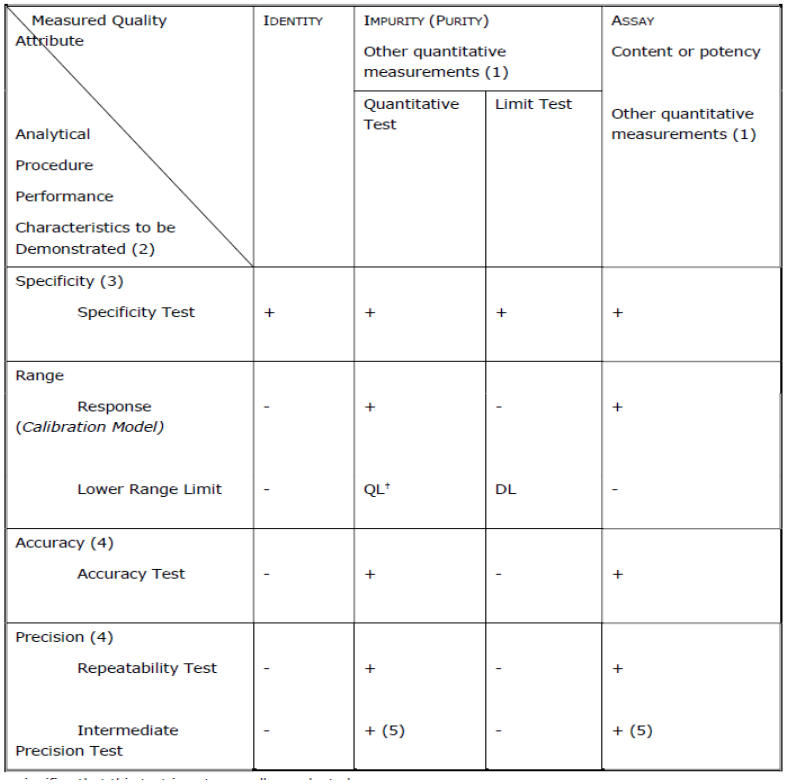
Type IA/IA$_{IN}$ submission checklist for nationally authorized medicinal products **Note:** For submissions of documentation for variations of medicinal products via CESP, the State Agency of Medicines of Latvia accepts documents without originally signed cover letters and application forms. It is not required to submit originals in paper format in parallel. More information is available on the CMDh web page: https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/procedural_guidance/eSubmissions/CMDh_006_2008_Rev_28_2025_06_clean_-_eSubmission_for_Variations_and_Renewals.pdf.	**Yes**	**N/A**
TECHNICAL SUBMISSION REQUIREMENTS		
Dossier is submitted in eCTD format and is technically valid (i.e. has passed eCTD technical validation criteria).		
COVER LETTER		
Present, dated and signed.		
Refers to the same medicinal product(s), marketing authorisation number(s) and procedure as listed in the application form.		
APPLICATION FORM		
Present, correct version, dated and signed by the contact person authorised for communication. A letter of authorisation is attached, if necessary.		
States the name and address of the MAH and of the contact person as previously notified to the Agency		
Variation procedure number		
Variation procedure number is valid and not used in any previous variation procedure. The principle for creating a variation procedure number for nationally authorized medicinal products in Latvia is the following: **MA No./variation procedure type/ chronological number**. If a grouped (two or more variation codes) variation procedure is submitted, the highest variation type is indicated in the procedure number and letter G is added: **MA No./variation procedure type/ chronological number/G**		
Type of application		
Type of application correctly identified by ticking the box(es) Type IA and/or Type IAIN, as applicable.		
It is indicated whether it is a single or a grouped submission.		
Products concerned by this application		
Marketing authorisation number(s) of all affected medicinal products are listed.		
They are the same as those indicated in the Cover letter.		
Type of changes		
All changes applied for are correctly classified according to the Guideline on the details of the various categories of variations (C/2025/5045).		

When two or more changes fall under the same category the scope number is indicated as many times as there are changes (e.g. scope Q.II.e.6.a.1 is repeated 'x' times for 'x' additional new pack sizes; scope E.4 is repeated for each manufacturing site affected by the change), except for E.5 when more than one manufacturer can be deleted with single E.5 variation (detailed present/proposed for each manufacturer and their functions is still necessary).		
The date of implementation is provided and variation has been submitted immediately following implementation (Type IA_{IN}) or as an annual update , part of a grouping, part of a super-grouping or applying exceptions to the annual update in justified cases (Type IA).		
No additional changes have been made to the marketing authorisation documentation beyond those already indicated in the section "Types of change(s)" and described in the sections "Scope and background" and "Present/proposed".		
Precise scope and background for change		
A scope contains precise description of <u>each</u> change applied for in the section "Types of Change(s)", even when two or more different changes fall under the same scope (e.g. scope Q.II.e.6.a.1 is indicated for each additional new pack size).		
Present and Proposed table (or attachment)		
Reflects all the changes applied for in the section 'Types of Change(s)'.		
Shows the precise present and proposed wording as in the relevant sections of the dossier and, if applicable, in the Product Information.		
Dossier section number(s) is/are indicated at the lowest possible level.		
Annexed documents (where appropriate)		
Relevant boxes are selected or left un-ticked as appropriate.		
Declaration of the Applicant		
Boxes relating to: 1. "There are no other changes than those identified in this application [...]". 2. "Where applicable, all conditions as set for the variation(s) concerned are fulfilled". 3. "For type IA notifications: the required documents as specified for the changes concerned have been submitted". are ticked.		
In case of variation(s) affecting more than one Marketing Authorisation, ensure that all Marketing Authorisations belong to the same marketing authorisation holder and that the following boxes: 1. [...] the MAs concerned belong to the same MAH (under 'Declaration of the Applicant') 2. [...] the main signatory confirms authorisation to sign on behalf of the designated contacts [...] (under 'Signature') are also ticked.		
SUPPORTING DOCUMENTATION		
Classification Guideline		

Relevant conditions and documentation, as specified in the Guideline (C/2025/5045), are ticked.		
Documentation listed in Annex IV of the Variations Regulation and in the Commission Classification Guideline		
Included and presented in accordance with the appropriate EU-CTD format headings and numbering.		
Is complete, updated, and correctly reflects the changes listed in the Present and Proposed table.		
Affected section(s) of the dossier correctly show(s) the change(s) applied for.		
Product information		
The Product Information (PI) includes only changes declared in the Present and Proposed table in the application form.		
The PI is provided in Word format (with tracked changes and clean version).		
The PI correctly reflects the scope of the variation and is based on the latest approved version.		
Q.III.1.a.2, Q.III.1.a.1		
QP declaration		
Section A and C contains information on all manufacturers mentioned in the corresponding CEP (including intermediate manufacturers, micronization sites) that will supply an active substance to finished product manufacturer.		
Section B contains information on all finished product manufacturing sites (EEA) that will use the active substance as starting materials and batch release sites (EEA).		
If non-authorised manufacturers are mentioned in QP declaration part A, B and/or C, it is clearly stated that they are not applicable for Latvian marketing authorisation documentation.		
3.2.S.2.1 Manufacturers		
If any of the active substance manufacturers indicated in the CEP is not used by the finished product manufacturer, it is clearly stated in the marketing authorisation documentation. The declarations are provided in module 1 from the CEP holder/active substance manufacturer and the finished product manufacturer that the active substance supplied to the finished product manufacturer is not manufactured by the particular active substance manufacturer (audit data of active substance manufacturing site not used is not necessary in part C of QP declaration).		
All manufacturers indicated in section 3.2.S.2.1 comply with the current marketing authorisation documentation including their names, addresses and functions.		
3.2.S.4.1 Specification		
In case there are additional parameters mentioned in CEP (new CEP from new or existing manufacturer and changes in these parameters/limits in case of CEP update) and there are more than one supplier of active substance, one combined specification of active substance is issued by finished product manufacturer for the control of active substance that can differs only in manufacturer-specific additional parameters such as residual solvents etc.		

Finished product manufacturer controls all parameters of active substance that are controlled by active substance manufacturer and are critical in the scope of pharmaceutical dosage form. This is applicable to CEP, Ph.Eur. and any additional parameter, otherwise justification of irrelevance of that parameters are provided. Note – reference to supplier's analytical results is considered as GMP issue and should not be part of documentation.		
3.2.S.4.4 Batch data		
Batch analysis data from active substance manufacturer are provided. Batch data from active substance manufacturer are mandatory for new CEP, and necessary in the case of CEP update if changes are related to manufacturing process, scale up/scale down of batch size, changes in manufacturing sites etc.		
Active substance batch analysis data from finished product manufacturer are provided.		
Other		
In case full sections 3.2.S.2.2-3.2.S.2.6 and/or 3.2.S.3.1 and/or 3.2.S.6 and/or 3.2.S.7 (packaging and re-test period is stated on the CEP) have been submitted in marketing authorisation documentation, declaration is provided that the content of sections corresponds to the information provided to EDQM for assessment.		
Information mentioned on the CEP corresponds to the one mentioned in the marketing authorisation documentation – the name and address of CEP holder, active substance, intermediate manufacturing and micronization site, packaging, re-test period (including storage conditions if mentioned), any additional parameter and acceptance criteria.		
The copies of corresponding CEP(s) and annexes are provided in documentation.		
Q.II.b.3.a		
Detailed present/proposed has been provided indicating all changes in manufacturing process not only versions of manufacturing process descriptions.		
All changes made in marketing authorisation documentation are mentioned in the application form and corresponds to the nature of the change of Type IA. Note - introduction of holding times if they exceed the ones mentioned in the corresponding guidelines, as well as introduction/change of bulk storage (conditions, equipment etc), changes in sub-batches etc. are not considered as type IA variations.		
There are no editorial changes made out of scope of the Q&A of EMA Classification of changes: questions and answers (Section 4).		
Information in sections 3.2.P.3.3, 3.2.P.3.4 and 3.2.P.3.5 complies regarding the manufacturing process, intermediates (their control), in-process control and intermediate/in-process acceptance criteria.		
Declaration that: ✓ stability studies have been started under ICH conditions (batch numbers are indicated) on at least one pilot/industrial scale batch ✓ assurance is given that these studies will be finalized		

✓ competent authority will be informed in case of out of specification or potentially out of specification results with proposed action has been provided.		
In cases when stability data are provided instead of stability declaration, the stability data complies with the shelf-life specification and assay results does not differ by more than 5% comparing with initial/release value, otherwise the reasonable explanation has been provided regarding the assay increase/decrease.		
Q.II.d.2.a		
Information regarding testing method conforms between sections 3.2.P.5.2 and 3.2.P.5.3 (adjustments that comply with Ph.Eur.2.2.46 – adjustment of chromatographic conditions - are acceptable).		
Comparative analytical results or validation data are provided.		
Typical performance characteristics and related validation tests for measured quality attributes as per ICH Q2(R2): 		
There are no editorial changes made out of scope of the Q&A of EMA Classification of changes: questions and answers (Section 4).		

Measured Quality Attribute / Analytical Procedure Performance Characteristics to be Demonstrated (2)	Identity	Impurity (Purity)		Assay
		Other quantitative measurements (1)		Content or potency
		Quantitative Test	Limit Test	Other quantitative measurements (1)
Specificity (3)				
Specificity Test	+	+	+	+
Range				
Response (*Calibration Model*)	-	+	-	+
Lower Range Limit	-	QL†	DL	-
Accuracy (4)				
Accuracy Test	-	+	-	+
Precision (4)				
Repeatability Test	-	+	-	+
Intermediate Precision Test	-	+ (5)	-	+ (5)

Method description is detailed enough that competent authority could repeat it. Information on preparation of test and standard solutions are provided, equipment and testing conditions are described. Procedure and system suitability parameters as well as calculation of results are provided.		
Q.III.2.b		
Variation concerns only active substances, reagents, intermediates, excipients, immediate packaging materials and active substance starting materials as per CMDH Q&A on variations (question 3.8)..		
If compliance to National Pharmacopoeia is proposed the copy of corresponding monograph with translation (if necessary) is provided.		
Batch data on two production batches are provided.		
All parameters in the specification/batch data comply with the requirements of corresponding monograph (parameters, acceptance criteria etc.)		
There are no other changes proposed in the specification except those to comply with the monograph. No deletion of other supplementary tests/parameters that were part of specification before variation. Note – if company proposes to delete one or more supplementary parameters from specification out of scope of Q.III.2.b additional variation should be added to support deletion and leading to grouped variation procedure application (type IA, IB or II).		
Specification does not contain any reference to results from supplier (note - reference to supplier's analytical results is considered as GMP issue and should not be part of documentation).		
Note. Change/addition of microbiological purity testing method needs validation data since method suitability should be demonstrated (even for Ph.Eur 2.6.12 and 2.6.13).		
Variations leading to changes in section 3.2.S.2.1 or 3.2.P.3.1 (Q.III.1.a.2, E.5, Q.II.b.1.a, E.4.b + other)		
Besides the proposed changes in section 3.2.S.2.1/3.2.P.3.1, all other manufacturers mentioned in this section comply with the current marketing authorization documentation (including names, addresses, functions).		
QP declaration is not necessary in the case of administrative changes.		
Present/proposed of manufacturers and their functions are clearly stated in the application form.		
The address and name of manufactures comply with the one mentioned in the other sections of documentation and GMP/MIA certificate.		
Deletion of non-significant specification parameter (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, Q.II.e.4.c).		
The specification parameter deleted is not an identification (except colorant), impurity, assay, critical physical parameter etc. Only truly obsolete tests that are no longer part of normal specifications for newer products, but have remained for historical reasons in older products are deleted. See EMA Questions and answers – what is considered to be non-significant in-process control or specification parameter (question 7.2.5).		

The variation is not related to deletion of quality parameters from shelf-life specification. Note - since the quality of finished product already marketed is controlled according to shelf-life specification, all parameters present in release specification should be part of shelf-life specification as well, however footnote can be added stating that specific parameter will not be tested in shelf life but will comply if tested.		
Other		
If other modules not relevant within the scope of proposed variation has been submitted as supporting documentation for some reasons, declaration is provided that the content of those modules complies with the marketing authorization documentation in force.		
There are no editorial changes made out of scope of the Q&A of EMA Classification of changes: questions and answers (Section 4).		