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The Variations Regulation (EC) No 1234/2008:
The legal framework after the revision

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Outline

- Definition of variation
- The new Variations Regulation 1234/2008
- The revision of the variation framework
- Main points of improvement
- Summary

What is a variation?

An amendment to the contents of the marketing authorisation dossier

Including the particulars and documents referred to in:

- veterinary use: Articles 12(3), 13, 13a, 13b, 13c, 13d and 14 Directive 2001/82/EC and Annex I thereto as well as Article 31(2) Regulation 726/2004/EC

- human use: Articles 8(3), 9, 10, 10a, 10b, 10c and 11 Directive 2001/83/EC and Annex I thereto as well as Article 6(2) Regulation 726/2004/EC, point (a) of Articles 7(1) and 34(1) Regulation 1901/2006/EC and Articles 7 and 14(1) of Regulation 1394/2007/EC

The new Variations Regulation

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

- applicable as of 1 January 2010;
- repeals Regulations 1084/2003/EC and 1085/2003/EC;
- applies to MRP, DCP and CAPs and authorisations granted following a CHMP/CVMP full harmonisation referral;
- does not apply to homeopathic and traditional medicinal products (no MA but subject to simplified registration procedures).

Objectives of the revised legal framework

- Introduce a simpler, clearer and more flexible legal framework
- Reduce administrative burden
- Adapt to ICH concepts
- Further harmonise handling of variations in the EU

... while maintaining the same level of public and animal health protection.

Main points of improvement

1) Harmonisation: NCA and central level
2) Simpler, clearer and more flexible: Classification
3) More flexible: Do-and-tell Type I As
4) Simpler: Annual reporting
5) Simpler and more flexible: Grouping and Worksharing

Harmonisation: NCA and central level

- **Before: two Regulations** differentiating between MRP + DCP products and centrally authorised products (CAPs)
- the majority of variations fell outside the scope of the Community rules and were resolved nationally leading to:
    - Lack of harmonisation
    - Big administrative burdens for industry and national
- Objective: one common set of rules for MRP, DCP and CAPs
- **Now: one Regulation** applying the same rules: Chapter II for MRP/DCP products and Chapter III for CAPs

Simpler, clearer and more flexible: Classification

Variations are classified according to the level of risk to public and animal health and the impact on the quality, safety and efficacy of the medicinal product concerned into the following categories: Minor variations Type IA; Minor variations Type IB; Minor variation Type II; Extension of marketing authorisation.

Before: Variations conditions listed in Annex of the Regulation

Now: - The "Commission guideline on the details of the various categories of variations" ('the **Classification Guideline**') provides details for the classification of variations into the categories.

- possibility of **scientific recommendation on classification** under Art. 5(1) of the Regulation via the coordination groups (CMDh/CMDv) or the EMA

More flexible: Do and tell procedure for Type IA variations

Type 1A = a variation which has only a minimal impact, or no impact at all, on the quality, safety or efficacy of the medicinal product concerned.

Before: Tell, wait and then do procedure for Type 1A -> validation of a notification within 14 days

Now: Do and tell procedure -> these variations do not need prior approval

Within Type 1A distinction:

- Type 1 A: Agency notified within 12 months following implementation

- Type 1 A IN: Agency notified immediately after implementation (applies to changes for which continuous supervision is required)

Simpler: Annual reporting

The new variations regulation introduces the possibility of annual reporting for Type I A variations not requiring immediate notification:

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.

Simpler: Type I B by default

Before: Type II by default (Type II= a variation which cannot be deemed to be a minor variation nor an extension)

Now: Type I B by default

When the Agency is of the opinion that the proposed variation may have a significant impact on the quality, safety or efficacy of the medicinal product, the MAH will be notified that the applied change cannot be handled as a Type IB and that the variation will have to be reclassified as a Type II variation.

MAH will be requested to revise and supplement its variation application so that the requirements for a Type II variation application are met.

Simpler and more flexible: Grouping and Worksharing

The new Regulation introduces the possibility to combine the notification of several types of notifications through

Grouping and Worksharing

Grouping:

Article 7(2)(a) :group several Type IA/ IAIN variations affecting one or several products of the same MAH under a single notification to the same relevant authority, or to group them with other types of variations.

Article 7.2(b) : group several types of variations affecting one medicinal product, under a single notification/application.

Simpler and more flexible: Grouping and Worksharing

Worksharing:

Article 20 sets-out the possibility for a MAH to submit the same Type IB or Type II variation, or the same group of variations affecting more than one marketing authorisation from the same MAH in one application.

These possibilities to group variations reduce the burden for administrators and industry.

Summary

The revision of the variations framework clarified, simplified and increased the flexibility of the variations procedures and reduced the burden for administrative bodies and the industry through:

- Harmonisation
- Classification Guideline
- Do and Tell Type IAs
- Grouping
- Worksharing

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