

Variation eAF v1.24.0.0

Changes introduced in v1.24.0.0 of the variation form Guidance for applicants – **Updated 26.10.20**

Kristiina Puusaari Go-live of the new version 15th September 2020 Mandatory use from 15th of December 2020



Summary of changes in v1.24.0.0



The v1.24.0.0 provides a **major technical change in the variation application form** (H&V)

- Connection between sections 1 and 3 of the form;
 - The selections made in section 1 'Type of Application' now directly affects the section 3 and depending on the selection, only the relevant scopes are available for selection in section 3.
 - Note: It is very important to note that any changes in section 1 'Type of Application' will lead
 into deletion of any already selected scopes in section.
- The variation scopes are now selected using controlled terminology lists (from RMS)
 instead of hard coded lists. This will bring significant performance improvements as the
 form is now much shorter and lighter
- The 'Conditions and Documentation' are now integrated in to the form and applicable conditions and documentation are automatically shown together with the scope(s) that have been selected. This means that separate Annex to the application form should no longer be provided. The applicant can indicate, using a tick box, the relevant selections and additionally, a free text field has been provided to include any justification/details for example why certain condition is not met/document is not provided or simply to provide more details

Important reminders about using the eAF forms

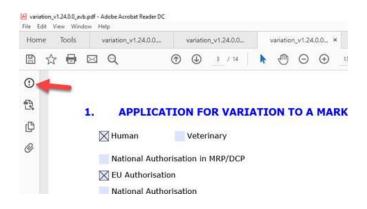


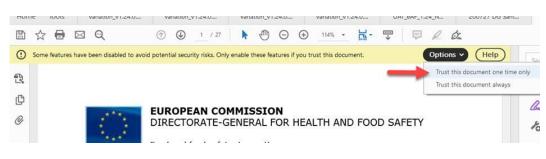
- The eAFs should be edited using Adobe Reader DC
- Please note that the conditions and documentation provided as a part of the scope, unfortunately do not contain the numbering from the classification guideline and the ordering of the conditions/documentation may be different from the classification quideline. We are currently looking at options in relation to this issue, however, regardless there is no need to provide separate annex as this could lead into discrepancies and additional work.
- Please note that the forms must be signed using an image of a signature or a signature snippet. Adobe sign or other digital signature tools must not be used
- Please note that imports of data from an older version do not work when there are significant changes to the form from the previous version. For example, it is not possible to import data from variation form v1.23.x.x due to very extensive DES changes
- If you experience any issues with the forms please report these to the EMA Service Desk portal immediately
- If you notice that there is an error in the newly introduced RMS variations list, for example a typo, a **missing scope**, error in the Conditions or Documentation etc, please report these to the EMA Service Desk portal immediately. In most cases the missing scopes are not intentional!

Accessing control terminology lists – very important



- In order to access the control terminology lists, the forms must be trusted first
- Please save the form on your local drive potentially with another name and open the saved form using adobe reader DC. It is important to use adobe reader DC to edit the forms instead of adobe acrobat or acrobat pro as using these will result in issues with locking the forms and may lead to rejection
- Once you open the form, there should be an exclamation mark on the top of the left hand pane. If the pane is closed, click the small sideways arrow to open the pane
- When you click exclamation mark, a yellow banner will open across the top, please select trust this document one time only

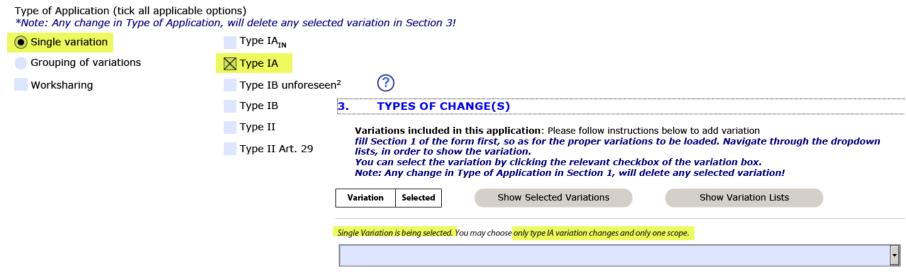






The selections made in section 1 'Type of Application' will now directly affect the section 3 and depending on the selection, only the relevant scopes are available for selection in section 3.

If a 'single' variation has been selected in section 1, it is only possible to select a single scope in section 3





If a grouping has been selected in section 1, a form validation error will be raised if only single scope is selected with the exception of Type IA_{IN} or Type IA variations where a single scope can be selected without a validation error

*Note: Any change in Type of Applic	ole options) Cation, will delete any sele	lected variation in Section 3!	
 Single variation 	Type IA _{IN}		
Grouping of variations	Type IA		
Including a line extension ³	? Type IB unf	foreseen ²	
Worksharing	Type IB		
	Type II		
	Type II Art.	. 29 ⁴	
Grouping of variations is being sales	ted You may choose yar	riation changes of types that are selected on section 1.	
Grouping or variations is being selec	tea. Tou may choose van	3	
Grouping of variations is being select	rou may choose var		•
FORM VALIDATION	rou may choose var		_
FORM VALIDATION Validation Errors: 1			_
FORM VALIDATION Validation Errors: 1		of variations is selected in Section 1 and re-validate.	



The selection of scopes in section 3 is done by drilling down dropdown menu which displays different available scopes based on the selections in section 1

Please note that any changes in Type of Application in section 1 will delete any

selected variations!

Variations included in this application: Please follow instructions below to add variation fill Section 1 of the form first, so as for the proper variations to be loaded. Navigate through the dropdown lists, in order to show the variation.

You can select the variation by clicking the relevant checkbox of the variation box.

Note: Any change in Type of Application in Section 1, will delete any selected variation!

		Ch	C-1td-Vi-ti		Ch \ \ \ i - t i -	- 11-b-		
Variation	Selected	Show	Selected Variations		Show Variation	n Lists)	
ingle Variation	ngle Variation is being selected. You may choose only type IB variation changes and only one scope.							
B. QUALITY	CHANGES						•	•
B.I ACTIVE S	UBSTANCE						•	-
B.I.a) Manufa	B.I.a) Manufacture							
							,	-
B.I.a.2 Chang	ges in the ma	anufacturing pro	carting material/reage cess of the active subs tch size ranges) of acti	tance		_		ı
3.I.a.3 Change in batch size (including batch size ranges) of active substance or intermediate used in the manufacturing pro 3.I.a.4 Change to in-process tests or limits applied during the manufacture of the active substance 3.I.a.5 Changes to the active substance of a seasonal, prepandemic or pandemic vaccine against human influenza								
B.I.a.z Re-arr	angement a	nd amendment	of equipment in the pl	asma poolin	g line of the activ	e substance v	vhich has already	/



In order to **select** the chosen scope, it is important to tick the 'select' tick box. If this box is not ticked and you make changes in the dropdown menu, the selected options will be deleted

Variat	ion	Selected		Show Sele	ected Variation	s		Show Variation	on Lists	
B.I.a.2	2.a 1	l								
Single Var	riation is	being select	ed. You may	y choose only typ	e IB variation char	ges and only or	ne scope.			
select	B.La.2.a - QUALITY CHANGES - ACTIVE SUBSTANCE - Manufacture - Changes in the manufacturing process of the active substance -									
Procedure Types: IA IB										
Condition The		bstance is no	t a biological	immunological su	bstance.					
Note:	Note:									
The change is fully described in the open (applicant's') part of an Active Substance Master File, if applicable.										
Motor				1						

If only one procedure type, for example IB is possible, based on the selection in section 1, or due to classification guideline, the procedure type will be automatically ticked by the system and cannot be manually changed



For Type IA and Type IA_{IN} the implementation date and implementation note are available.

Single Variation is being selected. You may choose only type IA variation changes and only one scope.
B. QUALITY CHANGES
B.II. FINISHED PRODUCT
B.II.b) Manufacture
B.II.b.2 Change to importer, batch release arrangements and quality control testing of the finished product
B.II.b.2.a Replacement or addition of a site where batch control/testing takes place
select B.II.b.2.a - QUALITY CHANGES - FINISHED PRODUCT - Manufacture - Change to importer, batch release arrangements and quality control testing of the finished product - Replacement or addition of a site where batch control/testing takes place
Procedure Types: IA IB IB Implement. Note:
Conditions:
The site is appropriately authorised.
Note:
The product concerned is not a biological/immunological medicinal product.
Note:



Where relevant the Art 5. checkbox will be automatically ticked and cannot be manually unticked.

Single variation is being selected. Fou may choose only type IA variation changes and only one scope.						
B. QUALITY CHANGES						
B.I ACTIVE SUBSTANCE						
B.I.c) Container closure system						
B.I.c.1 Change in immediate packaging of the active substance						
B.I.c.1.z Deletion of one of the authorised bulk or final containers						
select B.I.c.1.z - QUALITY CHANGES - ACTIVE SUBSTANCE - Container closure system - Change in immediate packaging of the active substance - Change in immediate packaging of the active substance						
Procedure Types: IA IB II						
Implement. Date: Article 5						
Conditions:						
The remaining packaging must be adequate for the storage of the bulk or final active substance at the authorised conditions.						
Notes						



When grouping is selected in section 1, and different procedure types have been selected in section 1, you will need to **manually** select the procedure type.

+ and – buttons, as well as 'clone' button to add additional scopes/clone scopes you have selected are available

select	B.II.b.2.a - QUALITY CHANGES - FINISHED PRODUCT - Manufacture - Change to importer, batch release arrangements and quality control testing of the finished product - Replacement or addition of a site where batch control/testing takes place Clone				
Procedu	re Types: IA 🔀 IB 🗌				
Impleme	ent. Date: 6 months after approval				
Conditio	vns:				
The site is appropriately authorised.					
Note:					
The product concerned is not a biological/immunological medicinal product.					
Note:					
Method transfer from the old to the new site or new test laboratory has been successfully completed.					



The relevant Conditions and Documentation are now available directly in the form and those relevant to the selected procedure type and scope are shown as a part of the scope.

If the condition/documentation tick box is not ticked, the free text field is **mandatory**. The free text field is always available and any necessary information can be included in it, as previously done in the separate annex to the application form.

select	B.II.b.2.a - QUALITY CHANGES - FINISHED PRODUCT - Manufacture - Change to importer, batch release arrangements and quality control testing of the finished product - Replacement or addition of a site where batch control/testing takes place Clone				
Procedu	re Types: IA 🔀 IB 🗌				
Impleme	ent. Date: Implement. Note: 6 months after approval				
Conditio	ns:				
The	e site is appropriately authorised.				
Note:					
⊠ The	product concerned is not a biological/immunological medicinal product.				
Note:					
⊠ Me	thod transfer from the old to the new site or new test laboratory has been successfully completed.				
Note:	Note: Details on the documentation provided that the applicant wishes to provide for the regulatory authority the application is addressed to. This text does not have size limit and the field is wrapped for ease of reading.				
At least one batch control/testing site remains within the EU/EEA or in a country where an operational and suitably scoped GMP mutual recognition agreement (MRA) exists between the country concerned and the EU, that is able to carry out product testing for the purpose of batch release within the EU/EEA.					
Note:					
Docume	ntations:				
Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 68 format for veterinary products, as appropriate) including revised product information as appropriate.					
١	Classified as internal/staff & contractors by the European Medicines Agency				

Please note:

The separate annex is no longer expected to be provided as a part of the submission.



Always ensure that you have **selected the scope** and ensure that the details are shown in the summary box before moving on. This is especially important for grouping variations if you need to select a different scope as this will be done by repeating the selections using the dropdown menu.

3. TYPES OF CHANGE(S) Variations included in this application: Please follow instructions below to add variation fill Section 1 of the form first, so as for the proper variations to be loaded. Navigate through the dropdown lists, in order to show the variation. You can select the variation by clicking the relevant checkbox of the variation box. Note: Any change in Type of Application in Section 1, will delete any selected variation! Variation Show Selected Variations Show Variation Lists Selected B.II.b.2.a Grouping of variations is being selected. You may choose variation changes of types that are selected on section 1. select B.II.b.2.a - QUALITY CHANGES - FINISHED PRODUCT - Manufacture - Change to importer, batch release arrangements and quality control testing of the finished product - Replacement or addition of a site where batch control/testing takes place Clone Procedure Types: IB Implement. Date: Implement, Note: 6 months after approval Conditions



For groupings, if you have used the 'Show Selected Variations' button and wish to continue adding different scopes, please click the 'Show Variation Lists' which will display a 'fresh' dropdown menu to continue scope selection.

If you have not used 'Show Selected Variations' button and wish to continue adding other scopes, simply start over by selecting the relevant scope using the required level of detail – as long as you have selected the previous scope and can see it in the summary box, you are not overwriting the previous selection.

TYPES OF CHANGE(S) Variations included in this application: Please follow instructions below to add variation fill Section 1 of the form first, so as for the proper variations to be loaded. Navigate through the dropdown lists, in order to show the variation. You can select the variation by clicking the relevant checkbox of the variation box. Note: Any change in Type of Application in Section 1, will delete any selected variation! Show Selected Variations Show Variation Lists Variation Selected B.II.b.2.a Grouping of variations is being selected. You may choose variation changes of types that are selected on section 1. A. ADMINISTRATIVE CHANGES B. OUALITY CHANGES C. SAFETY, EFFICACY, PHARMACOVIGILANCE CHANGES D. PMF / VAMF



In order to **select** the chosen scope, it is important to tick the 'select' tick box. If this box is not ticked and you make changes in the dropdown menu, the selected options will be deleted

Variation	Selected	Show Selected Variations	Show Variation Lists				
B.I.a.2.a	1						
Single Variat	on is being selec	ted. You may choose only type IB variation changes a	nd only one scope.				
<u> </u>							
select	5 OHAUTV	CHANGES ACTIVE CHESTANISE IA					
			nanges in the manufacturing process of the active substance -				
M	Minor change in the manufacturing process of the active substance						
Procedure T	Procedure Types: IA IB IB						
		1					
Conditions		1					
The acti	ve substance is no	ot a biological immunological substance.					
Note:	Note:						
The cha	nge is fully describ	bed in the open (applicant's') part of an Active Substance I	Vlaster File, if applicable.				
Matai		1					

If only one procedure type, for example IB is possible, based on the selection in section 1, or due to classification guideline, the procedure type will be automatically ticked by the system and cannot be manually changed

Any questions?

Further information

EMA Service Desk

Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us Send us a question Go to www.ema.europa.eu/contact Telephone +31 (0)88 781 6000

