INFORMED CONSENT APPLICATIONS
IN MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES
RECOMMENDATIONS

Doc. Ref.: CMDh/070/1999/Rev3
September 2010
April 2015

This document was produced by the CMDh in order to facilitate and harmonise the regulatory issues for submission of informed consent applications in mutual recognition procedure and decentralised procedure.

I Legal framework: Extracts from European legislation

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 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 module 4 and 5. In such case the legal basis for the application is Article 8(3).”

II Definition of the Reference product and Informed consent applications

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 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.

2. Informed consent application

An Informed consent application is an application according to Article 10c of Directive 2001/83/EC as amended.
- The marketing 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 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 authorised, i.e. the 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 EC note “Handling of Duplicate Marketing Authorisation Applications” of 30.03.2010 (ENTR/F/2/RSReD(2009) 380166.

- The applicant for the second 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 second product.

- The applicant could be the same as the marketing authorisation holder for the reference product or not

- The two products must have different tradenames.

- The informed consent application is not legally obliged to cover all pharmaceutical form(s)/strength(s) of the reference medicinal product.

III Dossier requirement
The applicant is advised to contact the 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.

IV Situation
The same or a different marketing holder wish to obtain a marketing authorisation for a product, which is the same in term of active substances to a product which has already been granted a marketing authorisation in the same Member State(s). The application is an application based on article 10c in Directive 2001/83/EC as amended.

Two different situations should be considered:

1. When the informed consent application is submitted in the Reference Member State;
2. When the informed consent application is only submitted in one or several Concerned Member States.

Situations where the informed consent application is submitted in the Reference Member State

Example 1
The reference product is harmonised by a mutual recognition procedure (MRP) or a decentralised procedure (DCP) in some Member States
National phase in the RMS
An informed consent application for A’ can be submitted nationally in the Reference Member State for A. The company could choose to stay nationally with this authorisation in the actual Member State.

Mutual recognition/Decentralised procedure
A 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.

<table>
<thead>
<tr>
<th>RMS=DE</th>
<th>Inf.cons.</th>
<th>RMS=DE</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>DE/H/135/01</td>
<td>A’</td>
</tr>
<tr>
<td>MAH: X</td>
<td>DE/H/145/01</td>
<td>MAH: X or Y</td>
</tr>
<tr>
<td>CMS=FR</td>
<td>Inf.cons.</td>
<td>CMS=AT</td>
</tr>
<tr>
<td>A</td>
<td>CMS=AT</td>
<td>A’</td>
</tr>
</tbody>
</table>

Example 2
The reference product is authorised nationally (application submitted before January 1, 1998) in some Member States.

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

Mutual recognition phase
Any subsequent applications for A’ in other Member States submitted by the same (or a linked) company should follow the mutual recognition procedure.

Alternatively

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.

1997

<table>
<thead>
<tr>
<th>A</th>
<th>A</th>
<th>A</th>
<th>MAH: X</th>
</tr>
</thead>
<tbody>
<tr>
<td>FR (national)</td>
<td>AT (national)</td>
<td>UK (national)</td>
<td></td>
</tr>
</tbody>
</table>

2006

↑ Inf. cons.

<table>
<thead>
<tr>
<th>↑ Inf. cons.</th>
<th>A’</th>
<th>MAH: X or Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Inf. cons.</td>
<td>AT=RMS</td>
<td>AT/H/44</td>
</tr>
<tr>
<td>↑ Inf. cons.</td>
<td>AT=DE</td>
<td>A’</td>
</tr>
</tbody>
</table>
**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.

**Situations where the informed consent application is submitted in a Concerned Member State**

The reference product has been authorised in several Member States following a mutual recognition procedure or a decentralised procedure. An informed consent application is subsequently submitted in one of the Concerned Member States.

Two situations are described as the applicant for the informed consent application could be:

a) the same (or linked) as the Marketing Authorisation Holder for A or

b) an independent company.

**Situation a)**
The applicant is the same (or linked) as the Marketing Authorisation Holder for A

**Example**
A’ is applied nationally 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 his 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 company 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 company 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.

**RMS=IRL**
**Situation b)**
The applicant is independent of the Marketing Authorisation Holder for A

**Example**

National phase in a CMS
A’ is applied nationally in a Member State which is a Concerned Member State for A, and a marketing authorisation is granted in this Member State.
The company could choose to stay nationally with this authorisation in the actual Member State.

Mutual recognition phase
A mutual recognition procedure for A’ could be initiated with this Member State as Reference Member State (RMS\(_2\)) for A’ in some of those Member States, which were Concerned Member States for the reference product A.

Alternatively

**Decentralised procedure**
Provided that A’ haven’t been applied nationally in a CMS a DCP can be initiated for A’ with any of the concerned Member States for A as acting RMS

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.