EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

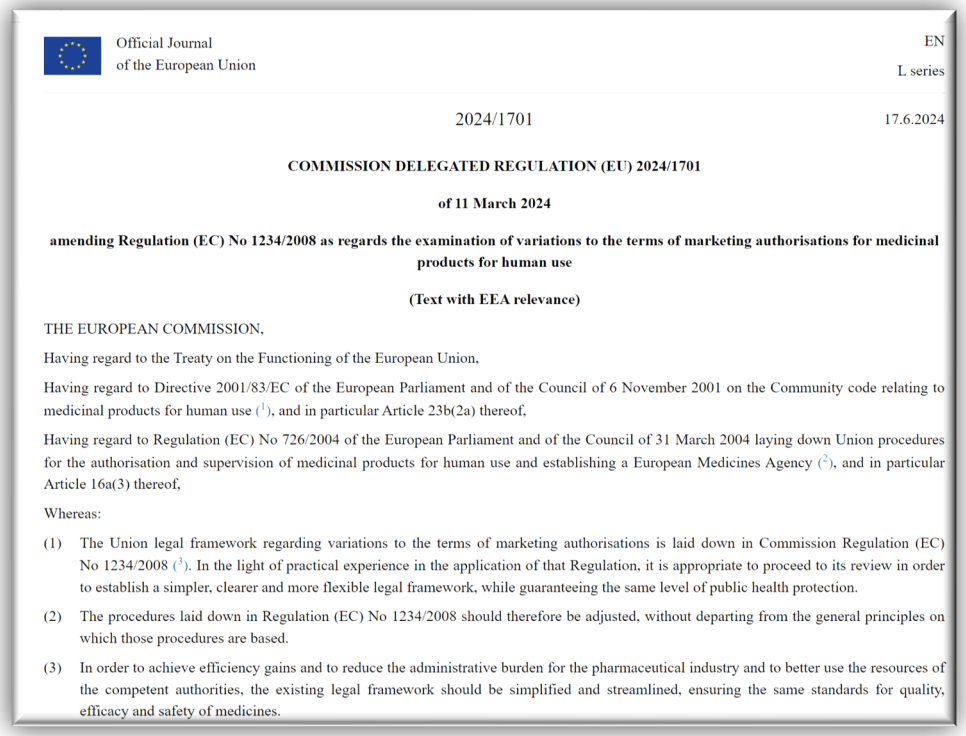
Amended Variation Regulation (transitional measures)

Regulation (EU) 2024/1701 of 11 March 2024

Presented by Thomas Girard (Regulatory Affairs Office) on 22 November 2024

Variations Regulation - version history since 2008

- Regulation(EC) No 1234/2008 of 24 November 2008
- Regulation (EU) No 712/2012 of 3 August 2012
- Regulation (EU) 2021/756 of 24 March 2021 (COVID-19 related revision)
- **Regulation (EU) 2024/1701 of 11 March 2024** (applicable from 1 January 2025)



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COMMISSION DELEGATED REGULATION (EU) 2024/1701

of 11 March 2024

amending Regulation (EC) No 1234/2008 as regards the examination of variations to the terms of marketing authorisations for medicinal products for human use

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use ([1]), and in particular Article 23b(2a) thereof,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency ([2]), and in particular Article 16a(3) thereof,

Whereas:

(1) The Union legal framework regarding variations to the terms of marketing authorisations is laid down in Commission Regulation (EC) No 1234/2008 ([3]). In the light of practical experience in the application of that Regulation, it is appropriate to proceed to its review in order to establish a simpler, clearer and more flexible legal framework, while guaranteeing the same level of public health protection.

(2) The procedures laid down in Regulation (EC) No 1234/2008 should therefore be adjusted, without departing from the general principles on which those procedures are based.

(3) In order to achieve efficiency gains and to reduce the administrative burden for the pharmaceutical industry and to better use the resources of the competent authorities, the existing legal framework should be simplified and streamlined, ensuring the same standards for quality, efficacy and safety of medicines.

1 Amended Variation Regulation

Implementation (overview)

Amended Variations Regulation

From 1st January 2025

Procedural aspects implemented from 1 January 2025:

- e.g. annual update of Type IA variations
- super-grouping
- mandatory/voluntarily WS procedure
- Article 5 recommendations
- recommendations for annual update of the Variations Guidelines

Details on the implementation Guidance for stakeholders published on a dedicated EMA and CMDh webpage on 31 October

Some measures dependent on the revision of the Variations Guidelines (ongoing).To be implemented after Q2 2025:

- e.g. downgrade of variations for Biological products
- new/updated scopes
- revise documentation and classification requirements
- additional regulatory tools

Details on the implementation to be provided in EC Guidelines on variations and EMA/CMDh guidance

After Q2 2025 (TBC)

Comments/questions - Type IA annual update

Reference date for annual update

- Cycle of the annual update will be determined by the first implementation of the type IA in the period
- Several exemptions foreseen in the revised Variation Regulation and accepted by the Agency are listed in the guidance
- No annual update required if no change implemented in the past 12 months (and not reported already as part of supergrouping/grouping)

Comments/questions - Type IA annual update

3-month submission window (between 9 and 12 months) in the guidance introduces complexity/proposal to remove reference to 3-month submission window

- The amended Variation Regulation provides that Type IA variation(s) should be notified *within 12 months* following their implementation as an *annual update*
- Fixed date was considered too rigid -> flexibility of an optional 3-month submission window was introduced for planning flexibility

Comments/questions - Type IA annual update

Exceptions to the type IA annual update

- EMA guidance lists the exception to the annual update of Type IA variations
- Specific exception for third countries relying on the proof of acceptance in EU under certain circumstances (shortages, critical need or part of an international reliance program)
- Updating the list in the light of experience acquired will be considered in the future

Comments/questions - Type IA annual update

Risk of having to 'un-implement' a change/Lack of predictability

- Type IA variations are minor in nature and are expected to be accepted if the requirements are met. Very low level of rejection
- Type IA variations rejected can be submitted immediately outside the annual update
- Type IA rejected can also be rectified within the 9-12 months period

Comments/questions - Type IA annual update

Transitional period

- Annual update will not be retroactive -> First annual updates are expected no earlier than from 1 September 2025 (for variations implemented on 1 January 2025) if use of the 9-months period

- *Clarification: "Type IA variations implemented in 2024 and not submitted by 31 December 2025": could this be simplified to "Type IA variations implemented, but not submitted, before 1 January 2025"?*
- *if only one variation in 12 months for a product, then still needs to be submitted according to the annual update (but may or may not be grouped with other variations)*

- Suggested wording noted
- Type IA variations should be submitted in the annual update (as a single notification or group, as appropriate), unless an exemptions applies and is used by the MAH

Comments/questions - Mandatory worksharing

There will be situations in which it is not possible, appropriate or necessary for the same change to be implemented for all affected authorisations at the same time

- Provided that the same Type IB/II variation(s) is/are not applicable to different MAs, the WS procedure would not be applicable

*The same variation or group of variations is made to several (not "all") marketing authorisations and is to be **implemented at the same timeframe** for the concerned authorisations*

- The mandatory WS procedure is applicable when the same Type IB/II variation(s) is/are applicable to different MAs from the same MAH
- Variation(s)/Group(s) *implemented at the same timeframe* is not a criterion foreseen in the amended Variations Regulation to exempt the mandatory worksharing procedure

What is meant by "identical changes" to be subject to worksharing?

- Absence or limited need for product specific assessment
- MAH are invited to liaise with the Agency in case of doubt

Transitional Period – classification of variation

- During the transition period (from 1 January 2025 and until the updated Variation Guidelines become applicable) MAHs should continue to rely on the current classification part of the Variations Guidelines and on specific procedural guidance that is available on the EMA and CMDh websites

- Date of application of the updated Variations Guidelines will be published in the OJUE