About this bulletin
Providing updates on GVSI activities

The GVSI Bulletin\(^1\) provides updates on the implementation of the Global Vaccine Safety Initiative (GVSI)\(^2\), a forum aiming to synergize the knowledge and expertise of its stakeholders to help ensure the safety of vaccinations through the implementation of the three strategic goals of the Global Vaccine Safety Blueprint\(^3\).

To optimize collaborative activities, the GVSI Bulletin aims to provide all stakeholders of the Initiative with a practical overview of activities identified. Components of the portfolio\(^4\) and activities of GVSI stakeholders that match the eight objectives of the Global Vaccine Safety Blue print and profiles of stakeholders are presented to increase visibility of actions and support synergies.

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\(^4\) [http://www.who.int/vaccine_safety/initiative/GVSI_portfolio_directory_1_July_2014.pdf?ua=1](http://www.who.int/vaccine_safety/initiative/GVSI_portfolio_directory_1_July_2014.pdf?ua=1)
Focus on Africa - Tanzania  
Capacity building for Adverse Events Following Immunization (AEFI) monitoring: a joint NRA and EPI initiative in Tanzania.

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As a follow up of the workshop held in Ghana in April 2014 for eight African countries, a four day workshop on vaccine safety monitoring, investigation and causality assessment was conducted in August 2014 in the United Republic of Tanzania. The workshop brought the different stakeholders and partners to a common forum to achieve national goals.

The Expanded Programme of Immunization (EPI) started in Tanzania in 1975 providing BCG, OPV, DPT, measles and TT vaccines. An AEFI reporting system was established through the EPI system. In 2002, the country introduced hepatitis B and in 2009, HiB in combination with DPT. However, these introductions did not result in an increased attention to vaccine safety, as demonstrated with the low number of AEFI reported over time (fig 1). In 2013 and 2014, the country introduced rotavirus vaccine, PCV13 and measles 2nd dose. These new vaccines’ introduction resulted in an increased number of doses of vaccines administered and urged the country to recognize the need to prioritise a formal process in AEFI surveillance and monitoring.

Despite the high immunization coverage, rumours related to vaccines safety existed in Tanzania in very small communities which were not easily picked during routine immunization services but mostly picked during mass campaigns. Standard procedures and guidelines to deal with such situations did not exist. To address this issue, the Ministry of Health and Social Welfare through National Regulatory Authority in collaboration with the National Immunization and Vaccine Programme supported by the World Health Organization (WHO) organised a four-day workshop on AEFI surveillance, investigation and causality assessment in Bagamoyo town, Tanzania, from 11 – 14 August 2014. The workshop came at a critical moment as the country was in the process of introducing other new vaccines such as Measles and Rubella (MR) vaccine, Human Papilloma Virus vaccine (HPV) and Injectable Polio Vaccine (IPV - as part polio end game strategy) in the routine immunization schedule.

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The MR vaccine was administered through a mass immunization campaign for children 9 months to 14 years of age. The campaign was planned to be integrated with other child health survival interventions of vitamin A supplement and deworming with mebendazole for children under five years. Also the campaign was integrated with ivermectin and albendazole given to all people above 5 years as part of the Neglected Tropical Diseases programme.

The main objectives of the AEFI workshop in Bagamoyo were to;

- Strengthen Post Marketing Surveillance capacity for all vaccines
- Ensure consistent AEFI investigation and causality assessment practices as per the revised WHO methodology for the upcoming campaign and subsequently in routine immunization
- Enhance national capacity for AEFI data analysis and data management
- Communicate effectively on vaccine safety issues
- Identify the roles and responsibilities of different stakeholders in Tanzania
- Finalize the national AEFI guidelines based on global standards

The 21 Tanzanian participants included National AEFI Committees members from the Muhimbili University of Health and Allied Sciences (MUHAS), retired professors of Epidemiology, practicing clinicians and also representatives of the National Regulatory Authority, Immunization and Vaccine Development (IVD) and WHO. Also, international participants representing the national EPI, National Regulatory Authority, Pharmacovigilance Centres and WHO Country Offices of Ethiopia, Ghana, Kenya, Malawi, Nigeria, and Zimbabwe participated in the workshop.

The workshop was facilitated by International experts from University Department of Paediatrics, Women's and Children's Hospital, Adelaide, Australia, the Office of Public Health Practice, Public Health Agency of Canada Ottawa, Canada and the WHO Headquarters in Geneva, Switzerland.

One of the important outcomes of the workshop was the finalization of the National Guideline for Monitoring AEFI. This guideline incorporates the updated concepts of vaccines and AEFI, prevention and management of AEFIs, reporting structure of AEFI in Tanzania, overview of the revised AEFI causality assessment methodology recommended by WHO, actions and responses towards AEFI, and communication and media management. The significant impact of this training was the reporting of 22 AEFI cases such as rash, itching and swelling at the injection site during the measles rubella (MR) campaign that was conducted in October 2014.
Communicating about vaccines – Updated guidance as part of good pharmacovigilance practices for the EU

Priya Bahri

Just over a year ago, revised guidelines for vaccine pharmacovigilance were issued by the European Medicines Agency (EMA) and the European Heads of Medicines Agencies (HMA) as part of the EU-GVP, the good pharmacovigilance practices (GVP) for the European Union.

This revision replaces the EMA’s vaccine pharmacovigilance guidelines of 2009 and was updated in accordance with scientific progress, new pharmacovigilance legislation in force since July 2012, and recent regulatory experiences, in particular with the pandemic influenza vaccines in 2009/10. It also takes into account the Report of the CIOMS/WHO Working Group on Vaccine Pharmacovigilance, published in 2012. Apart from strengthening data collection and assessment, the new guidance recognises communication as integral to the pharmacovigilance process and offers more specific recommendations on safety communication about vaccines to regulatory authorities and marketing authorisation holders. While the EMA and other regulatory bodies world-wide have previously published general principles and processes for communicating about safety of medicines including vaccines, issuing regulatory guidance on communicating about a specific medicinal product class is new.

Learning from communication research – a new approach for regulators

Improving information about medicines to patients/citizens and healthcare professionals has always been high on the EMA’s agenda, and over the last ten years, patient participation in the EMA’s regulatory work has been introduced with huge success, not least by consulting patient experts on statutory product information and ad hoc safety communication prior to publication. But what has hardly been done is reviewing and applying results from communication research, a scientific area, which is unfamiliar to those assessing benefits and risks of medicines. Of course, communication officers in regulatory bodies

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2 The views expressed in this article are the personal views of the author and may not be understood or quoted as being made on behalf of or reflect the position of the European Medicines Agency or one of its committees or working parties.
have their knowledge and skills but this is rarely product-specific. Would it be worth reviewing the scientific literature about impact of product-specific communication, in particular on healthcare practice and media debates, and translate this into guidance for regulators and the pharmaceutical industry? – That is a key question.

**Table: Selected recommendations on safety communication from the EU**

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<tr>
<th>GVP - Product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases</th>
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<tr>
<td>Integrate communication process with risk assessment and plan communication with public information needs and concerns in mind</td>
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<td>Monitor the media regarding debates on vaccines and ensure appropriate, timely and meaningful communication with the media</td>
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<td>Consider multiple stakeholders for communication exchange, e.g. vaccine-targeted and vaccinated persons, parents/carers, healthcare professionals, health policy makers and the general public</td>
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<td>Arrange for fulfilling the communication objectives of:</td>
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<td>• providing information for informed decision-making in healthcare practice and vaccination programmes;</td>
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<td>• prevention of anxiety-related reactions;</td>
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<td>• avoiding vaccination errors;</td>
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<td>• reiterating precautions for use and warnings.</td>
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<td>Include information on the benefit-risk balance, the target disease, risks of non-vaccination, key functions of vaccine pharmacovigilance systems with the roles or responsibilities of those involved as well as on how a decision on vaccine safety has been reached</td>
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<td>Address frequent public information needs, such as excipients, residues, special populations</td>
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<td>Explain concepts, if need to refer to, such as coincidental event, temporal (but not necessarily causal) association between an adverse event and vaccination, a single case of an adverse event, mock-up vaccine and a safety monitoring need (which does not necessarily refer a confirmed risk)</td>
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<td>Advise healthcare professionals on how to manage vaccination/needle anxiety and frequent concerns of vaccine-targeted/vaccinated persons and carers, such as pregnancy, puberty, immunosensitive conditions, general anxiety/mood disorders, epilepsy</td>
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<td>Keep stratified exposure and background rates for causal and coincidental events up-to-date for contextualising safety concerns</td>
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<td>Prepare and test standard texts</td>
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<td>Foster a collaborative approach between regulatory authorities and international partners</td>
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In the EU, there have been a number of communication challenges with vaccines, for example MMR, HPV and pandemic influenza vaccines. A pilot project was conducted at the EMA, comparing what the communication science literature had already found out with the experiences gained with later vaccine incidents by regulatory authorities in the EU. There was congruence between the findings, suggesting that the communication science literature has potential to provide evidence to help design better safety communication strategies, which proactively address public concerns and information needs of specific population segments. The findings from the literature have translated into specific recommendations (see Table) and as such are now included in the vaccines pharmacovigilance guidelines of GVP.
For the EMA, the next step will be to gain experience with the consistent application of the recommendations in communication operations and to monitor how these improve safety communication, in particular in terms of addressing communication needs of the public in the EU. Evaluating the public health impact of improved communication interventions will not be easy, but should be a further step in the future.

WHO invited a presentation of the guidelines and especially its new communication section at their GVSI meetings in Tianjin in October 2014, and the meeting participants welcomed the recommendations in this international context.

Innovation in Sri Lanka

Successful piloting of Vaccine Adverse Events Information Management System (VAEIMS) in Sri Lanka and its full-scale adaptation.

Ananda Amarasinghe¹, Paba Palihawadana¹, Madhava Ram Balakrishnan²

The Vaccine Adverse Events Information Management System (VAEIMS) is a software developed to transfer Adverse Events Following Immunization (AEFI) data from the periphery of the health care system, efficiently and effectively into a central database for processing and conversion of raw data to information for action. This was conceptualized by WHO and developed by the International Vaccine Institute (IVI), Republic of Korea in 2013.

Sri Lanka is the first country to test the beta-version of VAEIMS and pilot test the same using its national reporting system since August 2013. From 2015, it is operating in routing AEFI data entry with a capacity of possible data sharing with WHO to a Global database.

The opinion of the end users in Sri Lanka about VAEIMS is that it is user friendly right from the point of installation and data entry and also assess program performance in parallel by the mid-level and national level program managers. This is because there is absolutely no change in the existing Sri Lanka AEFI data collection procedures; reporting forms and routes of reporting. This software is simple to use, it collects information through a front-end screen that is identical to the Sri Lanka national AEFI reporting

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form facilitating accurate data entry; it includes a system of in-built alerts so that the end user knows if the entries contain mismatches and inaccuracies. There is also real time data analysis with graphs generated and a built in data error check and audit trail utility to accurately track changes and assess performance.

Sri Lanka will soon be working on incorporating VAEIMS into the national indigenously developed Web Based Immunization Information System (WEBIIS) which too is currently being introduced all over the country. The information obtained from VAEIMS will be used by the National AEFI committee and the EPI program for decision making. It will also be shared with the relevant stakeholders in the Ministry of Health including the National Regulatory Authority.

By adapting this path breaking innovation first, Sri Lanka has demonstrated to the world the benefits of a system to ensure standardization of AEFI related information through the use of global standards recommended by the WHO. And by being the first country to demonstrate successful bridging opportunity to the global database VigiBase, Sri Lanka has led the way to a path-breaking global solution for pooling of vaccine safety data to encourage AEFI reporting and vaccine safety monitoring.

Active surveillance in Singapore
Active surveillance of Adverse Events Following Immunisation (AEFI) at a sentinel paediatric hospital in Singapore

Sally Bee Leng Soh¹, Chee Fu Yung², Dorothy Toh³, Koh Cheng Thoon⁴

In 2009, in preparation for scaled-up nation-wide immunisation with pandemic Influenza A(H1N1) 2009 vaccines, the Health Sciences Authority (HSA), Singapore, collaborated with the primary paediatric and women hospital in Singapore, KK Women’s and Children’s Hospital (KKH) to initiate an active, inpatient surveillance of AEFI with the H1N1 vaccines.¹ A sentinel site was established at KKH², to monitor the safety of the H1N1 vaccines both in children and pregnant women. The surveillance was subsequently expanded to include AEFI with common childhood vaccines.

Since the sentinel site started operations in November 2009, active surveillance has enhanced the detection of AEFI. From 2010 to 2014, HSA has received more than 180 reports every year from the sentinel site, which contributed for more than 80% of the total AEFI reports received in children below 18 years old or around 70% for all age groups. This was a significant increase from less than 50 reports on average per year for all age groups from 2005 to 2008, when there was only a passive surveillance system. With the close monitoring of AEFI at the sentinel site by a multidisciplinary team composed of paediatricians, nurses and public health physician at KKH, this active surveillance framework has proven

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to be an integral part of vaccine safety surveillance in Singapore. It has provided data for MOH Expert Committee on Immunisation (ECI) to better evaluate the risk-benefit ratio of specific vaccines in the local context and aids in public health policy assessment. Examples of safety signals detected by KKH and presented to ECI for deliberation include BCG-associated lymphadenitis\(^3\) and vertical transmission of hepatitis B infections despite vaccination.\(^4\)

In the case of the BCG-associated lymphadenitis, a thorough investigation into an outbreak of lymphadenitis with the BCG vaccine was made possible using data collected by the sentinel site. Our investigation had shown that the outbreak may have been linked to vaccine manufacturing challenges associated with BCG vaccine, which were subsequently addressed by the manufacturer.\(^5\) This further demonstrates the value of sentinel site in the close monitoring of AEFI as vaccine manufacturing is a complex biological process and a minor change in a manufacturing condition can greatly impact the quality of any vaccine, including vaccines that have been in use for the past decades.

The team has also recently investigated the safety of rotavirus vaccine in the context of intussusception, taking into consideration the risk benefit of a national rotavirus vaccination programme.\(^6\) We found an 8 fold increased risk of intussusception in the first week after receiving the first dose of RV1 (Rotarix™) in Singapore (which was a similar finding from other studies conducted in Americas and Australia). The risk benefit analysis estimated that a rotavirus vaccination programme with 90% coverage in Singapore could prevent about 70% of all rotavirus hospitalization, with a low risk of 1 excess intussusception hospitalization for about every 65,000 infants vaccinated and protected over a 5-year period. These findings provided real data to support recent WHO recommendations to remove the age restrictions on rotavirus vaccination of older infants as well as reassurance to providers working to implement rotavirus vaccination in geographical regions outside Americas and Australia on the safety profile of the vaccine.

Our active surveillance at the sentinel site, together with appropriate clinical advice, provides confidence for healthcare practitioners as well as patients and parents regarding suitability for repeat vaccinations. On a national level, continued support in the collection of local data to support the safety of the vaccines and close monitoring of AEFI is critical in ensuring public confidence in national vaccination programmes. We believe that such a system could be duplicated by overseas public health authorities working on vaccine safety regionally and globally, where capacity to perform post-market AEFI surveillance remains limited or non-existent. With potentially more new vaccines being introduced into the National Immunisation Schedule, active surveillance of AEFI plays an increasingly important role to provide continued evidence on the positive benefit/risk assessment of vaccines used in our country.
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