PCWP/HCPWP joint meeting

28 June 2023

Co-Chairs: Juan Garcia-Burgos (EMA) and Rosa Giuliani (HCPWP)

Welcome and introduction

Juan Garcia Burgos (EMA) opened the meeting, welcoming all participants in person and online as well as the Working Party co-chairs.

1. Ongoing EMA activities

1.1. Update on RWE including DARWIN EU®

Andrej Segec (DARWIN EU® Project manager) and Kelly Plueschke (scientific administrator, workstream leader for RWE advice and patient registries) provided an update on real world evidence (RWE) activities and described the vision which is to enable the use of RWE in regulatory decisions taken on medicines and to establish its value across the different stages of medicines lifecycle, from the development phase through evaluation up to post-marketing supervision.

There are three pathways for studies available to EMA that include i) those conducted in-house by a team of pharmacoepidemiologists and data scientists using six databases containing mainly primary care medical records from different European countries, ii) those conducted via DARWIN EU® and iii) those commissioned to one of eight research organisations and consortia via the Agency's framework contracts.

Andrej began by providing an overview of the RWE experience report that summarises the experience to date. He described the DARWIN EU® network and the coordination centre that contracts the individual data partners and performs scientific studies. EMA is the entry point and the principal user of DARWIN EU that request studies provides strategic direction and oversees the coordination centre, on behalf of the EU medicines regulatory network.

In the first phase of the network, ten data partners from eight countries were included covering approximately 26 million active patients. RWE use is foreseen across the regulatory lifecycle in any of EMA's committees and working parties supporting orphan designations, scientific advice, paediatric investigation plans and the evaluation of benefits and risks. The network establishment is on track and the current focus is on growing the network and increasing the volume of the studies. The catalogue of standard data analyses includes both off the shelf and complex studies that can be found on a dedicated website. Applications have been created that enable users to personalise the visualisation of the results. He concluded with an overview of the studies currently in progress. See presentation for more details.

Kelly then presented an update on the third pathway (framework contract studies) and described the process for EMA funded studies. She listed the priority topics for registries and focused on leveraging the CHMP guideline on registry-based studies, which objective is to provide key recommendations on

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methodological and operational aspects on the planning and conduct of registry-based studies. Actions being taken to address the priority topics were described with an emphasis on where patients and HCP could also contribute to communication, engagement and training aspects specifically. She concluded with the messages that patient data is instrumental in optimising medicines development and that more patient and HCP involvement is needed. It is important to better understand patient and HCP needs in terms of training and communication and a call for volunteers was made to collaborate in the development of the patient communication and engagement strategy and preparation of the upcoming workshop. See presentation for more details.

This was then complemented by Elizabeth Vroom (PCWP patient representative on the DARWIN EU® Advisory board) who commented that RWE is clearly very relevant for patients but raised the question regarding the use of OMOP-based coding rather than Orphacode for rare diseases and described limitations with regards to coding of PROMs. She was supportive of EMA and DARWIN EU analysing healthcare data from real world data sets, but this may not be the solution for all needs of RWE by EMA and other bodies including HTA. While patients and HCP look at the real value of the data collected, she asked specifically about how to collect patient experience data and how this can be brought to the regulators. Elizabeth concluded that what has been done is impressive and more still needs to be done. She also requested that PCWP/HCPWP members contact her if they have any contributions on the use of RWE.

1.2. Piloting creation of electronic product information (ePI) for EU medicines

Elizabeth Scanlan (ePI Product Owner) described the pilot of electronic product information. The information for patients and HCP such as summary of product characteristics (SmPC) and package leaflet (PL) are provided in pdf form or printed, and in recent years this information has become available electronically. However, medicines information providers that provide the information electronically all do so via their own individual standards and platforms. The vision in that EU is for a common technical electronic standard that would be used by regulators across EU to provide information that would allow information to flow across borders more easily, to support patients as they travel, that would help regulators and improve efficiency across the regulatory network.
A standard was established and adopted by the European Medicines Regulatory Network in 2021, which is based on an international standard called FHIR and an initiative to create e-PI that complies with the common standard is currently being piloted with several EU regulatory agencies.
ePI will be created via a portal (called PLM) that is already being used by companies for other activities related to their applications, and once authorised the ePIs will be publicly available. The purpose of the pilot is to test the portal and the guidance documents to see how well ePI can fit into the regulatory procedures in the future.

The expected key benefits of ePI include support for challenges faced by patients and consumers, such as health literacy, improving timely access to information in different formats (including video), rapid updates of information, easier searching and increased accessibility of information by offering the options of different formats. Similarly, regulators, national competent authorities and medicine developers benefit from the ensuing administrative efficiencies that ultimately contribute to improved public health. See presentation for more details.

1.3. Monitoring of events and preparedness for Public Health Emergencies/Major Events

Monica Dias (Head of Supply and Availability of Medicines and Devices) provided an update on EMA activities in the area of shortages and availability. The extension of EMA's mandate with regard to monitoring and mitigating shortages has now been fully implemented, which includes the establishment of the Medicines Shortages Steering Group (MSSG), whose role in the context of EU coordination was described. The key milestones for the extended mandate were presented that include the MSSG and the medicine shortages single point of contact (SPOC) working party.

In addition, the medical device shortages steering group (MDSSG) and supporting working party have been established with an IT tool for reporting of shortages of critical medical devices along with supply and demand data. It is important to note that this part of the mandate is only applicable during a public health emergency; the structures and processes are in place and ready.

Preparedness is a key focus, and the process for managing shortages with stakeholders and partners was described. In terms of preparedness activities, a toolkit of measures is being established with a focus on critical shortages and how to mitigate the impact on different stakeholders. The toolkit has been shared with the MSSG to help them determine the most appropriate measure to use in any particular case. Antibiotic shortages were presented as a case example along with the measures that were undertaken.

With respect to what can be done to better prepare for any potential key antibiotic shortages for next autumn and winter. A joint EU (EMA HERA) exercise to match supply and demand was performed to understand if actions were needed to ensure sufficient supply, by contacting key suppliers and asking for supply forecasts. Demand forecasts were generated using modelling programmes and potential gaps are being identified and measures are being put in place.

The revision of pharmaceutical legislation foresees two key areas i) monitoring and management of withdrawals and shortages including critical shortages and ii) security of supply. A change to the reporting obligations is seen with the possibility of early notification for better and earlier preparation and possibly even prevention. This would result in a strengthened role for the MSSG, not only during a public health emergency or major events but for any critical shortage. For more information, see presentation.

1.4. Feedback on the pilot on collecting information on shortages by EMA eligible organisations

Inga Abed, Medical writer, gave an update on a pilot launched in November 2022 asking eligible patient, consumer and HCP organisations to report on shortages. She also gave an overview of EMA's structures dedicated to shortages and availability and how they interact. During the six-month pilot, reports were received on 33 active substances, of which most were already monitored through SPOC working party and/or otherwise managed or resolved. Most reports concerned nationally authorised products. To make the process more efficient, EMA will continue the pilot with modified criteria. As a follow-up action EMA will report back in November 2023 including the results surveys on recent shortages conducted in different languages on specific products. For more details, see the presentation. The updated form for reporting shortages was shared with WP members in the post-mail.

1.5. Implementation of the Good practice guide on prevention and possible re-launch of the sub-group

Inga Abed continued with a presentation of the Good practice guide on prevention of shortages, published in July 2022, which was drafted in a subgroup including patients and HCPs, EMA and HMA. Despite promotion through a social media campaign and a dedicated factsheet summarising the guidance, awareness among patients and HCPs of the guidance and its recommendations is lower than it could be, and EMA would welcome feedback from WP members on what more could be done to promote and implement the guidance. For more details, see the presentation. A Slido survey was shared with members in the post-mail to explore what further actions could be taken, together with a call for interest to join a small group to work on this topic.

1.6. Update on activities linked to presence of N-nitrosamines in human medicines

Antonio Azevedo, Nitrosamine team coordinator in the Inspections office and Robin Ruepp, Procedure Manager in the Referrals office, gave an update on nitrosamine impurities. Since 2018 when reviews of nitrosamines started, progress has been made in understanding and controlling the risk of
Their presence in human medicines. The focus is on balancing patient safety and availability of medicines,

and members were updated about the dedicated mechanism and groups that have been established. A new approach for determining the limits for nitrosamines through the use of the Carcinogenic Potency Categorisation Approach (CPCA) and the Enhanced Ames test (EAT) was presented and has been published recently in the EMA nitrosamines Questions & Answers document available at this link (please see Q10). This pragmatic and science-based approach is based on significant progress in the scientific understanding of the issue and will further support the objective of achieving the best possible balance between patient safety and availability of medicines.
For more details, see the presentation and the EMA dedicated webpage on nitrosamines.

1.7. Patient Experience Data update

Reinforcing patient relevance in evidence generation is a key priority in EMANs and the Regulatory Science Strategy. Patient Experience Data (PED) is relevant in the context of medicines development and benefit-risk evaluation as well as HTA but is still not systematically included. PED is seen as a new scientific discipline that requires multi-disciplinary expertise across the EMA and the EU network as well as stakeholder consultation. Rosa Gonzalez-Quevedo presented an update on progress since last year's workshop. This year, as a priority EMA will draft a reflection paper to provide advice on the best EU approach to generate and collect PED. Public consultation is planned for Q1 2024 and there will be an advance consultation with the working parties. Work is also ongoing regarding a second priority action to explore how to reflect PED in the CHMP's assessment report. For more details, see the presentation.

2. Pharmacovigilance

2.1. Minimisation of opioid use disorder (OUD)-risk with opioid-containing medicinal products: consultation on possible outer package warning

This topic formed part of a discussion that may be revisited with the PCWP and HCPWP and published at a later stage.

2.2. Report on pharmacovigilance tasks from EU Member States and EMA - 2019-2022

Aniello Santoro (Signal Management Lead) and Stephanie Cohen (Scientific communication officer) presented a brief update on the four-year report on pharmacovigilance tasks. The report consists of two sections, the focus areas of the EU network during the reporting period and the key pharmacovigilance activities.
The focus areas include the response to the COVID-19 pandemic, the measurement of the impact of pharmacovigilance activities, the use of real-world evidence and process simplification. The key pharmacovigilance activities include those that are led by the PRAC (e.g. assessment of signals, PSURs, RMPs, etc.) and other activities that are equally critical for the good functioning of the EU pharmacovigilance system, e.g. adverse drug reaction reporting (where patients and HCPs had a direct role). To accurately describe and reflect this information, statistics and quantitative elements as well as case studies and examples were included, as applicable. Details regarding the EU response to the pandemic and the example of thrombosis with thrombocytopenia syndrome (TTS) and Vaxzevria vaccine were provided to illustrate how the different components of the system worked together to minimise the risks associated with the vaccine. Other take-home messages included that the framework for measuring the impact of pharmacovigilance activities was strengthened through the systematic follow up on outcomes of the studies and through greater stakeholder engagement, as a way to improve the implementation of risk minimisation measures (i.e., PRISMA). Other key milestones during the reporting period were the launch of DARWIN EU enabling access to large healthcare databases across the EU and greater use of RWE in decision making and the simplification/ automation of processes with the objective of increasing efficiency. Patients and HCPs were thanked for their contributions to ADR reporting and for their participation in the various pharmacovigilance activities. See presentation for more details.

3. Clinical trials

3.1. ACT EU – feedback from kick off meeting of multi-stakeholder platform (MSP)

Peter Arlett (Head of Data Analytics and Methods Task Force) described the current landscape for clinical trials and the role of ACT EU within this. A kick off workshop for the ACT EU multi-stakeholder platform was held on 22-23 June to discuss specific issues on the priority areas as well as a model for establishing a multi-stakeholder platform. There was good representation of patients and HCP in the seven panels. He described the four sessions of the workshop, the main discussions that took place and the key outcomes. He concluded by stating that the stakeholders requested harmonisation and simplification of processes for clinical trials and ensuring that they are patient centric. There should be a focus on developing impactful clinical trials that are context-appropriate and transparent. There was agreement on the need for an EU ethics platform and to start the MSP from a strategic advisory group. The next steps include reviewing the feedback from all stakeholders and drafting selection criteria and a mandate for the MSP advisory group. See presentation for more details.

3.2. Decentralised clinical trials (DCT)

Monique Al (CCMO) (scientific lead of the DCT project) presented the EU recommendations on decentralised clinical trials. She began by defining various elements of trials that can be decentralised that render the trial more accessible and introduce more flexibility for trial participants however this also results in less direct interaction between the investigator and trial participants. The recommendations are the result of a very large and diverse collaboration that includes the European Commission, Heads of medicines Agencies (HMA) and EMA as well as the PCWP and HCPWP. The outcome of the collaboration was the recommendation paper and national provisions overview, which are specific member state provisions where national legislation does not allow for alignment. The opportunities and challenges of the recommendations as well as the content of the paper were described.

She focused on clarity in roles and responsibilities of sponsor and investigator, home health visits, electronic informed consent and direct shipment of investigational medicinal products and described the pros and cons for each. One of the many considerations is that the general medical rules to protect trial participants' safety should be upheld in particular when patients are separated from their traditional care centres. Which trial elements can be decentralised should also be decided in conjunction with patients and trial investigators. The next steps include the regular update of the national provision overview, translation of the recommendation paper into a best practice document for assessors of CT applications and to collect and track experience from DCT. See presentation for more details.

3.3. Good Clinical Practice (GCP) ICH E6 R3

Ivana Silva, Healthcare Professionals Liaison, gave a progress report on the work undertaken by the PCWP/HCPWP drafting group preparing a proposal for a PCWP/HCPWP contribution to the ICH E6(R3) GCP public consultation. She explained this was the culmination of the early engagement initiated in 2020 on this topic, when an ICH E6(R3) good clinical practice workshop with PCWP and HCPWP was organised. Following the PCWP/HCPWP written consultation in March, the joint drafting group agreed that very good progress had been achieved with the joint position on comments to present to ICH although divergent views between HCPs and patients were noted for 4 principles. The additional feedback collected to understand the extension of the divergency was presented during the meeting.

In parallel to this work, a more detailed draft version of the guideline was released in May upon the launch of the ICH public consultation and to be addressed in detail during the ACT EU PA04 – multistakeholder workshop on ICH E6 (R3) public consultation in July. Kim Pietsch, Seconded National Expert in the Quality and Safety of Medicines Department provided more details on the workshop.

To finalise whether and how PCWP/HCPWP comments may be submitted in the context of the ongoing

public consultation, a written procedure will be organised.

4. EMA communications and reporting

4.1. Introduction to the revamp of the Human Medicines Highlights newsletter project and results of the stakeholder survey

Kaisa Immonen, Patients and Healthcare Professionals Liaison, introduced the revamp project. All EMA newsletters are being transitioned to a new tool, and this brings an opportunity to make improvements to the HMH Newsletter. A survey was conducted among eligible organisations and subscribers in May-June 2023. The results indicated an overall positive perception of the newsletter and pointed to areas for improvement. For more details, see the presentation. As a next step the team will conduct some interviews building on the results of the survey. Interest was expressed during the meeting by Tove Frisch (ELPA), Christine Dehn (EHN), and Russell Wheeler (EURORDIS), and members were invited in the post-mail to email EMA if interested in participating.

4.2. Stakeholder Engagement report

Giulia Gabrielli introduced as a point of information that the Stakeholder engagement report will in future include the activities of all stakeholders – patients, consumers, healthcare professionals, academia and industry associations – and will continue to be published biennially.