



AGES

Österreichische Agentur für Gesundheit
und Ernährungssicherheit GmbH

*Health. Nutrition. Safety.
Our Concern.*

Information bezüglich der EU-Verordnung EG 1234/2008 (Variation Regulation)

AGES Gespräch
31. März 2009

Dr. Christa Wirthumer-Hoche
AGES PharmMed, Wien

Review project launched in 2006 „Better Regulation“

Simplification of the regulatory environment for the benefit of European Businesses and Citizens

Objectives:

- Clearer, Simpler, more flexible
- Reduce administrative burden
- Adapt to ICH concepts
- Further harmonise

To guarantee the same level of public and animal health protection



Erstellt: Christa Wirthumer-Hoche

Wo finde ich die Information?

EUROPEAN COMMISSION
Enterprise and Industry

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Important legal notice

Pharmaceuticals

Better Regulation

Review of the pharmaceutical legislation

Regulation on Maximum Residue Limits

Review of the Variations Regulations



Better Regulation

The regulatory framework in which businesses operate is a key factor of their competitiveness, growth and employment performance. Therefore, a key objective of the European Union's Enterprise policy is to ensure that the regulatory environment is simple and of high quality. This is why "better regulation" is a centrepiece of the European Commission's "Partnership for Growth and Jobs" - the renewed 'Lisbon Strategy' launched in spring 2005.

To make sure that regulation is used only when necessary and that the burdens they impose are proportionate to their aim, the Commission has a number of processes and tools in place:

- Withdrawal or modification of pending legislative proposals
- Measures to [simplify existing legislation](#)
- Better quality of new Commission proposals: systematic use of [impact assessment](#) and [public consultation](#) in the development of new policy proposals
- Monitoring and reducing administrative burdens thanks to CUT 25% on-line questionnaire

For more detailed information see the [Secretariat General's website on Better Regulation](#).

Better regulation and the pharmaceutical sector

In the context of the renewed Lisbon Strategy, refocused on growth and jobs, the Commission has taken a clear and strong position in favour of better regulation and committed to reinforce efforts to deliver concrete

Simplification of the regulatory environment for the benefit of European Businesses and Citizens

Progress achieved to date :

- 2008 - Review of the Variations Regulations
Revision of [Regulation \(EC\) No 1085/2003](#) concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products falling within the scope of [Council Regulation \(EC\) No 2309/93](#). The objective is to reduce the administrative burden for industry by streamlining the circumstances obliging industry to file applications for variations of human and veterinary medicinal products.
[Read more >>>](#)
- 2007 - Regulation on Maximum Residue Limits
Review of [Regulation 2377/90](#) laying down a Community procedure for the establishment of maximum residue limits (MRLs) of veterinary medicinal products in foodstuffs of animal origin in order to:
- reduce the number of lists of substances;- enhance transparency in the assessment procedure;- ensure compliance with international trade standards;- provide instruments to improve the availability of veterinary medicinal products for food-producing animals.
[Read more >>>](#)
- 2005 - Review of the pharmaceutical legislation
Simplified regulatory framework and incentives for SMEs, which are developing pharmaceuticals including reduced fees, etc.

Update – Variation Reg. - steps carried out (1)

- 20 October 2006 – Commission released a Consultation paper – outlining key items for possible improvements
 - Deadline for comments – end 2006
- Consultation on the extension of the legal basis of the Var. Reg. - summer 2007:
 - Deadline for comments – Sept. 07
- 24 October 07 – publication of a proposal for the Var. Reg. + public consultation paper
 - For comments to all stakeholders (Industry + Authorities) until 4 January 2008

Update – Variation Reg. - steps carried out (2)

- 19 March 2008 – new proposal for Var Reg – including the comments received during the consultation phase
 - 3 April 08 – Standing Committee
- New version to be elaborated – including the comments received during the Standing Committee meeting
 - 2 June 2008 – Standing Committee
 - 10 June 2008 – Stand. Com. – adoption
- Parliamentary scrutiny process – comments until end of Sept 2008
- **Nov 2008** – publication (not including nat. procedures)

Erstellt: Christa Wirthumer-Hoche



10/03/2009

EudraLex - Volume 1 - Pharmaceutical Legislation Medicinal Products for Human Use



Volume 1 of the publications "The rules governing medicinal products in the European Union" compiles the body of European Union legislation in the pharmaceutical sector for medicinal products for human use.

[Directives](#)
[Regulations](#)
[Miscellaneous](#)

EC/1234/2008 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 (*Official Journal L 334, 12/12/2008 p. 7 - 24*).

BG	CS	DA	DE	EL	EN	ES	ET	FI	FR	HU
IT	LT	LV	MT	NL	PL	PT	RO	SK	SL	SV

Erstellt: Christa Wirthumer-Hoche

VERORDNUNG (EG) Nr. 1234/2008 DER KOMMISSION

vom 24. November 2008

über die Prüfung von Änderungen der Zulassungen von Human- und Tierarzneimitteln

(Text von Bedeutung für den EWR)

DIE KOMMISSION DER EUROPÄISCHEN GEMEINSCHAFTEN —

gestützt auf den Vertrag zur Gründung der Europäischen Gemeinschaft,

gestützt auf die Richtlinie des Rates vom 21. Juni 2001 (2001/18/EG) zur Angleichung der Rechtsvorschriften der Mitgliedstaaten über die Zulassung von Arzneimitteln, insbesondere auf Artikel 39

- (2) Die in den Verordnungen (EG) Nr. 1084/2003 und (EG) Nr. 1085/2003 festgelegten Verfahren sollten daher angepasst werden, ohne dabei von den allgemeinen Grundsätzen abzuweichen, auf denen diese Verfahren beruhen. Aus Gründen der Verhältnismäßigkeit sollten homöopathische und traditionelle pflanzliche Arzneimittel, für die zwar keine Zulassung erteilt wurde, die jedoch einem vereinfachten Registrierungsverfahren unterliegen, nicht

Artikel 28

Inkrafttreten

Diese Verordnung tritt am 20. Tag nach ihrer Veröffentlichung im *Amtsblatt der Europäischen Union* in Kraft.

Sie gilt ab dem 1. Januar 2010.

Abweichend von Absatz 2 dürfen die Empfehlungen zu unvorhergesehenen Änderungen gemäß Artikel 5 ab dem in Absatz 1 genannten Datum des Inkrafttretens angefordert, abgegeben und veröffentlicht werden.

Diese Verordnung ist in allen ihren Teilen verbindlich und gilt unmittelbar in jedem Mitgliedstaat.

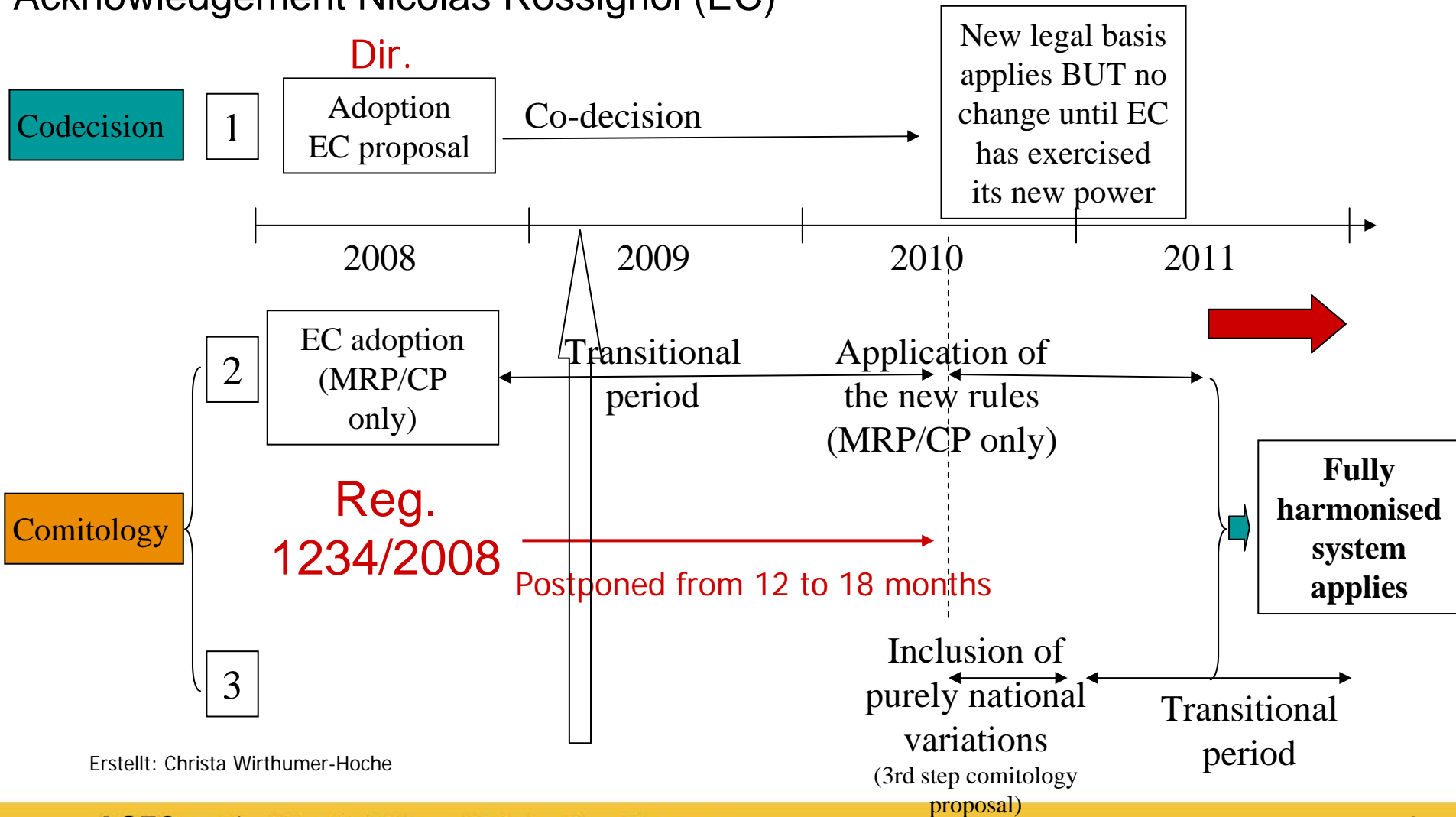
Erstellt: Christa Wi

Brüssel, den 24. November 2008

Next Steps & Timing

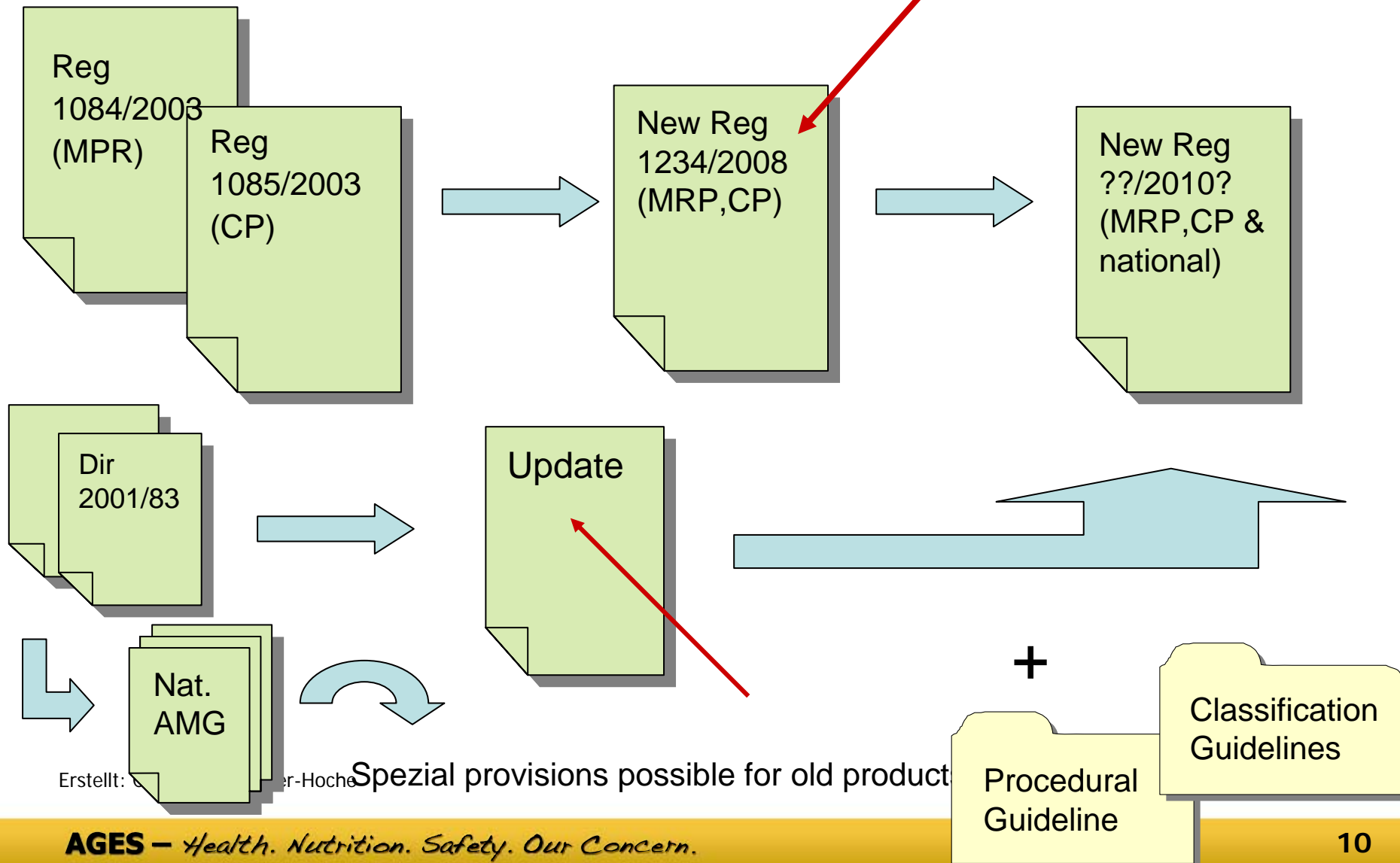
3-steps approach

Acknowledgement Nicolas Rossignol (EC)



Erstellt: Christa Wirthumer-Hoche

Development of the new Var Reg



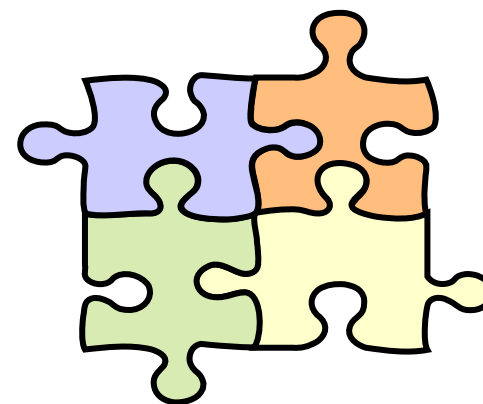
Amendments to Dir.2001/83/EC & Dir. 2001/82/EC

Article 2 - The following Article 23b is inserted:

- 4. A MS may continue to **apply national provisions** on variations applicable at the time of entry into force of this implementing regulation to **MA s granted before 1 January 1998** to MPs authorised only in that MS. Where a MP subject to national provisions in accordance with this Article is subsequently granted a MA in another MS, the implementing regulation shall apply to that MP from that date (MRP).
- 5. Where a MS decides to continue to apply national provisions pursuant to the previous paragraph, it shall **notify the Commission thereof**. If a notification has not been made by [date of transposition of amending directive], the implementing regulation shall apply."

Harmonisation – what does it mean in AT?

- In AT – we loose our independent national Variation-System for MA (§ 24 AMG)
 - It will stay for registration procedures
 - Update?
- EU classification of variations & time lines
- One common template
- New national Fee Regulation



Amendments to the Reg

- Review and rewording of the definitions of all categories of variation
 - Classification guideline
- Type IB by default
 - Procedure for unclassified variations – Art 5
- „Do & Tell“ procedure IA
 - Annual reporting system
 - IA requiring immediate notification
- Grouping of variations
 - Defined in Annex III
- Worksharing procedure
- Disagreement among MSs
 - Discussion at the CMD

Erstellt: Christa Wirthumer-Hoche

Variation – any amendment to the content of the MA dossier

- Type IA Minor variation
 - minimal or no impact on Q/S/E
- Type II Major variation
 - may have significant impact on Q/S/E – has to be assessed
- Extension variation listed in Annex I of the Reg
 - New strength, new pharm. form
- Type IB Minor variation
 - neither Type IA, Type II or extension

- Type IA and Type II pre-defined in Annex II
+ Commission classification guideline
- Extension pre-defined in Annex I
- Unlisted variation
 - Type IB by default, with the option
 - MAH to submit as Type II
 - NCA to require Type II

Unlisted Variations

Art. 5 procedure

- Art 5 procedure provides recommendation for the classification of „unforeseen variations“
- 45 days procedure, specific application form, specific submission dates
- Coordination:
 - CAPs by the EMEA
 - National MA by the CMD

Basis for the periodic review of the guideline and Annex II

- **Design space**
 - Annex II – Classification of variations
 - The following variations shall be classified as major variations of type II:
 - Variation related to the introduction of a new design space or the extension of an approved one
 - Where the design space has been developed in accordance with the relevant European and international scientific guidelines.

- **Continuous improvement of manufacture:**
 - ICH Q8, Q9, Q10:
 - Modern tools (risk management, quality systems)
 - facilitate continuous improvement
 - ICH work is still ongoing
 - Implementation at this stage not fully clear, but
 - Further flexibility to manufacturers, who have undertaken efforts to put this tools in place.

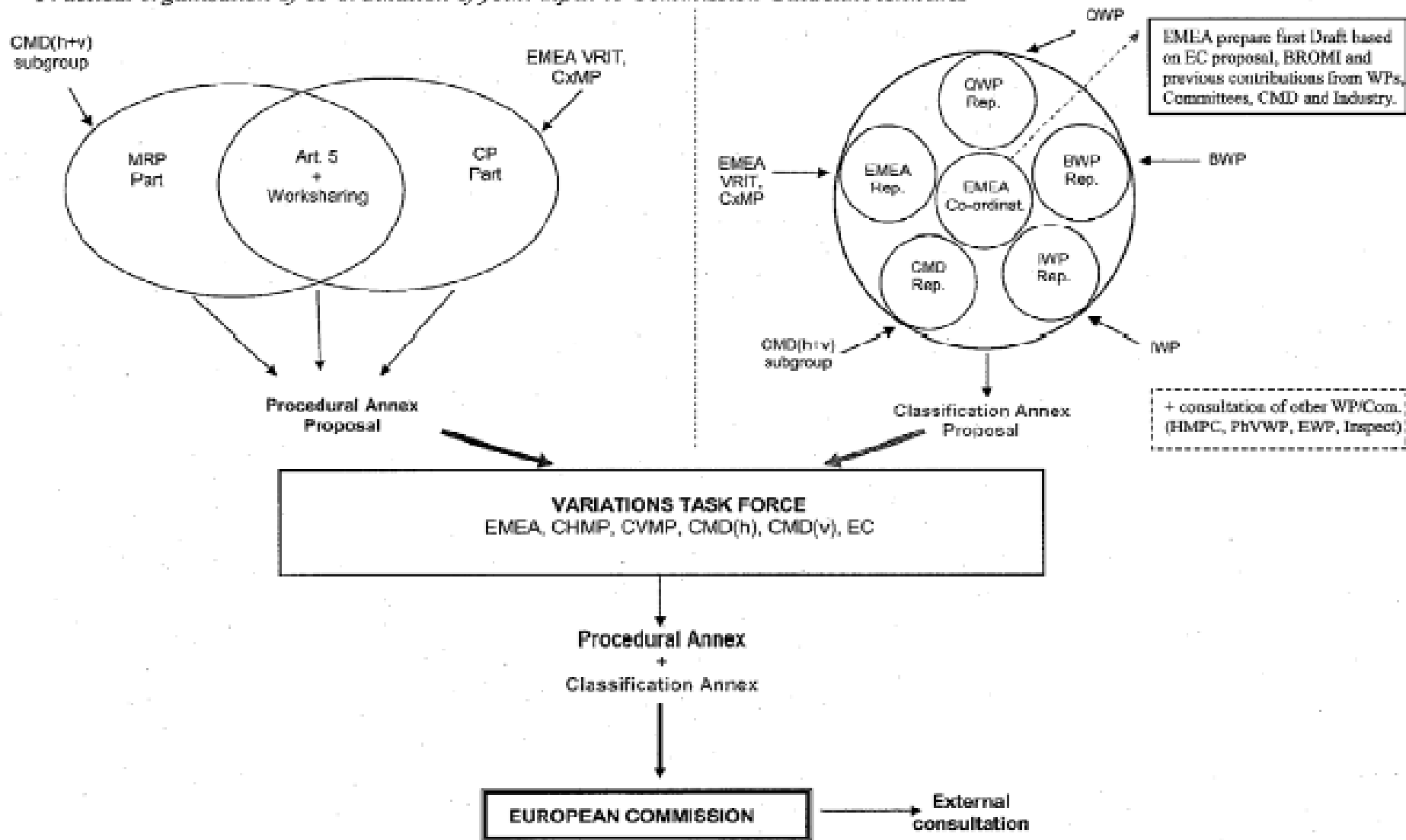
COM Guidelines

EC 1234/2008, Art. 4

Article 4

Guidelines

1. The Commission shall, after consulting the Member States, the Agency and interested parties, draw up:
 - (a) guidelines on the details of the various categories of variations;
 - (b) guidelines on the operation of the procedures laid down in Chapters II, III and IV of this Regulation as well as on the documentation



QWP=Quality Working Party, BWP=Biologics Working Party, IWP=Immunological Working Party, PhVWP=Pharmacovigilance Working Party, EWP=Efficacy Working Party, VRIT=Variation Regulation Implementation Team

EUROPEAN COMMISSION

EC 1234/2008

Documents to be revised

- **Commission documents – NTA**
 - Vol 2A, Chapter 5 „Variations“
 - procedural guideline
 - Vol 2B
 - electronic application form for variations
 - Vol 2C
 - application form for variations
 - Guideline on dossier requirements for Type IA & IB
 - Classification guideline

APPLICATION FOR VARIATION TO A MARKETING AUTHORISATION



HUMAN <input type="checkbox"/>		VETERINARY <input type="checkbox"/>																												
<input type="checkbox"/> NATIONAL AUTHORISATION IN MRP	MRP variation number ^{1A} : _/ _/ _/ _/ _/ _/																													
<input type="checkbox"/> COMMUNITY AUTHORISATION	EMA variation number ^{1B} : EMEA/ JCI/ _/ _/ _/																													
<input type="checkbox"/> NATIONAL AUTHORISATION	Worksharing number: _/ _/ _/ _/ _/																													
Reference Member State / Reference NCA for worksharing																														
<input type="checkbox"/> AT	<input type="checkbox"/> BE	<input type="checkbox"/> BG	<input type="checkbox"/> CY	<input type="checkbox"/> CZ	<input type="checkbox"/> DE	<input type="checkbox"/> DK	<input type="checkbox"/> EE	<input type="checkbox"/> EL	<input type="checkbox"/> ES	<input type="checkbox"/> FI	<input type="checkbox"/> FR	<input type="checkbox"/> HU	<input type="checkbox"/> IE	<input type="checkbox"/> IS	<input type="checkbox"/> IT	<input type="checkbox"/> LI	<input type="checkbox"/> LT	<input type="checkbox"/> LU	<input type="checkbox"/> LV	<input type="checkbox"/> MT	<input type="checkbox"/> NL	<input type="checkbox"/> NO	<input type="checkbox"/> PL	<input type="checkbox"/> PT	<input type="checkbox"/> RO	<input type="checkbox"/> SE	<input type="checkbox"/> SI	<input type="checkbox"/> SK	<input type="checkbox"/> UK	
Concerned Member State(s)																														
<input type="checkbox"/> AT	<input type="checkbox"/> BE	<input type="checkbox"/> BG	<input type="checkbox"/> CY	<input type="checkbox"/> CZ	<input type="checkbox"/> DE	<input type="checkbox"/> DK	<input type="checkbox"/> EE	<input type="checkbox"/> EL	<input type="checkbox"/> ES	<input type="checkbox"/> FI	<input type="checkbox"/> FR	<input type="checkbox"/> HU	<input type="checkbox"/> IE	<input type="checkbox"/> IS	<input type="checkbox"/> IT	<input type="checkbox"/> LI	<input type="checkbox"/> LT	<input type="checkbox"/> LU	<input type="checkbox"/> LV	<input type="checkbox"/> MT	<input type="checkbox"/> NL	<input type="checkbox"/> NO	<input type="checkbox"/> PL	<input type="checkbox"/> PT	<input type="checkbox"/> RO	<input type="checkbox"/> SE	<input type="checkbox"/> SI	<input type="checkbox"/> SK	<input type="checkbox"/> UK	<input type="checkbox"/> NONE
Type of Application																														
<input type="checkbox"/> Groupe^{1C}																														
<input type="checkbox"/> Annual Report^{1C}																														
PERIOD COVERED BY REPORT																														
From		To																												
Month	Year	Month	Year																											
<input type="checkbox"/> Worksharing																														
<input type="checkbox"/> Type IA IN																														
<input type="checkbox"/> Type IB																														
<input type="checkbox"/> Type II																														
<input type="checkbox"/> Indication																														
<input type="checkbox"/> Paediatric Indication																														
<input type="checkbox"/> Safety																														
<input type="checkbox"/> following Urgent Safety Restriction																														
<input type="checkbox"/> Quality																														
<input type="checkbox"/> Annual variation for human influenza vaccines																														
<input type="checkbox"/> Other																														

Gelöscht: ONLY

Formatiert: Einzug: Links: 0 cm

^{1A} Human Medicinal Products: Number to be completed by the Marketing Authorisation Holder, reflecting the correct sequential Mutual Recognition Procedure Number according to Chapter 1 of the 'Best Practice Guides for the submission and processing of variations in the Mutual Recognition Procedure' (<http://www.hma.eu>). In case of a grouped variation concerning more than one marketing authorisation, a list of authorisations in tabular format should be appended to this form.

Veterinary Medicinal Products: Variation number to be issued by the Reference Member State before submission of the application according to the corresponding VMRFG Best Practice Guide (<http://www.hma.eu>)

^{1B} Number to be completed by the MAH, reflecting the correct sequential EMA procedure number (not the MAH's numbering system) which takes into account any previous/ongoing variation, notification, extension, renewal and annual re-assessment procedures for the product.

^{1C} Individual variations included should be listed in tabular format and appended to this form.

Guideline for handling variations

Var Reg **1234/2008** effective **1 January 2010**

- Commission Guideline:
 - high-level EU procedural guideline Annex
- Additional:
 - EMEA: „Post-Authorisation Procedural Guidance“
 - CMD: Best Practise Guide

MAH – to inform RMS/EMA of upcoming post-authorisation submissions for the following 6-12 months (pre-submission meeting can be organised)

- Electronic application form will be revised
 - eVAF
- Solution for eCTD has to be sought
 - Update of the BPG „eCTD in MRP/DCP“





AGES

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Danke!



Fragen?

*Gesundheit. Ernährung. Sicherheit.
Unsere Verantwortung.*

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