EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use

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

Draft

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This guideline replaces 'Guideline on the procedure for Accelerated Assessment pursuant to Article 14(9) of Regulation (EC) No 726/2004' (EMEA/419127/05).

Comments should be provided using this template. The completed comments form should be sent to AA_guideline@ema.europa.eu

Keywords	***Accelerated Assessment***

Note for the public consultation on this draft revision: The European Medicines Agency is developing a scheme to facilitate development and accelerated assessment of innovative medicines of major public health interest and in particular from the viewpoint of therapeutic innovation to address unmet needs. The criteria for accelerated assessment laid down in this guideline are being considered for the access to this scheme.

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Executive summary

Based on the experience gathered by reviewing the approach taken to the assessment of past applications since the last version of the guideline in July 2006, it became apparent that some areas of the guideline would benefit from further clarifications, in particular with regards to the justifications provided by the applicant that the medicinal product falls within the scope of the accelerated assessment.

1. Introduction

Recital 33 of Regulation (EC) No 726/2004[1] states that "in order to meet, in particular the legitimate expectations of patients and to take account of the increasingly rapid progress of science and therapies, accelerated assessment procedures should be set up, reserved for medicinal products of major therapeutic interest, and procedures for obtaining temporary authorisations subject to certain annually reviewable conditions".

Article 14 (9) of Regulation (EC) No 726/2004, states that "when an application is submitted for a marketing authorisation in respect of medicinal products for human use which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. The request shall be duly substantiated.

If the Committee for Medicinal Products for Human Use (CHMP) accepts the request, the time limit (of 210 days to give an opinion) laid down in Article 6(3), first subparagraph, shall be reduced to 150 days"

The accelerated assessment procedure is applicable to marketing authorisation applications for medicinal products for human use falling within the scope of articles 3(1) and 3(2) of Regulation (EC) No 726/2004. This includes medicinal products for treatment, prevention or diagnosis.

Recital 7 of Regulation (EC) No 507/2006[2] states that "applications containing requests for conditional marketing authorisations may be the subject of an accelerated assessment procedure in accordance with Article 14(9) of Regulation (EC) No 726/2004".

2. Scope

The scope of this guideline is to provide applicants with guidance on the accelerated assessment request and the practical arrangements necessary to implement the legal provisions on the accelerated assessment procedure. It forms the basis for requesting an accelerated assessment, and should be followed unless otherwise justified. This guideline has to be read in conjunction with Notice to Applicants (Eudralex Volume 2), as well as other pertinent EU guidelines.

3. Legal basis

This guideline has been developed in accordance with Article 14 (9) of Regulation (EC) No 726/2004 which refers to marketing authorisation applications for medicinal products of a major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation.

[1] OJ L 136, 30/4/2004 p. 1 - 33.
[2] OJ L 92, 30/3/2006 p. 6 – 9.

4. Justification that the medicinal product falls within the scope of the accelerated assessment

Based on the legislation, a medicinal product of major public health interest may be reviewed under an accelerated assessment procedure. However, there is no single definition of what constitutes major public health interest. This should be justified by the applicant and assessed by the CHMP on a case by case basis. 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. It is noted that a new mechanism of action or a *technical* innovation *per se* may not necessarily represent a valid argument for justifying major interest from the point of view of public health.

The items to be described in the justification, and the appropriate level of detail, should be evaluated on a case-by-case basis. The request should be presented as a short but comprehensive document (ideal length of 5-10 pages). The following aspects could be considered, as appropriate, in the justification:

- The unmet medical need and the available methods of prevention, diagnosis or treatment. In general, the justification may be more convincing if based as much as possible on epidemiological data about the disease (e.g., life expectancy, symptoms and duration, health-related quality of life). The claims could be substantiated e.g., from published literature or registries. If relevant, the unmet medical need could be described separately for different indications or subpopulations. In addition, a description of the available treatment options/standard of care (SOC), including all relevant treatment modalities, e.g., medicinal products used in clinical practice (whether approved or not), devices, surgery, radiotherapy could be included. The effect of available treatments could also be described together with a description of how the unmet medical need is not fulfilled by the available treatments.
- The extent to which the medicinal product is expected to fulfil the unmet medical need. This could include a description of the medicinal product's effects, their importance, the added value of the medicinal product and its impact on medical practice. This could include benefits and risks based on traditional efficacy and safety endpoints or other health outcomes (e.g., patient-reported outcomes, number of hospitalisations).
- The strength of evidence to support justifying major interest from the point of view of public health, for example the available evidence to establish that the product fulfils an unmet medical need, taking into account the regulatory requirements applicable for the intended application. It is acknowledged that in a number of situations (e.g., within the context of a conditional marketing authorisation) that comprehensive clinical data may not be available. The description of the strength of evidence could include a brief outline of the main available evidence (e.g., number and types of clinical trials, sample size, design and key results) on which the applicant bases its claim of addressing a major public health interest.

5. General considerations regarding the granting of an accelerated assessment procedure

5.1. Pre-submission dialogue

The applicant is strongly advised to proactively enter into dialogue in order to prepare for an evaluation under accelerated assessment. When preparing the submission of a marketing authorisation

application, applicants have the opportunity to contact the PM to discuss relevant procedural or regulatory issues on the proposed submission. In view of a potential request for accelerated assessment, applicants should seek guidance from the PM to ensure timely submission of their request.

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.

It is strongly recommended that the applicant requests pre-submission meetings with the Rapporteurs and EMA as early as possible, to discuss details of the upcoming accelerated assessment procedure including the available data package. The pre-submission meeting might be a joint meeting with Rapporteurs and the EMA product team attending. 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. The rapporteurs might then advise on the submission strategy for the marketing authorisation application. It should be noted that applications should be mature in terms of the data submitted at the start of the evaluation, and that the planned submission timing is to be respected.

5.2. Timing of the request for an accelerated assessment and general considerations

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. This is to allow the relevant evidence to be included into the justification (see 4). In practice, the request should be submitted 2-3 months before the actual submission of the marketing authorisation application in order to allow sufficient time for its assessment.

The applicant should ensure that the indicated date for submission of the Marketing Authorisation Application is accurate for planning purposes as changes to the date might impact availability of assessment teams.

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 information relevant information with the request for accelerated assessment to allow identifying such need.

The request (consisting of the form and the justification) should be sent electronically. For procedural details please refer to the pre-authorisation guidance. It is recommended to copy the PM in the correspondence.

Depending on the applicant's submission date, the PM will set a timetable for the assessment of the request.

The Rapporteurs will produce a briefing note including the Rapporteurs' recommendations as to the appropriateness of an accelerated assessment.

Based on the request, the argumentations provided, and the recommendations of the Rapporteurs, the CHMP will take a decision on the request for accelerated assessment. If necessary, the CHMP may request clarifications from the applicant about the request.

The CHMP conclusion will be communicated to the applicant. The reasons for accepting or rejecting the request will also be summarised in the final CHMP assessment report of the marketing authorisation.

A decision on accelerated assessment will be taken without prejudice to the CHMP opinion (positive or negative) on the granting of a marketing authorisation.

5.3. Possible change to standard timetable

Following the granting of a request, the CHMP shall adhere to the accelerated timetable in accordance with Article 14(9) of Regulation (EC) No 726/2004 for the assessment. However, at any time during the marketing authorisation application assessment, if 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.

The new timetable will be communicated to the applicant. Where appropriate, the CHMP will explain the reasons for the change to the assessment timetable.

The applicant may also submit a justified request for a change to a “normal” assessment procedure, for example if additional time is needed for the applicant to provide any information requested by the CHMP. The CHMP shall consider such requests on a case-by-case basis and if appropriate adopt a revised timetable following Article 6 (3) of Regulation (EC) No 726/2004. The new timetable will be communicated to the applicant.

6. Timetable for the accelerated assessment procedure

6.1. Pre-submission phase

– 6 – 7 months before the actual submission of the marketing authorisation application: Notify the intention to submit a request for accelerated assessment as part of the letter of intent.

– Pre-submission meetings with the Rapporteurs and the EMA

– 2 – 3 months before the actual submission of the marketing authorisation application: Submission of request for accelerated assessment:

- Circulation of Rapporteurs’ briefing note to the CHMP with recommendations on the request for accelerated assessment.
- CHMP discussion and conclusion on the request for accelerated assessment. The conclusions are communicated to the applicant at the end of the CHMP meeting during which the request was discussed.

6.2. Accelerated assessment procedure

– Day 1 Start of the procedure.

- CHMP Rapporteurs’ assessment reports
- PRAC Rapporteur updated assessment report
- Peer-review phase

– Day 90 CHMP week with adoption of either:

- CHMP positive opinion or;
- CHMP list of questions to the applicant to be addressed in writing and at an oral explanation if necessary with maintenance of the accelerated timetable. The CHMP may also adopt questions for a Scientific Advisory Group, as applicable; or
- CHMP list of questions to the applicant to address in writing and at an oral explanation if necessary with switch to a standard timetable (see 5.2).

– Stop of the clock: One month stop of the clock by default.

– Day 91 Restart of the clock by submission of the applicant's written responses.

- CHMP and PRAC assessment report of the responses

– Day 120 CHMP week with either:

- CHMP positive opinion or;
- CHMP list of questions to the applicant to address in writing if necessary with maintenance of the accelerated timetable.
- CHMP list of questions to the applicant to address in writing and at an oral explanation if necessary with switch to a standard timetable (see 5.2).

– No Stop of the clock: The CHMP would request the submission of the written responses without clock-stop

– D121 Submission of written responses

- CHMP and PRAC assessment report of the responses

– Day 150 CHMP opinion

Applicants are reminded of the importance in complying with their intended submission date of the application as any unexpected delay may considerably impact the CHMP and PRAC Rapporteurs' team organisation in handling the procedure under the accelerated timetable. Any changes to the submission time should be communicated promptly to the Agency.

In case of Advanced Therapy Medicinal Products, the timetable would be arranged to include the review by the Committee for Advanced Therapies. Also a request for accelerated assessment would be reviewed by this committee before endorsement of the outcome by CHMP.

In order to allow for adequate evaluation periods the Agency will not initiate any accelerated assessment evaluation with a starting date in December.

Definitions

CHMP: Committee for Medicinal Products for Human Use

EC: European Commission

EMA: European Medicines Agency

EU: European Union

GCP: Good Clinical Practice

GMP: Good Manufacturing Practice

MAA: Marketing Authorisation Application

SAG: Scientific Advisory Group

SOC: Standard of Care

PM: Procedure Manager