The treatment of pain in children: What can the EMEA do?

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EMEA: a networking Agency

- EMEA is not FDA for Europe
- EMEA co-ordinates existing scientific resources of Member States
- Activities: *Scientific Advice, Orphan drug designation, Marketing Authorisation (centralised), Pharmacovigilance, Databases (EUDRACT), etc.*

The European Regulatory Framework

GRANTING MARKETING AUTHORISATION

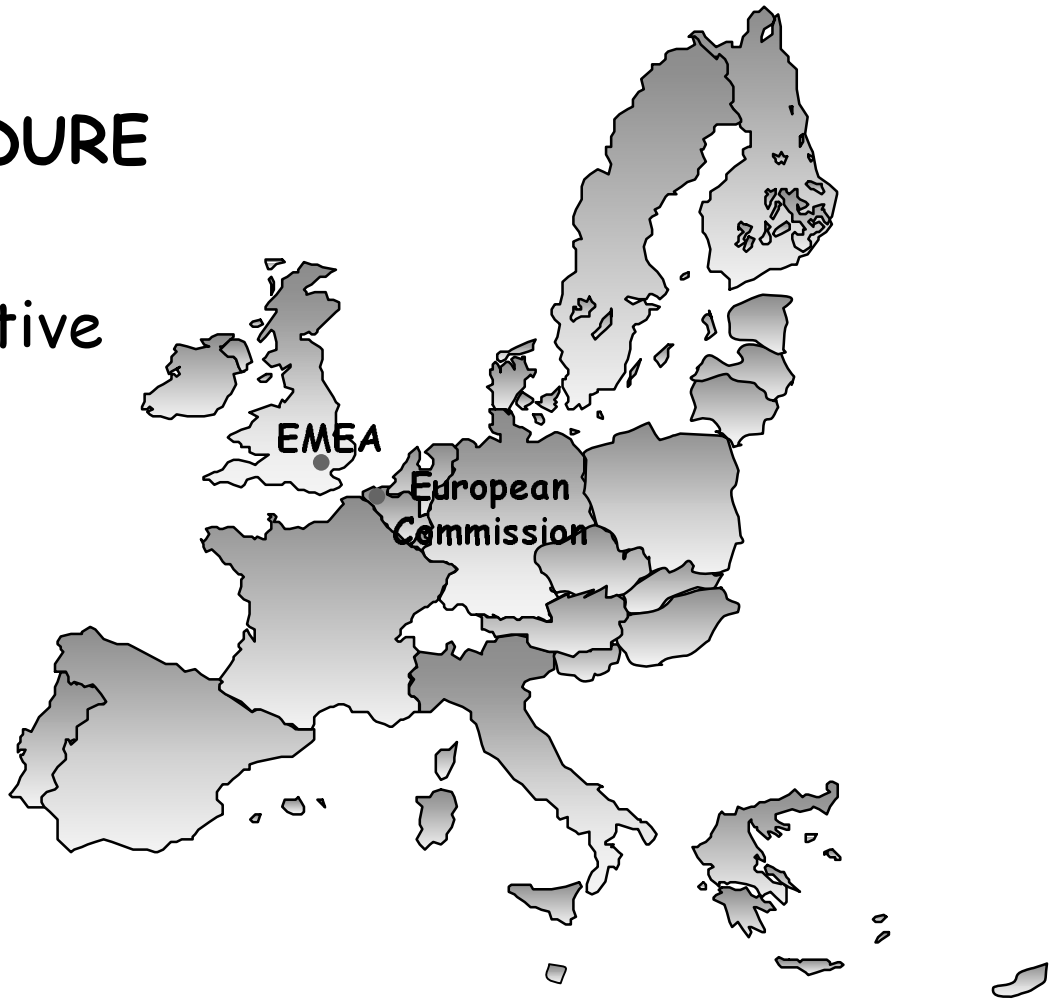
CENTRALISED PROCEDURE

Rapid and EU-wide authorisation for innovative medicines

1 evaluation (<210 days),

1 authorisation,

19 languages!



Why do we need a Regulation?

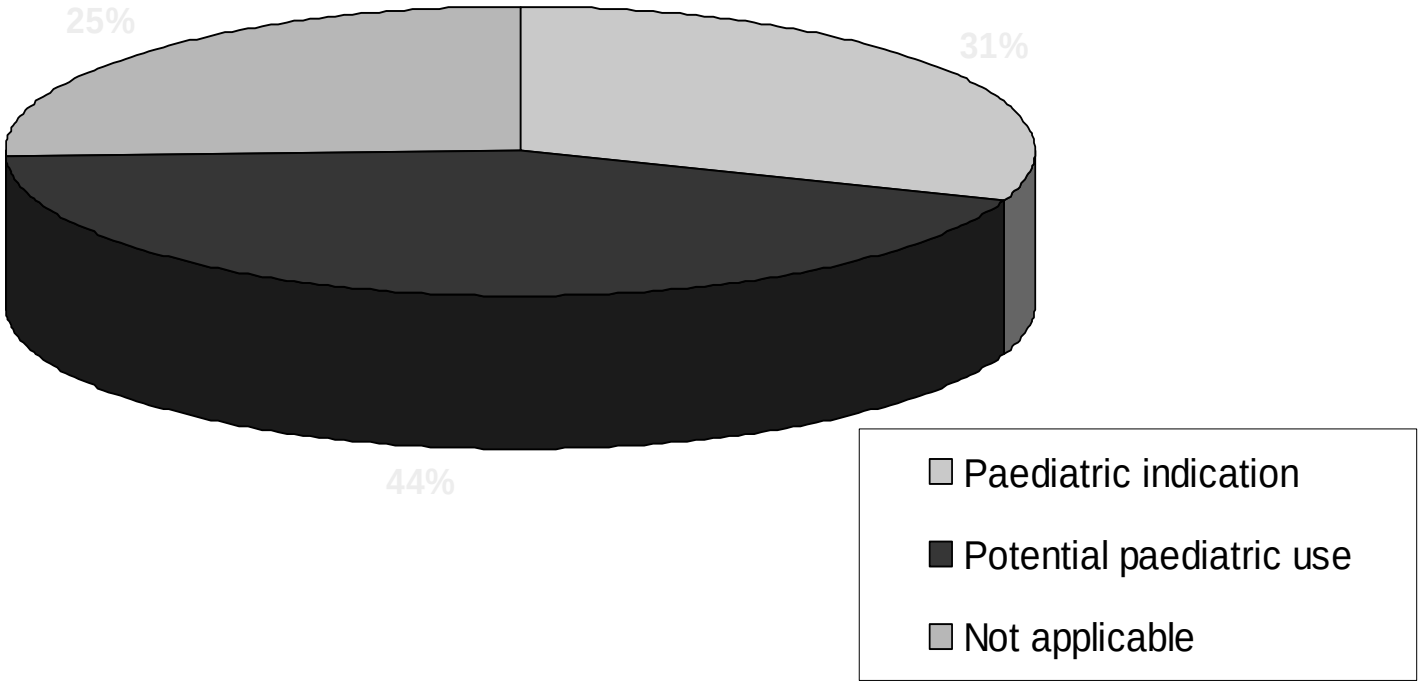
The current situation:

- ~22% of the EU population, 100 million, aged less than 18
- 50-90% of paediatric medicines have not been tested and evaluated
- No request from industry, no reliable information available to prescribers
- Risks of adverse effects (over-dosing) or inefficacy (under-dosing)
- Proper formulation often not available
- Children may be denied innovation

Why do we need a Regulation?

Medicines for children: experience with centralised procedure

Total number of approved substances: 175 (January 2003)
Corresponding to 234 MA



European Initiative

- Started in 1997
- 2000: Council Resolution (December)
- 2001-2002: 'Better Medicines for Children' - Public Consultation
- 2003-2004
  - Extended Impact Assessment
  - Consultation and Draft proposal

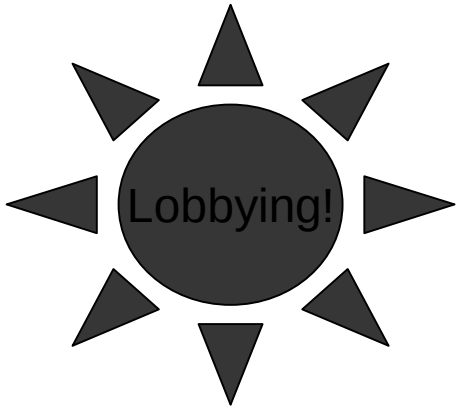
The legislative process

2004

- **Draft Regulation** after Public consultation (4/2004)
- Adoption of Commission proposal
- Official Draft Regulation (9/2004)

What's next?

Co-Decision process



European Commission

MS
Council of Ministers

European Parliament

- - 1st readings 2005
  - 2nd readings 2006
- Entry into force 2007

Objectives of the Regulation

- Improve the health of children
  - Increase high quality, ethical research into medicines for children
  - Increase availability of authorised medicinal products for children
  - Improve information available
- Achieve the above
  - Without unnecessary studies in children
  - Without delaying authorisation for adults

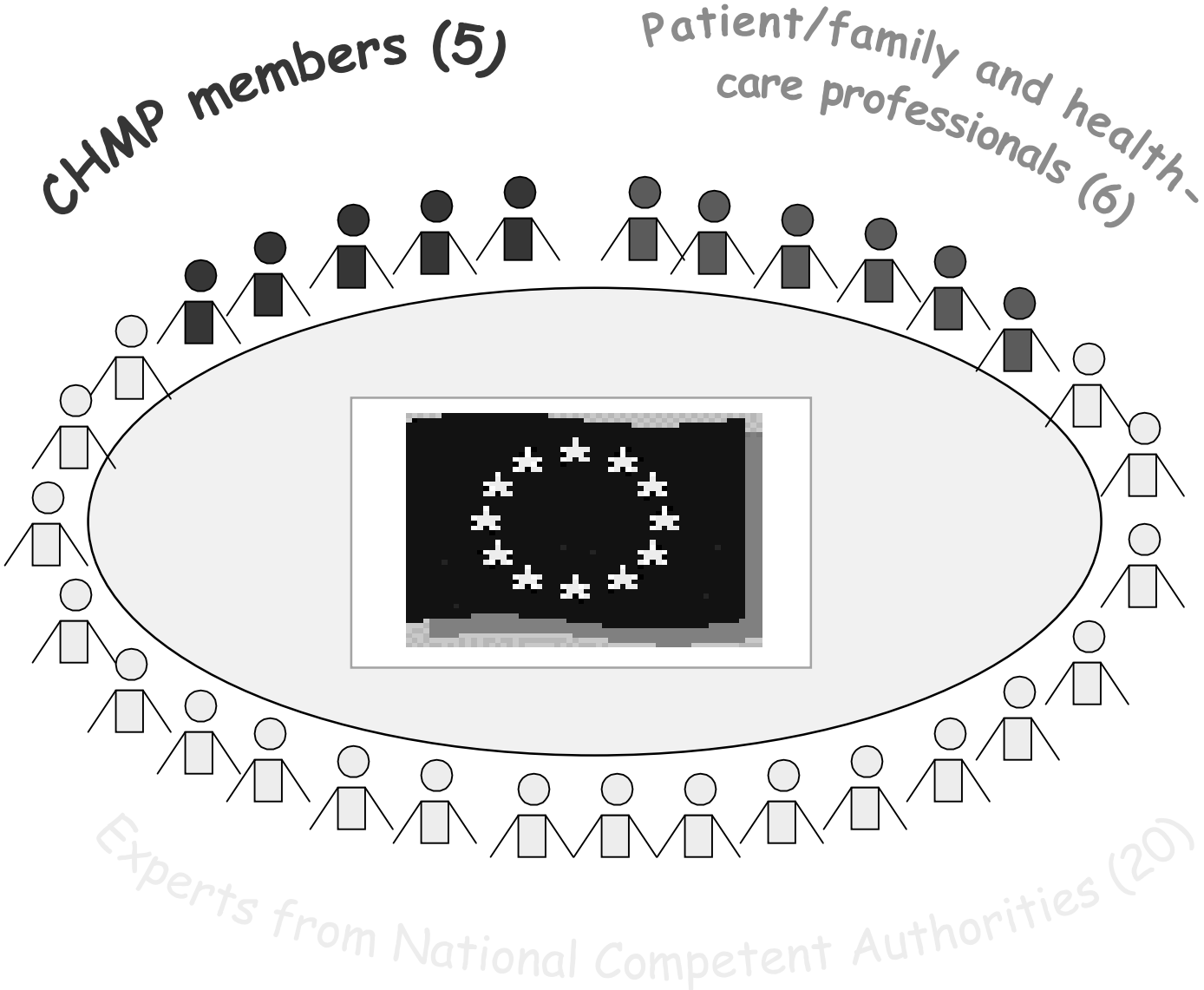
New products

- **Patent-protected products**
  - Obligation to submit Paediatric Investigation Plan (PIP) before marketing authorisation, or variation
  - **Reward**: 6-month extension of the patent protection (= Supplementary Protection Certificate)

'Old' products

- **Off-patent products**
  - Paediatric Use Marketing Authorisation (PUMA)
    - Incl. Formulation
    - Optional
  - **Incentive**: Data protection/exclusivity: 10 years (*as for new products*)

Paediatric Committee



Paediatric Investigation Plans

- Ensure availability of data in the paediatric population
- Waivers
- Deferrals

- Agreed plan and results serve as basis for evaluation of the marketing authorisation application

In the meantime . . .

Creation of the Paediatric Expert Group (PEG) by the Committee for Human Medicines (CHMP)

PEG

- Assessment of paediatric NEEDS (e.g. pain)

- List of PRIORITIES for research on old products
- Recommendations and contributions to guidelines

  (e.g. neonates, pharmacovigilance, Pharmacokinetics, formulations of choice)

- Liaison with Learned Societies (e.g. ESPGHAN)

PEG and pain

- Methodology
  - Use of needs list established by the French 'Comité d'Orientation Pédiatrique', in liaison with learned societies and experts
  - Consultation of all Member States to get a 'European' list
  - Consultation of European and national Learned Societies
  - Finalisation of list by PEG
  - NEXT STEPS?

PEG and pain NEEDS

- Agreed List
  - Products of interest, old and new/future
  - Excluding migraine (another list)
  - Assessment to be done?
  - Clinical trials to be performed/availability of data?
  - Paediatric formulations?

- Consultation of Industry
  - Trade association (EFPIA's paediatric group)
  - Individual companies

PEG and pain NEEDS

- Limitations of the method
  - No real legal framework
  - Need for thorough assessment of available data*
  - Formulations –if any- not available in all Member States
  - What if little interest from companies?

  - Preparatory work for Paediatric Committee

PEG and pain NEEDS

- Products identified by PEG:
  - Acute pain / Chronic pain
  - Mild / Moderate/ Severe

PEG and acute pain

- Severe:
  - Morphine
  - Fentanyl
  - S-Ketamine
  - *local anaesthetics (bupivacaine)*
- Moderate:
  - Tramadol
  - Diclofenac
  - Metamizol?
  - Clonidine
  - (Cox-2 inhibitors?)
  - Sucrose (neonate only)
  - *topical anaesthetics*
- Mild:
  - Paracetamol
  - Ibuprofen

PEG and chronic pain

- **Severe:**
  - Morphine
  - Opioids/antiepileptics
  - Opioids/antidepressants?
  - Fentanyl
  - S-Ketamine
  - *Local anaesthetics (Lidocaine transdermal?)*

Moderate:

- Piroxicam (melt)
- Ketoprofen?
- Naproxen
- Tramadol
- Metamizol?
- Clonidine

- Mild
  - Paracetamol
  - Ibuprofen

Next steps

- Publication of the list
- Liaison with Industry
- Awareness of Learned Societies on the need to perform trials
- Feed back from Workshop

Conclusions

- Pain is common to all children

- Marketing authorisations are not simply administrative burden!
- New Regulation intended to improve the future
- Harmonisation of practices and discussion of needs.
- Work of PEG to be shared/discussed

- Preparation of the Work of the Paediatric Committee

Websites

- EMEA www.emea.eu.int (+ links to EU national agencies)
- European Union www.europa.eu.int
- DG Enterprise pharmacos.eudra.org
- DG Research www.cordis.lu