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Report on the "ENCePP in the time of COVID" virtual ENCePP Plenary meeting

20 November 2020 – chairs: Xavier Kurz (EMA), Tom MacDonald (University of Dundee)

This report covers the key discussions points of the event that followed the presentations. All presentations mentioned in the report are available here.

1. Welcome and adoption of agenda

Tom MacDonald welcomed the participants (over 100 representatives of various organisations) of the webinar, including ENCePP partners and Steering Group members. Xavier Kurz outlined the agenda and the objectives of the event:

- To discuss key methodological considerations for observational studies on COVID-19 and how ENCePP could promote best practice, especially in the current context of preparedness for the monitoring of the safety and effectiveness of COVID-19 vaccines.
- To present the recommendations of the HMA-EMA Big Data Task Force, the proposed platform for a Data Analysis and Real-World Interrogation Network in the European Union (DARWIN EU), and discuss the interface between ENCePP activities and the Task Force recommendations.
- To summarise the achievements of the current ENCePP Steering Group at the end its term, introduce the members of the new ENCePP SG and discuss proposals for a draft ENCePP mandate.

2. Session 1: The COVID-19 pandemic, vaccines monitoring and the contribution from ENCePP

2.1. Key considerations for observational studies on COVID-19

Olaf Klungel gave a presentation on ***Key considerations for observational studies on COVID-19*** which was followed by a discussion with the following **key points**:

- Many studies published in the first months of the pandemic had methodological limitations. This may be due to the number of manuscripts generated in a short period of time under exceptional circumstances and heterogeneous knowledge of the authors in epidemiological methods. The importance of peer-reviewing of study protocols was highlighted, although often impaired by lack

of disclosure of formal study protocols and time/resources. Many ENCePP members were asked to review several protocols or study results a day, and they prioritised therefore studies to be published in high-profile journals. Many studies were published in journals without a proper peer review process. A balance needs therefore to be found between appropriate peer-review and the need to publish the findings rapidly to inform clinical practice. Several possible solutions were discussed:

  - a journal dedicated to the publication of protocols, though the EU PAS Register already serves this purpose;
  - a peer-review of protocols organised by EMA;
  - publication in journals without peer-review, but with the possibility to external reviewers to post comments on the design and the results.

- Transparency on study protocols was considered a key aspect for evidence generation, to allow replication of studies and decrease heterogeneity.
- Data governance is another important aspect to secure the quality of patient-level data; there is a need to understand the process of data generation and the provenance of data.

Conclusion of the discussion: Importance of publication/disclosure of protocols; definition of a quality index for protocols and results; importance of transparency on data provenance. ENCePP could have a role in:

- providing guidance on best methodological practice in situations of public health emergency;
- proposing processes for a fast review of protocols and results.

This topic should be further explored by Working Group 2 on Independence and transparency.

2.2. Development, authorisation and monitoring of COVID-19 vaccines

Marco Cavaleri gave a presentation on the ***Development and authorisation status of COVID-19 vaccines,*** followed by presentations by various colleagues on ongoing projects: ***EU regulatory network vaccine monitoring strategy*** (Georgy Genov), ***ACCESS and CONSIGN*** (Miriam Sturkenboom), ***I-MOVE*** (Marta Valenciano), ***DRIVE*** (Javier Diez-Domingo).

Key topics discussed:

- Status of COVID-19 authorisation: even with several thousands individuals included in Phase III clinical trials, it does not allow for the generation of evidence on adverse reactions occurring at a rate <1/1,000. Therefore, collection of safety data post-approval is extremely important. The speed at which the vaccines were developed and are being evaluated is unprecedented. Lessons learnt should be identified for a faster development of vaccines in the future, even if the amount of resources allocated to COVID-19 vaccines could probably not be repeated outside of an emergency situation.
- COVID-19 safety monitoring strategy: unprecedented level of collaboration; importance of transparency and exchange of information between academic centres, regulatory authorities and public health agencies based on high quality protocols.
- Presentation of projects on the monitoring of the safety and effectiveness of vaccines (ACCESS, CONSIGN, COVIDRIVE, I-MOVE): these projects involve a large number of centres, and capacity assessment is being performed in Europe. There are opportunities for ENCePP centres to contribute to one or several of these networks to protect public health. It is important that projects with the

same objective (e.g. vaccine effectiveness) align protocols to apply the most appropriate methods. These projects meet the same challenges: accessibility to high quality data, leveraging expertise (e.g. better representation from Eastern European countries) to address the need for rapid assessments and the implementation of new approaches to measure vaccine safety and effectiveness.

There were suggestions that ENCePP centres should find solutions locally on how to document information on vaccinations. The presenters encouraged the centres to contact them if they have questions or seek collaborations.

3. Session 2: ENCePP mandate and the new ENCePP Steering group

3.1. Achievements of the current ENCePP Steering Group, 2016-2020

Tom MacDonald presented the ***Achievements of the current ENCePP Steering Group 2016-2020,*** which was followed by short updates on the ***ENCePP Working Group and Special Interest Group activities*** presented by the chairs or topic owners:

- ENCePP WG1 - ENCePP research standards and guidances: Xavier Kurz provided a feedback on the ENCePP Guide on Methodological Standards in Pharmacoepidemiology revision 8.
- ENCePP WG2 - Independence and transparency: Rosa Gini updated the audience on Code of Conduct revision 4.
- ENCePP WG3 - Inventory of EU data sources and methodological approaches for multi-source studies: Gianluca Trifirò emphasised the importance of the registration of datasets in the ENCePP Resource Database, and outlined the review performed by WG3 on the characteristics of the studies in the EU PAS Register, which was presented in more details during Session 2.
- ENCePP SIG on Measuring the Impact of Pharmacovigilance Activities: update from Agnes Kant on the development of a guide on methods for modelling health outcomes of pharmacovigilance activities.
- ENCePP SIG on Drug Safety in Pregnancy: Corinne de Vries gave an overview on the work on an annex to the ENCePP Methods Guide on pregnancy and breast feeding and on CONCEPTION network.

3.2. Results of the ENCePP Steering Group election; Proposal of ENCePP mandate

Julianna Fogd presented the results of the ***New ENCePP Steering Group 2021-2023*** election. It was reassuring to see the interest generated by ENCePP, given the large number of applications received to be part of the ENCePP SG; and the selection of members appointed by the EMA Committees and international societies (ISPE, ISoP, ISPOR). The kick-off meeting of the new Steering Group will be held in January 2021.

Gianluca Trifirò presented the ***Review of post-authorisation studies registered in the EU PAS Register***. The aim of the work was to review the characteristics of studies in the EU PAS Register with special interest on multiple database studies (MDSs). The main conclusions reported were that assessing the studies requires multidisciplinary and advanced expertise; a large number of studies are based on primary data collection, without any comparator and just descriptive; and that the number of MDSs is increasing.

Xavier Kurz gave an update on the Proposals for an ENCePP mandate and next steps**.** Since August 2020, the current ENCePP SG has developed a hand-over document for the new ENCePP SG, which includes lessons learnt during its term and perspectives for the next years. This document will help the new ENCePP SG to prioritise the ENCePP activities and finalise the ENCePP mandate. ENCePP entrusts the new ENCePP SG to further develop ENCePP and successfully integrate the network into the new research environment that will prevail from 2021.

The new ENCePP SG members were advised to focus on the quality and speed of data analysis as well as the accessibility of databases, and increase the capacity to best leverage expertise across different countries and centres.

4. Session 3: Interface between ENCePP and the HMA-EMA Big Data Task Force recommendations on real-world evidence

Nikolai Brun gave a presentation on the ***HMA-EMA Big Data Task Force: Recommendations and workplan***, followed by the presentations on ***The Data Analysis and Real-World Interrogation Network in the European Union (DARWIN EU)*** by Gianmarion Candore and François Domergue, and ***Metadata for electronic health care records*** by Katerina-Christina Deli.

The work of the Task Force is to be integrated in the EU Digital Strategy and the European Health Data Space. The DARWIN EU network is planned to transform the research environment in Europe based on a federated network, taking into account the already existing networks. In this context, the Big data Task Force issued ten recommendations, and ENCePP should be an actor at every step of these recommendations. ENCePP could particularly provide important contributions to data discoverability, including definition and implementation of metadata, the development of a data quality framework, the development of guidance and training modules and the improvement of the EU PAS Register.

Xavier Kurz closed the webinar with a summary of the meeting, calling the ENCePP Partners for participating in the projects and contact the project coordinators, and thanking the four-year work of the ENCePP Steering Group and the leaving co-chair, Tom MacDonald.