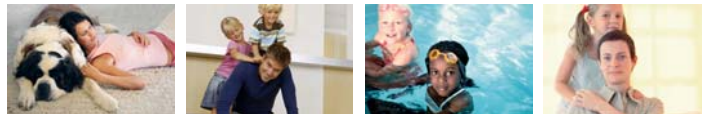




## Variations Update

### Industrial Perspective – First Experiences



DGRA Annual Congress, June 2010

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## Overview

- **What did we expect?**
- **Where are we today?**
- **What did we experience?**
- **Where do we (hope to) go next?**

## What did we expect?

### MORE...

- ... **Clarity** (definitions and examples, clear timelines)
- ... **Simplification** (e.g. type IB by default, grouping options)
- ... **Harmonization** (e.g. worksharing options)
- ... **Flexibility** (e.g. annual reports)

### LESS...

- ... **Redundancies** (during individual country assessment)
- ... **Processes** (to be maintained for different procedure types)
- ... **Workload** (for both, industry and agency)

## Where are we today?

- **So far, only limited number of submissions acc. to new rules**
  - Many variations were still submitted end 2009 ...
  - Companies like to wait for others to serve as guinea pig ...
- **First submissions according to new rules are still ongoing**
- **However, first examples are available showing**
  - Diversity of opinions and interpretation ...
  - Pitfalls and gaps ...
  - Areas of hope for the future ...

## What did we experience? Clarity

### Example: Type IA Variation Implementation Date



- Agency did not accept a future implementation date
  - Rationale:  
Type IA would mean „do and tell“, not the other way round
- However, future dates cannot be avoided by a global company:
  - Change in production is affecting all countries at the same time
  - New EU regulation has not yet been implemented in all EU countries for national MAs
  - In those countries change cannot be implemented first and then submitted afterwards
- Agency opinion not in line with explanatory note for the application form
- Turned out to be individual case manager opinion, could be settled

## What did we experience? Simplification

### Example: Grouping of Type IA Variations



- Company specific grouping of Type IA variations for change of QPPV was accepted (instead of product specific)

### Example: Type II Variation: New Indication



- So far, this was handled as single variation.
- Now, RMS requested during validation a split into a number of individual variations for all dossier components that changed e.g. Environmental Risk Assessment (ERA), Risk Management Plan (RMP)
- Following intense discussion, a compromise was achieved (one type II variation, but detailed description of all individual changes in application form and resubmission during validation phase)
- This affected 8 MAs in all EU Member States, took significant resources and delayed the start of the procedure by two weeks
- A few weeks before, a different RMS did not request such additional burden for a comparable variation

## What did we experience? Harmonization

- **Worksharing**

- First guinea pigs are running, which were planned in close co-operation with key agencies involved
  - Combination of MAs with different RMS was possible
  - Pragmatic approach so far by designated WS-RMS
  - Guidance for handling of eCTD-submission was given
- **Cave:** diverging implementation of new rules into national law is a potential read-block for harmonization!
  - Not critical for CMC-variations (only notification in Germany), but a major issue and potential source for disharmonisation regarding labeling

## What did we experience? Harmonization

### Example: Worksharing for Labeling Change

- Planned changes affected > 20 products all over EU including national MAs as well as MRP/DCP
  - About 50% of the affected products were out of scope of current worksharing options due to lacking national implementation of new rules
  - Pitfalls identified:
    - National agency assessors may be different for EU worksharing and national variations
    - Member States may try to enforce national perspective not accepted on EU level at least for national MAs
- ⇒ Both may end up in different national wording as agreed on EU level...
- National review timelines different from EU ⇒ esp. relevant for Germany

EU	2 months preparation	ca. 9 months review	referral?
Worksharing	<hr/>		
DE	Approval or rejection after 3 months		

## What did we experience? Flexibility



- **Annual Reports**
  - Promising, but too early to judge...
  - No possibility to benefit from this for national MAs
- **Worksharing and Grouping**
  - Promising, but too early to judge...
  - No possibility to benefit from this for national MAs
- **Prerequisites:**
  - Flexible planning by MA-Holder will only work if agencies deliver to promises and keep agreed procedure timelines
  - High-skilled project management on both sides must keep oversight on all running / overlapping procedures

## Where do we go next?

### Today...

- ... we must establish excellent planning and tracking tools within companies and agencies
- ... we should try as much worksharing and grouping to gain more experience
- ... we need agreement on pragmatic approaches

### Tomorrow (= in 2012?)...

- ... we must expand the established excellent planning and tracking tools within companies and agencies to the huge number of national MAs
- ... we will face significant changes in internal workflows and see an increase in resource needs (for both, CMC and labeling changes on national level)
- ... we will be able to benefit from worksharing, grouping and annual reports also for national MAs

**Are you ready?**