



**GUIDELINE BEST PRACTICE GUIDE ON THE ASSESSMENT REPORT
FOR MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES**

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1. INTRODUCTION

Art 28 of Dir 2001/83 EG provides for an assessment report (AR) which describes the assessment of the medicinal product and states the reasons for the conclusions.

The purpose of this guideline is to describe the structure and requirements of the assessment reports used in Mutual Recognition Procedures (MRP) and Decentralised Procedures (DCP).

~~1.1 Legal basis~~ 2. LEGAL FRAMEWORK

According to Article 28, 1st paragraph of Directive 2001/83/EC, as amended one Member State, acting as Reference Member State (RMS) shall prepare an assessment report on the medicinal product.

The 2nd paragraph of this article describes the procedure and timelines for the assessment report in case the product has already received a marketing authorisation in one member state, i.e. the MRP, while the 3rd paragraph deals with these issues for products which do not have a marketing authorisation in Europe at time of application, i.e. the DCP.

In the 4th and 5th paragraphs the important role of the assessment report of the RMS during the procedures is explained, stating that the Member States concerned shall approve the assessment report and shall adopt the decision amongst others in conformity with the assessment report:

2.1.2 In general

This document should be read in conjunction with the following guidelines, Best Practice Guides and Standard Operating Procedures:

- Best Practice Guide for [the decentralised and Mutual Recognition Procedure](#)
- Best Practice Guide for the Reference Member State in the ~~Mutual Recognition and Decentralised Procedures~~ [MRP/DCP](#)
- Decentralised Procedure —Member States' Standard Operating Procedure
- Position Paper on Repeat Use of the Mutual Recognition Procedure
- [Procedural Advice on Repeat Use](#)
- CMD(h) Best Practice Guide for the Public Assessment Report in the Decentralised and Mutual Recognition Procedures

~~2.2~~ 2.3. PURPOSE OF THE ASSESSMENT REPORTS

The assessment reports in the MRP and DCP are the key documents explaining why a marketing authorisation and each of the proposed indications have been or can be approved or rejected by the RMS and detailing the ~~risk to benefit considerations~~ [risk assessment](#) for the product. It also serves as an audit trail explaining why an authorisation has been proposed, granted, or rejected and explaining the terms of the summary of product characteristics ([SPCSmPC](#)), package leaflet (PL) and label. The reports should be sufficiently detailed to allow for secondary assessment by other Member States experts. As such these reports are central to the efficient operation of the mutual recognition procedure and the decentralised procedure.

An explanation of, and justification for each part of the [SPCSmPC](#), PL and label should be made referring to the relevant supporting data in the dossier.

Where it is recommended that a marketing authorisation to be granted is subject to conditions, these should be set out, clearly indicating the rationale and the timetable for receipt of results necessary to fulfil the additional requirements.

3.4. QUALITY ASSURANCE

The AR ought to be subject to a quality assurance programme within the RMS and the recommendations should be endorsed as representing the final opinion of the RMS.

4.5. CONTENT OF THE ASSESSMENT REPORT

In general, [there are five parts of](#) the assessment report in MRP and DCP ~~all consist of four parts~~:

- Overview
- Quality
- [Active Substance Master File \(ASMF\)](#)
- Non clinical data
- Clinical data

~~Templates have been developed for all parts.~~ For generic products it is possible to combine the non-clinical and clinical parts in one report and a separate template is available

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The Overview part will be the basis for the Public Assessment Report and has the following Index of Contents

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Cover page
I Recommendations
II Executive summary
II.1 Problem statement
II.2 About the product
II.3 General comments on the submitted dossier
II.4 General comments on compliance with GMP, GLP, GCP and agreed ethical principles
II.4 General comments on the submitted dossier
III Scientific overview and discussion
III.1 Quality aspects
III.2 Non clinical aspects
III.3 Clinical aspects
IV Benefit Risk Assessment
V Proposed List of Questions/Proposed List of Outstanding Issues *
V List of questions as proposed by the RMS*
VI Recommended conditions for marketing authorisation and product information
VI.1 Conditions for marketing authorisation
VI.2 Summary of Product Characteristics

VI.3 Package Leaflet and User Testing
VI.4 Labelling

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VII Appendix: QRD guidance and checklist for the review of user testing results

** This chapter is not applicable for the AR in the MRP*

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Bioequivalence data

A confidential attachment (not to be disclosed to the applicant) should state the full composition of and specification for the reference product used in the bioequivalence studies in [the OMS Other Member States](#) to enable the concerned Member States to compare it with that of the approved products marketed in their own countries.

EDMF

~~In Annex 1 of this guideline information is given on the content of the EDMF. The assessment of the EDMF has to be included in the assessment of the Quality part of the dossier. However, assessment of the closed part of the EDMF should be added as confidential annex not to be disclosed to the applicant.~~

5.

ASMF

The overall content of the ASMF should contain detailed information as indicated under the various headings of the relevant Notice to Applicants for Marketing Authorisations for Medicinal Products in the Member States of the European Union, CTD format, section 3.2.S.

The marketing authorisation holder applicant must be supplied by the ASMF holder with sufficient information to be able to take responsibility for an evaluation of the suitability of the active substance specifications to control the quality of the substance in the specified medicinal product. This information need to be present in the Applicants part of the ASMF, which is to be submitted by the ASMF holder to both the applicant and the competent authorities/EMA. Detailed information on the individual steps of the manufacturing method such as reaction conditions, temperature, validation and evaluation data for certain critical steps of the manufacturing method etc. and on quality control during manufacture may contain valuable know how. Such information may be present in the closed part, which is to be submitted to the competent authorities/EMA only.

6. ASSESSMENT REPORTS IN MRP AND DCP

~~5.4 The templates for the assessment reports in the MRP and DCP are published on the CMDh website.~~

~~Further guidance with regard to the Overview in MRP and Overview and List of Questions in the DCP can be found in the concerned templates, in which further guidance is given on what kind of information is expected under the different headings.~~

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Phase	Time in procedure (days)	Report	Parts of the report	Content
<i>MRP</i>				
Start	-14 d	AR	AR Overview AR Module 3 AR Module 4* AR Module 5*	—Overview with summary of scientific discussion, recommendations. The SPC, PL and label are attached. —Scientific discussion Module 3, 4 and 5
After day 90/150	97/157	FAR	FAR Overview	—Overview with summary of scientific discussion, recommendations and, if applicable, a short summary of discussion in breakout session and/or CMD(h). The final SPC, PL and label are attached
<i>DCP</i>				
Assessment step 1	70	PrAR	PrAR Overview PrAR Module 3 PrAR Module 4* PrAR Module 5*	—Overview with summary of scientific discussion, recommendations, List of Questions. The SPC, PL and label are attached with comments included. —Scientific discussion Module 3, 4 and 5
Assessment step 2	120	DAR	DAR Overview DAR Module 3 DAR Module 4* DAR Module 5*	—Update of the Overview of the PrAR with summary of scientific discussion, recommendations, List of Outstanding Issues. The SPC, PL and label are attached with comments included. —Assessment of applicant's responses on Module 3, 4 and 5
After day 210/270	217/277	FAR	FAR Overview	—Overview with summary of scientific discussion, recommendations and, if applicable, a short summary of discussion in breakout session and/or CMD(h). The final SPC, PL and label are attached

* for generics, these parts can be combined

[5.2](#)For further guidance on the Quality, Non-clinical and Clinical parts reference is made to the Day 70 Guidance documents aimed to be used for the initial assessment of any new drug application in the centralised procedure. As the format of the CTD dossiers is the same in centralised, decentralised and mutual recognition procedure the same guidance can be used. There is a separate guidance available for the combined report on Module 4 and 5 for generic products. This guidance can be used for MRP as well as DCP.

6.1 Assessment Report in MRP

Before the start of a Mutual Recognition Procedure, the final decision on an application in the RMS takes place after several stages in the national authorisation procedure. At each stage of the assessment, a national draft-AR or pre-AR will be generated, and subsequently amended and updated in the light of new information from the applicant, oral explanations and discussion in Committees. By this iterative process the national pre- or draft- reports lead to the production of the AR, which will be the document exchanged between Member States in the mutual recognition procedure.

For the national draft-AR or pre-AR it is highly recommended to start with the day 70 CHMP or DCP templates. This structure will facilitate the drafting of the AR for the MRP.

The Quality part of the AR used in the MRP should be based on the updated, integrated dossier. The assessment of non-clinical and clinical parts of the AR may either be an integrated document reflecting the final position of the RMS or it will be produced from the submission as first made with clear indications how this has been augmented by responses to objections. (It is recommended to use the CHMP templates day 70 and day 150)

However the [CMD\(h\)](#) expressed a preference for an integrated report for the non-clinical and clinical parts.

5.36.2 Assessment Reports in DCP

In the Decentralised Procedure, the RMS will generate a Preliminary Assessment Report (PrAR) and subsequently a Draft Assessment Report (DAR), which are the basis for decision making process between Member States. The Overview part of the DAR is an update of the Overview part of the PrAR in which new information from the applicant submitted with the response document and conclusions from the RMS thereof have to be processed.

5.4 Final6.3 Preparations for the Public Assessment Reports

The Best Practice Guide for the Public Assessment Report has highlighted the need for a Final Assessment Report, which forms the basis for the Public Assessment Report. The RMS will compile a final assessment report for all procedures. This consists ~~to an update~~ of the Overview Part of the AR in case of MRP and [an update](#) of the DAR in case of DCP in which the scientific discussions between Member States and the final conclusions are reflected. If applicable, a short description of the discussion in break-out sessions and [CMD\(h\)](#) is included. The final [SPC/SmPC](#), PL and label are attached.

This report forms the basis of the PAR and should therefore be finalised as soon as possible after the finalisation of the procedure.

The report will be released to the applicant.

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5.56.4 Updated assessment reports for repeat use procedures

Before the start of a repeat use procedure, there is a need for updating of assessment reports from MRPs and DCPs. Such a report could also form the basis for dealing with requests for MRP assessment reports from other regulatory authorities (the permission of the applicant would be required).

This updated Assessment Report will comprise:

1. the initial assessment reports (AR in MRP; PrAR and DAR in DCP)
2. a list of the initial Concerned Member States
3. minutes of the break out session if held
4. minutes of the [CMD\(h\)](#) meeting during referral procedure if held
5. a note of any withdrawals and the reasons for the withdrawal
6. A copy of the approved specification for the active substance(s) and copies of the approved release and shelf-life specifications for the finished product or a statement that no changes to the original were necessary.
7. The Final Assessment Report, including the agreed [SPC/SmPC](#), PL and label

The updated assessment report should be accompanied by a chronology to take account of any subsequent variations (for example variation assessment reports, decisions or notifications) to ensure that the updated mutual recognition assessment report is current as issued.

If the medicinal product has been the subject of a referral to the CHMP which is finalised, the Commission decision and background scientific information should be included but it will not be necessary to include the assessment reports of the rapporteur/co-rapporteur.

6.5 Procedural overview

<u>Phase</u>	<u>Time in procedure (days)</u>	<u>Report</u>	<u>Parts of the report</u>	<u>Content</u>
<u>MRP</u>				
Start	-14 d	AR	AR-Overview AR-Module 3 AR-Module 4* AR-Module 5*	- Overview with summary of scientific discussion, recommendations. The SmPC, PL and label are attached.. - Scientific discussion Module 3, 4 and 5
After day 90/150	97/157	FAR	FAR-Overview	- Overview with summary of scientific discussion, recommendations and, if applicable, a short summary of discussion in breakout-session and/or CMDh. The final SmPC, PL and label are attached

* for generics, these parts can be combined

<u>DCP</u>				
Assessment step 1	70	PrAR	PrAR-Overview PrAR-Module 3 PrAR-Module 4 * PrAR-Module 5 *	- Overview with summary of scientific discussion, recommendations, List of Questions. The SmPC, PL and label are attached with comments included. - Scientific discussion Module 3, 4 and 5
Assessment step 2	120	DAR	DAR-Overview DAR-Module 3 DAR-Module 4 * DAR-Module 5 *	- Update of the Overview of the PrAR with summary of scientific discussion, recommendations, List of Outstanding Issues. The SmPC, PL and label are attached with comments included. - Assessment of applicant's responses on Module 3, 4 and 5
After day 210/270	217/277	FAR	FAR-Overview	- Overview with summary of scientific discussion, recommendations and, if applicable, a short summary of discussion in breakout-session and/or CMDh. The final SmPC, PL and label are attached

* for generics, these parts can be combined

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7. SPECIAL FEATURES WITH REGARD TO THE ASSESSMENT REPORT FOR GENERIC OR HYBRID APPLICATIONS

Directive 2001/83/EC, as amended precisely stipulates the cases where the results of pharmacological and toxicological tests or clinical trials do not have to be provided, thus allowing for a generic, or a 'hybrid' application to be made.

See also NTA Vol 2A Chapter 1, section 5 and 6 for detailed information concerning, data protection and bridging data in the case of hybrid applications under Art 10 (3) of Dir 2001/83/EC.

If the [SPCSmPC](#) is different from that of the original product, the assessment report should outline the data supporting the modifications. In particular, if the RMS granted more indications for the reference product than the CMS, information on the underlying documentation for this additional indication should be given

In case of European Reference Product (ERP) and the information provided in the [SPCSmPC](#) of the ERP (e.g. indications, contraindications, warnings) is different or even unknown in the RMS, a scientific dialogue should be initiated with the member state of the ERP to try to support the [SPCSmPC](#) with data.

Where the [SPCSmPC](#) and/or PL of the brand leader has been approved by a Commission Decision after a Referral based on Art 30 of Dir 2001/83 these [SPCSmPC](#) and/or PL should be used for products with the same active substance and pharmaceutical form, unless justified.

For generic and hybrid applications the usual templates for the Overview and Quality parts of the AR can be used, but there is a separate, combined template for Module 4 and 5.

It was agreed between the Member States that only bioequivalence and new data should be discussed in this part of the AR.

~~7. TEMPLATES AND GUIDANCE~~

~~7.1 Templates~~

~~The following templates are available for the assessment reports in the MRP and DCP. These templates are published on the CMD website.~~

~~MRP~~

- ~~— Overview (*has to be updated*)~~
- ~~— Non-clinical and Clinical of a generic application~~

~~DCP~~

- ~~— RMS Day 70 Preliminary Assessment Report~~
 - ~~— Overview and List of Questions~~
 - ~~— Quality~~
 - ~~— Non-clinical~~
 - ~~— Clinical~~
 - ~~— Non-clinical and Clinical of a generic application~~
- ~~— RMS Day 120 Draft Assessment Report~~
 - ~~— Overview and List of Questions~~

- ~~-Quality~~
- ~~-Non-clinical~~
- ~~-Clinical~~

~~The Overview templates follow the same structure as the CHMP templates used in the centralised procedure for new active ingredients.~~

~~For the Overview a separate template is prepared for the mutual recognition assessment report. It has the same structure as the CHMP template, however the table of content is different as it serves as a general overview of the dossier and explains why the RMS has granted a marketing authorisation.~~

~~The English translations of the SPC, PL and label as approved by the RMS in case of MRP or as proposed by the applicant in case of DCP are part of the Overview report.~~

~~In principle, for Module 3, 4 and 5 the same templates should be used in the centralised procedure, the mutual recognition procedure and the decentralised procedure. The only difference in MRP is that there will be no list of outstanding questions because the RMS has already approved the medicinal product. Any outstanding issue should be discussed under Section V of the Overview.~~

~~There is a separate template for a combined report on Module 4 and 5 for generic products, specifically aimed for an extensive summary of the bioequivalence studies.~~

7.2 Guidance

~~There are guidance documents available in the form of annotated templates on Overview in MRP and Overview and List of Questions in the DCP, in which further guidance is given on what kind of information is expected under the different headings.~~

~~For the Guidance documents for the Quality, Non-clinical and Clinical parts reference is made to the Day 70 Guidance documents aimed to be used for the initial assessment of any new drug application in the centralised procedure. As the format of the CTD dossiers is the same in centralised, decentralised and mutual recognition procedure the same guidance can be used.~~

~~There is a separate guidance available for the combined report on Module 4 and 5 for generic products. This guidance can be used for MRP as well as DCP.~~

ANNEX

Assessment of EDMF

Introduction

The overall content of the EDMF should contain detailed information as indicated under the various headings of the relevant Notice to Applicants for Marketing Authorisations for Medicinal Products in the Member States of the European Union, CTD format, section 3.2.S.

The marketing authorisation holder applicant must be supplied by the EDMF holder with sufficient information to be able to take responsibility for an evaluation of the suitability of the active substance specifications to control the quality of the substance in the specified medicinal product. This information need to be present in the Applicants part of the EDMF, which is to be submitted by the EDMF holder to both the applicant and the competent authorities/EMA. Detailed information on the individual steps of the manufacturing method such as reaction conditions, temperature, validation and evaluation data for certain critical steps of the manufacturing method etc. and on quality control during manufacture may contain valuable know-how. Such information may be present in the closed part, which is to be submitted to the competent authorities/EMA only.

The EDMF should consequently follow the following structure:

- 1st section — Table of contents
- 2nd — Quality overall summary on Applicants Part
- 3rd — Quality overall summary on Closed Part
- 4th — Applicants part
- 5th — Closed part

The Applicants part would normally contain the following headings:

- 3.2.S.1 — **General information**
 - 3.2.S.1.1 — **Nomenclature**
 - 3.2.S.1.2 — **Structure**
 - 3.2.S.1.3 — **General properties**

- 3.2.S.2 — **Manufacture**
 - 3.2.S.2.1 — **Manufacturer(s)**
 - 3.2.S.2.2 — **Description of Manufacturing Process and Process controls**
 - flow sheet and short description is regarded sufficient, if detailed information is presented in the closed part
 - 3.2.S.2.4 — **Control of critical steps and intermediates**
 - in so far the information is also relevant for the marketing authorisation holder

- 3.2.S.3 — **Characterisation**
 - 3.2.S.3.1 — **Elucidation of Structure and other Characteristics**
 - 3.2.S.3.2 — **Impurities**

- ~~3.2.S.4 — Control of Drug Substance~~
- ~~3.2.S.4.1 — Specification~~
- ~~3.2.S.4.2 — Analytical procedures~~
- ~~3.2.S.4.3 — Validation of analytical procedures~~
- ~~3.2.S.4.4 — Batch analysis~~
- ~~3.2.S.4.5 — Justification of specification~~

- ~~3.2.S.5 — Reference Standards or Materials~~

- ~~3.2.S.6 — Container Closure System~~

- ~~3.2.S.7 — Stability~~
- ~~3.2.S.7.1 — Stability Summary and Conclusions~~
- ~~3.2.S.7.2 — Post approval Stability Protocol and Stability Commitment~~
- ~~3.2.S.7.3 — Stability data~~

The Closed Part would normally contain the following headings:

- ~~3.2.S.2.2 — Description of Manufacturing Process and Process controls~~
~~————— detailed information~~
- ~~3.2.S.2.3 — Control of Materials~~
- ~~3.2.S.2.4 — Control of critical steps and intermediates~~
~~————— in so far the information is related to the detailed description of the manufacturing process and in so far this information is not relevant for the Marketing Authorisation Holder~~
- ~~3.2.S.2.5 — Process validation and/or Evaluation~~
- ~~3.2.S.2.6 — Manufacturing Process Development~~

- ~~3.2.S.3.2 — Impurities~~
~~————— in so far the information is related to the detailed description of the manufacturing process and in so far the EDMF holder sufficiently justifies that there is no need to control these impurities in the final active substance~~

- ~~3.2.S.4.5 — Justification of specification~~
~~————— in so far the information is related to the detailed description of the manufacturing process, control of materials and process validation~~

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