DG Pre Marketing Authorisation

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FAMHP advice in function of procedures for clinical trials and marketing authorisations

Discussion paper 5.0

Introduction

Due to the introduction of the national scientific/technical advice procedure, there is a greater need to establish a clear distinction between situations where:

1) the FAMHP advice is possible according to the application procedures for clinical trials (initial application or amendment) or for marketing authorization (granting or variation)

2) the scientific/technical advice procedure must be followed

This document defines the possibilities and conditions for advice according to the application procedures for clinical trials and MA. This advice may fall under the following categories:

a) Pre-submission Meeting
b) Discussion of proposal responses during the procedure
c). Explanation of specific questions asked by the FAMHP
d) Consultation Regulatory Planning
e) Meetings Portfolio

Requests for advice that do not meet these conditions must be treated in accordance with the formal scientific advice procedure (provided they do fall within the legal scope of scientific/technical advice).

The Royal Decree of 16.07.2012 in modification of the Royal Decree of 31.03.2009 applies to requests for scientific and technical advice addressed to the FAMHP in accordance with Article 6sexies of the Law of March 25, 1964 on medicines:

- either the scientific issues regarding research and development
- or the technical issues in Belgian and European legislation insofar as it appears from the response that the existing legislation and regulations are insufficient in the current state of scientific knowledge

Are excluded from the scope of this RD:

- the interpretation of existing European or national legislation and regulations
- the ad hoc advices linked to divergences between the medicines legislation in Belgium and at European level

There are different possibilities for consultations based on the application procedures for clinical trials or for the marketing authorisation. They are discussed below. On the occasion of such consultations, attention may be drawn to the existence of the scientific/technical advice procedure.

This document does not aim to analyze the practical organization of these various consultations. This must be defined in specific procedures. Several divisions of the FAMHP may be involved. During the discussion on a new application for marketing authorization, for example, the PRE MA Division is responsible while the division “POST MA” take the initiative in the discussion on a variation application. In both cases, the division “Vigilance” may also be involved in the evaluation system of vigilance. For specific GMP issues, it can for example be necessary to involve in the consultation the division “Industry” of the DG “Inspection”.

Discussion

a) Pre-submission meetings

For a clinical trial application

Pre-submission meeting before submitting a CTA file concerning a medicinal product containing genetically modified organisms (GMOs):

Since the procedure is complex and involves the review of the Biosafety Council in the event of deliberate release into the environment (Royal Decree of 21 February 2005), this pre-submission meeting is recommended by the division "R & D" but is not mandatory.

Wherever possible, the concerned firm provides a draft of the CTA dossier and a dossier concerning the biosafety aspects before the meeting.

For a MAA

Such meetings are normally accepted only for dossiers (new applications, line-extensions or variations) for which Belgium is RMS within a mutual recognition procedure (MRP) / decentralized procedure (DCP) or for which Belgium is (co-)rapporteur within a centralized procedure (CP).

The pre-submission meeting takes place after the FAMHP has confirmed that it will act as RMS or after the CHMP has assigned the dossier to the Belgian (co-) rapporteur.

In exceptional cases, for example, if differences exist between existing legislation and / or guidelines and after approval of the Board office of the Medicines Commission, a pre-submission meeting may be accepted for a national application for marketing authorization.

The pre-submission meeting must contribute to the success of the procedure for MA variations applications. We must avoid that the preparation of the pre-submission meeting requires a scientific study by the assessors that the investment is not adequately offset by greater efficiency of the evaluation work (saving of time) during the procedure.

To ensure the effectiveness of the pre-submission meeting, the company is asked to forward in time to the FAMHP the draft of the agenda and relevant documents (eg a presentation, a draft of SPC, specific points of discussion, etc..). The company is asked to prepare a report of the meeting which is then corrected / validated by the FAMHP. A SOP that describes this in more detail is in preparation.

A pre-submission meeting for an MRP / DCP where Belgium is CMC is with difficulty defensible since the issues or potential problems must be addressed by the RMS. In this case, the formal national scientific / technical advice procedure can be used to prepare an MRP / DCP procedure where Belgium is CMS.

b) Discussion of questions /draft of responses during the procedure

For a clinical trial application

In rare cases, if the expert wishes to meet the firm to ensure that his questions were well understood or if the firm makes the request and that it was acceptable to the R&D division, a meeting or a teleconference for clarification on the GNA (Grounds for Non Acceptance) will be organized. This approach, however, must remain an exception.

A meeting with the firm could also be organized where the answers given by it to the request for additional information is not satisfactory. It should however be limited to special cases (eg. the failure to the authorization would be harmful to patients) because only a single round of questions is authorized by the Law of May 7, 2004 relating to experiments on human.

For a MAA

The MRP, DCP and CP provide that the draft response of the firm should be discussed with the RMS or rapporteur.

In exceptional cases, it is acceptable for a national marketing authorization application (new application, line-extension or variation) that the draft response should be discussed with the firm. Such a discussion may for example be appropriate if this leads to more efficient treatment of official responses (saving of time for evaluators) or in the case of very urgent procedures.

The discussion takes place after the full draft response had been introduced and that the evaluators have had sufficient time to study this draft. When Belgium is CMS in a MRP or DCP, a draft response can only be discussed at the request and in consultation with the RMS (eg when the arbitration is required).

c) Explanation of specific issues raised by the FAMHP

The firm may submit a request for clarification on specific issues that were raised by the FAMHP.

In this case, the dossier manager, the assessor and if necessary the scientific coordinator work together to decide if further explanations are indeed useful. Explanations are recommended if this contributes to the effective completion of the procedure. The explanations are usually given in writing (not meeting).

An explanation of issues is possible in all procedures.

d) Regulation concertation planning

For a clinical trial application

It may be useful for a firm to come present his submission program of clinical trials (eg. phase 1) to the division R & D of the FAMHP to agree on the planning.

This will allow efficient processing of the applications and an efficient organization of the work planning of the division, because the time limits for the dossier's processing are very short.

If an applicant submits many files repeating the same error(s) or does not clearly respect the recommendations of the Circular 528 relating to the submission of CTA dossiers, an interview may be arranged on request of the Division R & D in order to clarify the situation.

For a MAA

If a firm considers the introduction of several applications, it may be useful for FAMHP or for the client beforehand to consult together on the planning of the submissions. The initiative for the meeting may be taken by the client or by the FAMHP.

This may for example relate to different variations for a same product and to different products in a range of products and different procedures.

The planning meetings can be accepted if the dossier's managers and / or assessors estimate that this contributes to greater efficiency in the following of the procedure or whether it allows a more efficient planning work within the FAMHP.

e) Portfolio meetings

During a portfolio meeting, the company presents the products in development and for which a marketing authorization application could eventually be introduced.

The portfolio meetings are important for the identification of interesting products for which the FAMHP would assume the role of RMS or (co-) rapporteur, for example in the policy of spearheads.

If during the portfolio meeting, the company is looking for answers to specific questions related to the product development program, we must refer for the treatment of these questions to the procedure for national scientific-technical advice requests.