

<p style="text-align: center;">EXAMPLES FOR ACCEPTABLE AND NOT ACCEPTABLE GROUPINGS FOR MRP/DCP PRODUCTS</p>

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For future variation applications comparable to those listed below as acceptable groupings applicants do not have to contact the RMS for acceptance as these grouped applications are already accepted by all EU member states.

1. ACCEPTABLE GROUPINGS

- All minor notifications of type IA and type IA_{IN} may be grouped in one application without any relation to each other, if the group includes only type IA and type IA_{IN}.
- Only notifications of type IA or IA_{IN} may be grouped for more than one MA.
- The update of Module 1 incl. User Test, Braille, Environmental Risk Assessment, DDPS, RMP, QPs declaration etc., e.g. in preparation of a Repeat Use MRP may be submitted as one single application according to type II. The change may be introduced under classification category C.I.z – Update of Module 1 in preparation of a RUP.
- After a transfer of the MA in one or more member states to a new MAH – which itself is an independent purely national application – all other changes related to that transfer, e.g. change in product name in that member state, new DDPS for the new MAH etc. may be grouped in one application according to the highest variation type for the single changes.
- In connection with the introduction of a new manufacturing site other changes, e.g. changes in batch size, changes in batch releaser and controller, changes in the manufacturing process of the finished product including in-process controls etc. may be submitted in one application as a grouped variation according to the highest variation type for the single changes. All these changes are regarded as belonging to the same project as described in Annex III of the Regulation “All variations in the group relate to a project intended to improve the manufacturing process and the quality of the medicinal product concerned or its active substance”.

- Addition of more than one pack size, where at least one of the proposed pack sizes is outside the range of currently approved pack sizes.
- The update of an Active Substance Master File and any consequential changes to the active substance and if relevant finished product specifications (see also Q/A 3.4 <http://www.hma.eu/96.html>).
- The update of the finished product specification (limits and analytical procedures)
- The update of the method of manufacture of the active substance (*supported by ASMF or as part full dossier*) and any consequential changes to the active substance and if relevant finished product specifications.
- Changes in the manufacturing process of the finished product including batch size, in-process controls etc. may be submitted in one application as a grouped variation.
- Changes to the composition of the finished product and if relevant any related changes to the method of manufacture, finished product specification (limits and analytical procedures), shelf life and storage conditions and product information (SmPC, label and PL).
- Changes to the primary packaging of the finished product in relation to qualitative/quantitative composition, dimensions, if relevant supplier and pack sizes, if related.
- Changes to the shelf life and storage conditions of the finished product.
- Changes to the re-test period and storage conditions of the active substance.
- Any updates to the pharmacovigilance system.
- Updates in line with the agreed Core Safety Profile (C.I.3.a or b) and brand leader/innovator product (C.I.2.a or b).
- Changes following assessment of a given PSUR (C.I.3.a or b). (Regulation Annex III – example 11).
- Updates in line with PhVWP/CMDh agreed wordings relating to a class (Regulation Annex III – case 10)/specific active substance (C.I.3.a or b).
- Updates in line with the Company Core Safety Information, provided the changes are related (C.I.4).
- Updates in line with the brand leader/innovator (C.I.2.a or b) and NCA recommendations following the review of a PSUR (C.I.3.a or b).

- Updates in line with Paediatric Worksharing (C.I.3.a) and PhVWP wording (C.I.3.a or b) (Q&A 4.13 on variations published on CMDh website).
- Updates in line with the Company Core Safety Information (C.I.4) and related changes, which are independent of the CCSI, following a further review of current literature e.g. National Formulary in relation to safety information.
- Updates in line with the minimum clinical particulars for a product/class, recommendations made during assessment of a renewal (as type IB under C.I.z).
- Updates in line with the brand leader/innovator/reference product and the excipients guideline (which impact the content of the dossier) (grouped application C.I.2 (a or b) and C.I.z (Type IB/II), see also Q/A 3.11 <http://www.hma.eu/96.html>).¹
- Update in line with agreed Core Safety Profile, excipients guideline and QRD template (which impact the content of the dossier) (grouped application according to C.I.3 (a or b) and C.I.z (type IB or type II)).¹
- Updates in line with different guidelines affecting a product and impacting the content of the dossier e.g. SmPC, excipient and QRD template guidelines and any published agreed core SmPCs (C.I.z and C.I.3 as type IB or type II).¹

2. NOT ACCEPTABLE GROUPINGS

- Introduction of a new API manufacturer with a new ASMF may not be grouped with other unrelated quality changes concerning the active substance or the finished product but have to be submitted as separate applications.
- Variations for several minor changes of type IA and type IB though related to each other may not be grouped for more than one MA. In these cases a worksharing procedure should be followed.
- Changes to module 3 may not be grouped with a change in the product name if there is no relation between these changes and a common assessment is not justified. In exceptional cases where the changes to module 3 and the change in the product name are related with each other, e.g. changes in flavour, a grouping would be acceptable. However, the applicant should liaise with the RMS before submission.
- The combination of more than one acceptable grouping if the groups are not directly related with each other.

¹ Purely editorial changes can automatically be included as part of another variation to the same part of the dossier, provided that they do not change the actual content of the dossier and therefore the meaning of any text. This also includes editorial changes to the SmPC (see also Q/A 3.16).

- The inclusion of unrelated Quality, Non-Clinical and Clinical changes.
- The inclusion of additional non-related changes to an already agreed grouping.
- The inclusion of a new active substance manufacturer as part of a variation to introduce a new finished product manufacturer.
- The inclusion of changes to the active substance and finished product, unless they are totally related.
- The inclusion of a safety related change that would delay its implementation.
- Addition or change of several active substance manufacturers that do not fully meet the Type IA conditions and documentation requirements.