



**FINAL PAPER**

**September 2005**

<p align="center"><b>MRFG/CMD(h) CONCEPT PAPER – ACHIEVING HARMONISED PATIENT INFORMATION</b></p>
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**Patient information leaflets and labelling and the need to take account of patients' views**

**INTRODUCTION**

1. In accordance with Article 28 of Council Directive 2001/83/EC as amended by Directive 2004/27/EC, a marketing authorisation granted in accordance with the Mutual Recognition (MR) or Decentralised (DC) procedures will have harmonised labelling and patient information leaflets in the member states concerned. This new legal requirement takes effect from 30 October 2005. This document aims to assist marketing authorisation holders understand the overarching principles to be applied and points to additional guidance which is available.

**NEW REQUIREMENTS**

**Harmonisation of Patient Information Leaflets and Labelling**

2. The legal provisions for both labelling and patient information leaflets are already set out in Title V of Council Directive 2001/83/EC (as amended). There is a need for a commonality of approach by all member states in order to achieve a harmonised position on the product information which accompanies medicines following either MR or DC application. To this end, the MRFG/CMD(h) will take an active role to oversee the operation of the new process and to improve the quality of patient information. Together with the QRD group, the aim will be to apply the same standards to patient information approved through the Centralised and MR/DC procedures. Assessment of patient information and labelling will form part of the overall approval procedure. A new standard operating procedure on assessment and the associated MR/DC timetables is under development.
3. The reference member state (RMS) will take the lead on agreeing the product information. Applicants should ensure that mock-ups of packaging components accompany the application and are submitted to all member states concerned. Text versions alone will not be acceptable. Member states will agree a harmonised leaflet and label involving agreement of the content, but not the lay-out. National translations may be submitted at the end of the procedure. The issue of the need for good quality translations remains under discussion and further advice will be offered in due course.

Where there are particular national requirements for the labelling and patient information leaflets these will be accommodated using the “Blue Box” concept similar to that used for products authorised through the centralised system. Further information on the “Blue Box” requirements for CP/MR/DC will be made available through the Commission website.

4. There is current guidance from the European Commission dating from 1999 on the readability of the package leaflet and on the label (the Readability Guideline). <http://pharmacos.eudra.org/F2/eudralex/vol-2/C/g1981002.pdf> This is being updated to take account of the new requirements and will reflect the principles detailed at points 5 – 8 below.
5. To assist applicant companies comply with new legislative requirements, guidance concerning consultation with target patient groups has been made available through the Commission website [\[http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/08\\_05/USERTESTING\\_20050817.pdf\]](http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/08_05/USERTESTING_20050817.pdf).
6. Careful thought needs to be given to the writing of the information which goes directly to patients. Frequent criticisms of the information include that the language used is complex and alienates patients from the document. To assist those involved in the writing of patient information updated guidance will aim to help in the production of high quality patient information.
7. How the information is set out and the size and types of fonts which should be used to prepare interesting and accessible documents are also important factors. To this end updated guidance is being prepared within the readability guideline. Communication of risk within the patient information leaflet and label is known to be difficult and stakeholders will be consulted in due course regarding additional guidance on information provision in this respect.
8. The QRD templates have been updated to complement the changes proposed above and are available through the EMEA website [\[http://www.emea.eu.int/htms/human/qrd/qrdplt/24530905en.pdf\]](http://www.emea.eu.int/htms/human/qrd/qrdplt/24530905en.pdf)
9. For generic medicines, where patients may be given supplies of medicine from a variety of manufacturers over the course of treatment, it is important to encourage the uniformity of information for particular drug substances. To assist in achieving this, individual applicant companies may wish to collaborate on the production of common elements of package leaflets and agree to use a common text supported by the harmonised SPC. Nevertheless, in the absence of a common package leaflet text agreed amongst MAHs, and supported by appropriate testing, each applicant will need to justify the content and layout of his PL by reference to his own data concerning consultation with target patient groups.
10. The EMEA is currently developing the product information management (PIM) project to facilitate electronic exchange of SPC, labelling and patient information leaflet between the applicant and the EMEA for centralised marketing authorisations. It is proposed that PIM will be extended to encompass both MR and DC applications. Further information is available at <http://pim.emea.eu.int/>

## Patient Involvement

11. Further amendments to the directive now place an obligation on marketing authorisation holders to ensure that the resultant patient information leaflet reflects the results of consultations with target patient groups (article 59(3)) and that the supporting data should be provided to the competent authority (article 61(1)).

*Article 59 (3) states:*

*“The package leaflet shall reflect the results of consultation with target patient groups to ensure that it is legible, clear and easy to use.”*

*Article 61(1) states:*

*“... The results of assessments carried out in cooperation with target patient groups shall also be provided to the competent authority.”*

12. Since the introduction of the readability guideline in 1999, the usual approach suggested to ensure that the information provided meets patients’ needs has been for applicants to undertake a diagnostic user test. Although other methods may be valid updated guidance is now available (see point 5 above) which expands upon this earlier document and identifies diagnostic user testing as being one method of demonstrating compliance with this requirement. Alternative user consultation methodology will have to be justified by the applicant/MAH and will be considered on a case-by-case basis.
13. The guidance available through the Commission website recognises that it may not always be necessary to undertake a user test on all leaflets. It may be appropriate in certain cases for applicants to rely on aspects of a test carried out on a sufficiently similar medicinal product and to use these data in a complementary manner. However, discussion of compliance with article 59(3) will be required for all applications whether a test has been carried out or reliance on a test for a similar product is referenced.
14. Therefore, responsibility remains with the MAH to meet their obligations under article 59(3) by recourse to their own data or justification for its absence within the application. Applicants may discuss their plans for meeting their obligations under article 59(3) with the RMS in advance of making an application. CMS will have opportunity to comment at an early stage of the procedure if they disagree with the RMS position on requirements for user consultation.
15. It will not be essential to undertake testing on leaflets drawn up in more than one language and the testing may be done on leaflets prepared in any official language of the EU which may not necessarily be the language of the RMS. In all cases the leaflet which is subject to testing should be a full colour mock-up reflecting the fonts and layout intended for marketing. Results of such tests should be presented in English to permit the assessment of the test to be undertaken by RMS and CMS as necessary.

It will be helpful if applicants present the results in a standardised Summary Outcome Report. Guidance on the format to be used has been provided by the Commission and is available at [\[http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/08\\_05/USERTESTING\\_20050817.pdf\]](http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/08_05/USERTESTING_20050817.pdf). Only the English language version of the leaflet will be agreed during the approval process. At the end of the procedure the responsibility for the production of faithful translations will rest with the MAH in consultation with the MS within the 30 day process.

16. Performing the test or providing a justification for its absence will be essential prior to the completion of the MR or DC procedures. However, prior to the issuing of the national licence documents, requirements for translations and provision of national language mock-ups must be met. The timetables already include provision for this within it. It will not be considered appropriate to test retrospectively to an authorisation being granted.

## **Maintaining harmonisation of patient information**

### Variations

17. Following the grant of the marketing authorisation, there will be occasions when the summary of product characteristics is amended resulting in changes to the patient information leaflet and/or label. Amended mock-ups of packaging components must accompany the application to the MS and these will be subject to the approval process in the manner described above. For Type IA and IB notifications, the RMS will approve the packaging components on behalf of all CMS. For Type II variations, the CMS will have the opportunity to comment during the procedure. Again only the English language version of the leaflet and the labelling text will be agreed during the approval process. At the end of the variation procedure the responsibility for the production of faithful translations will rest with the MAH in consultation with the MS within the 30 day process.

### Repeat use

18. Where a MR or DC application follows the repeat use procedure, the RMS will coordinate the approval of all packaging components during the procedure. Both “new” CMS and existing MS should follow agreed principles for repeat use as detailed in the MRFG SOP [\[http://heads.medagencies.org/mrfg/docs/inter/position.pdf\]](http://heads.medagencies.org/mrfg/docs/inter/position.pdf). New issues concerning the summary of product characteristics should not be raised unless new data presented give cause for concern in relation to public safety. Transitional arrangements for repeat use procedures starting after 30 October 2005 will require harmonisation of the patient information. The MAH may achieve this using a Type II variation procedure involving the existing MS before the repeat use procedure starts. For the transitional period a Type II variation to harmonise patient information will be acceptable in parallel to the repeat use procedure. The RMS should coordinate this activity. Mock-ups of the proposed packaging components must accompany the application and again only the English language version of the leaflet and the labelling text will be subject to the approval process.

At the end of the procedure the responsibility for the production of faithful translations will rest with the MAH in consultation with the MS within the 30 day process.

#### Other changes

19. Guidance will be issued on the procedure to follow should changes be required to the packaging components subsequent to licence grant which are not connected to a change in the summary of product characteristics.

#### **Provision of Patient Information Leaflets in Formats Suitable for the Blind and Partially Sighted.**

20. Article 56(a) places a new obligation on marketing authorisation holders to include the name in Braille on the packaging of the medicinal product. In addition there is a requirement that the patient information leaflet is made available on request in formats suitable for the blind and partially sighted patient population.

*Article 56(a) states:*

*“The name of the medicinal product as referred to in article 54 point (a) must also be expressed in Braille format on the packaging. The marketing authorisation holder shall ensure that the package information leaflet is made available on request from patient organisations in formats appropriate for the blind and partially sighted”.*

Guidance has been prepared on this aspect through the Notice to Applicants group and is available

[\[http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/04\\_05/Braille\\_text20050411.pdf\]](http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/04_05/Braille_text20050411.pdf)

#### **GLOSSARY OF LINKS AND DOCUMENTS REFERRED TO ABOVE**

Guidance from the European Commission on Readability

<http://pharmacos.eudra.org/F2/eudralex/vol-2/C/g1981002.pdf>

PIM (Project Information Management) Project

<http://pim.emea.eu.int/>

MRFG position paper on repeat use of the mutual recognition procedure

<http://heads.medagencies.org/mrfg/docs/inter/position.pdf>

Guidance on Braille

[http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/04\\_05/Braille\\_text20050411.pdf](http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/04_05/Braille_text20050411.pdf)

Quality Review of Documents templates for product information – human medicinal products.

<http://www.emea.eu.int/hums/human/qrd/qrdplt/24530905en.pdf>

Guidance from the European Commission on undertaking consultation with target patient groups for package leaflets for compliance with articles 59(3) and 61(1)

[http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/08\\_05/USERTESTING\\_20050817.pdf](http://pharmacos.eudra.org/F2/pharmacos/docs/Doc2005/08_05/USERTESTING_20050817.pdf)

## **Abbreviations**

CMD(h)	Co-ordination group for Mutual Recognition and Decentralised Procedures
CMS	Concerned Member State
CP	Centralised Procedure
DC	Decentralised
EMA	European Medicines Agency
MAH	Marketing Authorisation Holder
MR	Mutual Recognition
MRFG	Mutual Recognition Facilitation Group
MS	Member State
PIM	Product Information Management
QRD	Quality Review of Documents
RMS	Reference Member State
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics