INTRODUCTION AND GENERAL COMMENTS

This document is intended to provide more clarification on how the new Variation Application Form should be completed. It will be regularly updated as more experience is gained.

The following provisions from Chapter 1 of the CMDh Best Practice Guides For The Submission And Processing Of Variations In The Mutual Recognition Procedure need to be noted:

‘A grouped application or worksharing application is a single procedure for the variation. It is not bulk or multiple single procedures and a single application form needs to be used for all products involved.

For the purpose of handling grouping and worksharing, the following definition of a marketing authorisation is used: all strengths and pharmaceutical forms of a certain product. For MRP/DCP products this would imply that all products belonging to e.g. AT/H/1234/001-sss will be considered to belong to the same marketing authorisation.’

For products authorised via the Centralised Procedure, this corresponds to the usual granting of a Marketing Authorisation, covering all strengths and pharmaceutical forms of the product concerned, which was already applicable prior to the new Variations Regulation (i.e. EU/0/00/000/001-nnn).

Therefore when a single variation is being submitted affecting more than one pharmaceutical form or strength within the above mentioned definition, a single application form should be completed (e.g. for AT/H/1234/001-002/IB/034 only 1 application form is needed instead of the 2 forms that were to be submitted under the previous Variation Regulation).

When a variation is submitted as part of a group of variations which include an extension application, the variation application form needs to be completed for the already authorised product presentations which are affected. The MAA form will need to be completed for the extension application. Note that the procedure will still be handled as one submission and that the variation application form is considered to be an annex to the application form for the extension application.

PAGE 1

Variation number
For Centrally authorised products the European Medicines Agency will assign the variation number on receipt of the application. For guidance on the structure of variation procedure numbers, please refer to the Agency’s Post-Authorisation Procedural Advice.
For products in MRP the variation procedure number should be assigned by the authorisation holder if only one MA is affected. In cases of worksharing and grouping affecting more than one MA the variation procedure number should be obtained from the Reference Authority or Reference Member State, as applicable.

In cases of worksharing or grouped applications MRP variation numbers are to be assigned (previously indicated to be virtual variation numbers, see below under PAGE 3): these are however not to be used in the communication by the MAH and involved Member States: only the variation procedure number on the first page should be used as reference in the cover letter, email headers etc..

For a single variation concerning several strengths within one MA the usual rules apply but under the new Regulation one application form can be used containing more than one MRP variation number. E.g.:

AT/H/0111/001/IB/033
AT/H/0111/003/IB/033
AT/H/0111/004/IB/033

Or alternatively: AT/H/0111/001+003-004/IB/033

Note that for the EU electronic application form the above mentioned alternative option of indication of a range is not appropriate and separate numbers need to be listed.

See Chapter 1 of the CMDh Best Practice Guides for the submission and processing of variations in the Mutual Recognition Procedure for more details. Especially ANNEX II Decision tree for allocating procedure numbers for grouped and worksharing procedures may be of interest.

Concerned Member States
Please tick all boxes for the countries which are involved in the procedures. Further specification on which Member States are involved per particular product should be provided in the table on page 3.

For centralised procedures please leave this section of the application form blank.

Type of application
On the first page of the application form it should be indicated which type of variations are included in the submission, whether a single or grouped variation is submitted and whether the worksharing procedure is followed. Note that all relevant boxes need to be ticked.

However with regard to type IB variations the following is applicable:

For all type IB variations the box “Type IB” should be ticked, unless it concerns a type IB variation where a “z”-category is ticked and which has not been classified as “z”-category following Article.5 recommendations. These type IB variations should be classified as type IB unforeseen variation and the box “type IB unforeseen” should be ticked.

Type IB variations classified as “z”-category following Article.5 recommendations should be submitted as type IB variations.

If for instance a worksharing procedure is followed for a grouped submission containing two Type II, one Type IB and one Type IB where a “z”-category is ticked (and no Article 5 recommendation is given) variations the following boxes should be ticked:

Type of Application (tick all applicable options)

☐ Type IA
☐ Type IA
☐ Single variation
☐ Grouping of variations
Type IB unforeseen

Type IB

Type II

Type II Art. 29

Or in case a single Type II variation is submitted in a grouped submission with an extension application:

**Type of Application (tick all applicable options)**

- [ ] Type IA<sub>IN</sub>
- [ ] Type IA
- [ ] Type IB unforeseen
- [ ] Type IB
- [ ] Type II
- [ ] Type II Art. 29
- [ ] Single variation
- [ ] Grouping of variations
- [ ] Including a line extension
- [ ] Worksharing

In the variation application form it is stated that:

“A variation is considered ‘unforeseen’ when the proposed variation is not considered a minor variation of Type IB following the Commission Guideline, or has not been classified as a Type IB variation in an Article 5 recommendation.

When one or more of the conditions established in the guideline for a Type IA variation are not met, the concerned change may be submitted as a Type IB variation unless the change is specifically classified as a major variation of Type II.”

The box “Type IB” should therefore be ticked for those Type IB variations which:

1. are listed as examples of Type IB in the Variations Guidelines;
2. are recommended to be Type IB following an Article 5 procedure;
3. are listed as Type IA but do not meet all of the conditions set-out in the Guideline and they are not listed as Type II variations in the Variations Guidelines.

**Change(s) concern(s):**

The following definitions apply:

**Change(s) concern(s) (for Type IB and Type II variations only, tick all changes applicable):**

- [ ] Indication
- [ ] Paediatric requirements
- [ ] Safety
- [ ] Following Urgent Safety Restriction
- [ ] Quality
- [ ] Annual variation for human influenza vaccines
- [ ] Non-food producing target species
- [ ] Other

The following guidance is on the interpretation of the above terms is provided for variations for medicinal products for human use. There is no specific guidance for medicinal products for veterinary use, however these boxes need to be ticked also in the variation application form for veterinary products.

**Indication:**

This category should be selected for an application in which a change is a new indication or an amendment to the indication, excluding a paediatric indication.
Paediatric requirements:
This category should be selected for an application in which a change is a new paediatric indication or for an amendment to the paediatric indication, and for variations related to the implementation of the Paediatric Investigation Plan or related to the implementation of the outcome of the assessment of studies under Article 45/46 of the Paediatric Regulation.

Note: if an extension/change in indication covers both the adult and (part of) the paediatric population both boxes need to be ticked.

Safety:
This category should be selected for an application in which a change relates to a change of the safety information (e.g. section 4.3 to 4.9 of the SmPC). Whether a 30 or 60 day timetable will be followed, is to be decided by RMS or the Agency.

Safety following Urgent Safety Restriction:
This category should be selected for an application to adapt the Product information following an Urgent Safety Restriction.

Quality:
This category should be selected for an application in which a change relates to a change in module 3.

Annual variation for human influenza vaccines:
This category should be selected for the annual update for human influenza vaccines. See the guideline on Fast track Procedure for Human Influenza vaccines.

Other:
This category should be selected for an application in which a change does not fall into one of the above categories.

PAGE 2

Name and address of the Applicant/MA holder
Name and address of contact person

For worksharing or grouped variations affecting more than one MA, in case of individual MAHs belonging to the ‘same MAH’ (as defined in the Commission Variations Guidelines), a single MA holder* and contact point need to be designated.

* Note that in Chapter 7 of the CMDh Best Practice Guides For The Submission And Processing Of Variations In The Mutual Recognition Procedure it is stated that …..The above principle also applies for MRP/DCP products with different companies as MAH in RMS and CMS, since these MAHs do fulfil the definition of the same MAH as given in the Commission Communication 98/C 229/03.

PAGE 3

PRODUCTS CONCERNED BY THIS APPLICATION

In cases of worksharing or grouped applications product specific MRP variation numbers are to be assigned (previously indicated to be virtual variation numbers) for MRP/DCP products: these are however not to be used in the communication: only the variation number on the first page should be used as reference. See the Best Practice Guide on Variations, Chapter 1.

For products in MRP the following examples are provided.
Example 1) Worksharing

- NL/H/0111/001; CMS: AT, DE, FR, UK (MA-number in The Netherlands: RVG 12345)
- NL/H/0222/001; CMS: AT, DE, FR (MA-number in The Netherlands: RVG 23456)
- DE/H/0333/001; not authorised in NL; CMS: NO
- The Worksharing consist of a Grouped submission (sequential variation numbers respectively: 33 for NL/H/0111, 44 for NL/H/0222 and 55 for DE/H/0333).

For the worksharing procedure for these three dossiers the completed table would be:

<table>
<thead>
<tr>
<th>(Invented)Name(s):</th>
<th>Active substance(s)</th>
<th>Pharmaceutical form</th>
<th>Strength</th>
<th>MA holder name(s):</th>
<th>MA number(s):</th>
<th>MRP Variation Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL: WonderPill A 20 mg&lt;br&gt;AT: &lt;to be completed&gt;&lt;br&gt;DE: &lt;to be completed&gt;&lt;br&gt;FR: &lt;to be completed&gt;&lt;br&gt;UK: &lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>20 mg</td>
<td>PharmaCompany&lt;br&gt;AT: &lt;to be completed&gt;&lt;br&gt;DE: &lt;to be completed&gt;&lt;br&gt;FR: &lt;to be completed&gt;&lt;br&gt;UK: &lt;to be completed&gt;</td>
<td>NL: RVG 12345&lt;br&gt;AT: &lt;to be completed&gt;&lt;br&gt;DE: &lt;to be completed&gt;&lt;br&gt;FR: &lt;to be completed&gt;&lt;br&gt;UK: &lt;to be completed&gt;</td>
<td>NL/H/0111/001/WS/033</td>
</tr>
<tr>
<td>NL: WonderPill B 20 mg&lt;br&gt;AT: &lt;to be completed&gt;&lt;br&gt;DE: &lt;to be completed&gt;&lt;br&gt;FR: &lt;to be completed&gt;&lt;br&gt;UK: &lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>20 mg</td>
<td>PharmaCompany&lt;br&gt;AT: &lt;to be completed&gt;&lt;br&gt;DE: &lt;to be completed&gt;&lt;br&gt;FR: &lt;to be completed&gt;&lt;br&gt;UK: &lt;to be completed&gt;</td>
<td>NL: RVG 23456&lt;br&gt;AT: &lt;to be completed&gt;&lt;br&gt;DE: &lt;to be completed&gt;&lt;br&gt;FR: &lt;to be completed&gt;&lt;br&gt;UK: &lt;to be completed&gt;</td>
<td>NL/H/0222/001/WS/044</td>
</tr>
<tr>
<td>DE: &lt;to be completed&gt;&lt;br&gt;NO: &lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>20 mg</td>
<td>PharmaCompany&lt;br&gt;NO: &lt;to be completed&gt;&lt;br&gt;NO: &lt;to be completed&gt;</td>
<td>DE: &lt;to be completed&gt;&lt;br&gt;NO: &lt;to be completed&gt;&lt;br&gt;NO: &lt;to be completed&gt;</td>
<td>DE/H/0333/001/WS/0055</td>
</tr>
</tbody>
</table>

\(^1\) Indicate the MA numbers affected (a range may be appropriate). For the MRP variation number, which is a product specific number, see the Best Practice Guide on Variations, Chapter I, example: NL/H/0123/001-004/IB/033/G.
Example 2) Grouped variation within one MA

- NL/H/0111/001-003; CMS: AT, DE, FR, UK (MA-numbers in The Netherlands: RVG 12345, RVG 12346, RVG 12347);
- Grouped submission includes a Type IB variation (sequential variation number: 33);

<table>
<thead>
<tr>
<th>For the grouped variation for this MA the completed table could be (Invented)Name(s):</th>
<th>Active substance(s)</th>
<th>Pharmaceutical form</th>
<th>Strength</th>
<th>MA holder name(s):</th>
<th>MA number(s): ¹</th>
<th>MRP Variation Number ³</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL: WonderPill A 10 mg AT: &lt;to be completed&gt; DE: &lt;to be completed&gt; FR: &lt;to be completed&gt; UK: &lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>10 mg</td>
<td>PharmaCompany AT: &lt;to be completed&gt; DE: &lt;to be completed&gt; FR: &lt;to be completed&gt; UK: &lt;to be completed&gt;</td>
<td>NL: RVG 12345 AT: &lt;to be completed&gt; DE: &lt;to be completed&gt; FR: &lt;to be completed&gt; UK: &lt;to be completed&gt;</td>
<td>NL/H/0111/001/IB/033/G</td>
</tr>
<tr>
<td>NL: WonderPill A 20 mg DE: &lt;to be completed&gt; FR: &lt;to be completed&gt; UK: &lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>20 mg</td>
<td>PharmaCompany DE: &lt;to be completed&gt; FR: &lt;to be completed&gt; UK: &lt;to be completed&gt;</td>
<td>NL: RVG 12346 DE: &lt;to be completed&gt; FR: &lt;to be completed&gt; UK: &lt;to be completed&gt;</td>
<td>NL/H/0111/002/IB/033/G</td>
</tr>
<tr>
<td>NL: WonderPill A 30 mg AT: &lt;to be completed&gt; DE: &lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>30 mg</td>
<td>PharmaCompany AT: &lt;to be completed&gt; DE: &lt;to be completed&gt;</td>
<td>NL: RVG 12347 AT: &lt;to be completed&gt; DE: &lt;to be completed&gt;</td>
<td>NL/H/0111/003/IB/033/G</td>
</tr>
</tbody>
</table>

Or, alternatively (note however that for the electronic application form the below mentioned alternative option of indication of a range is not appropriate separate MA and MRP Variation numbers need to be listed):

¹ Indicate the MA numbers affected (a range may be appropriate). For the MRP variation number, which is a product specific number, see the Best Practice Guide on Variations, Chapter 1, example: NL/H/0123/001-004/IB/033/G.

EMACMDh explanatory notes on Variation Application Form
<table>
<thead>
<tr>
<th>(Invented)Name(s):</th>
<th>Active substance(s)</th>
<th>Pharmaceutical form</th>
<th>Strength</th>
<th>MA holder name(s):</th>
<th>MA number(s):</th>
<th>MRP Variation Number:</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL: WonderPill A 10/20/30 mg</td>
<td>&lt;INN&gt;</td>
<td>Tablet</td>
<td>10/20/30 mg</td>
<td>PharmaCompany</td>
<td>NL: RVG 1234/6/7</td>
<td>NL/H/0111/001-002/IB/033/G</td>
</tr>
<tr>
<td>AT: &lt;to be completed&gt;</td>
<td></td>
<td></td>
<td>10/30 mg</td>
<td>AT: &lt;to be completed&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DE: &lt;to be completed&gt;</td>
<td></td>
<td></td>
<td>10/20/30 mg</td>
<td>DE: &lt;to be completed&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FR: &lt;to be completed&gt;</td>
<td></td>
<td></td>
<td>10/20 mg</td>
<td>FR: &lt;to be completed&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK: &lt;to be completed&gt;</td>
<td></td>
<td></td>
<td>10 mg</td>
<td>UK: &lt;to be completed&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For submissions to the Agency, only the presentation(s) affected by the change(s) applied for should be listed. Annex A of the centrally authorised product(s) concerned can also be provided as an Annex to the application form. For worksharing procedures submitted to the Agency, which include nationally authorised products, relevant product and Member State details (including the product specific MRP variation numbers, if applicable) should be provided as an Annex B to the application form.
EXAMPLE of a completed ANNEX B)

- DE/H/0155/001; CMS: CY, FR;
- DE/H/0165/001; CMS: AT, BE, FR, PT;
- The Worksharing consist of a Grouped submission (sequential variation numbers respectively: 38 for DE/H/0155 and 34 for DE/H/0165).

<table>
<thead>
<tr>
<th>Member State EU/EEA¹</th>
<th>MRP/National variation number²</th>
<th>Marketing Authorisation number</th>
<th>Marketing Authorisation Holder³</th>
<th>(Invented) name⁴</th>
<th>Active substance(s)</th>
<th>Strength(s)</th>
<th>Pharmaceutical Form⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>DE/H/0165/001/WS/034</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>Belgium</td>
<td>DE/H/0165/001/WS/034</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>Cyprus</td>
<td>DE/H/0155/001/WS/038</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>Germany</td>
<td>DE/H/0155/001/WS/038</td>
<td>&lt;to be completed&gt;</td>
<td>PharmaCompany WonderPill A</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>DE/H/0165/001/WS/034</td>
<td>&lt;to be completed&gt;</td>
<td>PharmaCompany WonderPill B</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>DE/H/0165/001/WS/034</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>France</td>
<td>DE/H/0155/001/WS/038</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>Portugal</td>
<td>DE/H/0165/001/WS/034</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;to be completed&gt;</td>
<td>&lt;INN&gt;</td>
<td>20 mg</td>
<td>Film-coated tablets</td>
</tr>
</tbody>
</table>

¹ List all the EEA Countries where the medicinal product(s) included in the worksharing are authorised, in alphabetical order (i.e. all medicinal products authorised in Austria, all medicinal products authorised in Belgium, etc.)
² If applicable
³ Name and address of the Marketing Authorisation Holder in each EEA Countries where the medicinal product is authorised
⁴ As registered in the respective official language of the EEA Country (no strength or pharmaceutical form should be mentioned unless it is an integral part of the authorised (invented) name)
⁵ It is possible to combine in the same row several strengths for the medicinal product in each Country. A separate row should however be used for each pharmaceutical form.
⁶ Information in English - use current standard terms from the Ph. Eur.
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**TYPE(S) of CHANGE(S)**

In case of several variations under the same classification the type of change, number and title of each of these variations should be mentioned. E.g. a grouped type II variation application of 3 type II variations C.I.4, this category should be repeated 3 times and the changes of each type II variation should be explained under the precise scope and background for change.

For Type IA variations and those Type IB changes listed in the Variations Guidelines a copy of the relevant section from the Variations Guidelines needs to be provided as an annex to the variation application form and the relevant boxes for conditions and documentations need to be ticked. For Type IA variations, all documents in the guideline should be provided (unless the guideline indicates that their absence may be appropriate or can be justified). For Type IB variations, to ease validation applicants are advised to provide all documents suggested in the Guidelines, including the documentation required for Type IA variations, but which are submitted as a Type IB variation since not all of the Type IA conditions are met.

For Type IA variations following an Article 5 recommendation a copy of the conditions’ needs to be provided and the relevant boxes for conditions need to be ticked.

Only the main header of the change from the Variations Guidelines with the specific variation applied for needs to be selected.

So from the list of changes presented as:

<table>
<thead>
<tr>
<th>B.I. a.2</th>
<th>Changes in the manufacturing process of the active substance</th>
<th>Procedure type</th>
<th>Implement. Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a) Minor change in the manufacturing process of the active substance</td>
<td>□ IA □ IB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b) Substantial change to the manufacturing process of the active substance which may have a significant impact on the quality, safety or efficacy of the medicinal product.</td>
<td></td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>c) The change refers to a biological / immunological substance or use of a different chemically derived substance in the manufacture of a biological/immunological substance, which may have a significant impact on the quality, safety and efficacy of the medicinal product and is not related to a protocol.</td>
<td></td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>d) The change relates to an herbal medicinal product and there is a change to any of the following: geographical source, manufacturing route or production.</td>
<td></td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>e) Minor change to the restricted part of an Active Substance Master File</td>
<td>□ IA □ IB □ II</td>
<td></td>
</tr>
<tr>
<td></td>
<td>z) Other variation</td>
<td>□ IA □ IB □ II</td>
<td>Art 5 Implement.</td>
</tr>
</tbody>
</table>

* the conditions are included in the publication of the advice by CMD(h/v) or the Agency.
1 If one of the conditions is not met and the change is not specifically listed as Type II.
the following information needs to be included in the application form when applying for variation B.I.a.2.c).

<table>
<thead>
<tr>
<th>B.I.a 2</th>
<th>Changes in the manufacturing process of the active substance</th>
<th>Procedure type</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑</td>
<td>c) The change refers to a biological / immunological substance or use of a different chemically derived substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol.</td>
<td>II</td>
</tr>
</tbody>
</table>

Further explanation

<table>
<thead>
<tr>
<th>B.I.a 2</th>
<th>Changes in the manufacturing process of the active substance</th>
<th>Procedure type</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑</td>
<td>a) Minor change in the manufacturing process of the active substance</td>
<td>☑ IA ☑ IB</td>
</tr>
</tbody>
</table>

If one of the conditions is not met and the change is not specifically listed as Type II.

Since Type IA variations are ‘do and tell’ variations the implementation date of the change concerned needs to be specified in the last column. For all other variations the implementation date needs to be provided at the end of the application form. When a Type IA change is part of a grouped submission with Type IB or Type II changes or if a Type IA change is included in a worksharing procedure and when a specific implementation date can not be included here (i.e. when the Type IA change has not yet been implemented by the MAH) reference should be made to the Declaration of the Applicant section of the application form (i.e. ‘See Decl. Appl.’).

Where the change applied for does not meet all the conditions of a particular Type IA variation as given in the Variations Guidelines and the change is not listed as a Type II variation this is considered to be a Type IB variation and this should be indicated on the application form. Such variation is to be included as follows:

<table>
<thead>
<tr>
<th>B.I.a 2</th>
<th>Changes in the manufacturing process of the active substance</th>
<th>Procedure type</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑</td>
<td>a) Minor change in the manufacturing process of the active substance</td>
<td>☑ IB⁹</td>
</tr>
</tbody>
</table>

Other variations

<table>
<thead>
<tr>
<th>B.I 2</th>
<th>Changes in the manufacturing process of the active substance</th>
<th>Procedure type</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑</td>
<td>z) Other variation</td>
<td>☑ Art 5</td>
</tr>
</tbody>
</table>

To apply for variations not listed in the guideline, MAHs should declare such other variation (“z”) under the specific guideline section concerned at the lowest possible level i.e. either within a specific
variation or under the appropriate guideline section title, as appropriate, including its proposed classification. Please indicate whether the variation has been subject to an Article 5 procedure.

These changes can only be submitted as a Type IA variation, when such classification has been recommended following an Article 5 procedure.

Note that ‘other variations’ recommended to be Type IB via an Article 5 procedure, should be considered as ‘Type IB’ and not as ‘Type IB unforeseen’ variations on the first page of the application form.

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PRECISE SCOPE AND BACKGROUND FOR CHANGE, AND JUSTIFICATION FOR GROUPING, WORKSHARING AND CLASSIFICATION OF UNFORESEEN CHANGES (if applicable)

The actual changes that are being applied for should be stated in a concise way and a brief explanation provided of why the change is required. For grouping, where applicable, the justification should include a reference to Annex III of the Commission Regulation, or to examples published by CMD or the Agency, or to any pre-submission contacts with the RMS/NCA or the Agency (as appropriate).

For example, where variations within a group are considered by the applicant to be consequential to each other (cases 2 and 3 in Annex III of the Commission Regulation), this should be clearly stated and appropriately justified by the applicant in this section of the application form.

For worksharing procedures, the justification should refer to the pre-submission contacts with CMD or the Agency.

For type IB variations where the “z”- category is ticked - except type IB variations classified as “z”- category following Art.5 recommendations - a justification for classification as a type IB has to be given.

In the present/proposed table: specify the precise present and proposed wording or specification, including dossier section number(s) at the lowest possible level according to CTD. For SPC, labelling and package leaflet changes, underline or highlight the changed words presented in the table or provide as a separate Annex.

If applicable, the D-U-N-S (Data Universal Numbering System) number and/or EU or National ASMF reference number should be provided.

OTHER APPLICATIONS
This section should only be completed for submissions relating to one MA and should contain a concise and general description of the changes.

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Declaration of the Applicant
All applicable boxes need to be ticked, the implementation date for the Type IB and Type II variation(s) need(s) to be indicated here, as appropriate. The implementation date for Type IA changes is normally to be indicated in the TYPE(S) of CHANGE(S) section of the form (see also ‘Page 5’ above.

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In case of worksharing/grouping for more than one MA a single MA holder and contact point need to be designated and the box declaring that the main signatory is authorised on behalf of all designated contact points (as specified in the dossiers) needs to be ticked.