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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Variations

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Veterinary Regulation 2019/6 Webinar

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Main Changes arising from Regulation EU 2019/6

There will only be two categories of variations:

- **V**ariations **N**ot **R**equiring **A**ssessment = **VNRA**
- **V**ariations **R**equiring **A**ssessment = **VRA**

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Variations not requiring assessment (VNRA)

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- The Standing Committee on VMP adopted the Implementing Regulation establishing the list of variations not requiring assessment. Translation and publication is complete and Commission Implementing Regulation (EU) 2021/17 of 8 January 2021 establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council has been published in the Official Journal.
- The Implementing Regulation includes all variations not requiring assessment along with any associated conditions and documentation requirements.
- The format and categorisation is familiar but different!
- CMDv Best Practise Guide is under development.

ANNEX

Variations not requiring assessment

	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
A	**Administrative changes**		
1	Change in the name or address or contact details of:		
a)	— the marketing authorisation holder	The marketing authorisation holder shall remain the same legal entity.	
b)	— a manufacturer or supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance or a quality control testing site (where specified in the dossier) where no European Pharmacopoeia (Ph. Eur.) Certificate of Suitability (CEP) is part of the approved dossier.	The manufacturing or quality control site and all manufacturing operations shall remain the same. The manufacturer or supplier shall already be incorporated in the Union IT systems storing and providing organisational data.	
c)	— an active substance master file (ASMF) holder	The manufacturing site and all manufacturing operations shall remain the same. The ASMF holder shall already be incorporated in the Union IT systems storing and providing organisational data.	Updated 'letter of access' to the Active Substance Master File.
d)	— a manufacturer of an excipient (where specified in the dossier)	The manufacturing site and all manufacturing operations shall remain the same. The manufacturer shall already be incorporated in the Union IT systems storing and providing organisational data.	
e)	— a manufacturer or importer of the finished product (including batch release or quality control testing sites)	The manufacturing site and all manufacturing operations shall remain the same. The manufacturer or importer shall already be incorporated in the Union IT systems storing and providing organisational data.	

Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
10	Change to in-process tests or limits applied during the manufacture of the active substance	The change shall not be a consequence of any commitment from previous assessments to review specification limits. The change shall not result from unexpected events arising during manufacture e.g. new unqualified impurity; change in total impurity limits.	Amendment of the relevant section(s) of the dossier for the new test method validation and batch data, as appropriate Comparative table of former and new in-process tests and limits.
a)	— tightening of in-process limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	
b)	— addition of a new in-process test and limits	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way. The new test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance, except if this method is a standard pharmacopoeial microbiological method.	
11	Change in the specification parameters or limits of an active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance or of the immediate packaging of the active substance	The change shall not result from unexpected events arising during manufacture (e.g. new unqualified impurity or change in total impurity limits). The change shall not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation procedure according to Article 62 of Regulation (EU) 2019/6) unless it has been previously assessed and agreed as part of a follow-up measure in a previous procedure under Regulation (EU) 2019/6.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new specification parameters and limits.

Variations not requiring assessment (VNRA)

The MAH will

- Record the change in product database within 30 days of implementation including required documents (no application form)
- Documents submitted directly to UPD. No CESP submission. Documents include those listed in the Implementing act as well as SPC, package leaflet, label, PuAR

The RMS/EMA/NCA will

- Approve/reject the variation
- Inform CMS & MAH by recording decision in database
- Amend the MA

The decision, along with updates to SPC, labels etc is published via UPD

Details intrinically linked to UPD processess and functionalities

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Variations requiring assessment (VRA)

Variations requiring assessment (VRA)

- Every change not listed in the Implementing act
- CMDv and EMA have worked on a new variation guideline to replace Regulation 1234/2008, which will no longer apply for variations to VMPs from the 28 January 2022.
- The format and categorisation is familiar but different!
- z-categories to address unlisted variations and VNRA if requirements not met
- 'Article 5 type' procedure for unlisted variations
- CMDv Best Practise Guide is under development.

Classification guide for VRA

Classification codes:
VRA E,F,G….
(VNRA: A,B,C,D)

Documentation requirements for some variations – as previous IB variations

Similar structure:
Sections on Admin, Quality, S&E etc.
Main change
Sub category 1
Sub category 2 ……

S = Standard timetable — 60 Days

R = Reduced timetable — 30 Days

E = Extended timetable — 90 Days

Grouping and worksharing

- Worksharing procedure is compulsory for VRA (Article 65).
- CMDv guidance will apply until implementing act on worksharing is developed
- Grouping is catered for in Article 64
- Article 66: Re-examination: no new data can be provided
- VRNA cannot be included in worksharing or grouping – can only be dealt with via UPD (in UPD it is envisaged that it will be possible to link variations to multiple marketing authorisations while recording the change)

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Next Steps

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- CMDv / EMA Guideline on VRA – expected in June
- CMDv BPG's – under development
  - Variations requiring assessment (almost complete)
  - Variations not requiring assessment (on hold for clarification of UPD interactions)
  - Classification of unlisted variations (almost complete)
  - Grouping
  - Worksharing
  - Re-examination procedure

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Thank you

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