1. Classification of changes

1.1. Administrative changes

1.1.1. How to apply for a change in name and/or address of a marketing authorisation holder manufacturing site? NEW Nov 2025

Classification category E.4 should be used as long as there is no change in the physical location of the facility, and all manufacturing operations remain the same. This scope is only for changes in name and/or address that are purely administrative in nature (e.g. the municipality decides to change the name of the street or there is a change in the postal code). If the facility moves to a different physical location, classification under the appropriate Q section should be used (e.g. Q.I.a.1 for a manufacturer or a batch control/testing site of an active substance, Q.II.b.1 for a manufacturer of a finished product, Q.II.b.2 for a release site or batch control/testing site for the finished product).

Classification category E.4 should also be used for administrative changes to the name and/or address of manufacturing sites for active substance or finished product intermediates or any other materials mentioned in the dossier.

In case the site impacted by the change in name and/or address is performing multiple activities, they can be included in the same Type IA submission as long as they are all part of the same classification category. For example:

a) The same change concerns the MAH and the batch release site: a grouping of a Type IA, E.4.a and a Type IA, E.4.b should be submitted, since the conditions to be fulfilled are different and need to be declared for each activity.

b) The same change concerns a site where manufacturing of final product, primary and secondary packaging and quality control are performed: a single Type IA, E.4.c can include all activities, since the conditions and documentation are the same. The company needs to confirm explicitly in the application form that conditions and documentation are met for all activities.

In case a CEP is used, changes in the name and/or address of the sites listed in the CEP are covered under scope Q.III.1 when the new version of the CEP is submitted. A parallel variation under classification category E.4 is not required.

An official document from a relevant official body including the new name and address needs to be provided (e.g. Chamber of Commerce registry, manufacturing authorization or importation (MIA), GMP certificate…). A self-declaration issued by the MAH is not considered sufficient.

1.1.2. How to apply for the deletion of more than one manufacturing site? *Rev. Nov 2025*

In case more than one manufacturer in one MA has to be deleted a single variation of type IA under classification category E.5 to delete all manufacturing sites may be submitted. However, it has to be assured that there is still one approved manufacturing site left in the documentation performing the same function as the one(s) concerned by the deletion.

1.2. Quality changes

1.2.1. Introduction of a new manufacturing site for the finished product. What changes can I submit under a single Type II scope? (Classification category Q.II.b.1) *Rev. Nov 2025*

Multiple related extensive changes could be considered for submission under a single Type II scope Q.II.b.1 – Change in the manufacturing site for part or all of the manufacturing process of the finished product.

Multiple related changes submitted under a single type II should always be clearly identified in the application form as following: a clear description of all the related changes should be provided in the precise scope. All the related changes should be listed in the present/proposed table.

Changes affecting the FP not directly related to the introduction of the new manufacturing site such as changes in excipients, specification parameters /limits for the FP, container closure system including suppliers should be submitted as additional grouped variation scopes.

It should be highlighted, that for variations introducing additional manufacturing or batch control/testing sites (including sub-contractors), each additional site should be declared as a separate variation on the variation application form. Such variations can be submitted as a grouping application. The precise scope should include the full name and full address of the site, and clearly list all activities performed at each site.

Any pre-submission queries related to the intended submission of multiple related changes under one single Type II variation should be addressed to the Quality Specialist assigned to your product. See also question 'Who is my contact at the European Medicines Agency during type II variation including extension of indications?'.

1.2.2. Introduction of a new manufacturing site for an active substance. What changes are covered by a single Type II scope? (Classification category Q.I.a.1) *Rev. Nov 2025*

The introduction of a new manufacturing site for an active substance supported by an ASMF should be submitted under a single Type II, Q.I.a.1.f.

The introduction of a new manufacturer of the active substance not supported by an ASMF or intermediate that requires extensive updates to 3.2.S section should be submitted under a single Type II, Q.I.a.1.b).

It should be noted that, in cases where the introduction of the new active substance manufacturer has an impact at the level of the finished product manufacturer (e.g. changes to the active substance specifications or related analytical methods) separate variations have to be submitted under the corresponding Q.I.b categories and may be grouped together, if related to the introduction of the new active substance manufacturer.

It should be highlighted that, for variations introducing additional manufacturing or batch control/testing sites (including sub-contractors), each additional site should be declared as a separate variation on the variation application form as a grouped application, and the precise scope should include the full name, full address of the site and list all activities performed at each site.

Any pre-submission queries related to upcoming submissions pertaining to such Type II changes should be addressed to the Quality Specialist assigned to your product. See also question 'Who is my contact at the European Medicines Agency during type II variation, including extension of indications?'.

1.2.3. How should multiple changes to Module 3.2.S or the update of an ASMF, which is part of Module 3 of a marketing authorisation be submitted? (Q.I.z) *Rev. Nov 2025*

An update of Module 3.2.S can be submitted as a grouped variation application, if conditions 5 or 6 of Annex III of the Variation Regulation (EC) No 1234/2008 are met.

An update or change of a stand-alone ASMF is not foreseen and can only be addressed in connection with a marketing authorisation. The type of variation(s) is dependent on the type of changes introduced in the updated version. The update – including changes to the open and /or restricted part - can be submitted as a grouped application, if condition 5 of Annex III of the Variation Regulation (EC) No 1234/2008 is met.

In case of substantial changes or multiple minor changes to Module 3.2.S or the ASMF, it is recommended to submit a single Type II variation under category Q.I.z. It is a prerequisite for the validation of these single variations that the "present/proposed" section of the application form is filled in correctly and completely.

In all cases, updates of the ASMF must be submitted by the ASMF holder (open and closed part to EMA, open part to marketing authorisation holder (MAH)) whilst the variation to the Marketing Authorisation has to be submitted by the MAH. We encourage a close dialogue between MAH and ASMF holder to ensure that the ASMF update has been submitted before or at the same time as the variation application to avoid validation issues. A clear present and proposed table listing all changes should be included in both submissions (a table of changes should be included in the ASMF submission and the same table of changes and a present and proposed section for the applicant's part should be included in the MAH variation application). The application form needs to include the specific ASMF version number the submission relates to.

Minor changes to the restricted part of an ASMF are not acceptable as Type IA variations and should be submitted using classification category Q.I.a.2.d.

Any pre-submission queries related to upcoming submissions pertaining to extensive changes to Module 3.2.S or extensive ASMF updates should be addressed to the Quality Specialist assigned to your product. See also question 'Who is my contact at the European Medicines Agency during a type II variation, including extension of indications?'.

1.2.4. How should I submit a revised Certificate of Suitability (CEP)? (Q.III.1a.2) *Rev. Nov 2025*

In line with the Marketing Authorisation Holder's (MAH) obligation to keep the dossier up to date, a new or revised Certificate of Suitability (CEP) for an active substance (AS), excipient or starting material/reagent/intermediate used in the manufacturing process of the AS should be submitted as a variation. It is however understood that only the versions of the CEP (i.e. revised certificates) which were used in the manufacturing process of a batch of finished product (FP)/ AS need to be included in the dossier, provided that there are no quality and/or safety concerns that have led to the revision of the CEP.

In case of CEP revision related to quality and/or safety issues, the revised CEP should be implemented immediately and the appropriate variation should be submitted, even if the revised CEP is not linked to a specific production batch for the finished product.

CEP revisions should be submitted under the appropriate variation classification scope within subsection Q.III.1. Each CEP revision should be submitted as a variation scope, i.e. an update covering more than one CEP version should be submitted as a grouped variation.

When submitting a revision of an approved CEP, the MAH should refer to the previously agreed version of the CEP within the 'Present/Proposed' section of the application form.

If with the submission one or more revisions of the CEP are omitted, the MAH should confirm in the variation application form (section 'Precise scope and background for change') that substance/material from the omitted CEP version(s) was not used in the manufacture of the FP and/or AS during the validity of this certificate(s). Additionally it should be confirmed that any changes introduced by the omitted CEP revision(s), do not affect the quality of the AS and/or FP. In case such confirmation is missing, a negative Type IA notification may be issued.

The MAH should also clearly indicate in the 'Present/Proposed' section all changes introduced in the CEP between the latest approved version and the new revision, including all revisions that were not notified. Any changes e.g. to manufacturing sites, additional residual solvents introduced in the CEP by subsequent revisions should be declared.

Example

Submission of a revised CEP version for an already approved manufacturer: R0-CEP-xxxx-xx-rev02 when the current certificate in the dossier is: R0-CEP-xxxx-xx-rev00.

If during the validity of R0-CEP-xxxx-xx-rev01, material of the CEP was used in the manufacture of the FP and/or the AS, then the MAH should submit a grouping of two IA variations to include both certificates (rev. 01 and rev 02) in the Module 3. The foreseen conditions for each of the respective variations should be met.

If during the validity of R0-CEP-xxxx-xx-rev01, material of the CEP was not used in the manufacture of the FP and/or AS, the MAH should only submit a single Type IA variation to include the revised certificate R0-CEP-xxxx-xx-rev02 in Module 3. The foreseen conditions for the variation should be met.

The MAH should also confirm in the variation application form that material/substance from R0-CEP-xxxx-xx-rev01 was not used in the manufacture of the FP and/or AS during the validity of this certificate and that changes introduced by the revision R0-CEP-xxxx-xx-rev01 do not affect the quality of the AS and/or the FP. MAH should also clearly list within the 'Present/Proposed' section of the application form all changes introduced to the CEP with revisions 01 and 02.

1.2.5. What is considered to be a non-significant or an obsolete in-process control, specification attribute or acceptance criteria? (Classification category Q.I.a.4.c, Q.I.b.1.d, Q.I.c.2.c, Q.II.b.5.c, Q.II.c.1.c, Q.II.d.1.d and Q.II.e.4.c) ***Rev. Nov 2025***

Variation scopes Q.I.a.4.c, Q.I.b.1.d, Q.I.c.2.c, Q.II.b.5.c, Q.II.c.1.c, Q.II.d.1.d and Q.II.e.4.c of the EC 'Variations Guidelines (2025)', deal with the deletion of a non-significant or an obsolete in-process control (IPC) test, specification attribute or acceptance criteria. Provided all relevant conditions and documentation requirements are met, all these variations fall under the Type IA category (do-and-tell).

The variation categories listed above are intended to be used for non-significant or obsolete IPC test, specification attribute or acceptance criteria that are no longer in line with the technical and scientific progress and part of normal specifications for newer products but have remained for historical reasons in older products (e.g. description of odour and taste). It is not intended to include changes in relation to revisions of the control strategy with an intention to minimise redundant testing of parameters and attributes (critical or non-critical) that are tested at different stages during production, or cases where process/ product characterisation performed after authorisation has shown that the attribute/ parameter is non-critical. Such changes require regulatory assessment and are to be handled as Type IB or II variations as appropriate.

1.2.6. Which variation category should be used to remove/replace the Rabbit Pyrogen test from marketing authorisation dossiers? NEW Nov 2025

Please refer to the EMA's webpage of 'Quality of medicines questions and answers: Part 1 - European Pharmacopeia (Ph. Eur.) - Phasing out Rabbit Pyrogen Test'.

1.2.7. When applying for a new pack size, what is considered to be within /outside range? (Classification category Q.II.e.6) *Rev. Nov 2025*

The introduction of a new pack size (i.e. in addition to currently approved pack sizes) should be submitted as a variation under scope Q.II.e.6.a).

A range is defined from the smallest to the largest approved pack size (i.e. not from '0') for the same pharmaceutical form and strength. The pack size equals to the number of units of the pharmaceutical form (e.g. tablets, sachets, ampoules, etc.) contained in the outer packaging. Pack sizes not included within this range are considered to be outside of the range.

For the addition of a new pack size where the number of units of the pack is within the range of the currently approved pack sizes for the strength and pharmaceutical form, applicants should submit a Type IA_{IN} variation Q.II.e.6.a.1.

For the addition of a new pack size where the number of units of the pack is outside the range of the currently approved pack sizes for the strength and pharmaceutical form, applicants should submit a Type IB variation Q.II.e.6.a.2.

In support of a timely introduction of new pack sizes to the market, EMA accepts the following approach for the introduction of various pack sizes falling outside the range within a single grouped submission. The biggest or the smallest pack size per strength outside the range should be classified as Type IB variation Q.II.e.6.a.2. This presentation defines the new limits of the range so that any intermediate pack size for the strength and pharmaceutical form can be classified as Type IA_{IN} variation Q.II.e.6.a.1.

Example 1

The "Medicinal Product A" has currently two approved pack sizes of 30 and 60 tablets for the pharmaceutical form "film coated tablets" and the strength "20mg" and the MAH intends to apply for two new pack size(s) of 90 and 120 tablets at the same time.

The introduction of a new pack size of 120 tablets for the "20mg" strength is considered outside the range of packs and should be classified as variation Q.II.e.6.a.2 (IB). This pack size defines a new limit for the range (30-120), so that the introduction of a pack size of 90 tablets as a grouped (or a latter) submisison can be classified as a variation Q.II.e.6.a.1 (IA_{IN}).

The MAH should therefore apply for a grouped variation of 1 x Type IB - Q.II.e.6.a.2 variation and 1x type IA_{IN} Q.II.e.6.a.1 variation.

Example 2

The "Medicinal Product B" has currently two approved pack sizes of 2 and 10 pre-filled syringes for the pharmaceutical form "solution for injection" for both strengths of "20mg" and "40mg". The MAH is applying for four new pack sizes: 5 prefilled syringes for the "20 mg" strength; 30 pre-filled syringes for the "20 mg" strength; 5 prefilled syringes for the "40 mg" strength; 30 pre-filled syringes for the "40 mg" strength.

For the "20mg" strength, the introduction of a new pack size of 5 pre-filled syringes strength is considered within the range of approved packs (2-10) and should be classified as variation Q.II.e.6.a.1 (IA_{IN}) and the introduction of a new pack size of 30 pre-filled syringes is considered outside the range of approved packs (2-10) and should be classified as variation Q.II.e.6.a.2 (IB).

For the "40mg" strength, the introduction of a new pack size of 5 pre-filled syringes strength is considered within the range of approved packs (2-10) and should be classified as variation Q.II.e.6.a.1 (IA_{IN}) and the introduction of a new pack size of 30 pre-filled syringes is considered outside the range of approved packs (2-10) and should be classified as variation Q.II.e.6.a.2 (IB).

The MAH should therefore apply for a grouped variation application under the scopes referred above.

It should be highlighted, that for variations introducing additional presentations or pack sizes for centrally approved products, each additional presentation or pack size should be declared as a separate variation on the variation application form under the section 'variations included in this application'.

Changes to strength, pharmaceutical form and route of administration are to be submitted as an Extension of a marketing authorisation.

For additional guidance on changes to an existing presentation that can trigger new EU number(s) please see the EMA post-authorisation guidance for Type IA, Type IB and Type II variations.

1.2.8. How should I submit a new working cell bank (WCB)? (Classification category Q.I.a.2 a) *Rev. Nov 2025*

If a new WCB is introduced using the limits/conditions as detailed in an approved qualification protocol, the new WCB is covered by the existing quality assurance system and there is no need to submit a variation.

If the documentation of the WCB in the dossier does not include an approved qualification protocol for introducing new WCBs, the MAH should file a Type IB variation under Q.I.a.z.

To introduce a qualification protocol for preparation of a new WCB, the MAH should file a variation Type II Q.I.a.2.b. The addition of the new WCB can be covered as part of this single variation Type II.

Changes to an approved qualification protocol should be filed using Q.I.a.2.a, or Q.I.a.2.b, as relevant depending on the complexity of the change. The addition of a new WCB can be covered as part of this single variation.

1.2.9. How should I submit a new in-house reference standard/preparation for a biological medicinal product or excipient? *Rev. Nov 2025*

If a new in-house reference standard/preparation for a biological active substance, excipient and/or finished product is introduced using the limits/conditions as detailed in an approved qualification protocol, the new in-house reference standard/preparation is covered by the existing quality assurance system and there is no need to file a variation.

For other changes to an in-house reference standard/preparation for a biological active substance, excipient and/or finished product, classification scopes under Q.I.b.3 should be used.

1.2.10. What changes in manufacturing sites, buildings and rooms are covered by the company Quality Assurance System (GMP)? *Rev. Nov 2025*

Provided that module 3 is not impacted, with the exception of section 3.2.A.1 (for biological medicinal products), the changes listed below (not an exhaustive list) are covered under the company's quality management system and do not require a variation to the Marketing Authorisation:

- Transfer of a manufacturing activity from one building to another in the same authorised site
- Transfer of a manufacturing activity from one room to another in the same authorised building
- Transfer of QC activity from one building to another in the same authorised site
- New filing line identical to an already approved one in an authorised room, building, manufacturing site (in case of a duplication of line to increase the batch size of the final product, a variation under Q.II.b.4 should be submitted).
- New isolator in an authorised building
- New media or buffer preparation room in an authorised building
- Changes in the layout of an authorised manufacturing site

If as a result of any of the changes listed above, any amendments are introduced to module 3 (with the exception of section 3.2.A.1 for biological medicinal products), such as changes to the manufacturing site address detail, changes to the manufacturing process, changes to the batch size, etc., the MAH should file the appropriate variation(s).

1.2.11. Changes in equipment used in the manufacturing process. What changes are covered by the company Quality Assurance System (GMP)? *Rev. May 2018*

Provided that the new equipment is equivalent to the one currently used, and operates in the approved range of process parameters, the change is covered by company's quality assurance system.

If the introduction of new equipment has any impact on the processes and details registered in module 3 (with the exception of section 3.2.A.1 for biological medicinal products), the MAH should submit the appropriate variation(s).

1.2.12. How should I update section 3.2.A.1 for Biotech medicinal products? *Rev. Nov 2025*

Notice to applicants for Medicinal products for human use (Eudralex – Volume 2B) establishes that information on facilities and equipment should be included in Appendix 3.2.A.1 for biotech medicinal products.

Any update of this section can be included as part of any upcoming variation affecting Module 3. In case the MAH wants to update this section and does not foresee any upcoming variation affecting Module 3 in the short/medium term, the MAH may consider submitting a Type IB variation (Q.II.z).

1.2.13. What do I need to consider if there are any changes to my medical device post-authorisation? *Rev. Nov 2025*

Information on the lifecycle management of a medical device when used in combination with a medicinal product can be found in 'Questions & Answers for applicants, marketing authorisation holders

of medicinal products and notified bodies regarding medicines used in combination with medical devices and consultation procedures by notified bodies for certain devices'.

1.2.14. How should I submit the transfer of test methods for testing of medicinal products to a new or already authorized testing site? Which variation classification category is applicable and what type of supporting documentation is expected? Rev. Nov 2025

Although, the need to submit a variation to approve an existing QC testing site for additional testing activities after analytical test transfer has been completed is not specifically foreseen by the EC Variation Classification Guideline submission of a variation following by analogy the existing foreseen variation category Q.I.a.1.i, Q.I.a.1.j, Q.II.b.2.a, Q.II.b.2.b, Q.II.b.2.c.2 or Q.II.b.2.c.3 may be necessary as outlined below under ii.

i. In case of **physical, chemical and microbiological test methods** to be transferred to a **new** testing site (i. e. not yet listed in the dossier) submission of a variation is required (category Q.I.a.1.j, Q.II.b.2 or Q.II.b.2.c.2). The documentation to be submitted is defined in the EC Variation Classification Guideline.

ii. In case of biological, immunological, or immunochemical test methods (e.g. in vivo bioassays, in vitro bioassays, enzymatic assays, binding assays, neutralisation assays, immunochemical assays) to be transferred to a **new** testing site or to an **already approved** testing site, a variation of type Q.I.a.1.i or Q.II.b.2.b or Q.II.b.2.c.3 is to be submitted.

The documentation should include at a minimum, the method transfer protocols in accordance with Eudralex Volume 4 Chapter 6 article 6.39 (which pre-define the acceptance criteria), from the old site to the new site (or new test laboratory). Depending on the variability of the specific method and the potential risk, to the quality, safety or efficacy of the product, posed by the proposed change, additional data such as a summary of the analytical method transfer test results may be required.

1.2.15. Do I need to record in the dossier a new manufacturing site for physical importation? NEW Mar 2021

The Member States shall ensure that the import of medicinal products into their territory is subject to an authorisation in accordance with Article 40(3) of Directive 2001/83/EC.

Please note that physical importation and batch certification of imported products are different operations that can take place at the same or different authorised manufacturing sites located in the Union (EEA).

It is not a requirement to register in the dossier of your marketing authorisation the manufacturer(s) responsible for the physical importation of the finished product, hence no variations applications are required for changes in physical importation sites. The Manufacturing and Importation Authorisation (MIA) holder responsible for batch certification of imported medicinal products should ensure that the site(s) of physical importation is appropriately authorised for this operation. The physical importer needs to hold a MIA with an entry in section 2.3.1 according to the Union Format for MIAs. A technical agreement between the physical importer and the batch release site shall be in place. For more information on the certification by a QP and on batch release in the EU, also with regards to importation, see GMP annex 16.

1.3. (Non-) Clinical changes

1.3.1. What should I consider in relation to the quality documentation in case of a change in the clinical use of marketed products meaning change in therapeutic indication, posology or maximum daily dose (MDD)? NEW Nov 2025

In case of a change in the clinical use of marketed products, meaning change in therapeutic indication (including a change in the target population), posology or maximum daily dose, a review of the quality documentation should always be performed. In this review the MAH should perform an assessment of the impact on the quality documentation of the proposed clinical change. Confirmation that the assessment has been performed should be included as part of the clinical variation. This also applies to generic products and hybrids.

The review performed by the MAH on the quality documentation could lead to the following scenarios:

- The submission of a quality variation is not required (e.g. the change in MDD does not affect the authorised acceptance criteria and control strategy for impurities). A declaration confirming the conclusions of the assessment needs to be included in the Application Form or as a separate Annex in Module 1.
- The submission of the appropriate quality variation under the Quality Changes chapter is needed (e.g. acceptance criteria for an impurity should be changed). A quality variation should be submitted under the appropriate classification according to the Variation classification guideline and grouped with the clinical variation.

For both scenarios non-exhaustive examples are given below:

1. Changes to the clinical use of marketed products can warrant a re-evaluation of the **mutagenic impurity** limits:

   a. An increase in clinical dose, e.g. changes in the MDD could impact the authorised control strategy for mutagenic impurities, including N-nitrosamines, in active substances and medicinal products.

   b. An increase in duration of use, e.g. when a mutagenic impurity was controlled above the lifetime acceptable intake for a previous indication that may no longer be appropriate for the longer treatment duration associated with the new indication.

   c. A change in indication from a serious or life-threatening condition where higher acceptable intakes were justified to an indication for a less serious condition where the existing mutagenic impurity acceptable intakes may no longer be appropriate, e.g. for products initially intended for advanced cancer only as defined in the scope of the ICH S9 guideline, where N-nitrosamine impurities controlled according to ICH Q3A(R2) and ICH Q3B(R2) guidelines is no longer applicable.

2. Changes to the clinical use of marketed products can warrant a re-evaluation of **organic impurities** limits according to ICH Q3A and Q3B guidelines since reporting, identification and qualification threshold are established based on the MDD.

3. Changes to the clinical use of marketed products can warrant a re-evaluation of **elemental impurities**, as individual permitted daily exposures (PDEs) are set based on the MDD and the route of administration, according to ICH Q3D.

4. Changes to the clinical use of marketed products can warrant a re-evaluation of **endotoxins limits** for parenteral products considering the calculation formula included in European pharmacopoeia General chapter 5.1.10.

5. Changes to the clinical use of marketed products can warrant a re-evaluation of the appropriateness of the **pharmaceutical form, container closure system or dosing devices** where a new target population is applied for (e.g. paediatric population, home versus hospital setting); refer to question on 'Will I need to provide a (new or updated) EU declaration of conformity/certificate of conformity issued by a notified body/notified body opinion if there are changes to the device (or device part) after the initial marketing authorisation of the integral DDC?' in 'Questions & Answers for applicants, marketing authorisation holders of medicinal products and notified bodies with respect to the implementation of the Regulations on medical devices and in vitro diagnostic medical devices (Regulations (EU) 2017/745 and (EU) 2017/746)'.

6. Changes to the clinical use of marketed products can warrant a re-evaluation of the **compatibility studies** with reconstitution diluents in the extremes of concentration of the product to be administered due to a change in the posology/target population.

7. Changes to the clinical use of marketed products can warrant a re-evaluation of **instructions for administration** and the feasibility of dosing (e.g. with regards to volumes to be measured, measuring device to be included or recommended, and dilutions to be used).

8. Changes to the clinical use of marketed products can warrant a re-evaluation of the **excipient safety** and the need for excipient warnings, as excipient safety should be based on daily exposures (mg/kg), which are set based on the MDD and the route of administration. Excipient safety should also consider target population, changes in age range, in particular where younger subsets are included.

1.3.2. How should I submit a study protocol? Rev. Nov 2025

For imposed, non-interventional safety studies, the initial protocol submission should follow the provisions under Article 107n of Directive 2001/83/EC. Substantial amendments of such study protocol should be submitted under the provision of Article 107o of Directive 2001/83/EC (please also refer to guidance on PASS).

For other studies (i.e. non-imposed studies and/or interventional studies), if the initial assessment or the amendment of a study protocol does not result in a consequential change of the condition as reflected in Annex II and/ or the description of the study in the RMP it can be provided as a post-authorisation measure (PAM) (please also refer to the EMA guidance on post-authorisation measures: 'Under which procedure should I submit my PAM?').

Once agreed, the MAH can take the opportunity of a regulatory procedure affecting the RMP to include the final updated protocol in the appropriate RMP annex(es).

If the study description in the Annex II condition and/ or in the RMP is affected, the study protocol/ or the protocol amendment, together with the proposed updated Annex II and/or RMP should be provided as part of a type II variation application under category C.9.c.

A change that affects the due date of the milestones for non-imposed studies and/or interventional studies listed in the Annex II and/or RMP can be submitted as Type IB variation under category C.9.b.

1.3.3. How should non-clinical and/or clinical study reports be provided? Rev. Nov 2025

In line with the 'Variations Guidelines' all 'final' non-clinical or clinical study reports concerning a marketing authorisation granted under the centralised procedure will have to be submitted to the Agency as part of a type II variation application, unless otherwise specifically covered in the annex to the classification guideline on variations or listed below:

- Results of imposed non-interventional safety studies covered by the Art. 107q of the Directive 2001/83/EC;
- Submissions of final study results in support of extension of marketing authorisation applications, annual renewals or annual re-assessments;
- Submission of study results related to paediatric population in line with Article 46 of Regulation 1901/2006. Submissions pursuant to Article 46 should continue to follow the procedure for post-authorisation measures, unless the MAH concludes that changes to the product information (PI) are warranted based on the data submitted. In such cases, the relevant variation should be submitted;
- Studies in the context of an environmental risk assessment (ERA). These are expected to be assessed during the initial marketing authorisation or relevant post-marketing procedures (e.g. extension of indication, extension applications). In the exceptional case that ERA study results are provided stand-alone, they should be submitted as a type IB C variation;
- Results including reports from bioequivalence studies to support quality changes to the marketing authorisation should be submitted under the applicable variation category for quality changes.

As a general rule, the 'final' study report is considered the one including the primary analysis of the study. In case the final study report has previously been submitted, further updates of data from the study without formal statistical significance after the primary analysis do not trigger additional variations, unless they lead to changes to the product information and/or to the Risk Management Plan (RMP). On the other hand, a formal extension study, generally with a different study design and objectives as compared to the initial study, is considered a separate study and it generally carries a separate study number. The submission of the final report for such an extension study triggers a variation.

When a change to the product information is proposed as a consequence of the final study report, the type II variation should be submitted under variation classification categories C.a (extension of indication), C (other changes involving the SmPC, Annex II, labelling and/or Package Leaflet) or C.9.c (changes limited to the Annex II conditions). When no changes to the product information are proposed, the variation should be submitted under category C.12.

When a final non-clinical or clinical study report is provided as part of a variation submitted under category C.12, it should be noted that one separate type II variation per study report is required. This requirement applies also in situations where the CHMP has requested several non-clinical or clinical studies to be undertaken as part of a specific post-authorisation measure (PAM) in order to address a specific issue; one type II variation under category C.12 per final study report will still be requested (provided that the product information remains unaffected) .

It should be noted that these requirements also apply to all non-clinical studies, including the provision of final study reports for *in vitro* studies.

In case the final non-clinical or clinical study report leads to consequential changes to the RMP, the MAH can include an updated RMP version as part of the type II variation regardless of whether it is submitted under category C.6, C.4, C.9 or C.12.

With regard to 'interim' non-clinical or clinical study results, the timelines of the progress reports for a given study should be pre-specified and indicated in the protocol. These progress reports may include available interim results, but there is in general no obligation or recommendation to include interim results in RMPs unless required as part of an agreed pharmacovigilance plan. In this case, for CAPs, the specified progress report(s)/interim results should be submitted as PAM unless the MAH considers that the interim data would require consequential changes to the product information and/or the RMP in which case a type II variation should be submitted instead. On the other hand, interim results should be reported in relevant PSURs.

When interim results have been requested by the CHMP and are provided in order to address a specific post-authorisation measure (PAM), the data should be submitted in line with the requirements of the PAM procedure, unless the MAH considers that the interim data result in consequential changes to the product information and/or the RMP in which case a type II variation should be submitted instead.

With reference to analyses across studies on specific topics (e.g. a biomarker report from more than one study) for which the individual final study reports have previously been submitted, the analysis should be submitted under category C.4 (in case of changes to the product information), under category C.9 (changes limited to the Annex II conditions) or as a PAM (no changes to the product information and/or the RMP are warranted). When the analyses should be submitted as variations, one variation scope per analysis (and not per study included in the analysis) should be submitted.

Final results from an imposed non-interventional post-authorisation safety study (PASS category 1 and 2 in the RMP and reflected in Annex II) should be submitted within 12 months of the end of data collection unless a written waiver has been granted by PRAC, as appropriate (please refer to guidance on imposed post-authorisation safety studies). It should be noted that the submission of final results of imposed non-interventional studies should follow the relevant Art 107q of Directive 2001/83/EC procedure (please also refer to guidance on post-authorisation safety studies), regardless of whether or not the MAH considers that changes to the product information are warranted.

When a change to the product information is proposed for a medicinal product containing more than one active substance to implement changes that were already assessed by a EU competent authority for a medicinal product containing one of the active substances and the same wording is proposed, the change and supportive data should be submitted as a Type II variation under category C.4.

Any pre-submission queries in this regard should be addressed to the appointed Product Lead.

1.3.4. What changes to the product information (PI) can be included as part of one type II variation? Rev. Nov 2025

In principle, one change to the PI supported by one set of data constitutes one assessment and subsequently one scope i.e. one type II variation.

All data/study reports provided as part of a variation must support the same changes to the SmPC. If this is not the case, i.e. some data support one change (update A), and other data support another change (update B), it will be necessary to submit separate stand-alone variations or a group of variations, as appropriate; one variation for SmPC update A including the data supporting A, and one variation for SmPC update B including the data supporting B.

In the event that some of the data/study reports proposed to be part of an application do not support any of the proposed changes to the SmPC, the reports give rise to separate variation scopes (category

C.12 – one variation per final study report as explained under 'How should non-clinical and/or clinical study reports be provided?'), which could potentially be grouped in the same submission or may need to be removed from the proposed variation application and submitted as a separate appropriate application.

Thus, only when changes are consequential to the same supporting data, can one type II variation application propose changes to several different sections of the SmPC as well as corresponding changes to the Package Leaflet. Any additional changes to the PI that are consequential to the assessment of another set of data will have to be submitted as part of a separate variation (stand-alone or part of a grouped application to be decided on a case-by-case basis).

Some theoretical examples are being provided below to illustrate the principles explained above.

Example 1

Proposed application: Provision of final clinical study reports (CSR) for 3 PK studies (studies X, Y, Z).

- If the data from the 3 CSRs support the same SmPC updates, the reports should be submitted as part of one single type II variation under category C.4 (scope = 'update of the SmPC based on the results from studies X, Y and Z').
- If two study reports (X, Y) support one SmPC change (update A), and the 3rd study report (Z) supports a different SmPC change, the applicant should submit one type II variation under category C.4 for SmPC update A and one type II variation under category C.4 for SmPC update B. The two variations can in this case be submitted as part of a grouped application, as it makes sense to assess the 3 PK studies together (scope = 'update A of the SmPC based on the results of studies X and Y, and update B of the SmPC based on the results of study Z').
- If two study reports (X, Y) support all proposed SmPC changes and the 3rd study report (Z) does not result in any consequential changes to the SmPC at all, the applicant should submit a grouped application including one type II variation under category C.4 (studies X, Y) and one type II variation under category C.12 (study Z). The two variations can in this case be submitted as part of a grouped application, as it makes sense to assess the 3 PK studies together (scope = 'update of the SmPC based on the results of studies X and Y. The applicant also provides study Z as a grouped variation as a common assessment of these changes is considered meaningful').

Example 2

Proposed application: Provision of one CSR for study A supporting SmPC changes regarding efficacy in patient population A and overall clinical safety, and one CSR for study B supporting SmPC changes regarding efficacy in patient population B and overall clinical safety.

- In view of the fact that the efficacy data are unrelated and concern two separate patient populations, two separate assessments will need to be undertaken and two separate Type II variations will be required. However, as the scopes of the two variations are both partly related to overall clinical safety, it is meaningful to assess them together and the applicant should therefore provide the two variations as part of one grouped application.
- However, in the event that the data sets would be completely unrelated - e.g. because of different safety profiles in the two patient populations due to different posology - the reports should be provided as part of two separate stand-alone Type II variations; one for patient population A (efficacy and safety) and one for patient population B (efficacy and safety).

Example 3

Proposed application: Update of the SmPC section 4.8 in order to add three new ADRs; 'dyspnoea' and 'chromaturia' following a review of the MAH's safety database undertaken upon request by PRAC following a PSUSA procedure, and 'Kounis syndrome' following the MAH's own signal detection.

- As the three ADRs are supported by two separate data sets the MAH should submit two variations as part of a grouped application; one type II variation under category C.3.c to add 'dyspnoea' and 'chromaturia', and one Type II variation under category C.4 to add 'Kounis syndrome'. Both variations are related to clinical safety and it makes sense to assess them together hence the acceptability of the grouping.

Example 4

Proposed application: Type II variation under category C.6.a in order to propose an extension of indication, which will include both non-clinical and clinical studies.

- Provided that all non-clinical and clinical data that will be submitted as part of the application are supportive of the new claimed indication, the studies should be provided as part of the application without the need for any additional variation.
- However, in the event that e.g. one of the non-clinical studies is not supportive of the proposed extension of indication, it will need to be submitted as part of a separate variation application (stand-alone or part of a grouped application to be decided on a casebycase basis).

Any pre-submission queries in this regard should be addressed to the Product Lead.

1.3.5. How do I submit changes to the Summary of Pharmacovigilance System for medicinal products for human use? Rev. Nov 2025

As of 1 February 2016, changes to the summary of the pharmacovigilance system – changes in QPPV (including contact details) and/or changes in the Pharmacovigilance Master File (PSMF) location are to be notified to the authorities through the Art 57 database only without the need for any further variation.

Upon a change in the QPPV or location of the PMSF, the Art 57 database should be updated by the MAH immediately to allow continuous supervision by the Competent Authorities.

Please also refer to Question How to inform the authorities of a change in the summary of the pharmacovigilance system? in the Pharmacovigilance system section of the Post-Authorisation Guidance.

References

- News Item: Regulatory information – Green light for reliance on Article 57 database for key pharmacovigilance information on medicines for human use in Europe
- Art 57 Reporting requirements for Marketing Authorisation Holders
- Detailed Guidance on electronic submission of information on medicines

1.3.6. How should I submit data requested as a follow-up to a prior regulatory procedure? Rev. Nov 2025

Occasionally, the outcome of a regulatory procedure may require the MAH to follow-up on certain aspects in a subsequent regulatory submission. The type of submission required depends on the nature

of the data requested and whether the implementation impacts the Product Information (PI) and/or the Risk Management Plan (RMP).

If the outcome of the prior regulatory procedure requests the submission of a (non-)clinical study report, this should always be submitted as a variation (unless this is a paediatric study submitted under Article 46 of the Paediatric Regulation (EC) 1901/2006). Any other requested information (e.g. cumulative safety review) should be submitted as a variation if it has impact for the PI or the RMP. In other cases, it can be accepted as a Post Authorisation Measure (PAM).

Similarly, if the prior procedure already recommends changes to the PI or the RMP, these should be submitted as variation, unless the MAH would like to provide a justification why such changes are not supported by the MAH. In the latter case, the rationale for not submitting a variation proposing the indicated PI and/or RMP changes and any requested data supporting the rationale can be submitted as a PAM. If however the data requested involves the submission of a final (non-)clinical study report, a variation should always be submitted even if no changes to the PI and/or RMP are proposed (with the exception of submissions under Article 46 of the Paediatric Regulation (EC) No 1901/2006).

The classification of the variation depends on the nature of the prior procedure the outcome of which is being implemented:

- for implementation of the outcome of a Union referral procedure, the applicable variation category is C.1.
- for implementation of the outcome of a PSUR, PASS protocol or PASS results procedure, or the outcome of a PRAC signal recommendation, or to adapt to a joint recommendation of EU competent authorities, the applicable variation category is C.3. It should be noted that PI changes resulting from PSUR data should ideally be implemented within the PSUR procedure itself; only if additional data are required to support the PI changes which cannot be submitted and assessed during the PSUR procedure, should a follow-up variation of the C.3 category be submitted.
- in case of a procedure under article 46 of Paediatric Regulation No (EC) 1901/2006, the applicable variation scope is C.3 only in case changes to the PI are proposed. In principle, it is expected that in most cases PI changes are to be proposed. In the exceptional case that no changes to the PI are proposed, a PAM procedure should be applied for (see also question How should non-clinical and/or clinical study reports be provided?)
- for the alignment of the PI of a generic, hybrid or biosimilar medicine to that of the reference product the applicable variation category is C.2 with the exception of the implementation of wording from PSUR and PASS procedures; the applicable scope category in such cases is C.3.
- any other prior regulatory recommendation should be implemented via: a C.4 variation category, if changes to the PI are proposed; a C.9 variation category, if changes to the conditions in Annex II of the PI or in the RMP are proposed; a C.12 variation category, if a final (non-)clinical study report is being submitted; a PAM, if a paediatric final study report is being submitted under the requirements of Article 46 of Paediatric Regulation 1901/2006 and in all other cases where requested data and analyses are being submitted without an impact to the PI (including Annex II) and the RMP (please also refer to question Under which procedure should I submit my PAM?).

1.3.7. What is considered a new or modified therapeutic indication? Rev. Nov 2025

Applications proposing changes to the therapeutic indication aiming to extend the target population (either by modifying an existing indication(s) or by extending in a completely new indication/target disease) trigger paediatric and orphan requirements (please refer to questions 'What aspects should I

consider at time of submission of a Type II variation if there are orphan medicinal products designated or authorised for a condition related to my proposed therapeutic indication?', 'Do I need to address any paediatric requirements in my type II variation application?', 'What aspects should I consider at time of submission of an extension application if there are orphan medicinal products designated or authorised for a condition related to my proposed therapeutic indication?' and 'Do I need to address any paediatric requirements in my extension application?' in the post-authorisation guidance for type II variations and Extension of Marketing Authorisations).

The EC Guideline on the elements required to support the significant clinical benefit in comparison to existing therapies of a new therapeutic indication in order to benefit from an extended (11-year) marketing protection and the EC Guideline on a new therapeutic indication for a well-established substance provide a definition of what is considered a 'new indication'. More specifically, a new (or modified) indication is:

- a new target disease;
- different stages or severity of a disease;
- an extended target population for the same disease, e.g. based on a different age range or other intrinsic or extrinsic factors;
- a change from first-line treatment to second-line treatment (or second-line to first-line treatment), or from combination therapy to monotherapy, or from one combination therapy (e.g. in the area of cancer) to another combination;
- change from treatment to prevention or diagnosis of a disease;
- change from treatment to prevention of progression of a disease or to prevention of relapses of a disease;
- change from short-term treatment to long-term maintenance therapy in chronic disease.

However, in some particular situations a case-by-case assessment may be needed to determine whether the target population is extended. For example, the following may not be considered a new indication:

- information on the use of the medicinal product in the authorised target diseases in patients with renal or hepatic impairment;
- information on the use of the medicinal product in the authorised target diseases in pregnant women;
- for vaccines, information on the concomitant administration with other vaccines.

In addition to applications extending the target population, orphan similarity requirements are also triggered by any extension of the Marketing Authorisation (line extension, please refer to question 'What aspects should I consider at time of submission of an extension application if there are orphan medicinal products designated or authorised for a condition related to my proposed therapeutic indication?').

Paediatric requirements are triggered by an extension of the Marketing Authorisation (line extension) for new pharmaceutical forms and/or new routes of administration (please refer to question 'Do I need to address any paediatric requirements in my extension application?').

From a procedural point of view, extensions of indication can be submitted as type II variations or extensions of the Marketing Authorisation depending on whether the change in the target population is accompanied by other changes e.g. changes to the strength, pharmaceutical form, route of

administration (please refer to question 'When will my variation application be considered a Type II variation or an Extension application?').

For extensions of the Marketing Authorisation, in case the change in the indication is only intended for the new pharmaceutical form/ strength being added, the extension of indication is covered by the scope of the MA extension application. In case the change(s) in the therapeutic indication also applies to existing presentations, the application should be presented as a grouping of a line extension(s) and C.6.a scope variation.

When the extension of indication is submitted as a type II variation application, the C.6.a scope category (i.e. addition of a new therapeutic indication or modification of an approved one) typically applies. However, not all variations under the C.6.a. scope category are actual extensions of indication (e.g. restrictions of an existing indication also fall under this scope category). The contrary is also the case: there are variations which aim to extend the target population but which do not affect the wording of the approved therapeutic indication in section 4.1 of the SmPC. So the variation category is not C.6.a but rather C.4 (changes in the Product Information due to new quality, preclinical, clinical or pharmacovigilance data). Ultimately, if the 'target population' is extended, the orphan and/or paediatric requirements are triggered, even though the variation may not have been submitted as a C.6.a 'extension of indication'.

In case of a change in therapeutic indication, a review of quality documentation should be performed. Any resulting change to the quality documentation (e.g. change to impurity limits) should be proposed with the submission of the relevant grouped quality variation. Please see also question on 'What should I consider in relation to the quality documentation in case of a change in the clinical use of marketed products meaning change in therapeutic indication, posology or maximum daily dose (MDD)?'.

1.3.8. When is the submission of assessments carried out on target patient groups in order to comply with Article 59(3) of Directive 2001/83/EC and any resulting change(s) to the Package Leaflet a stand-alone variation? NEW Nov 2025

Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended, require that the package leaflet reflects the results of consultations with target patient groups ('user consultation') to ensure that it is legible, clear and easy to use and that the results of assessments carried out in cooperation with target patient groups are provided to the competent authority.

It is expected that 'user consultation' results in support of post-approval changes that require a regulatory application are provided as part of the same application. However, if the 'user consultation' results need to be updated outside the scope of another regulatory procedure, it should be submitted as a stand-alone variation type IB, C.11.

- 'User consultation' results should not be provided as part of a type IA/IAIN variation. The review of the results requires the involvement of the rapporteur as part of a type IB or type II variation.
- A stand-alone variation type IB, C.11 can be submitted both for cases where the 'user consultation' results affect the product information Annex III, as for cases that do not lead to an update of Annex III.

1.4. Editorial changes

1.4.1. What can be considered an editorial change and how can it be submitted as part of a type IA/IB/II variation? Rev. Nov 2025

The European Commission 'Variations Guidelines' 2013/C 223/01 specifies that "If amendments to the dossier only concern editorial changes, such changes should generally not be submitted as a separate variation, but they can be included in a variation concerning that part of the dossier". Changes that can be classified as a variation as per Variations Guidelines are not considered editorial changes and should be submitted under the appropriate variation category.

Editorial changes in module 3

Provided that the above condition is fulfilled, the following changes to the Module 3 may be considered editorial: adding headers for ease of use, reordering of existing information without changing the meaning, alignment of information among/within the sections provided that it can be demonstrated what is the correct reference that had been previously agreed (e.g. alignment of information in flow charts to process description), punctuation changes and grammar/orthographic corrections that do not alter the meaning of the text.

Examples of changes that cannot be considered editorial: removal of specification parameters or manufacturing description, update of information to bring the dossier content in line with the current manufacturing process, etc.

Editorial changes should always be clearly identified in the application form as follows: A brief description of the editorial changes should be provided in the Precise Scope. All the editorial changes should be listed in the **present/proposed table**, and a **justification** as to why the holder considers them 'editorial' (i.e. why they should not trigger a specific variation) should be **provided** for each change.

In addition, the MAH should provide a **declaration** in the 'Precise scope and background…' section of the application form confirming that the changes proposed as editorial do not change the content of the concerned part(s) of the dossier beyond the scope of the variation within which the editorial changes are being submitted.

The Agency strongly recommends the submission of editorial changes within procedures with an administrative validation phase e.g. type IB or type II variations. This allows the appropriate review of proposed editorial changes during the administrative validation phase and the consequential amendment of the submission prior to assessment if needed. The editorial changes proposed should affect the same part of the dossier concerned by the variation procedure i.e. fourth level of the eCTD dossier (e.g. "3.2.S.x" or "3.2.P.x"). For example, if a variation affects section 3.2.S.2.1 editorial changes can be submitted in sections from 3.2.S.2.1 to 3.2.S.2.7.

Exceptionally, the Agency may accept minor editorial changes as part of IA variations, if affecting the same eCTD section impacted by the variation submitted (i.e. at the fifth level 3.2.S.2.1). This is due to the fact that IA notifications are of administrative nature and do not have a validation phase. In case of doubt on the acceptability of editorial changes in future type IA applications, please contact the Agency by raising a ticket via EMA Service Desk, selecting the tab "Business Services", category "Human Regulatory". The subcategory to be selected is "Post-authorisation - Human", followed by the sub-option: "Variation IA queries".

If you do not have an EMA Account, you may create one via the EMA Account Management portal. For further information or guidance about how to create an EMA Account reference the guidance "Create an EMA Account".

MAHs are reminded to follow this guidance and ensure the high quality of variation applications in support of a timely processing of submissions.

The Agency expects MAHs to keep proportionality between the submissions of editorial changes versus the change which is the scope of the variation application. If the editorial changes affect sections in module 3 not impacted by any upcoming variation, the MAH may consider submitting these changes as a separate type IB variation (Q.I.z or Q.II.z respectively).

Editorial changes in module 4 and 5

Editorial changes in module 4 and 5 are in principle not foreseen.

Only in case of alignment of information within the dossier, provided that it can be demonstrated which is the correct reference that has been previously agreed, a change to a report in module 4 and 5 can be accepted as editorial and the update submitted as part of an upcoming type II non-clinical or clinical variation submitted under the C scope categories that involves the relevant committee for the specific study. If no such variation is foreseen, a type IB variation C.z can be submitted.

Other updates cannot be considered editorial and require assessment under a variation, for example correction of information in module 4 and 5, updated calculation, etc.

Editorial changes should be clearly identified in the application form as follows: A brief description of the editorial changes should be provided in the Precise Scope. The editorial changes should be listed in the **present/proposed table**, and a **justification** as to why the change is editorial should be **provided**.

In addition, the MAH should provide a **declaration** in the "Precise scope and background…' section of the application form confirming that the changes proposed as editorial do not change the content of the dossier beyond the scope of the variation within which the editorial changes are submitted.

Please contact the Agency in advance of an upcoming submission by raising a ticket via EMA Service Desk, selecting the tab "Business Services", category "Human Regulatory". The subcategory to be selected is "Post-authorisation - Human", followed by the relevant sub-option: "Variation IA queries" or "Variation IB queries".

If you do not have an EMA Account, you may create one via the EMA Account Management portal. For further information or guidance about how to create an EMA Account reference the guidance "Create an EMA Account".

Editorial changes to the product information in module 1.3

Formatting changes, correction of typographical errors and/or mistakes to the English Product Information (PI) or translations of the Product Information are considered editorial changes provided that the meaning of the text is not altered. These changes can be included within the scope of any upcoming variation impacting the product information.

Changes in the scientific content cannot be accepted as an editorial change. These changes should be classified under the scope of the relevant variation as per Variations Guidelines (e.g. Type II C.4). If no relevant scope is available, a variation type IB C.z may be appropriate.

Proposed changes that may require confirmation by the rapporteur or linguistic review will only be accepted by the Agency when submitted within the scope of an upcoming variation type IB or type II under chapter C which impacts the product information and where linguistic review is foreseen, if applicable.

Editorial changes should generally not be submitted as a separate variation and therefore no reference to a variation category is required. Should there be no upcoming variation to include the editorial changes, these could also be submitted as a stand-alone IB C.z if they affect the English SmPC. If they affect the PIL/labelling of all language versions an Art. 61(3) notification should be submitted. If other languages are affected but not the English version and in case no variation affecting the product information is upcoming, the MAHs are advised to contact the Agency to discuss how to handle these necessary changes.

The MAH should liaise with the Agency without delay if the mistake concerns an incorrect or missing important information (e.g. contra-indication or adverse event) in the EN or any of the other languages, that could affect the safe and effective use of the medicinal product and/or lead to a potential medication errors (e.g. wrong strength, wrong posology, wrong route of administration).

The editorial changes should be clearly identified in the application form as editorial changes. A brief description of the editorial changes should be provided in the precise scope of the application form. Furthermore, editorial changes should be presented in the **present/proposed table** or provided as a separate Annex. A statement confirming that the proposed editorial change(s) do(es) not change the content of the previously approved Product information should be provided.

Any changes proposed by the applicants as editorial will be carefully considered by the Agency at time of submission and may be subject to further assessment at the same time as the variation. Proposed editorial changes that cannot be accepted as such will be rejected. In case of doubt, applicants can contact the Agency in advance of the planned submission by raising a ticket via EMA Service Desk, selecting the tab “Business Services”, category “Human Regulatory”. The subcategory to be selected is “Post-authorisation - Human”, followed by the relevant sub-option: “Variation IA queries” or “Variation IB queries”.

If you do not have an EMA Account, you may create one via the EMA Account Management portal. For further information or guidance about how to create an EMA Account reference the guidance "Create an EMA Account".

References

- Commission Regulation (EC) No 1234/2008
- Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures (EC Variations Guidelines (2013))
- Guidelines on the details of the various categories of variation, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use, and on the documentation to be submitted pursuant to those procedures (EC Variations Guidelines (2025), applicable from 15 January 2026)