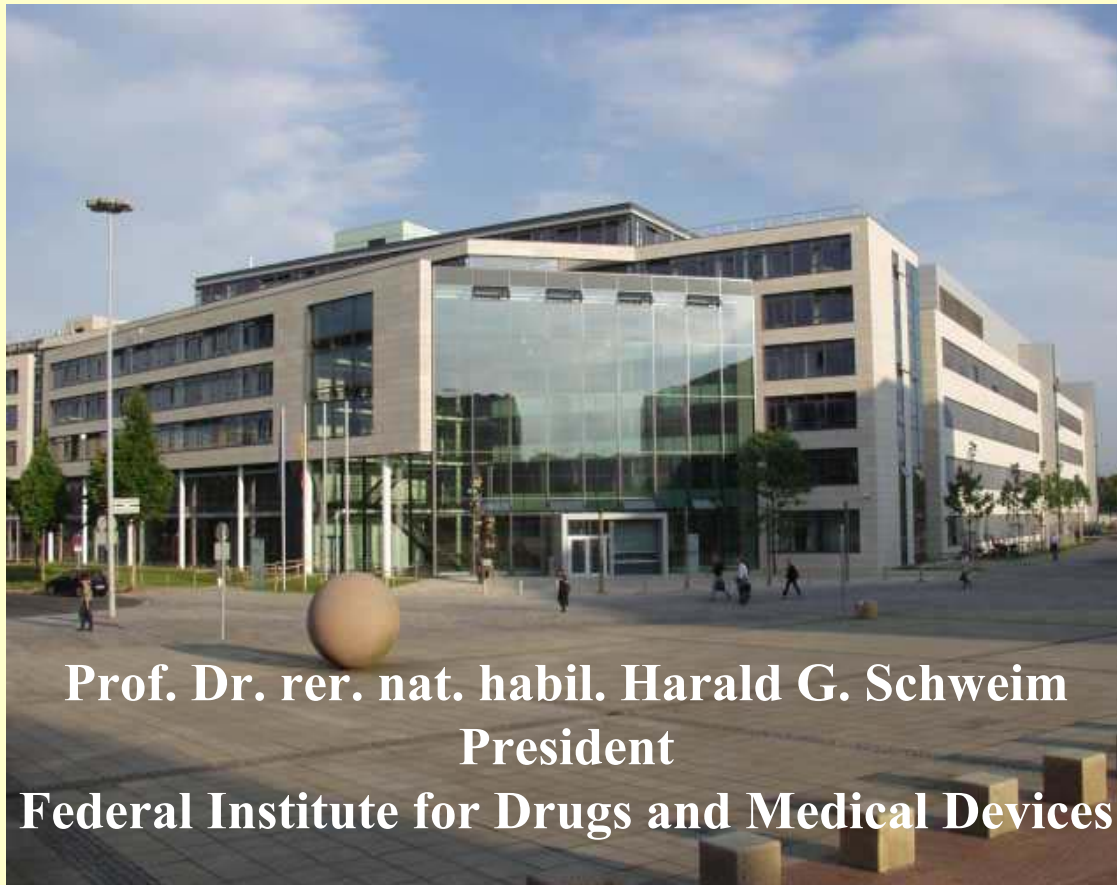


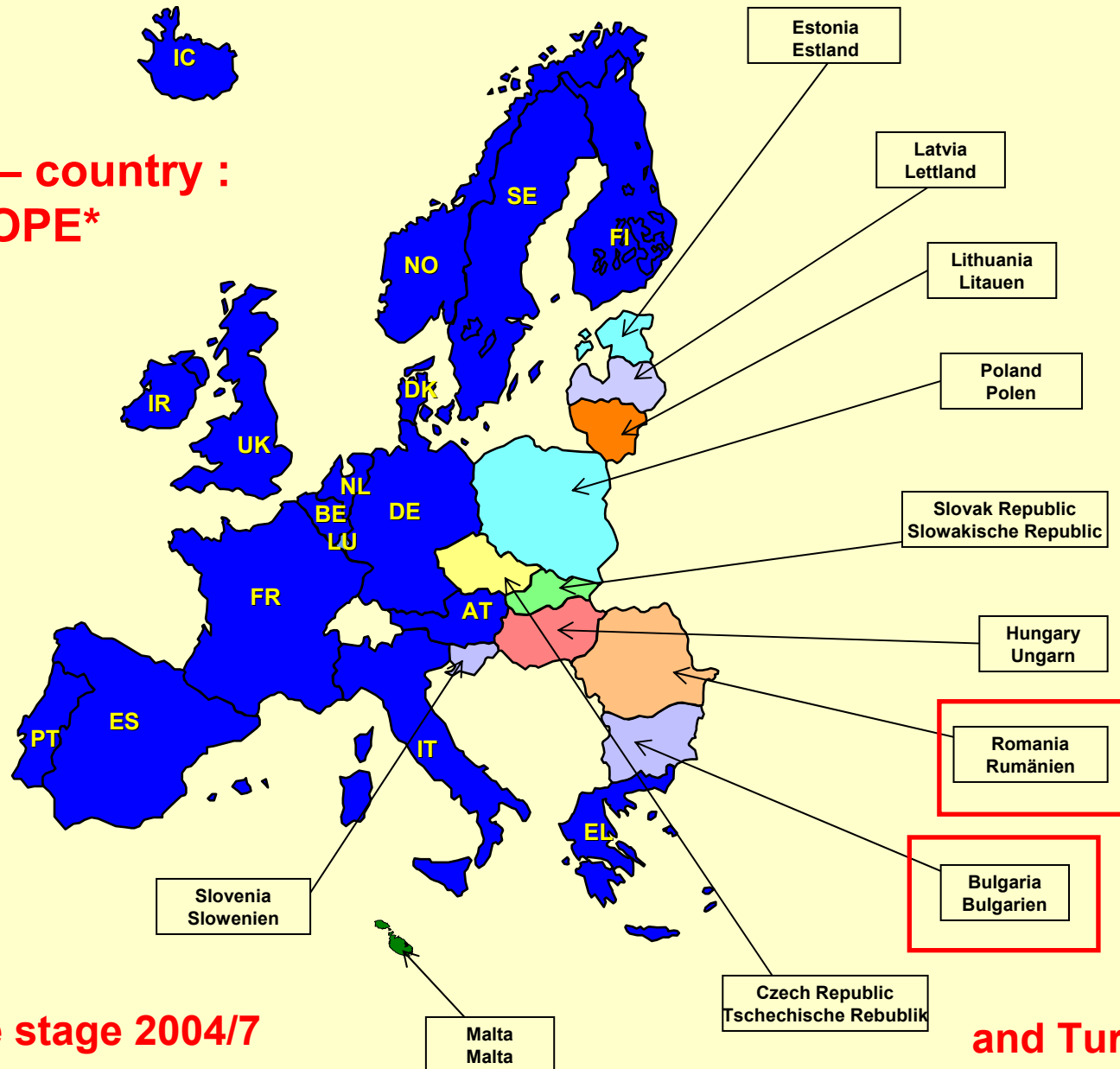
Reform des Zulassungssystems von Arzneimitteln und „enlargement“: Position des BfArM



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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 "example" approvals („Muster“)
 - ~ 10,000 "freshly" appr. "old products" ("Nachzulassung")
 - ~ 20,000 MRP-ready defined approvals (Assesment 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 "example" („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

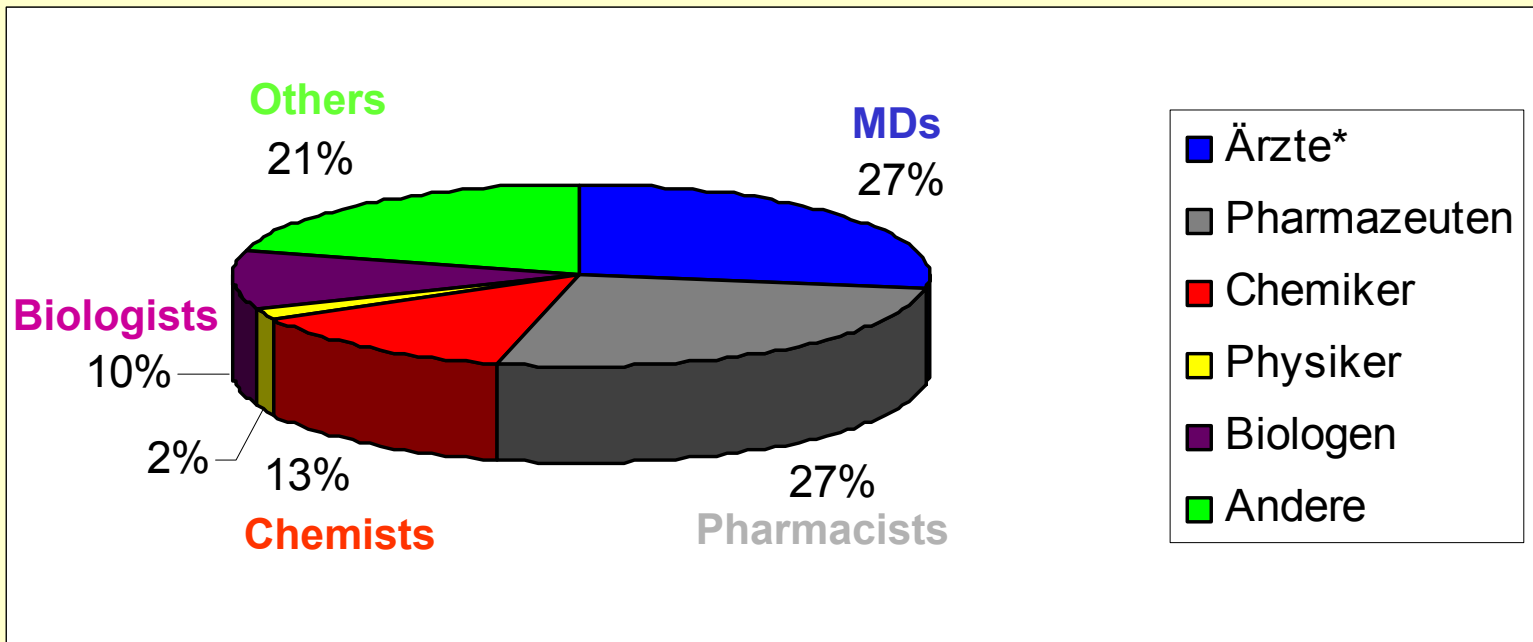
standard approvals according to § 36 AMG

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



Use of Experts in BfArM

- 1 -

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

Experts in BfArM

- 2 -

- 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)

BfArM – European Workload 1995 to 2002

<ul style="list-style-type: none"> • Centralised Procedure (incl. line extension) 	Number 368	BfArM as (Co)Rapp 54 (ca. 16 %)
<ul style="list-style-type: none"> • Mutual Recognition 	Number Projects: 1877 Single: 3562	as RMS Projects: 258 Single: 466 as CMS 1362

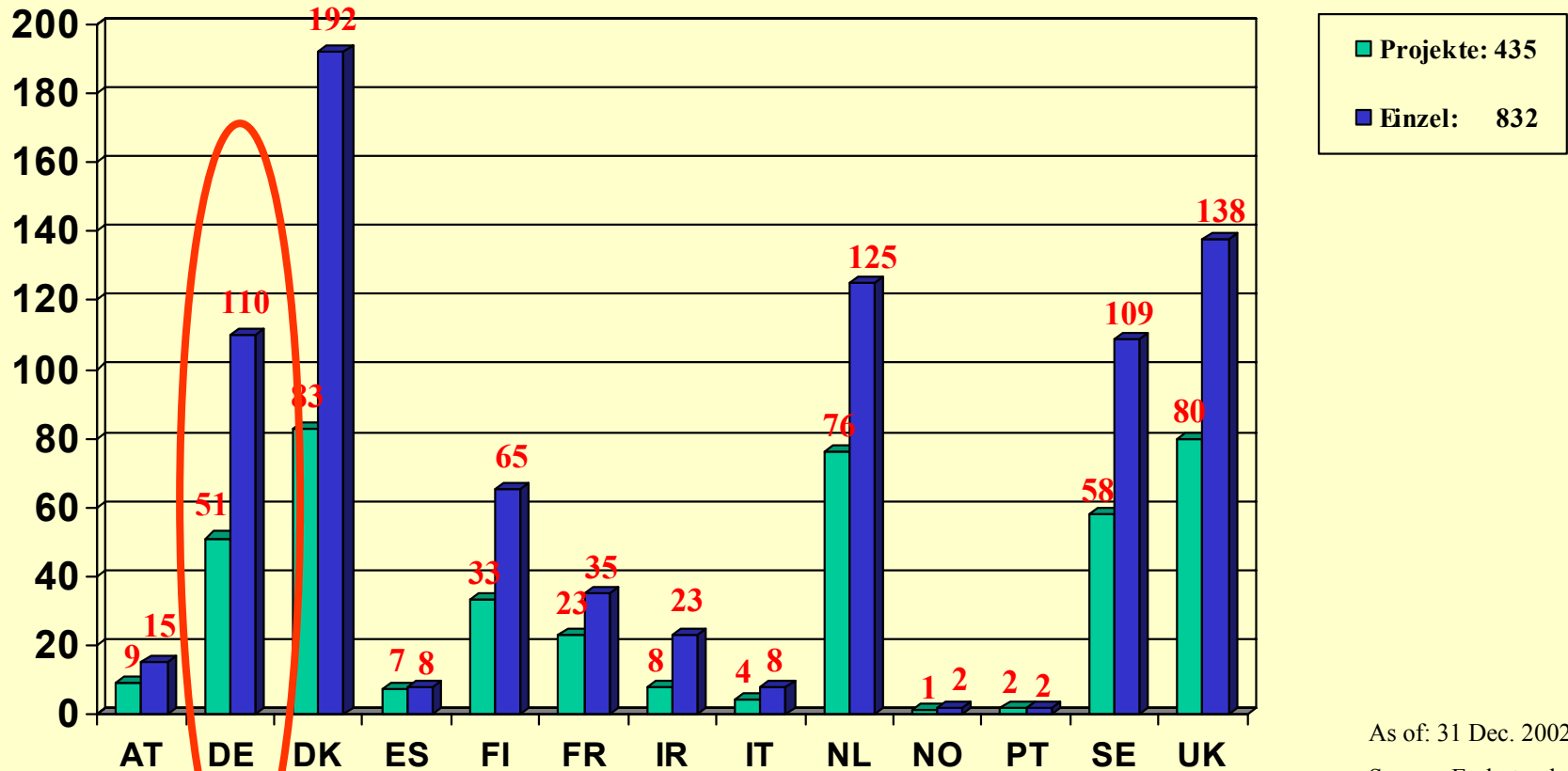
DE holds rank 4 of RMS countries (2002)

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 -

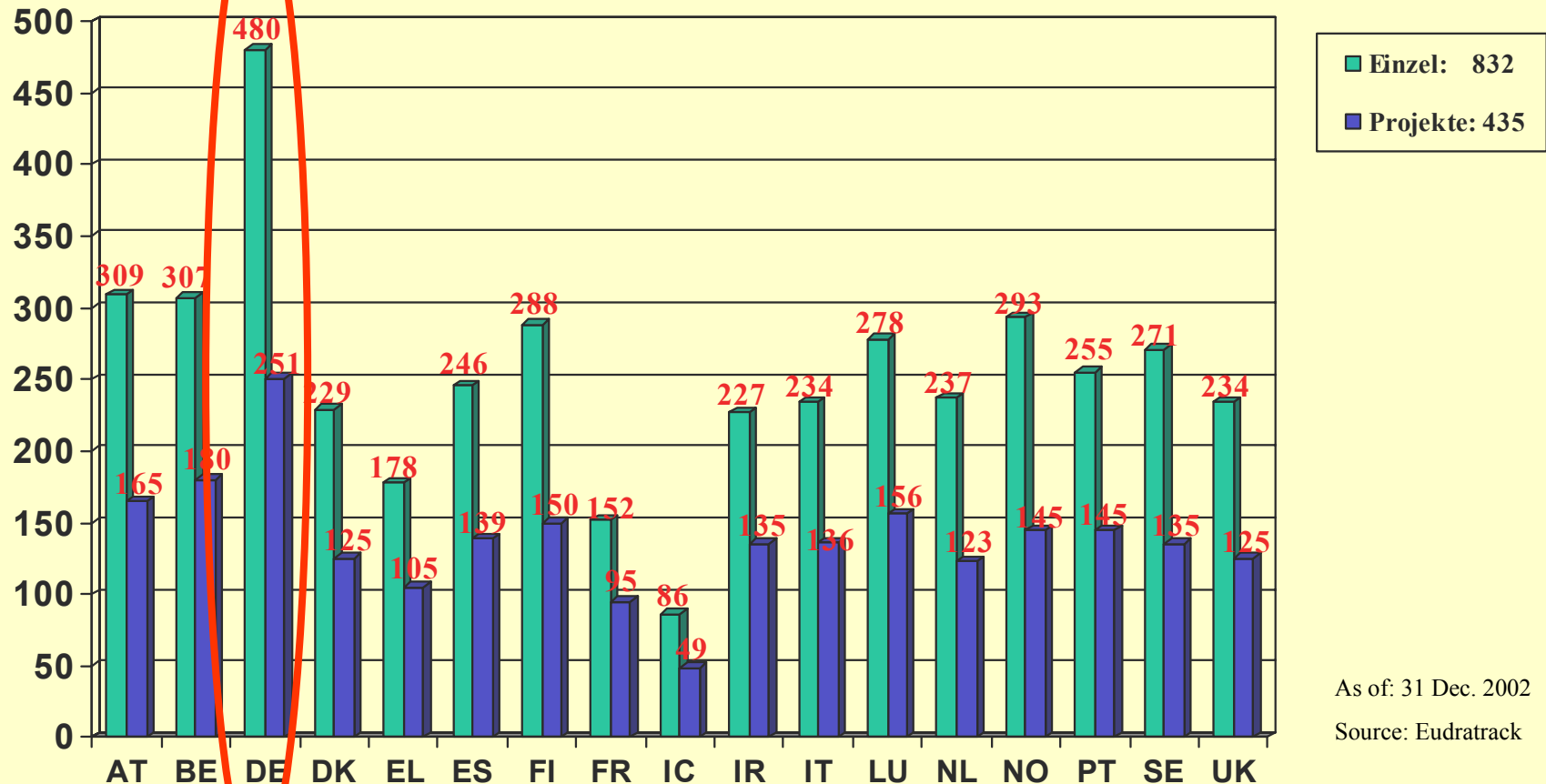


As of: 31 Dec. 2002

Source: Eudratrack

Overview of Concerned Member States in Decentralised Procedures

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



As of: 31 Dec. 2002

Source: Eudratrack

Proposals of the Commission

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

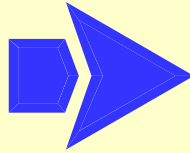
Most Important Aspects of the Review for Us:

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

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 , but time frame ?**

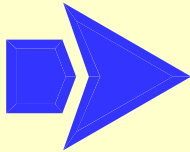
centralised



**Council Regulation (EEC) No. 2309/93 - Annex
new drugs **obligatorily (?)****

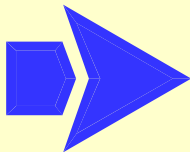
**CENTRALISED
(and who supports it really ?)**

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 (MR) procedures ?**
and how to keep scientific knowledge ??
- **abolishment of renewal procedure ?**
and then what about outdated claims ??

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

So it's absolutely 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 defined their Position for the Future:

- **Team leader or/and 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
- "Off-label use - ", "orphan drugs - ", "fast-track drug – development“
- 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
 - "Bread-and-butter products"  mutual recogn./national
 - "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 NCE need the MRP

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

Windows of Opportunity - Vision

CPMP as a trend-setter for pharmaceutical science

- **centralised procedure focussed on**
 - **therapeutic innovations, technologies,**
 - **new therapeutic principles**

national authorities ("better regulation") in MR-Procedures

- **known biotechnological products (e.g. insulins)**
- **known chemical substances and combinations thereof**
- **other new substances**

**Implementation and surveillance of consolidated opinions within the MRFG
outside the complex and elaborate Centralised Procedure**

Fulfilment of the EMEA Tasks („Sekretariat“ !)

- ++ 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 Agencies 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 CEEC) ??
or "full provider" ??**

BfArM's proposed Solution

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



Raubüberfall

Thank you for your kind attention

In Wirklichkeit würden die Ferkel ihrer Freundin Sai Mai nie etwas antun. Die Tigerin wurde nämlich selbst vier Monate lang von einem Schwein gesäugt, als sie noch ein Baby war.

ner Chance hatte dieser bedauernswerte bengalische Tiger, als er am Mittwoch von einer Bande blutrünstiger Banditen-Ferkel überwältigt wurde.



Task of DGRA