%)
0903 - Does the NMRA use an electronic information management system to keep and recover all information relative to product licensing, registration, inspections, etc.?	18 (72%)
0908 - Are there legal provisions that require manufacturers to implement adequate Good Manufacturing Practices (GMP)?	18 (72%)
0913 - Does a national laboratory exist in the country for quality control testing?	18 (72%)
0917 - Are there legal provisions that provide for pharmacovigilance activities as part of the NMRA mandate?	17 (68%)
0918 - Does a national adverse drug reactions database exist in the country?	17 (68%)
0901 - Does the NMRA have a website?	16 (64%)
0905 - Are there legal provisions that require the NMRA to make publicly available information of registered pharmaceutical products with defined a periodicity?	14 (56%)
0915 - Are there legal provisions that exist requiring the agreement by an ethics committee/ institutional review board of the clinical trial to be performed?	14 (56%)
0914 - Are there legal provisions that exist requiring NMRA authorization for conducting clinical trials?	13 (52%)
0916 - Are there legal provisions requiring the sponsor and investigator to comply with Good Clinical Practices (GCP)	12 (48%)
0919 - Do routine and crisis communication strategies exist?	11 (44%)
0906 - Are there legal provisions requiring the NMRA to publish the Summary Product Characteristics (SPCs) of the pharmaceuticals registered?	5 (20%)

4. Characterization of the level of achievement by income

- The correlation between a country’s basic medicines regulatory capacity by its income level (according to the [World Bank](#) classification) was evaluated for the 25 countries.
- Figure 3 shows the regulatory capacity of countries grouped by income level. A higher level of income does not necessarily imply a correlation with a high degree of achievement. In this dataset, lower-income countries have achieved a higher level of the basic indicators when compared with the average profile in the Americas.

Refer to page 3.

Figure 3. Basic medicines regulatory capacity by income level: achievement average of 20 regulatory basic indicators in 25 countries of the Americas



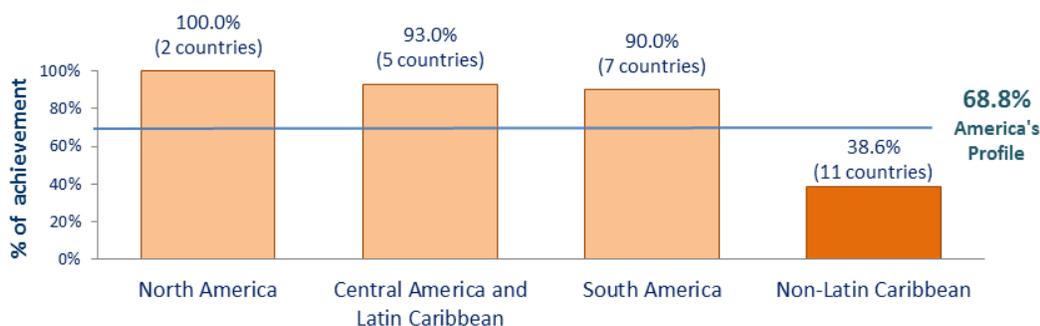
Source: Observatory-PRAIS, 2014

High Income (5 countries)	Upper middle income (16 countries)	Lower middle income (4 countries)
Antigua and Barbuda Chile Saint Kitts and Nevis Trinidad and Tobago United States	Argentina Barbados Brazil Colombia Costa Rica Cuba Dominica Dominican Republic Grenada Jamaica Mexico Panama Peru Saint Lucia Saint Vincent and the Grenadines Suriname	Bolivia Guatemala Guyana Paraguay

5. Characterization of the level of achievement by geographical subregion

- The different subregions of the Americas tend to have health systems with similar characteristics and levels of development. In order to determine whether this correlation extends to their level of regulatory capacity, Figure 4 shows achievement level by geographical subregion. The Figure shows large differences between geographic areas: North America shows the highest achievement level (100%), while the countries of the Non-Latin Caribbean show much lower attainment (36.6%).
- It is important to emphasize the limitations of this analysis: first, there are different numbers of countries in each subregion and the list of countries in subregions is incomplete; and second, levels of achievement can vary significantly between countries within a single subregion. However, this analysis allows us to infer which subregions have the greatest need for improvement.
- The Region of the Americas could take advantage of having many countries that can share their successful regulatory experience with countries in the same subregion and others.

Figure 4. Basic regulatory medicines capacity by subregion: achievement average of 20 basic indicators in 25 countries of the Americas



Source: Observatory-PRAIS, 2014

6. Opportunity for improvement by indicator

• In order to establish the regulatory areas that most need strengthening in the region, the 20 basic indicators were ranked by non-achievement (Figure 5 and Table 2).

• Indicator #0906 (20 countries) “the requirement to publish a summary of product characteristics” has the highest level of non-achievement. This indicator presents information that serves as a guideline for the safe and effective use of medicines information (package leaflets or brochures accompanying the medicines packaging) that should be based on official technical documentation. It is good practice for a regulatory authority to publish this information to provide health professionals access to this document.

• Other indicators with sub-optimal achievement include:

- ◊ Indicator #0919 - lack of a clear risk communication strategy for routine and crisis communication (14 countries);
- ◊ Indicator #0916 - lack of legal provisions requiring the sponsor and the investigator to follow good clinical practices (13 countries);
- ◊ Indicator #0914 lack of legal provisions requiring clinical trials authorization (12 countries); and
- ◊ Indicator #0905 - lack of legal provisions requiring the NMRAs to make available to the public and periodically provide list of registered pharmaceutical products (11 countries).

Figure 5. Opportunity for improvement by order of non-achievement of each basic medicines regulatory indicator in 25 countries of the Americas - March, 2014



Source: Observatory-PRAIS, 2014

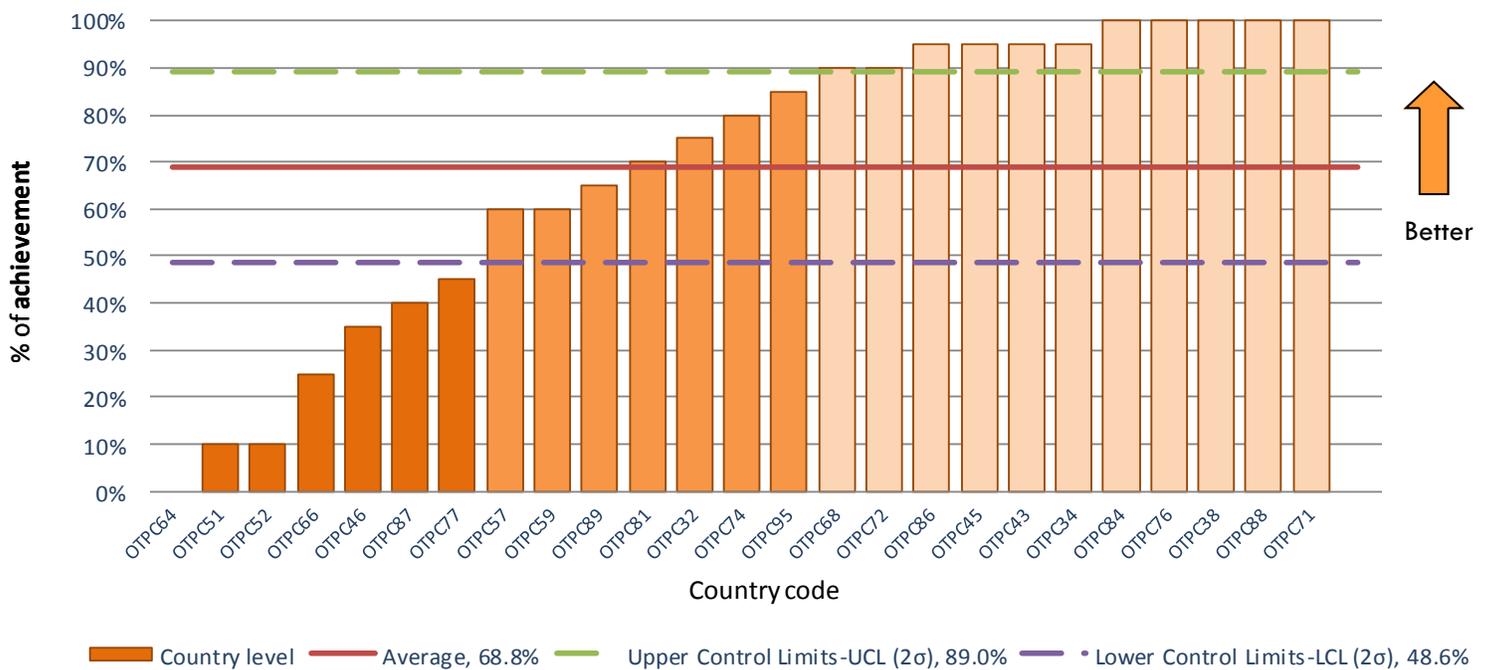
Table 2 - Basic medicines regulatory indicators

	No. of countries with non-achievement (%)
0906 - Are there legal provisions requiring the NMRA to publish the Summary of Product Characteristics (SPCs) of the pharmaceuticals registered?	20 (80%)
0919 - Does a routine and crisis communication strategy exist?	14 (56%)
0916 - Are there legal provisions requiring the sponsor and investigator to comply with Good Clinical Practices (GCP)	13 (52%)
0914 - Are there legal provisions that exist requiring NMRA authorization for conducting clinical trials?	12 (48%)
0905 - Are there legal provisions that require the NMRA to make publicly available registered pharmaceutical products with defined periodicity?	11 (44%)
0915 - Are there legal provisions that exist requiring the agreement by an ethics committee/ institutional review board of the clinical trial to be performed?	11 (44%)
0901 - Does the NMRA have a website?	9 (36%)
0917 - Are there legal provisions that provide for pharmacovigilance activities as part of the NMRA mandate?	8 (32%)
0918 - Does a national Adverse Drug Reactions database exist in the country?	8 (32%)
0903 - Does the NMRA use an electronic information management system to keep and recover all information relative to product licensing, registration, inspections, etc.?	7 (28%)
0908 - Are there legal provisions that require manufacturers to implement adequate GMPs?	7 (28%)
0913 - Does a national laboratory exist in the country for quality control testing?	7 (28%)
0912 - Are there legal provisions for quality control of the pharmaceutical market?	6 (24%)
0900 - Are legal provisions that establish the functions and responsibilities of the NMRA in place?	5 (20%)
0904 - Does the NMRA have a legal provision that requires a marketing authorization (registration) for all pharmaceutical products on the market?	5 (20%)
0910 - Are there legal provisions that exist allowing the sampling of imported products for testing?	4 (16%)
0909 - Are there legal provisions that exist requiring authorization to import medicines?	3 (12%)
0911 - Are there legal provisions that exist requiring manufacturers to be licensed? If yes please attach the appropriate document or provide the URL.	3 (12%)
0907 - Are there legal provisions that exist permitting inspectors to inspect premises where pharmaceutical activities are performed?	2 (8%)
0902 - Does the NMRA participate in harmonization or collaboration initiatives?	1 (4%)

7. Establishing regional benchmarks

- To ensure continuous improvement countries prioritize areas of work and take action in accordance the institutional development plans (IDP), and the degree of achievement of the indicators. Considering that the goal should be to achieve 100% of the basic indicators and that a country, whatever its initial situation may be, can advance toward that goal, Figure 6 offers a metric to short- and medium-term goals for regulatory capacity development.
- Benchmarks were set for each country and the upper and lower control limits were set according to the level of achievement of the regional average. The graphic in Figure 6 was prepared by adapting the “Six Sigma” control methodology in order to establish metric-based improvement targets and propose recommendations to the countries. The upper and lower lines were calculated taking as reference a two-fold variance (2 sigma) around the average number. Theoretically, it would be expected that 95% of the country results would lie within the range of the lower control limit (LCL) and the upper control limit (UCL).
- Based on this metric it is possible to make the following recommendations,
 - ◇ Countries under the lower control limit (LCL) can set the goal of reaching this LCL before the next evaluation cycle (one or two years planning);
 - ◇ Countries under the upper control limit (UCL) can set the goal of surpassing the UCL before the next evaluation cycle (one or two years planning); and
 - ◇ Countries that have already reached or are above the LCL can set the goal of achieving and/or improving the quality of 100% achievement.

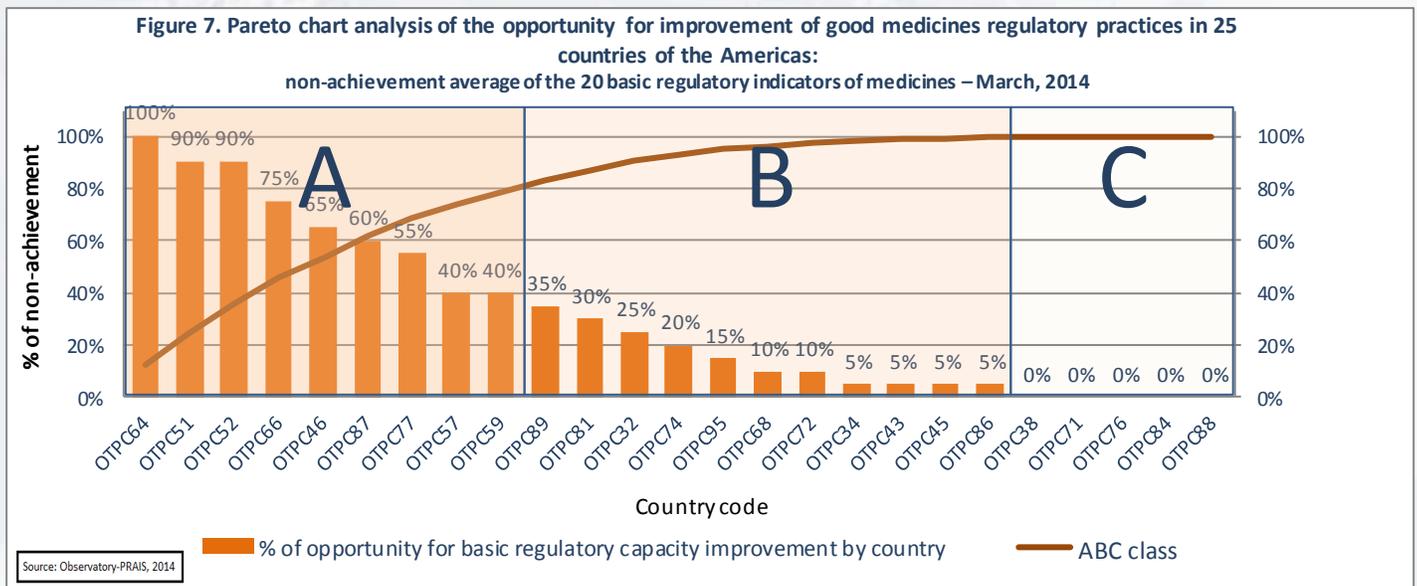
Figure 6 - Basic medicines regulatory capacity benchmarking in 25 countries of the Americas: achievement average of 20 basic indicators - March, 2014



Source: Observatory-PRAIS, 2014

8. Opportunity for improvement of good medicines regulatory practices in the Region of the Americas

- In order to determine groups of importance and optimize the potential impact in improving good regulatory practices, a "Pareto chart" was applied to sort the countries by decreasing order of the percentage of non-achieved indicators and arbitrarily group them, as follows: A-class: countries contributing up to an 80% to global non-achievement; B-class: additional 20%, and C: 0% (Figure 7).
- The analysis indicates that nine countries of the Region in A-class, should receive more attention and or prioritization (e.g. cooperation). This is because there are countries with great potential to increase the regulatory capacity development to 80% of the Region of the Americas average.
- Eleven countries in B-class should continue and deepen the implementation of basic indicators and start a specific analysis of their regulatory systems though advanced indicators.
- The five countries in C-class should maintain the already implemented basic indicators, as well as leveraging advanced indicators as a monitoring tool to achieve high standards of regulatory practices. They may also support other countries through regional cooperation processes.



9. Limitations of the data and analysis

- This initial effort to prepare a regional profile of basic medicines regulatory capacity in the Americas has the following methodological limitations:
 - ◊ In principle, there is a set of regulatory functions and processes that is hard to evaluate using only one or a small number of indicators, due to the complexity of related processes;
 - ◊ Different methodologies applied to collect data and information;
 - ◊ A “yes”, “no”, or “not applicable” response was requested with regard to the level of achievement of this group of basic indicators. This type of approach does not allow an evaluation of partial achievement, or of the depth of achievement in the case of a positive response;
 - ◊ Data are from a sample of 25 of the 35 Member States of the Region of the Americas. While this is a significant and representative number of countries, a regional analysis would ideally include all the countries of the region; and
 - ◊ Another natural limitation is related to the time interval in which data were collected and the analysis was prepared: from 2009 until the first quarter of 2014.
- However, we hope that from now on data can be collected periodically (annually or biannually) in order to better monitor the development and trends of medicines regulatory capacities over time.

10. Discussion and recommendations

- This bulletin represents an initial effort to prepare a profile of basic medicines regulatory capacities in the Region of the Americas, based on data processed in the Observatory — PRAIS. It is a useful tool to support the monitoring and prioritization of medicines regulatory capacity in the region.
- Based on this methodology, we estimate that on average the basic medicines regulatory capacity in the Americas is at approximately 69% of what it should be, indicating an opportunity for strengthening these capabilities. This figure can be used as reference and benchmark for the next evaluation of data in the Observatory — PRAIS. In this regard, the region could set the goal of surpassing this figure collectively and collaboratively.
- This analysis reflects a wide degree of variance in achievement among participating countries (range from zero to 100%). This heterogeneity should be taken into account when preparing technical cooperation plans, which should give particular priority to the countries and subregions with the lowest levels of achievement, according to different countries context.
- The large number of positive responses regarding participation in harmonization initiatives reflects the interest that the countries of the Americas have in sharing information and working jointly with other countries, particularly within the framework of the Pan American Network for Drug Regulatory Harmonization ([PANDRH](#)), established in 1999.
- A lack of legal provision to publish the Summary of Product Characteristics (SPCs) of the pharmaceuticals registered, is noted. This result, in the same way for other indicators, can be used to prioritize areas in the NRA institutional development and technical cooperation plans for both PAHO and between countries.
- The analysis indicates that a high level of socioeconomic development does not guarantee sufficient regulatory capacity. It is therefore reasonable to conclude that a country's income level should not be considered a strong predictor of its regulatory capacity and that the availability of financial resources in a country does not in itself guarantee

an adequate medicines regulatory system. A more in-depth analysis will determine whether the allocation and distribution of resources is a better predictor: this includes per capita health spending; health spending, by sector, as a percentage of gross domestic product (GDP); health spending in the regulatory area; spending on research and development; and priorities in pharmaceutical policies, among others. An analysis of the allocation of funds to and within the health sector will reveal whether countries allocate sufficient resources to the regulatory system despite having a high socioeconomic level. In contrast, adequate achievement of the indicators by countries with lower socioeconomic development shows that sufficient regulatory capacity can still be achieved with limited resources.

- Such analysis is only possible through systematic, standardized data collection with the support of the health and regulatory authorities of the Member States. The analysis should be enhanced by collecting data in all the countries of the region.
- In future issues of this newsletter, a more accurate analysis of the level of development of medicines regulation in the Americas will be made; taking as a reference 166 indicators considered "advanced". This will support the scope of specific strengthening regulatory capacities of medicines of Member States.
- The cooperation of the countries of the Americas is essential in order to periodically update the Observatory's data. This will make it possible to evaluate trends in the development of medicines regulatory capacities and to prioritize actions aimed at improving regulatory capacity in the region. The gaps identified above require national authorities and principal stakeholders in the region of the Americas to implement joint activities, with the support of PAHO and other partners, aimed at facilitating technical cooperation to ensure access to safety, effectiveness and quality of medicines.

About the Observatory — PRAIS

- [The Observatory — PRAIS](#) contains a set of data from countries that provide information for profiles of: access to health technologies; intellectual property management; health technology governance; research, development, and innovation in health technology; and the regulation of drugs and biologicals.
- These profiles are made up of basic and advanced indicators, selected according to their level of importance, simplicity, access, sustainability, and timeliness, in order to reflect the regional situation and regional performance in health technologies.
- The basic medicines regulatory indicators were selected with a view to providing the basic information necessary for a general understanding of a country's performance, based on the frequency of yes/no responses from ["the Pharmaceutical Sector Country Profile data collection tool,"](#) WHO document.
- The advanced medicines regulatory indicators stand out for their specificity, complexity, or fine detail, allowing a deeper evaluation of the issues. This indicators were chosen from the "Manual for the assessment of national regulatory authorities of regional reference for basic and biologicals, 2011" PAHO. Both basic and advanced indicators were presented to PANDRH Steering Committee in 2011 and approved as a data collection tool.
- PRAIS was officially launched on May 7, 2012, year when the Observatory had regulatory data from 8 countries and has been increasing, adding data from Member States and participant states of the Americas.

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