CMDv/BPG/012

BEST PRACTICE GUIDE
for
Informed consent for MRP and DCP procedures

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ANNEX 1: TEMPLATE FOR LETTER OF ACCESS FOR AN APPLICATION UNDER ARTICLE 13C OF DIRECTIVE 2001/82/EC ('INFORMED CONSENT' APPLICATION)
1. Introduction
Notice to Applicants, Volume 6A, Chapter 1, includes the possibility for obtaining a marketing authorisation based on consent to refer to the documentation supporting the marketing authorisation of an already authorised product. Such an application is known as an informed consent application.

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

3. Legal framework

Extracts from European legislation
Informed consent, as a legal basis for a marketing authorisation, is defined according to the Article 13c of Directive 2001/82/EC as amended, defined as follows:

“Marketing authorisation holder for a medicinal product grants a consent to an applicant for a marketing authorisation to refer to the pharmaceutical, pre-clinical and clinical parts of the authorised medicinal product dossier (parts II, III and IV) for the purpose of evaluation of a subsequently submitted application for a marketing authorisation with respect to another product with the same qualitative and quantitative composition of the active ingredients and with the same dosage form.”

Notice to Applicants- Volume 6A, Chapter 1, Section 5.6

"It is a prerequisite for the use of Article 13c that consent has been obtained for all three parts containing the pharmaceutical, safety and residues and pre-clinical and clinical data. It is not possible to use Article 13c a legal basis for an application consisting of the applicant’s own Part II and for which consent has been given for Parts III and IV.”

4. References and related documents
» Directive 2001/82/EC as amended
» Notice to Applicants, Volume 6A, Chapter 1
» Notice to Applicants, Volume 6A, Chapter 2
» Commission Communication 98/C 229/03
» Informed consent applications in MRP and DCP, CMDh/70/199/Rev3 Sept 2010

5. General
Definition of the reference product, definition of the Informed consent application and dossier requirements

5.1. The Reference product
For the purpose of the mutual recognition procedure and the decentralised procedure, the CMDv has agreed that the reference product is defined by a marketing authorisation holder and a marketing authorisation for a veterinary medicinal product supported by a complete dossier.
Consequently the marketing authorisation for the reference product cannot be based on an Article 13 application.
5.2. Informed consent application

An Informed consent application is an application according to Article 13c of Directive 2001/82/EC as amended. In this BPG the resulting authorised product is named “the second product”, or A’.

- The marketing holder for the reference product has consented that the applicant can refer to Part IC, II, III and IV containing the pharmaceutical, safety and efficacy data (including residue data and ERA as applicable) for the reference product.
- In practice this means that the product applied for must be exactly the same as the reference product on the day of submission informed consent application.
- It is not possible to use Article 13c for an application with the applicants own data for Part II and for which consent has only been granted for Parts III and IV.
- ERA data should be documented anyway: to the extent that the first application does not contain an environmental risk assessment, this assessment must be performed in connection with any subsequent application made under Article 13c.
- An informed consent application can only be submitted in Member States where the reference product is currently 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.
- The applicant for the second product must during the lifetime of the product have permanent access to the documentation for the reference product or be in possession of this information. It is the responsibility of the holder of the reference product and the applicant of the informed consent product to ensure that permanent access is maintained.
- 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, linked or different from the marketing authorisation holder for the reference product.
- The two products must have different trade names.
- The informed consent application is not legally obliged to cover all pharmaceutical form(s)/strength(s) of the reference medicinal product.

5.3. Dossier requirements

- In general, Part IA and IB of the dossier should only be submitted by the applicant.
- The applicant should in practice refer to Part IC, II, III and IV of the reference product.
- An exemption can be made when a new ERA data should be documented together with part IA and IB, if there were no ERA data in the dossier of the reference product.
- Letter of access for an “Informed consent application”regarding the dossier references between the initial MAH and new MAH should be submitted together with an Informed consent application (see Annex 1 of this guideline).

6. Description of the procedure

Possible situations

The same or a different marketing holder wish to obtain a marketing authorisation for a product, which is exactly the same as a product already authorised in the same Member State(s). The application is an application based on article 13c in Directive 2001/82/EC as amended.
The following situations should be considered:

1. The informed consent application is submitted in the Reference Member State of the reference product and the reference product is authorised through DCP or MRP.
2. The informed consent application is submitted in a Member State, where the reference product is nationally authorised.
3. The informed consent application is only submitted in one or several Concerned Member States of the reference product;
   a. and the MAH is the same (or linked)
   b. and the MAH is an independent company

**Situation 1**

An informed consent application is submitted in the Reference Member State of the reference product which is authorised through DCP or MRP.

The MAH can be the same (or linked) or an independent company.

- An informed consent application for A’ can be submitted nationally in the Reference Member State for the reference product A. The company could choose to stay nationally with this authorisation in this Member State.

After that an informed consent application via MRP for A’ could be initiated based on the authorisation of the national informed consent application described immediately above in all or some of those Member States, which are Concerned Member States for the reference product A.

- Alternatively, an informed consent application via DCP for A’ could be initiated with the same Reference Member State as for the reference product A in all or some of those Member States, which are Concerned Member States for the reference product A.

See illustration 1 below.

**Illustration 1**  Submission of informed consent application nationally or via DCP where the reference product A is authorised via MRP/DCP.
Situation 2

The reference product is authorised nationally in a number of Member States. An informed consent application is submitted in a Member State where the reference product is authorised nationally. The MAH can be the same (linked) or an independent company.

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

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

- Alternatively, an informed consent application via DCP for A’ could be initiated with one of the Member States where the reference product A is already authorised as RMS.

See illustration 2 below.

*) It should be confirmed by the applicant that the pharmaceutical, preclinical and clinical documentation in the dossiers for reference product A, which are referred to in the application for A’, are the same in the Member States concerned. 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 reference product 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.
Situation 3
The reference product has been authorised in several Member States following MRP or DCP. An informed consent application is subsequently submitted in one of the Concerned Member States.

Situation 3.a
The applicant is the same (or linked) as the Marketing Authorisation Holder for the reference product A. An informed consent application is submitted in the Concerned Member State of the reference product which is authorised through DCP or MRP.

A national as well as DC procedure cannot be accepted.

As the informed consent application for A’ is exactly the same as the reference product A, which is already authorised by the same (or a linked) company in other Member States, the applicant should submit an application according to article 32 of Directive 2001/82/EC as amended.

See illustration 3.a. below.

**Illustration 3.a.** Submission of informed consent application nationally or via DCP where the reference product A is authorised via MRP/DCP and where the applicant is the same (linked).
Situation 3.b.
The applicant is independent of the Marketing Authorisation Holder for the reference product A. An informed consent application for A’ is submitted in the Concerned Member State of the reference product A which is authorised through DCP or MRP. The MAH is different.

- An informed consent application for A’ can be submitted nationally in a Concerned Member States, where the reference product A is already authorised.

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

- Provided that an informed consent application for A’ have not been applied nationally in a CMS a DCP can be initiated for A’ with any of the Concerned Member States for reference product A as acting RMS.

See illustration 3.b. below.

**Reference product, A**
The reference product A authorised through MRP or DCP.

**Informed consent, A’**
Different MAH
National informed consent in CMS of reference product A. ✓

MRP informed consent in MS where reference product A is authorised.

Different MAH
DCP informed consent in MS where the reference product A is authorised with any MS as RMS. ✓

**Illustration 3.b.** Submission of informed consent application nationally or via DCP where the reference product A is authorised via MRP/DCP and where the applicant is different.

**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.
Annex 1: Template for letter of access for an application under Article 13c of Directive 2001/82/EC ('Informed consent' application)

<table>
<thead>
<tr>
<th>Section to be completed by the MAH of the reference product</th>
</tr>
</thead>
<tbody>
<tr>
<td>I, the undersigned acting in my capacity as &lt;Job title&gt; of &lt;name of the MAH for the reference product&gt; whose registered office is located at &lt;address of the MAH for the reference product&gt; hereby confirm that permanent and full access has been granted to &lt;name of the MAH for the proposed informed consent MA&gt;, whose registered office is located at &lt;address of the MAH for the proposed informed consent MA&gt; to Part IC, II, III and IV of the MA dossier for the following medicinal product:</td>
</tr>
<tr>
<td>&lt;name and MA number of the reference product&gt;</td>
</tr>
<tr>
<td>This access has been granted for the purposes of the submission of a marketing authorisation application under Article 13c of Directive 2001/82/EC as amended to &lt;name of competent authority(ies) to which the application has been submitted&gt; for the following product:</td>
</tr>
<tr>
<td>&lt;name of the proposed informed consent MA and procedure number if available&gt;</td>
</tr>
<tr>
<td>In the event that the Marketing Authorisation is granted to &lt;name of the MAH for the proposed informed consent MA&gt;, access to the data will be available to &lt;name of the MAH for the proposed informed consent MA&gt; and &lt;name of the competent authority(ies) to which the application has been submitted&gt; for as long as the product is authorised. The data in the dossier may be used in the assessment of any variation or renewal of the Marketing Authorisation or for any other purposes whatsoever relating to the Marketing Authorisation and we can confirm that &lt;name of the MAH for the proposed informed consent MA&gt; will have full access to the dossier to enable them to fulfil their obligations as MAH as described in Directive 2001/82/EC as amended.</td>
</tr>
<tr>
<td>For and on behalf of &lt;name of the MAH for the reference product&gt;</td>
</tr>
<tr>
<td>Date and place</td>
</tr>
<tr>
<td>Signature</td>
</tr>
<tr>
<td>Name, Job Title</td>
</tr>
</tbody>
</table>
I, the undersigned acting in my capacity as <Job title> of <name of the MAH for the proposed informed consent MA> whose registered office is located at <address of the MAH for the proposed informed consent MA> hereby confirm that we have received full access to Part IC, II, III and IV of the MA dossier for <name and MA number of the reference MA> by <name of the MAH for the reference product>, whose registered office is located at <address of the MAH for the reference product>.

This access has been granted for the purposes of the submission of a marketing authorisation application under Article 13c of Directive 2001/82/EC as amended to <name of the competent authority(ies) to which the application has been submitted> for the following product:

<name of the proposed informed consent MA and procedure number if available >.

Submitted by the applicant:

<name and address of the MAH for the proposed informed consent MA>

We can confirm that <name of the MAH for the proposed informed consent MA> has full access to the dossier and that we are in a position to fulfil our obligations as MAH as described in Directive 2001/82/EC as amended, in the event that the Marketing Authorisation is granted.

For and on behalf of <name of the MAH for the proposed informed consent MA>

Date and place
Signature
Name
Job Title