EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Variation eAF v1.24.0.0

Changes introduced in v1.24.0.0 of the variation form (to NCA users) – **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

EUROPEAN MEDICINES AGENCY

- 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
- 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 order.[1]

Important reminders on the use of eAFs

EUROPEAN MEDICINES AGENCY

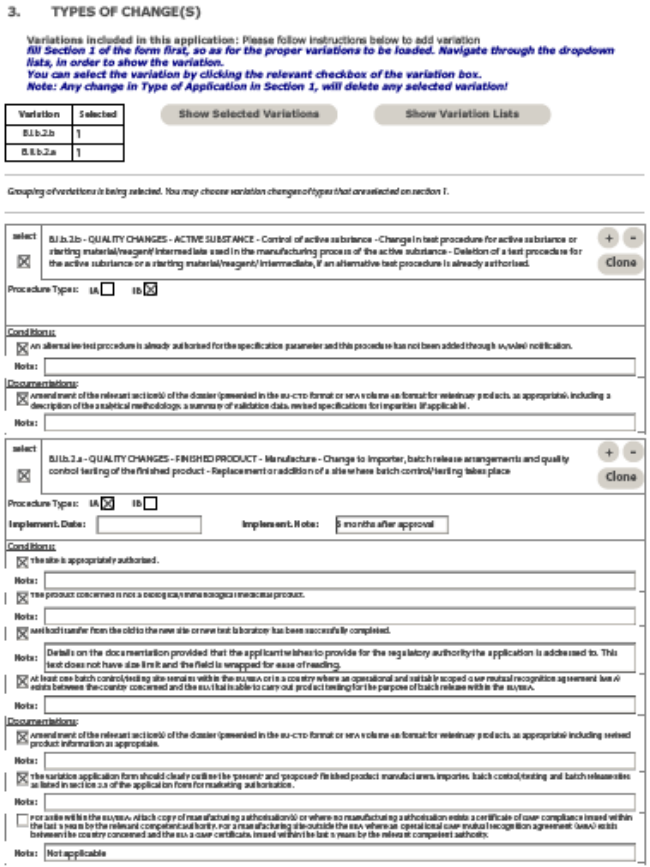
These points are very important to the applicants filling in the forms, however, it is good to be aware of this points in case you are asked or come across a form with an issue;

- 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 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 follow the updated eAF new term request process

Details of the changes

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.



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	Selected
B.II.b.2.b	1
B.II.b.2.a	1

Show Selected Variations | Show Variation Lists

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

select ☒ B.II.b.2.b - QUALITY CHANGES - ACTIVE SUBSTANCE - Control of active substance - Change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance - Deletion of a test procedure for the active substance or a starting material/reagent/intermediate, if an alternative test procedure is already authorised. Clone

Procedure Type: IA ☐ IB ☒

Conditions:
☒ An alternative test procedure is already authorised for the specification parameter and this procedure has not been added through a variation notification.
Note:

Documentations:
☒ Amendment of the relevant section(s) of the dossier (presented in the EU CTD format or NeeS volume as format for veterinary products, as appropriate) including a description of the analytical methodology, a summary of validation data, revised specifications for impurities if applicable).
Note:

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

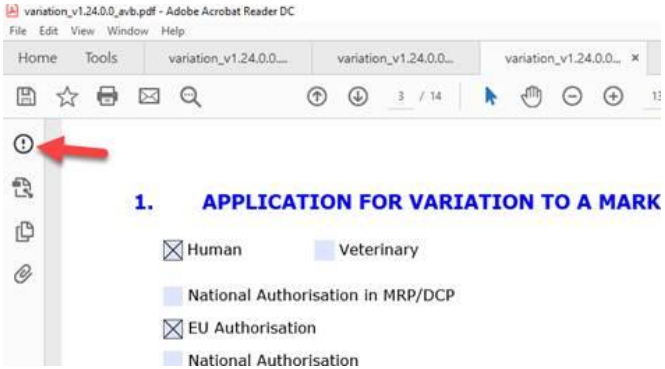
Procedure Type: IA ☒ IB ☐
Implement. Date: Implement. Note: 3 months after approval

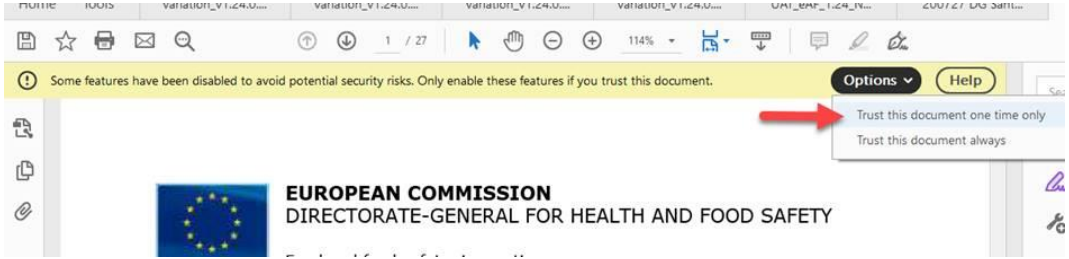
Conditions:
☒ The site is appropriately authorised.
Note:
☒ The product concerned is not a biological/immunological medicinal product.
Note:
☒ Method transfer from the old to the new site or new test laboratory has been successfully completed.
Note: Details on the documentation provided that the applicant 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 user mutual recognition agreement (user 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:

Documentations:
☒ Amendment of the relevant section(s) of the dossier (presented in the EU CTD format or NeeS volume as format for veterinary products, as appropriate) including revised product information as appropriate.
Note:
☒ The variation application form should clearly outline the 'present' and 'proposed' finished product manufacturers, importers, batch control/testing and batch release sites as listed in section 2.2 of the application form for marketing authorisation.
Note:
☐ For sites within the EU/EEA: Attach copy of manufacturing authorisation(s) or where no manufacturing authorisation exists a certificate of user compliance issued within the last 3 years by the relevant competent authority. For a manufacturing site outside the EEA where an operational user mutual recognition agreement (user MRA) exists between the country concerned and the EU a user certificate, issued within the last 3 years by the relevant competent authority.
Note: Not applicable

Accessing control terminology lists

- 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

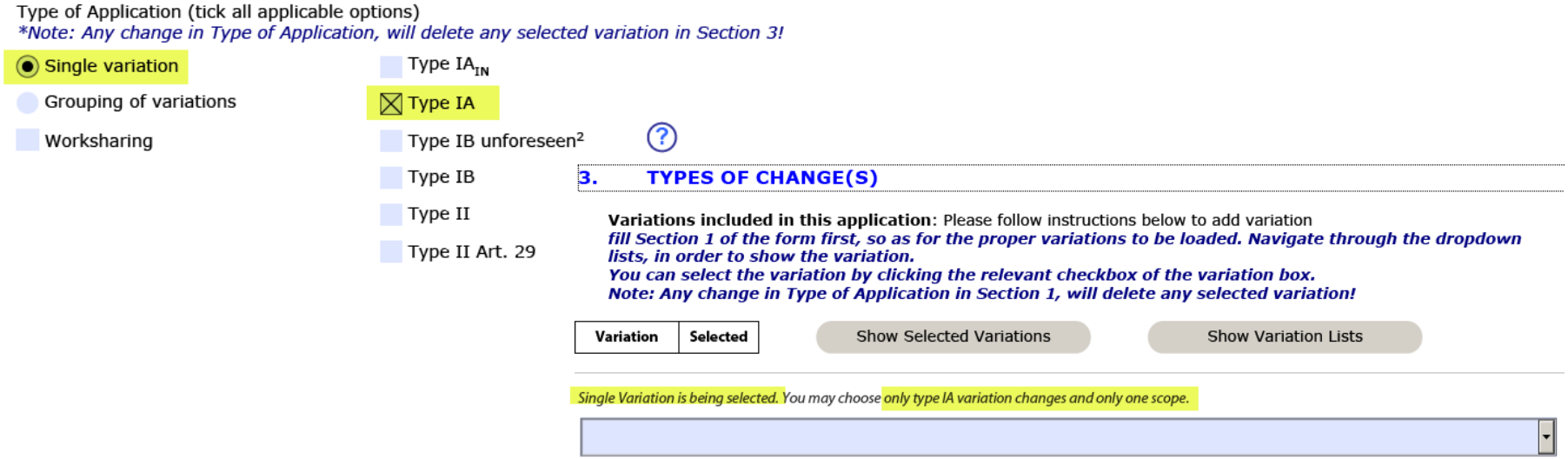




Details of the changes - Connection between sections 1 and 3

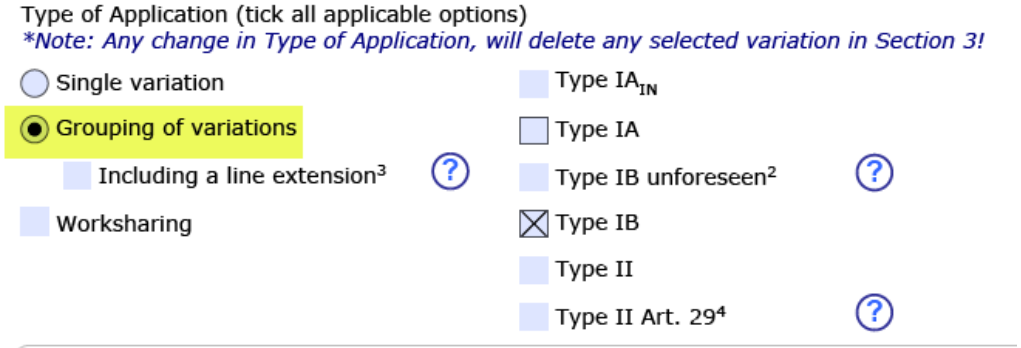
The selections made in section 1 'Type of Application' will now directly affect the section 3 and depending on the selection, only the relevant scopes are available for selection in section 3.

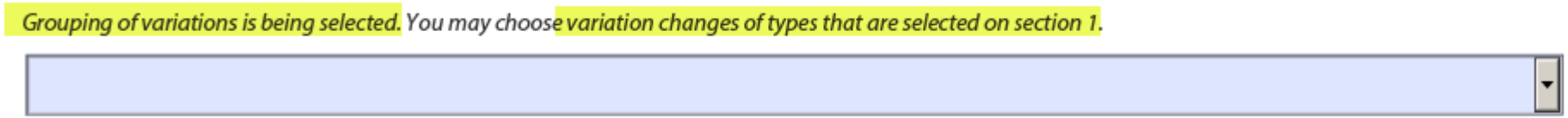
If a 'single' variation has been selected in section 1, it is only possible to select a single scope in section 3



Details of the changes - Connection between sections 1 and 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

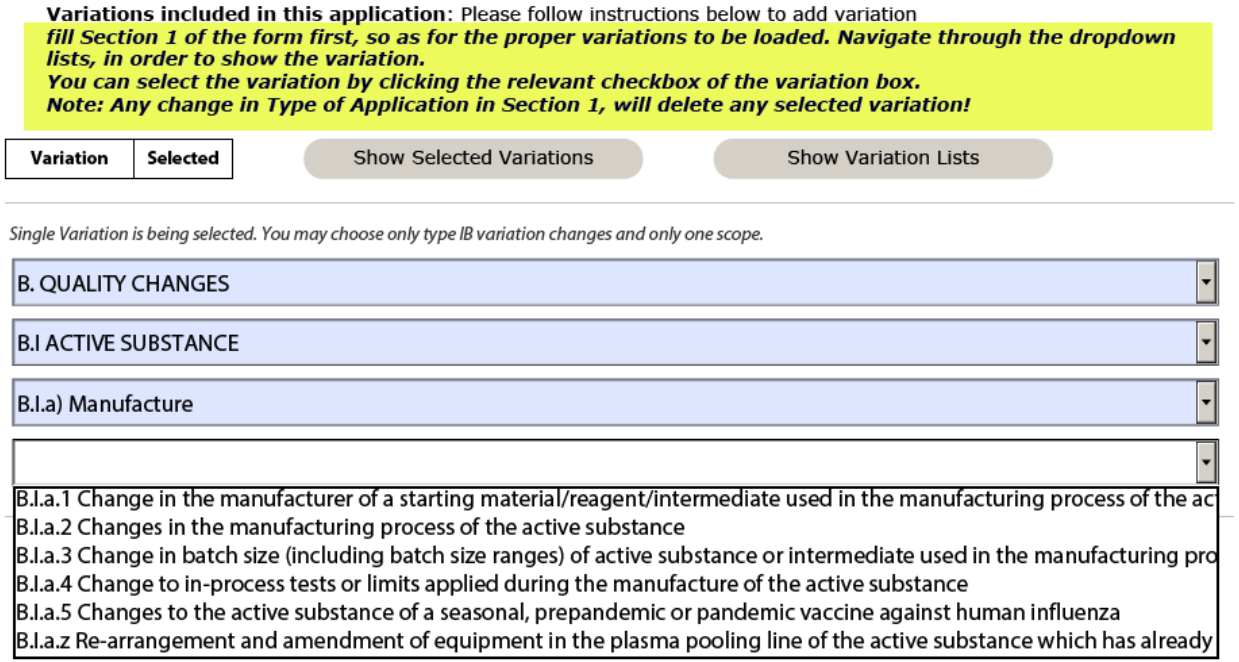




Details of the changes - Connection between sections 1 and 3

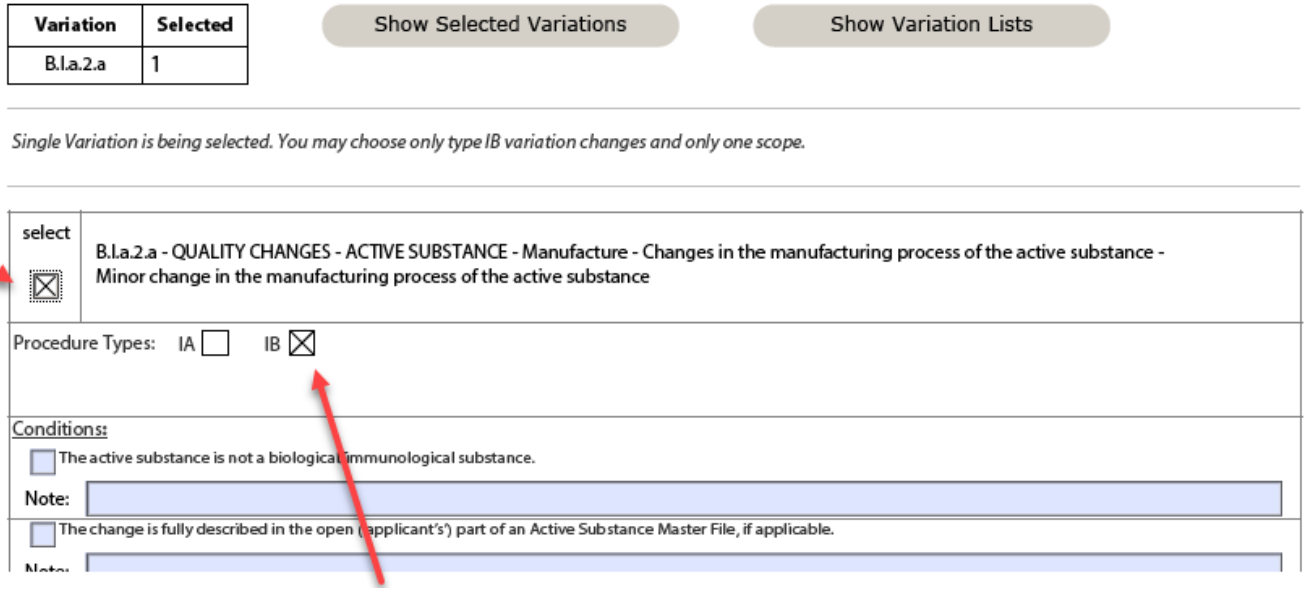
The selection of scopes in section 3 is done by drilling down dropdown menu which displays different available scopes based on the selections in section 1

Please note that **any changes in Type of Application** in **section 1 will delete any selected variations!**



Details of the changes - Connection between sections 1 and 3

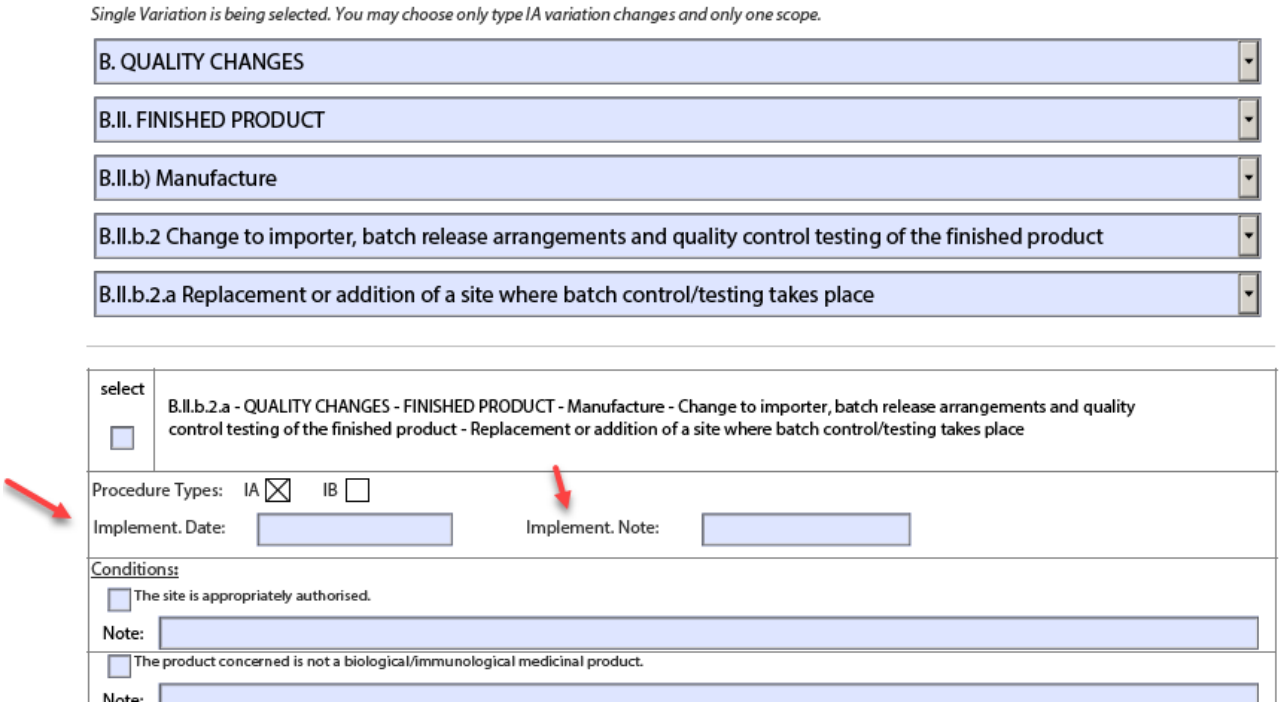
In order to **select** the chosen scope, it is important to tick the 'select' tick box. If this box is not ticked and you make changes in the dropdown menu, the selected options will be deleted



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

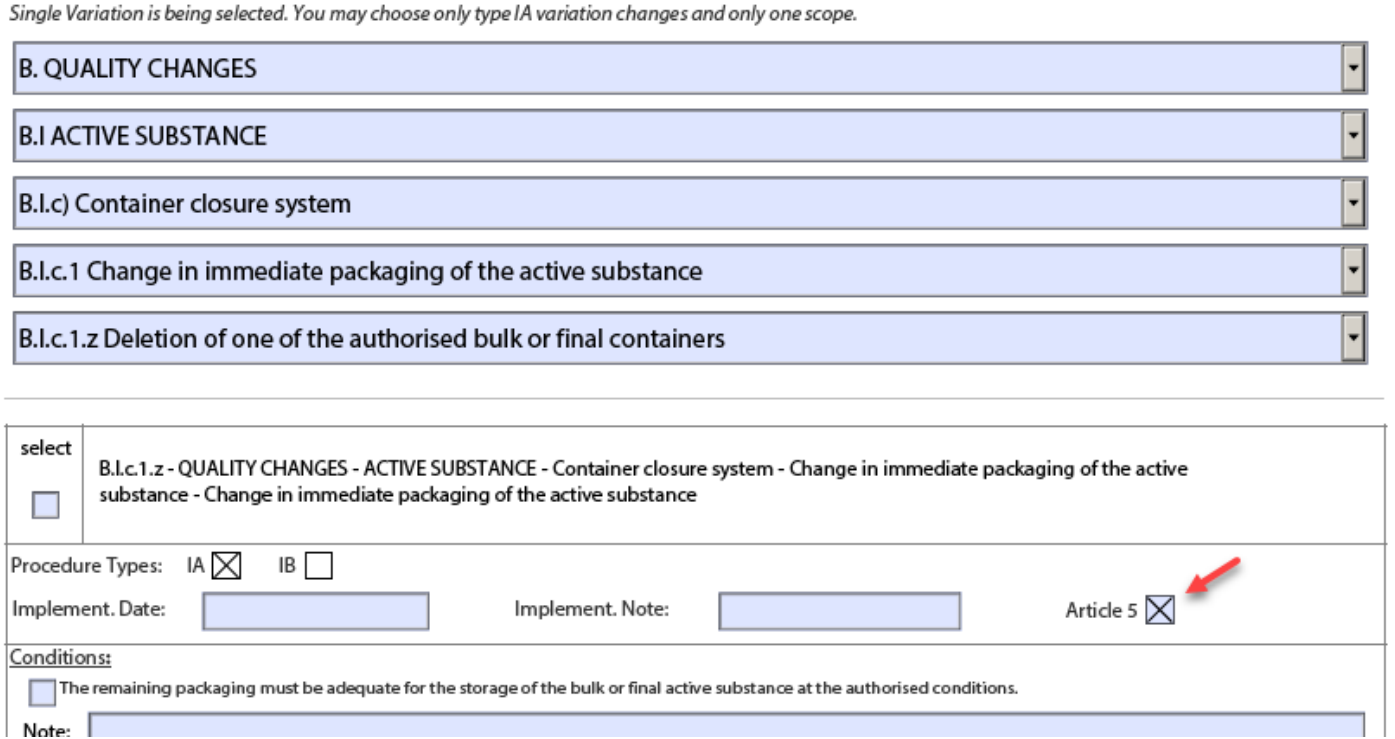
Details of the changes - Connection between sections 1 and 3

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



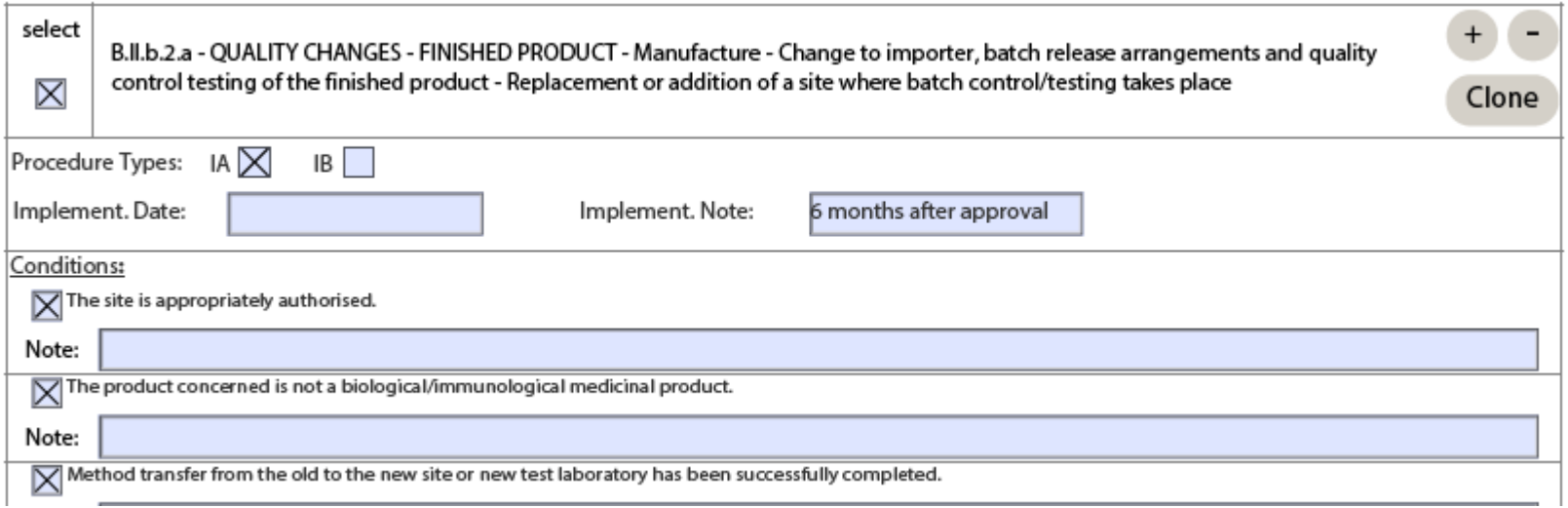
Details of the changes - Connection between sections 1 and 3

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



Details of the changes - Connection between sections 1 and 3

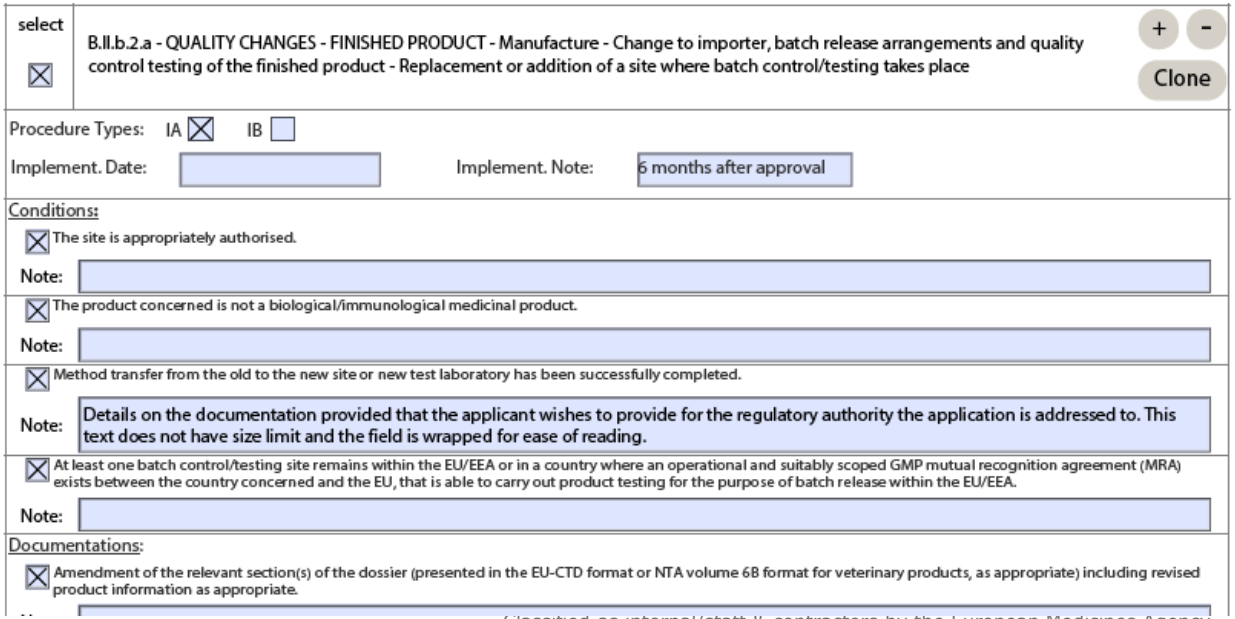
When grouping is selected in section 1, and different procedure types have been selected in section 1, you will need to manually select the procedure type. + and – buttons, as well as ‘clone’ button to add additional scopes/clone scopes you have selected are available



Details of the changes - Connection between sections 1 and 3

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.

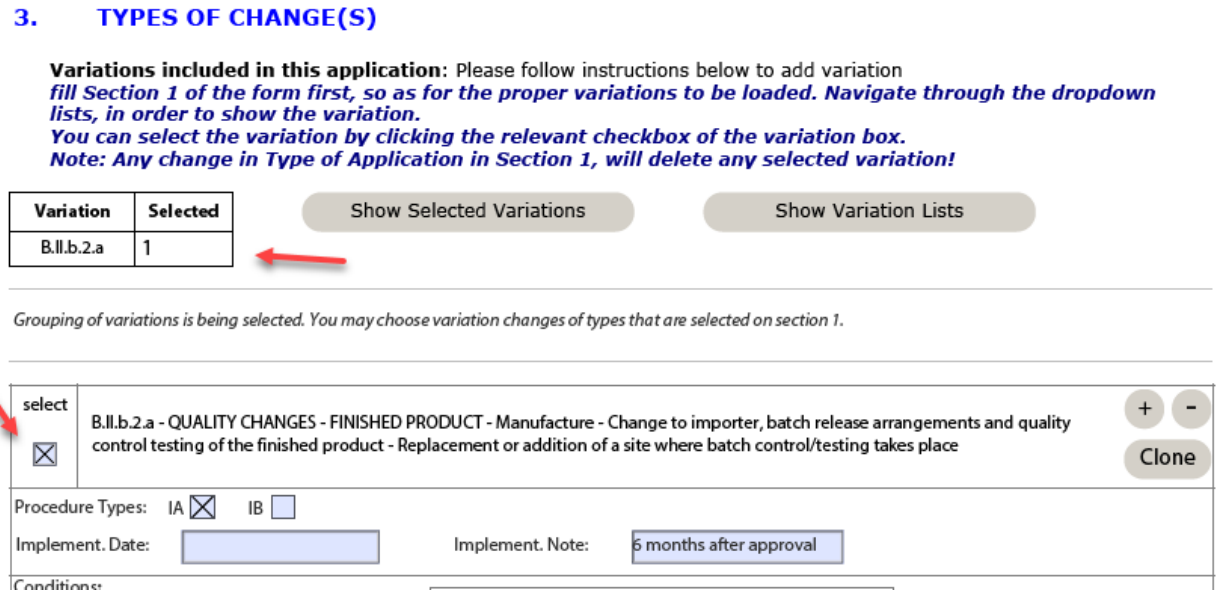


Please note:

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

Details of the changes - Connection between sections 1 and 3

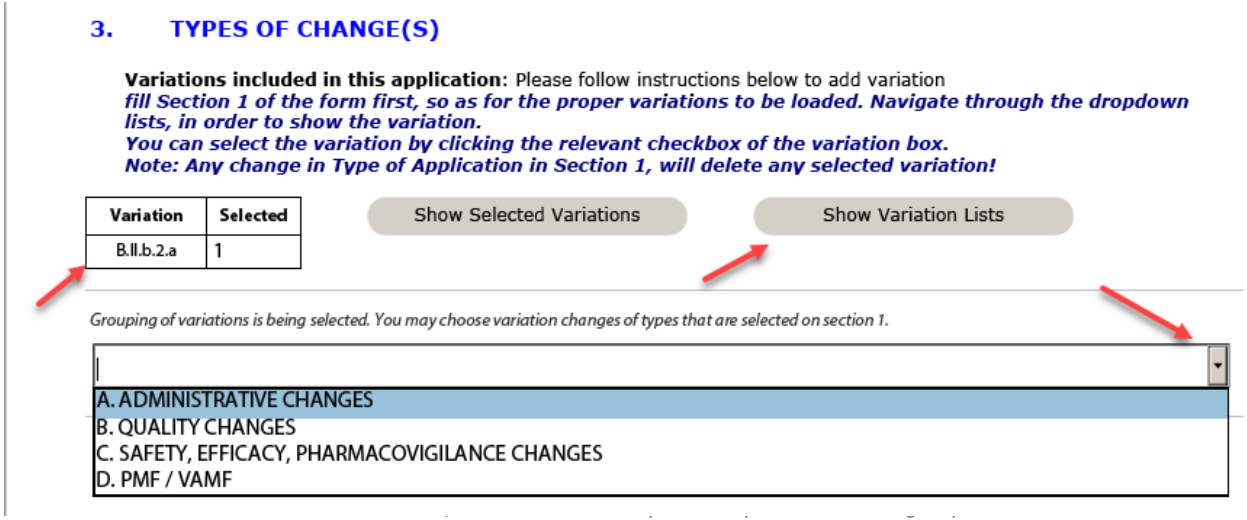
Always ensure that you have selected the scope and ensure that the details are shown in the summary box before moving on. This is especially important for grouping variations if you need to select a different scope as this will be done by repeating the selections using the dropdown menu.



Details of the changes - Connection between sections 1 and 3

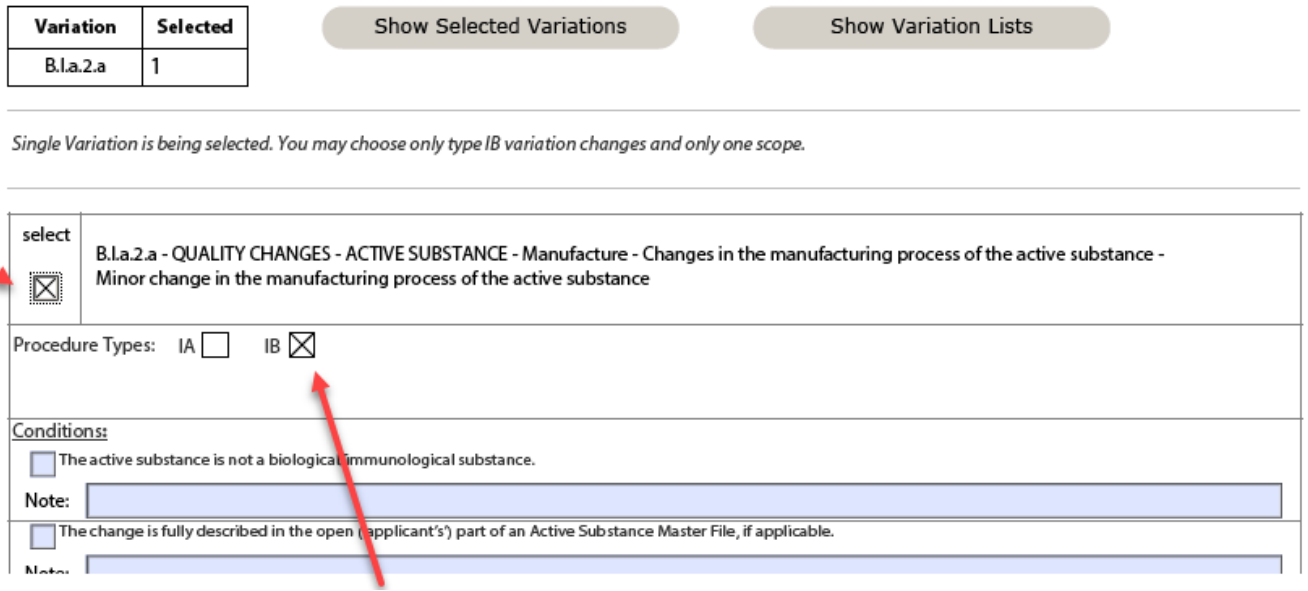
For groupings, if you have used the 'Show Selected Variations' button and wish to continue adding different scopes, please click the 'Show Variation Lists' which will display a 'fresh' dropdown menu to continue scope selection.

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.



Details of the changes - Connection between sections 1 and 3

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



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

Follow us on **@EMA_News**