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Procedure Management and Committees Support Division

Pre-notification check for type IB Variations

This pre-notification checklist is aimed at facilitating submission of complete and correct Type IB variation notifications by Marketing Authorisation Holders (MAHs).

Guidance for Marketing Authorisation Holders

The Agency strongly recommends that this checklist is used in advance of submission of any Type IB variation; you should be able to answer to every item listed below "Yes" unless a specific point is not applicable "n/a" to the application in question. Please note that this checklist should not be included in the submission.

Commission Regulation (EC) No 1234/2008 ('the Variations Regulation') defines a minor variation of type IB as a variation that is neither a type-IA variation nor a type-II variation nor an extension. Such minor variations must be notified to the national competent authority or the European Medicines Agency by the MAH before implementation, but do not require a formal approval. Upon acknowledgement of receipt of a valid notification, the MAH must wait a period of 30 days to ensure that the notification is deemed acceptable by the national competent authority or the Agency before implementing the change ('tell, wait and do' procedure).

Upon receipt of a type IB application, the procedure manager proceeds to validate the documentation submitted in accordance with the checklist included below. The validation issues included in the checklist are presented below in different fonts (**bold**, *italics* and normal) to facilitate understanding on the points that would prevent the start of the procedure until they are addressed satisfactorily from those that facilitate validation or assessment:

- **Bold** corresponds to blocking validation issues that need to be satisfactorily addressed by the MAH before the start of the procedure;
- *Italics* corresponds to validation issues that relate to information needed for documentation check but not blocking;
- Normal corresponds to information considered for completeness of the submission and not blocking. These issues can be either raised at validation together with other **Bold** or *italic* validation issues or, if no bold or italic validation issues are identified, they are highlighted in the variation report for improvement of future submissions.

Issues identified during validation will be notified to the MAH via email. The MAH will be requested to provide responses to the issues raised within 5 working days. Delayed or insufficient responses will

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lead to complete or partial invalidation (in case of grouped variations) of the application as only one request for supplementary information will be issued during the validation phase.

For variations affecting an Active Substance Master File (ASMF), an additional section of the checklist is presented addressing the specific submission requirements.

Type IB Pre-notification checklist

Type IB submission checklist[1]	Yes	n/a
TECHNICAL SUBMISSION REQUIREMENTS		
• Dossier is submitted in eCTD format[2] and is technically valid (i.e. has passed eCTD technical validation criteria)		
COVER LETTER[3]		
• Present, dated and signed. • Refers to the same medicinal product(s), EU numbers and procedure as listed in the application form. • Where applicable, previous regulatory and/or procedural advice requested to the Agency is attached.		
APPLICATION FORM[4]		
• **Present, correct version, dated and signed by the contact person authorised for communication as specified in section 2.4.3 of the initial Application Form or a letter of authorisation is attached.** • **States the name and address of the MAH and of the contact person as previously notified to the Agency.**		
'Type of application' • Correctly identified by ticking the box(es) Type IA, Type IA_{IN} (in case of grouped variations) and Type IB. It should also be specified whether the procedure is foreseen or unforeseen in the classification guidance. • Indicates whether it is a single or a grouped submission.		
'Products concerned by this application' • EU marketing authorisation number(s) of (all) affected presentation(s) is/are listed.[5] • Is/are the same as that/those indicated in the Present/Proposed table, Precise Scope and cover letter.		
'Types of change(s)' • **All changes applied for are correctly classified according to the Guideline on the details of the various categories of variations (2013/C 223/01).** • **When two or more changes fall under the same indent, the scope number is indicated as many times as there are changes (e.g. scope B.II.e.5.a.2 is repeated 'x' times for 'x' additional new pack sizes).** • **In case of grouped variations including changes categorised as type IA,** **- the date of implementation for Type IA changes is provided,**		

1 Guidance for submitting type IB variations is provided in the post-authorisation guidance 'Q&A: type IB variations':
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000085.jsp&mid=WC0b01ac058013af9c

2 Please refer to the "EMEA implementation of electronic-only submissions and mandatory eCTD submissions in the Centralised Procedure: statement of intent"
www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500004098

3 Preferably by using the template www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500106371

4 As published on the Commission's website in Volume 2C of the Notice to applicants

5 Please avoid stating 'See Annex A' if **not** all presentations are affected by the change(s) applied for.

Type IB submission checklist[1]	Yes	n/a
- the Type IA variation has been submitted within 1 year (Type IA) or immediately following implementation (Type IA_{IN}), as appropriate		
'Precise scope and background for change' It contains for each change applied for in the section 'Types of Change(s)': • A scope number and a precise description of the change. If the PI is affected, the sections updated should also be provided here. • When two or more different changes fall under the same scope, the scope number is indicated as many times as there are changes (e.g. scope B.II.e.5.a.2 is indicated for each additional new pack size).		
'Present and Proposed' table (or attachment) • *Reflects all the changes applied for in the section 'Types of Change(s)'.* • Shows the precise present and proposed wording as in the relevant sections of the dossier and, if applicable, in the Product Information. For further guidance, see footnotes 9 and 10 of the application form. • Dossier section number(s) is/are indicated at the lowest possible level.		
'Annexed documents (where appropriate)' • Relevant boxes are selected or left un-ticked as appropriate. If changes to the Annex II of the Product Information are proposed, the box "Manufacturing Authorisation Holder responsible for batch release and conditions of the Marketing Authorisation" should be ticked.		
'Declaration of the Applicant' The boxes relating to the aspects below are ticked: • **"There are no other changes than those identified in this application [...]".** • "Where applicable, all conditions as set for the variation(s) concerned are fulfilled". • "For type IA notifications: the required documents as specified for the changes concerned have been submitted" (if included as part of the grouped variations). **In case of a worksharing involving medicinal products approved within the mutual recognition procedure or nationally, this application has been submitted simultaneously, to the relevant National Competent Authorities and the EMA.** • **Date of implementation of the Type IB changes is inserted.**		
Grouping is acceptable, either as outlined in Annex III of Reg. (EC) No 1234/2008 or previously agreed with the Agency.		
SUPPORTING DOCUMENTATION		
Classification Guideline • *Copy of the relevant page(s) from the Classification Guideline is/are attached for each change applied for. This does not apply to changes that are unforeseen in the classification guideline (.z scopes).* • *Relevant conditions and documentation, as specified in the appropriate Guideline*[6]*, are ticked.*		
Documentation listed in Annex IV of the Variations Regulation and in the Commission Classification guideline. • *Included and presented in accordance with the appropriate EU-CTD format headings and numbering.* • *Is complete, updated, and correctly reflects the changes listed in the Present and Proposed table.* • *Affected section(s) of the dossier correctly show the change(s) applied for.*		

6 Guideline on the details of the various categories of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (2010/C 17/01)

Type IB submission checklist[1]	Yes	n/a
PRODUCT INFORMATION (SMPC, ANNEX II, LABELLING, PL) AND ANNEX A		
• The Product Information (PI) includes only changes declared in the Present and Proposed table in the application form. • **The PI provided in all EEA languages in Word format (with tracked changes) and as clean PDFs correctly formatted[7]. No other versions or formats are included.** • **The PI correctly reflects the scope of the variation and is based on the latest approved version.** • **Annex A is provided in all EEA languages in Word format (with tracked changes) and as clean PDFs when its content is modified by a change (e.g. addition or deletion of a presentation).**		
New EU number(s) • Reserved with the EMA[8] • Correctly inserted in Annex A and in the Product Information.		
CHANGES TO THE RMP		
• **The Version number correctly reflected.**		
• The changes to the RMP should be included in the Application Form in the 'Present and Proposed' table or provided as a separate Annex (except in case of update to the latest RMP template). • **RMP, based on the latest approved version, only including the changes covered by the scope of the variation with tracked changes, or** • **RMP including a summary of changes from the previous RMP version (mandatory in case update to the latest RMP template).**		
CHANGES TO AN ASMF		
MAH should submit: • **Application form listing the ASMF number in the 'Present and Proposed' table (last row).** In order to avoid validation comments, the EMA strongly recommends submission of the variation application once the ASMF holder has requested and obtained an EMEA ASMF reference number[9] and has successfully carried out the submission of relevant sections of the ASMF in the appropriate eCTD format. • **Revised sections of the dossier (open part) corresponding to ASMF open part.**		
MAH should liaise with ASMF holder to ensure that the following documentation is submitted: • Submission letter and administrative details (Annex 3 of the ASMF Guideline)[10,11]. • Detailed table of changes, clearly showing the present and proposed situation. Dossier section number(s) is/are indicated at the lowest possible level. • **Revised sections of the ASMF dossier (open/restricted part) reflecting changes to the previously accepted version, as applicable.**		

This checklist is published for transparency purposes and does not preclude that during the actual validation of the submitted application the Agency may identify other issues that could impact the validation outcome.

7 Please refer to the User guide on the preparation of PDF versions of the product information

8 New EU sub-numbers for Type IB variations concerning an additional presentation (e.g. new pack size) should be requested from the European Medicines Agency.

9 Please refer to Q.27 of the Pre-submission guidance

10 Guideline on Active Substance Master File Procedure

11 Additional guidance on documents relating to an ASMF