

**CMDh STANDARD OPERATING PROCEDURE  
PROCEDURE FOR ARTICLE 61(3) CHANGES TO PATIENT INFORMATION**

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**Issue**

1. Maintaining the harmonisation of labels and package leaflets (PLs) approved through the Decentralised (DC) and Mutual Recognition (MR) procedures concerning changes not connected to the Summary of Product Characteristics (SmPC), the so-called “non-variations”.

**Scope**

2. Article 61(3) of Directive 2001/83/EC relates to a provision to amend the labelling or PL of a marketing authorisation in respect of aspects not connected to the SmPC. Following implementation of the new pharmaceutical legislation in October 2005 this applies to the harmonised label and PL resulting from DC/MR procedures. For DC/MR approved products, the scope of the provision extends to those European aspects of the label and PL where a harmonised position has previously been reached and is to be maintained.
3. Changes to information agreed on a national basis, for example the content of the ‘blue box’ information, or changes resulting from a translation issue, are outside the scope of this procedure and should be agreed with the Member States concerned according to national procedures (See also paragraph 6).

**Principles:**

- Applications under Article 61(3) are notifications concerning minor changes to PL or labelling.
- The majority of Notifications will be determined by the RMS on behalf of the CMS.
- The CMS have an opportunity to provide comments to the RMS however, it is envisaged that these will only be required as an exception.
- The Article 61(3) notification procedure will be simple with minimal administration and in most cases would be completed by Day 20. Directive 2001/83/EC allows for a 90-day procedure for Article 61(3) notifications. This reflects a maximum timeline and the procedure should only be extended in exceptional circumstances where the MAH is required to amend the PL or labelling before the notification can be accepted.

## Background

4. Once approved through DC or MR, harmonisation of labels and PLs should be maintained as changes are made by the MAH. This will involve the variation procedure for changes affecting the SmPC, and an Article 61(3) procedure for changes not affecting the SmPC (with the exception of PL and label changes resulting from a variation –see paragraph 6).
5. Labels and PLs should have been harmonised with respect to content, but excluding national specific information including product name, MAH and name of the representative, MA number, and additional blue box information. It follows that lay-out may not be harmonised.

## When to use the notification procedure

6. A MS co-ordinated Article 61(3) procedure is applicable to changes to the label and PL that are not associated with a change to the SmPC and are not the subject of a variation application. These will include but are not restricted to:
  - A change in user instructions in the PL, not resulting in a change in the SmPC
  - A change in storage instructions or arrangements, not resulting in a change in the SmPC
  - A change in expression of side effects in the PL, not resulting in a specific SmPC change

However, MAHs are encouraged to introduce all changes at an opportune time within a variation procedure, rather than as a separate Article 61(3) notification. Changes to packaging resulting from a variation to the SmPC will be considered and assessed as part of the particular variation application. Where the results of user consultation indicate that changes are required to the SmPC these should be submitted by the appropriate variation.

Submission of the results of user consultation is considered outside the scope of this notification procedure. Following implementation of Commission Regulation (EC) 1234/2008 CMDh was asked to recommend a classification (under Article 5) for submission of the results of user consultation. The resulting recommendation was that the results of such assessments to comply with Article 59(3) of Directive 2001/83/EC (including and resulting change to the Package Leaflet) should be submitted as Type IB variation procedures under category C.I.Z. This includes situations where the results of user consultation may indicate that no changes or only minor changes are required to the product information.

Changes relating to national issues and translation issues are outside the scope of the notification procedure and are not encompassed by this standard operating procedure.

7. Local national arrangements will continue for changes such as changes in the local representative on the PL, layout of information on packs and in package leaflets, translation issues to DC/MR authorised products.

## Outline Procedure

8. The Article 61(3) notification procedure will be simple with minimal administration. The RMS will co-ordinate the process allowing for CMS to comment if required using the MRVE mailbox and CTS system for communications and tracking.
9. The applicant should notify the RMS of their wish to amend the label and/or PL on the attached form specifying the nature of the proposed change. The form should specify the MR/DC product information amendment procedure number, which is characterised as follows:

CC/D/nnnn/sss/P/vvv

Where the information in the sections are:

CC:	the initials of the RMS
D:	H for Human or V for Veterinary
nnnn:	specific medicinal product number
sss:	sequential speciality number characterising the pharmaceutical form/strength
P:	denotes Product Information amendment notification
vvv:	sequential number

Article 61(3) notifications have their own series of sequential numbers and are separate to other procedures.

Copies of the notification should be submitted to all CMS at the same time together with national translations of the amended label and/or PL.

10. The application is validated within 5 days of receipt and the RMS notifies the CMS of the procedure start date (Day 0) by CTS.
11. The RMS circulates its position concerning the English version of the amended texts to the CMS by Day 15 of the procedure.
12. CMS should notify the RMS early in the procedure (by Day 20) of their comments on the English version. The CMS should advise the MAH directly of any comments on the national translation and may advise the RMS that they have comments on the translation. In cases where conflicting comments are received on the English version of the texts the comments to be communicated to the applicant will be decided by the RMS.
13. Directive 2001/83/EC allows for a 90-day procedure for Article 61(3) notifications. This reflects a maximum timeline. However as the changes permitted under this notification are minor the need for amendment to the proposed changes should only be required as an exception. The procedure should only be extended beyond 20 days in exceptional circumstances such as when an MAH requires time to respond to a request for amendment. Between Day 20 and Day 89 the RMS considers the CMS comments and may close the procedure (approve/refuse) on behalf of the CMS.
14. Amendments to the application and/or supplementary information may be requested by the RMS by Day 25 of the procedure.

15. The applicant will usually have 10 days to respond (i.e. by Day 35) but this may be extended if the MAH requires additional time to provide updated product information. The amended English version should be provided together with the relevant national translations.
16. On receipt of the updated documentation the RMS will circulate, within 10 days, a final position on the English version for agreement. If a CMS requires additional time to review the updated information this should be indicated to the RMS before Day 45.
17. The RMS will make the final decision on behalf of CMS as to whether the amended product information can be approved or is rejected.
18. The RMS may close the procedure at any time between Day 20 and Day 90
19. The RMS will notify all CMS and the applicant at the end of the procedure that the process has been concluded. The RMS will circulate the final agreed texts and indicate if any amendments have been made compared to the version submitted by the MAH at the start of the procedure.