Methodology for the rapid review and updating of lists of medicines in the Dominican Republic

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Background

The drafting or updating of lists of essential medicines (LEM) is often a painstaking task. The most commonly used methodology involves setting up teams made up of specialized clinicians, clinical pharmacologists, health workers and, in some countries, representatives of the pharmaceutical industry. Over a period of several workdays, either sequential or spread over a period of several weeks or months, these teams analyze the advisability of modifying, retaining or excluding each of the active principles and dosage forms included on the list being reviewed, along with requests for the inclusion of new molecules, all in accordance with criteria set forth by the World Health Organization (WHO) [4,5]. In 2007, at least 134 countries had LEMs and most had updated them within the preceding five-year period[5].

The countries of Latin America have available limited numbers of trained professionals in the areas of clinical pharmacology, pharmacoepidemiology and pharmacoeconomics. Such professionals constitute indispensable resources for the LEM review process, given their more in-depth knowledge of the pharmacokinetics and pharmacodynamics of molecules, as well as of their efficacy, safety and cost-effectiveness. Their skills in the systematic review of scientific evidence enable them to help bring about consensual agreement among clinical specialists, using criteria developed at the time a decision is made to include or exclude a given medicine. Often, the drafting or review of an LEM is postponed or delayed due to the limited in-country availability of such pharmacological experts, or to difficulties in obtaining technical assistance of this type from other countries.

For the above reasons, the Dominican Republic's LEM had not been reviewed since 2005. In about 2014, the Ministry of Public Health (MPH) also saw the need to conduct a review of both the therapeutic formulary in use at the primary level of care and the list of high-cost medicines, as well as to draft a list of over-the-counter medicines. The MPH requested technical assistance from the United States Agency for International Development (USAID) to address these needs.

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[4] World Health Organization. Promoción del uso racional de medicamentos: componentes centrales. Perspectivas políticas sobre medicamentos de la OMS 5. WHO: Geneva; September 2002.
[5] World Health Organization. Selection of essential medicines. In: The World Medicines Situation Report. 3rd ed. Geneva: WHO; 2011.

Methodology

The Systems for Improved Access to Pharmaceuticals and Services (SIAPS)[6] program proposed a methodology for reviewing the above-mentioned lists and formularies, with the potential to achieve optimum results in short periods of time and with a minimal investment of resources. The methodology consisted of identifying an expert international pharmacologist with experience in the LEM process and the following procedural steps:

1. **Design of an instrument for drafting the proposal:** An instrument was designed that would enable the expert pharmacologist to record, for each product, i.e., each active principle in its various dosage forms, his or her proposal for *retaining, excluding,* or *replacing* that product (with either a therapeutical equivalent or a safer or more effective dosage form) or for *adding* that product to the list. For those products proposed for *exclusion, replacement* or *addition*, it would be necessary to record the documentary source supporting the proposal. The instrument, which included columns for *agree*, *disagree*, *proposal*, and *source consulted,* would enable the proposal to be subsequently validated at workshops attended by expert consultants, who would give mark the columns accordingly. Below is a sample of the instrument designed.

Product	Expert proposal				Review and validation by consultation group			
	Retention	Exclusion	Replacement/ addition	Observations/source consulted	Agree	Disagree	Proposal	Observations/ source consulted
Ampicillin, suspension, 125mg/ml, vial 120 ml			x	Amoxicillin, suspension, 125mg/ml, vial 120 ml	x			
Acetylsalicylic acid, tab 81 mg	x							

2. **Drafting and review of proposal by the expert:** Three weeks prior to traveling to the country, the expert was given the current list of medicines along with requests for inclusions, exclusions or modifications, all of which had been previously routed through the appropriate pharmacy and therapeutics committees, if any. On this basis, the expert proposed the retention, exclusion or replacement of each product, basing his or her decision on reference lists (WHO, similar lists from countries with well-established regulatory entities, or evidence-based clinical guidelines prepared by independent authorities, such as those prepared by the WHO and the *National Institute for Health Care and Excellence* – NICE) and consultations with reviews of the literature using indexed databases, such as those of NICE, the Cochrane Database, the Canadian Agency for Drugs and Technology in Health, the National Guidelines Clearinghouse, the NHS Economic Evaluation Database and the Health Technology Assessment Database. Drafting of this initial review proposal required approximately 10 workdays at the expert's place of residence.

3. **National workshop to review and validate the proposal:** The expert's proposal was presented to and validated by a consultation group made up of clinical specialists, health workers, pharmacists, technical staff from the national regulatory authority and representatives of the pharmaceutical industry. The work session required three days to carry out the following agenda:

[6] Project implemented by Management Sciences for Health (MSH) since 2011 with funding provided by USAID.

- ***Presentation and agreement on the methodology for studying the efficacy, safety and cost-effectiveness of the medicines:*** Either the expert or the work session facilitator presented the working methodology that would make it possible, at a two-day meeting, to review and validate the list of medicines.
- ***Summary presentation of the proposal drafted by the expert:*** The systematic methodology used to review the safety, efficacy and cost-effectiveness of each product and to develop the proposed list was explained to the work group, with the proposed list subsequently presented to the group for its consideration. Participants were offered suggestions as to the most reliable sources of information for conducting electronic consultations during the work session.
- ***Organization of work*****:** Groups of between five and eight participants each were formed, with each group assigned to review one section of the list of medicines. Steps were taken to ensure that participant specialties were consistent with the therapeutic groups included in the section of the list assigned to each. Each work group had available computers with Internet access, enabling them to perform electronic consultations, and each was given an electronic copy (Excel) of the proposal drafted by the expert. The group was asked to complete, within a pre-determined period of time (six to eight hours of work), the instrument columns labeled *Review and validation by consultation group*. Each group was asked to appoint a discussion moderator, along with a *rapporteur* to record on the electronic spreadsheet the consensus reached by the group.
- ***Review of the proposal drafted by the expert:*** The groups reviewed the proposal drafted by the expert for each product, recording their agreement or disagreement. In cases of disagreement, they recorded their reasons and the bibliographic reference supporting the consensus reached by the group.
- ***Presentation of the consensus reached by the groups:*** In a plenary session, the *rapporteur* for each group presented the products with regard to which the group was in disagreement with the expert, together with the reasons given and the bibliography justifying the group's decision. The expert and/or plenary session participants then presented their counter-arguments, if any, after which the group consensually reached a definitive determination. Each medicine analyzed was thus definitively included, excluded or modified on the new list. Only by exception and by group decision were decisions postponed in order to gather additional evidence not available at the time of the meeting.
- ***Presentation and validation of the complete list:*** The expert then consolidated in a single list the consensually reviewed and validated sections and presented the list to the work group for confirmation of the overall consensus reached. For the few products for which a decision was still pending, the algorithm that would lead to its eventual inclusion or exclusion (*" will be included on the final list if a review of literature confirms that ….; otherwise it will be excluded"*) was made explicit.
- ***Commitments regarding editing and publication of the list:*** A period of eight days was agreed upon for the participants to deliver to the expert any additional evidence so that the latter could make a final decision regarding the inclusion, exclusion or modification of a given product. Likewise, a period of 30 days was established for the expert to forward on to the national health authority the list of medicines validated by the group of experts. Health authorities present at the closing ceremony will make known to the participants the procedures and dates for final editing and publishing of the list of medicines.

Results

Using the above methodology, SIAPS supported a review of the list of high-cost medicines in 2014. Ninety-eight medicines used to treat some 10,700 patients accounted for expenditures totaling 4,800 million Dominican pesos (USD 106 million) in 2014, an amount 15% greater than that allocated for the treatment of all patients receiving care in public hospitals and primary health facilities in that same year. In a three-day work session, the list was reduced from 98 to 45 medicines, leading to a reduction of 893 million DOP (USD 20 million) in the pharmaceuticals procurement budget.

The LEM, which had not been updated since 2005, was reviewed in 2014. The validated list reduced the number of products from 1039 to 762, increasing from 64% to 82% the percentage of products included on the WHO model list and other international reference lists. The LEM was published and officially approved for use as a purchasing standard in August 2015. The therapeutic formulary for the primary level of care, which had not been reviewed since 2008, was also updated to ensure its consistency with the new version of the LEM, as regards both medicines included and the levels of care authorized to use them.

April 2015 saw the development of the first proposed list of over-the-counter medicines in the Dominican Republic. The list was based on the country's database for drug control and registration (in which products are registered as either over-the-counter or available by prescription only), on predetermined criteria established by the health authority (for example, exclusion of antibiotics, narcotics, parenterals), and on reference lists from countries with sound and well-institutionalized health authorities (Colombia, Canada, United States and Spain). Using the above-described methodology, a list of 670 over-the-counter products was consensually established. Official approval will follow publication of the supporting Ministerial Declaration.

Analysis and conclusions

The combination of an initial systematic and documented review of LEMs by a professional expert followed by validation by a group of national experts has proven to be both effective and efficient. The times traditionally required to achieve these results were reduced significantly, as were the financial and material resources involved. In addition, the methodology designed made it possible for opposing positions taken by clinical specialists to be resolved on the basis of evidence that was systematically identified and documented on the working instruments. The databases that contributed to the review of the above-mentioned lists will make it possible for subsequent review exercises to be carried out with an even greater degree of efficiency.