EU Variations Regulations

Consequences for the pharmaceutical industry – Will the changes make the EU a more competitive market place?

Dr. R. Faust / 10th DGRA Annual Congress 2008

Agenda

- Why is it important to change the existing situation?
- Type IA
- Type IB
- Guideline on Variations
- Grouping of Variations
- Worksharing
- Coordination Group & Referrals
- Summary

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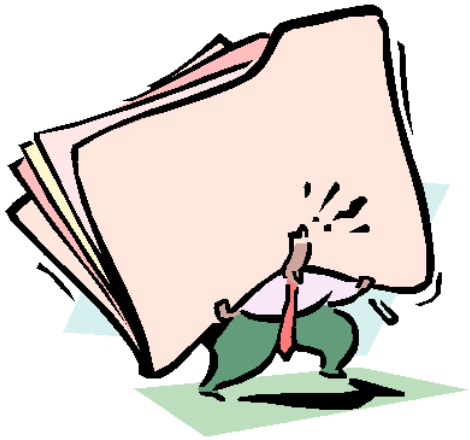
Why is it important to change the existing situation? (1)

- Current system has become more and more inefficient due to the increasing numbers of variations
  - A medium sized company can already easily have 2000 – 4000 variations/year



- The currently used variation system is a time and resource consuming process with no harmonised rules
- More than 80% of the procedures are still national variations
- Necessity obvious to simplify the existing variation system e. g. with regard to purely administrative changes

Why is it important to change the existing situation? (2)

- Type II variation “by default” leaves no room for regulatory judgement and tends to create high burden without any benefit for the safety of patients
- Companies should be able to implement a variation at the same time in all Member States
- Same rules should apply for variations of products that were nationally approved before 1995 and subsequently via MRP in other EU countries

Why is it important to change the existing situation? (3)

- An improved regulatory framework is needed with the opportunity to make variations simpler, clearer and more flexible
- This will help to reduce resources and improve consisting planning on both sides
- Focus might even be increased on the patients safety because the authorities manager may allocate more staff to scientific work rather than to administrative tasks

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Type IA – From *Tell&Do* to *Do&Tell*

- Minor Variations to be reported within 12 months (via annual reporting)

or

- Minor Variations requiring an immediate notification

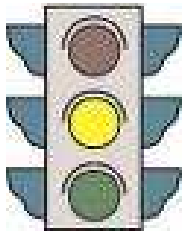
- Changes could be implemented any time before completion of the variation procedure

Type IA – Reportable within 12 months (1)

- Type IA variations to be reported within 12 months

  - Variations would not require any prior approval
  - It is supported that in case of no variations an annual report has not to be submitted

Type IA – Reportable within 12 months (2)



Could be rejected by the authorities post-hoc

Annual report to be kept simple and standardised

The respective template needs to be compatible with eCTD requirements

The planned guidelines on the classification of the variations will play a major role

Type IA – With immediate notification

- Type IA variations requiring immediate notification

The variation does not require any prior approval

From acknowledgement within 2 weeks to active closure within 1 months

Can be rejected post-hoc

Type IA – Rejection risks…

- Article 21 „Closure of Procedure“ allows rejection of a variation

- To achieve a real benefit
  - Predictable situation needed
  - If inevitable, rejection be allowed only in case of defined situations such as required documents missing etc.

Type IA – Summary
Redefinition of Type IA variations

Change is expected

To significantly simplify the current system

To improve rescource needs and the change management on both sides

Discussions should start early

On the guidelines for the variation classification

On the reasons allowing to reject a Type IA variation

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Type IB – Change from *Type II* to *Type IB* by default (1)

- ✓ From Type II by default to Type IB by default
- ✓ Chance to reduce administrative burden on both ends
- ✓ Classification of Type II changes via guideline is fully supported

Type IB – Change from *Type II* to *Type IB* by default (2)

It would be desirable

That in case of questions, e. g. special situations; not all criteria/conditions of a Type IB met,

- Classification could be discussed together with Competent Authority / RMS / EMEA
- Possibility to keep Type IB status based on risk assessment

Type IB – Change from *Type II* to *Type IB* by default (3)

To achieve a real benefit

Clear timelines are needed

- For seeking advice on classification
- For validation period
- For variation procedure

Type IB – Safeguard clause (1)

Clear rules needed for the upgrade to Type II (safeguard clause), e. g.

- Only in cases of serious potential risk to public health
- Reasons to be clearly expressed by the Competent Authority/Agency
- Introduce fixed timelines for the decision to upgrade to Type II (e. g. not more than 14 calendar days)

Type IB – Safeguard clause (2)

Clear rules needed on the documentation needs after an upgrade to Type II, e.g.

- No additional quality overall summary, non-clinical or clinical overview
- No reformatting/amending of the existing documentation
- No resubmission of the variation

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Guideline on variations (1)

The publication of an explanatory guideline is fully supported to address

- The classification of variations (Type IA and Type II)
- Which is ideally comes into force in parallel to the regulation
- Which is regularly reviewed and updated
- Taking into account the classification on variation needs previously unforeseen

Guideline on variations (2)

Discussion on the guideline should start soon to

- Fully evaluate the simplification opportunities
- Add new changes focussing purely on administrative changes, e. g.
  - changes to a supplier’s address
  - the name of the QPPV if she/he marries

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Grouping of Variations (1)

- ✓ The option to group variations is clearly supported
  - Same variations to multiple marketing authorizations could be submitted as one
  - Several variations to one or all related marketing authorizations could be submitted at the same time

Grouping of Variations (2)

- ✓ Will help to reduce the duplication of information and thus resource needs at company and Competent Authority
- ✓ Will improve the change management of multiple changes e. g. to a manufacturing process
  - Single review for multiple variations
  - Single date of approval
- ✓ Will contribute to further improved regulatory compliance

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Worksharing

Meaning a single evaluation for

- One medicinal product authorised in several Member States
- One change relevant for different medicinal products

✓ Expected to eliminate / minimise the multiplication of evaluations for the same change by different Competent Authorities

Potential pitfalls with worksharing

To achieve a real benefit

The MAH should have the option to request a worksharing procedure

The same evaluation timelines should apply as for the established variations categories

The worksharing procedure should adhere to the same timelines for the approval / implementation of a variation

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Coordination Group & Referrals

In case of disagreement the variation procedure would be referred to the Coordination Group (MRP/DCP approved products, art. 16)

- Would give a similar situation to DCP/MRP referrals

It would be desirable if

Referrals would only be applicable for Type II variations

- Would avoid possible delays for Type IA and Type IB variations caused by referrals

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Summary

- An improved framework for variations is needed
  - Which is clear, simple and flexible
  - Has harmonised rules and
  - Clear timelines
- The proposed changes are fully supported and will be a significant step forward to improve the current system – if implemented correctly.
- There are still some open points which warrant further discussion
- Clear wording and definitions in implementation guidelines will be essential to achieve the intended objectives!

Thank you!