



**APPLICANT'S RESPONSE DOCUMENT IN  
MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES  
RECOMMENDED CTD FORMAT**

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**INTRODUCTION**

The recommendations described in this document should be followed by the applicant for compiling and sending a response document during a Mutual Recognition (MRP) and Decentralised Procedure (DCP), including the CMD(h)-referral phase of these procedures. This document should enable the applicants to have precise and consistent information of location in the CTD format allowing the Competent Authorities to assess applications in an efficient and timely manner.

It is important to emphasise that a well-prepared response document greatly facilitates the task of the Competent Authorities in evaluating the dossier. Moreover, since the Member States have a short time period to assess the response document, it should be clear, brief and focused on the questions raised.

It concerns response documents to be submitted during a MRP and DCP, especially at the following phases:

- at Day 60 in MRP
- at Day 106 (to be prepared during clock-off period) in DCP
- at Day 160 in DCP
- at Day 25 of the 60-Day referral procedure to CMD(h), applicable for MRP and DCP

However, when a further response document should be circulated at other time points during the procedure, these recommendations should apply.

This document should be read in conjunction with the following guidelines:

- Best Practice Guide for Mutual Recognition Procedure
- Decentralised Procedure – Member States' Standard Operating Procedure
- CMD(h) Standard Operating Procedure – Disagreement in procedures – Referral to CMD(h)

## **GENERAL PRINCIPLES**

1. The applicant should answer all questions raised by the Member States.
2. In MRP and DCP, the applicant should provide a draft response document in due time to the Reference Member State (RMS) , in order that the Reference Member State could discuss the proposed answers with the applicant before the final response document is sent to all Member States concerned. Moreover, the RMS should comment on the final responses in a letter or a report to the CMS, clearly stating if the applicant's response document is considered as satisfactory.
3. During the clock-off period of the DCP, the applicant should agree with the RMS on the timing of submission of the draft and final response documents.  
The response document in MRP and in Assessment Step II of DCP should be received by the Member States (RMS+CMS) not later than ten days (at Day 60 of a MRP or at Day 160 of a DCP) following the deadline for the Member States' comments. The timelines for submission of the response document in the 60-day referral procedure are mentioned in the SOP for this procedure.  
The applicant should comply with these timelines in order to facilitate assessment and if necessary, discussion during the break-out session or an oral hearing in CMD(h).
4. Answers to outstanding issues not solved by the company's first response document should be sent to all Member States concerned with a further response document  
All the answers should always be circulated to all involved Member States even if only one CMS raised a question.
5. Additional studies are not acceptable during the MRP, during assessment step II of the DCP nor during the 60-Day referral to the CMD(h). However, it is allowed to supplement the dossier with new data related to the questions raised by the Member States in the response document submitted during the clock-off period of the DCP.
6. After finalisation of the procedure, the applicant should provide the RMS with:
  - an updated table indicating all changes made to the SPC, PL and Labelling during the procedure
  - the approved release and end of shelf-life specifications for the finished product
  - the approved specifications for the active substance.

Any change made during the procedure should be clearly indicated.

## **FORMAT OF THE RESPONSE DOCUMENT**

The response document should follow the same presentation as the initial dossier. The applicant should include in section called “Responses to Questions” of the Module 1 (EU CTD) a document which lists the questions with the corresponding narrative text response for each question (see Notice to Applicants - Volume 2B, Presentation and format of the dossier CTD - current edition). This section will not be used for supporting technical documentation which will be included to the relevant Modules. Each question should be followed by the initials of the Member State who raised the question, the name of section and page number where the answer can be found in the concerned Module.

### **Module 1: Regional Administrative information**

- Module 1.2. Application form  
The applicant should answer questions, if any, on the application form (administrative data, samples, manufacturing and marketing authorisations).
- Module 1.3.1 Summary of Product Characteristics, Package Leaflet and Labelling  
This part should include the new proposed SPC/PL and Labelling including relevant tabular format with the answer to the questions raised by the Member States on the different sections of the SPC/PL and the Labelling.

#### 1. New proposed SPC/PL and Labelling

In agreement with the RMS, the applicant should propose a new version of the SPC/PL and Labelling including all revised wording clearly identified, preferably using track-changes function.

#### 2. Questions raised on SPC/PL and Labelling : tabular format (*landscape paper format*)

The proposed changes on the SPC/PL and Labelling should be presented in a separate tabular format.

The tabular format may be adapted as necessary for an individual marketing authorisation application by expanding or contracting sections or omitting sections where not relevant. Each objection or question should be mentioned and followed by the initials of the Member State. Cross-references could be useful from one response to another. The final proposal should include clear and appropriate answer to support the new proposal.

Alternative tabular presentations may be used. However, the heading of such tables must be of the same structure, i.e:

- New proposed SPC

<b>Initial Proposed SPC plus proposed revisions</b> (using track-changes function)	<b>Objections/Points for consideration raised by Member States</b>	<b>Company response (with cross reference to the response document when applicable)</b>

- New proposed PL

<b>Initial Proposed PL plus proposed revisions</b> (using track-changes function)	<b>Objections/Points for consideration raised by Member States</b>	<b>Company response (with cross reference to the response document when applicable)</b>

- New proposed Labelling

<b>Initial Proposed Labelling plus proposed revisions</b> (using track-changes function)	<b>Objections/Points for consideration raised by Member States</b>	<b>Company response (with cross reference to the response document when applicable)</b>

### **Module 2: Common Technical Document Summaries**

Module 2.6 – Non clinical Written summaries

Module 2.7- Clinical Written Summaries

This Module should be updated when responses contain extensive data which would require inclusion of the relevant summaries/overview sections.

### **Module 3: Quality**

The applicant should answer questions, if any, on chemical, pharmaceutical and biological documentation.

### **Module 4: Nonclinical study reports**

The applicant should answer questions, if any, on toxico-pharmacological documentation.

### **Module 5: Clinical study reports**

The applicant should answer questions, if any, on clinical documentation.

### **Appendices**

A copy of the questions sent by the Member States should be appended to the document.

For purpose of flexibility, the option to provide a presentation per Member State remains available.

For the template, please refer to the Notice to Applicants Volume 2B – Common Technical Document <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/>

## **SUBMISSION OF RESPONSE DOCUMENT**

### **During MRP and DCP**

The applicant should send in due time the whole response document to the RMS and all CMS by courier according to national requirements as described in the Notice to Applicants/Volume 2A/Chapter 7 – current edition. The applicant is invited to send the response document via e-mail addresses to National Competent Authorities. The applicant should check national recommendations for the sending of documents via Eudralink or contact national authorities to know requirements before sending documents via Eudralink. Even if the response document is sent via e-mail, hard copies of the response document might still be needed and should be sent according to national requirements.

#### *E-mail addresses*

The E-mail-addresses to be used by the applicants for their response documents are published at the websites of the national agencies and in the Notice to Applicants/Volume 2a/Chapter 7 – current edition. Attention is made that personal mail addresses cannot be used unless requested.

#### *Heading of the E-mail*

Applicants are requested to standardize the header of the E-mail as follows: Procedure Nr.\_Name (can be shortened if too long)\_Company\_Response-Day of Procedure.

#### *Eudralink*

The response document should be sent via Eudralink using the E-mail header as mentioned above. The following rules should be taken into account:

- All files should be zipped to facilitate saving of the files,
- The option that E-mail addresses of all recipients are visible should be chosen.

### **During referral to the CMD(h)**

The applicant should send the response document in electronic format via e-mail to all National Competent Authorities and to the EMEA, with one paper copy to the RMS. An overview of the e-mail addresses to be used by the applicants is available on the Heads of Medicines Agencies website.

Applicants are requested to standardise the header of the e-mail as follows: Procedure Nr. \_ Name (can be shortened if too long)\_Company\_Response-CMD Referral. The following rules should be taken into account for sending the files via Eudralink:

- All files should be zipped to facilitate saving of the files,
- The option that e-mail addresses of all recipients are visible should be chosen.

## **NUMBER OF COPIES OF THE RESPONSE DOCUMENT**

### **During MRP and DCP**

The number of copies of the Applicant's response document for submission to the Concerned Members States are set out in the Notice to Applicants/Volume 2A/Chapter 7 – current edition.

- Note:
- i) The written response should be bound in separate volumes so that the pharmaceutical assessor can review the response to Modules 1 and 3, the pre-clinical assessor the response to Modules 1, 2 and 4 and the clinical assessor the response to Modules 1, 2 and 5.
  - ii) On the request of the Reference Member State, the Applicant should provide the response document in electronic form.

**During referral to the CMD(h)**

One paper copy of the response document during the 60-day referral procedure to the CMD(h) should be submitted to the RMS. Electronic submission to other Member States and EMEA is sufficient.