

Position on EU-Directive Mutual Recognition Procedure View of the National Authority - BfArM

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Approval of Drugs in Germany

regulatory framework

**Regulations, Directives and publications in the EU
German Drug Law (AMG)**

how to gain marketing authorisation in Germany :

centralised procedure according to 2309/93/EEC

decentralised procedure according to 75/319/EEC

**national procedure for new and known substances
according to §§ 21, 25, 48, 49 etc. AMG**

homoeopathics etc. according to §§ 34

standard approvals according to § 36 AMG

parallel import approval

old drugs ("Nachzulassung") according to § 105 AMG

Life cycle of an approval (national)

Development incl. clinical trials (GMP, GLP, GCP §40,41 AMG)

Application according to §21 AMG

Approval according to § 25 AMG

Report according to § 29 para 1 AMG every 6 months, years 1 + 2

PSUR according to § 49, 6 AMG **variation** end of year 2

Report according to § 29 para 1 AMG once a year, years 3 + 4 + 5

"Prescription only" according to § 49 / 48 AMG end of year 5

Renewal **variation** according to § 31 end of year 5

Drugs in the EU

- **Quality**
 - **Efficacy**
 - **Risk - Benefit**
-
- **Reimbursement ?**
 - **Pricing ?**
-
- **"Unified" Market ?**

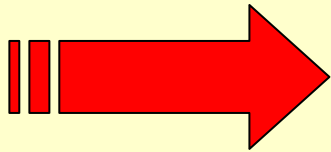
Proposals of the Commission

- **Centralised or decentralised - balance**
 - **Mutual Recognition Committee**
 - **Empowerment of the Mutual Recognition Procedure**
 - **Abolishment of renewals ???**
 - **However, lacking definitions on:**
 - **NCE**
 - **Public health**
 - **Serious risk to public health**
- "Better regulation" ?**
- Postmarketing pharmacovigilance ?**

Need for Definition : "Serious Risk to Public Health"

- **national views / definitions differ from case to case and from country to country ?**
- **are national views always objective?**
- **maybe national views are "historical" ?**
- **are national views applicable to European harmonisation / single market ?**
- **are national views "for home use" only or a "mission" to other countries?**

**Conclusion: A European definition is highly necessary.
Already on the commission agenda ?**

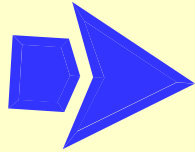


Changes in

Directive 2309/93/EEC



centralised

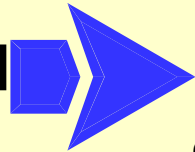


**Council Regulation
(EEC) No. 2309/93
Annex**

Part A - Biotech

**Part B deleted = means new drugs **obligatorily (?)
CENTRALISED****

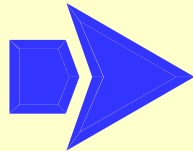
decentralised



Generics

**centralised and decentralised
line-extension**

national



**FOR ONE MEMBER STATE ONLY;
bibliographic approval;**

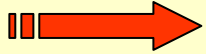


Changes in the Committees in accordance with Directive 2309/93/EEC



CPMP "renamed" to Committee for Human Medicinal Products

Only one representative per Member State



Committee on Orphan Medicinal Products



**Committee on Herbal Medicinal Products
one representative per Member State**



Changes in the Committees in accordance with 2309/93/EEC



Members of the Management Board :

4 members from the Member States,

4 members from the EU Commission,

4 members from the European Parliament,

4 members from patient (groups) and industry (?)

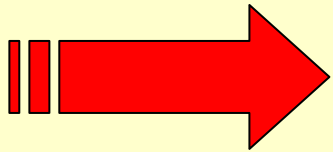


Heads of Agencies as Advisory Board

One representative per National Authority



'New'



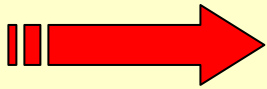
Directive 2001/83/EEC

= combination of all existing Directives

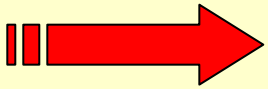
e.g. 65/65/EEC; 75/319/EEC; 92/27/EEC



Directive 2001/83/EEC



Mutual Recognition Procedure



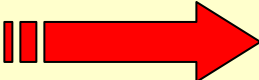
Decentralized Procedure



Directive 2001/83/EEC

Title III

Mutual Recognition Procedure and Decentralised Procedure



Chapter 4 Article 28

Applicants choose RMS

A) Mutual Recognition Procedure

MA granted: RMS prepares or updates **AR within 60 days**

AR and SPC to CMS

within 90 days CMS shall approve **SPC, Labelling, Package Leaflet**

all MS where an application in accordance [...with Directive

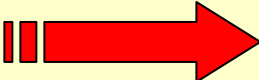
2001/83/EEC...] , **shall adopt a decision within 30 days**



Directive 2001/83/EEC

Title III

Mutual Recognition Procedure and Decentralised Procedure



Chapter 4 Article 28

Applicants choose RMS

A) Mutual Recognition Procedure

MA granted

CMS  disagreement referred to co-ordination group

MS fail to reach an agreement within 60 days  Agency



Directive 2001/83/EEC

Title III

Mutual Recognition Procedure and Decentralised Procedure



Chapter 3 Article 17 and Chapter 4 Article 28

Applicants choose RMS

B) Decentralised Procedure

Medicinal Product not authorised

RMS: **draft AR , draft SPC, draft labelling** within 120 days to CMS

within 90 days CMS shall approve **SPC, Labelling, Package leaflet**

all MS where an application in accordance [...with Directive

2001/83/EEC...], **shall adopt a decision within 30 days**

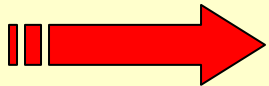


Directive 2001/83/EEC

Title III

Mutual Recognition Procedure and Decentralised Procedure

Chapter 3 Article 17 and Chapter 4 Article 28



Applicants choose RMS

B) Decentralised Procedure

Medicinal Product not authorised

Questions: Application to RMS and CMS: How to avoid parallel evaluation?

Start/information of national procedure to all CMS by RMS?

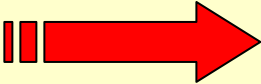
Clock-stop? Involvement of applicant? Deficiency letter ? Final AR?



Directive 2001/83/EEC

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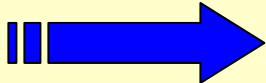
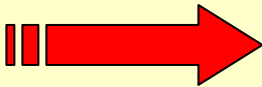


Directive 2001/83/EEC

Title III Placing on the market

Chapter 3 Article 21

Public MR-Assessment Report

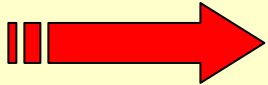


**At the request of any interested party,
the competent authorities shall make available the
assessment reports on the product,
together with the reason for their opinion after deletion of information
of a commercially confidential nature**



Directive 2001/83/EEC

Title III



Mutual Recognition Procedure and Decentralised Procedure

Chapter 4 Article 27

Mutual Recognition Facilitation Group = **co-ordination group**

„examination of any question relating to MA of a medicinal product

in two or more Member States

„composed of one representative per Member State ..

term of 3 years..renewable ...experts



Directive 2001/83/EEC

Title III

Mutual Recognition Procedure and Decentralised Procedure

Chapter 4 Article 30

MS may, each year, forward to the **co-ordinating group** ..

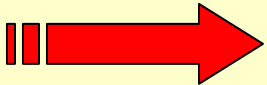
a list of medicinal products for which harmonised

Summary of Product Characteristics should be drawn up

co-ordination shall agree on list

Commission or an MS, in agreement with the Agency and

taking into account the views of interested parties



German (BfArM) historical workload:

“Nachzulassung“ : Applications : 12500*

Of these : 7300* (scientific work)

5200* (withdrawals, only formal work)

5300* (expired)

Rest : 5300* (homoepathics with indication) + 4700* (without indication)

Backlog from former years : 4700 applications

*rounded

"Eurotasks" for BfArM

- present: 10 - 15%
- future: 20 - 30% (after finishing "Nachzulassung")

EU → BfArM: innovation, orphans, biotech

BfArM → EU: generics, OTCs

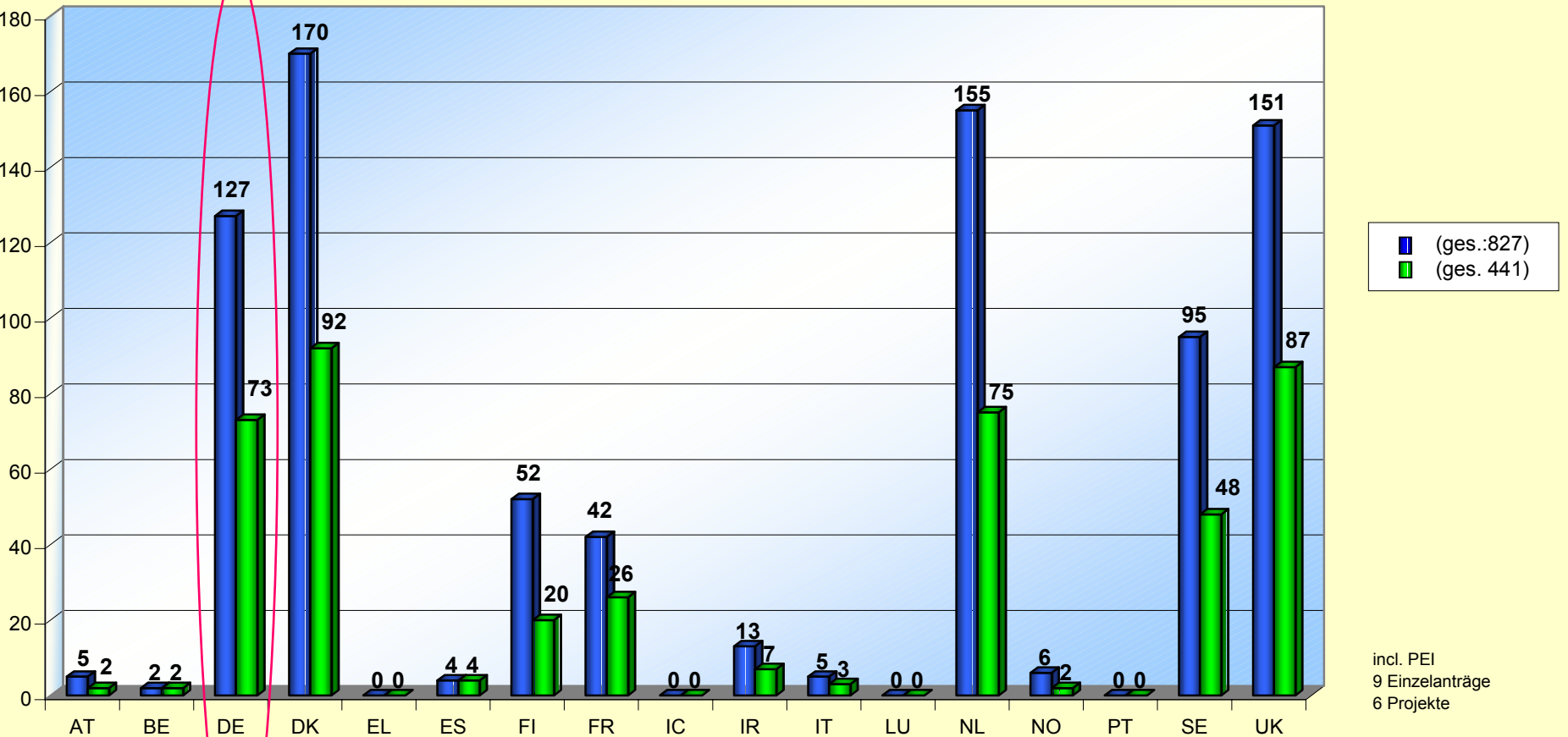
BfArM – Europ. Workload 1995 to 2001

➤ Centralised Procedure	Number	BfArM as (Co)Rapp
	325	43
	(235 / 36 substances)	
➤ Mutual Recognition	Number	BfArM as RMS
	2388	299
		BfArM as CMS
		1362

Comparison of the countries in MRP 2001 RMS

Übersicht der 'Reference Member States' im dezentralen Verfahren

- abgeschlossene Verfahren (Tag 90) 1.01.01-31.12.01 -



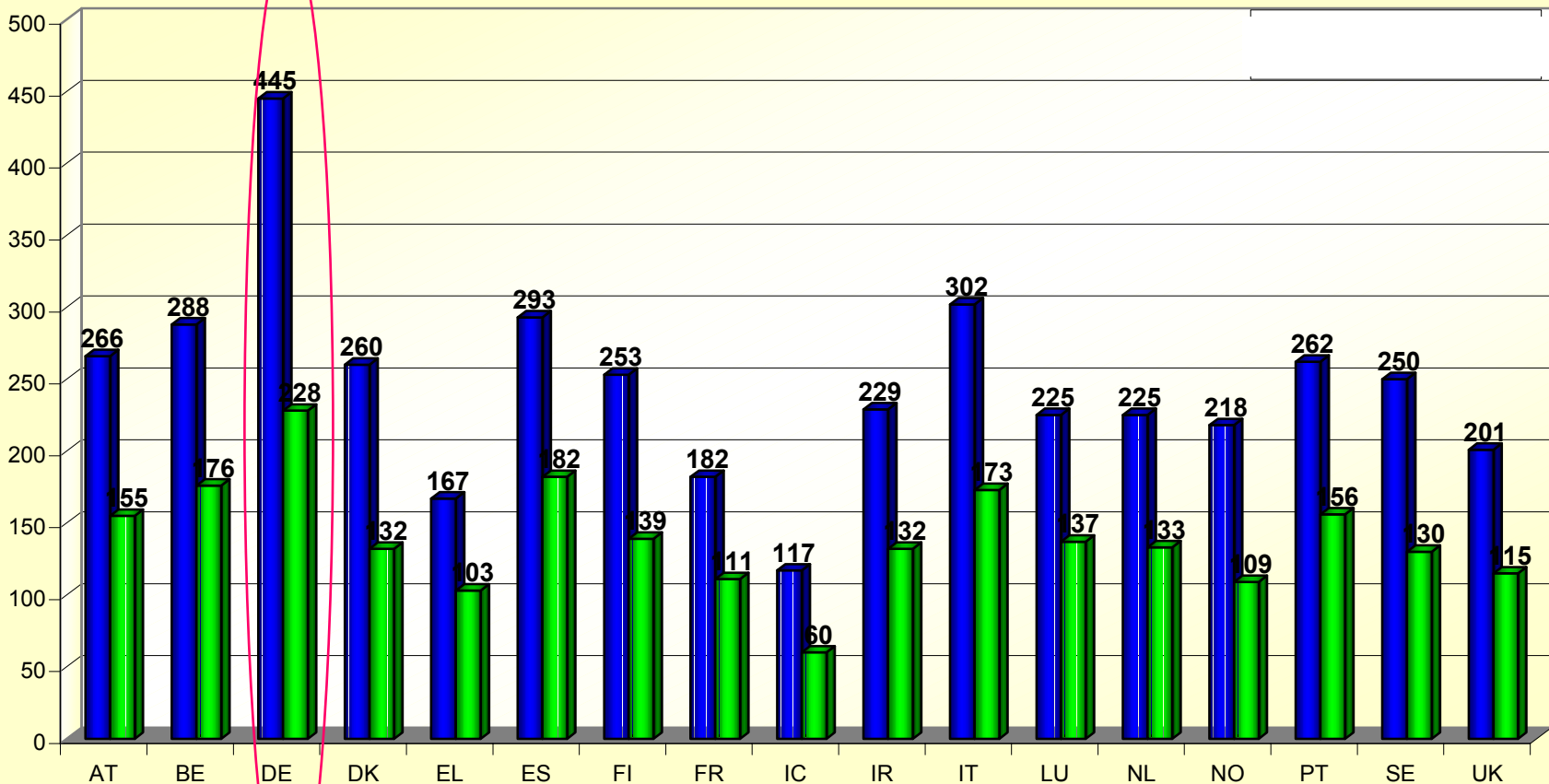
incl. PEI
 9 Einzelanträge
 6 Projekte
 Stand: 31.12.01
 Datenquelle: EudraTrack

By number of approvals: projects-green; approvals-blue

Comparison of the countries in MRP 2001 CMS

Übersicht der 'Concerned Member States' im dezentralen Verfahren

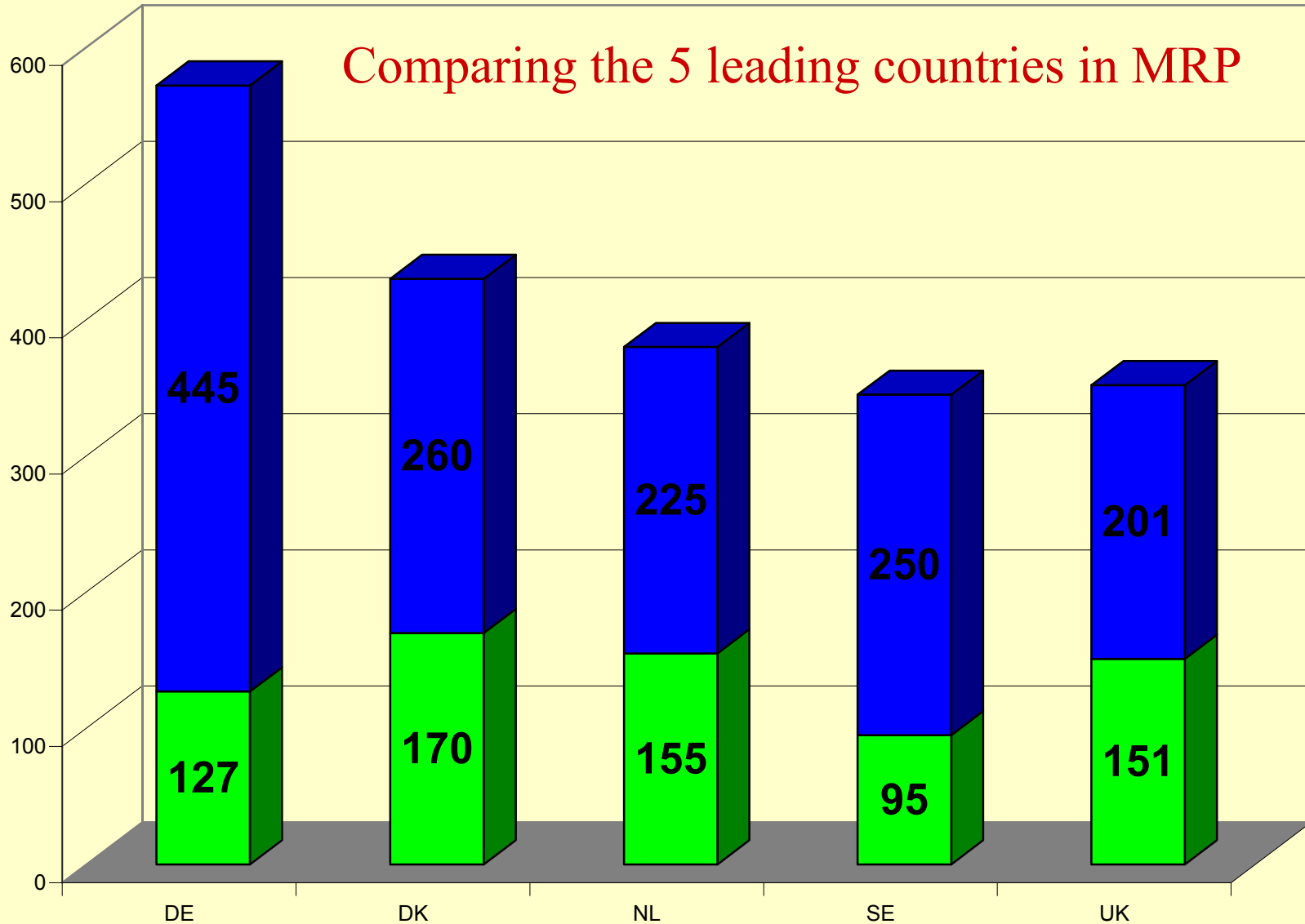
- abgeschlossene Verfahren (Tag 90) vom 1.1.01-31.12.01-



incl. PEI-Anträge
aus dem Jahr 2001
4 Einzelanträge
4 Projekte

Stand: 30.12.01
Datenquelle: EudraTra

By number of approvals: projects-green; approvals-blue



**Gesamtanzahl
Einzelanträge
1.1.01-31.12.01
827**

incl. PEI
9 Einzelanträge RMS
4 Einzelanträge CMS



Stand: 31.12.01
Datenquelle: EudraTrack

By number of approvals, RMS = green, CMS = blue

Future of national procedures ?

- abolishment of the EU – "uncommon" § 49 AMG ?**
- abolishment of renewal procedure ?**
- what about outdated claims ?**

Our Proposal for the Future European System

- "Premium products" (innovative)  centralised
- "Bread-and-butter products"  mutual recogn.
 - "me too"
 - "former" innovative classes of products
 - OTC's
 - generics
 - "important" herbals

-
- the balanced status (centralised/decentralised) must survive :
 - fast access for innovations, not overloading CP
 - but some NEC need the MRP

"Diamonds are forever ! (Premiums are not !)"

Role and Tasks of the BfArM in the Future

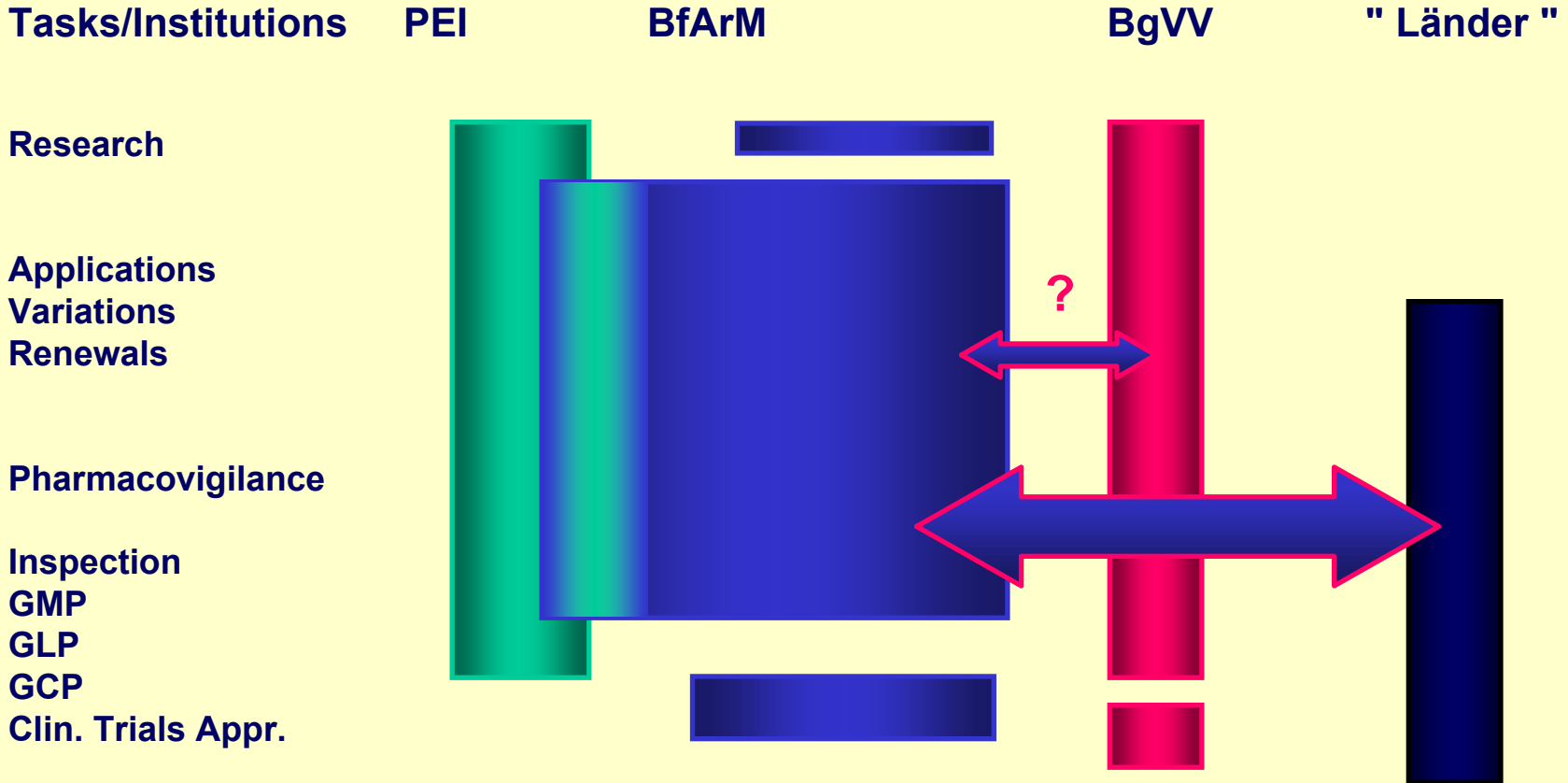
to be clarified :

- **Centre of excellence (EU und CEEC) ??**
- **Therapeutic working groups ??**
- **Excellent national and EU 'scientific advice' ??**

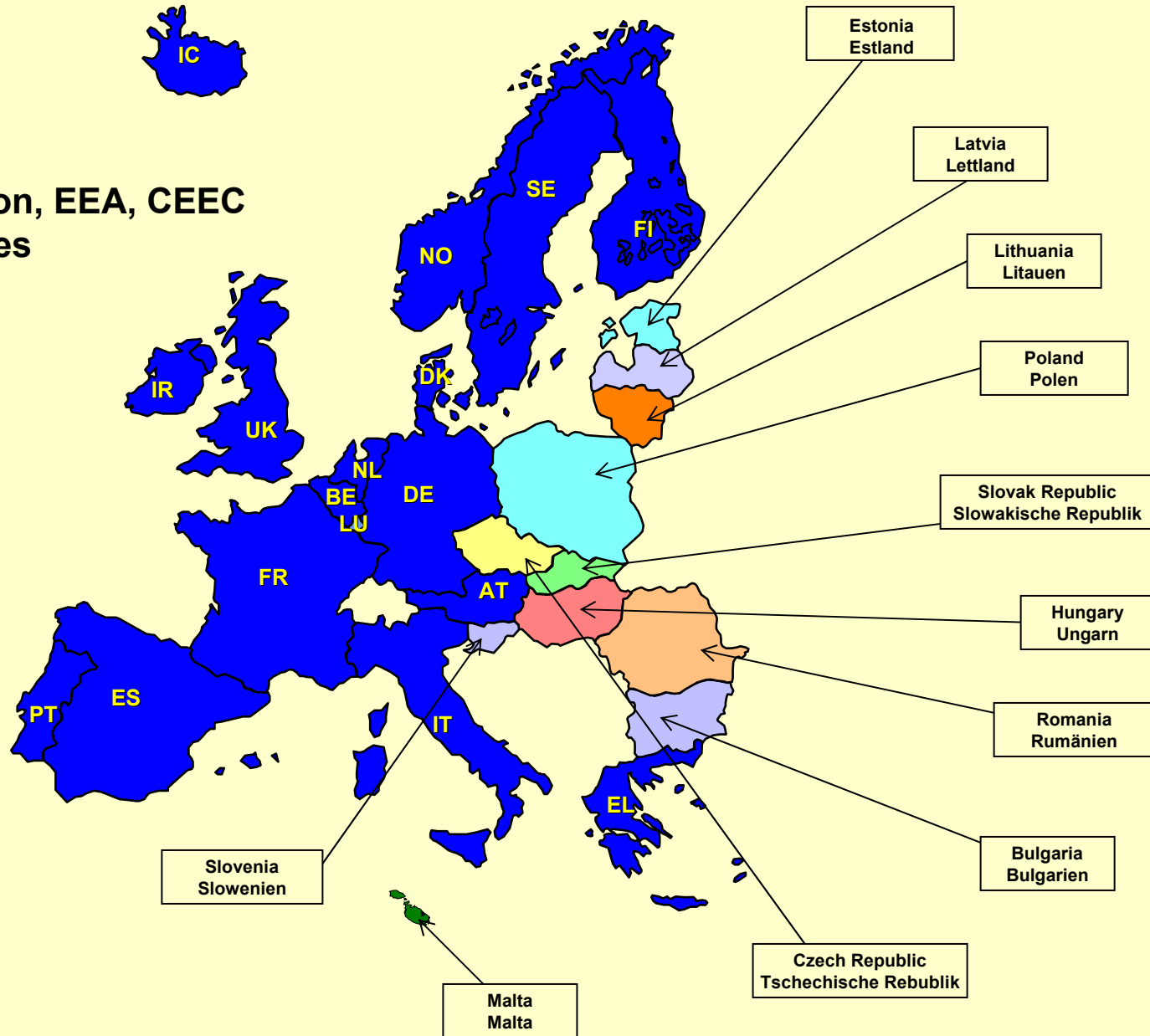
Self - defined Future Position of BfArM

- **Team leader and opinion leader**
 - ❖ according to approvals :
 - MRFG – RMS
 - Centralised - Rapporteur
 - ❖ according to projects / indications (e.g. antibiotics, HIV)
 - ❖ according to topics (Notes for Guidance, Points to Consider, Working Parties)
- **Team player in all other cases**

Germany : Complications for Europe co-operation and ourselves = federal structures



European Union, EEA, CEEC Member States





Thank you for your attention