30 September 2015

Submission of comments on 'Guideline on the scientific application and the practical arrangements necessary to implement the procedure for **accelerated assessment** pursuant to article 14(9) of regulation (EC) No 726/2004' (EMA/CHMP/697051/2014-Rev. 1)

Comments from:

| Name of organisation or individual |
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*Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.*

*When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).*

1. General comments

| Stakeholder number  *(To be completed by the Agency)* | General comment (if any) | Outcome (if applicable)  *(To be completed by the Agency)* |
| --- | --- | --- |
|  | EFPIA welcomes the revised draft guidance document on the practical applications regarding the accelerated assessment (AA) procedure in particular the **more detailed and revised timeline schedule**. EFPIA particularly welcomes the clarification that products which are subject to a **conditional marketing authorisation, should be eligible for an accelerated assessment following specific request by the applicant**. On the procedural side, EFPIA is very supportive of the introduction of a **second possibility to submit written responses** without clock-stop.  For the revision of the guideline the following aspects are of key importance which will be followed by detailed comments: |  |
|  | * Distribution of the Rapporteur’s assessment report (AR) is not provided for in the revised guideline. Inclusion of a step for **timely provision to the applicant of the draft Rapporteur’s Assessment Report** is critical in order to be prepared at Day 90 and to evaluate if a one-month clock stop can be maintained. Background: Under the current process applicants are provided the draft assessment reports at Day 80 which enables draft response preparation if desired to help ensure that the one month response deadline is met following the ratified list of questions at Day 120. |  |
|  | * Applicants should be allowed to **request a meeting** with the CHMP rapporteur and Co-Rapporteur **outside of pre-specified timings upon justified requests** being accepted by the (Co-) Rapporteurs.Organisation of these meetings could follow the same as for clarification meetings. |  |
|  | * In line with the reduced timetable for the scientific evaluation, EFPIA would also welcome the possibility **to reduce the timetable (5 + 10 instead of 5 + 20) for translations post CHMP opinion** prior to the Commission Decision procedure initiation if this is requested by Applicants. |  |
|  | * EFPIA requests clarification of how **Orphan Maintenance review** will be performed alongside an accelerated assessment for an Orphan Medicinal Product.   Background: Presumably, the OMP maintenance report will be submitted in parallel as per current Orphan Medicinal Product guidelines but it is not clear whether or not the assessment will be conducted by the COMP in parallel. |  |
|  | * EFPIA would also welcome additional EMA guidance as to how accelerated assessment can relate to **Type II variation** or line extension applications (e.g. for new indications), which has to be seen in the context of the stated objective to improving of existing therapies (line 83). |  |
|  | While the below points supporting accelerated access to patients are not in EMA’s remit, EFPIA flags the importance of:   1. **Accelerated decision making by the European Commission** to reduce the timeline from max. 67 days to max. 30 days to reflect the public health importance of the product evaluated under accelerated assessment.   Particular focus should be given to the reduction of the Standing Committee procedure to significantly less than 22 days (max. 5 days for situations where there is a high public health interest and which stipulate an ‘urgency’ or ‘extreme urgency’. (ref. Rules of Procedures for the Standing Committee on Medicinal Products for Human Use (SANCO/D/3/PB/SF/ddg.1.d.3 (2011)1118442), in particular Art 3(2) and 8)  2. **Acceleration of the scientific assessment of relative effectiveness by HTA Bodies and on pricing and reimbursement following** the EU Commission Decision on the marketing authorisation. |  |
|  | A **review of and report on the experiences** with the revised system latest within 1-2 years after adoption of the guideline will be important to allow adjustments in scope with expectations. |  |

1. Specific comments on text

| Line number(s) of the relevant text  *(e.g. Lines 20-23)* | Stakeholder number  *(To be completed by the Agency)* | Comment and rationale; proposed changes  *(If changes to the wording are suggested, they should be highlighted using 'track changes')* | Outcome  *(To be completed by the Agency)* |
| --- | --- | --- | --- |
| 45-64 |  | Comment:  The clarification that an accelerated assessment procedure is compatible with conditional marketing authorisation and that reduced review timelines can accommodate a SAG consult or review by the CAT (for an ATMP) without extension of the timelines is appreciated.  Proposed change:  In addition, the accelerated assessment procedure should also be applicable to a marketing authorisation under exceptional circumstances as it could also justify for a major interest of public health. |  |
| Section 4 (75-112) |  | Comment:  “*Major public health interest*” vs “*Unmet medical need*”:  One of the objectives of the guideline is to further clarify the justification needed to support that a medicinal product is of “*major public health interest*”. The current text focusses on the justification to be provided to support a claim that a medicinal product addresses an “*unmet medical need*”.  This may be perceived and interpreted as too restrictive as there may be situations where a medical product while not addressing an “*unmet medical need*” can still be of “*major public health interest*”. The guideline should not a priori exclude aspects other than purely medical ones (e.g. significant cost savings for public health systems, addressing emerging or anticipated drug shortages, etc.)  Proposed change: Lines 77-85 “Based on the legislation, a medicinal product of major public health interest may be reviewed under an accelerated assessment procedure. *The concept of major public health interest may cover several aspects, e.g. addressing unmet medical needs but is not limited to that.* Typically, the justification could present the arguments to support the claim that the medicinal product addresses to a significant extent the unmet medical needs for maintaining and improving the health of the Community, for example, by introducing new methods of therapy or improves existing ones…”..” |  |
| Section 4 (75-112) |  | Comment and Proposed change:  In order to be consistent with the aim of Regulation 726/2004 and to ensure that products of major public health interest are not just interpreted based on prevalence, the guideline should be specific on the qualification aspects for an AA procedure: The justification to support the need for AA will also include the proof of the product helping patients affected by a chronically or seriously debilitating disease or whose disease is considered to be life threatening, and who cannot be treated satisfactorily by an authorised medicinal product. |  |
| Section 4 (75-112) |  | Comment:  The orphan legislation criteria listed in the Regulation EC No 141/2000 refers to high unmet need and major contribution to patient care, specifically, its Recital 11 states that “rare diseases have been identified as a priority area for Community action within the framework for action in the field of public health”.  Proposed change:  In reference to Section 4, EFPIA seeks clarification that an Orphan Medicinal Product will be eligible for an accelerated assessment.  The maintenance of the Orphan drug designation (i.e Maintenance report) could serve as basis for requesting the AA procedure |  |
| 112 |  | Comment:  In line with the EFPIA comment submitted on the 'Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No726/2004’ (EMA/CHMP/509951/2006, Rev1), EFPIA believes it is important that applications for a conditional marketing authorisation application automatically qualify for an accelerated assessment procedure once requested by the applicant.  Proposed change:  Addition after line 112  “Applications which are submitted for a conditional marketing authorisation application will, upon request by the applicant, be automatically granted an accelerated assessment procedure.” |  |
| 120-121 |  | Comment:  The intent to submit a request for accelerated assessment may be data driven. Pivotal data may become available only 3 – 4 months before submission of a marketing authorisation application (MAA), which is later than the recommended timing for submission of a notification of intent to submit an MAA (6 – 7 months before MAA).  Proposed change:  “The intent to submit a request for an accelerated assessment should be notified as part of the notification of intent to submit a marketing authorisation application, **if possible**.” |  |
| 125-126 |  | Comment:  As outlined in the guideline, it is particularly important in the context of planning for an accelerated assessment that alignment is gained rapidly between sponsor, EMA and Rapporteur(s). Therefore, in order to make the pre-submission meetings, which the Agency is strongly recommending, most fruitful, it is important that all parties can be present. Therefore, the current proposed wording should be changed to make a joint meeting more systematic.  Proposed change: “The pre-submission meeting ~~might~~ **should** be a joint meeting the Rapporteurs and the EMA product team attending.” |  |
| 126-130 |  | Comment:  EFPIA welcomes the concept of a ‘rolling review’ for data which can be submitted prior to the official start of a centralised procedure or during the evaluation procedure, as a main support to achieve a formal conclusion under accelerated timelines.  Proposed change:  It is crucial for the accelerated assessment to achieve a mutual understanding of the data package that is planned to be included in the application. In case the applicant might foresee that relevant supplemental data will become available during the evaluation, details should be provided about timelines and how these supplemental data are considered of relevance for their marketing authorisation application and can be reviewed within an accelerated review.  It would be useful if some concepts of the rolling review prior to the start of the evaluation procedure as applicable in the US on Expedited Programs can be included. Similarly, concepts of rolling review for pandemic flu (EMA Work instructions on Rolling Review: IPM 7.2 Non-core dossier approved MA: rolling review (prior to submission of marketing authorisation application) as part of the EMA Pandemic Influenza Crisis Management Plan) or as referenced for ebola would be useful to bring into perspective for an accelerated review. |  |
| 132 |  | Comment:  It is unclear what should be considered as ‘mature’ applications in the light of the possibility to submit supplemental data.  Proposed change:  Suggest to remove this statement. Within the paragraph it is mentioned that there is a mutual understanding of the data package that is planned for submission and if additional data are forthcoming during review that timelines and relevance of these additional data are discussed with the Agency and rapporteurs. |  |
| 136-140 |  | Comment:  The new proposed timing for submitting the formal request for an accelerated assessment appears somehow too early. Very often, pre-submission meetings with the EMA and Rapporteurs occur 2-3 months prior to the intended submission date. Considering that during those meetings the possibility of an accelerated assessment would be discussed, providing an appropriate forum to address any open questions and align all parties on the path to submission, it may not be feasible to submit the formal request at the same time.  It is also noted that the Agency anticipates that it would take about 2-3 months to review the applicant’s request for accelerated assessment. Under this proposed revised process, there might be situations where the time needed to come to a recommendation on accelerated assessment might hold up submission and as such delay availability of the medicines in the Union. In summary, consideration should be given to a wider range of submission timeframe (allowing later submission than currently proposed) and to retaining the timelines for the pre-submission phase and assessment of the request for accelerated assessment outlined in the currently valid guideline. However, given the complexity of global development programmes and associated regulatory processes an early request maybe appropriate in specific situations, such as for medicinal products which have been granted accelerated procedures early in development in other regions**.**  Proposed change:  “The formal request for an accelerated assessment is submitted in a second step, as early as possible before the actual submission of the marketing authorisation application but preferably after discussion at the pre-submission meeting. This is to allow the relevant evidence to be included into the justification (see 4). If the pre-submission meeting happens early enough, then the request for an accelerated assessment should be submitted 2-3 months before the actual submission of the marketing authorisation application in order to allow sufficient time for its assessment. However, if the pre-submission meeting happens closer to the submission date, the request for an accelerated assessment should be submitted as early as possible no less than 10 to 30 days ahead of the MA submission” |  |
| 144-147 |  | Comment:  (1)The information to be provided by the Applicant to enable early identification of a GMP or GCP inspection is not clear and clarification would be welcomed.  In addition, it is not clear why an inspection identified at D90 (for example) would impact the procedure.  (2)In addition, the current guidance notes that the need for a GCP or GMP inspection would only impact the timeline if this was identified late in the procedure.  Proposed change:  (1) A summary of the pre-submission guidance described in the EMA website would be useful (EMA's questions and answers on pre-submission guidance: <http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000021.jsp&mid=WC0b01ac0580022711>)  “Furthermore, an early identification of a need for pre-authorisation Good Manufacturing Practices (GMP) or Good Clinical Practices (GCP) inspections is advisable. The applicants should provide relevant information with the request for accelerated assessment to allow identifying such need. For procedural details please refer to the pre-authorisation guidance and Q&A on accelerated evaluation.“  (2) In order to avoid any delays and ensure AA timelines are met, the notification of a GMP assessment should be notified as early as possible. |  |
| 151-152  155-157  186-192 |  | Comment:  Timetables on the assessment of the request were included in previous guideline.  Proposed change:  Further it would be helpful to clarify what the timeline would be for CHMP to decide on a request for AA. Furthermore, a timetable is suggested also for the revised guideline. |  |
| 158-159 |  | Comment:  The CHMP concludes on a request for an accelerated assessment at a very early stage and this is based on summary information. The reasons for this conclusion may no longer be consistent with CHMP views on the interest of the medicinal product at the end of the centralised procedure after their in depth assessment of the full marketing authorisation dossier. Consequently, as a general rule, the reasons for accepting or rejecting a request for an accelerated approval should not be summarised in the final CHMP assessment report of the marketing authorisation. Only the CHMP decision on the request (i.e. accepted or rejected) should be indicated.  Proposed change: The CHMP conclusion and rationale for the conclusion will be communicated to the applicant. The ~~reasons~~ decision to accept or reject the request will also be ~~summarised~~ mentioned in the final CHMP assessment report of the marketing authorisation. |  |
| Section 5  114  161 |  | Comment: In the view of the European Early Medicines Designation and the PRIME Scheme (PRIority MEdicines) currently being established by EMA and discussed with stakeholders EFPIA believes it is important to explicitly link the accelerated assessment with the evolving concept of early and frequent dialogues between the applicant and the Agency.  Applicants should be allowed to request a meeting with the CHMP rapporteur and Co-Rapporteur outside of pre-specified timingsupon justified requests being accepted by the (Co-) Rapporteurs.Organisation of these meetings could follow the same process as for clarification meetings. Further detailing in this guidance is requested:   * After the review starts, meetings between assessors, EMA and applicants should be allowed (considering the same rationale as changes proposed by the EMA on recommending pre-submission dialogue and guidance on meetings with applicants on the responses to CHMP adopted questions during the evaluation within the centralised procedure (EMA/636600/2014). * At a minimum, clarification meetings with applicants on the responses to CHMP adopted questions during the evaluation within the centralised procedure should be explicitly allowed as a possibility. * In addition to these meetings, EFPIA believes that in order to facilitate maintenance of the accelerated assessment timetable, both regulators and applicants would benefit from having more flexibility in this approach. For instance, meetings before the adoption of the list of questions may be particularly important to retain an accelerated clock.   Proposed changes:  Insertion after line 161  “In order to allow for clarifications between the CHMP (Co-) Rapporteurs, the EMA and the applicant, the applicant may contact the EMA Procedure Manager at any time during the procedure to request a meeting with the CHMP (Co-) Rapporteurs. A clarification meeting is particularly recommended after the adoption of the CHMP Day 90 or Day 120 List of Questions (See further guidance in EMA/636600/2014): These meetings are intended to discuss with the applicants their response strategy and the potential need to adjust the response timelines, ahead of the formal response submission within the legal timeframe.  The applicant may consider requesting a similar meeting at any other stage of the review, upon justified reasons being accepted by the (Co-) Rapporteurs. For instance, a meeting before the adoption of the list of questions may be particularly important to retain an accelerated clock. Applicants should carefully consider the appropriateness to request such meetings” |  |
| 164-175 |  | Comment:  Section 5.3 could be strengthened to recognize the careful weighing of unmet medical needs of patients and major public health interest. The currently stated examples suggest that at any time in the accelerated assessment the application could be switched to a standard timeline without weighing the impact on patients.  It would be welcomed if the guidance could clarify several aspects relating to switch to a ‘normal’ timeline:   * Clarification under which conditions a switch triggered by an inspection would occur. * EFPIA suggests that in general, the accelerated assessment timetable should still be maintained in the case of an oral explanation (OE). Yet, in such cases, it appears that the EMA reserves the right to switch automatically to a standard timetable. While this makes sense when applicant cannot respond in time to questions, in case of an OE, which is the final step of the procedure, it seems unrealistic to switch to a standard timetable, unless any major objections following the OE are remaining.   Proposed change (if any):  *Line 164-173* “However, at any time during the marketing authorisation application assessment, if after weighing the impact on the unmet medical needs of patients, the CHMP considers that it is no longer appropriate to conduct an accelerated assessment, the CHMP may decide to continue the assessment under the standard centralised procedure assessment timelines, following an appropriate timetable to be adopted by the CHMP, according to Article 6 (3) of Regulation (EC) No 726/2004.  Examples of such situations are when major objections have been identified that cannot be handled in an accelerated timetable, when a longer clock-stop ~~longer~~ is requested by the applicant (e.g. to prepare for the oral explanation), or when the need for GMP or GCP inspection becomes apparent. Similarly, in case of a negative trend following the oral explanation, the CHMP may decide to continue the assessment under standard assessment timelines.  After discussion with the applicant, the new timetable will be communicated to the applicant. In any case, the CHMP will explain the reasons for the change to the assessment timetable, including how the impact on the previously agreed major public health interest of the accelerated assessment has been considered in making this change.”  Further clarification under which conditions a switch triggered by an inspection would occur. |  |
| 176 |  | Comment:  The guidance is no longer using the term “normal” but instead “standard” assessment procedure.  Proposed change:  “The applicant may also submit a justified request for a change to a standard assessment procedure, for example if additional time is needed for the applicant to provide any information requested by the CHMP.” |  |
| Section 6: 181-229 |  | Comment and Proposed change:  EFPIA welcomes the introduction of (additional) reduced timelines and would appreciate further clarifications on the procedural timetable, given its importance for the applicant’s planning:   * Inclusion of timelines for circulation of rapporteurs briefing note to CHMP and for CHMP discussion and conclusion on the request for accelerated assessment, draft assessment reports (CHMP Rapporteurs and PRAC), clarification meetings, translations are included in the timetable. * Currently applicants receive the draft rapporteur assessment reports at day 80. In order for the applicant to be able to rapidly address potential questions and as such minimise the need for a clock-stop, applicants should receive the preliminary assessment report before the opinion or list of questions at day 90. The guidance should include a timetable for this.   The procedural timetable for accelerated assessment should be made public with all other procedural timetables. |  |
| 182-192 |  | Comment:  Notify the intention to submit a request for accelerated assessment as in the official letter of intent, if possible. See also comments on Line 120-121.  With regards to the timing of submission to the marketing authorisation application see comments on line 136-140.  Proposed change:  Line 184  Align wording on between line 183-184 and 122, in particular on “intent/notification of intent” and “letter of intent”  Line 186-187 Alignment needed with line 136-140 (see comments for those) |  |
| 198 |  | Comment:  The proposed assessment timetable (90-day) is an improvement compared to the current accelerated assessment timetable. The evaluation phase is more balanced with two time points for responses (D90 and D120) to questions, which improves the chances for an opinion at D120 and D150. Additional clarity on when the draft (Co-) Rapporteur assessment reports are available for the Applicant and when PRAC is involved in the initial assessment would be welcome. As an alternative for point 2 and seen the short timelines also for Applicants to respond, the list of questions on the different modules is usually sent at once, in totality, to the applicant. EFPIA believes that for AA as soon as a set of questions is finalised for each separate module, it could be sent to the applicant to allow work on the responses to be initiated as soon as possible. The date of the last set of questions sent to the applicant should be the actual starting the clock-stop.  Proposed change:  D80: PRAC list of questions and draft Rapporteur and Co-Raporteur’s list of questions to be sent to the applicant by the EPL (cc PM, Rapporteur, co-Rapporteur) |  |
| 193-219 |  | Comment:  There is no indication as to when a GMP or GCP request for inspection may be received by the applicant and when the inspection would occur during the accelerated assessment. An indication as to when this may occur could be added. |  |
| 219 |  | Comment:  Considering the recent guideline (May 2015) on the pre-opinion technical labeling review, the Technical Labeling Review comments will be incorporated into the scientific comments; a single set of comments will be sent to the applicant as part of the list of questions at Day 120.  Both types of comments are to be taken into account when submitting the revised EN product information as part of the responses to the list of questions at Day 121.  Upon receipt of the revised EN product information at Day 121, the Agency will review the implementation of the Technical Labeling Review comments by the applicant and will forward the revised EN product information to all QRD members for comments (via written procedure) by Day 140 as well as to representatives of Patients’ and Consumers’ Organizations and the EMA medical writers.  The Day 140 Technical Labeling Review comments will be incorporated into the scientific comments and a single set of comments will be sent to the applicant as part of the Day 150 set of documents.  Proposed change:  Clarification that this process will also be applicable in case of an accelerated assessment while including an earlier PIQ/QRD feedback. |  |
| 224-226 |  | Comment: “In case of ATMP, the timetable would be arranged...”  The guidance document acknowledges the assessment needed by the CAT committee. It would be helpful to mention that this is done within the possible accelerated CHMP opinion timetable.  Further, EFPIA would welcome an integrated approach not only for ATMPs but also when product assessments need the intervention of other assessment committees such as COMP for ‘significant benefit’, PDCO, (…).  Proposed change:  “In case of involvement of other assessment committees such as Advanced Therapy Medicinal Products (CAT), COMP, PDCO, ( …) the timetable to possible accelerated CHMP opinions would be arranged to include the review by these Committees.”” |  |

Please add more rows if needed.