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Patient Health Protection

Summary - EMA workshop with EU pharmaceutical industry associations on the implementation of Article 57(2), second subparagraph of Regulation (EC) No. 726/2004

14.00 – 16.30 on Monday, 14th May 2012

BACKGROUND:

On 14 May 2012, representatives of the European Medicines Agency (EMA) met members of the European pharmaceutical industry associations (EVM, EUCOPE, EUROPABIO, EFPIA, EGA, EBE, ECI-EEIG and AESGP) in order to provide an update and current status on Article 57 (2)), second subparagraph of Regulation (EC) No. 726/2004 implementation and to provide European pharmaceutical industry associations with an opportunity to share their implementation experience and raise any potential issues. Susanne McDonald (Irish Medicines Board-IMB) attended via teleconference as the HMA observer.

The meeting was co-chaired by Noel Wathion (Head of Patient Health Protection Unit) and Luc Verhelst (Head of Information and Communications Technology Unit); the European pharmaceutical industry associations welcomed the Agency's constructive and open dialogue.

DISCUSSION and OUTCOME:

The Agency presented the scope of the EudraVigilance Data Quality Management contract signed in December 2010 between the Agency and its external contractor (Kinapse), as well as the main achievements of the first year and half of activity. It was emphasised that this activity represents a significant investment (6.4 Millions of Euros over 4 years) and commitment made by the Agency in order to improve the quality of the data within the EudraVigilance System. It was announced that at the end of May, the Agency will publish aggregated data related to centrally authorised products for the general public and health care professionals. (Relevant presentation attached as Annex1).

In the second part of the meeting, the Agency presented the current status of the Article 57(2) implementation. (Relevant presentation attached as Annex 2).

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Noel Wathion introduced the new EMA XEVMPD training strategy, which can be summarised as follows:

- The Agency recognises the utmost importance of data quality in EudraVigilance (EV) and in the eXtended Medicinal Product Dictionary (XEVMPD) due to their important role in the protection of public health. The Agency confirms the need to ensure that users of EV and XEVMPD have an adequate level of understanding of the various aspects of data reporting requirements and rules before being allowed to use the systems. Therefore users will need to attend training and successfully pass a knowledge evaluation before registering with EudraVigilance.
- There are now two options for MAHs to be trained on the use of XEVMPD:
  - Attending the current face to face training. The following change is introduced: the notification process of successful completion of the knowledge evaluation will be managed by the Agency. Users who successfully pass the XEVMPD knowledge evaluation will receive a notification email directly from the Agency.
  - Attending in a new e-learning course. The Agency will publish an XEVMPD e-learning training programme by 18/5/2012 at the latest (Post-meeting note: the e-learning course has been published on 16/05/2012). The e-learning will be free of charge. The notification process of successful completion of the knowledge evaluation will be managed by the Agency. Users who successfully pass the XEVMPD knowledge evaluation will receive a notification email directly from the Agency. The XEVMPD knowledge evaluation will consist of 2 parts: A Multiple Choice Questionnaire and a Product Report Exam Case, where participants will be requested to enter a fictitious XEVPRM in the XEVMPD training environment based on the supporting documents provided.
- MAHs will have the possibility to attend either the current face to face XEVMPD training or the e-learning training course published by the Agency.
- Users, who successfully attended either the face-to-face or the e-learning training, will receive a notification of successful completion of the XEVMPD knowledge evaluation directly from the Agency. It was emphasised that since the Agency does not have the possibility to acquire additional dedicated resources for the knowledge evaluation process, some notifications may be provided by the Agency with delays.
- At least one user from each marketing authorisation holder should be trained to understand how to submit medicinal product data to the Agency and to ensure quality of medicinal product data submitted to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD). A notification of successful completion of the XEVMPD knowledge evaluation will be required for one user before the electronic submission process can be initiated by an MAH.

The Agency took the opportunity to enquire about the views of the Industry Associations on two unresolved aspects of electronic submission of medicinal product information: the handling of marketing authorisation numbers for different pack sizes for nationally authorised medicinal products and how to present the quantitative declaration of active substances for salts, hydrates and esters in the XEVPRM. The Agency presented the background of these aspects, as well as proposed options on how to proceed and invited the Industry Associations to select which option they prefer to use.

The EU Pharmaceutical Industry Associations presented their implementation experience and raised a number of issues. (Presentations attached as Annex 3).

Since the Agency did not receive the aforementioned presentations in time for the involved colleagues to provide sufficient feedback, the Agency undertook to provide/confirm official feedback in writing within this summary. The Agency also confirmed that all questions related to maintenance of the data

and long term strategy and roadmap will be noted and used as basis for the next workshop which will be organised in June.

The aspects emerging from the presentations and clarified by the Agency are reported below:

- AESGP presentation:
  - EV-Web generally acceptable, however the interface could be more user friendly. A user manual would be desirable.

    EMA feedback: the Agency is currently reviewing the EVMPD User Manual to align it with the new technical specification; the e-learning course will support the users on how to interact with the XEVMPD data entry tool

    Post Meeting Note: XEVMPD user manual has been published on the EudraVigilance Website on 16 May 2012;

  - Duplicate records submitted for each language (and products available under multiple product names) which increases the workload.

    EMA feedback: this is acknowledged, however MAHs should not be concerned about duplicates as the Agency will validate and de-duplicate the data received. In addition, the Agency will be publishing the newly received substance and translation names on a weekly basis to minimize any duplication of effort.

  - Required values not always available in controlled vocabularies, for example no option available for Article 126a under Authorisation Procedure.

    EMA feedback: This question is currently being assessed by the EMA legal service.

  - Lack of the critical “mass update” functionality which means MAHs will have to update each record individually.

    EMA feedback: the Agency acknowledges this issue and is looking into finding a solution to improve the system capabilities in terms of cumulative updates.

  - At least one user needs to be trained and certified before access can be granted but the face to face is training fully booked and e-learning not yet available. In addition, it can take up to 20 working days to register new users. This means several weeks before a company has access.

    EMA feedback: the Agency will make the e-learning available within the coming days. This should reduce the time for registering in the XEVMPD. The Agency will further discuss the possibility of increasing the available number of face-to-face trainings with DIA.

    Post-meeting note: The e-learning course materials have been made available on the 16 May 2012.

  - Substances vocabulary needs improvement: better organisation, removal of duplicated entries and spelling mistakes.

  - Currently, all new aliases and translations are based on the “untidy” vocabulary.

    EMA feedback: the Agency reviewed and updated some of the published controlled vocabularies with current standard terms. Unfortunately, due to time constraints, this was not possible to achieve for the Substance controlled vocabulary. The Agency will reconcile the data during the validation; in addition and in order to reduce number of duplicate entries in the XEVPMD, the Agency will publish new terms as received via XEVPRM on a weekly basis.

- Uncertainty on whether to submit substances as aliases or as new substances.

  EMA feedback: No detailed feedback was provided for this point

  Post Meeting Note: MAHs should locate a substance in the published Controlled Vocabulary. If the substance is not present, MAHs will need to add it as a new substance. If a substance entry for the specific chemical entity is already present, but the name used in the XEVMPD is not the one that the MAH needs to use to be aligned with the SPC, then the MAHs need to add the specific name as an alias. EMA will validate the data in the future.

- Substance updates can be made by multiple MAHs at the same time resulting in overwriting of entries. This is likely to be relatively common as it seems that processing of the submitted XEVPRM can take days to be available in EVWEB and in the published controlled vocabulary.

  EMA feedback: this is a known issue. However, the system is keeping the history of every version of substance received together with the aliases and translation submitted. The Agency will validate the complete data, including the historical submission for substances.

- Could rationalisation of Controlled Vocabulary result in the EMA issuing a list of 'redundant' EV substance codes and requiring companies to discontinue use and replace old by new one? If so, what would be the timeline?

- If it's the case, old codes will still exist within companies' reference computer systems and will have to be changed there even if no updates are required into EVMPD.

  EMA feedback: this is still under discussion. However, the Agency is considering to introduce the concept of master substances that are created following the validation. If this concept will be implemented, old entries will be then linked to the appropriate master substance and their EVCODEs will still be usable. The Agency emphasised that it is considering various options and will make efforts to minimize the impact of data validation on Industry's systems.

- EFPIA presentation:

  - We seek confirmation that EMA will not add additional data requirements to EVMPD in advance of the finalisation of the ICH M5 Implementation Guide. We reiterate our commitment to work with EMA in building a roadmap for the transition to IDMP.

    EMA feedback: the Agency does not have the intention to apply major changes to the XEVMPD before a roadmap for the long term strategy is available. With regards to the implementation of the structured substance information, this will be defined in the context of the roadmap for the long term strategy. The maintenance is under discussion in the June ICH Meeting in the Japan.

  - We request further information on the EVMPD Implementation Group i.e. scope, participation and timing.

    EMA feedback: During the last EudraVigilance Steering Committee meeting it was agreed to establish an implementation group with members of EU Pharmaceutical industry associations. Each EU Pharmaceutical industry association is asked to provide 1 or 2 nominations for this group.

  - A mechanism for uploading bulk changes is essential to support variations such as change of MAH name or change of QPPV, which impact a large number of EVMPD records.

    EMA feedback: the Agency acknowledges this and is working in order to find a solution to improve the system capabilities for bulk updates.

- A general principle applied to the use of MedDRA is to code and submit new data in the latest version of MedDRA, but once that data has been reported there is no requirement to recode to a later version. This should be applied to coding of indications in EVMPD.

  EMA feedback: As indicated in the published XEVPRM Q&A document, we rely on the MedDRA Points to Consider document (ENGLISH Release 4.2 (.pdf) based on MedDRA Ver. 14.1 http://www.meddramsso.com/subscriber_library_ptc.asp). The coding is required at LLT level. With regards to versioning, EMA follows the same principles used for ICSRs reporting. If there is a major difference from a medical perspective, MAHs should update the information accordingly.

- MedDRA codes do not necessarily map cleanly to the text that describes the approved indications in the SmPCs or equivalent.

  EMA feedback: If a MAH needs a term not available in MedDRA, the MAH has to follow the normal MedDRA change request procedures.

- Where products are approved at the National level and the approval documentation is in the local language then a translation needs to occur before the MedDRA codes can be allocated.

  EMA feedback: the Agency acknowledges that MedDRA is not available in all the EU languages.

- In some circumstances, the business rules of XEVMPD make it impossible to incorporate all the translations of the substance name under a single EVCode due to duplicate substance name which may already contain partial translations.

  EMA feedback: This is due to a duplicate prevention mechanism in place in the XEVMPD system, preventing the same substance name to be entered in the XEVPMD (based on the same spelling). It is acknowledged that the presence of duplicated EVCode and substance name (with different spelling or language code for translation) can cause issues; to minimize this, the Agency suggests to first check which are the missing translations in the overall substance controlled vocabulary and then submit only the missing terms to one of the available EVCode/Substances. EMA will validate and reconcile the data in the future.

- Updates to controlled vocabularies need further clarification. There must be a defined change process.

- Any changes to terms that have been used in XEVMPD data sets must be clearly communicated in order to allow appropriate updates of all impacted records. EMA should not update any impacted datasets owned by the MAH, as this will result in a loss of synchronization between the EMA database and the in-house database of a MAH.

  EMA feedback: Terms previously present in the Controlled Vocabularies have not been modified, only new terms will be added. This is with the exclusion of the Organisation Controlled Vocabulary where the Agency, upon request from an organisation, may update or nullify its term: in this scenario, being a request of the organisation itself, it does not have any impact on all the other organisations. The Agency will put in place the change control system indicating the new terms added.

- EGA:

  - It was noted that some questions raised during previous workshop have not been answered yet.

    EMA feedback: the Agency will verify which questions remain open.

Post-meeting note: Following the workshop Remco Munnik clarified that the mentioned open questions were all related to the maintenance of the submitted data and variations. It was formally agreed during the first workshop that those open questions will be discussed in the workshop foreseen to take place in June 2012.

- A concern was raised about registration for gateway users in the test environment. Acknowledgements are not received.

  EMA feedback: no feedback provided during the workshop.

  Post-meeting note: The Agency needs to have specific examples. If there are some issues, these can be addressed on a case by case basis.

- The added value of some information requested was questioned (e.g. splitting of the name, coding of indications, etc.)

  EMA feedback: The information requested has been mutually agreed between the Agency and the EU Pharmaceutical industry associations during the previous workshop.

- A concern was raised with regard to the low quality of the Controlled Vocabularies.

  EMA feedback: the Agency reviewed and updated with current standard terms some of the published controlled vocabulary. Unfortunately, due to time constraints, this was not possible to achieve for Substance controlled vocabulary. The Agency will reconcile the data during the validation; in addition and in order to reduce the number of duplicates entries in the XEVPMD, the Agency is publishing on weekly basis new terms as received via XEVPRM.

- A request for providing more details on technical aspects was risen. For instance, the list of errors in the acknowledgement is not available.

  EMA feedback: no feedback provided during the workshop

  Post-meeting note: European Pharmaceutical Industry Associations are invited to provide the EMA with the list of information missing. The Agency will make this information available.

- There is a request for allowing gateway users to access the Controlled Vocabularies in real time and not as off-line excel files.

  EMA feedback: at the moment the XEVMPD does not allow this. EMA noted this requirement for future development.

- It is requested to implement a change control system for Controlled Vocabularies.

  EMA feedback: the Agency noted this requirement for future development.

- Cut-off date for data submitted (e.g. the SmPC provided as a part of the message may no be longer the latest one by 2 July 2010 (as some changes may happen in the meantime). If it happen, does the message need to be resubmitted?

  EMA feedback: MAHs need to make the initial submission of the medicinal product information by 2 of July 2012. MAHs will need to update the initial submission only after 2 July. EMA will organise an additional workshop in June to address the maintenance processes.

- Clarification was requested as to whether MAHs have to submit the information within 15 days from the official approval from NCA or from the date of closing of the procedure.

  EMA feedback: The “official approval from NCA or from the date of closing of the procedure” currently refers to the date as of when the “authorisation status (AP.12.3) valid =1” becomes

effective (e.g. the date when the initial marketing authorisation or the renewal of the marketing authorisation becomes effective). For centrally authorised medicinal products this refers to the date of notification of the Commission Decision".

- Outsourcing of EVMPD activities by small companies.

  EMA feedback: Delegates were reminded that the legal obligation and the responsibility for submitting the medicinal product information stay with the MAHs even if they delegate to an external party.

  Post Meeting note: If a MAH delegates the submission of Medicinal Product Information to a third party service provider and this is correctly reflected at the time of registration in the XEVMPD community, sufficient requirements for the MAHs to start the submission is to demonstrate that the selected third party service provider has at least one user successfully trained in the XEVMPD.

The next steps and actions can be summarised as follows:

1. The Agency to provide slides discussed during this meeting to the EU Pharmaceutical Industry Associations (Post Meeting note: presentations were sent in the morning before the meeting).
2. The Agency to provide a summary of the workshop prior to the next meeting.
3. The Agency to set up in June the next Workshop aiming to discuss maintenance of the information on Medicinal Information after 2 July 2012. The points on maintenance and variations listed in the presentations from EU Pharmaceutical Industry Associations will be used as basis for discussion.
4. EMA to provide problem statement regarding unresolved issue presented in EMA slides. The problem statement will outline the pros and cons from a public health perspective for each of the options and should be circulated to EU Pharmaceutical Industry Associations. EU Pharmaceutical Industry Associations to communicate preferred option within a week from EMA communication.
5. EMA to provide the mandate for Art.57 implementation group together with a list of members representing EU Pharmaceutical Industry Associations.

Annex 1:

- EudraVigilance Data management activities_14 May 2012

EudraVigilance Data management activitie

Annex 2:

- Current status of Art57 implementation and next steps_14 May 2012

Current status of Art57 implementation

Annex 3:

- AESGP presentation for article 57(2) meeting

AESGP presentation for article 57(2) meet

- EFPIA EBE EVM Feedback - EMA workshop 14May12

EFPIA EBE EVM Feedback - EMA work

- EGA 2012-05-14 Article 57 update

EGA 2012-05-14 Article 57 update.ppt