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Informed consent applications in mutual recognition and decentralised procedures

Recommendations

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1. Introduction

The scope of this document is to facilitate and harmonise the regulatory issues for submission of informed consent applications in mutual recognition procedure (MRP) and decentralised procedure (DCP).

2. Legal framework

Article 10c of Directive 2001/83/EC as amended:

"Following the granting of a marketing authorisation, the authorisation holder may allow use to be made of the pharmaceutical, preclinical and clinical documentation contained in the file on the medicinal product, with a view to examining subsequent applications relating to other medicinal products possessing the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form".

Notice to Applicants - Volume 2A, Chapter 1, Section 5.6

"It is a prerequisite for the use of Article 10c that consent has been obtained for all three modules containing the pharmaceutical, preclinical and clinical data. It is not possible to use Article 10c as legal basis for an application consisting of the applicant's own module 3 and for which consent has been given for modules 4 and 5. In such case the legal basis for the application is Article 8(3)."

3. Definition of the reference product and informed consent applications

3.1. The reference product

For the purpose of the mutual recognition procedure and the decentralised procedure, the CMDh has agreed that the reference product is defined by a marketing authorisation holder (MAH) and a marketing authorisation for a medicinal product supported by a complete dossier.

Consequently, the marketing authorisation for the reference product cannot be based on an Article 10 application.

The concept of "reference medicinal product" is laid down by Article 10 of Directive 2001/83/EC as amended and is applicable in case of applications in accordance with Article 10. It does not apply in the context of applications under Article 10c. Therefore, when the term "reference product" is used throughout this guidance it should not be mistaken for "reference medicinal product" in the context of abridged applications according to article 10.

3.2. Informed consent applications

An informed consent application is an application according to Article 10c of Directive 2001/83/EC as amended.

- The marketing authorisation holder for the reference product has consented that the applicant could refer to all three modules containing the pharmaceutical, preclinical and clinical data for the reference product.

- The medicinal product applied for must have the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form as the reference product.
- It is not possible to use Article 10c for an application with the applicants own data for module 3 and for which consent has been given only for module 4 and 5.
- An informed consent application can only be submitted in Member States where the reference product is already authorised (valid marketing authorisation), i.e. the informed consent application cannot be submitted in parallel to the application for the reference product.
- The authorisation of the informed consent application should follow the same authorisation route as the initial authorisation. Therefore a national, MRP or DCP informed consent application cannot refer to a centralised approved medicinal product cf. Commission Communication 98/C 229/03 and Commission Notice 'Handling of duplicate marketing authorisation applications of pharmaceutical products under Article 82(1) of Regulation (EC) No 726/2004' (2021/C 76/01).
- The applicant for the informed consent product must during the lifetime of the product have permanent access to the references in the documentation for the reference product or be in possession of this information.
- If an Active Substance Master File has been used for the reference product a new letter of access should be included in the application for the informed consent product.
- The applicant could be the same as the marketing authorisation holder for the reference product or not.
- The two products must have different trade names.
- The informed consent application is not legally obliged to cover all pharmaceutical forms/strengths of the reference product.

4. Dossier requirements

The applicant is advised to contact the relevant national competent authorities regarding dossier requirements.

In case other modules than module 1 are submitted according to the requirements of the relevant national competent authorities, these other modules have to be identical with the reference product dossier.

Member states that only require Module 1 accept the submission of Modules 1-5, in case other Member states concerned in the procedure have this as national requirement.

5. Guidance for different situations

In principle, two different situations are possible when an applicant wishes to obtain a marketing authorisation for a product by submitting an application based on article 10c in Directive 2001/83/EC as amended.

For guidance in the situation where the reference product is authorised through MRP/DCP see section 5.1.

For guidance in the situation where the reference product is authorised through purely national procedure see section 5.2.

5.1. The reference product is authorised through MRP/DCP

5.1.1. Purely national procedure in the RMS of reference product A

An informed consent application for A' can be submitted nationally in the Reference Member State for the reference product A.

The MAH could choose to stay nationally with this authorisation in the actual Member State.

5.1.2. Mutual recognition/Decentralised procedure with same RMS as for reference product A

An MRP or a DCP for A' could be initiated with the same Reference Member State as for A in all or some of those Member States, which are Concerned Member States for A.

5.1.3. Purely national procedure in a CMS of reference product A – same (or linked) applicant as the MAH of reference product A

A' is applied for via purely national procedure in a Member State, which is a Concerned Member State for A.

A national procedure cannot be accepted.
According to article 18 of Directive 2001/83/EC, as amended the authority shall reject the application unless it was submitted in compliance with Articles 27 to 39, as A' is possessing the same qualitative and quantitative composition in terms of active substances to A, which is already authorised by the same (or a linked) company in other Member States.

The applicant will have the opportunity to withdraw the application and to submit an application according to article 28 of Directive 2001/83/EC, as amended. However, this will have one of the following consequences:

- Scenario 1: If the applicant withdraws the national application and submits an application for a mutual recognition procedure according to article 28 of Directive 2001/83/EC as amended with a dossier identical to the dossier submitted for A, the application for A' should refer to a marketing authorisation in the Reference Member State for A.

  It is not possible for the Concerned Member State to recognise more than once the marketing authorisation granted for A in the Reference Member State.

- Scenario 2: If the applicant does not withdraw the national application, article 18 of Directive 2001/83/EC as amended has to be triggered and the application will be rejected by the competent Authority.

  When the applicant submits a dossier corresponding to the dossier assessed by the Reference Member State for A, the result will be as described under Scenario 1.

  In the case the applicant does not submit a dossier, which corresponds to the dossier assessed by the Reference Member State, the Concerned Member State could consider the application as invalid.

5.1.4. Purely national procedure in a CMS of reference product A – different applicant compared to the MAH of reference product A

When the applicant is independent of the MAH for the reference product A then informed consent product A' can be applied for nationally in a Member State which is a Concerned Member State for the reference product A, and a marketing authorisation can be granted in this Member State, provided that the A' application has not been submitted/approved in other Member States with the same applicant/MAH.

The MAH could choose to stay nationally with this informed consent authorisation in the actual Member State.

5.1.5. Mutual recognition procedure – following national procedure in a CMS of reference product A

Mutual recognition procedure

A mutual recognition procedure for A' could be initiated with this Member State as Reference Member State (RMS2) for A' in some of those Member States, which were Concerned Member States for the reference product A.

5.1.6. Decentralised procedure - RMS is a CMS for reference product A

Decentralised procedure

Provided that A' hasn't been applied for nationally in a MS, a DCP can be initiated for A' with any of the concerned Member States for A as acting RMS, however it is recommended to use the RMS for A whenever feasible.

Note: In case of a mixture of national and mutual recognition procedures for A before 1998, a national submission of the first informed consent application for A' is possible in any Member State where a marketing authorisation for A was granted, either nationally or following a mutual recognition procedure. The second application for A' will then follow a mutual recognition procedure. Alternatively, a DCP can be initiated for A' with one of the Member States acting as RMS.

5.2. The reference product is authorised through purely national procedure

The reference product is authorised nationally (application submitted before January 1, 1998) in some Member States.

5.2.1. Purely national procedure in one of the Member States

Purely national procedure in one of the Member States

An informed consent application for A' can be submitted nationally in one of the Member States, where A is already authorised.

5.2.2. Mutual recognition procedure

Any subsequent applications for A' in other Member States submitted by the same (or a linked) marketing authorisation holder should follow the mutual recognition procedure.

5.2.3. Decentralised procedure

An informed consent application can be started for A' with one of the Member States where A already is authorised acting as RMS.

It should be confirmed by the applicant that the pharmaceutical, preclinical and clinical documentation in the dossiers for A, which are referred to in the application for A', are identical in the Concerned Member States. If this is not the case the authority in the Concerned Member States could consider the application for A' as invalid.

Note: In case of a mixture of national and mutual recognition procedures for A before 1998, a national submission of the first informed consent application for A' is possible in any Member State where a national marketing authorisation for A was granted or in the Reference Member State for the mutual recognition procedure. The second application for A' will then follow a mutual recognition procedure. Alternatively, a DCP can be initiated for A' with one of the Member States acting as RMS.

6. Maintenance of the dossier following granting of the informed consent marketing authorisation

A marketing authorisation based on an article 10c of the 2001/83/EC Directive informed consent application is considered a stand-alone authorisation.

After the marketing authorisation has been granted, the marketing authorisation holder can make changes to the dossier independently of the reference product dossier. There is no requirement that the two dossiers remain identical after approval of the informed consent application, i.e. the informed consent product (A') can over time deviate from the reference product (A).

For any variations all necessary data needs to be submitted with the variation application and classified according to the Variation classification guideline. It is not sufficient to make reference to the reference product dossier.