Guidance

Apply to change a veterinary Marketing Authorisation or Homeopathic Remedy

Guidance for the pharmaceutical industry on how to apply to vary a veterinary Marketing Authorisation (MA) or Homeopathic Remedy.

Scope

These variation procedures apply to MAs authorised in Great Britain (GB).

They also apply to MAs that have been authorised in Northern Ireland (NI):

- via a national procedure, that is, not subject of an EU procedure such as the Mutual Recognition Procedure (MRP), Decentralised Procedure (DCP) or Centralised Application Procedure (CAP)
- via an EU procedure where the variation is dealt with on a national basis, such as change of legal entity of MA holder.

Further guidance about variation procedures for MAs authorised in NI via an EU centralised procedure can be found on the European Medicines Agency (EMA) website.

Marketing Authorisation Holders

All products included in a variation application must belong to the same marketing authorisation holder (MAH).

In GB and NI, an MAH is identifiable by their unique company number, which forms the first part of a product's Vm number, which appears on its labels, for example, 12345/5010.

Product ranges

An MA includes all products that are part of a so-called 'product range' and includes all strengths and pharmaceutical forms of that product.

An example of a product range is as follows:

- Product Name 10 mg tablet for cats and small dogs

- Product Name 20 mg tablet for medium size dogs
- Product Name 30 mg tablets for large dogs

One change to one MA (one product or one product range) is considered a single variation.

Types of variation

There are two types of variation:

- Variations NOT requiring assessment (VNRAs)
- Variations requiring assessment (VRAs)

Variations not requiring assessment

VNRAs have little or no impact on the safety, quality or efficacy of a product. These changes are listed in the European Commission guidance.

Variation requiring assessment

Any change that is not listed as a variation not requiring assessment will be considered a variation requiring assessment.

VRAs are listed in the European Commission guidance

Not all possible variations are included in the lists of VNRAs and VRAs. If you wish to apply for a variation that is not listed, please email the VMD prior to submission, s.response@vmd.gov.uk and include 'variation classification request' in the subject line.

If you wish to apply for a change that isn't listed to an NI MA, please follow the procedure on the EMA website.

Some unlisted variations that have already been classified by the VMD as unforeseen variations, and are dealt with on a national basis regardless of the scope of the MA, have been given a national 'U' classification category. See Unforeseen Variations section below.

Variations not requiring assessment

A VNRA application may only include one change to one MA, a single variation.

However, to reduce administrative burden on you, we will accept the following VNRA change combinations in a single national application form:

- One VNRA change to multiple products, a maximum of 10 products
- Multiple VNRA changes to one product, a maximum of 10 changes

Multiple VNRA changes to multiple products is NOT permitted.

Combined application forms will be progressed as individual applications and may not all be approved at the same time.

VNRA cannot be grouped with VRA applications but can run concurrently. If the VNRA is dependent on the outcome of a concurrent VRA assessment, the application will be placed on hold pending the VRA approval.

You must notify us of VNRA within 12 months of implementation of that variation.

These notifications are checked to ensure that:

- the correct variation type and category has been selected
- no other changes have been made that haven't been applied for
- all conditions have been fulfilled
- all relevant documentation has been provided and is accurate

You will be informed as to whether the variation is approved or rejected within 30 days of receipt. The fee applies regardless of the outcome.

Where at least one of the requirements cannot be fulfilled, the VNRA will be rejected, and you will still be charged. You will need to reapply using the correct VRA category.

For Northern Ireland MA authorised via a European procedure, most VNRA should be submitted via the Union Product Database. Changes to the name, address or contact details of the Marketing Authorisation Holder (A.1.a), or Changes to the labelling or the package leaflet which are not connected to the SPC – administrative information concerning the holders representative (C.10.a) or inclusion of traceability stickers in or on the product carton (C.10.c) should be submitted via national applications, as described above.

Further guidance is available from the EMA on Centralised NI MA submissions.

Variations requiring assessment

A VRA is known as one of the following depending on the specified timeframe for that change.

- VRA – standard / extended
- VRA – reduced

Refer to Timetables for national applications for further information.

The ‘shortened’ timetable will be used for VRA – reduced and the ‘standard’ timetable will be used for VRA – standard / extended.

Extensions

Formerly known as ‘extensions’ there are some variations that fundamentally alter the terms of an MA to either create a new stand-alone MA (new-extension) or change an existing MA (variation-extension).

These former extension changes weren’t included in the old classification guideline, however they are now included in the list of VRAs with all the other changes requiring assessment.

If you are applying for a former extension that amends an existing MA (variation-extension), this will be dealt with as a VRA – standard / extended.

If you are applying for a former extension that results in a new stand-alone MA, it will be dealt with in accordance with new MA procedures and timeframes.

Parallel submissions are not possible for applications that result in a new stand-alone MA due to the different timescales and procedures used on a national basis and in the EU.

Consequential changes to product literature

If a variation results in consequential changes to the Summary of Product Characteristics, labelling or package leaflet, these will be considered as part of the same variation application.

Single variation

An application including one change to one MA, that is one product or one product range.

Grouped variations

An application including either:

- several VRA changes to one MA; that is one product or one product range
- one VRA change to several different MAs; that is several different products or different product ranges
- several VRA changes to several MAs; that is several different products or different product ranges

A grouped variation will be handled using the longest timeframe associated with any change included in the application.

All changes included in a grouped application must apply to all products.

You can't include a VNRA in a grouped variation.

You can't include a former extension that results in a new stand-alone MA in a grouped variation. However, you can include former extensions that amend an existing MA, a variation-extension, in a grouped variation; this application will still be known as an 'extension-led grouped variation' for fee purposes.

It is recommended that you avoid groupings that are entirely unrelated for example, grouping of unrelated quality and safety / efficacy variations. If you do the VMD may decide to run the application on a longer timeframe and additional costs may be incurred.

Workshare variations

EU workshare procedures can be applied to MAs in NI issued following an EU procedure (DCP/MRP/EUCE) only.

It is recommended not to include MAs aligned between GB and NI as this is likely to result in MA number separation for GB and NI territories (where products were authorised pre-2021) and may result in de-alignment. Contact VMD for further guidance should you need to submit an EU workshare involving aligned MAs.

Variations to parent products

Informed consent ('copycat')

A parent MA holder has a responsibility to notify a copycat holder when changes have been made and should provide them with at least the categories used for the variation(s) and ideally, the application number. The copycat holder needs this information to apply for the same changes.

Changes to copycats and parents belonging to the same MAH may be included in a grouped application.

Marketing Authorisations for Parallel Import (MAPIs)

If the SPC or product literature of the UK authorised parent product is changed, you must submit a national Unforeseen Variation to align the MAPI product.

Change of legal category

The legal category may also be referred to as the distribution category.

A product may only be distributed on the marketplace in accordance with the distribution category shown on the product label. Therefore, until the change in distribution category has been implemented onto the packaging of a product it must continue to the distributed in accordance with the distribution category shown on the product label.

For further information about distribution categories see the guidance on Retail of veterinary medicines. When applying for a legal category change select U.II.z.g) in the application form.

Legal category variations will usually be considered by the Veterinary Products Committee (VPC) unless the VPC has already provided advice on

the appropriate legal category of products containing the same active ingredient(s) and indicated for use in the same target species.

If you apply to make a national legal category change to a NI MA authorised via MRP / DCP , for example, POM-V to POM-VPS and it is likely that the variation will be approved, your national application will be placed on hold and you will need to submit further applications to introduce any proposed changes to the EU SPC or wording in the product literature. Once the European variation is approved, we will conclude the national legal change variation.

NI only - centralised products

A change to the legal category from prescription to non-prescription, or vice versa, will be dealt with by the EMA via a centralised variation procedure.

Unforeseen variations

A number of unforeseen variations have been identified and these are listed below. These variations are dealt with on a national basis regardless of whether the MA is nationally authorised or mutually recognised.

You should complete the application form including the relevant variation category given here, and include a clear, concise description of the variation in the present and proposed sections.

Administrative changes – U.I.z

Refer to MAHs, Named Distributors and Local Representatives of veterinary medicines for guidance on how to make changes.

SPC or Product literature changes - U.II.z

Change	Description	Confirmation/Justification (must be provided)	Packaging to be provided
U.II.z.a) Dosing Instructions	changes to simple dosage instructions intended to remove ambiguity	the change is not the result of safety concerns, no new studies are required to support the change and the dosing regimen remains the same	
U.II.z.b) Safety Warnings	change or addition to safety warnings	no other aspects of the dossier are changed, no safety warnings are removed, no new studies are required to support the change and the proposed warnings serve to increase the protection of the user, the environment or target species. As appropriate justify the change	revised labels, package leaflet and SPC
U.II.z.c) Corrections to layout	normal corrections or simple text layout changes to SPC or product literature (including multilingual labelling)	no other aspects of the dossier are changed, the changes are not the result of any safety concerns, the legibility is not compromised and the indications or warnings are the same in all languages; justify the change	revised labels, package leaflet and SPC

Change	Description	Confirmation/Justification (must be provided)	Packaging to be provided
U.II.z.d) Joint-labelling	to obtain joint-labels between the UK and Ireland for nationally authorised products or to obtain joint-labels for the first time for mutually recognised products	no other aspects of the dossier are changed, the changes are not the result of any safety concerns, the legibility is not compromised and the indications or warnings are the same in all languages	revised labels, package leaflet and SPC current SPCs for the UK and Ireland and a proposed joint SPC - only applicable for joint-labelling variations on nationally authorised products
U.II.z.e) Changes to MAPIs	changes to the SPC and product literature of a MAPI as a direct consequence of a change to the SPC and product literature of the UK authorised product (parent)	the only changes are those required to bring the MAPI back in line with the parent	revised labels, package leaflet and SPC
U.II.z.g)	Change in distribution (legal) category of the veterinary medicinal product	Need a new user risk assessment for products based on new legal distribution category	mock-ups for the relevant pack size(s) and an updated package leaflet if applicable

Miscellaneous changes - U.III.z

An abbreviated resubmission of a previously refused variation (Type II or VRA – standard / extended), you must:

- confirm that at the time of refusal the VMD gave you permission to resubmit under this category, and that the application has been resubmitted within 3 months from the date the previous application was refused
- provide responses to the refusal points
- choose category U.III.z.a)

Following formal advice of the VMD, you must:

- confirm that the VMD has already assessed the relevant data and formed an opinion on these, and that the change is not required as a result of your failing to keep the Part II (quality) data in accordance with current practice, or in line with current CVMP guidelines
- if required, provide revised labels, package leaflet and SPC
- choose category U.III.z.b)

These changes will be dealt with on a standard timetable: See Timetables for national applications for further information.

Alignment of MAs in GB and NI

MAs may be considered aligned if they:

- are the same pharmaceutical form
- have the same qualitative and quantitative composition
- are intended for the same target species with the same indications
- have the same dossier. Except for certain differences that make no impact on the scientific requirements or regulatory framework such as sites of batch release

NI MA authorised via MRP / DCP

To maintain alignment of your MAs in GB and NI, you must submit post authorisation applications to both the EU and the VMD for assessment at

the same time, known as parallel submissions. Not submitting identical applications to either authority may introduce divergence and result in MA de-alignment.

If changes occur during the respective assessment by the GB and EU authorities, that either contravene UK or EU regulations or change the terms of authorisation valid in GB compared to NI, this may result in MA dealignment .

NI MA authorised via Centralised procedure

For EU Centralised procedure biological applications, upon CVMP approval recommendation, it is critical that you provide VMD with a copy of any approved revisions/changes to the finished product tests and specifications, at release and at the end of shelf life, in order that NI IVMP batch release activities can be completed post approval.

Parallel submissions

Since January 2021, VMD have been accepting EU (NI) applications to run in parallel with National (GB) applications where the products are aligned.

Both applications will run in accordance with the EU timeline.

You must submit your applications to the EU and UK within 2 working days of each other and ensure you cross-reference them in your applications.

As the procedure progresses you must submit updated GB SPC and QRD documents every time you submit updated EU SPC and QRD documents. This is to include the final version of key documents upon completion of the decision period.

Parallel submissions are not possible for:

- VNRA – if you submit your EU and GB applications within 48 hours of each other, subject to identical approval outcomes, your GB and NI MAs will not dealign
- applications involving former extensions that result in a new stand-alone MA due to the different timescales and procedures used on a national basis and in the EU
- EU Workshare procedures
- EU Centralised procedures

For non-parallel applications, if you wish to increase the likelihood of a shared GB and NI label being possible, we require you to submit EU procedural information; Lists of Questions, your responses, assessment report, as part of your GB national procedure company responses, that will enable your GB assessors to try and align GB QRD text with the EU procedure decisions.

NI MA authorised nationally

For aligned MAs authorised on a national basis in GB and NI which are separate and have different authorisation numbers (3xxx in NI and 5xxx in GB) or where the variation is dealt with a national basis regardless of the scope of the NI MA, you are encouraged to include all products in the same, single application (for VNRAs) or grouped application (for VRAs). Not doing so may introduce divergence and result in MA dealignment.

You may also submit them separately.

MA Separation (Pre 2021 authorisation)

If a pre-2021 UK-wide MA, that retains a Vm 4000 authorisation number, becomes de-aligned during a variation procedure or results in separation of MA documentation, such as separate GB SPC and QRD documents and EU SPC and QRD documents. You will be issued with a new authorisation number for GB (Vm 5000) and NI (Vm 3000), which will result in changes to product literature and packaging.

We will notify you where applications result in splitting of pre-2021 MA numbers as early in the procedure as possible. You have 12 months from the date of the notification to implement the new MA numbers on packaging and leaflets.

If you choose to separate a Vm 4000 MA number and there are no other changes to the dossier:

- Select category U.I.z.c)
- Do not submit revised SPC, QRD text or mock-ups for administrative changes. We will annotate the agreed changes onto the latest authorised versions held on file and issue them back to you at the end of the variation procedure

How to submit your application

Refer to Submission of applications to an animal medicines for guidance.

You must be registered to use the Veterinary Medicines Digital Service (VMDS).

If your application affects the SPC and/or QRD text, no other applications that also affect these documents should be ongoing on the product when the variation is submitted. You must ensure that you time submission of applications, so that they do not clash.

Application forms

Application forms are available through VMDS.

For applications involving former extensions, you need to use the VRA application form if you are amending an existing MA (variation-extension), but the new MA electronic application form if you are creating a new stand-alone MA (new-extension).

The application form to vary a product authorised in NI via an EU procedure, not to be dealt with on a national basis, is available.

Validation

Variations requiring assessment (VRA) will be validated upon receipt to check that everything has been provided, so that assessment can begin.

It is up to you to identify and submit all the necessary information in support of your application. If the application is incomplete, we may not be able to progress it. For variations involving more than one change and / or more than one product, the application will only pass validation once all aspects are considered acceptable. We will contact you if further information is needed.

Fees

Once an application has passed validation or upon receipt for applications that do not have a validation period, you will be sent an invoice for the fee by email so you must provide a valid email address in your application.

Information on fees are here: Application fees for animal medicines.

Assessment timescales

Once the application has passed validation, or upon receipt for an application that does not have a validation period, it will go into the assessment phase. Refer to Timetables for national applications.

Applications being run in parallel with an EU procedure, a parallel submission, will run in accordance with the EU timeframe. We will send our questions and our decision whether to approve or refuse around the same time as the corresponding EU procedure.

The timescales for mutual recognitions applications are in the relevant Best Practice Guides, available on the CMDv website. Timescales for Centralised applications will be provided by the EMA.

If during the assessment phase we need further information from you, our timescales will be suspended until the information is received.

Assessment outcome

If the assessment outcome is to approve an application, we will send you the authorisation documentation using the secure messaging service available on the VMDS. Documentation will be sent to the application contact unless otherwise stated in the 'other information' field in the application form.

It is possible that not all changes included in a group application will have the same outcome and can be a mixture of approved and refused. You will be notified of the outcome of each change along with the authorisation documentation.

Contact us

- To request a company meeting prior to applying email: postmaster@vmd.gov.uk and include 'Request a company meeting' in the subject line
- Once you have applied, contact the people assigned to the application given in the validation passed email
- For all other enquiries email: postmaster@vmd.gov.uk