EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Evaluation Division

European Medicines Agency post-authorisation procedural advice for users of the centralised procedure
Type IA Variations

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

1. Type IA Variations

1.1. When shall I submit my Type IA/IA$_{IN}$ variation(s)? ~~Rev. Dec 2016~~

Commission Regulation (EC) No 1234/2008, as amended, ('the Variations Regulation') and the Commission 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 and on the documentation to be submitted pursuant to those procedures ('the Variations Guidelines') set-out a list of changes to be considered as Type IA variations. Such minor variations have only a minimal impact or no impact at all, on the quality, safety or efficacy of the medicinal product, and do not require prior approval before implementation ("Do and Tell" procedure). The Classification Guideline clarifies the conditions which must be met in order for a change to be considered a Type IA variation.

Such minor variations are classified in two subcategories, which impact on their submission:

Type IA variations requiring immediate notification ('IA$_{IN}$')

The Classification Guideline specifies which Type IA variations must be notified (submitted) **immediately** to the National Competent Authorities/European Medicines Agency ('the Agency') following implementation, in order to ensure the continuous supervision of the medicinal product.

Type IA variations NOT requiring immediate notification ('IA')

Type IA variations implemented in 2024 and not submitted to the Agency by 31 December 2025:

Type IA ~~Variations~~variations that do not require immediate notification may be submitted by the MAH ~~within~~ no later than 12 months after implementation.~~, or may be submitted earlier should this facilitate dossier lifecycle maintenance or when necessary, to ensure that the latest product information is reflected in certificates of pharmaceutical products, for example.~~

The 12 months deadline to notify minor variations of Type IA allows for an 'annual reporting' for these variations, where a MAH submits several minor variations of Type IA which have been implemented during the previous twelve months.

Type IA variations implemented from 1 January 2025 (inclusive):

Type IA variations which do not require immediate notification should be collected and submitted by the marketing authorisation holder (MAH) as a 'Type IA annual update', within 12 months after the oldest variation IA implementation date. The submission should be done as a single submission covering all minor variations of Type IA implemented during the period. The application should be submitted no earlier than 9 months and no later than 12 months after the first implementation date of the IAs included in the 'type IA annual update'.

As an example, if an applicant has three Type IA variations to the same marketing authorisation implemented on 1 February 2025, 7 March 2025 and 21 April 2025 respectively, an annual ~~report~~update of Type IA variation grouping the three variations would be expected between 1st November 2025 (9 months after 1st February 2025) and 1st February 2026 (12 months after 1st of February 2025), since the first implementation date of the variations included in the grouping is 1st of February 2025, unless one of the exceptions below applies.

A submission outside the Type IA annual update is possible in the following cases:

- as part of an acceptable grouping together with variations of other types (IAIN, IB or II).~~,~~
- as part of a super-grouping (one or more Type IA variations for multiple marketing authorisations from the same MAH).
- when a single T~~t~~ype IA variation in an annual update was refused and the company needs to resubmit to comply with the 12 months reporting period.
    - exceptionally, an individual submission immediately after implementation when duly justified. This encompasses the following cases listed below:
    - When the Type IA variation is needed to mitigate a shortage, and regulatory flexibilities have been agreed with the MSSG (Executive Steering Group on Shortages and Safety of Medicinal Products).
    - When the Agency deems the immediate update of the marketing authorisation dossier in relation to a public health concern necessary (e.g. an emerging or declared public health emergency).
    - When the IA variation is needed to update the marketing authorisation dossier prior to a routine site inspection or a MAH transfer.
    - When a third country is requesting proof of acceptance in EU (e.g. by the means of a Certificate of Pharmaceutical Product (CPP) or EU authorisation letter) for a -particular change intended to mitigate a shortage or a critical need in the third country or the medicinal product is part of an international reliance program that has been accepted by the Agency.

The Type IA annual update must fulfil the conditions for grouping or super-grouping, if it concerns more than one Type IA variation and/or more than one marketing authorisation:

- all Type IA variations affect the same marketing authorization approved via centralised procedure, or
- the Type IA variation(s) affect several marketing authorisations approved via centralised procedure owned by the same holder, provided that the variation(s) notified is/are identical for all marketing authorisations concerned ("super-grouping").

Please note that currently it is not operationally possible to have super-grouping of Type IA variations including simultaneously marketing authorisations approved via the centralised procedure and non-centralised procedure. Additional cases taking into account the experience acquired may be identified in the future and appropriate operational guidance will be provided on Agency and CMDh websites accordingly.

In line with the objective of a single review and to ensure its effectiveness, it is expected that the individual supporting data for the variation(s) applying to the several marketing authorisations are identical

It is also not acceptable to combine a grouping with a super-grouping in the same application (i.e. having variations not applicable to all marketing authorisations concerned). Separate submissions should be done in such case.

Most ~~of these~~ Type IA variations do not impact ~~on~~ the product information. However, in case of an upcoming submission of a variation, extension or other regulatory procedure which will affect the product information, the MAH should also include any Type IA change(s) affecting the product

information as part of a grouping application, in order to keep the product information up-to-date and to facilitate document management.

~~There are no recommended submission dates for Type IA. However, MAHs are encouraged to avoid submitting Type IA notifications shortly before or during the Agency holiday periods (e.g. end July and Christmas).~~

Meaning of "implementation" for Type IA variations

For quality changes, implementation is when the Company makes the change in its own Quality System.

This interpretation allows companies to manufacture conformance batches and generate any needed stability studies to support a Type IA_{IN} variation before making an immediate notification~~[1]~~ because the change will not be made in their own Quality System until these data are available.

For product information, it is when the Company internally approves the revised product information. The revised product information will then be used in the next packaging run.

~~[1] For example the type IAIN for addition, deletion or replacement of components in the flavouring or colouring system requires stability data on at least two pilot scale or industrial scale batches.~~