CHAPTER 3
CMDh BEST PRACTICE GUIDE FOR THE PROCESSING OF TYPE IA MINOR VARIATIONS (NOTIFICATIONS) IN THE MUTUAL RECOGNITION PROCEDURE

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1. INTRODUCTION

This Best Practice Guide has been produced by the CMDh in order to facilitate the processing of Type IA minor variations in the MR procedure. Guidance is given on the role of the Reference Member State (RMS) as co-ordinator of the notification process, and to reflect good practice of the Concerned Member States (CMS) in ensuring a consistent approach is maintained. This will ensure that the notifications are processed in an efficient and timely manner. Moreover, it is considered that the quality of the submission and supporting documentation, which are the responsibility of the marketing authorisation holder (MAH), are crucial to the overall process. From 4 August 2013 the same rules will apply to purely national MAs.

Variation Regulation (EC) No.1234/2008 effective 1 January 2010 identifies the category of variation that can be processed as Type IA Notifications. According to the Regulation, a Type IA variation is a category of change which is specifically identified in the Commission guideline on the classification of variations as a Type IA notification and where all the required conditions and data requirements are met.

According to the Regulation minor variations of Type IA do not require prior approval but can be implemented prior to notification to the relevant authorities (“Do and tell”). Type IA notifications are listed in the Commission guideline on the classification of variations and these notifications should be submitted within twelve months following implementation, so called “annual reports”, taking into account the guidance on possible grouping of variations. However, the notification should be submitted immediately after the implementation of the variation in the case of specific minor variations requiring immediate notification. These notifications are specifically identified as IA-IN in the guideline.

It is possible for a MAH to include a Type IA variation in the submission of a Type IA-IN variation, or with another upcoming variation, rather than waiting to include it in an annual report. Further information about the grouping of Type IA variations is available in Chapter 6 of this Best Practice Guide; however, the timetable and principles for grouped variations, consisting of Type IA changes only, is the same as the procedure outlined in this Chapter of the Best Practice Guide.
2. MINOR TYPE IA VARIATIONS (NOTIFICATIONS: “DO AND TELL”)

Allocation of the MR notification number

Information on the allocation of the MR notification number is presented in Chapter 1 of this Best Practice Guide. In case of doubt, the RMS or Reference Authority should be contacted. The MAH will insert the MR variation number on the application form and in the cover letter. Virtual variation numbers should not be inserted on the application form and in the cover letter.

Start of notification process (Day 0)

The MAH will submit simultaneously to the RMS and CMS an application containing the elements listed in Annex IV of the Regulation, presented as follows in accordance with the appropriate headings and numbering of the EU-CTD format:

- Cover letter.
- Application form, including the MR variation number, a description of the variation(s) submitted and the date(s) of implementation.
- A copy of the relevant page(s) of the Commission Guideline, indicating that all conditions and documentation requirements are met, or a copy of the relevant published Article 5 Recommendation, if applicable.
- Supporting documentation as appropriate.
  - For variations that affect the SmPC and/or labelling or package leaflet, both the English texts and the national translations should be submitted. Mock-ups or specimens should be provided according to Chapter 7 of the NtA, or as discussed with the RMS on a case-by-case basis.

Additionally, the RMS submission should include the list of dispatch dates (all the dates of dispatch to the CMS) and declaration that the relevant national fees have been paid at the time of submission).

The RMS creates the CTS record.

CMS should check they have received the application and relevant fee. The acknowledgement of an acceptable notification which is issued by the RMS on completion of the process will reflect that these documents have been submitted simultaneously to all CMS and that relevant fees have been paid. The notification process start date (Day 0) is set by the RMS on the day of receipt of the above documentation. The RMS completes the CTS record as the means of informing the CMS of the start of the notification process. The CMS are only notified via CTS, there will be no additional e-mail. Day 0 should be backdated as necessary to coincide with the actual date of receipt of the notification.

For purely national MAs the variation application has to be submitted to the relevant Competent Authority of the member state concerned including the same documents.
Review phase (Day 0–30)

The RMS will perform a check of the notification to confirm that the required supporting documentation has been submitted. The MAH’s checklist which has been appended to the application form will assist with this. The checklist must have positive confirmation e.g. by manually indicating “YES” or “tick” against each item to indicate that all the required conditions are satisfied and all documentation has been submitted. If all the documentation has not been provided, the notification will be deemed unacceptable and the MAH should immediately cease to apply the concerned variation(s) or the MAH may decide to submit a new variation, which will require a new variation procedure number.

Neither RMS nor CMS will perform a full assessment of the supporting data in detail. The RMS will be responsible for undertaking a check (which is more extensive than an administrative check) to establish the acceptance of the notification based on the submitted documentation. CMS should not comment to the RMS or MAH about the acceptance in respect of content. CMS may comment only in the case of non-receipt of documentation or non-payment of fees (highlighted from CTS and via email to the RMS and the applicant). Where a Type IA notification affects product information, it is acknowledged that the change will have already been introduced prior to submission. It is the MAH’s responsibility to ensure that the text has been correctly updated, including in any required translations. Consequently, the updated product information, including translations will not be the subject of a separate assessment. Therefore, there will be no national phase after the end of the procedure.

For Type 1A variations, there is no request by the RMS for clarification, information or documentation from the MAH and there is no clock-stop or suspension of the process.

Outcome of the notification process

The RMS will make the decision as to whether the notification is accepted or rejected. The following actions will be taken on or before Day 30.

- **For an acceptable notification**: The RMS will inform the MAH on behalf of the CMS that the Variation is considered acceptable and a letter of “Acknowledgement of an acceptable Notification” will be issued. CMS are informed of the outcome by means of the updated CTS record.
- **For an unacceptable notification**: The RMS informs the MAH in writing that the Variation is not acceptable and provides brief reasons as well as a course of action. CMS are notified via the updated CTS record, which should also state the reasons for non-acceptance.

Examples of suitable text to be used for notification acknowledgement letters issued to the MAH on completion of the process are provided in Annex 1.

For grouped variations a different outcome may apply to the different variations included in the notification, i.e. some changes may be accepted, whilst others may be rejected. In these cases please refer to Chapter 6 if this BPG for details on the possibilities of outcome.

Competent authorities should implement the decision nationally within two months in the case of a variation(s) that does not require immediate notification or six months if the variation(s) does require immediate notification.
ANNEX I

Sample text for acknowledgement notification letters to be issued to the MAH on completion of the procedure

Example 1

ACKNOWLEDGEMENT OF AN ACCEPTABLE NOTIFICATION

The <<competent authority>> acknowledges that the Type 1A variation detailed in your application is acceptable. The following change(s) has been notified:

<< enter change introduced by notification>>

The notification is considered acceptable on the basis of the Marketing Authorisation Holder undertaking that:

i. The notification of change complies with all conditions specified in the Commission guideline on the classification of variations.

ii all supporting documentation as listed in the Commission guideline on the classification of variations have been provided.

iii the application has been submitted simultaneously to all Concerned Member States and the relevant fees have been paid as required by national competent authorities.

Failure to comply with any of the above may subsequently deem the notification unacceptable.

Example 2

NON-ACCEPTANCE OF NOTIFICATION

The <<competent authority>> cannot accept your Type IA variation as being acceptable because of the following:

<<enter reason for non-acceptance>>
### ANNEX II

<table>
<thead>
<tr>
<th>Submission phase</th>
<th>To the RMS and CMS the MAH submits the application accompanied by supporting documentation as appropriate. The MAH submits list of dispatch dates to the RMS.</th>
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</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>The RMS starts the procedure and completes the CTS record. The CMS are only informed via CTS, there will be no additional mail</td>
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<tr>
<td>Until Day 30</td>
<td>The RMS checks if the notification can be accepted. The CMS only checks if the notification has been received and if the fee has been paid as appropriate.</td>
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<tr>
<td>Day 30</td>
<td>The RMS will inform the MAH on behalf of the CMSs of the outcome of the variation notification. CMS are informed accordingly via the updated CTS record. Where applicable, the MAH provided the RMS during the procedure highlighted and clean versions of the SmPC, labelling or package leaflet in electronic format. The RMS checks the highlighted (changed) text, and circulates these documents together with a statement that it has endorsed the changes made, to the MAH and CMSs. All changes in the text, in comparison with the previously approved version of product information, should be marked with track-changes in the highlighted versions circulated at the end of procedure or the RMS should confirm that these are unchanged since submission. It is recommended to upload the clean documents to CTS for transfer to the MRI index.</td>
</tr>
</tbody>
</table>
| Within 2 or 6 months after acceptance | Competent authorities should implement the decision nationally within:  
- Two six months in the case of a variation(s) that does not require immediate notification or  
- Six months if the variation(s) does require immediate notification. |