EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Procedure Management and Committees Support Division

Pre-notification check for type IA/IA$_{IN}$ Variations

This pre-notification checklist is aimed at facilitating submission of complete and correct Type IA and Type IA$_{IN}$ 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 IA or Type IA$_{IN}$ variation; you should be able to answer "Yes" to every item listed below 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 Type IA/IA$_{IN}$ variations as minor variations which have only a minimal impact, or no impact at all, on the quality, safety or efficacy of the medicinal product and do not require prior approval before implementation ("Do and tell" procedure). Type IA/IA$_{IN}$ variations are reviewed by the Agency within 30 days following receipt, without involvement of the Rapporteur or Co-Rapporteur. These are simple procedures without clock-stop and for which interactions with Applicants are not envisaged.

However, in exceptional cases, the Agency may issue a Request for Supplementary Information, responses to which should be provided within 4 working days. Failure to respond within the specified deadline may lead to an unfavourable outcome.

For variations classified as Type IA or Type IA$_{IN}$ relating to:
- changes to the Risk Management Plan (RMP)
- implementation of a PRAC signal recommendation wording (when classified as Type IA$_{IN}$)
- changes to an Active Substance Master File (ASMF)

an additional section of the checklist is presented addressing the specific submission requirements.

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Type IA and Type IA_{IN} Pre-notification checklist

Type IA / IA_{IN} 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 number(s) 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 and/or Type IA_{IN}, as applicable. • 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.1 is repeated 'x' times for 'x' additional new pack sizes; scope A.4 is repeated for each manufacturing site affected by the change). • The **date of implementation** is provided. The variation has been submitted immediately following implementation (Type IA_{IN}) or within 1 year (Type IA), as appropriate. In case of variation(s) affecting more than 1 Marketing Authorisation (IG): • the same (group of) variation(s) is applied for all Marketing Authorisations but the scope(s) is/are not repeated for each product[6]		
'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[7]. 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.1 is indicated for each additional new pack size).		

[1] Guidance for submitting Type IA variations is provided in the post-authorisation guidance 'Q&A: type IA variations'.
[2] Please refer to the "EMEA implementation of electronic-only submissions and mandatory eCTD submissions in the Centralised Procedure: statement of intent".
[3] Preferably by using the template.
[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.
[6] It is understood that the same change(s) apply/ies to all products included in the application.
[7] A 'Guidance for applicants for the preparation of the 'precise scope' section of the variation application form' has been prepared to support marketing authorisation holders in completing this section.

Type IA/IA$_{IN}$ submission checklist[1]	Yes	n/a
'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**' Boxes relating to: • "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". are ticked. In case of variation(s) affecting more than 1 Marketing Authorisation (IG applications), ensure that all Marketing Authorisations belong to the same marketing authorisation holder[8] and that the following boxes: • […] the MAs concerned belong to the same MAH (under 'Declaration of the Applicant'). • […] the main signatory confirms authorisation to sign on behalf of the designated contacts […] (under 'Signature'). are also ticked. MAHs are reminded that with the introduction of the Common Repository (mandatory as of July 1st, 2015) separate submissions to all CHMP members/(Co-)Rapporteur are no longer required.		
SUPPORTING DOCUMENTATION		
Classification Guideline • Copy of the relevant page(s) from the Classification Guideline is/are attached for each change applied for. • Relevant conditions and documentation, as specified in the appropriate Guideline[9], 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(s) the change(s) applied for.		
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 is provided in all EEA languages in Word format (with tracked changes) and as clean PDFs correctly formatted[10]. 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		

[8] As per Commission Communication 98/C 229/03 'applicants belonging to the same mother company or group of companies and applicants having concluded agreements or exercising concerted practices concerning the placing on the market of the relevant medicinal product have to be taken as one entity'

[9] Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures (2013/C 223/01)

[10] Please refer to the "User guide on how to generate PDF versions of the Product Information and other annexes - human"

Type IA / IA$_{IN}$ submission checklist[1]	Yes	n/a
PDFs when its content is modified by a change (e.g. addition or deletion of a presentation, change in product name). • The formatting checklist[11] has been completed and included in the submission.		
New EU number(s) • Reserved with the EMA[12]. • Correctly inserted in Annex A and in the Product Information.		

Additional checklists addressing specific submission requirements for changes to RMP, implementation of PRAC recommendations and changes to ASMF

Type IA / IA$_{IN}$ submission checklist[1]	Yes	n/a
CHANGES TO THE RMP		
• The version number is 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. Changes to RMP as part of IA variations need to include the **exact** wording as agreed within the context of a previous regulatory procedure. • **RMP,** based on the latest approved version, only including the changes covered by the scope of the variation **with tracked changes**		
IMPLEMENTATION OF OUTCOME OF A PRAC SIGNAL RECOMMENDATION		
• The agreed wording is correctly reflected in all applicable sections of the SmPC and PIL as published on the EMA website[13].		
• Annexes provided in Word version (with tracked changes) and as clean PDF correctly formatted[8]. No other versions or formats are included.		
CHANGES TO AN ASMF		
The 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[14] and has successfully carried out the submission of relevant sections of the ASMF in the appropriate eCTD format. • Revised sections of the dossier (Applicant's Part), which should correspond to the ASMF Holder's Open Part.		
The MAH should liaise with the ASMF Holder to ensure that the following documentation is submitted: • Submission letter and administrative details (Annex 3 of the ASMF Guideline)[15, 16]. • 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 review of the submitted application the Agency may identify other issues that could impact the outcome.

[11] Formatting checklist.
[12] As of 1st April 2011, new EU sub-numbers for Type IA variations concerning an additional presentation (e.g. new pack size) should be requested to the European Medicines Agency prior to submission similarly to the procedure already in place for obtaining new EU sub-numbers for Type IB variations. Please refer to Q.11 of the published post-authorisation guidance 'Q&A: type IA variations'
[13] Please refer to "PRAC recommendations on safety signals".
[14] Please refer to Q.3.3.6 of the Pre-submission guidance How shall I submit an Active Substance Master File (ASMF)?
[15] Guideline on Active Substance Master File Procedure.
[16] Additional guidance on documents relating to an active substance master file.