Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

CMD(h) BEST PRACTICE GUIDE FOR THE PUBLIC ASSESSMENT REPORT IN THE DECENTRALISED AND MUTUAL RECOGNITION PROCEDURES

January 2006

According to Art 21 (3) and (4) of Directive 2001/83 as amended the competent authorities shall make publicly available a Public Assessment Report (PAR) of marketing authorisations issued via the Mutual Recognition Procedure (MRP) or the Decentralised Procedure (DCP). These articles read as:

> 3. The competent authorities shall make publicly available without delay the marketing authorisation together with the summary of product characteristics for each medicinal product which they have authorised.
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> 4. The competent authorities shall draw up an assessment report and comments on the file as regards the results of the pharmaceutical and preclinical tests and the clinical trials of the medicinal product concerned. The assessment report shall be updated whenever new information becomes available which is of importance for the evaluation of the quality, safety and efficacy of the medicinal product.
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> The competent authorities and the Agency shall make publicly accessible without delay the assessment report, together with the reasons for their opinion, after deletion of any information of a commercially confidential nature. The justification shall be provided separately for each indication applied for.

This document addresses the structure and content of the PAR for Decentralised and Mutual Recognition Procedure as well as the actions to be taken to its publication.

1. The competent authority, in the role of the RMS, should draft a public assessment report (PAR) after finalisation of the MRP or DCP. This PAR should provide insight into the regulatory process and present information on the underlying data.

2. The PAR should be drafted according to the table of contents, mentioned in the Annex 1 to this BPG.

3. The basis of the PAR is formed by the overview part of the Final Assessment Report of the RMS in both the MRP and DCP. Therefore, the assessment reports should be written according to agreed guidance, and assessor's should take into account this purpose of their assessment reports.

4. The PAR prepared by the RMS should be written in the English language. It is the decision of the national agencies to make publicly available a PAR in national languages.

5. Competent authorities should ensure that PARs are released within 60 calendar days after finalisation of the MRP or DCP (see timetable in Annex 2).

6. The PAR should be made publicly available by publication on the website of the Heads of Medicines Agencies on the MRP Product Index (http://heads.medagencies.org/index.html). Active publication will contribute to transparency of the regulatory process and avoid a lot of individual requests.

7. Information on discussion in CMD, if applicable, should be mentioned in PAR by a short summary of the discussion.

8. To deal with confidentiality issues, the PAR has to be drafted by the RMS in consultation with the MAH according to the same principles as applied by EMEA. As a general rule the non-clinical part and clinical part of the assessment reports are not confidential with some exemptions, such as new technology. With regard to the quality part the same principles as applied by EMEA should be followed. This means, that in general the chemical-pharmaceutical data can be considered to be commercially confidential with the exception of certain items of information, like qualitative and quantitative composition in terms of active substances, qualitative composition in terms of excipients, pharmaceutical form, shelf-life and storage conditions, chemical incompatibilities.

9. Abstract in lay language is not part of the PAR to be published at the website of the Heads of Agencies on the MRP Product Index. Lay summaries can be prepared at a national level depending on national policies. If the RMS prepares an abstract in lay language, they are encouraged to circulate this document to the CMSs, because it might be useful basis for publication in the national languages.

10. Withdrawals during the initial applications will be discussed in CMD, unless the withdrawal is done before sending the draft AR in DCP. This implies that withdrawals of initial applications will be published, because the discussion in CMD is briefly described in the PAR. Publication of withdrawals of applications for a new indication should not be done on a routine basis, however if there is an overriding Public Health interest to inform prescribers and patients this information should be disclosed. The decision should be made on a case by case basis and the decision should be justified.

11. Competent authorities should ensure that the PARs are updated in line with major updates of the dossier. It is not the intention to update the PAR with Type 1A and type 1B variations.
    These changes will be reflected in updated SPC's, PLs and labelling, if applicable.
    The scientific discussion in the PAR on the initial procedure (Module 5) will not be updated with information approved afterwards via variations, article 61(3) procedures, renewals, pharmacovigilance issues etc. The RMS should describe major changes in the dossier in the tabulated format of Module 6 (see Annex). Relevant assessment reports of these post-authorisations procedures have to be appended, by example if major changes in SPC or PL are introduced during the procedure. A proposal for appending the assessment report or not will be done by the RMS during the MRP of the change in the dossier. The principles on confidentiality issues and consultation with the MA holder applied during the drafting of the initial AR should also be

applied during drafting of the update. The SPC, PL and label have to be updated if applicable.

12. Member States will actively publish a PAR for all DCPs and MRPs ended after 30 October 2005. For procedures started before the date of entry into force of the new legislation, but day 90 is after 30 October 2005 Member States are recommended to publish a PAR, but will take account of status and timing of the pending application at 30 October 2005.

13. Publication of PAR of MRPs finalised before 30 October 2005 is only required if considered necessary, e.g. after a fundamental change in the dossier. This will be decided by RMS and CMSs during the procedure on this change. To this end, the RMS should give a proposal in the assessment report. In this case it is not necessary to draft a complete PAR afterwards, but the assessment report on the variation might be sufficient. On case by case basis it has to be decided whether it is necessary to add the AR of the initial procedure.

Annex 1 Table of content of the PAR for MRP- and DCP- products

Note: The subheadings of the chapter 2-4 of module 5 can be adapted to make them more appropriate for the type of application

Module 1: Information about the initial procedure

1 Type of application (level 1-5)
2 Active Substance
3 Form
4 Strength
5 MA Holder
6 RMS
7 CMS
8 Procedure-number
9 Timetable

Module 2: Summary of Product Characteristics

Module 3: Package Leaflets

Module 4: Labelling

Module 5: Scientific discussion during the initial procedure

1. Introduction
(type of marketing authorisation, main features of disease/condition etc, discussion in CMD)

2. Quality aspects
2.1 Introduction
(pharmaceutical form, formulation, container system, etc)
2.2 Drug Substance
(INN; chemical features like chemical class, chirality, manufacturing, specifications, stability)
2.3 Medicinal Product
(pharmaceutical development, manufacture of the product, product specification, stability of the product)
2.4 Discussion on chemical, pharmaceutical and biological aspects

3 Non-clinical aspects
3.1 Introduction
3.2 Pharmacology
3.3 Pharmacokinetics
3.4 Toxicology
3.5 Ecotoxicity/environmental risk assessment
3.6 Discussion on the non-clinical aspects
For generics: brief explanation that abridged applications avoid the need for repetitive tests on animals and humans. Reference to the reference medicinal product

4. Clinical aspects
4.1 Introduction
4.2 Pharmacokinetics
4.3 Pharmacodynamics
4.4 Clinical efficacy
4.5. Clinical safety
4.6. Discussion on the clinical aspects
For generics: brief explanation that abridged applications avoid the need for repetitive tests on animals and humans. Reference to the reference medicinal product. For these applications the bioequivalence studies are pivotal and should be described.

5 Overall conclusion, benefit/risk assessment and recommendation
(Discussion in CMD, specific obligations, follow-up measures, if applicable)

Module 6: Steps taken after the initial procedure with an influence on the Public Assessment Repor (Type II variations, PSURs, commitments)

Scope	Procedure number	Type of modification [1]	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

Annex 2 Timetable for drafting the Public Assessment Report

Step	Calendar days (after finalisation of the procedure)	Action	By
1	1-7	Electronic version of FAR to applicant requesting them to identify those issues that are considered to be commercially confidential and to make a proposals including justifications for the deletions/alternative wordings, within 10 working days (see annex 1 for a template)	RMS
2	7-14	Comments	Applicant
3	14-21	Check applicant's proposals for the PAR Inform the applicant if they cannot be agreed.	RMS and applicant
4.1	21-59	Complete Module 5 of the PAR	RMS
4.2	21-59	Complete Module 1 (information about the initial procedure)	RMS
5	60	Publication on the website of the Heads of Agencies of the Modules 1, 2, 3, 4, and 5	RMS

For variations the same timetable will be followed, but the updated reports will contain the relevant parts of the Dossier