# DGRA – Annual Congress 2001

Bonn, 21 – 22 May 2001

# Future EU-Regulatory System

# Future Regulatory System

**Will Registrations of**

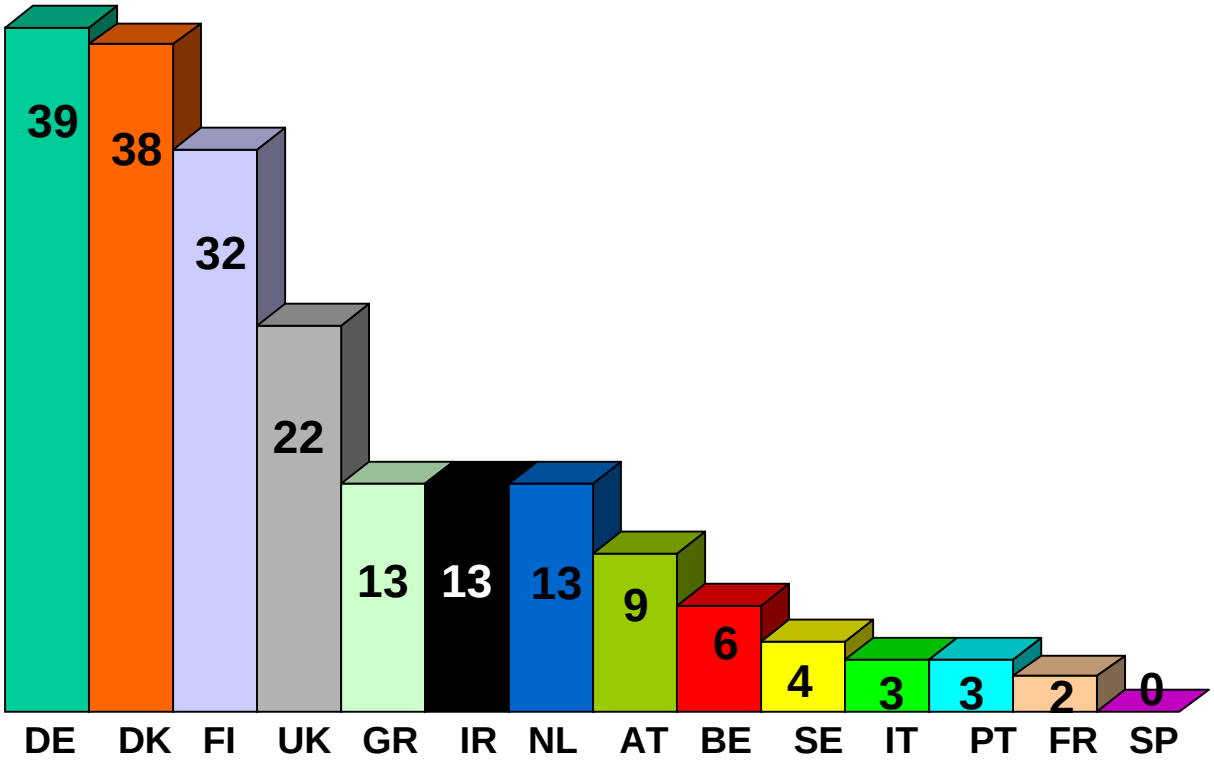
**Generic Medicines Benefit**

**from the**

**Future EU-Regulatory System ?**

# Current Situation

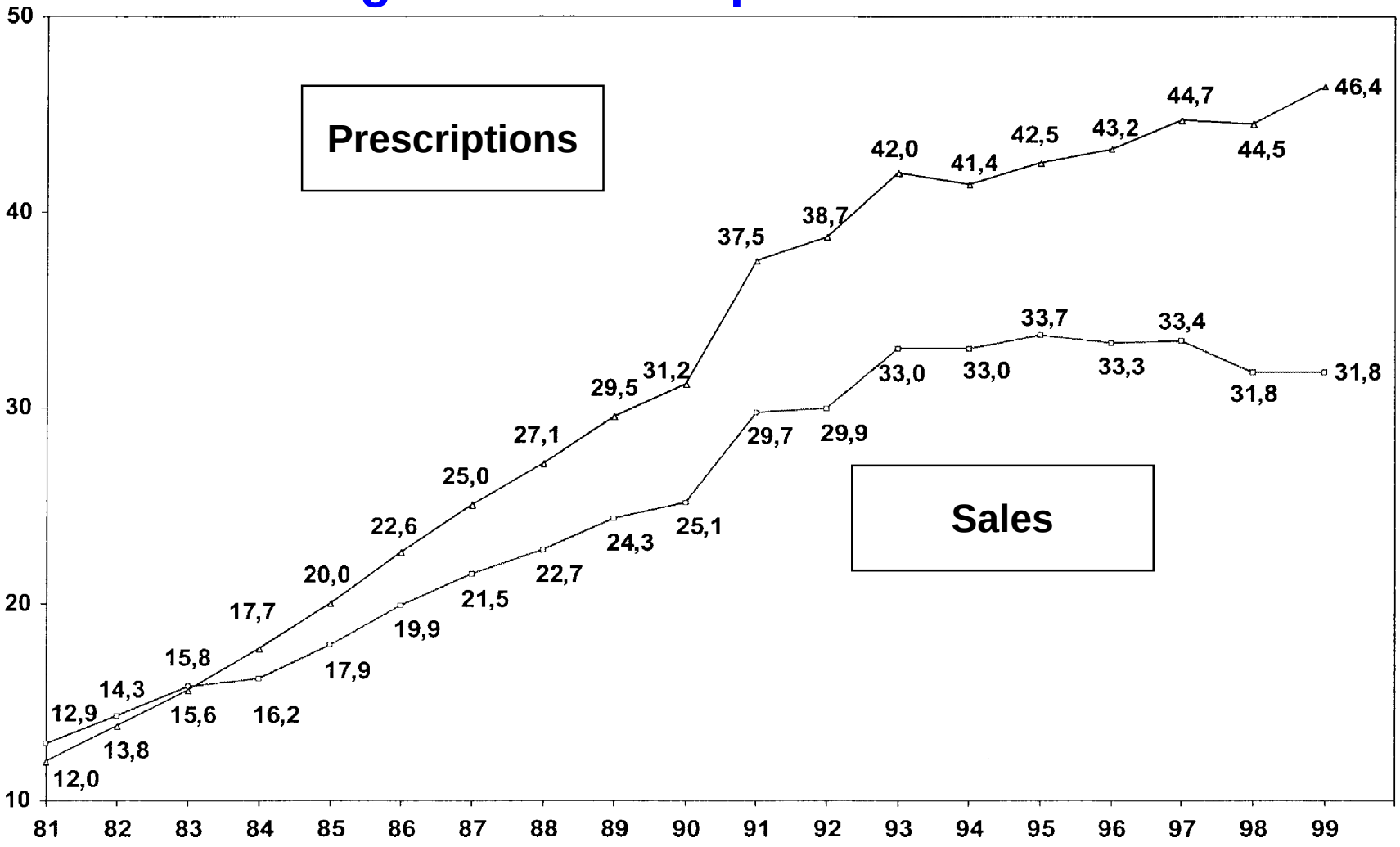
## Share of Generic Products in the EU Prescription Market 1997



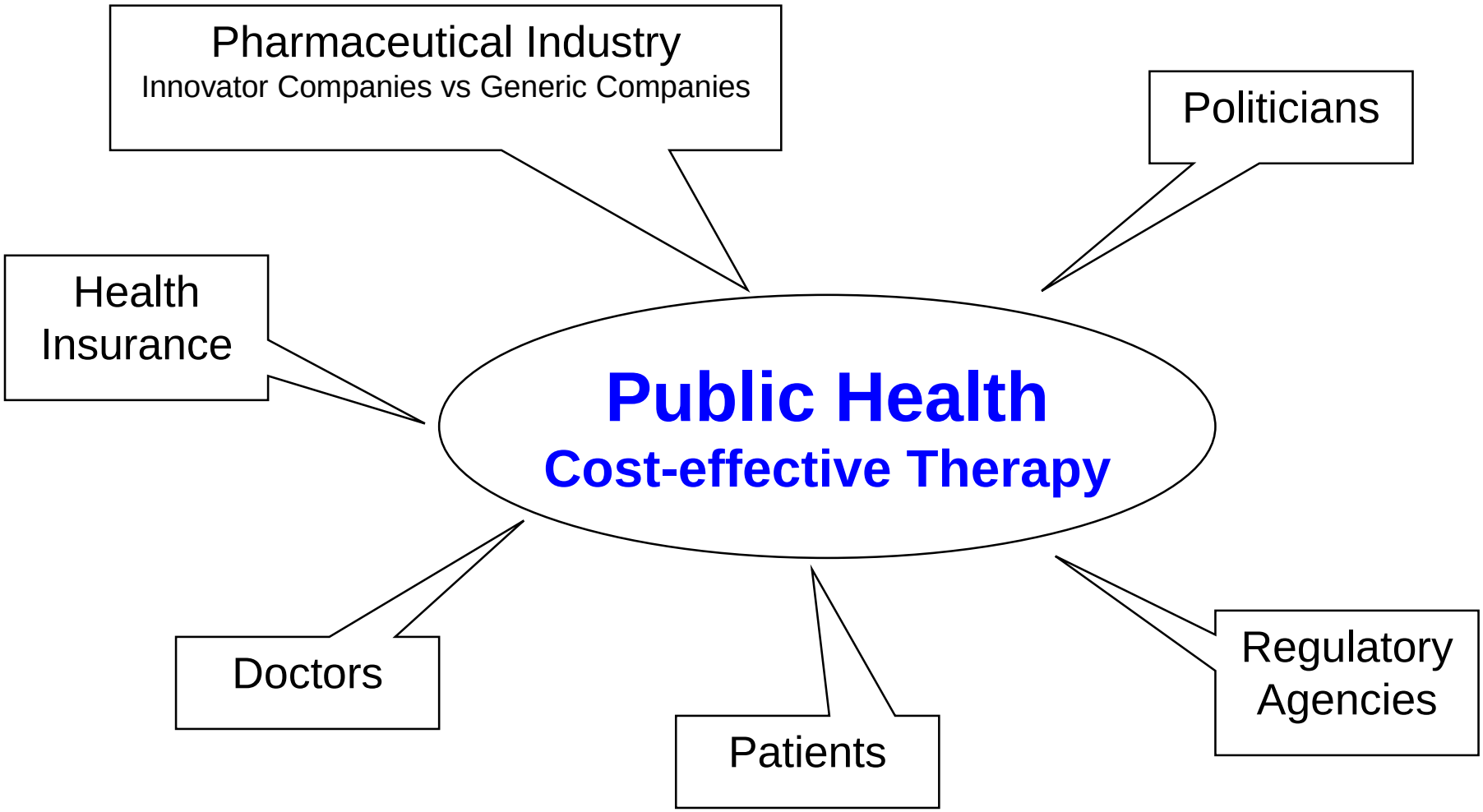

DE = Germany; DK = Denmark; FI = Finland; UK = Great Britain; GR = Greece; IR = Irland; NL = Netherlands; AT = Austria; BE = Belgium; SE = Sweden; IT = Italy, PT = Portugal; FR = France; SP = Spain

# Current Situation

## Share of Generics in Germany with Regard to Prescriptions and Sales



# Current Situation



# Political Support for Generics

- EU Member States dedicated to increasing the use of generic medicines. Access to medicine is critical issue for CEE region.
- The European Parliament has constantly called for measures to promote generics.
- The European Commission has committed itself to ensuring early access to the post patent market to generics.

# The New Legislation and Generic Medicines

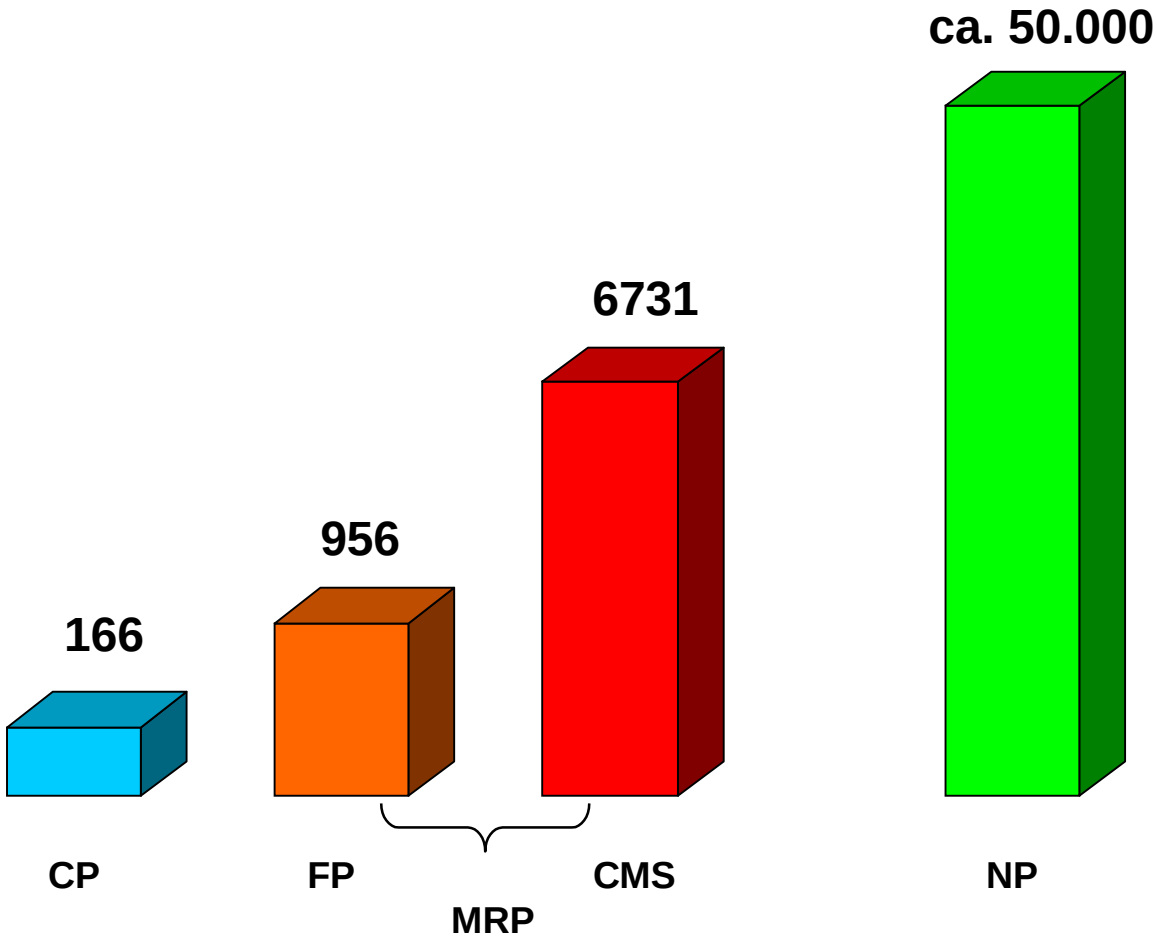
- Legislation should ensure that:

„*the licensing process for generic products operates speedily to ensure that consumers have access to lower priced generics as soon as possible after patent protection of the original product has expired*“

European Commission‘s Communication
on the Single Market in Pharmaceuticals, 25 November 1998

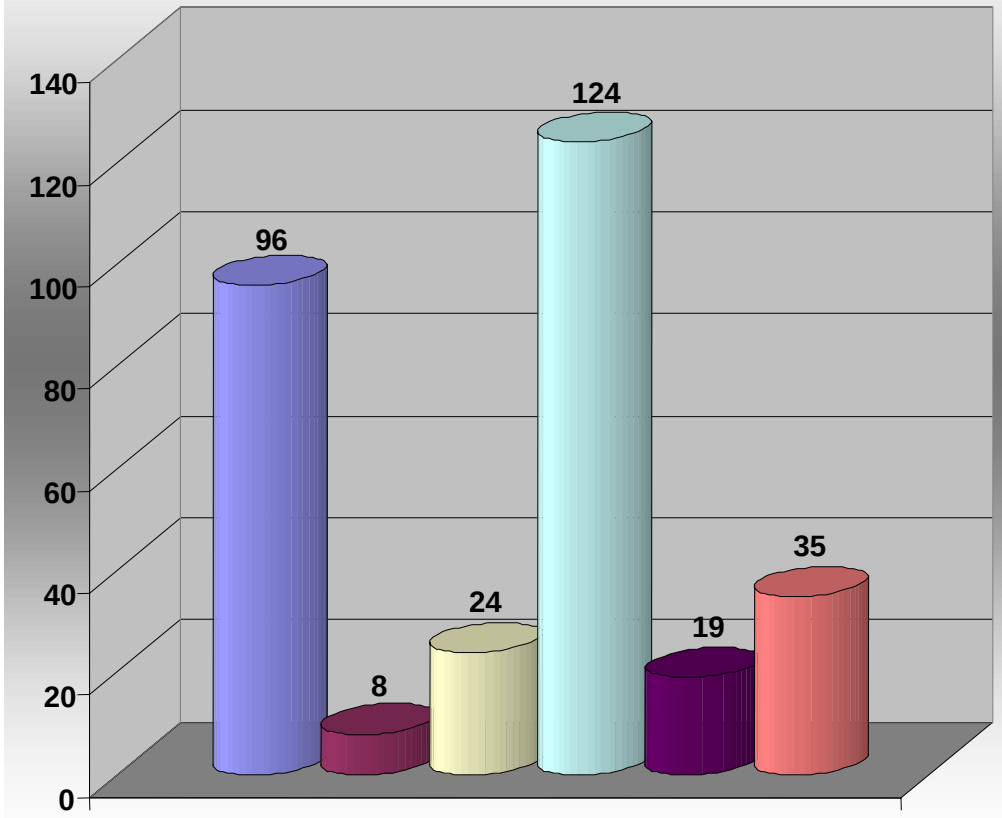
# Current Situation

## EU-Wide Authorised Medicinal Products 1995 - 2000




CP = Centralised Procedures NP = National Procedure CMS = Concerned Member States
FP = Finalized Procedures MRP = Mutual recognition procedure

# Mutual Recognition Procedure

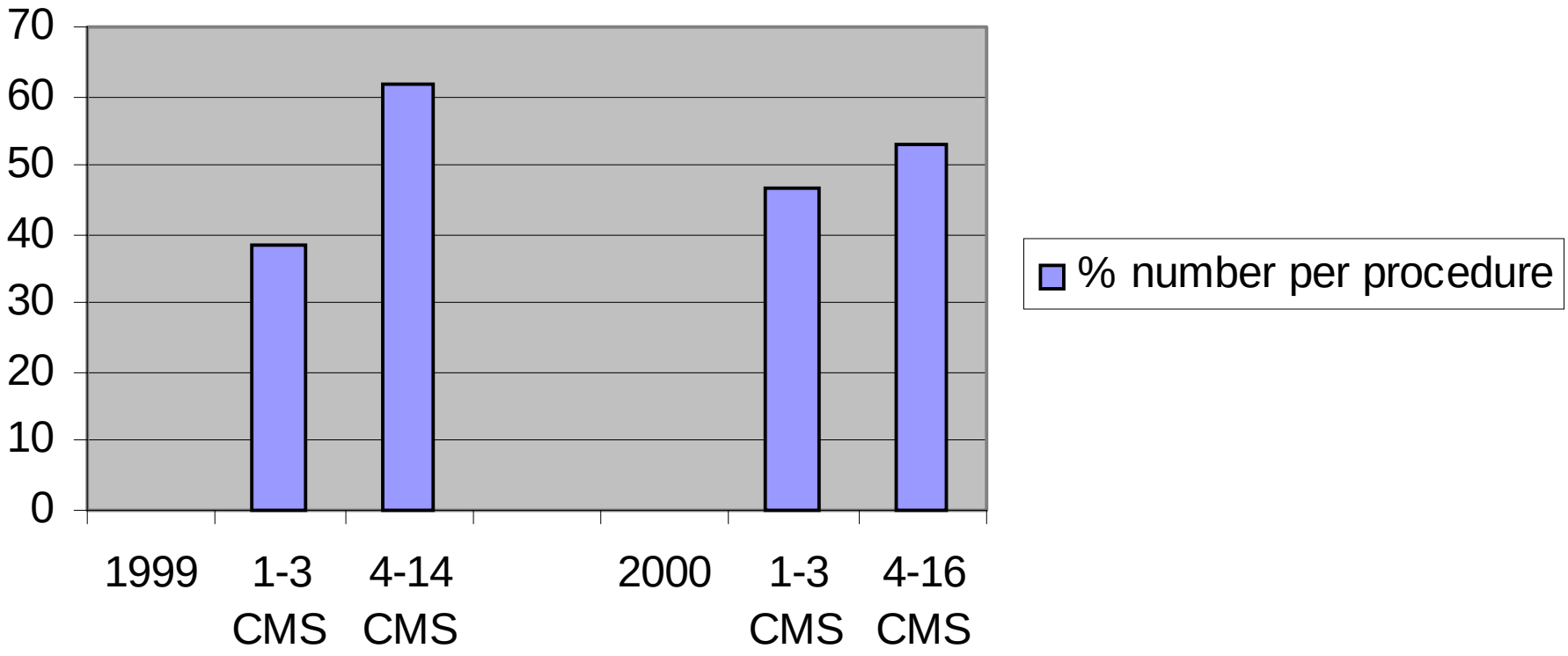



- Full dossier (Article 4.8, Directive 65/65)
- Informed Consent (Article 4.8(a)i, Directive 65/65)
- Bibliographic (Article 4.8(a)ii, Directive 65/65)
- Generic (Article 4.8(a)iii, 1st paragraph, Directive 65/65)
- Fixed Combination (Article 4.8(b), Directive 65/65)
- Different use, route or dose (Article 4.8(a)iii, 2nd paragraph, Directive 65/65)

MRFG
Mutual Recognition Facilitation group

HEUMANN

# Number of CMS per Procedure



# Withdrawals (1)

| | *1995 - 1997* | *1998* | *1999* | *2000 (30/09)* | *total* |
|---|---|---|---|---|---|
| Procedures finalised | 249 | 180 | 253 | 183 | 865 |
| No & % of procedures with at least 1 CMS withdrawn | 112 (46%) | 85 (47%) | 71 (28%) | 67 (36%) | 335 (39%) |
| % of CMS withdrawn in relation to the total number of CMS | 12% | 16,5% | 8,2% | 5,5% | 10,5% |

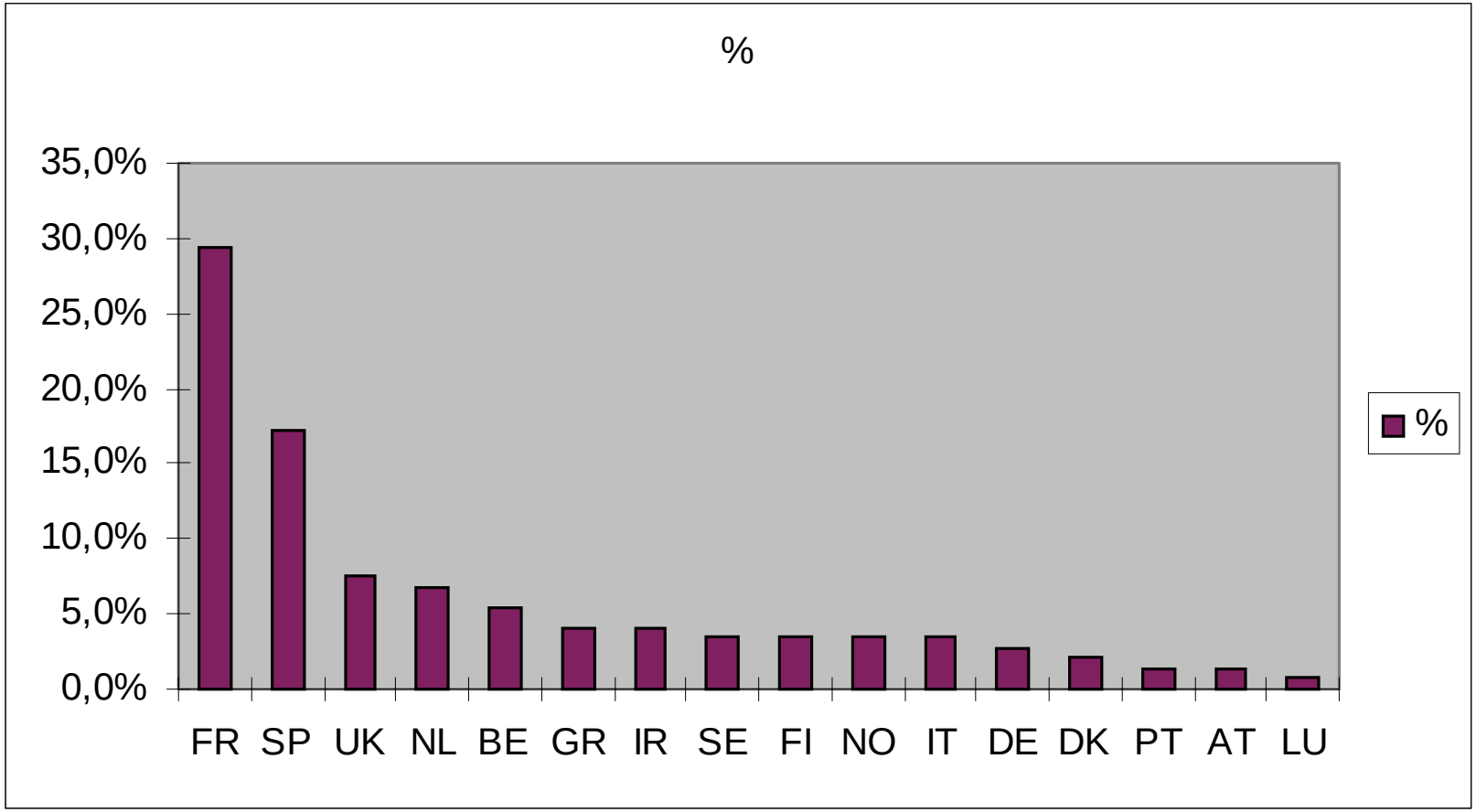
# Withdrawals (2)

| | |
|---|---|
| NEW APPLICATIONS | 30,8 % |
| GENERICS | 48,7 % |
| OTHERS | 20,5 % |

# Withdrawals (3)

| | |
|---|---|
| **DOSSIER** | **38 %** |
| *Safety/Efficacy* | *23 %* |
| *Quality* | *10 %* |
| *Bioequivalence* | *5 %* |
| **SPC** | **57%** |
| **Miscellaneous** | **5 %** |

# Withdrawals (4)



# CMS

# Serious Public Health Concerns

- **NTA** “refers to the quality, safety and efficacy”
- **CMS** negative risk-benefit-evaluation

  ⇒ indication / posology / treatment-duration

  ⇒ bioavailability / bioequivalence

Das dezentrale Zulassungssystem – Dresden 2001

# Current Situation

# for Known Chemical Entities (Generics)

**CP:** not possible

**MRP:** not working

**NP:** to slow

# Objectives of a Generic Applicant

- Free choice of CP, MRP or NP independent where the dossier is
- Based on one EU-reference product
- Conducting one EU-bioequivalence study
- Obtaining all applicable indications
- Marketed immediately after patent expiry/ end of protection period
- Registration time according to the legal given time lines

# Proposal for Future Improvement of Generic Registration

1. Harmonisation exercise
2. Improved registration procedures
3. Simplified procedures for maintenance
4. Business flexibility
5. Preparatory work under patent protection

# Harmonisation Exercise

## Conclusion

Key cause of the problem for generic applications is the differences in SmPCs for the same originator product in different Member States

## Measures

Harmonisation of SmPCs

Maintenance of Harmonisation

# Disharmony in SmPCs

- Main concerned sections are:
  - Indications
  - Contra-indications
  - Special warnings and precautions
  - pregnancy.

- Sometimes the disharmony with the originator's indications and contra-indications reflects local practices & nomenclature of diseases at the time when the medicinal product was licensed

- European "class-labelling" – difficulties with the national implementations & the update.

# Harmonisation of SmPCs according to Article 11

- ***2 April 2001:*** Request for information regarding SmPCs (focusing on sections 4.1 to 4.4) to be sent to the concerned Marketing Authorisation Holders and trade association

- ***23 April 2001:*** Selection of coordinating Member States

- ***1 May 2001:*** Response from the Marketing Authorisation Holders

# Harmonisation Exercise

## Harmonisation of SmPCs according to Article 11

- ***21 May 2001:*** Assessment of responses by Coordinator Member States
- ***28 May 2001:*** Final selection of medicinal products for the first wave of harmonisation through article 11 procedures
- ***12–13 June 2001:*** Final list of medicinal products to the Heads of Agencies meeting for adoption

# Improved Registration Procedures

## Future Centralised Procedure (CP)

- Open for all known chemical entities independent of the route of registration of the originator
- Abbreviated CP to facilitate applications for known chemical entities
- Multiple marketing names for generics to take into account national realities and substitution requirements

# Improved Registration Procedures

## Future Mutual Recognition Procedure (MRP)

- Open for all known chemical entities independent of the route of registration of the originator
- Revised time frames,
  30 days (must) for the CMS to grant MA

# Improved Registration Procedures

## Future National Procedure (NP)

- Still possible for the registration of known chemical entities
- Open for all known chemical entities independent of the route of registration of the originator
- Registration time frames according to the legal given time lines

# Improved Registration Procedures

## Dossier

- One EU-dossier
  - one EU-reference product
  - “is marketed issue” must be solved
  - one EU-bioequivalence study
- SmPC
  - all applicable indications
  - one SmPC for different strengths and presentations

# Improved Registration Procedures

## New definition of active ingredient (revised NtA)

Different salts, esters, derivatives etc. but with the same active moiety should not be considered a new active substance unless they differ significantly from each other in properties regarding safety and efficacy.

Burden of proof → applicant (new annex IV)

Decisions on a case by case basis during the evaluation phase

# Simplified procedures

## Variations

- **Type 0**
  - A variation, which does not affect the quality, safety and efficacy (tell and do)
    → exhaustive list
- **Type I**
  - A variation, which necessitates to demonstrate that it does not affect the quality, safety and efficacy (tell, wait and do)
    → a list as exhaustive as possible including “other”
- **Type II**
  - A variation, which elicits a change of the quality and/or safety and/or efficacy of a medicinal product and necessitates an assessment (approval required)
    → exhaustive list

# Renewal

- **MA's for medicinal products are "dynamic" and not "static"**
  - Dossiers must be regularly updated in order to assure that scientific progress & new regulatory requirements are respected
  - PSURs
- **Renewal**

  unnecessary bureaucratic burden

  → should be deleted

# Simplified procedures

- **One “working language” (English) during the EU-procedures**
  - no necessity for time consuming translations into all EU-languages (EU-enlargement !) at the time of submission
  - benefit for arbitrations ?
  - shorten the Decision Making Process at the Commissions level (Draft decision in English)

# Codification

New Legislation in Summer 2001

“Marketing Authorisation Holder Issue”

- **Business flexibility**

  - Co-promotion and
  - Co-marketing

must be possible in the future

# Preparatory work under patent protection

Roche-Bolar – type exemption in order to develop and approve generic products before patent expiry of the originator

# Advantages of New Regulations

- Benefit to Public Health (end of EU wide difference in product use/information).
- Enhance the single market.
- Reduce the work load of regulatory authorities and free up resources for other activities e.g. innovative applications.
- Meets the objectives of improving access to generic medicines.

# Future Regulatory System

**… at the End a ☺ Generics**