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Best practice guide on measures improving predictability of submissions/responses and adherence to communicated submission/responses deadlines

This best practice guide has been developed for Applicants / Marketing Authorisation Holders (MAHs) and Regulatory Agencies to optimise the operation and functioning of Mutual Recognition (MRP), Decentralised (DCP) and Centralised (CP) procedures relating to medicinal products for human and veterinary use. Compliance with the principles defined in this best practice guide, will enable both the Regulatory Agencies and Industry to improve workload planning and resourcing of relevant procedures for the benefit of patients/animals, to ensure their timely access to new medicines.

In particular it is intended to provide guidance on initial Marketing Authorisation Applications (MAA) submission dates, receipt of preliminary / draft assessment reports, draft List of Questions (LoQ) and/or draft List of Outstanding Issues (LoOI), LoQ/LoOI and responses to those.

Lack of compliance with initially communicated submission dates for initial MAAs, LoQs and/or LoOIs has been observed. Regulatory Agencies need to ensure that the relevant resources and expertise are available at the time of submission, which is of particular importance when dealing with very specialised/novel applications or veterinary applications where only a small number of individuals in the Network are available or have the appropriate expertise to undertake the work. Furthermore, deviations from communicated timetables may also be more difficult to manage when resources are scarce during certain periods and only short notice has been given.

Similarly for companies, the timing of receipt of (draft) assessment reports for new MAAs or (draft) LoQs/LoOI may create difficulties in resource and workload planning. Delays in the receipt of such reports can then affect the timing of the responses and could also have an impact on the time of approval and subsequent launch of a product. Additional elements such as the availability of experts and assessors in the National Competent Authorities (NCAs) and the number and clarity of questions may further affect the timing of responses.

Overall, it can be concluded that frequent and timely communication by both companies and Regulatory Agencies is key for ensuring adherence to deadlines and allow for any necessary adjustments. It is evident that better adherence to time tables is beneficial for all parties involved.

In order to improve predictability, adherence to initially communicated submission deadlines and procedural timelines to ensure the efficient functioning of the EU Network the following principles have been mutually agreed between the Regulatory Agencies and representatives of industry stakeholder associations. Both parties agreed to adhere and apply these principles across their respective organisations.



Industry

Initial MAAs submissions

1. Proposed submission dates communicated to EMA/NCAs for initial MAAs should be realistic and based on the most likely timing of completion of the application dossier, and should avoid being overly optimistic.
2. In the centralised procedure, submission dates communicated to the EMA/NCAs at the eligibility stage (and with requests for appointment of Rapporteurs, if applicable) will be re-confirmed 2-3 months prior to the initially communicated intended submission dates, to either confirm that the application will be submitted according to the previously agreed submission date or to inform the EMA/NCAs about any delay in submission or cancellations.
3. Prior to submitting an application applicants are advised to engage in early dialogue with the EMA/NCAs at the pre-submission stage. If appropriate, pre-submission meetings will be requested well in advance of the intended submission date to ensure there is sufficient time to update the application dossier in line with the regulatory guidance received. For advice relating to scientific aspects, scientific advice should be sought at EMA/NCAs.
4. Data submitted in support of an application should be sufficient to fully support dossier requirements or in line with discussions at pre-submission meetings, the legal basis of the submission and the proposed product information.
5. In addition, if at any time prior to submission, it becomes apparent that the initially indicated submission date for an initial MAA will not be met, this will be communicated to the EMA/NCAs as soon as possible. The reasons for the delay of the submission date and a proposal for an alternative submission date (based on realistic timings) will be communicated to the EMA/NCAs. Likewise, the reason for any cancellation of an intended submission will be communicated in a timely manner.
6. If an intended submission date is not met, a discussion should be initiated with the EMA/NCAs to assure the availability of assessment teams and explore the need for an adjustment of the submission date.
7. Failure to communicate changes to submission timelines or submission of applications outside the communicated and agreed timelines without prior agreement may require an amendment to the procedural timetable.

Responses to LoQ/LoOI

8. Upon receipt of the preliminary assessment reports, the applicant will inform the EMA/RMS of the intended timelines for the submission of their responses. Applicants (for DCP/CP procedures) will confirm the preliminary date as soon as possible and not later than within 2 weeks after receipt of the final LoQ/LoOI.
9. The date given by the applicant for responding to the LoQ/LoOI will be based on realistic timings and allow the applicant to compile a complete response to all questions (after the analysis of the LoQ/LoOI within their company/product teams).

10. Incomplete/partial responses to LoQ/LoOI should not be submitted, unless otherwise agreed with the EMA/RMS. Submission of additional responses and/or data after the deadline for submission of responses (during the assessment) should be avoided.
11. If the submission date proposed by the applicant for their responses to the LoQ/LoOI (as indicated within 2 weeks of their receipt of the final LoQ/LoOI) is not met a revision of the timetable will need to be discussed with the EMA/RMS
12. Any request for an extension of the clock-stop will be submitted as soon as possible to facilitate appropriate planning.
13. If clarification of any question is required, this should be limited to clarification of the question(s) and/or discussion on the applicant's approach to responding to questions but should not be used to pre-assess the responses.

Regulatory Agencies

1. EMA/NCAs will ensure the early appointment of contact points within their organisations (e.g. Procedure/Project Managers) to facilitate discussion with applicants, including updates on the status of procedures.
2. For procedures where the booking of submission slots is required:
 - procedures will be transparent and the booking process will be explained, e.g. on NCA's websites
 - in case of cancellation the slot will be allocated to another applicant, whenever feasible for the NCA
3. EMA/NCAs will facilitate the organisation of pre-submission meetings and the provision of regulatory guidance relating to the submission dossier. Such meetings will be organised well in advance to enable discussion on the intended submission date and to ensure that applicants have sufficient time for updating/revising their submission dossier in line with the regulatory guidance received.
4. EMA/RMSs will make every effort to ensure that preliminary/draft assessment reports, assessment reports and CMS comments are circulated on time and that any potential delays are promptly communicated to applicants and Concerned Member States (CMS), in case of MRP/DCP procedures.
5. EMA/NCAs will ensure that any comments/questions in the assessment reports are clear and unambiguous (accurately capture the concerns raised).
6. EMA/NCAs will make every effort to ensure that after adoption/completion of LoQs and/or LoOIs additional late questions or late proposed changes to the SmPC are avoided.
7. If clarification of any questions is required, the contact points at the EMA/NCAs (with the involvement of assessors, when relevant) will ensure that such clarifications are provided to the applicant in a timely manner.