BfArM
Bundesinstitut für Arzneimittel und Medizinprodukte

Innovations in the Decentralized Procedure and Mutual Recognition

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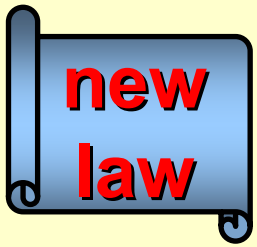
Setting the Scene: Review 2001 - (1) = Review of the EU-Legislation for Medicinal Products

Consists of three parts:

- **Directive 2001/82/EC**
  Community code relating to veterinary medicinal products
- **Directive 2001/83/EC**
  Community code relating to medicinal products for human use
- **Council Regulation (EEC) No 2309/93**
  Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of medicinal products



Setting the Scene: Review 2001 - (2)

Implementation

- published in the Official Journal: **30. 04. 2004**
- Council Regulation
  - Title IV: in force 20th May 2004
  - other parts will enter into force after 18 months (20th November 2005)
- transposition of the Directives into national law: max 18 months (30th October 2005)

The different licensing procedures

central	MRP/DC	national
Council Regulation (EEC) No 2309/93 Annex Part A Part B	More than one EU-MS	national MA for MRP MA for only one EEA-MS bibliographic application Article 10 (2) Dir. 2001/83

Mutual Recognition Procedure (MRP)

- describes the procedure to get national MAs in MSs if the same medicinal product is already approved in one MS (= RMS)

  → mandatory procedure

- method of work sharing between MS

Decentralized Procedure (DC)

- describes the procedure to get national MAs in MSs if the same medicinal product is intended to be licensed in more than one MS where the centralised procedure does not apply or neither the centralised nor the MRP are selected by the applicant

  → optional procedure, applicant's choice

- method of work sharing between MS, but early involvement of all CMS

new law

MRP and Decentralised Procedure (1)

What is new for both procedures?

Public Assessment Report

PL and labelling is part of the approval

harmonisation between MSs

'Blue Box' is required!

MRP and Decentralised Procedure - (2)

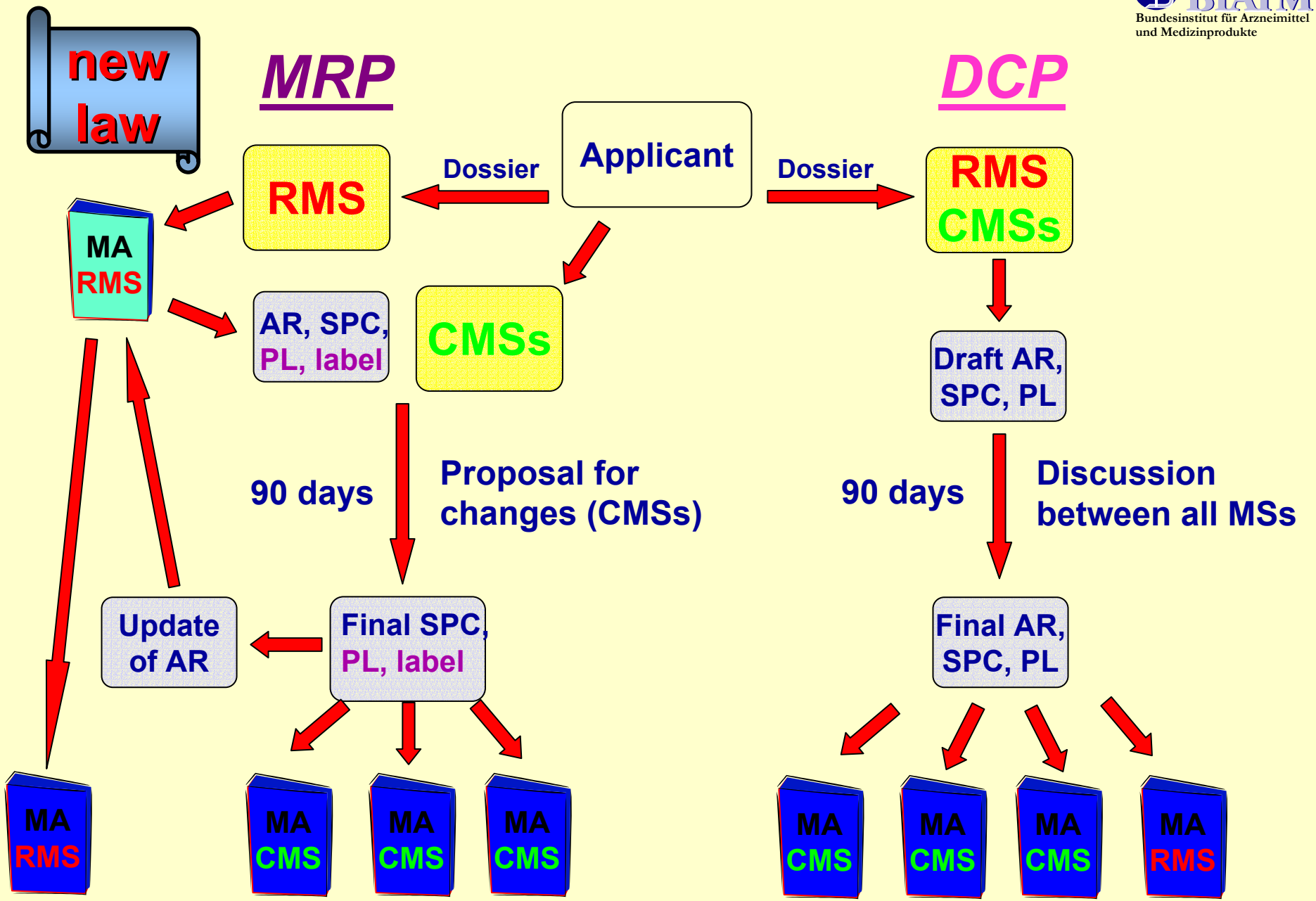
Two different routes for receiving a MA in more than one MS:

1. **Mutual recognition procedure - MRP**

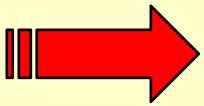
   where the medicinal product has already received a MA at the time of application

2. **Decentralised procedure - DCP**

   where the medicinal product has not received a MA at the time of application


new law
MRP
DCP
Applicant
Dossier
Dossier
RMS
RMS
CMSs
MA
RMS
AR, SPC,
PL, label
CMSs
Draft AR,
SPC, PL
90 days
Proposal for
changes (CMSs)
90 days
Discussion
between all MSs
Update
of AR
Final SPC,
PL, label
Final AR,
SPC, PL
MA
RMS
MA
CMS
MA
CMS
MA
CMS
MA
CMS
MA
CMS
MA
CMS
MA
RMS

Mutual Recognition Procedures - (1)



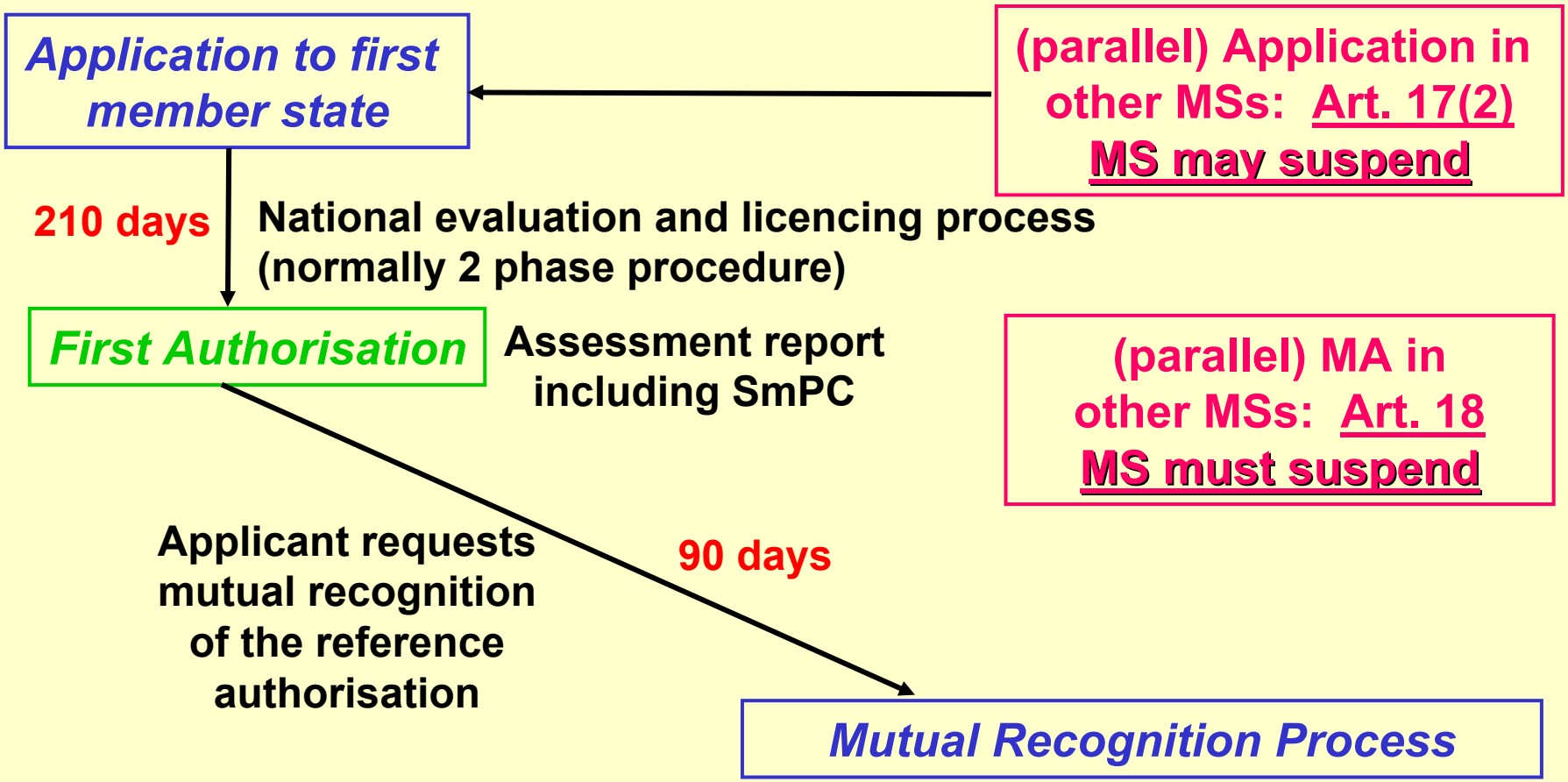
Article 28 Directive 2001/83/EC

' ... he shall certify that the summary of product characteristics proposed by him in accordance with Article 11 is identical to that accepted by the reference Member State...'

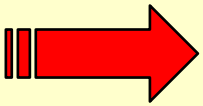
'... he shall testify that all the dossiers is identical …'

'... the holder of the authorization shall request the Reference Member State to prepare an assessment report ...'

Mutual Recognition Procedures - (2)



Mutual Recognition Procedures - (3)



Article 18 of Directive 2001/83/EC

'Within 90 days of the receipt of the assessment report the Member State concerned shall either recognize the decision of the first Member State and the summary of product characteristics as approved by it or, ... present a risk to public health ....

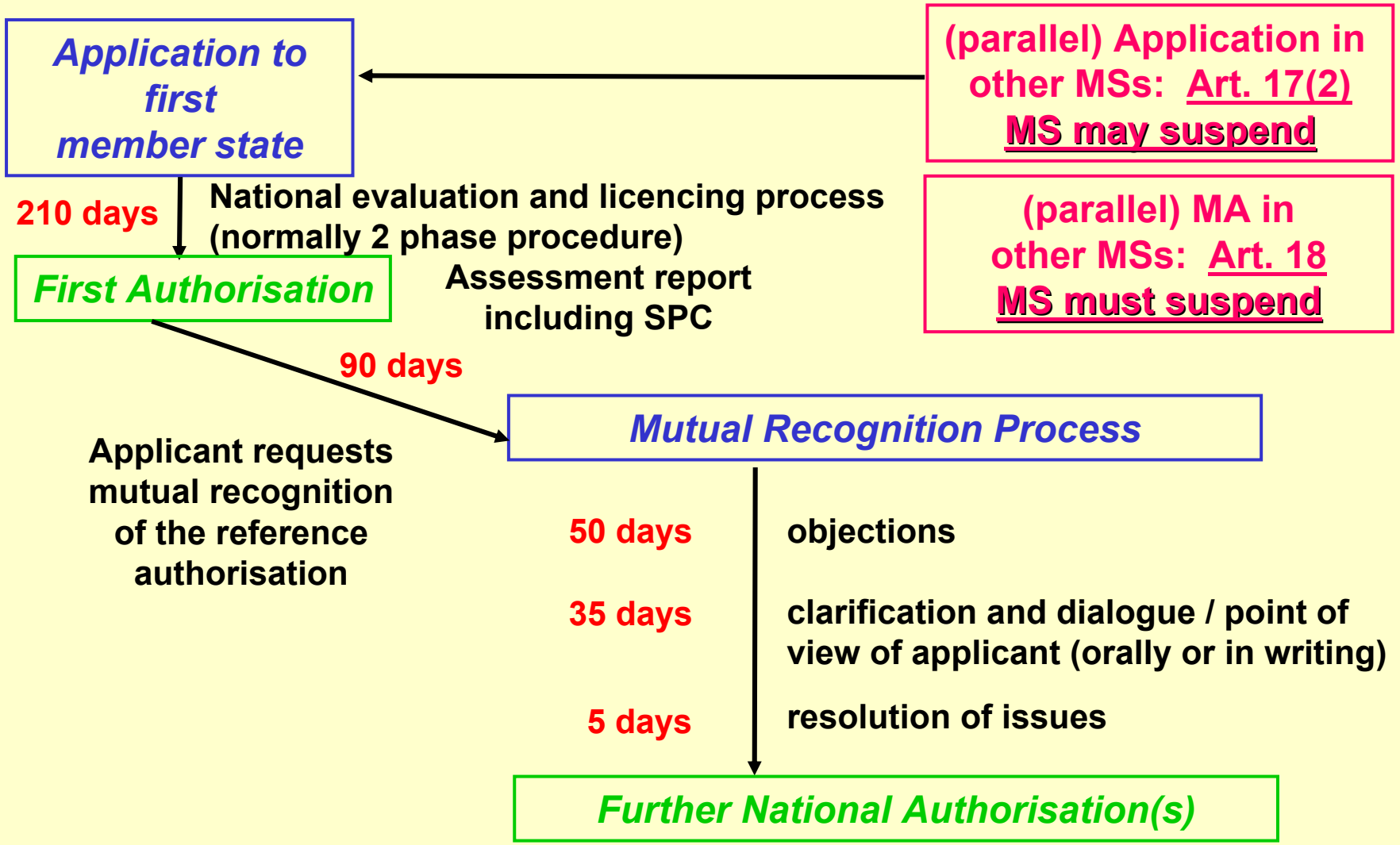
The Summary of Product Characteristics (= SmPC)

- basis of information for health professionals on how to use the medicinal product safely and effectively
- definitive statement between the competent authority and the marketing authorisation holder
- common basis of communication between the competent authorities of the Member States
- content cannot be changed except with the approval of the originating competent authority

The Package Leaflet (= PL)

- the content of the package leaflet must be consistent with the SmPC but in a wording that can be easily understood by non-professionals
- inclusion in the packaging of all products obligatory
- to be written in the official language(s) of the Member State where the product is placed on the market
- text must be approved by the competent authorities

Mutual Recognition Procedures - (4)



Risk to public health - (1)

NtA „refers to the quality, safety and efficacy“

CMSs negative risk-benefit-evaluation

- **indication / posology / treatment-duration**
- **bioavailability / bioequivalence**

Review 2001: „ … serious risk to public health … „
Guideline/definition to be published by the EC

Risk to public health - (2)

- Arbitration procedure
- Withdrawal of application possible (day 89/90)

Decentralised Procedure - (1)

What is new ?

- Applicant can choose procedure (and RMS)
- consultation between MS´s before the first MA is issued
- introduces a ‘clock-stop’ period
- final AR, SPC, PL and labelling
- MA is granted at the ‘same time’ in the selected MSs

Decentralised Procedure - (2)

Implications for competent authorities

- early involvement as CMS
- working together
- tighter time-limits, but also ´clock stop´
- discussion between MS will be positive for public health (if new active substance)

Decentralised Procedure - (3)

Possible procedure

Day - 30	pre-procedural step - *submission of dossier, validation*
Day 0-120	National step - *RMS assessment, Preliminary AR, comments from CMS, consolidated LoQ to applicant*
CLOCK STOP	*Applicants response document*
Day 120-210	European step - *draft AR/SPC/PL, CMS comments, break out, Final AR, approval and closure (or referral)*
Day 210-240	National step - *granting of MA*

DCP - proposed flow chart - (1)

!!!!!!! First ideas !!!!!!!

1. Pre-procedural Step

Day - 30 ***Submission of the dossier to RMS and CMSs Validation of the application***

Communication with the MS of the Reference Product, if applicable

new law

DCP - proposed flow chart - (2)

2. National step – 120 days

Day 0 *RMS starts the procedure and the assessment of the dossier*

Day 85 *RMS forwards Preliminary AR to CMSs and Applicant*

Day 110 *CMSs send comments to RMS*

Day 120 *RMS sends consolidated LoQ to Applicant*

→ **Clock-stop period**

DCP - proposed flow chart - (3)

Clock-stop period

- *recommended period of 6 months, which could be extended if justified*
- *Applicant sends the response document*
- *RMS validates the response document*
- *RMS prepares the draft AR, SPC, PL and labelling*

→ **European step**

DCP - proposed flow chart - (4)

3. European step – 90 days

Day 121 *RMS sends draft AR, SPC, PL and labelling to CMSs and Applicant*

Restart of the procedure

Day 150 *CMSs send comments on draft AR, SPC, PL and labelling to RMS*

Day 155 *RMS sends the consolidated LoQ to the Applicant*

Day 165 *Applicant sends the response document to RMS and CMSs*

DCP - proposed flow chart - (5)

Day 170 *Possibility of a Break-out Session*

Day 175 *CMSs send final comments*

Day 180 *RMS circulates the final AR*

Final discussion of AR, SPC, PL and labelling

Withdrawl from CMSs

Day 210 *Mutual approval of final AR, SPC, PL and labelling - closure of the procedure*

or disagreement and referral to the Coordination Group

DCP - proposed flow chart - (6)

4. National step – 30 days

Day 210-240 *granting of MA*

MRP/DCP
Proposed changes to procedures - (1)

If no agreement between RMS/CMS can be reached at end of procedure

- **Referred to Coordination Group (CG)**
  - **60 days for negotiation between the MS concerned (RMS and CMSs)**
  - **consultation of the applicant in written or oral form**

MRP/DCP
Proposed changes to procedures - (2)

- Still disagreement after this consultation
  - the elements of disagreement are forwarded to the Agency

→ arbitration

→ MS´s that are in agreement with the AR and SPC may authorise the medicinal product, without waiting for the outcome of the procedure

MRP/DCP
Proposed changes to procedures - (3)

necessary prerequisite:

Definition of ‘Serious Risk to Public Health’

EU-Commission together with MRFG / VMFRG

MRFG

is **M**utual **R**ecognition **F**acilitation **G**roup

- Meets once a month at EMEA in London
- Representatives from EU Member States, Norway, Iceland and Cadreac Observer
- Chaired by member from EU-Presidency

Tasks of MRFG

- informal Group started by the Heads of Agencies
- coordination and facilitation of the mutual recognition procedure
- provides a forum to reach a common understanding of the procedure and develop SOPs
- translates legal interpretations into practical recommendations
- holds break-out sessions on individual applications in order to facilitate agreement

Activities of MRFG

- Release of papers and recommendations
- Organisation of break-out meetings
- Improvement of transparency
- Organisation of informal meetings
- New activities
- Statistics
- Co-operation with the European Commission
- Facilitation of enlargment of the MRP

Coordination Group vs. MRFG

- legal basis for operation
- wide scope - to examine any question related to authorisation of medicinal products in more than one MS
- to assist procedures for authorisation of MPs in more than one MS
- new responsibilities – mix of procedural, regulatory and scientific work
- one representative from each MS, appointed for 3 years (renewable)
- members can be accompanied by experts
- rules of procedure for the CG – to be approved by the EC-Commission

Coordination Group - (1)

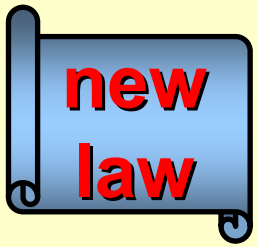
➢ Dialogue between MS´s

- **Procedural / Regulatory**
  - ✓ Regulatory SOP´s, guidelines and recommendations
  - ✓ Harmonised view on the interpretation of Directives and Regulations
- **Scientific**
  - ✓ Scientific discussion to resolve scientific problems, arbitration only in exceptional cases
  - ✓ Identification of the need to modify or develop new guidelines (establishment of ad-hoc groups)

Coordination Group - (2)

➢Harmonisation of SPC´s

- **once a year the CG will elaborate a list of products where the SPC needs to be harmonised**
  - ✓ proposal of candidates by the MS to CG
  - ✓ CG will discuss and compile a list to be send to the EU-Commission
  - ✓ EU-Commission (?) will start Article 30 procedures
- **Risk management**
  - ✓ close liaison with the Pharmacovigilance Working Party (PhVWP)
  - ✓ arrangements for work sharing of PSUR´s



Coordination Group - (3)

- **Organisational aspects**
- **Elected chairperson and vice-chair**
- **Rules of procedures**
- **Meetings**
  - ✓ monthly at the EMEA – plenary meeting
  - ✓ Break-out sessions – will be reported to the plenary meeting
- **Secretariat**
  - ✓ provided by the EMEA

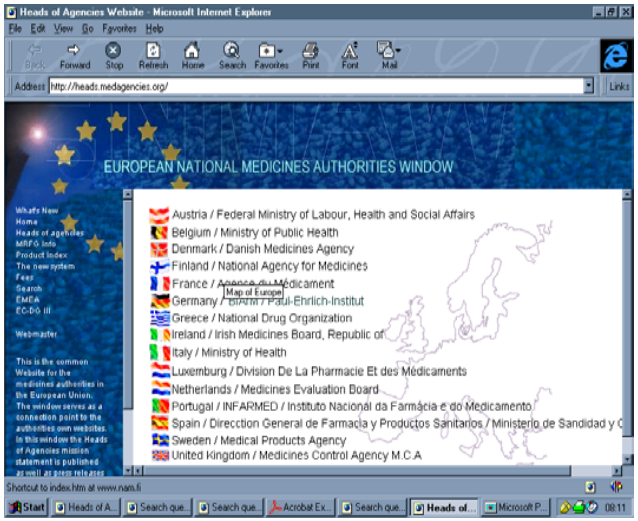
Information on Drug Regulatory Affairs

European Institutions

http://pharmacos.eudra.org
= European Commission, DG Enterprise

http://www.emea.eu.int
= European Medicines Evaluation Agency

http://heads.medagencies.org
= (National) Medicines Authorities in the European Union



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… thank you!