The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action:

Stakeholder Forum Report

Monday 21 September 2015

Royal Society of Medicine, London, UK

SCOPE Stakeholder Forum

On Monday, September 21 2015, 50 delegates from across the European Union (EU) met at the Royal Society of Medicine in London to participate in a Stakeholder Forum for the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action. The project was in its 23nd month, with 13 months remaining.

The aim of SCOPE is to improve the capabilities of medicines regulators in operating to the new pharmacovigilance (PV) legislation in all EU Member States (MSs). The forum reiterated this purpose and drive with SCOPE Work Package Leaders (WPLs) providing updates on the progress achieved so far in the project.

Organised by the Medicines and Healthcare Products Regulatory Agency (MHRA, UK) who are the coordinators of SCOPE, the Stakeholder Forum comprised of four sessions. Dr June Raine, Chair of the Pharmacovigilance Risk Assessment Committee (PRAC) and Director of the Vigilance and Risk Management of Medicines division at the MHRA opened the day. The attendees were welcomed and the aims for the day were outlined, namely to share, test, and enthuse attendees in helping deliver the Joint Action objectives.

Session I - An Overview of Progress in SCOPE

1. A view from the European Commission - Helen Lee, DG SANTE

Representing the Directorate General for Health and Food Safety (DG SANTE), Helen Lee outlined the characteristics of Joint Actions and focused on the impact and sustainability of SCOPE. Helen Lee explained that the European Commission (EC) Joint Actions are specific funding instruments under the EU health programme, which have clear EU added value and are co-financed by MSs. It was noted that that the main objectives of SCOPE are to facilitate collaboration among the MSs, and support work on a national level. The challenges for MSs and PRAC were highlighted, including the numerous PV procedures and activities, as well as timelines for assessment procedures. With the increased pressure on MSs, SCOPE aims to identify and promote best practices across the network to improve the quality of PV outputs, build capacity, and help MSs to achieve greater consistency. Helen Lee emphasised that SCOPE is expected to add a significant value to the PV network.

The key challenge is to ensure uptake and use of SCOPE deliverables. Helen Lee explained that the Joint Action will only impact PV practice if the tools developed are actually used by the primary target groups. The outputs of the project should also increase awareness of healthcare professionals (HCPs) and patients. The biggest challenges ahead are to ensure the delivery of adequate and appropriate training materials, alongside links to other activities and stakeholder initiatives within the network.

Discussion/Questions

An explanation of the relationship between the EC and the Consumers, Health, Agriculture and Food Executive Agency (CHAFEA) was requested so that participants could understand

the roles in terms of a Joint Action. The EC is responsible for the policy, and calls for projects and actions under the health programme. CHAFEA is the executive agency of the EC, established to manage EU projects and is responsible for the finances, support, and day to day management of projects.

A question was posed about the long term plans of SCOPE, and how National Competent Authorities (NCAs) could be expected to continue this collaboration. It was recognised that MSs had different capabilities at the time of implementation of the PV legislation. The Joint Action will help to bring MSs to the same level, which is considered a difficult achievement; however, SCOPE is a starting platform. All MSs must take a similar approach to reduce risks for patients. Harmonisation cannot be achieved by SCOPE alone, however, the project will help facilitate a common approach to PV at the EU level.

2. Progress in SCOPE - Mick Foy, MHRA

Mick Foy, representing the MHRA as Project Executive gave a summary of the progress achieved by SCOPE. Mick Foy informed delegates that 24 face-to-face meetings, and 80 teleconferences (TCs) had taken place since the start of the project. SCOPE Partners logged 4453 days of work, and responded to 764 questions posed in the SCOPE surveys. A summary of the deliverables achieved since the beginning of the project was presented, including technical, management and reporting milestones. The governance structure of the project was shown with different strategic, executive and implementation levels used to ensure a coordinated and cohesive network. Mick Foy gave thanks to WPLs – the National Authority of Medicines and Health Products (INFARMED, PT), Agency for medicinal products and medical devices Croatia (HALMED,HR), Medicines Evaluation Board (MEB, NL), Spanish Agency for Medicines and Health Products (AEMPS, ES), National Institute of Pharmacy (OGYEI, HU), and the Italian Medicines Agency (AIFA, IT).

Mick Foy highlighted that SCOPE priorities are to deliver the set of objectives on target, on time and on budget. The Work Package (WP) meetings have been a mechanism to facilitate coordination, and ensuring flexibility to remain current.

Brief details of the risk register were covered and these risks were emphasised: staff availability, timesheet difficulties, and resources. The SCOPE website has been regularly updated to keep all stakeholders up-to-date with progress. A calendar available on the SCOPE website lists all SCOPE events including TCs and face-to-face meetings, allowing interested parties to ask questions about meetings, and progress made so far.

Mick Foy outlined the coordination, communication, and dissemination responsibilities of SCOPE's horizontal WPs. As the coordinator, the MHRA's focus has been on managing progress and quality, supporting partners to achieve success, in order to ensure that SCOPE objectives are delivered.

The role of the General Advisory Board (GAB) was also presented. The board has been responsible for providing strategic advice on the project, including progress, risks, finances, quality, sustainability, and horizon scanning. It is formed of seven members who were collectively chosen by participants for their individual expertise, as well as one representative from each WP. The GAB have been providing a wider view of SCOPE objectives both within the EU network and beyond.

Mick Foy outlined SCOPE's financial systems process, covering both how partners have been receiving pre-financing payments, as well as the administrative information required. The importance of submitting all financial documents (timesheets, expenses claims) was highlighted as staff efforts recorded on timesheets allow for consolidation of spending and recalculation of contributions, prior to the next pre-financing payments. Two anonymised examples of budget spending were presented, where each graph presented a partner's (i.e. Topic Lead or WPL) pre-financing with predicted spend, alongside the actual WP spend, across the SCOPE period. In the example presented for an active SCOPE partner, the predicted and actual budget trends were in relative agreement. However, for a non-active partner, the predicted and actual budgets were largely different. Mick Foy encouraged all partners to bridge the gap between the actual spend and predicted budget by contributing to the review of SCOPE reports.

Overall SCOPE was to be allocated six pre-refinancing payments. It was highlighted that CHAFEA were currently reviewing the 18 month technical project report and that the next pre-financing payment would be transferred to all partners following approval of the report.

SCOPE has been reporting on a regular basis to CHAFEA through interim and technical reports, in addition to meetings at the European Medicines Agency (EMA), Pharmacovigilance Implementation Group (PIG), European Risk Management Facilitation Group, Heads of Medicines Agency (HMA) and Informal PRAC.

The project's year ahead will focus on delivery of guidance documents, toolkits, training and workshops.

Discussion/Questions

A question was posed around subcontracting within the SCOPE project. Areas of subcontracting were identified for products that could be delivered by NCAs, due primarily to a limitation of expertise. The training and documents delivered across all WPs must be delivered to a consistent, and high, quality. Therefore, a call for tender will go out in the coming months to ensure this consistency across all SCOPE outputs.

3. View from General Advisory Board - François Houyez, EUORDIS

François Houyez, representing the European Organisation for Rare Diseases (EURORDIS) as a GAB Member, gave a presentation on SCOPE progress from a patient's perspective. François

Houyez, referred to Articles 102 and 106 from the Directive 2010/84/EU which set out to provide different levels of engagement with patients and HCPs.

Two initiatives lead by NCAs were presented as examples of collaborations with patients. The first action, the Health Products Regulatory Agency's (HPRA, IE) PV Information Day (21 October 2014) was envisaged to support and stimulate patient reporting. In 2015, the HPRA also held a range of conferences and seminars for patient groups. The National Security Agency of Medicines and Health Products (ANSM, FR) has launched a call for patient's organisations with the main objective to stimulate and support independent associations aiming to reduce risks related to health products. From 2012 to 2014 there have been a number of projects received; some of these have been completed.

François Houyez presented two more examples of interesting patient support initiatives within the Behcet's community, and an example of a patient data post-authorisation project designed to improve tracking of adverse drug reactions (ADRs). François Houyez highlighted that patient communities must know who to report ADRs to, and that NCAs would be interested in collaboration. The importance of ADR reporting tools available to the public was also described.

Following from a brief explanation of WP4 (ADR reporting) survey results, François Houyez emphasised the importance of ADR reporting campaigns, engaging patients, and developing user friendly reporting tools. Feedback and acknowledgements to patients were recognised as vital tools to improve reporting systems. Media campaigns, target communication, leaflets disposed at local pharmacies, registrations in a service for first time users, and creating awards for the most useful spontaneous reports, were all suggested as potential improvements that could be tailored to needs and resources available at national levels. François Houyez spoke of issues with reporting forms across Europe: outdated designs, rough adaptations of a HCP's version, technical wording, difficulties with navigation on NCA's website, poor promotion, and a lack of consultation with patients prior to development. Innovative examples of ADR forms were also presented to the audience, including pop-up guidance with electronic forms, and efficient communication examples, presented as good practice.

Discussion/Questions

A discussion followed on various aspects of collaboration with ongoing initiatives, delivering outputs that would directly improve national PV systems, and sustainability. The importance of presenting 'golden nuggets' was agreed, WP4 would include case studies in order to share knowledge of well-established and successful PV systems. It was recognised that NCAs engagement with patients should be improved in two-way communication, including feedback sent back to patients, and sharing information on how European pharmacovigilance system works.

Session II – Effective Systems for Managing ADRs and Signals

Marie Lindquist, Uppsala Monitoring Centre (UMC), opened the second session of the day

1. Improving capabilities for ADR reporting - Dr Viola Macolić-Šarinić, HALMED

Dr Viola Macolić-Šarinić, representing the Agency for Medicinal Products and Medical Devices (HALMED, HR), and leader of WP4: ADR Reporting, started by thanking all NCAs for replying to SCOPE surveys. The responses were essential in developing WP4 recommendations. The key survey findings from all topics were presented to the audience. WP4 results were fully anonymised, and did not include any country specific indicators. WP4 recommendations formed a basis for the development of four deliverables: an overarching guidance document on ADR reporting systems, including sections on national reporting systems, medication errors, patient reporting, awareness levels, reporting forms, and IT systems, the publication of articles e.g. in scientific journals, creating a specification to the EMA regarding MS requirements for transition to E2B-R3, and finally creating training and awareness raising materials.

Dr Viola Macolić-Šarinić presented the next steps for WP4, namely that final reports would be published in January 2016. The efforts over the next months will focus on drafting guidance documents and articles, developing training materials, and drafting a position paper for the EMA. A summary of all key survey finding were presented to the participants.

2. Delivering Effective Signal Management - Alexandra Pacurariu, MEB

Alexandra Pacurariu, representing the Medicines Evaluation Board (MEB, NL) gave a summary of activities in WP5: Signal Management. The main objective of WP5 is creating a common understanding of best practice in signal management across the EU network. A web-based questionnaire was sent in July 2014, with 25 countries submitting a response. A review of available literature for this topic was also delivered by WP5. The key survey findings from all topics were presented to the audience. Alexandra Pacurariu stated that all MSs perform signal detection on national data, with methods fit for purpose. Good pharmacovigilance practices (GVP) compliance could be improved, especially with regards to validation, prioritisation and confirmation steps. It was also noted that MSs would like to communicate signals better through an integrated signal management tool in order to make more knowledge-based decisions in advance, without passing burdens on to signal management. Limited strategies are available for managing reports of special interest, except for vaccines, which are reported in high numbers in most MSs. WP5 plans to finalise work on a best practice guidance document in March 2016, and deliver a training session in October 2016.

3. Panel Discussion

Dr Marie Lindquist, representing the Uppsala Monitoring Centre (UMC, SE) chaired the panel discussion. The value of collaborative work with other EU activities (i.e. EudraVigilance, SMART) to achieve sustainable outcomes was discussed. The sustainability aspect was also discussed in terms of resources and funds available in EU NCAs, WP7: Quality Management will provide recommendations on how to manage and balance resources available in NCAs.

Concerns about time and effort required for processing paper ADR reports were highlighted. It was also noted that some MSs might have negative experiences with patient reporting. WP4 will deliver a web-based reporting form, compliant with E2B standards, for reporting suspected side effects of medicines and to facilitate spontaneous reporting from patients. Also awareness tools will be delivered for adaptation at national levels.

The integration of the deliverables from the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (PROTECT) project, specifically regarding the use of large databases, together with WP5 recommendations, and other SCOPE deliverables onto an EMA work programme was highlighted.

Session III - Evaluating and Maximising Risk Benefit Assessment

Prof Hervé Le Louet, International Society of Pharmacovigilance, opened the third session of the day

1. Tools for effective risk communication - Yvette Escudero, AEMPS

Yvette Escudero from Agencia Española de Medicamentos y Productos Sanitarios (AEMPS, ES), gave an overview of the key results and recommendations from all topics forming WP6: Risk Communication. WP6 collected information on risk communication practices in the EU. MS leadership was recognised as the key to developing interactive and two-way risk communication on national levels. A series of recommendations, presented in the form of a communication toolbox allowing MSs to select the most interesting and suitable tools for their own needs, will be developed by WP6.

Yvette Escudero stated that WP6 is aiming to define best practice in risk communication through the creation of the standardised toolkit, and a forum for interaction among European NCAs in order to strengthen regulatory collaboration. Work over the following months will focus on analysing results from a study conducted on the impact and effectiveness of risk communication, from a HCPs point of view, in addition to collecting input from patients and consumers on risk communication, developing a web-portals guide and risk communication toolkit, and finally organising a workshop on risk communication in 2016.

Discussion/Questions

An obligation to reach out to stakeholders outside of the SCOPE consortium in order to improve communication aspects was highlighted. Feedback on safety communications and awareness from HCPs and patient groups was recognised as essential in building good practice. A question was posed about a way of presenting recommendations in the toolkit. The WP6 deliverable will be a common toolkit for adaptation by MSs and will provide good examples of practice from the EU regulatory network.

2. Strengthening capabilities for benefit risk assessment – Dr Jelena Ivanovic, AIFA

Dr Jelena Ivanovic, representing Agenzia Italiana del Farmaco (AIFA, IT) as WP8 leader, gave an overview of key survey finding and recommendations. WP8: Lifecycle PV aimed to collect information on methods and process for PV assessment, explore competencies and useful alternative data sources in the context of various procedures (RMPs, PASS, PSURs, and referrals), support a competency framework, promote consistency in Benefit Risk assessment, and identify and develop appropriate training materials.

A common format for recommendations from the WP8 topics was developed, including a 'hints and tips' documents for various procedures. The 'hint and tips' documents were not intended as guidelines and will not replace the existing guidance and recommendations available in the PV network. These documents have been designed to share experience in the EU PV network, and offer advice on some aspects of assessment and of writing assessment reports. The 'hints and tips' were intended as reflection papers, based on the experience and advice from senior and junior assessors working in NCAs.

In June 2015, WP8 completed a catalogue of additional data sources, including examples from NCAs, as well as a list of useful training and literature. Over the coming months WP8 will continue working on the 'hints and tips' documents on RMP, PASS, referrals, PSUR/PSUSA, in addition to the concept paper on assessors exchange programme. The final report and training materials are planned for completion in June 2016 and face-to-face training will be scheduled for the third quarter of 2016.

Discussion/Questions

A question was posed about how WP8 deliverables would be reviewed, and whether PRAC would be involved in this process. It was recognised that PRAC's opinion would be beneficial, as WP8 outputs were intended to improve assessment process. However, this aspect will be brought for discussion with GAB members.

3. Quality Management Systems - Júlia Pallós, OYGEI

Júlia Pallós, representing National Institute of Pharmacy and Nutrition (OYGEI, HU), as WP7 leader presented an overview of WP7: Quality Management Systems activities. The main

objective of WP7 was to understand and provide recommendation on how to develop Quality Management Systems (QMS) for PV. WP7 is divided into three work streams: Topic 1 was designed to understand how national QMS work across the EU, Topic 2 was formed to investigate the resource management aspect, and Topic 3 aimed to explore PV inspection.

WP7 will deliver a practical guidance (toolkit) on how to improve QMS, and training materials for PV staff, including examples of good practice. These deliverables will be addressed to PV staff working in national agencies. The toolkit will contain guides, good practices on how to operate PV, case studies on quality planning, compliance, performance management, resource management and training development plans. As e-learning materials these will be designed as modules to increase knowledge on quality management and provide a general learning on QMS with a special focus on PV and PV inspection.

The efforts over the coming months will focus on the development of training materials and the toolkit, for presentation towards the end of the project. WP7 will organise two face-to-face meetings in November 2015 and March 2016. Site visits to two selected NCAs are scheduled for February and March 2016, which will inform development of the toolkit.

4. Content of SCOPE deliverables - Margarida Guimarães (INFARMED) and Louise Loughlin (MHRA)

Margarida Guimarães, representing the National Authority of Medicines and Health Products (INFARMED, PT) as leader of WP3: Evaluation, gave a brief overview of the evaluation process, and summarised all activities. SCOPE outputs refer to various aspects of PV, but have the same ultimate goal - to improve work on national levels and provide consistency across the EU. SCOPE aims to help medicines regulators to comply with PV legislation, and provide support to optimise their work.

Margarida Guimarães introduced Louise Loughlin, representing the MHRA as SCOPE project manager. Louise Loughlin spoke of SCOPE deliverables, and training sessions. SCOPE outputs designed by individual WPs will be delivered in various formats - toolkits, educational materials, guidance documents, cases studies, reports. However, all materials will be approved by WPLs, and have a consistent design across all the deliverables. Individual WPs will design their own training structure in a variety of forms - workshops, 'train the trainer' sessions, e-learning, case studies, and guidance documents. Pilot training sessions could also be delivered in order to provide high quality end products. Training is aimed at NCAs, and may be delivered in a variety of locations. WP2: Communication and Dissemination is also planning to organise a flagship event towards the end of the project, which would complement the training delivered by each individual WP. All SCOPE deliverables will be made available on a dedicated section of the SCOPE website.

Session IV – Questions and panel discussion

Panel Discussion on next steps

The forum's final session was dedicated to open questions from delegates, and discussion on the next steps. It was noted that presentations and all meeting papers will be made publicly available on the SCOPE website. PV was recognised as a constantly evolving field, and it was agreed that SCOPE should aim to provide different levels of guidance - from good practice to minimum standards.

A question was posed about further contributions from MSs. It was expressed that all partners who would like to contribute to the development of SCOPE deliverables would be welcome to comment and review SCOPE reports.

Questions in the panel discussion that followed were focussed on the training and sustainability of SCOPE deliverables. Training and workshop dates, as well as guidance documents will be advertised through the website. Timelines will be carefully planned to avoid clashing with other important meetings. As PV systems are moving forward and evolving, it was agreed that SCOPE materials should be living documents that could be incorporated into the PV network. Sustainability and maintenance of the project's foreground beyond the lifetime of the project was echoed in this discussion; it was noted that there is a need to identify a group able to maintain SCOPE's deliverables through the existing PV network.

Concluding Remarks

Dr June Raine concluded the day by returning to the three objectives set out in her opening presentation - to share, test, and enthuse attendees in helping to deliver SCOPE objectives. All WPs shared the impressive amount of work that has been achieved, and will share even more information with the network by providing examples of good practice, guidelines, and tools. Closer collaboration with patient organisations, and academia should be accomplished in order to involve all expertise available in the network.

Questions asked during the SCOPE Stakeholder Forum will be further explored to ensure the key issues are tackled and prioritised correctly. Dr Raine asked attendees to think about the future of SCOPE and posed a series of questions. "What items should be addressed now? Does everyone have access to the information available on national levels? Are we linked-in enough? Are we in line with the EMA, academia, and patient organisations? What links must be formed to keep the network up-to-date? What do we want achieve for the different bodies, patients, assessors and HCPs? What are the critical success factors? Who will maintain SCOPE deliverables?"

Dr June Raine acknowledged the enormous amount of work SCOPE has ahead in the next 13 months, and thanked all presenters and delegates for their contributions to the meeting.