28 May 2015
EMA/290883/2015

Highlights from the EMA industry platform meeting held on 24 April 2015 on the operation of the centralised procedure

The purpose of these "centralised platform" meetings is to promote awareness about the changes introduced in the centralised evaluation procedure, to have an open dialogue and exchanges of views, and to discuss ideas and proposals for continuous improvement. Initially these meetings will focus on procedural aspects, and may at a later stage extend in scope to also cover other topics related to the centralised procedure.

Status update of changes to the operations in the centralised procedure

This presentation gave a brief overview of recent changes introduced in the operation of centralised evaluation procedures and their implementation status. Some highlights of the session are listed below; the presentation can be found here:

- The overall aim of the changes introduced was to deliver efficiency and consistency gains in terms of procedural management and to optimise the support provided by the Agency to its Scientific Committees in their evaluation activities.
- Key changes include the implementation of the new product team concept; the redesign of the Agency's procedures in order to optimise the use of internal and network expertise depending on content complexity; and the simplification of document management.
- The key milestones in the implementation of the changes were:
  - 1st of April 2014, when the new product team concept was introduced for the first set of application/procedures' types (variations, PSURs/ PSUSAs, administrative Procedures (e.g. 61(3) Notifications) and
  - September 2014, when the new operations were implemented to all remaining centralised procedures (e.g. Initial MAAs).
  - In both phases transitional arrangements were implemented to ensure continuity of service.
  - By the end of Dec 2014 the new operations were fully implemented in the majority of the Agency's procedures.
  - Implementation is ongoing in the some areas like generics, non-Pharmacovigilance referrals and renewals procedures, and is expected to be finalised by Q3 2015.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

- Applicants / MAHs were informed proactively for each procedure of their products about any change that directly affected the interface with the Agency. The procedural guidance on the Agency's website has also been updated.
- The Agency highlighted some important changes that have been introduced recently such as the additional submission dates for certain Type II variations (effective from 1st of March 2015) and the new guidance on Pre-submission and Clarification meetings.

The following upcoming changes were also noted:

- The Risk Management Plan review process during the assessment of initial MAAs; this will be presented at the next Pharmacovigilance platform meeting
- The Product Information (PI) review process; this will be presented at the next Centralised Procedure platform meeting.
- Other CHMP initiatives in the centralised procedure like the introduction of the "Effects table" in the Benefit/risk assessment section of the CHMP Assessment Report for all MAAs and extensions of indications submitted as of February 2015 and the ongoing pilot project to integrate patients' views into CHMP discussions.

EMA product team and applicant / MAH interaction

In this session the Agency provided an overview of the tasks, composition and roles within the EMA product team followed by practical examples presented by PMs and EPLs. The presentations mainly focused on the practical aspects of the interface between applicants and EMA staff during evaluation procedures. Industry representatives shared their first experiences with the new EMA product team concept. Some highlights of the session are listed below:

- The Agency clarified that the procedure manager is the applicant's primary contact during the course of all evaluation procedures. At certain milestones and in the interest of efficiency the EPL may be in direct contact with the applicant /MAH to facilitate the discussion on the scientific evaluation (see exampes in the published presentations). Despite the fact that the Procedure Manager should be the primary contact point, the EMA Product Lead can be directly contacted in case of purely scientific questions. But in this particular case, the Procedure Manager should be kept informed.
- Industry expressed the need for clarification of the interfaces between the Agency, Committees and the applicant during the evaluation process across the different types of centralised procedures (pre- and post-MA) e.g. through flow-charts showing these interactions. The Agency recognised such need for clarification and informed that new Q&As have been developed for the pre- and post- authorisation guidance on the Agency's website. Specifically, clarifications on the roles and responsibilities of each product team members and who to contact during an initial marketing aurthorisation application and in the post- authorisation phase. *(Post–meeting note: the Q&As were published on 29 April 2015.)*
- Industry queried the EMA process for EPL/PM assignment and also asked clarification on the number of procedures and products supported by EPL/PMs. Industry stakeholders were informed that the stabilisation of EPL/PMs products appointment was reached, thus supporting better product and procedure oversight. Information was also provided that the Agency will focus on optimising the PM allocation post-authorisation to provide more stability in contact

points for Industry. Prior to any implementation, any changes which may affect EMA/Industry applicants or MAH interface will be communicated either at product/procedure level and where appropriate through relevant Q&A updates.

Variations process management from validation to EC decision, including classification and validation aspects

This session focused on explaining how the Agency is handling variations procedures, the role of the PM and EPL in these procedures and industry's experience so far. Some highlights of the session are listed below (see also presentations):

- During the post-authorisation phase of a medicinal product a Procedure Manager (PM) is allocated for each post-authorisation procedure submitted. This concerns all types of variations, extension applications, renewals, annual-reassessments, PSURs/PSUSAs, PASS protocols, referrals, post-authorisation measures as well as administrative procedures (marketing authorisation transfers, Article 61(3) notifications).
- When the MAH requires regulatory procedural guidance or has questions prior to submission of these applications he may contact the Pre-Submission Queries Service (PQS).
- The PQS consists of a dedicated team of experienced PMs that ensure consistency and accuracy in the advice provided. Queries may be submitted through dedicated mailboxes (see presentation). With the response the MAH is notified of the contact details of the PM dealing with the request in case follow-up/clarification via e-mail or telephone is required.
- The Agency strives to respond to these queries within 5 working days. Since its operations started the Service has a mean response time of 3.15 days. As suggested at the meeting, the PQS will be proactively notifying the MAH, when delays are expected because of the complexity of the request.
- For products with a high number of upcoming post-authorisation procedures, which may require detailed planning discussions, the PQS should be the first point of contact. The PQS will liaise with the relevant members of the product team to provide with a consolidated response which may be followed-up by a TC, if needed.
- Information on the PQS is included under the post-authorisation guidance for the relevant procedures. Upon request from Industry, a dedicated Q&A on the function of the PQS including the list of all the mailboxes and guidance on its operations will shortly be published in the post-authorisation guidance on the Agency's website.
- The Agency supports the request from Industry to apply consistently a pragmatic approach (across and within procedures) in the interpretation of the regulatory requirements and to facilitate an earlier finalisation of procedures, where possible. In the interest of transparency, the Agency will share examples of potential flexibility through updates of the Q&As or publication of relevant examples in the pre- and post- authorisation guidance on the Agency's website.
- In order to ensure that procedure starts are not delayed by minor issues, Industry raised the need for transparent, clear requirements for the validation of submissions that are applied consistently. The Agency acknowledges this need. Guidance on how to fill in the application form for Type IA and IB variations is already published on the Agency's website together with a pre-notification checklist for Type IA notifications. As a follow up to the platform meeting, the Agency will proceed to publish a validation checklist detailing the issues that may affect procedure start vs. issues that

could be addressed during the procedure. In addition the Agency will ensure that the advice provided from the pre-submission queries service is consistently followed during the validation of submissions.

- The Agency gave an update on the key changes introduced in the procedural management of Type IB variations, i.e. different ways of internal processing of Type IBs depending on complexity and the use of a single assessment report template throughout the procedure.
- The Agency shared results showing that the changes introduced have improved procedural efficiency by decreasing validation and processing time and increasing the number of right first-time submissions.
- The Agency gave an update on the key changes introduced in the procedural management of Type II variations, i.e. different ways of internal processing of Type II variations depending on content complexity (see next point), a single Assessment Report template used throughout the procedure and the implementation of weekly procedure start dates. The weekly procedure start dates are expected to apply to approximately 75% of Type II submissions. Clarifications were also provided on the timing of PRAC involvement for Type II variations.
- For complex Type II variations, particularly evaluations requiring Committee plenary discussions (e.g. extensions of indication) the product team is activated with involvement of the EMA Product Lead (EPL) and/or Risk Management Specialist (RMS); the direct interactions with the EPL are foreseen at key milestones like for the initial marketing authorisation; a dedicated Q&A is about to be published.
- Industry mentioned some difficulties experienced with delays in the provision of ARs and Opinions. The Agency noted these and provided during the meeting some explanations of certain delays. The Agency will review together with the regulatory Network potential measures to be taken to address this. In addition, it was agreed that MAHs will be notified proactively, if such delays are expected to occur.
- The Agency clarified how several procedures affecting the same product are handled, when they are submitted in parallel. Parallel procedures are identified by the PMs during validation. PMs/PAs use internal tracking tools to check the status of the parallel procedures and the correctness of Annexes at the time of Opinion/Notification.
- The difficulties in the procedural management of parallel procedures affecting the RMP were also noted. It was noted that discussions were ongoing in other fora e.g. the PhV platform meetings.
- EPARs are updated on the EMA website on a monthly basis. A dedicated team ensures that the update includes all EPAR changes related to the procedures finalised during the month.
- Variation classification issues were also discussed. In general, in case of doubt about the classification of changes, MAHs can seek regulatory advice by contacting the PQS service.

New practice for the management of clarification meetings

- The Agency introduced the new practice in the management of clarification meetings (See presentation) which is effective as of February 2015.
- Such meetings should provide applicants with opportunity to better understand the rationale behind the questions and discuss/present their response strategy. It was however clarified that

such meetings should not be expected to get pre-evaluation of the proposed responses. The committee Rapporteurs will review the proposed response approach and provide a perspective on how the Committee would see this approach. It is expected that these meetings will contribute in preventing incomplete or premature responses leading to prolongation of the procedural timelines in the second phase of the initial centralised evaluation and ultimately aimed at accelerating medicinal process market access.

- Industry expressed concerns about recent experience encountered in the practical arrangement for organising these meetings resulting in delays and highlighted the need for particular attention in case of accelerated initial evaluation procedures. The Agency took note of the comments and will review the experience.

EMA survey on experience with post-authorisation procedures

- The Agency informed Industry participants about the ongoing survey on certain post-marketing authorisation procedures (Type IB/II/PSURs). The survey will include procedures that are finalised in the period 01/04/15 – 30/09/15.
- The aim of the survey is to get direct feedback from MAHs on the various procedures managed by the Agency and to identify areas for improvement in the handling of procedures and the existing guidance.
- To ensure survey results are representative and to enable a productive and open dialogue, high response rates are needed.

The next platform meeting will take place in November 2015. One topic will be the review of the results of the EMA survey on post-authorisation procedures.