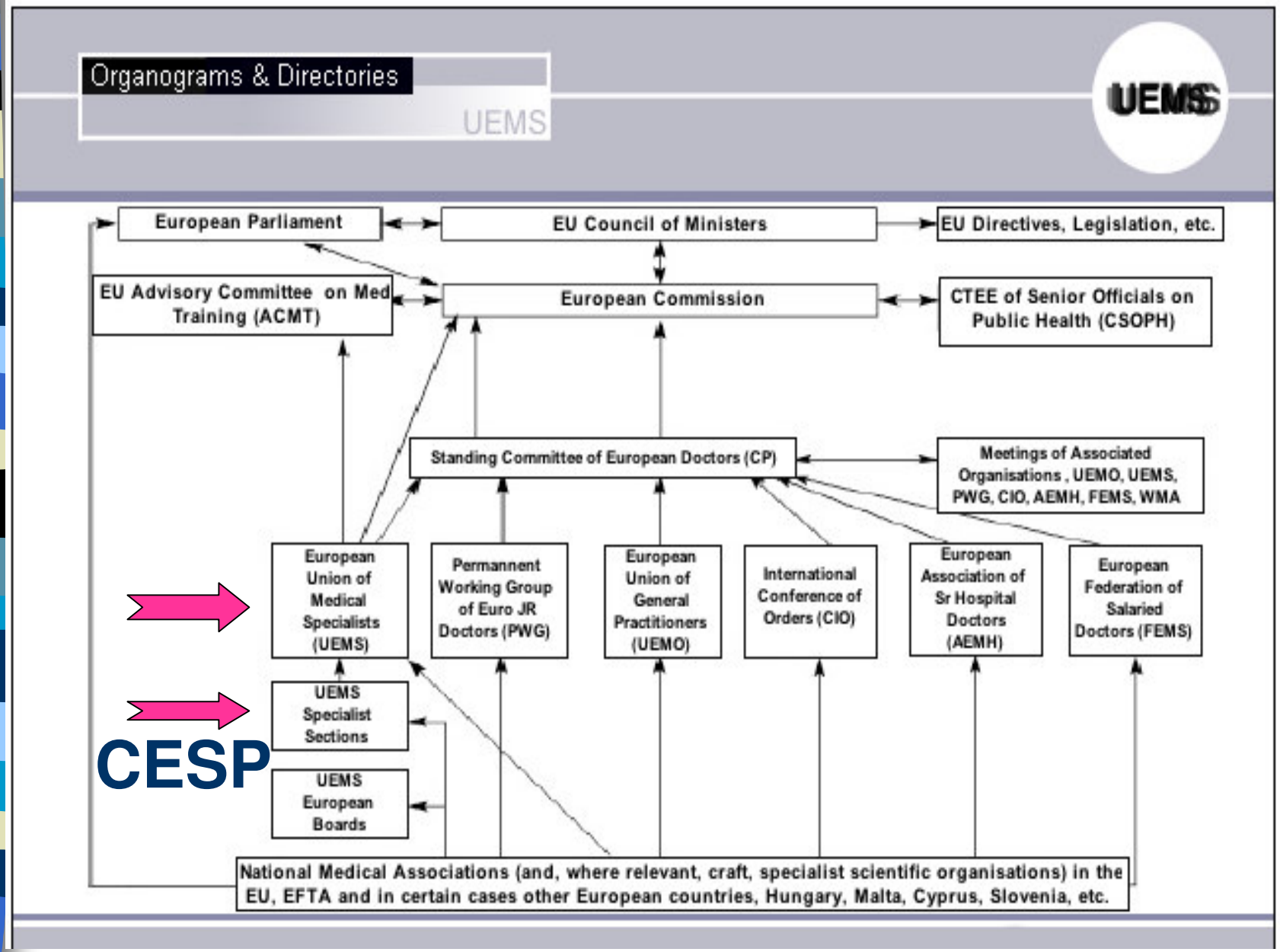
MEDICINES FOR CHILDREN

the paediatricians perspective

José Ramet MD PhD

C.E.S.P.


Organograms & Directories
UEMS
UEMS
European Parliament
EU Council of Ministers
EU Directives, Legislation, etc.
EU Advisory Committee on Med Training (ACMT)
European Commission
CTEE of Senior Officials on Public Health (CSOPH)
Standing Committee of European Doctors (CP)
Meetings of Associated Organisations , UEMO, UEMS, PWG, CIO, AEMH, FEMS, WMA
European Union of Medical Specialists (UEMS)
Permannent Working Group of Euro JR Doctors (PWG)
European Union of General Practitioners (UEMO)
International Conference of Orders (CIO)
European Association of Sr Hospital Doctors (AEMH)
European Federation of Salaried Doctors (FEMS)
UEMS Specialist Sections
UEMS European Boards
CESP
National Medical Associations (and, where relevant, craft, specialist scientific organisations) in the EU, EFTA and in certain cases other European countries, Hungary, Malta, Cyprus, Slovenia, etc.

Introduction

Treated with a medicine

ADULT

- sure : extensively tested
- to assure
  - safe
  - effective
  - high quality for use

CHILD

- may not be true
- over 50% of those used
  particularly in specialized medicine
- Potential risk
  - lack of efficacy
  - unexpected adverse effects
  - even death

Historical background

- drug catastrophes involving mainly children
  - sulphanilamide 1937
  - thalidomide 1962

- development of regulations concerning medicinal products

- stringent criteria of (pharmaceutical)
  - quality
  - safety
  - efficacy

unfortunate paradox :children benefited the least

→ “Therapeutic orphans”

H. Shirkey 1963 :reflect problems re. regulatory requirements

Current situation

- European Union
  - 0-16 years : about 75 million people

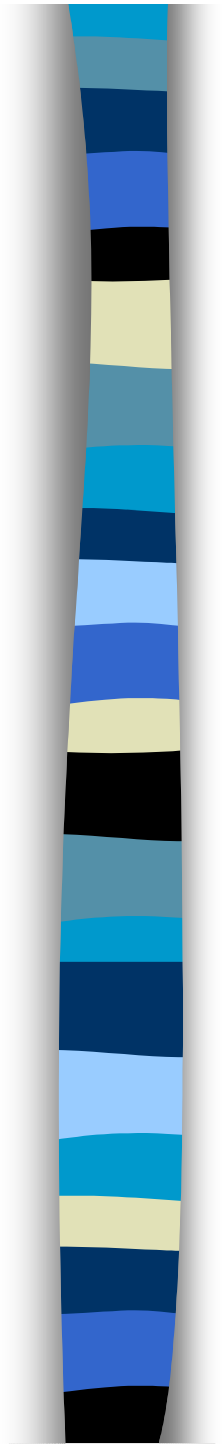
- 0-16 years group : specific sub-populations
  - Age groups: different developmental and behavioural characteristics
  - Age-specific needs

European pediatric hospitals

			Off-label	Unlicensed
Conroy	1998	Gen ped Hosp	39%	7%
Turner	1996	PICU	23%	14%
Conroy	1999	NICU	55%	10%

Consequences of unlicensed and off-label use of medicines in children

- Quality
- Safety
- Efficacy



Analgesia

Sedation

Antibiotics

Paralyzing drugs

Gastric protection

...

Consequences of unlicensed and off-label use of medicines in children

- **Quality:**
  - absorption characteristics and bioavailability unknown
  - most likely risk :

    inaccurate dosing inefficiency

- **Safety** : unknown adverse effects

- **Efficacy:**
  - new major therapeutic breakthroughs : not available for children
    - treated with older - less efficacious - products
    - new medicines used without appropriate studies
      - not same efficacy as in adults / effect not similar
      - increase morbidity and mortality of children

Indications... without research

- Promising case report published
- Uncontrolled study suggests benefit
- Use: standard for many years

Empiricism

- Empiricism : wrong?
- No, but

  Difficult to accept

  If strong evidence missing: rely on ... absence of data

  - Uncontrolled studies
  - Case reports / anecdotical reports
  - Not published information
  - Meta-analysis
    - Negative studies not published
    - Homogeinity bias
    - Size
    - Blinding

Child... Not a small adult
Infant... Not a small child
Preterm... Not a small infant

- Studies in adults not sufficient
  - Specificity disease
  - Kinetic characteristics
  - Effects on growth, development, maturation
  - Specific adverse reactions
- Additional problems
    - Incapable give legal consent
    - Medicines if clinical value
    - Best possible protection
    - Minimization risk and pain

EU regulatory initiatives on pediatric medicinal products?

- 1. Increase the availability medicinal products
- 2. Ensuring that pharmacovigilance mechanisms are adapted
- 3. Avoiding unnecessary studies
- 4. Procedure for determining priorities for research
- 5. Joined European efforts
- 6. Highest ethical criteria

initiatives on paediatric medicinal products?

- **1. Increase the availability** medicinal products
  suitably adapted to the needs of children by encouraging :
  - appropriate pediatric studies on new medicinal products
  - studies on existing products
  - development of suitably adapted formulations

- **2. Ensuring that pharmacovigilance mechanisms are adapted**
  - Possible long-term effects in specific cases

- **3. Avoiding unnecessary studies**
  - Publication of details of clinical trials already initiated

- **4. List of priorities for research**
  - on existing medicinal products
  - in accordance with health needs
  - priorities in different therapeutic classes

- **5. Expert group**
  - in the field of research
  - development and assessment of clinical trials

- **6. Highest ethical criteria**

Avenues to explore

- Positive Incentives for research
- specific rules to encourage the performance of clinical trials in children
- Legal EU requirements
- Transparency and central database
- Scientific expert group
- European network of clinical excellence

Future ?

“It is difficult to make predictions

... especially about the future”

Y. Berra