

Variation eAF v1.24.0.0

Changes introduced in v1.24.0.0 of the variation form (to NCA users) – $\ensuremath{\textbf{Updated}}$

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)
- The change **mainly affects the applicants** as the way of **selecting** the variation types and scopes has changed significantly

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- The change to the EMA and NCAs is less, however, opening of received forms should be much faster as the form has become much lighter and shorter as the variation scopes are now selected using controlled terminology lists (from RMS) instead of hard coded list
- The main change for the receiving authorities is in the **'Conditions and Documentation'** which are now **integrated in to the form** and are inherent part of the scopes that have been selected. This means that **there is no longer a need for a separate Annex** to provide these. The applicant can include justification/details why certain condition is not met/document is not provided or to provide any other details as necessary directly in the eAF section 3.
- Unfortunately, at the time of go live the, due to RMS system limitation, the conditions and documentations integrated into the eAF are not in the same order as in the Classification Guideline. The system does not allow manual ordering of the items and hence they are displayed in a different order. The numbers referred to in the Classification Guideline are not displayed, however, we are discussing if these should be added to RMS. These may provide ease of seeing which condition/documentation is in question, however, they may not appear in numerical ¹order.

Important reminders on the use of eAFs

These points are very important to the applicants filling in the forms, however, it is good to be aware of this points in case you are asked or come across a form with an issue;

- The eAFs should only be edited using adobe editing tools as using any other editing tools may lead to issues when the forms are received and may lead to rejection. If the received form appears not signed or is signed but is not properly locked, it may have been edited using Adobe Acrobat/Acrobat Pro or other non adobe tool
- 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 cannot 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 v1.23.x.x due to very extensive DES changes
- In general, if you experience any issues with the forms please report these to the <u>EMA</u> <u>Service Desk</u> 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 follow the updated eAF new term request process



TYPES OF CHANGE(S)

Please see example of a filled in, locked form section 3 using in v1.24.0.0 on the right.

Please note that the following slides provide details to the applicant on how to fill in the form and may not be so much interest to the EMA users, however, these could be useful in understanding the user experience of the applicant and the business rules.

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Nota: Not applicable

- 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. It is important to use adobe reader 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
- When you click this with your mouse, a yellow banner will open across the top, please select trust this document one time only

variation_v1.24.0.0_avb.pdf - Adobe Acrobat Reader DC File Edit View Window Help	
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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

Type of Application (tick all applicable *Note: Any change in Type of Applica	e options) tion, will delete any selec	cted variation in Section 3!
• Single variation	Type IA _{IN}	
Grouping of variations	🔀 Туре IA	
Worksharing	Type IB unforese	en² 🕐
	Type IB	3. TYPES OF CHANGE(S)
	Type II	Variations included in this application: Please follow instructions below to add variation
	Type II Art. 29	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 Selected Show Selected Variations Show Variation Lists
		Single Variation is being selected. You may choose only type IA variation changes and only one scope.
		·

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

Type of Application (tick all applicable options) *Note: Any change in Type of Application, will delete any selected variation in Section 3!

Single variation		Type IA _{IN}	
Grouping of variations		Туре ІА	
Including a line extension ³	?	Type IB unforeseen ²	?
Worksharing		🗙 Туре IB	
		Type II	
		Type II Art. 29 ⁴	?

Grouping of variations is being selected. You may choose variation changes of types that are selected on section 1.

FORM VALIDATION

Validation Errors: 1

Please select more than 1 Variations in Section 3 when Grouping 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!

ariation	Selected	Show Selected Variations	(Show Variation Lists	

Single Variation is being selected. You may choose only type IB variation changes and only one scope.

B. QUALITY CHANGES	▼
B.I ACTIVE SUBSTANCE	•
B.I.a) Manufacture	•
B.I.a. 2 Change in the manufacturing process of the active substance	ed in the manufacturing process of the ac
B.I.a.3 Change in batch size (including batch size ranges) of active substance or int	ermediate used in the manufacturing pro
B.I.a.5 Changes to the active substance of a seasonal, prepandemic or pandemic va	accine against human influenza



In order to Selected Show Selected Variations Show Variation Lists Variation B.I.a.2.a **select** the chosen scope, Single Variation is being selected. You may choose only type IB variation changes and only one scope. it is important to tick the select B.I.a.2.a - QUALITY CHANGES - ACTIVE SUBSTANCE - Manufacture - Changes in the manufacturing process of the active substance -Minor change in the manufacturing process of the active substance \boxtimes 'select' tick Procedure Types: IA ів 🖂 box. If this box is not ticked Conditions: and you make The active substance is not a biological immunological substance. Note: changes in the The change is fully described in the open (applicant's') part of an Active Substance Master File, if applicable. Mata dropdown menu, the If only one procedure type, for example IB is possible, based on the selected selection in section 1, or due to classification guideline, the options will be

procedure type will be automatically ticked by the system and cannot be manually changed

deleted

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	•
R II h 2 a Penlacement 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
Procedu Implem	re Types: IA 🔀 IB 🔄 🔹 ent. Date: 🔹 Implement. Note:
Conditio	
The	e 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. You 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
Procedu	re Types: IA 🔀 IB 📃
Impleme	ent. Date: Implement. Note: Article 5 📈
Conditio	ins:
The	e remaining packaging must be adequate for the storage of the bulk or final active substance at the authorised conditions.
Note:	

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	ure Types: IA 🔀 IB 📃						
Implem	ent. Date: 6 months after approval						
Conditio	Conditions:						
The	e site is appropriately authorised.						
Note:	Procedure Types: IA IB mplement. Date: Implement. Note: Conditions: Conditions: Conditions: The site is appropriately authorised. Note: The product concerned is not a biological/immunological medicinal product. Note:						
The	e product concerned is not a biological/immunological medicinal product.						
Note:							
Me Me	ethod 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	- one
Procedu	ire Types: IA 🔀 IB 📃	
Impleme	ent. Date: Implement. Note: 6 months after approval	
Conditio	ons:	
The	e site is appropriately authorised.	
Note:		
The	e product concerned is not a biological/immunological medicinal product.	
Note:		
X Me	ethod transfer from the old to the new site or new test laboratory has been successfully completed.	
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 I exi:	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) is 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	entations:	
M Am pro	nendment 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 revise oduct information as appropriate.	ied
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Please note:

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

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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!



Grouping of variations is being selected. You may choose variation changes of types that are selected on section 1.

select B.Il.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						
Procedu	re Types: IA 🔀 🛛 IB 🗌					
Impleme	ent. Date:		Implement. Note:	6 months after approval		
Conditio	un ct					



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.

3. TYPES OF CHANGE(S)

Variation	Selected	Show Selected Variations	Show Variation Lists	
B.II.b.2.a	1			
Grouping of va	nriations is being select	ted. You may choose variation changes of types that are	e selected on section 1.	

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In order to	Variation	Selected		Show Selected Variat	ions		Show Variation Lists		
select the	B.I.a.2.a	1							
chosen scope,	Single Variation is being selected. You may choose only type IB variation changes and only one scope.								
it is important									
to tick the	select B.I.a.	select B.I.a.2.a - QUALITY CHANGES - ACTIVE SUBSTANCE - Manufacture - Changes in the manufacturing process of the active substance -							
'select' tick		Minor change in the manufacturing process of the active substance							
box. If this box	Procedure Types: IA IB								
is not ticked	Conditions:								
and you make	The active substance is not a biological immunological substance. Note: The change is fully described in the open (applicant's') part of an Active Substance Master File, if applicable.								
changes in the									
dropdown	Nata			1					
menu, the	If only	one pro	oced	lure type, for	example	e IB	is possible, based on t	he	
selected	selectio	on in se	ectio	n 1, or due to	classific	atic	on guideline, the		

procedure type will be automatically ticked by the system and cannot be manually changed

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options will be



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



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