Chances of Co-operation with CADREAC
View of the National Authority - BfArM

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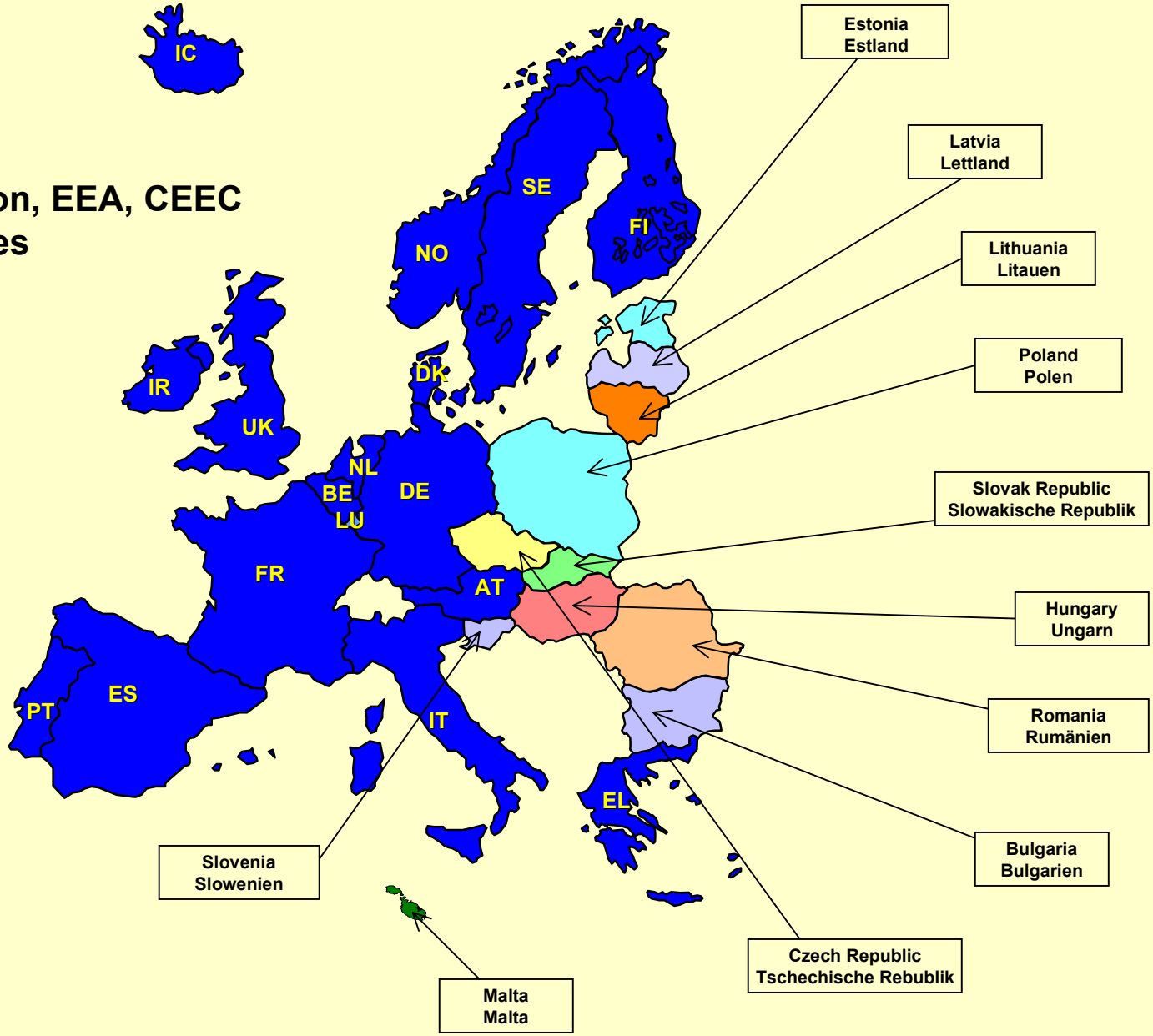
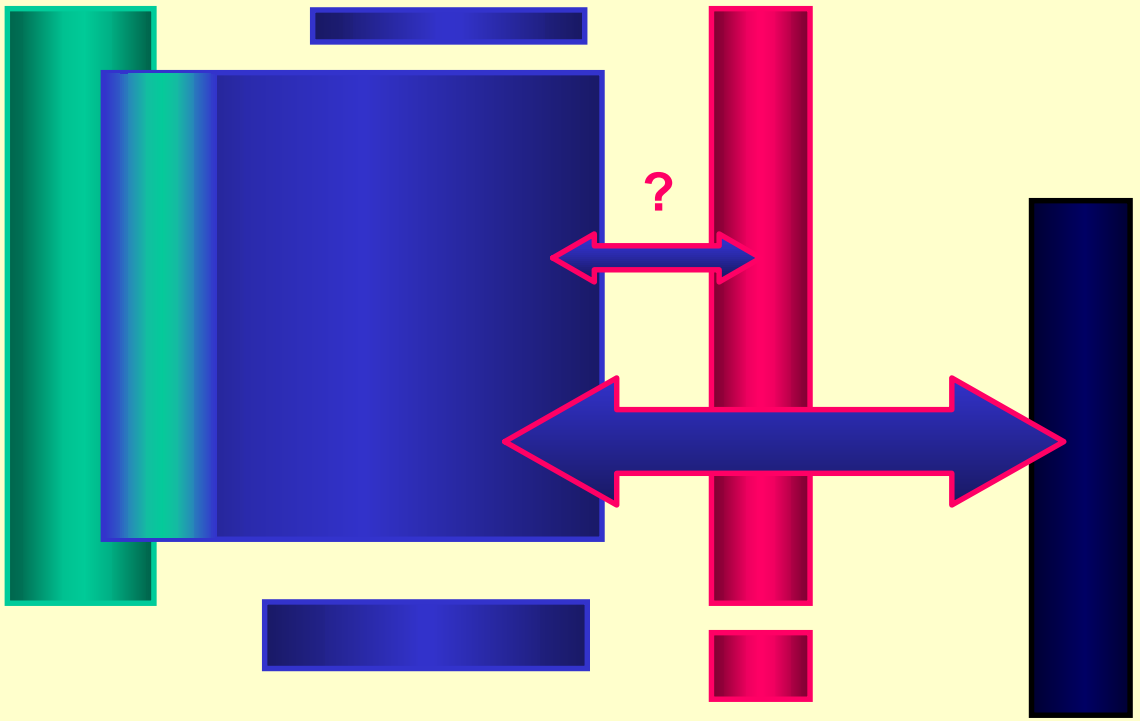
Europan Union, EEA, CEEC Member States



Germany : Complications for Europe

co-operation and ourselves = federal structures

Tasks/Institutions	PEI	BfArM	BgVV	"Länder"
Research				
Applications Variations Renewals				
Pharmacovigilance				
Inspection GMP GLP GCP Clin. Trials Appr.				



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 ?

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	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 according to § 31	end of year 5

variation

variation

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**

Drugs in the EU

- Quality
- Efficacy
- Risk - Benefit

- Reimbursement ?
- Pricing ?

- "Unified" Market ?

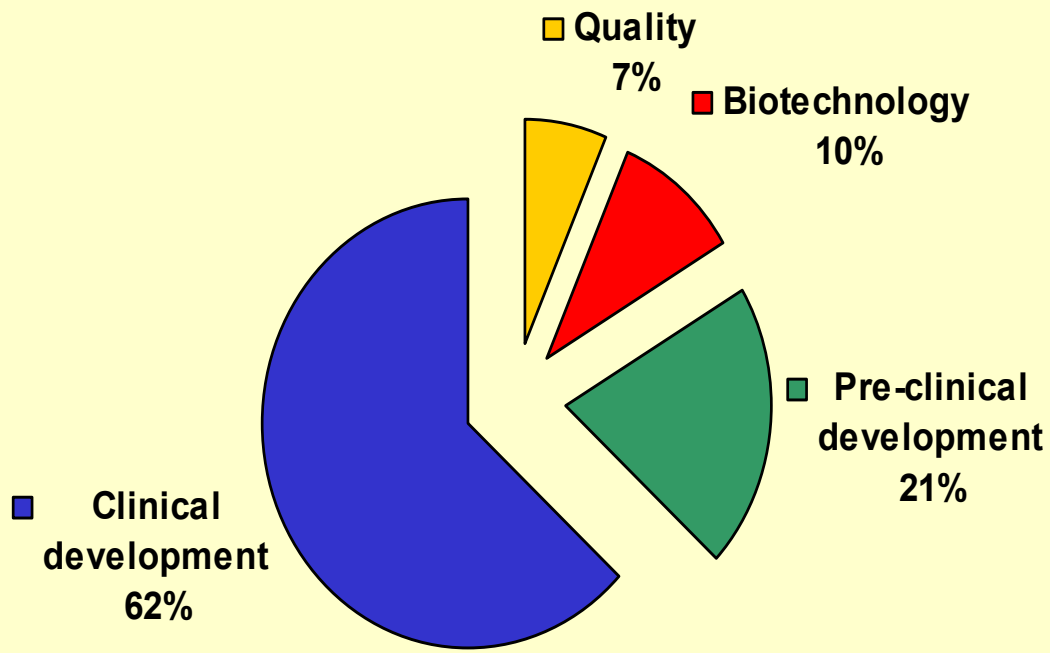
"Eurotasks" for BfArM

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

EU ➜ BfArM: innovation, orphans, biotech

BfArM ➜ EU: generics, OTCs, scientific advice

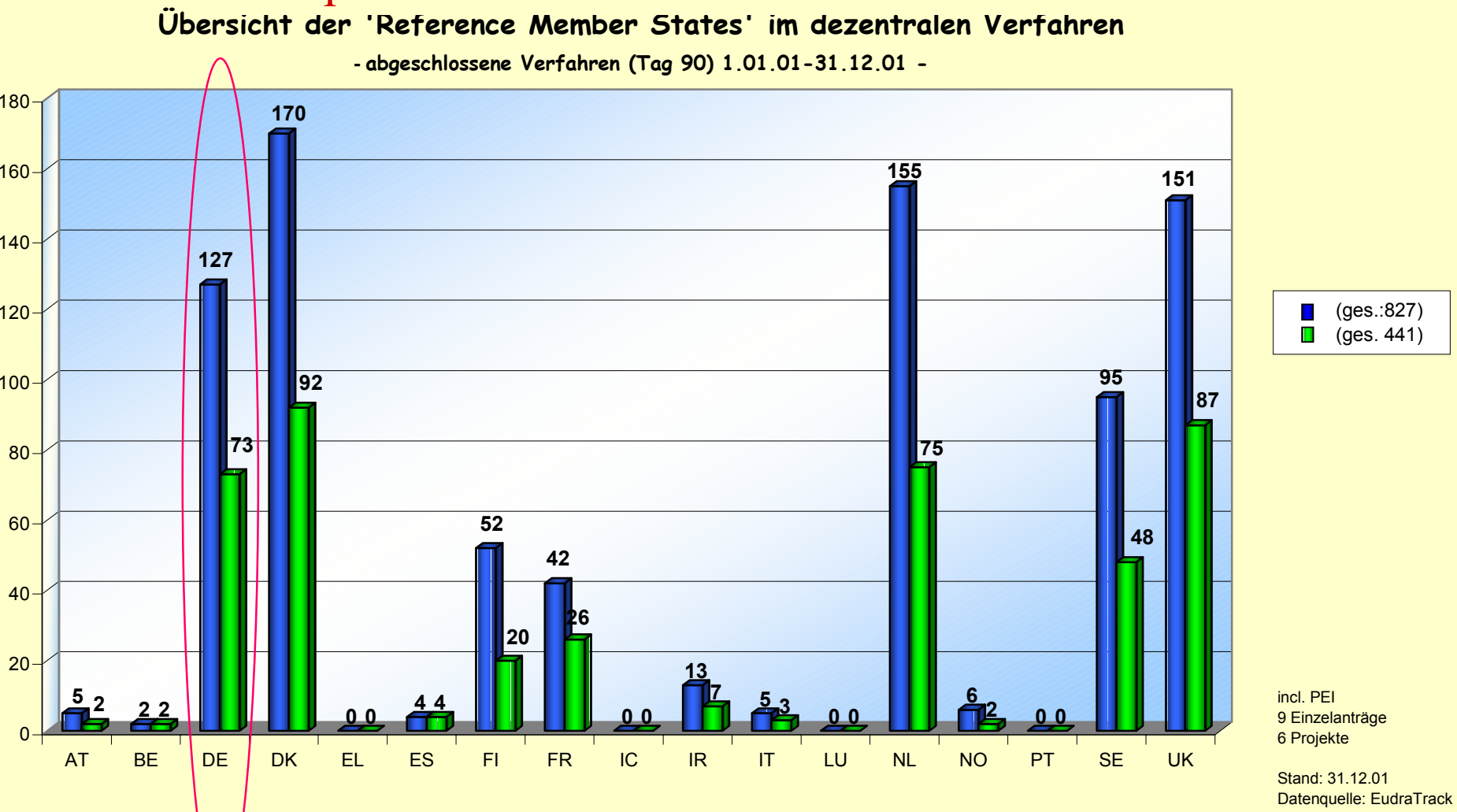
Distribution of scientific advice requests in 2000



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

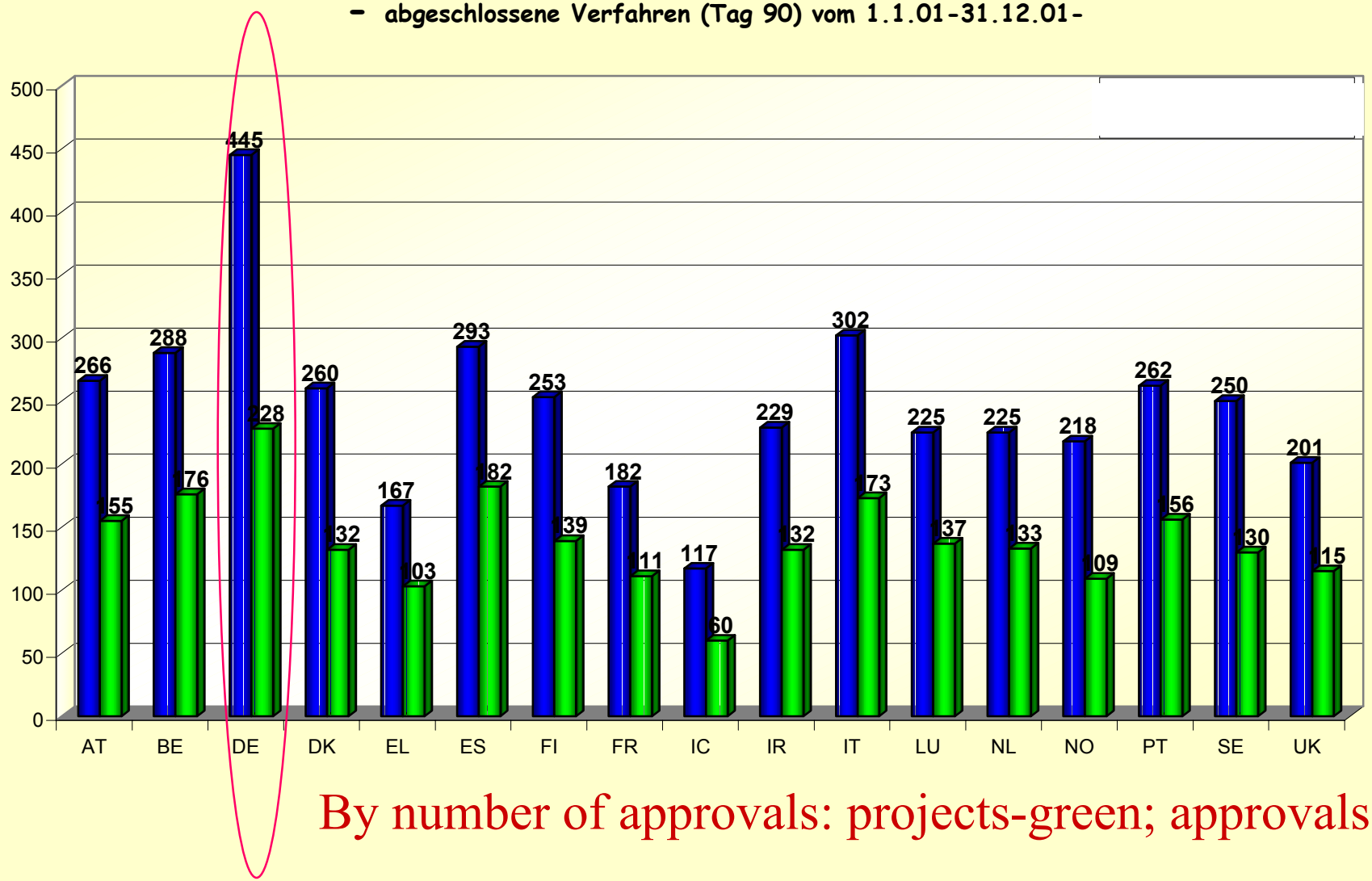


incl. PEI
9 Einzelanträge
6 Projekte

Stand: 31.12.01
Datenquelle: EudraTrack

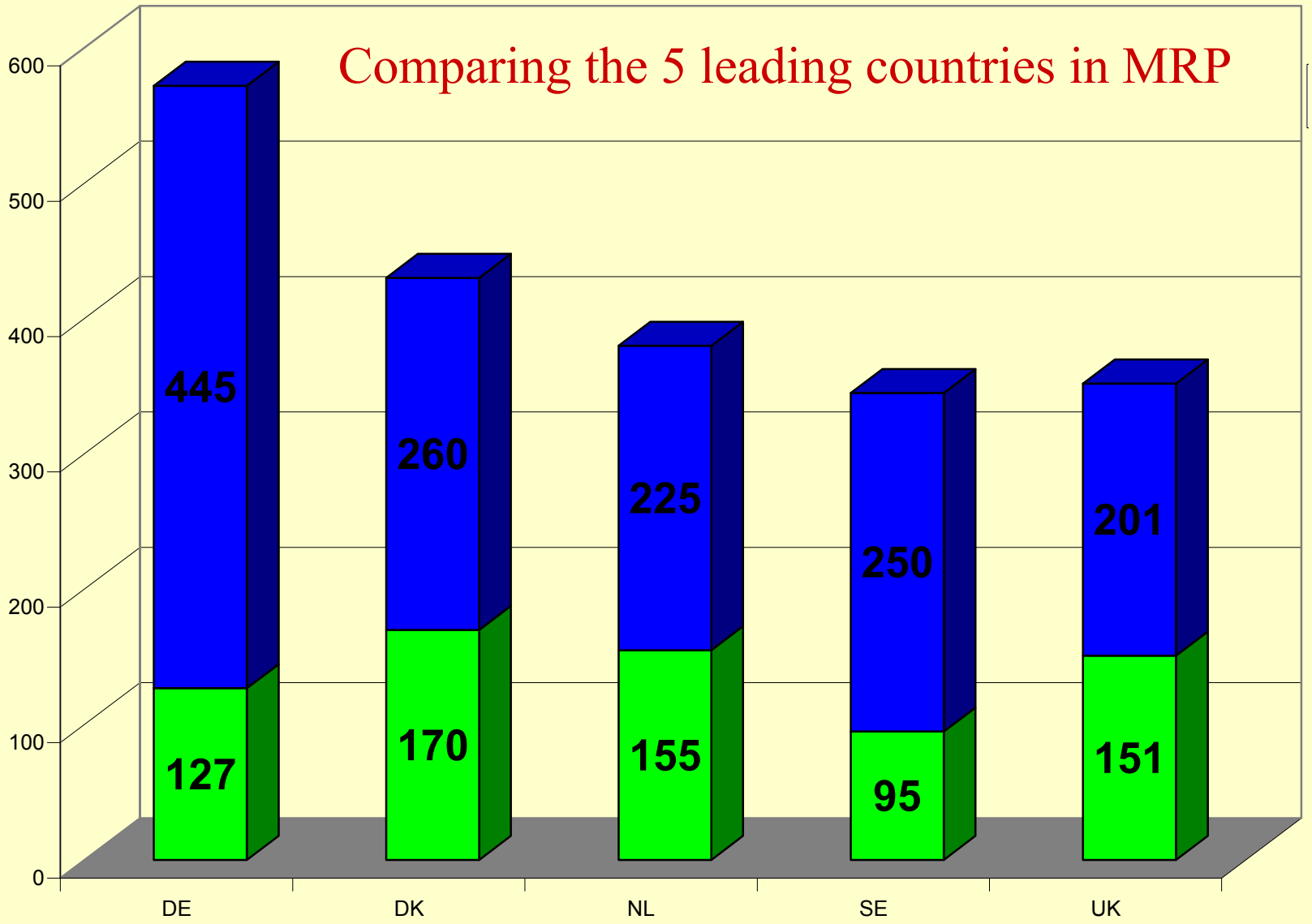
By number of approvals: projects-green; approvals-blue

Comparison of the countries in MRP 2001 CMS



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

Comparing the 5 leading countries in MRP



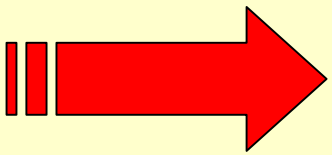
Gesamtanzahl Einzelanträge 1.1.01-31.12.01

827

incl. PEI
9 Einzelanträge RMS
4 Einzelanträge CMS

Stand: 31.12.01
Datenquelle: EudraTrack

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



Changes in

Directive 2309/93/EEC

centralised

Council Regulation (EEC) No. 2309/93 Annex

Part A - Biotechs

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 Committies in accordance with Directive 2309/93/EEC

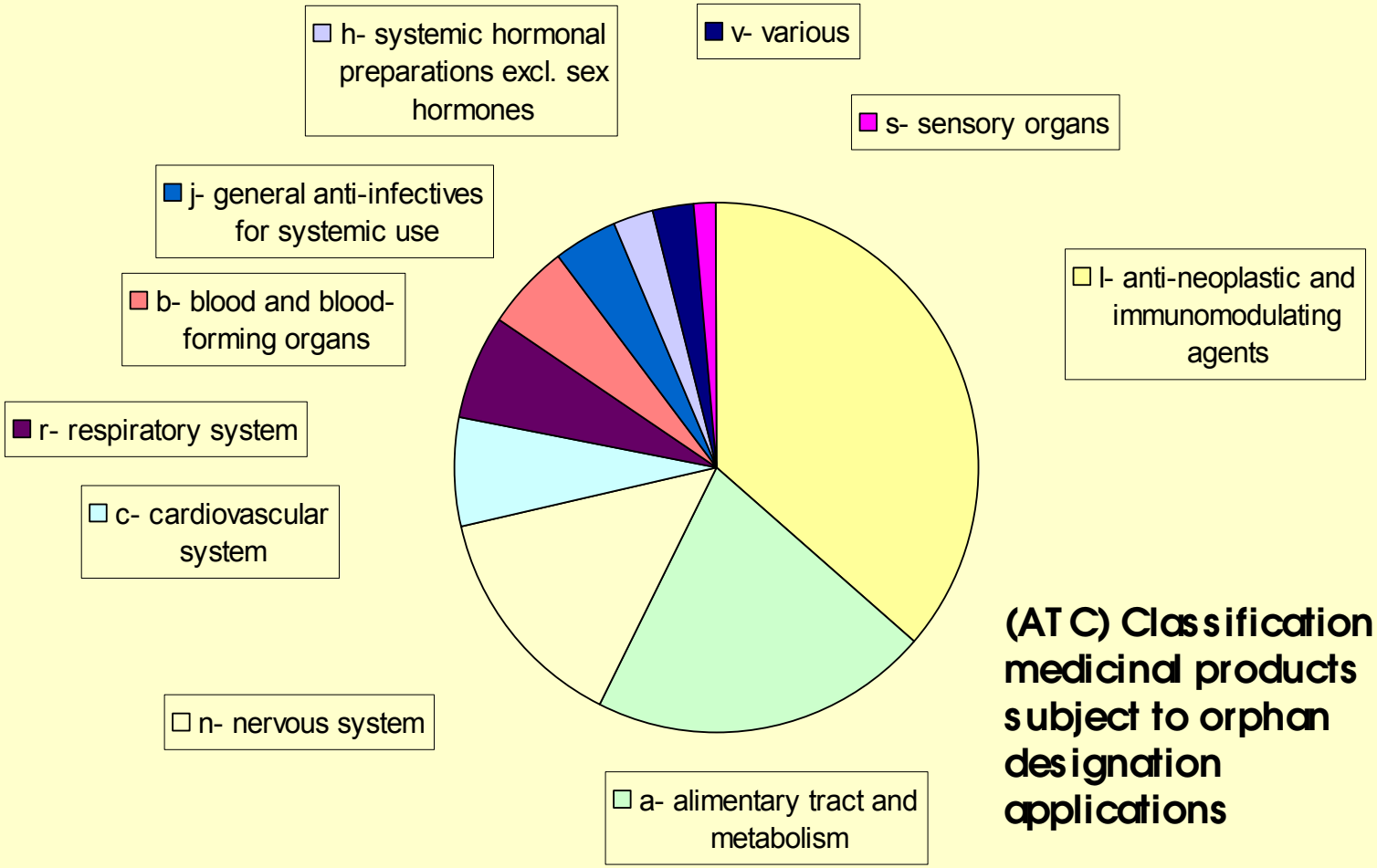
- CPMP "renamed" to Committee for Human Medicinal Products

  Only one representative per Member State

- Committee on Orphan Medicinal Products

- Committee on Herbal Medicinal Products
  one representative per Member State

Orphan Medicinal Products in the EU



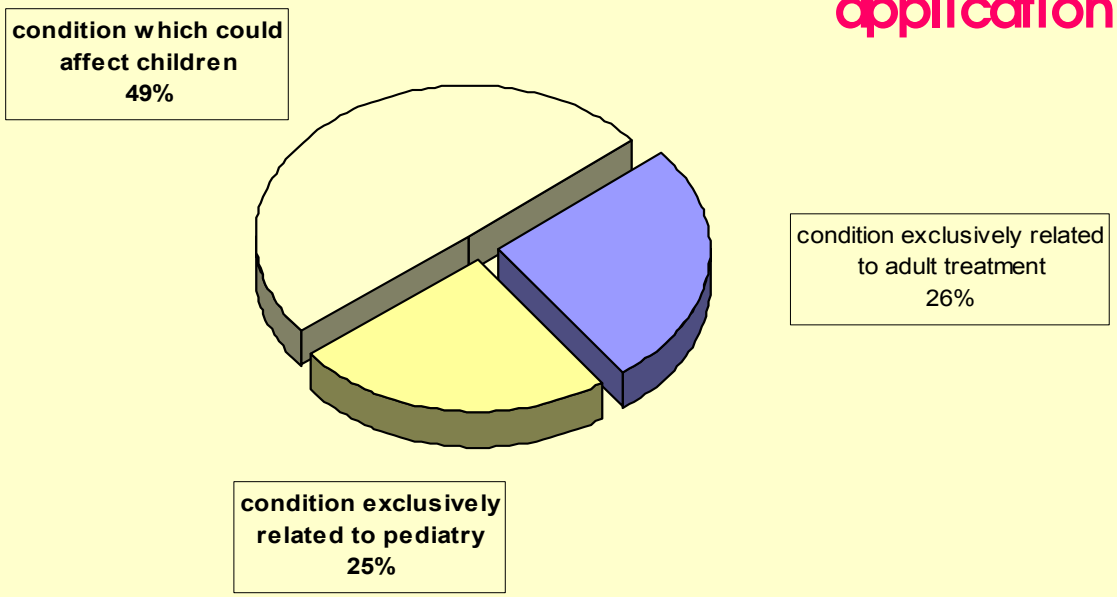
(ATC) Classification of medicinal products subject to orphan designation applications

March 2001

Orphan Medicinal Products in the EU

Status March 2001

Children and orphan designation applications



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

Members of the Management Board :

4 members from the Member States,

4 members from the EU Commission,

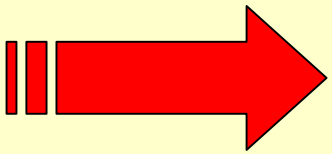
4 members from the European Parliament,

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

Heads of Agencies as Advisory Board

one representative per National Authority

'New'

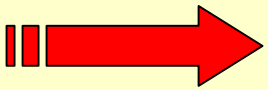


Directive 2001/83/EEC

= combination of all existing Directives

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

Directive 2001/83/EEC



Mutual Recognition Procedure

Decentralised 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 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

As an example : The great challenge "Harmonis/zation of Summary of Product Characteristics"

Article 10 75/319/EEC
Procedure for individual drugs

Article 11 75/319/EEC
Procedure for originator

Article 12 75/319/EEC
Procedure for "active substances"

Article 11

- **When?**

  Different national decisions on the drug

- **Why?**

  Harmonisation of national decisions

- **Who starts ?**

  Member States, EU Commission, applicant/holder of author.

- **Who is concerned ?**

  the drug

  applicant/holder of authorisation

  the reference drug

  Member States with existing authorisations

  Member States with withdrawn/suspended authorisations

Follow-up after Community Referral
Article 11

- **How ?**

The procedure harmonises the "Summary of Product Characteristics" especially Parts III and IV of the Dossier (pharm-tox, clinical)

Not Part II, Quality. This part of the SPC can remain unharmonised

However, the authorisation holder is seriously advised to harmonise voluntarily or to file the Quality Dossier as a 'European Dossier'

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
  - "some" 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**

Drugs in Germany

- big (German-speaking) market (~ 100 million)

- 60,000 approved drugs with :
- ~ 1000 usable "example"- approvals
- ~ 10,000 "freshly" appr. "old products" ("Nachzulassung“)
- ~ 20,000 MRP-ready defined approvals

- big market for homeophatics and herbals

- important medium-sized (co-operative) companies

- tradition in precision and exactness

- all global players in the market

Situation

- old market workload until 31 December 2005
- strict national regulations (AMG)
- well established court law
- strong (lobbying) trade associations
- need for equal treatment of appr.
- no pricing negotiations within approval procedure

Actions taken

- electronic application (partly) ("Einreichungsverordnung")
- many internal (partly public) databases for appr. drugs
- "electronic" marketing authorisation (in progress)

- use of "pattern" approvals for known drugs
- developing new database vigilance systems
- SOPs on nearly all topics

Chances for co-operation

- exchange and education of experts in co-op. with PEI via DGRA
- access to our databases
- exchange of Assessment Reports
- knowledge on "how to handle old products"
- "better understanding" by way of "cultural closeness"
- country-specific co-operation

Thank you for your attention