Vaccine safety and pharmacovigilance in the WHO African Region

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Every vaccine has a lifecycle, which starts with discovery, to clinical evaluation, licensure and eventual introduction and use in routine immunization programmes. During clinical trials of new candidate vaccines all adverse events associated with vaccination are monitored. Clinical trials are, however, limited in their ability to detect rare and late occurring adverse events associated with vaccination due to smaller sample size and limited participant follow-up time.1,2,3 Careful, systematic and regular monitoring for possible infrequent but serious adverse events following immunization is thus desirable during the post-marketing, widespread use of any vaccine. An adverse event following immunization (AEFI) is defined as any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.4

Vaccine safety and pharmacovigilance has, therefore, assumed more significance in the WHO African Region which has also seen a growth in clinical development of new vaccines as well as their introduction into the national immunization programmes in many countries. Some of the vaccines being introduced include pneumococcal conjugate, conjugate meningococcal A meningitis, human papilloma virus, rotavirus and rubella. For the first time a vaccine against malaria, RTS,S/AS01, is in phase 3 clinical trial in seven countries in the Region, which if licensed and pre-qualified could be added to the list.

SUMMARY—In recent years the WHO African Region has seen a growth in clinical development of new vaccines as well as their introduction into the national immunization programmes of many countries. Recognizing the critical need for vaccine safety and pharmacovigilance, WHO has been supporting individual and institutional capacity building in the Region to strengthen the monitoring and response to adverse events following immunization through implementation of the Global Vaccine Safety Blueprint. This framework is discussed along with general points about the importance of ensuring vaccine safety and the system needed to enable this. The article ends with a brief overview of the status of vaccine safety and pharmacovigilance and the key priorities for countries in the Region for the immediate future.

Voir page 66 pour le résumé en version française. Ver a página 66 para o sumário em versão portuguesa.

1 WHO Regional Office for Africa, Brazzaville, Congo. Immunization Vaccines and Emergencies, Routine Immunization and New Vaccines
2 Routine Immunization, WHO-AFRO Intercountry Support Team
3 Safety and Vigilance Team, EMP, WHO, Geneva

Participants at a workshop for the development of national plans for vaccine safety and pharmacovigilance, Accra, Ghana
Recognizing the critical need for vaccine safety and pharmacovigilance, WHO has been supporting individual and institutional capacity building for the countries of the Region to implement the Global Vaccine Safety Blueprint, a strategic framework for strengthening the monitoring and response to AEFIs.5

Pharmacovigilance is one of the six required regulatory functions of national regulatory authorities (NRAs) for vaccines. In this context, WHO has developed an assessment tool to support institutional capacity building of NRAs, consisting of seven indicators and 28 sub-indicators. This tool allows countries to prepare development plans that guide institutional building efforts and to identify technical support needs for all areas of regulation of medicines, including vaccines.

Key point

The Global Vaccine Safety Blueprint is a strategic framework which sets the parameters for the safety of vaccines through effective use of the principles and methods of pharmacovigilance, ensuring the minimal capacity required for vaccine safety capacity in all countries, enhanced capacity under specific circumstances and providing a reliable network of support for capacity building and crisis management to national authorities.

Key point

Evidence exists that the administration of several antigens in combined vaccines increases the burden on the immune system. Combining antigens does not increase the risk of adverse reactions and can, in fact, lead to an overall reduction in adverse reactions following immunization.

Requirements of a functional vaccine safety and pharmacovigilance system

The Global Vaccine Safety Blueprint defines the requirements for a functional vaccine safety and pharmacovigilance system. This requires collaboration between the national expanded programme on immunization (EPI), national regulatory authority, national pharmacovigilance centres (NPCs), AEFI review committee and other groups (interagency coordinating committee, national immunization technical advisory group, health professional associations etc.). The system should capture AEFI reports, investigate AEFIs, analyse the data, conduct causality assessment, define corrective actions and follow up the AEFIs and clearly communicate on AEFIs (see Figure 1).

This cycle depicts the steps for an effective AEFI surveillance system,
from identification, to notification, reporting, investigation, analysis, causality assessment, feedback and corrective action.

**WHO Global Vaccine Safety Blueprint**

Recognizing the need to strengthen capacity for vaccine safety especially in low- and middle-income countries, which lack this capacity, WHO and partners developed a strategic framework document on vaccine safety called the Global Vaccine Safety Blueprint, in 2011. The document sets out key indicators that aim to ensure that all countries have at least a minimal capacity to ensure vaccine safety. The Blueprint defines a strategy for strengthening safety activities globally.

The primary focus is to establish national capacity for vaccine safety in countries lacking this capacity through the coordinated efforts of all major stakeholders. The development of the document was achieved through consultations of experts globally and clearly defines its mission, vision and goals.

The Blueprint proposes three priority objectives:
- Establishing minimum capacity for vaccine safety and pharmacovigilance in each country;
- Enhanced approach in special situations; and
- Development of a global technical support network.

The eight strategic objectives of the Blueprint, which are being implemented by countries with the support of WHO are:
- Detection of AEFI;
- Adequate investigation of safety signals;
- Adequate communication of vaccine safety issues;
- Use of appropriate tools and methods;
- Ensuring a regulatory framework is in place;
- Technical support and training;
- Global analysis and response; and
- Public-private information exchange.

While the first four objectives relate directly to the components of vaccine pharmacovigilance systems, the last four address the supporting elements or prerequisites that must be in place for the vaccine safety system to function effectively. This Blueprint represents an excellent framework which if properly implemented can significantly strengthen vaccine pharmacovigilance in countries lacking the capacity, especially those of the African Region.

**WHO capacity building efforts for vaccine safety and pharmacovigilance**

Through workshops organized by WHO and bringing together national immunization staff, NRAs and pharmacovigilence centres, WHO has supported countries to develop work plans for vaccine safety and pharmacovigilance, which address their needs and are being implemented. These plans were developed in consultation with all stakeholders, WHO and partners in each country. The activities are defined, with timelines, defined roles and responsibilities and clear monitoring and evaluation plans.

The workshops evolved around a template for the development of work plans. The template defines the areas of activity, the baseline or current status, specific plans to fill gaps, estimated cost of achieving the results, source of funding, responsible person(s), partners and stakeholders, and a monitoring and evaluation framework to track progress made. The template is presented as Table 1.

WHO is also training the national AEFI committees for countries, who will in turn train provincial/regional and district committees. WHO has developed tools for causality assessment, training on vaccine safety and pharmacovigilance by countries.

### Table 1. Template for development of country work plans for vaccine safety and pharmacovigilance

<table>
<thead>
<tr>
<th>Specific activities</th>
<th>Current status</th>
<th>Needs to be addressed by 2015</th>
<th>Estimated cost</th>
<th>Source of funding</th>
<th>Responsible person(s)</th>
<th>Stakeholders and partners</th>
<th>Monitoring and evaluation</th>
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<td>AEFI committee</td>
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<td>Responsibilities and roles in vaccine safety</td>
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<td>Capacity for AEFI data analysis</td>
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<td>Written formal communications with all stakeholders including manufacturers</td>
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<td>Means for assessment of regional and district AEFI committees</td>
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Status of vaccine safety and pharmacovigilance in the WHO African Region

Eight anglophone countries (Ethiopia, Ghana, Kenya, Malawi, Nigeria, Uganda, United Republic of Tanzania and Zambia) and seven francophone countries (Burundi, Côte d’Ivoire, Cameroon, Democratic Republic of the Congo, Guinea, Madagascar and Togo) have been supported to develop work plans for 2014 and 2015. The countries have started implementation of their plans.

Prioritization and advocacy for pharmacovigilance and safety will ensure that it remains firmly on the global, regional public and national health agenda.

Clear definition of roles and responsibilities of each stakeholder institution ensures sustainability and attainment of goals.

Regular monitoring and evaluation of the status of implementation is essential to the success of building capacity for vaccine safety and pharmacovigilance.

Resource mobilization by all stakeholders is critical to success.

Partnerships at all level is also important.

This includes establishment or training of national expert committees, establishment of mechanisms for collaboration between stakeholders, collection, analysis and reporting of AEFI s. Evaluation of the status of implementation, and support where required, is ongoing through teleconferences and e-mail exchanges.

The national expert committee for AEFIs of the United Republic of Tanzania was trained in the use of the new WHO causality assessment tool by a panel of international experts. In addition, six international participants from Ethiopia, Ghana, Kenya, Malawi, Nigeria and Zimbabwe attended the meeting. Similar workshops will be conducted in their respective countries as part of a regional effort to strengthen national capacity for vaccine safety.

References


