Process for development of a revised National Regulatory Authority assessment tool harmonized across all medicines including vaccines

Background

Strengthening health systems including medicines regulatory systems is a mandate of WHO. In January 2014 the WHO Executive Board discussed a draft WHA resolution regarding strengthening of national regulatory systems which will be presented to the World Health Assembly (WHA) in May 2014. In the Americas’ region for example, a Regional Committee Resolution (CD50.R9), endorsed in 2010 urges Member States and PAHO/WHO to strengthen national regulatory authorities for medicines and biologicals across the region. Other WHO regions also emphasize the need to ensure access to medicines of assured quality. For example, the “Regional Strategy for Improving Access to Essential Medicines” in the Western Pacific Region (2005-2010) which was endorsed by all Member States, provides a comprehensive and practical approach to prioritizing goals for the pharmaceutical sector and identifies the strategies to attain them. This includes providing guiding principles on WHO’s role to continue to support medicines regulatory authorities strengthening.

The vaccines National Regulatory Authorities (NRA) strengthening programme is based on a five-step capacity building approach. It includes defining a benchmark using a set of indicators to measure performance for the recommended regulatory functions. It may entail either a self-assessment of functions by the NRAs or a WHO assessment of the functions by an international team of experts. This assessment leads to the identification of strengths and gaps to build upon strengths and address the gaps which are reflected in an Institutional Development Plan (IDP) or in special cases in a road map too. After endorsement of the IDP by the government (NRA and/or Ministers of Health) it can be used to tailor the technical support to the specific needs of that particular authority and country. Once the proposed activities as part of the IDP are implemented (including training and technical support), a re-assessment or other monitoring mechanisms allow verification of the progress achieved. Based on the progress made and the remaining gaps a new tailor made plan for technical support is developed and implemented.
Purpose of the revision process

The NRA assessment tool is an instrument used by countries, regions and WHO headquarters to assess, as part of the five-steps capacity building model, the strengths and weaknesses of the regulatory systems in place. The instrument as such is important and needs to be tailored to the needs, but the way in which the assessment is planned and conducted is another important component of the model as well as the way in which functions are scored and the final evaluation is done.

The fact that a number of slightly different tools have been developed for different products over the years raises the need to seek convergence among them. Although, the merger of the medicines, PAHO and vaccines tools is the ongoing effort, it is envisaged that in the future, other existing tools will be also merged with the medicines, vaccines and PAHO tool, so that a single consolidated tool is available for all product categories.

An additional challenge results from the fact that while the different tools are being used by different WHO programmes for different purposes they target the same institutions and staff using different procedures. Furthermore, the multiplication of assessment tools leads to confusion in the countries assessed which requires WHO to tackle the problem and seek some level of harmonization in the tools, assessment process, scoring system, terminology and policy.

Current status of development of the revised tool

The revision process started in January 2013 and has gone through a number of steps that led to the following results:

- The indicators and sub-indicators present in the medicines, vaccines and PAHO tool have been compared and those that were common have been combined, those that were not common or those functions that were relevant to one tool but not to others were kept separate. In the process of combining indicators and sub-indicators the wording may have been slightly modified in some cases, but the concept was not changed or revised. However, there was an agreement to regroup some of the functions, such as post-marketing
surveillance (PMS) which was merged with lot release. Vigilance and Risk Management remained as a separate function. In addition it was proposed to separate the ethics indicators from the clinical trial oversight function. Endorsement of the proposed changes will be a matter for discussion and decision making by the International Consultation of Experts. The regulatory functions listed in figure 1 were considered as harmonized.

- This version of the tool with the combined and non-combined indicators was entered into the database originally used only for the vaccines tool, and originated an electronic tool applicable when conducting joint assessments for medicines and vaccines.

- The new version of the tool was piloted during the self-assessment (2013) and the assessments carried out in Mexico (March 2014) and in China (April 2014). If a NRA is evaluated against one of the product categories (i.e. vaccines in the case of Mexico), the indicators of the vaccine tool that are common to the medicines and PAHO tools will be automatically filled in the respective fields. This feature facilitates the performance of either joint or separate assessments as it avoids unnecessary repetitions.

- In addition, a mapping of the technical standards (WHO or other internationally recognized standards) used to assess compliance with indicators and sub-indicators in the respective assessment tools has been conducted. This mapping allowed to define in a transparent manner the standards against which NRAs are assessed for each individual indicator and sub-indicator. It also showed that there may be a need to develop additional new indicators/sub-indicators and to delete some existing ones.
Next steps and expected timelines

The revision process will be completed in the coming months, in close collaboration with NRAs and WHO regional offices, to achieve the three following objectives at the same time:
1) The revision of the proposed tool and its guidance document;
2) The revision of the assessment process;
3) The development of a comprehensive policy on the WHO role in strengthening national and regional regulatory capacity in Member States.

The plan of the WHO secretariat is the following:

May 2014 - Public availability of prototype 1 of the harmonized (combined) tool

The WHO vaccine and medicine tools including the harmonized tool (prototype 1) are currently posted on the WHO website in excel format for comments. The computerized harmonized tool (prototype 1) is also available and posted on the WHO sharepoint site and can be accessed upon request. Through this process each interested NRA will have the opportunity to have access to the revised tool.
October/November 2014 - Establishment of the working groups

WHO secretariat will establish three working groups: one will be responsible to review the prototype tool for harmonization purposes, to fine tune the combined/harmonized tool and to revise and update the indicators and sub-indicators. This work may lead to the modification of some of the existing indicators/sub-indicators, the creation of new ones and the deletion of others. These changes would lead to a new version of the tool (Prototype II).

Another working group will review and provide recommendations for improvement of the NRA assessment process as required to meet the upcoming needs.

The third working group will provide recommendations for the development of a comprehensive NRA assessment policy defining the responsibilities of WHO taking into consideration the framework of the draft policy for strengthening regulatory capacity, the “to be established resolution on RSS” and the future perspectives regarding the prequalification programme.

The membership of the working groups will be decided through consultation with all WHO Regional Offices and consultation with EMP staff and staff from other relevant Departments in HQ. The criteria for selection of members will be defined in the Terms of Reference for the working groups.

The policy working group will be established in October. The first virtual meeting will take place the week starting on 6 October 2014, and the other two working groups will be established in November 2014. This time difference will allow the policy working group to advance work that will inform and guide the work of the other two working groups. These three working groups will be working remotely using a web-based communication system and through teleconferences from their establishment until the end of their assignments (30 November 2014). The WHO secretariat will provide the relevant background information, documents and guidelines and in particular share the experiences of the WHO regions in this domain. The working group dealing with the revised tool should develop a consolidated report including recommendations on new indicators or sub-indicators or other suggested changes to the WHO secretariat. These changes would lead to the development of
a proposed draft of the tool (Prototype II). The other two groups (assessment process and policy) will develop reports with proposals for consideration by the International Consultation of Experts.

**October 2014 - Briefing to WHO expert committees**

WHO Secretariat will brief the Expert Committee on Biological Standardization (ECBS) and the Expert Committee on Pharmaceutical Preparations (ECPP) on the on-going revision of the NRA assessment tool, assessment process and proposed policy for WHO’s role on regulatory capacity strengthening in their respective meetings of October 2014.

**October to December 2014 – Public consultation**

WHO secretariat will make publicly available the proposed draft tool and proposals from the two other working groups for public consultation through a web link on the WHO website and through posting on the WHO/RSS sharepoint.

**December 2014 – Online consultation of experts**

WHO secretariat will convene an online Consultation of Experts in the period 2 to 4 December 2014. This consultation will be primarily focused on the policy recommendations for an extended discussion of the proposals made by the policy working group. Inputs received during the online consultation will be integrated into the concept paper prepared by the policy working group for further consideration and discussion at the face to face International Consultation of Experts which will take place the week starting on 12 January 2014.

Similarly to the process followed for establishment of the working groups the composition of the International Consultation of Experts will be decided following the established rules and procedures and ensuring broad representation from NRAs and Regional Offices. The final reports of the three working groups (concept papers) will be presented to the International Consultation of Experts. In this respect the International Consultation of Experts may have to consider also the outcomes of the public consultations and that of the online Consultation meeting, organized at the previous step.
It is likely that the International Consultation Meeting will be dedicated the first day to discuss the policy proposal and the other two days to discuss the other aspects. It is expected that the International Consultation Meeting will finally recommend the adoption by WHO secretariat of a final draft of the harmonized tool, and will provide detailed recommendations on the amendment of the assessment process and on the development of the policy document.

This consultation may lead to the modification of some of the existing indicators/sub-indicators, the creation of new ones and the deletion of others. These changes would lead to the development by the WHO secretariat of a new version of the tool (Prototype III).

**February to July 2015 - Feasibility and usability studies by field testing**

WHO secretariat will organize field testing assessments or self-assessments with countries who wish to do so, to pilot the revised tool during a period of approximately six months.

**October 2015 - Endorsement by WHO experts committees**

The new harmonized tool, the assessment process and draft Regulatory Systems Strengthening (RSS) policy document as recommended by the International Consultation of Experts will be referred for endorsement to the Expert Committee on Biological Standardization (ECBS) and the Expert Committee on Pharmaceutical Preparations (ECPP) in October 2015.

**November 2015 - Official Publication**

The endorsed tool and its guidance document will be sent for publication following the WHO internal rules and procedures and made publicly available through a web link on the WHO website and posted on the WHO/RSS sharepoint.

**January 2015 to December 2016 - Transitional period**

As per WHO usual practice, the official use of the tool in countries will require a transition period to be determined by the International Consultation Meeting of Experts depending on the level and magnitude of the changes introduced. A grace period of between six months and one year may be given before official implementation. However, countries who wish to do so, may request WHO to apply the new tool even during the grace period as appropriate.
December 2016 - Official Implementation

At the end of the transitional period, the revised tool and its guidance will enter into full operation.

Conclusions

This very ambitious plan is based on the current experience at WHO HQ in developing a harmonized assessment tool in order to satisfy the needs of NRAs worldwide and is part of a continuous improvement process in an attempt to reflect the changes in the field of pharmaceutical regulation.
Process for development of a revised Assessment tool, assessment process and RSS policy document

1. Preliminary draft (Prototype 1)
   - On website

2. Revised tool (prototype 2) + Draft proposals
3. Final draft
   - Prototype 3 and final proposals
4. Official publication

Key milestones:
- WGs established
- International consultation of experts convened
- WHO Expert Committees convened

Timeline:
- May 2014
- Oct 2014
- Oct/Nov 2015
- Jan 2015
- July 2015
- Dec 2016