About this newsletter
Providing updates on GVSI activities

The GVSI Bulletin newsletter provides updates on the implementation of the Global Vaccine Safety Initiative (GVSI)\(^1\), 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\(^2\) which are summarized in a product portfolio.

To optimize collaborative activities, GVSI Bulletin\(^3\) aims to provide all stakeholders of the initiative with a practical overview of activities identified. Components of the portfolio and activities of GVSI stakeholders that match the eight objectives of the Global Vaccine Safety Blueprint and profiles of stakeholders are presented to increase visibility of actions and support synergies.

New CIOMS Working Group on Vaccine Safety
Developing collaboration mechanisms between the public and private sectors
Dr Christine Maure, Dr Patrick Zuber

The new CIOMS Working Group on Vaccine Safety has been established in 2013 to address one strategic objective of the Global Vaccine Safety Blueprint “To put in place systems for appropriate interaction between national governments, multilateral agencies, and manufacturers at national, regional and international levels.”

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The Group aims in particular at:

• Promoting a more efficient and rapid collection and exchange of information between national regulatory agencies, multilateral agencies and vaccine manufacturers.

• Developing and endorsing harmonized tools and methods for vaccine safety monitoring activities between national regulatory agencies, multilateral agencies and vaccine manufacturers.

• Proposing mechanisms for vaccine safety monitoring in difficult settings, i.e. those with minimal infrastructure.

The group is composed of representatives from regulatory and public health agencies, manufacturers, academia and technical agencies. It plans on meeting two times per year. During its second meeting on 18-19 September 2013 in Geneva, the working group consolidated the topics of interest identified during the first meeting. Several cross-sectorial teams were formed to develop those respective areas. The expected outcome of this working group is to produce a series of consensus publications.

Regional Update:
Africa Identifies Vaccine Safety as a Priority Area for 2014
Dr Bartholomew Dicky Akanmori, Dr Philipp Lambach

In June 2013, the Regional Office for Africa (AFRO) received the Final Report on the External Evaluation of the Regional Immunization Strategic Plan 2009-2013. This report recommends that a regional committee for reviewing adverse events following immunization (AEFI) be established and assist countries set up committees at national level, and to develop their own expertise. AFRO should implement the GVSI’s portfolio for Africa.

The committee will be a Working Group of the Taskforce on Immunization (TFI) which advises on vaccines and immunization in the region. With the support of the TFI AFRO will be able to implement the GVSI’s portfolio for Africa. To further support the implementation of the GVS Blueprint in countries of the region it has become necessary to support the development of Country Roadmaps for strengthening vaccine safety and pharmacovigilance. Selected francophone countries will meet to initiate this before the end of the year. Subsequently other groups of countries will also be supported to develop theirs, all in line with the Institutional Development Plans of their National regulatory Authorities (IDPs).

Because some issues related to adverse events are quite technical, a special committee – the Global Advisory Committee on Vaccine Safety (GACVS) – has been established since 1999 to address vaccine safety concerns of global importance. Increased access to vaccines, availability of new products and access to information resulted in an increased attention to vaccine safety in many AFR countries. In response, the Regional Office, with support from the Global Vaccine Safety Initiative plans to assist its member states in enhancing their vaccine safety systems, including building up local expertise through national experts committees. This would bring them into line with the GAVS recommendation to have in place a national committee with representation from a wide range of specialists relevant to reviewing AEFIs. In addition, a regional vaccine safety committee will be established in order to provide overall guidance in this capacity-building effort and serve as a regional technical reference.

Several AFR countries have already established AEFI review committees: Ghana, Ethiopia, South Africa, Senegal, Uganda, Tanzania, Mali, Burkina Faso, Nigeria, Mauritania and Benin. Uganda and Senegal also share individual case safety reports to the Global Programme for International Drug Monitoring. However, overall AEFI reporting
remains very low in most countries and a particular attention will be paid to facilitate the communication of vaccine safety concerns using current information technologies. With financial and technical support from key partners, national vaccine safety system development plans will be supported as a priority during 2014. It is expected that by the end of the biennium a regional pool of vaccine safety experts will be available to pursue the development of such national capacity and also address in a timely fashion along the lines proposed in the global vaccine safety Blueprint

AEFI Surveillance in Sri Lanka
A good model, but yet more to do
Dr Ananda Amarasinghe & Dr Madhava Ram Balakrishnan

In Sri Lanka, there has been significant progress in AEFI reporting and investigation since the establishment of a passive surveillance system for Adverse Events Following Immunization (AEFI) in mid 1990s. In 2012, as a part of the Global Vaccine Safety Initiative (GVSI), a study was carried out to evaluate the AEFI system in the country.

Fifty two (52) Medical Officer of Health (MOH) areas, two from each district (n=26) were selected into the study. Also, an immunization clinic from each selected MOH area was included in the study to describe AEFI reporting and record keeping at clinic level and, to describe AEFI related immunization service activities at the same level. AEFI registers and other relevant records too were reviewed to evaluate AEFI reporting and recording practices. Interviews of a sample of MOH and Public Health Midwives (PHM) were carried out to explore their knowledge on AEFI.

Only 51.1% cases have complete documentation in the Clinic AEFI Registers. AEFI status of previous vaccinations recorded in Child Health Development Records is 77%. The overall AEFI reporting in the country is 3.2 adverse events/1000 antigens administered. Most reports are from the northern part of the country (Figure). The highest rate of antigen specific AEFI was reported for DPwT vaccine (10.9/1000 doses administered), followed by Pentavalent vaccine (4.1/1000 doses administered). The reported AEFI rates by age group were 8.8/1000 doses of antigen administered for infants and 5.4/1000 for children aged over one year. Immunization safety practices adopted at clinics (screening, advices, and observation for immediate AEFI following immunization) and knowledge of MOH and PHM on AEFI is good.

With these observations, in 2013, Sri Lanka started piloting an indigenously developed Web Based Immunization Information System (WEBIIS) to minimize the gaps in its surveillance system.
Dr Ananda Amarasinghe (MD), has completed medical degree with honors, at Kharkov State Medical Institute, former USSR and Postgraduate studies in Community Medicine at the PGIM, Colombo. He has been trained in advanced Epidemiology at the New castle Upon Tyne University, UK, CDC Atlanta and National Institute of Epidemiology, Chennai, India.

Dr Amarasinghe is a consultant Epidemiologist at the Epidemiology Unit, Ministry of Health, Sri Lanka, since 2000. He is the leading technical advisor to introduce new vaccines and lead introduction of Hepatitis B and Penta-valent vaccines and the adoption of new health technologies including auto-disable syringes. He has developed guidelines for AEFI surveillance, Sentinel Site Surveillance, Immunization financing for the national immunization programme, Sri Lanka. He is the team leader of developing National Immunization Policy in the country. At present his main responsibility at the Epidemiology Unit is vaccine safety.

In 2008-2010, worked at the Pediatric Dengue Vaccine Initiative (PDVI), International Vaccine Institute (IVI), in Seoul, Korea, and was responsible for dengue vaccine development project activities in Asia.

Dr Amarasinghe is an adviser for several WHO Committees: the Global Advisory Committee on Vaccine Safety (GACVS), The Advisory Committee on Safety of Medicinal Products, SAGE working group on Japanese Encephalitis, TAG on dengue vaccine development. He has been a Short Term Consultant to WHO and has successfully undertaken numerous programmed projects, training activities, particularly in vaccine safety and introduction of new vaccines into the EPI in most of the WHO regions. He is the lead author of revised guidelines on Immunization Safety, published by WHO/WPRO. At present, he is assigned to develop WHO Global Manual on Immunization Safety.

He is the author or co-author of more than 30 peer reviewed publications.
Global Advisory Committee on Vaccine Safety (GACVS)\(^4\)

Report on Safety of Immunization during Pregnancy

Dr Philipp Lambach

At its meeting in December 2011, the Strategic Advisory Group of Experts (SAGE)\(^5\) asked GACVS to provide support to the review of current evidence on the safety of vaccinations in pregnant and lactating women. This request related to uncertainties about the safety of vaccination – whether intended or inadvertent – of pregnant women during mass vaccination campaigns. Such evidence would be particularly important in situations where manufacturers do not recommend the vaccination of pregnant women on solely precautionary grounds. However, evidence relating to this issue is limited. Clinical trials are not usually conducted among pregnant and lactating women prior to the licensure of vaccines. Experience from several countries suggests both a lack of available post-licensing data and a reluctance to include pregnant women in clinical trials. This in turn has limited the ability to make evidence-based decisions and provide optimal guidance for the use of vaccines in this population.

Vaccine-preventable infectious diseases are responsible for significant maternal, neonatal, and young infant morbidity and mortality. Immune alterations, thought to be a consequence of allowing the woman to tolerate the semi-allogeneic fetus, may interfere with the normal development of specific response to pathogens in the mother and fetus. These immunological changes may alter their susceptibility to certain infectious diseases.\(^6\) In addition, they may be at risk of more serious outcomes of infections. The immature adaptive immune systems of neonates and premature infants make them one of the most vulnerable age groups for morbidity and mortality due to infections.

Maternal immunization can protect the mother directly against vaccine-preventable infections, and provide a cocooning effect that can potentially protect the fetus. It can also provide further direct fetal/infant protection against infection via the transport of specific antibodies to the fetus prior to birth.

GACVS has evaluated the data on the safety of immunization of pregnant women for several inactivated and live attenuated vaccines. There is no evidence of adverse pregnancy outcomes from the vaccination of pregnant women with inactivated virus, bacterial vaccine, or toxoid. Therefore, pregnancy should not preclude women from immunization with these vaccines if medically indicated.

Live vaccines may pose a theoretical risk to the fetus. However, there is a substantial literature describing the safety of live-attenuated vaccines including monovalent rubella vaccines, combined measles mumps rubella vaccines, and oral polio vaccines. No significant adverse effects to the fetus following these live attenuated vaccines have been reported. Thus, the contraindication of MMR-containing vaccines is considered a purely precautionary measure. Inadvertent vaccination of pregnant women with MMR-containing vaccines is not considered an indication for termination of the pregnancy.

The benefits of vaccinating a pregnant woman generally outweigh the potential risks if she is at high risk of being exposed to a particular infection and the disease would pose a risk for her or her fetus/newborn, and if the vaccine is unlikely to cause harm. The use of selected vaccines in pregnancy is an important aspect of prenatal care, which not only improves maternal health but also benefits the neonate.

\(^4\) [http://www.who.int/vaccine_safety/committee/en/](http://www.who.int/vaccine_safety/committee/en/)


Vaccine Adverse Events Information Management System (VAEIMS)
An AEFI data collection and processing software for national use

Dr Ajit Pal Singh & Dr Madhava Ram Balakrishnan

For optimal vaccine safety monitoring and meaningful analysis of Adverse Event Following Immunization (AEFI) data, systematic and standard collection of critical parameters is essential. A limited number of variables are required to properly manage AEFI information. A WHO working group developed a core data set that was endorsed by the Global Advisory Committee on Vaccine Safety (GACVS) in June 2012. This data set includes 22 variables with 10 identified as critical. This simple structure provides countries with a harmonized data collection set that simplifies AEFI reporting and also allows for comparisons and pooling of essential information for action. The core variables are expected to ultimately ensure global standardization of data collection, analysis and interpretation. This will also promote global pooling of data and encourage signal detection in rare and extremely rare AEFI.

Currently, many countries in Asia and Africa lack the ability to create and maintain database for vaccine adverse events that is accessible to various stakeholders such as regulators, public health agencies and pharmacovigilance centers to collaborate on vaccine benefits and risks assessment. The creation of such a common Vaccine Safety database and it linkage to Vigibase (the global database) could generate useful information about the safety profile of vaccines in different parts of the world.

The Vaccine Adverse Events Information Management System (VAEIMS) is software that has been developed by IVI in technical collaboration with WHO to transfer quality AEFI data using the core variables from the periphery of a health care system, efficiently and effectively into a central database for processing and conversion of raw data to information for action. VAEIMS has been designed keeping in mind the diverse data collection, collation, transmission, analysis and feedback systems existing in different countries. It is tailor made to local conditions as a very user-friendly innovative software application that is able provide quick and reliable information for decision makers at all levels within a country, and if necessary shared with a global audience.

Sri Lanka expressed interest in piloting VAEIMS and incorporating some of its features into its own indigenously developed Web Based Immunization Information System (WEBIIS) which is currently in a piloting stage. When VAEIMS was demonstrated in Sri Lanka by a team from IVI/WHO in July, there was keen interest in the Ministry of Health (MoH). This was mainly because VAEIMS was tailor-made to the Sri Lanka context and ready to be deployed immediately with minimum training. The country decided that during the interim period until WEBIIS becomes full-fledged, VAEIMS will be used at the national level to pilot national data entry, data analysis and conversion of information for action. VAEIMS will also be piloted to transfer data from the national database to Vigibase (the global database). The potential for WEBIIS being made E2B compatible soon for global sharing of AEFI data was a feature that was considered important by the MoH. Sri Lanka is the first country to test beta-version of VAEMIS and pilot testing commenced in August 2013.

Encouraged by the experience from Sri Lanka, and based on feedback obtained from several countries, IVI have initiated work on a web based version of VAEIMS that will also be available to all countries free of cost. The features of web based VAEIMS include “live” data upload, storage and transfer. It also includes analytical tools to quickly analyse AEFI data from within a country and compare it to other reports across globe. A pilot version of Web based VAEIMS will be demonstrated to the participants at the GVSI meeting in New Delhi in November. IVI

http://www.who.int/wer/2012/wer8730.pdf
has also initiated discussions with Uppsala Monitoring Centre (UMC) to harmonise the software in order to integrate data from VAEIMS with Vigibase. At a later phase of development of VAEIMS, the prospects of collecting data from the field using smartphones and regular mobiles will also be explored.

Experience of a VAEIMS user…

In August 2013, Sri Lanka became the first country to test the beta-version of VAEMIS. We used it at national level to pilot data entry, data analysis and conversion of information for action. We are now working on incorporating some of its features into our own indigenously developed Web Based Immunization Information System (WEBIIS). We hope that through piloting VAEIMS, Sri Lanka would pioneer the transfer of AEFI data from the national database to Vigibase, the global database. We find VAEMIS user friendly and comprehensive to capture a wide range of information needed for AEFI surveillance. We acknowledge the technical and professional support of the International Vaccine Institute and WHO for developing this customized to our requirements. Dr Ananda Amarasinghe, Epidemiology Unit, Ministry of Health, Sri Lanka.