This document was produced by the CMD(h)MRDG in order to facilitate and harmonise the regulatory issues for submission of informed consent applications in mutual recognition and decentralised procedures.

**Legal framework: Extracts from European legislation and Commission Communication**

**Article 10.1.a.i) of Directive 2001/83/EC**

“The applicant shall not be required to provide the results of pharmacological and toxicological test or the results of clinical trials if he can demonstrate that the medicinal product is essentially similar to a product authorised in the country concerned by the application and that the person responsible for the marketing of the original medicinal product has consented to the pharmacological, toxicological or clinical references contained in the file on the original medicinal product being used for the purpose of examining the application in question.” 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).”

**Commission Communication C28/2016 of 16 July 1998**

“In case of Article 4 (3) paragraph 8 a) i) (“informed consent”) (now Article 10.1 a i) of Directive 2001/83/EC), the product to which essential similarity is claimed has to be authorised both in the reference and the concerned Member State(s) and essential similarity has to be demonstrated by the applicant in all these Member States (except for cases in which the “original product” has already undergone mutual recognition in the concerned Member States. In such cases the criteria of essential similarity are automatically met). Moreover, the consent of the marketing authorisation holder of the original product has to cover the use of the pharmacological, toxicological or clinical references contained in the file of the original medicinal product in each Member State concerned by the procedure.”

**Definition of the Reference Original product and Informed consent applications**

CMD(h) Recommendations
Informed consent applications in MRP/DCP

Revision 2, July 2006
1. The **Original Reference product**
For the purpose of the mutual recognition procedure and the decentralised procedure, the CMD(h) Member States have agreed that the original 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 original reference product cannot be based on an abridged dossier Article 10c application.

2. Informed consent application
An Informed consent application is an abridged application according to Article 10.1a1c of Directive 2001/83/EC as amended.

- The marketing holder for the original reference product has consented that the applicant could refer to all three modules containing the pharmaceutical, preclinical and clinical data the documentation in part III and/or part IV for the reference original product.
- The product applied for must have the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form be essentially similar to the original product and it might either be identical to the as the original reference product or not.
- 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 original reference product is authorised, i.e. the application cannot be submitted in parallel to the application for the original reference product.
- The applicant for the second product must during the lifetime of the product have permanent access to the references in the documentation for the original reference product or be in possession of this information.
- If an Active substance Master File DMF 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 original reference product or not
- The two products must have different tradenames

**Dossier requirement**
The applicant is advised to contact the national competent authorities regarding dossier requirements.

**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 essentially similar to a product which has already been granted a marketing authorisation in the same Member State(s). The application is an abridged application based on article 10.1a1c 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

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

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

Mutual recognition phase
A mutual recognition procedure 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.

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

First 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. The subsequent authorisation granted for A’ might be varied independently of A.

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 those parts of the pharmaceutical, preclinical and clinical documentation in of 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

19992006
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.

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

The original 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 should in principle initiate a mutual recognition procedure, as A’ is essentially similar 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.

As described in the MRFG SOP on article 18 of Directive 2001/83/EC, 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.

As it is not possible for the Concerned Member State more than once to recognise more than once the marketing authorisation granted for A in the Reference Member State, the company should initially obtain a marketing authorisation also for A’ in the Reference Member State for A as described under example 1.1. Subsequently a Mutual Recognition procedure for A’ could be initiated.
- 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.

<table>
<thead>
<tr>
<th>RMS=IRL</th>
<th>Not acceptable for the CMS more than once to recognise more than once the authorisation for A</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>IRL/H/157/01</td>
</tr>
<tr>
<td>CMS=IT</td>
<td>A</td>
</tr>
<tr>
<td>CMS=ES</td>
<td>National inf. cons. A’</td>
</tr>
<tr>
<td>Appl. : X</td>
<td></td>
</tr>
</tbody>
</table>

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

**Example**

*First 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 (RMS₂) for A’ in some of those Member States, which were Concerned Member States for the reference original 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.

<table>
<thead>
<tr>
<th>RMS₁=SE</th>
<th>MAH: X SE/H/155/01</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Inf. cons. A’</td>
</tr>
<tr>
<td>CMS=DK</td>
<td>CMS=PT CMS=NL</td>
</tr>
<tr>
<td>RMS₂=NL</td>
<td>MAH: Y NL/H/163/01</td>
</tr>
<tr>
<td>Inf. cons. Inf. cons.</td>
<td></td>
</tr>
<tr>
<td>CMS=DK</td>
<td>CMS=PT 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 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.**