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Pharmacovigilance and Epidemiology Department

Highlights from the 13th EMA Industry Platform meeting on the operation of EU pharmacovigilance legislation – 20 March 2018

The following records announcements and action points from the 13th Pharmacovigilance Industry Platform meeting. ACRO and EUCROF joined the meeting for the first two items only.

Pilot of MAH EudraVigilance Signal detection

- The industry provided their initial feedback on the EV signal detection pilot which started on 22 February including a set of proposed metrics for the evaluation of the pilot. The industry highlighted the implications of the switch from their current signalling processes into the EV enriched processes with resources implication especially for smaller organisations. Industry also emphasised the importance of a common understanding of the definition of a validated signal. The different industry associations attending indicated their support for the proposed metrics and their willingness to collaborate in data collection.
- The regulators followed up with the main features of the pilot including its planned duration, the substances covered, the frequency of eRMR screening, as well as the main metrics to be collated by EMA (e.g. the number of emerging safety issues reported, stand-alone signal notifications and related outcomes). The main objectives of the pilot (e.g. to test the network's operational capacity) as well as its limitations (e.g. short duration) were highlighted. EMA will aim to promptly discuss with European Commission (EC) colleagues the next phase of the implementation beyond Feb 2019 with a view to communicate to industry stakeholders as early as possible thereby allowing for adequate preparation.

  http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2018/05/WC500248596.pdf
- **Actions:**

  1. The regulators to signpost MAHs to the existing training materials.

  2. The regulators to set up a dedicated teleconference with industry on how the data and metrics should be collated.

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- **Post meeting note re action 1:**

The following documents will help familiarise the MAHs with the data, system and signal management requirements, processes and resources:

- EMA Signal Management webpage
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.jsp&mid=WC0b01ac0580727d1b

- GVP IX revision 1 and its addendum
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c

- EMA Questions & Answers on Signal Management
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/09/WC500150743.pdf

- Screening for Adverse Reactions in EudraVigilance
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/12/WC500218606.pdf

- Report of CIOMS Working Group VIII on Practical Aspects of Signal Detection in Pharmacovigilance

- EudraVigilance training page
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000162.jsp&mid=WC0b01ac0580a1a1fb

- EVDAS training for MAHs (EV-M5b)
http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2017/01/WC500219435.pdf

- EudraVigilance User Manual – Marketing Authorisation Holders – EudraVigilance access via the EudraVigilance Data Analysis System
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/11/WC500238986.pdf

- EudraVigilance User Manual - Individual Case Safety Report form
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/06/WC500229803.pdf

New EudraVigilance system

- The industry presented their initial feedback on the new EudraVigilance (EV) system pointing at the clear simplification in reporting requirements and the recent increase in stability and performance of the system. They then highlighted some ongoing issues including the increased workload due to the downloading and triaging of higher volumes of ICSRs to which they now have access (due to substance based access). They emphasised the need for clarification of their obligations regarding the processing of cases downloaded prospectively as well as those they access through signal management. Industry reported that they are benefiting from the simplification of reporting only to EV instead of multiple agencies; however this benefit is significantly negated by the increased workload associated with downloading and triaging higher volumes of ICSRs. A close cooperation with EMA was highlighted as a success factor to further simplify processes, including the clarification of MAH requirements for case download and further processing.

- The regulators provided a progress update; EMA reminded that any technical issues need to be recorded and tracked via the EMA IT helpdesk to allow for a timely prioritisation and resolution. In terms of case processing, the regulators presented the option favoured by the PRAC and supported by the inspectors, that only ICSRs from National Competent Authorities accessed by MAHs "prospectively" should be recorded by them, while their handling of cases originating from other MAHs would depend on how they met their pharmacovigilance obligations. It was noted that the final regulatory position on case handling will need input from the EC. While input is sought from the EC, the MAHs should proceed in line with their established processes. The industry representatives were invited to nominate volunteers to work with the EV-EWG on the development of criteria to determine "pharmacovigilance obligations" and the subsequent recording of cases.
- The regulators announced the updated Q&A document (v. 1.4)[1], which has now been published.

http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2018/05/WC500248595.pdf

PRAC Work Plan for 2018

- The regulators introduced the PRAC work plan[2] for the upcoming year including a number of initiatives in the product life-cycle. They highlighted the importance of cross committee work (e.g. with CAT, CHMP, PDCO), as well as of measuring the impact of the recent legislative initiatives (e.g. the additional monitoring experience analysis and the experience of the public hearings to engage patients and healthcare professionals). In terms of risk assessment, the committee will discuss a structured approach to hepatotoxicity in product benefit risk management, based on work conducted by different delegations and PRAC independent experts. This will follow a similar approach to that taken for serious cutaneous adverse reactions (SCARs) in 2017.

http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2018/05/WC500248594.pdf

Good pharmacovigilance practices for the EU

- A number of processes-dedicated GVP revisions have been published in 2017. The focus in 2018 will shift towards population-specific modules including the paediatric GVP expected to be published in May, followed by the public consultation of the geriatric GVP in Q2 2018. Work has also started on the pregnancy/breastfeeding GVP.

  http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2018/05/WC500248592.pdf

- The regulators presented the scope and objectives of the paediatric specific GVP.

  http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2018/05/WC500248593.pdf

United Kingdom's withdrawal from the European Union preparedness activities

- The regulators gave an update on EMA / EU Network preparedness activities further to the UK notification on 29 March 2017 of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on EU. It included the updates of the EMA Operation Relocation Preparedness (ORP)

[1] http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/07/WC500230934.pdf

[2] http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2018/03/WC500245931.pdf

task force organisation and activities and the network preparedness of UK portfolio re-distribution methodology.

- It was noted that 24-hours prior to this Industry Platform meeting the *Draft Agreement on the withdrawal of the United Kingdom of Great Britain and Northern Ireland from the European Union and the European Atomic Energy Community*[3] was published by the EC. Industry was told of the need to update of the Article 57 database for EU QPPVs currently based in the UK, as in line with Art 8 Dir 2001/83/EC the EU QPPV must reside in the EEA. It was noted that the industry enquiry regarding the need for the location of the deputy QPPV within the EEA (should one exist) was being considered at the EC level and clarifications expected to be made available in the next update of EMA-EC Q&A and EMA procedural guidance on Brexit related changes. Once available, these will be published in the enclosed [link].
- The regulators updated on the "Brexit preparedness" meetings with industry stakeholders planned for 2018.
  http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2018/05/WC500248591.pdf

Next meeting/topics:

The next meeting will likely be in September or Q4 2018.

The different industry associations indicated possible priority topics for the next meeting. These were:

- Pilot of MAH EudraVigilance Signal detection,
- EudraVigilance operation of the new functionalities,
- MLM,
- PSPs,
- Risk minimisation measures and GVP XVI,
- UK withdrawal from the EU,
- Feedback on the revised RMP template & guideline,
- Industry contribution to the impact of phV activities,
- Impact of the data privacy regulation,
- Registries,
- PASS impact and phV obligations,
- The analysis of the additional monitoring experience in the EU.

[3] https://ec.europa.eu/commission/publications/draft-agreement-withdrawal-united-kingdom-great-britain-and-northern-ireland-european-union-and-european-atomic-energy-community-0_en