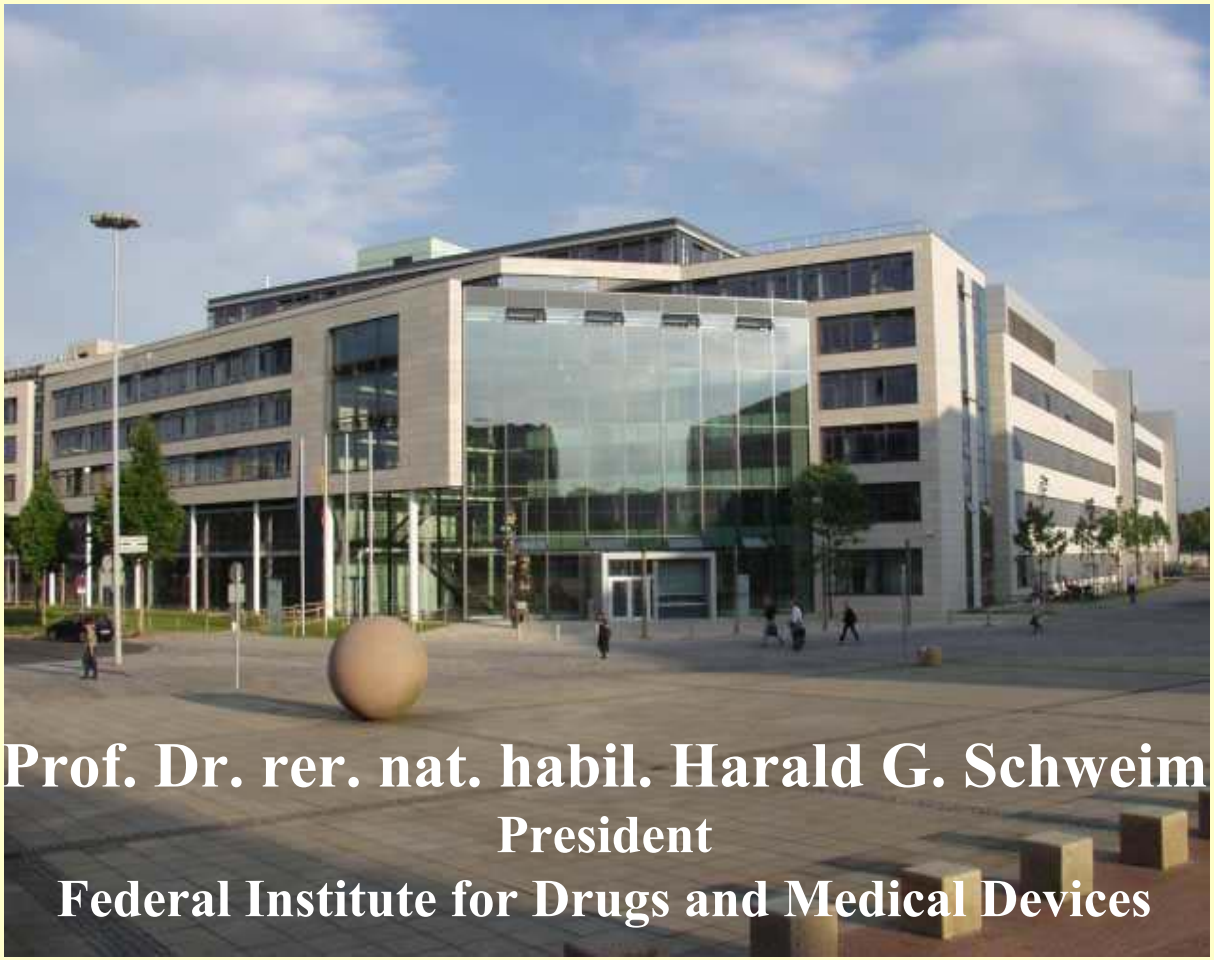
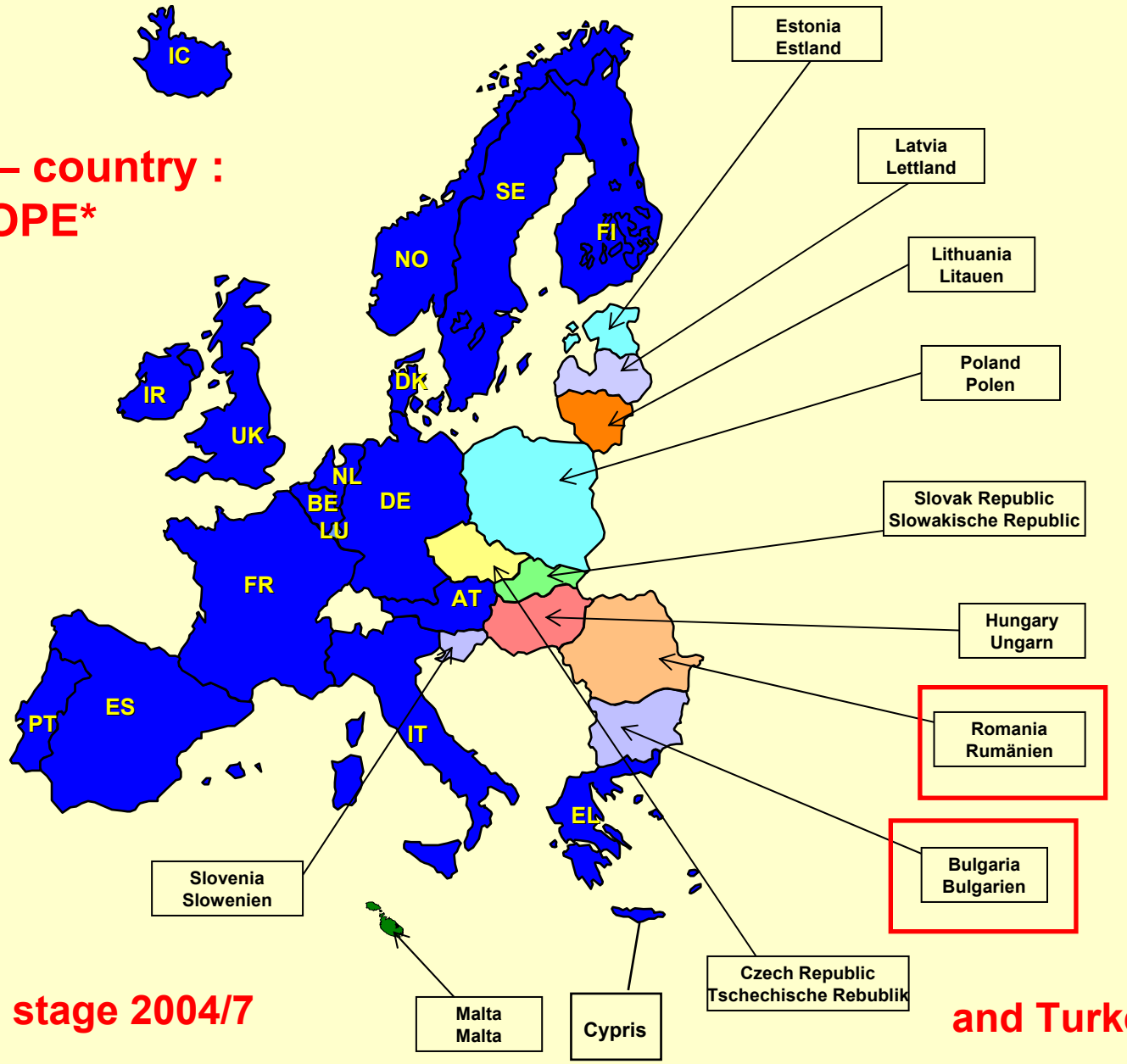
BfArM
Bundesinstitut für Arzneimittel

Das BfArM im System der europäischen Zulassungsverfahren



Prof. Dr. rer. nat. habil. Harald G. Schweim
President
Federal Institute for Drugs and Medical Devices

my home – country : EUROPE*



*Intermediate stage 2004/7

and Turkey ?

Drugs in Germany I

- big (German-speaking) market (~ 100 Mio. people)

- 60,000 approved drugs with :
- ~ 1000 usable approvals with standardised master texts ("Muster")
- ~ 10,000 "freshly" appr. "old products" ("Nachzulassung")
- ~ 20,000 MRP-ready approvals (Assessment Reports)

- big market for homeophatics and herbals

- important medium-sized (and cooperative !) companies

- tradition in precision and exactness

- all global players in the market

Drugs in Germany II

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

Drugs in Germany III

- partly electronic application obligatory ("Einreichungsverordnung")
- many internal (partly public) databases for approved drugs
- "electronic" marketing authorisation (in progress)
- broad use of standardised master text ("Muster") approvals for known drugs
- developing new database vigilance systems
- SOPs on nearly all topics in Regulatory Affairs
- Very active scientific regulatory affairs society (DGRA)

Approval of Drugs in Germany

regulatory framework

Directive 2001/83/EEC = Codification (65/65/EEC; 75/319/EEC; 92/27/EEC) Title II Article 2 and 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

Staff at BfArM (05/01/02)

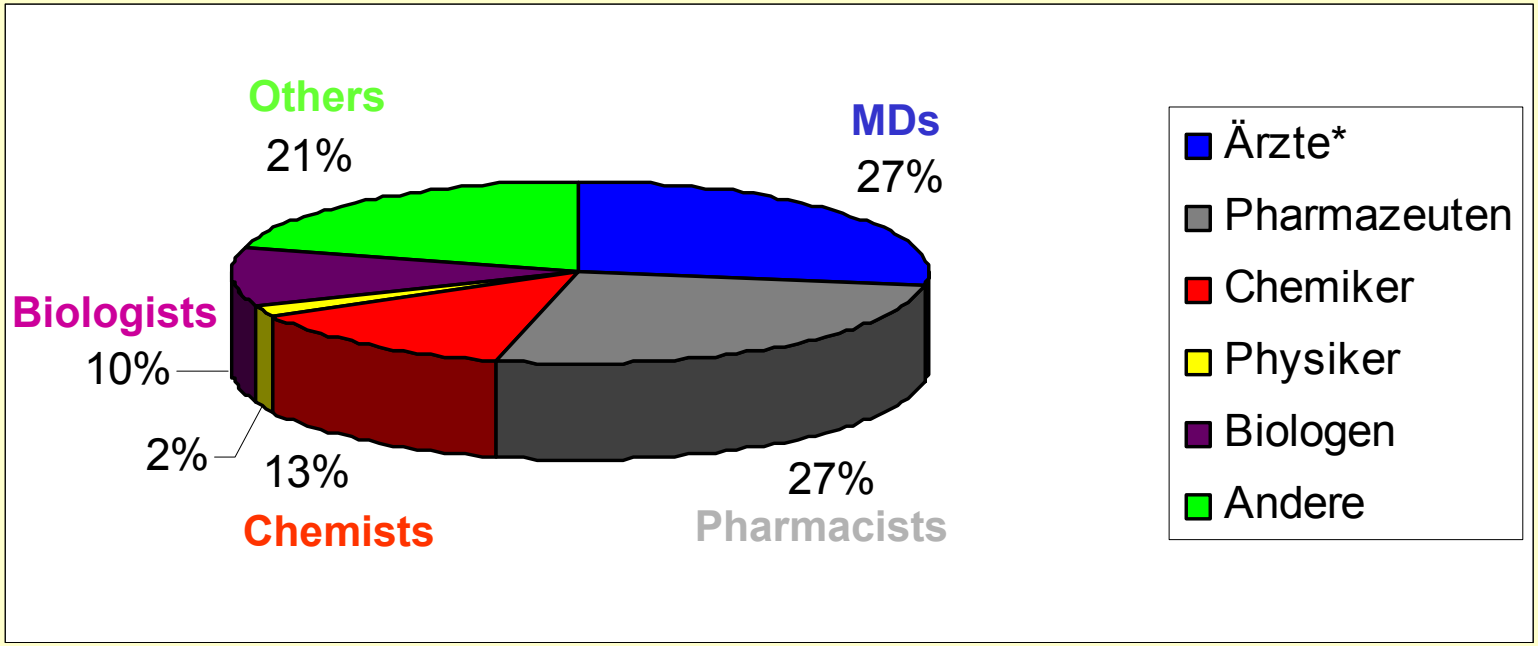
965 Employees;

630 thereof female and 335 male;

695 thereof in scientific Dep./270 in administrative Dep.;

342 thereof scientists;

184 thereof female and 158 male



BfArM – European Workload 1995 to 2002

- **Centralised Procedure (incl. Line-extension)**

Number	BfArM as (Co)Rapp	
368	54	(ca. 16 %)

- **Mutual Recognition**

Number	as RMS
Projects: 1877	Projects: 258
Single: 3562	Single: 466
	as CMS 1362

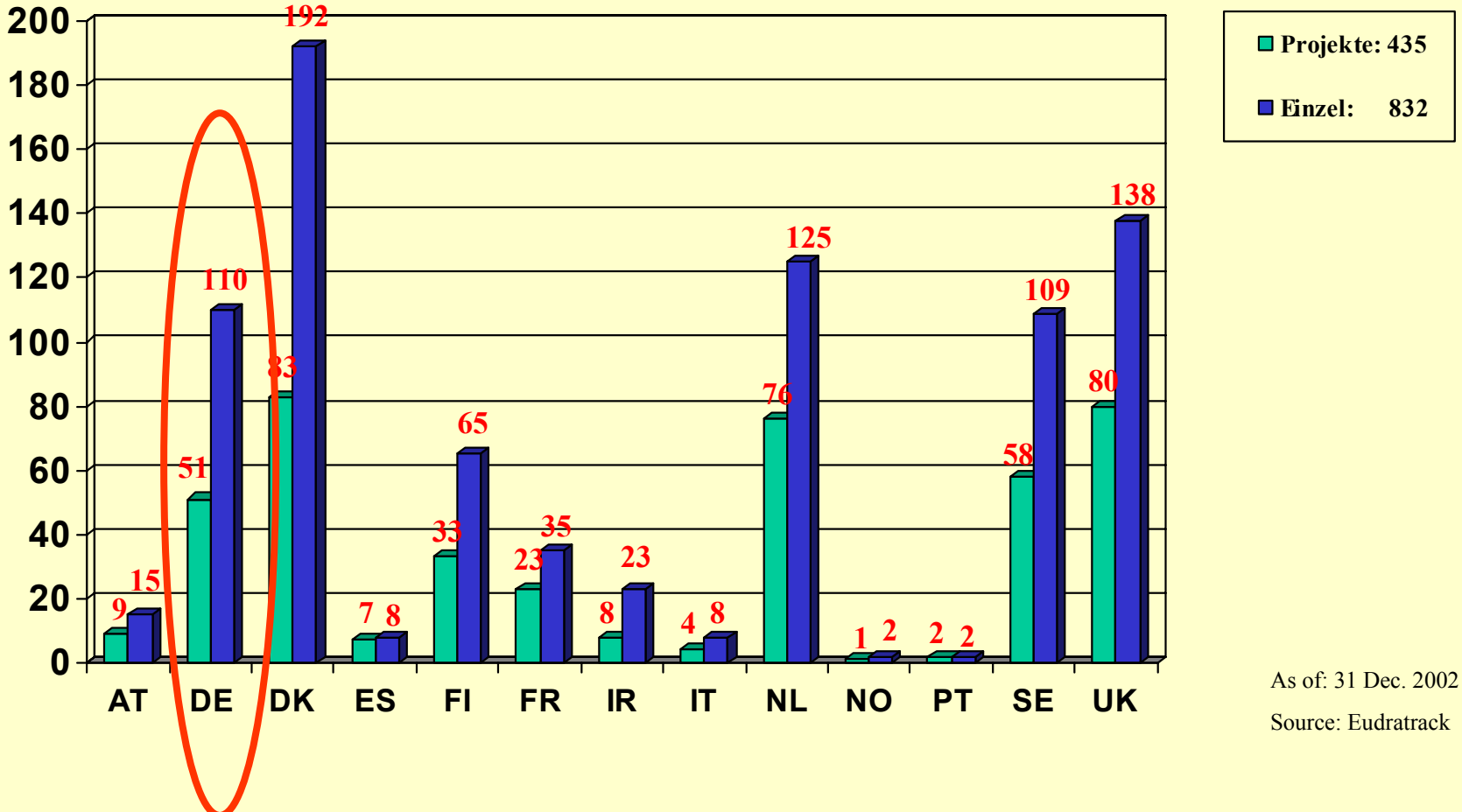
DE holds rank 4 of RMS countries (2002)

DE (together with SE) leading in the licensing of new substances in MR-Procedures

DE is concerned in more than 50% of all procedures and thus has the most MR licenses in Europe

Overview of Reference Member States in Decentralised Procedures

- completed procedures (Day 90) 1 January 2002 until 31 December 2002 -

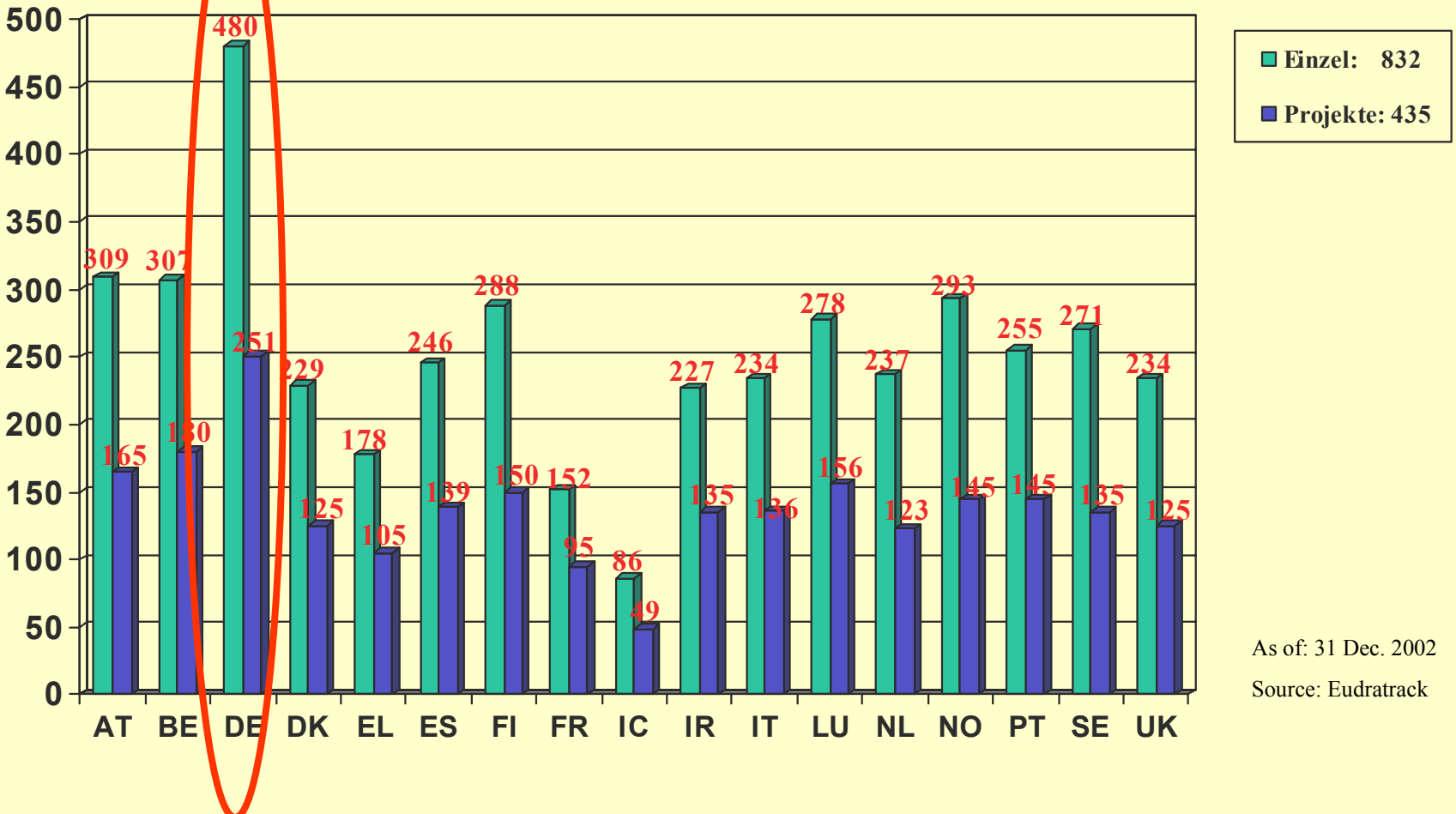


As of: 31 Dec. 2002

Source: Eudratrack

Overview of Concerned Member States in Decentralised Procedures

- completed procedures (Day 90) 1 January 2002 until 31 December 2002 -



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Source: Eudratrack

Proposals of the Commission

- Centralised or decentralised – now in balance* ?
- Mutual Recognition Committee – composition ?
- Empowerment of the Mutual Recognition Procedure
- One renewal after 5 years (?)
- "Pre-approval" pharmacovigilance ??
- "Better regulation" ?
- However, lacking definitions on:
  - NCE
  - Public health
    - Serious risk to public health

* New Commission proposal will follow a little later

Most Important Aspects of the Review for Us:

- Streamlining of Committees (number of members; process of selection; responsibility)
- Scope for centralised / decentralised procedures
- Importance of clear definitions (next slide)
- Renewal versus pharmacovigilance (following)

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 Commission agenda, but within which time frame ?

centralised

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

new drugs for: AIDS, oncology diabetes &

neuro-vegetative diseases (e.g. Alzheimer's)

obligatorily CENTRALISED

decentralised

Generics

centralised and decentralised

line-extension

national

FOR ONE MEMBER STATE ONLY;

bibliographic approval;

Future of national procedures ?

- abolishment of new substances in national procedures ?

  and how to keep scientific knowledge ??

- abolishment of renewal procedure ?

  and then what about outdated claims ??

  we recomend renewals all 10 (8) years

Deficits due to Centralisation/Globalisation of Product Development + Maintenance

- Loss of national identification for:
  - academic research
  - product development
  - licensing system
  - marketing/product maintenance
  - drug safety

Deficits due to Centralisation-(**ONLY**) of Licensing Procedures

- Medium-sized companies' development of innovative products is inhibited by

  in-house bundling of capacities
  for processing of centralised procedures

  in-house costs for pursuing centralised procedures
  fees for centralised procedures

It‘s necessary for companies to have (as free as possible) choice of access to market

Possible Development I (Risks)

- Shift from national + decentralised procedures to centralised procedures
- Increase in monopolisation of licensing systems
- Decrease in competition
- Decrease in national identification with products
- Shifting of decisions from national to centralised anonymous EU authorities

Development II (Advantages)

- Common market
- Quality of supply with medicinal products of a consistently high European standard
- Uniform regulatory system
- Transparency
- Orientation for consumer and patient

But Pharmacovigilance always stays a national responsibility !!

Agencies Have to Define Their Position for the Future:

- Team leader and/or opinion leader ?
- Centres of excellence for agencies or "full provider" ??
  - 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 ! (The Network-System !)

……otherwise ???

BfArM's Decisions for Contribution I

- "Full-provider"
- Scientific expertise
- Effective and efficient licensing system
- Customer orientation
- Scientific co-operation with other regulatory authorities
- Fulfilment of European and international standards
- Development of a worldwide pharmacovigilance network

National Contribution II

- Co-operation in detecting counterfeit medicinal products
- Co-operation in the field of inspections
- Development of a European strategy for consumer information
- Developments in "off-label use", "orphan drugs", and "fast-track drugs“
- We want to be part of the european network

Optimisation of European Procedures

- Excellent national and EU scientific advice
- High scientific level expertise
- Bridging of national / EU risk management
- Contribution to European pharmaceuticals market :

  Qualified "Nachzulassung" in the CC
- Quality / quality assurance
- Fast access to important drugs for all Europeans

Importance of European Procedures - Future

Regulation of access to Centralised/Mutual Recognition Procedures

Balance between Centralised and Mutual Recognition Procedures

- **For 2003, only few (22+16 orphans*) new substances can be expected within the Centralised Procedure. What is the EMEA's future? (costs ? , fees ?, 240 employees must be paid !)**
  - **Therapeutic advisory groups as "European FDA starting point"??**
  - **Variations Type IA (and some Type IB) to be handled by EMEA ??**

"An open door may tempt a saint"

*** source: EMEA/MB/057/02/en/Final**

Our Proposal for the Future European System

"Premium products" (innovative) ➡ centralised

centralised procedure focussed on AIDS, cancer, neuro-deg. diseases and

therapeutic innovations, technologies

new therapeutic principles

"Bread-and-butter products" ➡ mutual recogn./national

known* biotechnological products (e.g. insulins)

known chemical substances and combinations thereof

other new substances and generics

"former*" innovative classes of products

"important" herbals

* Only " Diamonds are forever ! "

Fulfilment of the EMEA Tasks ("Secretariate" !)

++	Co-ordination, project management
(+)	Platform for decision making
	(still possible after Court of Justice on OCs-3, anorectics, Capoten?)
+/-	Transparency, websites etc.
-	Archiving, documentation, data-bases (pending)
--	EUDRA xxx products (deficitary)
(+)	Success monitoring, cost-performance accounting, quality assurance
-	Personnel required per application (too much administration?)

Fulfilment of the Agency's Tasks ("Scientific Body" !)

+	Scientific evaluation (professional work = service for EMEA)
+	Experts in a stand-by mode
+	Implementation of the European idea in MR-Procedures
(+)	Translation of recognition into national licenses
-- !	Avoidance of double offers / double work

WHAT ? WHERE ?

- Expertise, co-coordination -- at home
- Co-operation -- on site (London, Brussels)
  - HoA, MRFG, MB, Ph-Com
  - CPMP, COMP,SciARG, ORGAM,WP's, ad hoc groups
  - “Topic Leader” of the BfArM at ICH:
  - eCTD; Quality; BIOTEC; SAFTEY; VIGILANCE
- Delegation
  - to Commission
  - to EMEA

Role and Tasks of the Agencies in the Future

to be clarified :

- **How to survive ?? (Especially small ones)**

- **Centre of excellence (EU and CC) ??**

  or "full provider" ??

BfArM‘s Proposed Solution

- **Cooperation on a network-basis**
- **Promotion of research and development via scientific expertise**
- **The lager ones as "full providers"**
- **The smaller ones as centres of excellence**
- **Cooperation within the procedures**

Frankfurter Rundschau of 8 May 2003 **Agency** **Industry**

Thank you for your kind attention

Use of Experts in BfArM

- BfArM as a large competent authority has many internal experts in the fields of
  - Regulatory affairs
  - Phamaceutical quality
  - Non-clinical issues
  - Clinical issues
  - Pharmacovigilance
- But wants (and practices) use of external experts from Candidate Countries

Experts in BfArM

- National procedures
  (Internal and external experts)
- Mutual recognition procedures
  (Internal experts*, external experts only in exceptional cases)
- Centralised procedures
  (Internal experts only*)

(* with the exception of CC colleagues)