



**Conclusions and Recommendations from the Fourteenth Meeting of the WHO  
Advisory Committee on Safety of Medicinal Products (ACSoMP)  
Geneva, Switzerland  
25 - 26 April 2017**

*The WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) has been constituted to provide advice on pharmacovigilance (PV) policy and issues related to the safety and effectiveness of medicinal products. The conclusions and recommendations from the Fourteenth meeting of ACSoMP are presented below.*

**WHO Medicines Safety & Vigilance (SAV/Rx) Updates:**

*2020 Strategy Focus:* The goals and core strategy of SAV/Rx for 2017-2018 are very much aligned with its overall 2020 strategy with the prevailing theme of “no country left behind: worldwide pharmacovigilance for safer medicines, safer patients”. The 2020 strategy is focused on building comprehensive, sustainable, resultsdriven pharmacovigilance (PV) systems. This strategy focuses on developing the right infrastructure, ensuring that good quality data are collected, analysed, used for decision-making and appropriately shared with public health programmes.

*Collaboration:* Much emphasis has been placed on encouraging global collaboration through platforms such as the WHO Annual Meeting of National PV Centres and knowledge-sharing in PV through the WHO Pharmaceuticals Newsletter and other publications. The bulk of this effort is focused on expanding regional and local networks and partnerships. WHO SAV/Rx continues to take a lead role in convening expert committees, for example, ACSoMP or the International Working Group on Drug Statistics Methodology. Country-level support is focused on the development of tools, approaches and norms for low and middle income countries (LMIC), supporting national assessments, providing technical support, training through interactive workshops, and in providing surveillance and risk management support.

*Implementation Approach:* The current process, which is being reviewed, is as follows:

1. At the WHO National PV Centres' Annual Meeting, feedback and recommendations on the plans and strategies for the WHO Programme for International Drug Monitoring (PIDM) are sought from Member States.
2. The WHO HQ SAV/Rx team and WHO Collaborating Centres (CCs) then integrate feedback and recommendations into work-plans.
3. Approval and advice are sought from expert committees on annual plans.
4. Grants are sought from donors to ensure sustainable resourcing for PV work.

5. Deliverables and results are shared with Member States at the WHO Annual Meeting of National PV Centres and through publications and presentations at other conferences and key meetings.

*2017 Goals:* Key SAV/Rx objectives for the year include further initiating new members into the WHO PIDM, aligning PV indicators into a Global Benchmarking Tool (GBT) for National Regulatory Agencies (NRA), assess country 'PV readiness' to support the risk evaluation of emerging products in new markets, drawing institutional development plans to address gaps in PV, supporting the implementation of new technologies, e.g. Mobile adverse events (AE) and adverse drug reaction (ADR) Reporting App in collaboration with the IMI WEBRADR project in a few Member States, providing continued support to public health programmes (PHP), delivering training on regulatory aspects, e.g. PV inspection workshops and MedDRA, as well as continuing work to encourage collaboration and knowledge-sharing among Member States.

*PV Patient & HCP Engagement:* More work needs to be conducted by the PV community to increase engagement with the broader health-care community. Further discussion on the right type and the amount of information to provide to patients is needed to ensure the prevention and management of ADRs. It is very important that messages are tailored to the appropriate stakeholder; the current approach adopted for communication in the labelling of medicines needs some improvement, e.g. with 'boxed' warnings in the US, where prescription habits vary greatly; in some cases, this results in a complete lack of a medicine's use rather than signifying controlled use.

### **WHO Collaborating Centres for Pharmacovigilance:**

WHO SAV works with 4 Collaborating Centres to advance pharmacovigilance (PV) in countries. These are, in the order in which they were established, the WHO Collaborating Centre for: International Drug Monitoring, Sweden; Advocacy and Training in Pharmacovigilance, Ghana; Strengthening Pharmacovigilance Practices, Morocco, and Pharmacovigilance in Education and Patient Reporting, the Netherlands.

The 4 WHOCCs were invited, as observers, to the 14th ACSoMP Meeting. The Committee had the following feedback to all 4 Centres:

*On-line Training:* Much of the training sessions outlined by the centres is conducted in a face-to-face setting. It was suggested this may limit outreach, and that supplementary online training programs that can be prerecorded with standard Q&As should be leveraged for the more standard work streams. It was noted that the UMC has already invested in building an online platform for training and numerous training videos can be found on the UMC YouTube channel. In addition, the British Pharmacological Society (BPS) has created an online assessment platform which includes questions on PV and PV communication that the General Medical Council (GMC) has made mandatory for prescribers. However, one of the challenges of using online technologies is ensuring its maintenance.

*Harmonizing Training:* It was also recommended that the training carried out by centres should leverage alternate global resources and more importantly should be coordinated to reduce duplication, to ensure harmonized content and maintenance of the curricula. In addition other available course material and resources should be leveraged in training, e.g. the International Society of Pharmacovigilance (ISOP) course material, the WHO-ISoP PV core curriculum, the

WHO CC Accra's PV Toolkit, and resources made available by the UMC on their website and through social media channels. A more challenging aspect of training is that universities will only add PV to their curricula if examiners are willing to test students on the subject; a majority of PV training at universities is run through practical workshops supporting more mature students to qualify for regulatory roles.

*The Committee recommended that all PV training activities across all centres should be mapped and included in the WHO repository of training courses and materials.*

*PV Career Path:* It was remarked that students who join relevant doctoral programmes have more success in developing a career path for themselves in PV, and this subsequently results in more sustainable engagement in PV. To encourage participation and ensure long-term engagement, the vocation prospects for trained individuals must be considered when creating training opportunities. The UMC is in the early stages of setting up a collaboration between UMC and the Consortium for Advanced Research Training in Africa (CARTA) which will offer PhD stipends for PV in Africa.

*Active surveillance:* WHO/SAV has published a series of handbooks in active surveillance approaches. All 4 Collaborating Centres have supported WHO in advancing these approaches in countries. ACSOMP advised that an overview and a guide on active surveillance best practices and applications will be developed by WHO, building on experience to date, emphasizing what currently works and what doesn't. The Committee noted that the new CIOMS Guide to Active Vaccine Safety Surveillance should be leveraged when developing such a best practice guidance, to help with the broader goal of harmonizing PV efforts in vaccines and medicines.

### **WHO-BMGF Smart Safety Surveillance/ Project Triple-S: Optimizing post-marketing surveillance of priority medicines and vaccines in low and middle-income countries**

Access to medicines and vaccines in low and middle-income countries (LMIC) has improved in the last few years. But there has not been a proportionate improvement in pharmacovigilance. This is of particular concern given the number of products in the development pipeline that will be launched exclusively in LMIC or simultaneously, in both LMIC and in High Income Countries (HIC), with little experience from advanced settings for LMICs to rely upon.

LMIC must, therefore, be supported to introduce new products, to identify, assess, and adequately manage the risks associated with these products. In September 2016, the WHO Safety and Vigilance (SAV) team signed an agreement with the Bill and Melinda Gates Foundation (BMGF) to manage a project to optimise post-marketing surveillance of priority medicines and vaccines in LMIC. The overriding project goal is to ensure timely and adequate ADR reporting and review, and action on ADR data in LMIC where priority Global Health products will be introduced. This will be achieved by implementing smart safety surveillance systems for three pilot products (two medicines and one vaccine) in a few pilot countries of varying PV readiness by:

1. Strengthening the functionality of current PV systems
2. Building capacity to analyse safety data
3. Improving capacity to use PV data for regulatory decision-making
4. Supporting the collaboration between public health programmes and the PV community

Project Triple-S should ideally implement a “launch and leave” system, which enables local stakeholders to manage safety monitoring for all products in the long-term. It is critical that the project’s PV efforts are sustained beyond the pilot, and so much advocacy work has been conducted since 2015 to engage external partners who can support the project by providing technical expertise, financial investment or coordination capabilities. To date, three key external partner meetings have been held; multiple partners have already provided their commitment to support the pilot. In addition, joint media communications from the BMGF and WHO have been published to generate interest in PV and in the pilot.

*Pilot products:* Criteria to help choose the pilot products were created and tested with external stakeholders and WHO disease-control programmes. The criteria focused on emerging LMIC launches, product approval type, prioritising on those with accelerated/conditional approval, the nature of adverse events identified in the clinical development, public health impact, and exclusive target populations. The criteria used and a proposed shortlist of medicinal products were fully endorsed by the ACSoMP committee. It was further recommended that the criteria used to choose the three pilot products should be shared in a joint WHO and BMGF communique or publication.

*Normative:* WHO/SAV established a working group to develop an up-to-date global set of indicators to assess LMIC for PV readiness within the context of Project Triple-S. These indicators are drawn from the WHO PV Indicators published in 2015 and other recognized global PV and assessment tools. The indicators were chosen for their ability to capture the core PV development aspects embedded in Project Triple-S encompassing policy, law and regulation, system structure and stakeholder coordination, signal generation and data management, capacity for risk assessment and risk management, communication and resourcing. These selected indicators will be used to measure the in-place PV infrastructure, competence, capacity and gaps in LMIC, to study their capacity to assess and act on the benefit-harm information of the Pilot products in Project Triple-S.

*Country Assessments:* Project Triple-S’ success will depend on the target countries’ ability to adopt and implement PV. An assessment of the potential target countries, and of relevant local stakeholders will be critical to ensure success. It was recommended that countries with PV systems of varying maturity be included in the pilot phase, to help understand the types of countries and systems that will benefit the most from external support. The pilot phase will include four to six countries. The pilot products will be used to build or enhance PV systems/capacity, while the processes and systems will be used to strengthen the data and information on these products.

*End-to-end PV for policy decisions:* ACSoMP members noted that Project Triple-S will be a “game-changer” in the PV space, in particular with its focus on building an end-to-end PV system which will very likely impact future product launches, but the entire safety data set that can instigate policy decision-making will likely not be available in Project Triple-S’ three-year timeframe. Nonetheless, impact and success can be measured through an assessment of the number of reports, their quality, and the ability of LMIC to analyse and use the data for decisions.

*Risk Management Plans (RMP):* It was noted that industry often pays little attention to local risk management plan requirements in developing markets. Often this is because many NRA do not

request this information from industry; regulatory requirements for PV are inconsistent and minimal in many LMIC, many NRAs simply request periodic safety update reports. RMP will be an integral part of the PV protocol in Project Triple-S; a spectrum of training activities has been embedded, including establishing a vigilance framework, ensuring that there is regulatory capacity for managing new submissions, close engagement with industry, outlining a risk management plan as part of a drug or vaccine's application process and ensuring the feasibility of RMP in local settings.

*Collaboration between medicines and vaccines:* The importance of close collaboration and aligned evaluation of both medicines and vaccines work is well recognized within Project Triple-S. The WHO teams are equally involved, and representatives from both ACSoMP and the Global Advisory Committee on Vaccine safety (GAVCS) will converge to form the Project Advisory Group (PAG), to ensure good alignment between medicinal and vaccines vigilance.

*Advisory Input:* WHO/SAV proposed inviting the co-chairs of ACSoMP as lead members of Project Triple-S Advisory Group, with other WHO Expert Committee members brought in as needed, for scientific guidance and oversight of specific project activities. This approach was endorsed by the members of ACSoMP. The ACSoMP fully endorsed Project Triple-S and the Committee co-chairs agreed to provide expert input as part of the Project Advisory Group (PAG).

*Pharmacovigilance Success Stories:* A key goal of Project Triple-S is to strengthen PV systems and practices. Although not all LMIC have resources to implement a comprehensive end-to-end PV system, this is the long-term goal. Understanding any individual successes in one or more key PV aspects in LMIC is critical to ensure optimal approaches to PV.

WHO/SAV undertook a review of LMIC that have demonstrated success in at least one specific PV function, to understand the reasons for the success and use the lessons learnt to develop a 'best practice' guidance to support PV development and implementation in LMIC. Six countries were included in the study that used a structured interview to gain insight on a specific PV topic per country, e.g. strategies that underpin the integration of PV in public health programmes (PHP); how to build a resilient PV infrastructure; introducing electronic reporting, etc. Insights were then analysed to identify interventions and "good working" practices that may lead to success. ACSoMP members agreed that this work is of particular importance because agencies that fund PV frequently request a measure of success in PV. It was recommended that the final summary and guideline capture the impact of PV in each country, the perceived challenges and successes, and finally, the potential consequences of not having a PV system in place.

The Committee recommended that the final output be published and presented at the WHO Annual Meeting of National PV Centres in 2017.

### **CIOMS update:**

Key CIOMS developments that are of interest to ACSoMP, such as CIOMS Working Group on Drug Induced Liver Injury, were briefly highlighted. In addition to the CIOMS Guide to Active Vaccine Safety Surveillance, a draft on safety communication in vaccines, created in collaboration with WHO and, ISO, is in the pipeline. The committee noted that WHO SAV will work closely with CIOMS to develop this protocol and will reach out to WHO CCs to pressure-test and refine the outcome.

## **Integration of PV with broader initiatives – “Coalition of Interested Partners”:**

As an increasing number of individual organizations have become involved in Strengthening Regulatory Systems, the WHO is in the process of establishing a ‘Coalition of Interested Partners’ or CIP framework to achieve better coordination, efficiency, outcomes and sustainability of these efforts in the same target Member States (MS) or region, to achieve better public health outcomes. The core objective is to create a more coordinated approach by defining roles and responsibilities amongst all stakeholders, share planned activities, reduce redundancies and identify opportunities for complementary action, and create a single development plan for countries involving all stakeholders.

The WHO is well positioned to lead this coordination effort by virtue of its mandate and experience. In general there has been a positive move towards regional collaboration in regulatory systems strengthening (RSS) as showcased by the African Medicines Regulatory Harmonization (AMRH) initiative, RSS discussions in South East Asia on malaria elimination, the “Call for Action” at the first Intergovernmental Authority for Development (IGAD) regulatory conference and the PV stakeholders meeting that took place in Rabat this year. Although regional meetings show a positive reception to CIP, it’s critical that individual Member States agree to the coalition approach.

No additional funding will be sought through this initiative; current donor relationships will be maintained. The Project Triple-S will also be used as a pathfinder pilot, establishing a more collaborative approach to PV knowledge-sharing, capacity building and implementation approaches, and reducing redundancies.

In December 2015, the concept was first presented at the second international consultation on the WHO global regulatory authority benchmarking tool. In 2016, the CIP framework approach was further developed with a meeting held at the Bill and Melinda Gates Foundation (BMGF) offices in Washington DC, and then again at a pre-International Conference of Drug Regulatory Authorities (ICDRA) meeting in Cape Town. The first pilot on the CIP approach was launched in Dhaka, Bangladesh, in May 2016; this is on-going. All relevant services and target countries are currently being mapped and a taskforce is being formed to lead development and implementation.

The committee congratulated the team on this important effort, fully endorsed the approach and agreed that Project Triple-S should take full advantage of the CIP approach. The committee requested that the proceedings of the CIP taskforce are published and recommended that a small PV working group be established to support this initiative.

## **The cardiotoxicity of antimalarials. A report from the WHO Evidence Review Group:**

The cardiotoxicity of antimalarial medicines has received renewed interest in recent years following the ‘Thorough QT’ assessment of the dihydroartemisinin-piperaquine formulation approved by the European Medicines Agency, which showed evidence of QT interval prolongation. Piperaquine is a bisquinoline antimalarial that is structurally related to chloroquine. Many drugs among the quinoline and structurally related medicines affect myocardial depolarization and repolarization. WHO currently recommends the artemisinin-

based combination treatment dihydroartemisinin-piperaquine for the treatment of uncomplicated malaria. This treatment is being considered alongside other antimalarial medicines for preventive therapy and mass drug administration.

To inform WHO recommendations, a group of experts met in October 2016 to review evidence on the cardiotoxicity risk of quinoline antimalarials and structurally-related medicines in people with and without clinical malaria. The following recommendations were proposed by the WHO Evidence Review Group (ERG) for consideration by the WHO Malaria Policy Advisory Committee and the WHO Advisory Committee on Safety of Medicinal Products:

1. Apart from halofantrine, antimalarial medicines that prolong the QT/QTc interval, such as quinine, chloroquine, artesunate-amodiaquine and dihydroartemisinin-piperaquine, have been associated with a low risk of cardiotoxicity.
2. Drug-induced QT/QTc interval prolongation is a surrogate indicator for increased risk of drug-induced torsade de pointes (TdP), a potentially lethal polymorphic ventricular tachycardia. Risk factors for drug-induced QT/QTc prolongation include female gender, structural heart disease, genetic defects of cardiac ion channels, electrolyte disturbances, bradycardia, hepatic impairment, and concomitant use of medications that prolong the QT/QTc interval or increase drug levels. Antimalarial medicines that can induce QT/QTc interval prolongation should be used with caution in individuals with known heart disease, a family history of sudden unexplained death consistent with cardiac arrhythmias, or who are already taking medicines that can prolong the QT/QTc interval.
3. Dihydroartemisinin-piperaquine and artemether-lumefantrine have been the most intensively studied antimalarial drugs. No sudden deaths have been attributed to cardiotoxicity following artemetherlumefantrine. However, among ~200 000 treated individuals with close follow-up, one possible sudden cardiac death associated with dihydroartemisinin-piperaquine was reported. This finding is consistent with the risk of fatal cardiotoxicity associated with other QT/QTc-prolonging medicines in current use.
4. Review of pharmacovigilance, clinical and preclinical data, along with preliminary results of PK/PD modelling, reveals no evidence of a significant difference in the risks of cardiotoxicity following exposure to piperaquine, chloroquine or amodiaquine at the current recommended doses. The risks of cardiotoxicity of piperaquine-containing medicines are probably similar for healthy volunteers and malaria patients.
5. Drug-induced TdP and life-threatening ventricular tachyarrhythmias are very rare events, and there are no simple screening tests to identify people at risk. Further studies are needed to identify genetic polymorphisms and other pre-existing conditions that may contribute to the risk of drug-induced cardiotoxicity. More evidence on the potential cardiotoxicity of chloroquine, amodiaquine and primaquine is needed.

The ACSoMP committee fully endorsed this comprehensive review and recommended that the findings be published in an open access journal. ACSoMP members noted that a simple risk minimization algorithm (exclusion criteria), that can be used by physicians in case management, should be developed by the WHO Global Malaria Programme in consultation with ACSoMP. A further recommendation was made that language in patient and physician information packages is carefully reviewed so as not to over-amplify the risks of cardiotoxicity

## **Safety Monitoring in Seasonal Malaria Chemoprevention (SMC) in the Sahel region:**

SMC is defined as “the intermittent administration of full treatment courses of an antimalarial medicine during the malaria season, with the objective of maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk, to prevent malaria. SMC is recommended in areas of high seasonal malaria transmission throughout the Sahel sub-region. Preventive treatment composed of sulfadoxine–pyrimethamine plus amodiaquine should be given to children aged 3–59 months at monthly intervals for 4 months, (provided both drugs retain sufficient antimalarial efficacy). Twelve African countries have included SMC since 2013. By 2016 the drugs had been administered to 16 million children.

Pharmacovigilance is being integrated into the SMC programme to detect and report all adverse events (AEs) related to SMC medicines with a focus on serious reactions, to define the safety profile of the drugs in SMC, and to strengthen PV systems in target countries. It started with a situational analysis that highlighted weaknesses in the Safety Monitoring Systems, and the training required for PV and malaria programme staff. Workshops were then conducted to strengthen PV country expertise, comprehensive support was provided to ensure effective implementation of safety monitoring, with a safety committee to review the outputs.

In general not all SMC ADR data seem to get reported to VigiBase, the WHO global Individual Case safety Reports (ICSR) database. The Reporting frequency seems to be a bit higher for phone (SMS)-based reporting than reporting through Cohort Event Monitoring (CEM), while both SMS and CEM reporting were higher than through spontaneous reporting systems. Due to the high frequency of vomiting, a risk management algorithm was created to help HCPs manage post-drug administration vomiting. There was some concern that the serious ADRs were reported only through emails, when requested, and not routinely to VigiBase. An assessment needs to be conducted on a larger scale to understand if this is a larger problem or specific to SMC. In addition, the current systems (VigiFlow) and practices of reporting to VigiBase must be assessed further to understand any additional reasons for the under-reporting.

Longer-term training and funds for the national PV department are essential to sustain and apply what was learned. The benefit of SMC can be quantified through the malaria surveillance systems. It showed 40-60% reduction in malaria cases in this vulnerable population. It was noted that the benefit-risk profile of SMC is positive and ACSoMP endorsed the activities undertaken so far to support the safe implementation of SMC.

## **Pharmacovigilance of TB Medicines :**

The goal of this session was to update ACSoMP committee on safety data on bedaquiline.

USFDA: There were fewer than 100 cases of multi-drug resistant TB (MDR TB) in the US in 2015. Bedaquiline is designated an orphan drug and in 2012 received accelerated approval based on surrogate data (time to sputum culture conversion over 24 weeks) with a boxed warning for two safety issues: increased mortality and QT prolongation. Approval was conditional based on seven post-marketing requirements and two post marketing commitments focused on registry formation and additional clinical data collection. Bedaquiline is not widely used in the US; to



date, the USFDA has not identified any important new safety signals, and subsequently, only limited label changes and safety precautions have been added since approval.

EMA: In Europe, bedaquiline was authorized by the EMA in 2013. Orphan drug designation was also assigned to bedaquiline and conditional approval was granted requiring additional monitoring efforts. Safety evaluation based on spontaneous reports is challenging because it is difficult to isolate individual effects of the drug on a patient due to severe comorbidities, concomitant medications and previously failed TB treatments. The RMP was important to identify risks including QT prolongation and increased transaminases. A confirmatory Phase III trial (STREAM) was requested in addition to an MDR registry, but they have both been slow to recruit subjects.

India: Bedaquiline was made available in India for 'compassionate, named patient use' before it was approved in May 2015 under the conditional access program, to be made available through the Revised National Tuberculosis Programme (RNTCP). Guidelines for use were approved in November 2015. A detailed procedure for recording and reporting ADRs was established and the Programmatic Management of Drug Resistant Tuberculosis (PMDT) guidelines were modified to include bedaquiline-specific information. In addition, patient information booklets, consent forms, cohort event monitoring forms and suspected ADR forms were developed.

A software bridge allows the seamless transfer of PV data between the TB programme database and the National PV database. A data safety committee has been set-up to assess the benefit-harm profile, and recommend regulatory action, if required. Regular meetings and health worker training workshops have taken place since 2016. Guidelines have been developed to support bedaquiline use, data entry and to emphasize the importance of pharmacovigilance.

389 patients have been enrolled so far. 155 ADRs have been reported; commonly reported ADRs include nausea, vomiting, anaemia, alanine aminotransferase (ALT) increase, acne, T-wave inversion, QT prolongation, lipase increase, abdominal pain and hypotension. In view of the potential safety benefit and unmet need, the Data & Safety Monitoring Committee (DSMC) has recommended the scale-up of access to all TB-sites capable of implementing the conditional approval protocol.

The Committee recommended that, given the scale-up of treatment, safety data from US FDA and EMA be shared with India. A pilot assessment of the ease and efficiency of collecting safety information from global regulatory sources should be conducted. The response time and quality of information provided should also be assessed. The Committee also noted that the experience from India would be useful in implementing data linkages between public health programmes and National PV databases in other countries.

### **Global Programme to Eliminate Lymphatic Filariasis (GPELF) – Alternative Mass Drug Administration Strategies:**

Lymphatic Filariasis (LF) is endemic in 73 countries with 946 million at risk of infection. The GPELF was launched in 2000 to stop transmission through Mass Drug Administration (MDA) and to reduce suffering and improvement of quality of life, through morbidity management and disability prevention (MMDP). MDA involves a combined dose of 2 medicines given annually to

an entire at-risk population in the following way: albendazole (400 mg) together with either ivermectin (150–200 mcg/kg) or with diethylcarbamazine citrate (DEC) (6 mg/kg). The MDA strategy takes time, mapping takes longer than 5 years typically and post-MDA surveillance can run for greater than 4 years.

Currently, 28 countries are not on track to achieving elimination. Alternative strategies are needed to reduce the time required to interrupt transmission. The new WHO guidelines (under development) will include a review of a new triple combination option of albendazole, ivermectin and diethylcarbamazine and an increased frequency of current MDA combinations compared to the current annual regimens. To date, efficacy, measured by a reduction in microfilaria levels (Mf) of the new triple combination therapy shows excellent results.

In the 'current' MDA strategy (that is, not triple combination therapy), observed adverse events (AEs) are more common in highly infected patients and areas of high endemicity, most frequent after the first MDA round, with a reduction after each round of treatment, and is more serious with filarial co-infections. This is thought to be due to the overall stress on the immune system in clearing MF. MF levels are lower in subsequent annual treatments during MDA. ACSoMP members have been providing feedback on safety monitoring and related -issues and can provide additional input before final submission of the new WHO GPELF guideline.

### **Pharmacovigilance Curriculum for Undergraduate Programmes in Universities:**

In collaboration with SAV/Rx, the WHO CC in Lareb is developing an undergraduate pharmacovigilance curriculum, to ensure that future health-care professionals are well equipped to manage ADRs and to improve patient safety in the long-term. The curriculum should enable the student to:

1. Understand the importance of pharmacovigilance in the context of pharmacotherapy
2. Prevent ADRs when possible
3. Recognize ADRs when they occur
4. Respond to ADRs (management, including treatment of ADRs)
5. Report an ADR

In order to develop these competencies, the student needs to have knowledge of clinical pharmacology, including pharmacokinetics and pharmacogenetics, pharmacotherapy, pathophysiology, the basics of drug development and registration, and the role of searching for and interpreting scientific literature. ACSoMP recommended that other than the core principles mentioned, communication of safety data and the ability to explain an ADR or AE should also be included. The Committee endorsed the framework outlined and recommended that the curriculum, when developed, should be published.

### **Measuring the Impact of Pharmacovigilance Activities:**

Throughout ACSoMP 2017, much discussion centred on measuring the impact of PV. The approach used by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) was outlined. As PV teams work through the risk management cycle, it's important to understand how well they are operating, how effective they are, and if they can do better.

The PRAC strategy on measuring PV activities was adopted in January 2016, and includes an evaluation of processes, e.g. signal detection, risk minimization, product-related risk minimization activity, stakeholder engagement and the identification or development of methods. A pilot was carried out by PRAC in 2016 to test the integration and prioritization of measuring PV impact in regulatory practice. A workshop on measuring the impact of PV was then carried out.

Recommendations from the workshop are to make use of robust science, ensure transparency and clarity of concepts, make use of innovative technologies, ensure prioritization into public health criteria, ensure there is systematic and routine data collection for all processes, leverage a multi-stakeholder collaboration, including patients and HCPs. Going forward, PRAC will team up with the European Network of Centres for Pharmacovigilance and Pharmacoepidemiology (ENCePP), patients, HCPs, and industry to develop this further. In addition, two studies initiated in April 2017 on diclofenac and hydroxyzine will be used to measure the success of PV implementation.