Working with regulators & policy makers

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„Declaration of interest”

- ✧ 2006: Alternate @ PCWP
- ✧ 2007 – 2009, 2009-2012: 2 terms PCWP EATG representative
- ✧ 2013 – 2016: Co-chair PCWP
- ✧ 2008 – 2016: ENCePP Steering Group for PCWP
- ✧ 2009: Pharmacovigilance Working Party, trial phase
- ✧ 2009 – 2014: PROTECT-IMI External Advisory Board, nominated by EMA
- ✧ Since 2014: Co-chair working PCO working group Swissmedic

- PCWP: Patient & Consumer Working Party; ENCePP: European Network of Centres for Pharmacoepidemiology and Pharmacovigilance; PROTECT: Former IMI project on pharmacovigilance methodology
- PCO: Patient & Consumer Organisations

Content

- Background & history of medicines regulation
- European Regulatory Network within global context
- Medicines regulation at European level
- Examples HIV history
- EMA structure (committees, working parties, working groups, advisory groups)
- Patients at EMA: representatives of their organisation, as members of committees, individual experts

Thalidomide, the „Big Bang”

- Thalidomide: mild sleeping pill considered safe incl pregnant women
- Developed 1950s by Chemie Grünenthal, Germany
- Perfect example of fashionable tranquilisers
- Licensed 1956 as OTC, Germany & Europe, prescription free
- Reduced morning sickness – popular with pregnant women
- >10‘000 babies worldwide born with malformed limbs
- First signs 1960, revealed 1962
- **Until 1962, all new drugs considered “safe for use“**
- Compensation settlements 1970s
- 2007: study shows thalidomide effective in bone-marrow cancer; 2008: EMA approval for multiple myeloma
- 2009: mystery explained – drug component prevents growth of new blood vessels in developing embryos, stunting limb growth
- OTC: Over-the-counter medicines; EMA: European Medicines Agencies

Medicines regulation: global picture & ICH

- Need for medicines regulation and safety/efficacy testing recognised at different times
- Thalidomide driver in Europe 1960s
- Most countries: 1960s &1970s rapid increase in laws, regulations & guidelines for reporting and evaluating the data on safety, quality and efficacy of new medicinal products.
- Harmonisation regulatory requirements pioneered by EC 1980s, as moving to single market
- EC success demonstrated harmonisation was feasible
- Bilateral discussions Europe, Japan & US on possibilities for harmonisation. WHO Conference of Drug Regulatory Authorities (ICDRA), Paris 1989, plans for action materialised.
- Authorities approached IFPMA to discuss joint regulatory-industry initiative on international harmonisation, ICH conceived April 1990 in Brussels

- ICH: International Committee for Harmonisations; EC: European Community; IFPMA: Intern. Federation of Pharmaceutical Manufacturers Associations

ICH today

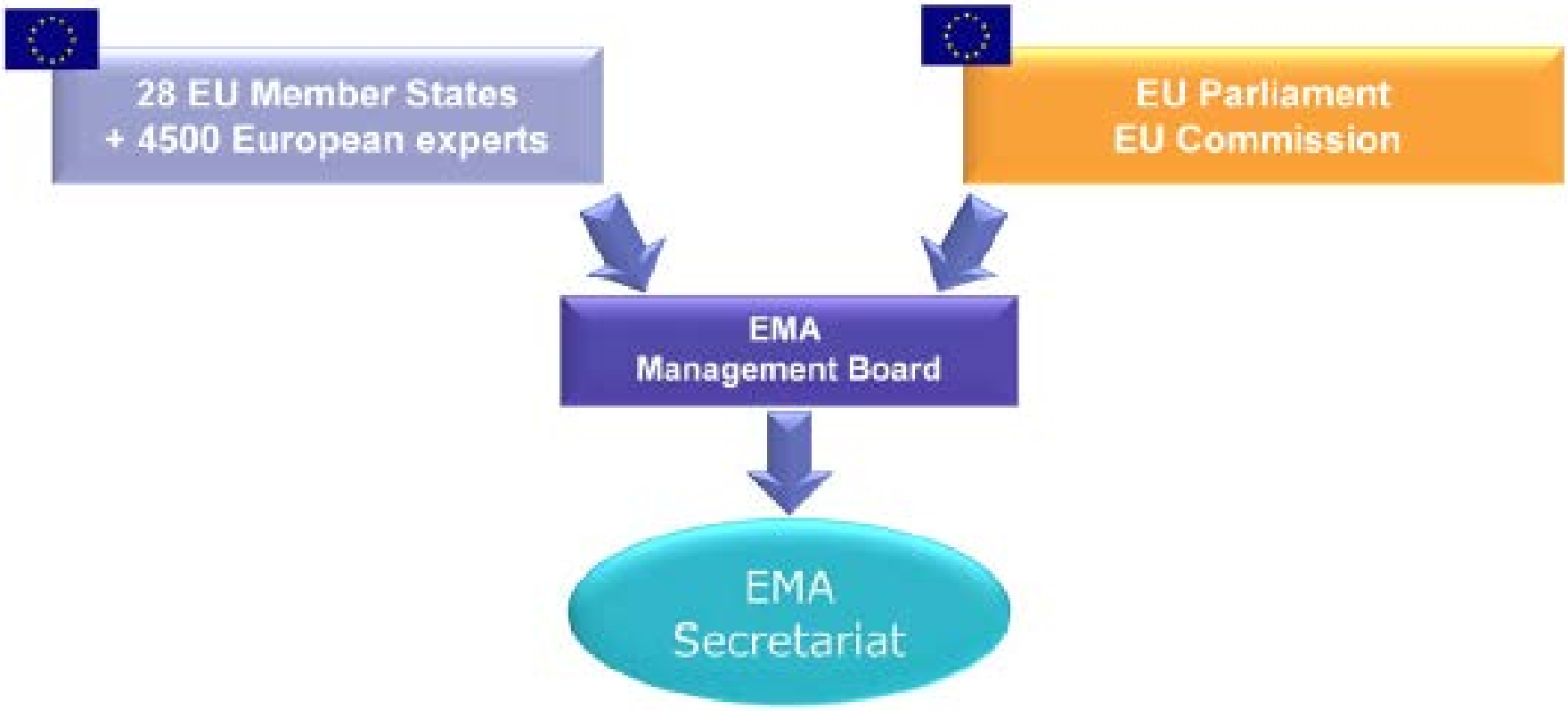
- 1990s: Tripartite ICH Guidelines on Safety, Quality and Efficacy topics
- From 2000: development of ICH Guidelines continued, but more attention given to evolving science & technology
- ICH standards progress as global standards
- Today: extending benefits of harmonisation beyond ICH regions
- Founding regulatory members: EC, FDA, PMDA
- Founding industry: EFPIA, JPMA, PhRMA
- Standing members: Health Canada, Swissmedic
- Standing observers: WHO, IFPMA
- Observers: ANVISA, Brazil; CDSCO, India; COFEPRIS, Mexico; HSA, Singapore; MFDS, South Korea; Roszdravnadzor, Russia; TFDA, Taiwan; TGA, Australia

European Regulatory Network

The European regulatory system for medicines is a unique model in the global regulatory environment.

This system is based on a network that includes all national medicines regulatory authorities (for both human and veterinary medicines) from Member States in the EU and European Economic Area, united in the Heads of Medicines Agencies (HMA), and the European Medicines Agency (EMA), working closely together in an integrated fashion.

EMA at the European level



What the EMA does not do?

The European Medicines Agency does not control:

- pricing of medicines
- access to medicines
- advertising of medicines
- patents on medicines
- medical devices
- homoeopathic medicines
- food supplements
- cosmetics

Are all medicines approved via the EMA?

No. In the European Union (EU), there are two ways of getting a marketing authorisation for a medicine:

1. the **centralised authorisation procedure**, via the European Commission after evaluation by the EMA, which results in a single marketing authorisation valid throughout the EU;

2. **National authorisation procedures**, where individual EU Member States authorise medicines for use in their own territory through 3 possible procedures:

   - National authorisation
   - Mutual-recognition procedure (MRP)
   - Decentralised procedure (DCP)

Additional information:
•EMA Basic video on 'The Centralised Procedure at EMA' for more information)
•For more information on the MRP/DCP procedures – http://www.hma.eu/medicinesapprovalsystem.html

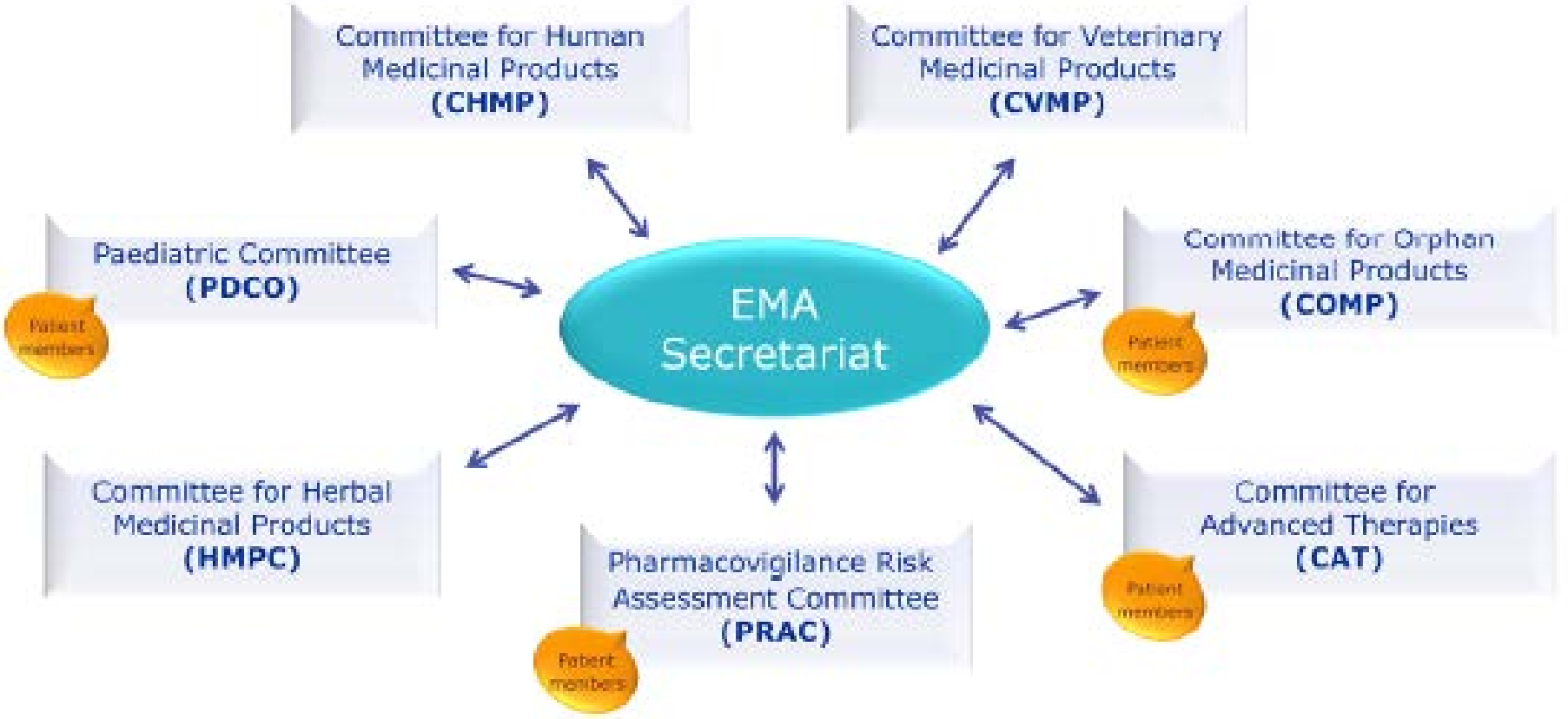
Medicines that are mandatory for evaluation at EMA

- Rare diseases
- HIV, cancer, neurodegenerative disorders, diabetes
- Auto-immune diseases, viral diseases
- All biotech products
- Gene therapy
- Monoclonal antibodies

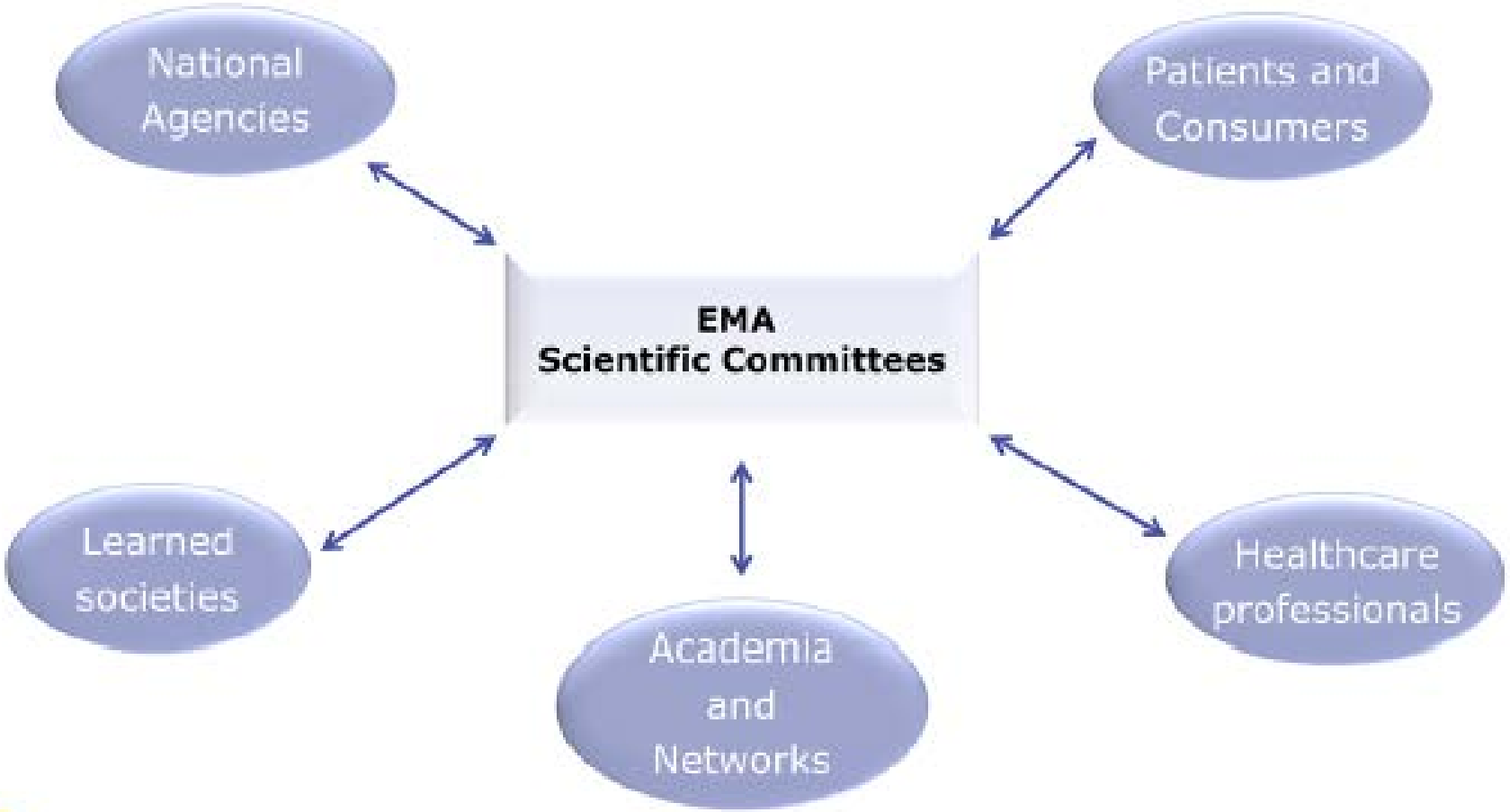
± Other innovative products

EMA and its scientific committees

The EMA committees contain members nominated by the medicines regulatory authorities of the EU Member States (the 'national competent authorities')



Experts who work with the scientific committees



Patients at regulatory bodies – The Denver Declaration 1983

- Californian & NY PWAs meet in Denver → “Denver Principles”, birth of “PWA empowerment”, as well as term “PWA”
- We recommend that people with AIDS…
  - Be involved at every level of AIDS decision-making and specifically
  - Be included in all AIDS forums with equal credibility as other participants, to share their own experiences and knowledge

"Nothing about Us, Without Us“

Pioneer 1: Project Inform

- 1985: Project Inform created (Martin Delaney & others)
- Smuggling runs to Tijuana for a cold remedy (ribavirin) Soon after, decision to take political action
- Project Inform started "medically supervised guerrilla trials" — community-based studies of the safety and efficacy of drugs, like ribavirin, without FDA approval
- Established National AIDS-treatment hotline
- Early 1990s: Delaney instrumental in introducing accelerated approval & expanded access programmes
- Delaney central figure in "Acceptable Risks" (Poseidon Press, 1992), "Who should decide which risks are acceptable, the bureaucracy in Washington or the patient whose life is on the line?"

FDA Demo
October 1988

"Storm the NIH"
May 1990

Pioneer 2: Act Up &
1st Wall Street protest March 24, 1987

To demand the following

1. Immediate release by the Federal Food & Drug Administration of drugs that might help save our lives.
   These drugs include: Ribavirin (ICN Pharmaceuticals); Ampligen (HMR Research Co.); Glucan (Tulane University School of Medicine); DTC (Merieux); ddC (Hoffman-LaRoche); AS 101 (National Patent Development Corp.); MTP-PE (Ciba-Geigy); AL 721 (Praxis Pharmaceuticals).
2. Immediate abolishment of cruel double-blind studies wherein some get the new drugs and some don't.
3. Immediate release of these drugs to everyone with AIDS or ARC.
4. Immediate availability of these drugs at affordable prices. Curb your greed!
5. Immediate massive public education to stop the spread of AIDS.
6. Immediate policy to prohibit discrimination in AIDS treatment, insurance, employment, housing.
7. Immediate establishment of a coordinated, comprehensive, and compassionate national policy on AIDS.

President Reagan, nobody is in charge!

ACT UP
AD MY LIPS

FEDERAL
DEATH
ADMINISTRA
PISD
PISD
B.S.

HIV activist & ECAB regulatory achievements

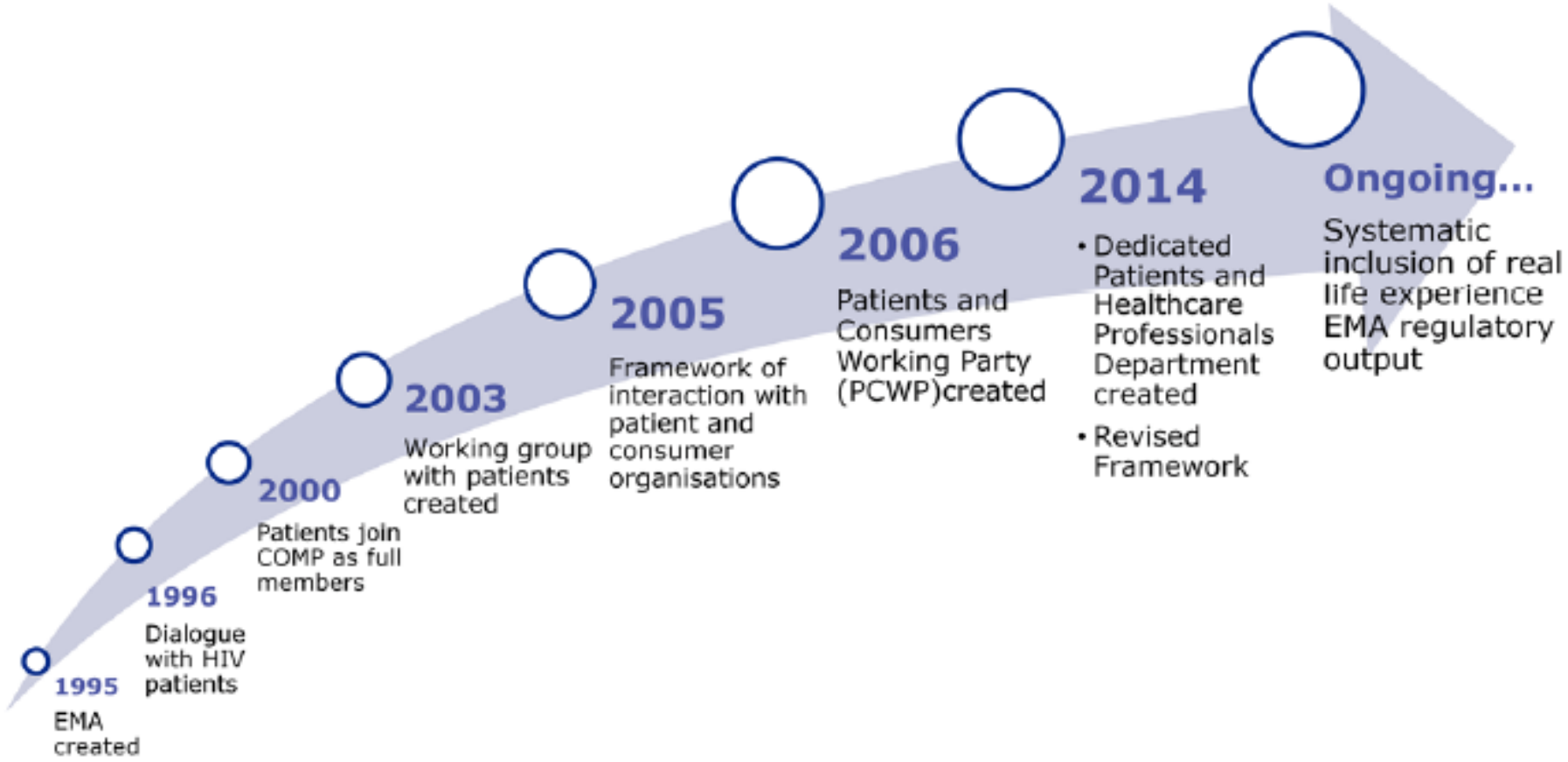
- Expanded access / compassionate use (FDA, 1987)
- Accelerated approval for life threatening conditions (FDA, 1992)
- Pushing for surrogate markers instead of clinical endpoints in pivotal trials (EMA, nevirapine approval 1997)
- EATG first to ring the alarm bells re. lipodystrophy in early HIV combination treatments 1997
- Influencing CD4 threshold in phII/phIII trials and other important changes in trial protocols
- Formal cooperation with EMA since 2003 (informal since 1996)
- Successful lobbying for a pivotal trial including two investigational compounds, ending exposure to monotherapy by multidrug resistant trial participants 2007

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Patients' and Consumers' Working Party (PCWP)

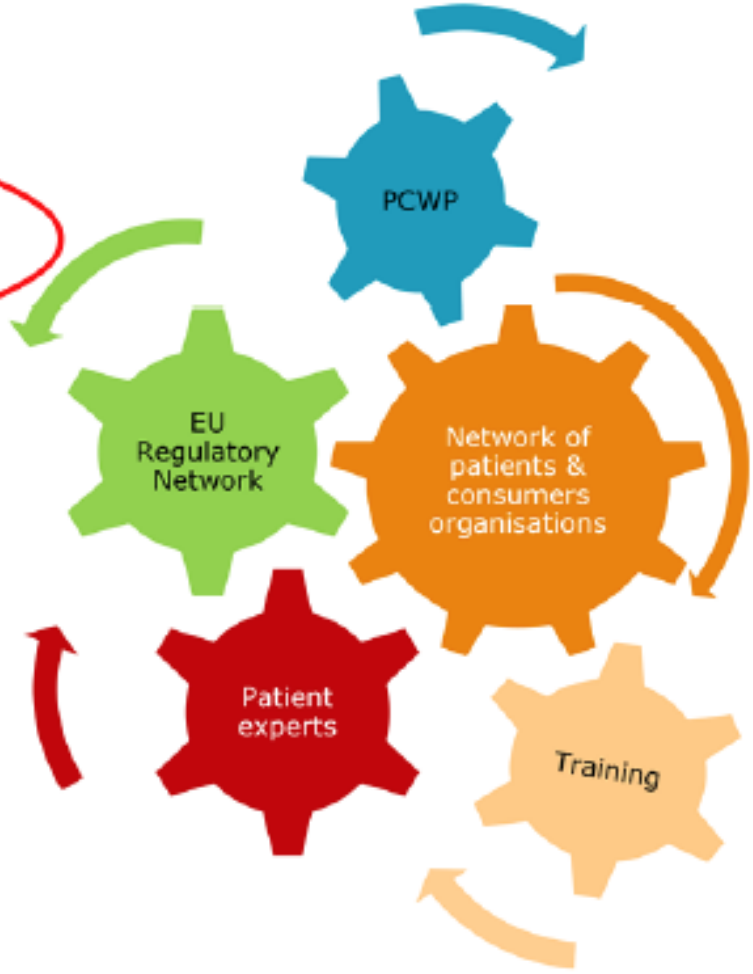
An agency of the European Union

Interaction with patients: the EMA journey… so far



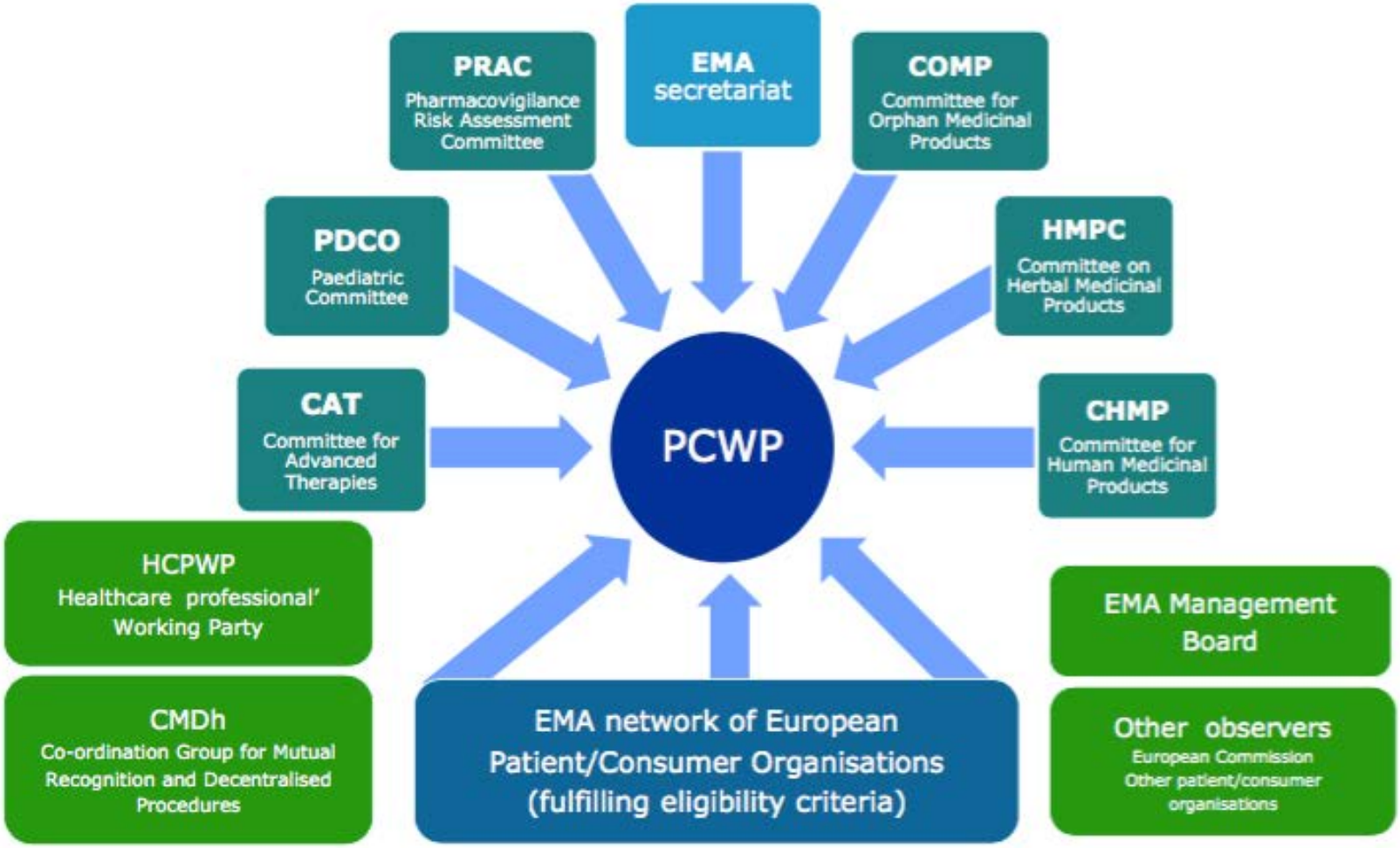
The framework relies on five critical elements

1. A network of European patients and consumers organisations
2. A forum of exchange: EMA Working Party with Patients and Consumers' organisations
3. A pool of patients acting as experts in their disease and its management
4. Interaction with the EU Regulatory Network
5. Capacity-building focusing on training and raising awareness about EU regulatory system



PCWP composition

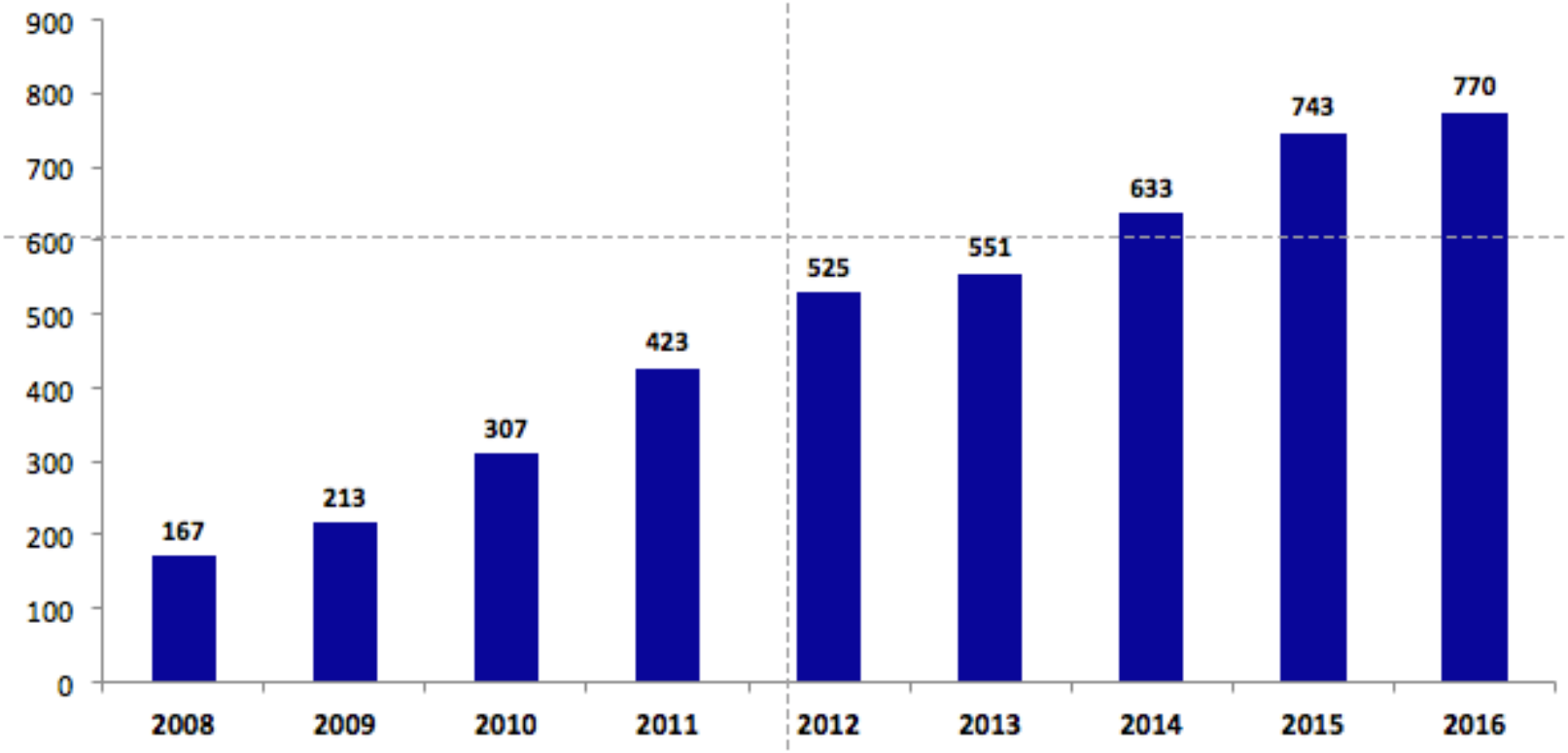
20 Patient/consumer organisations



PCWP input

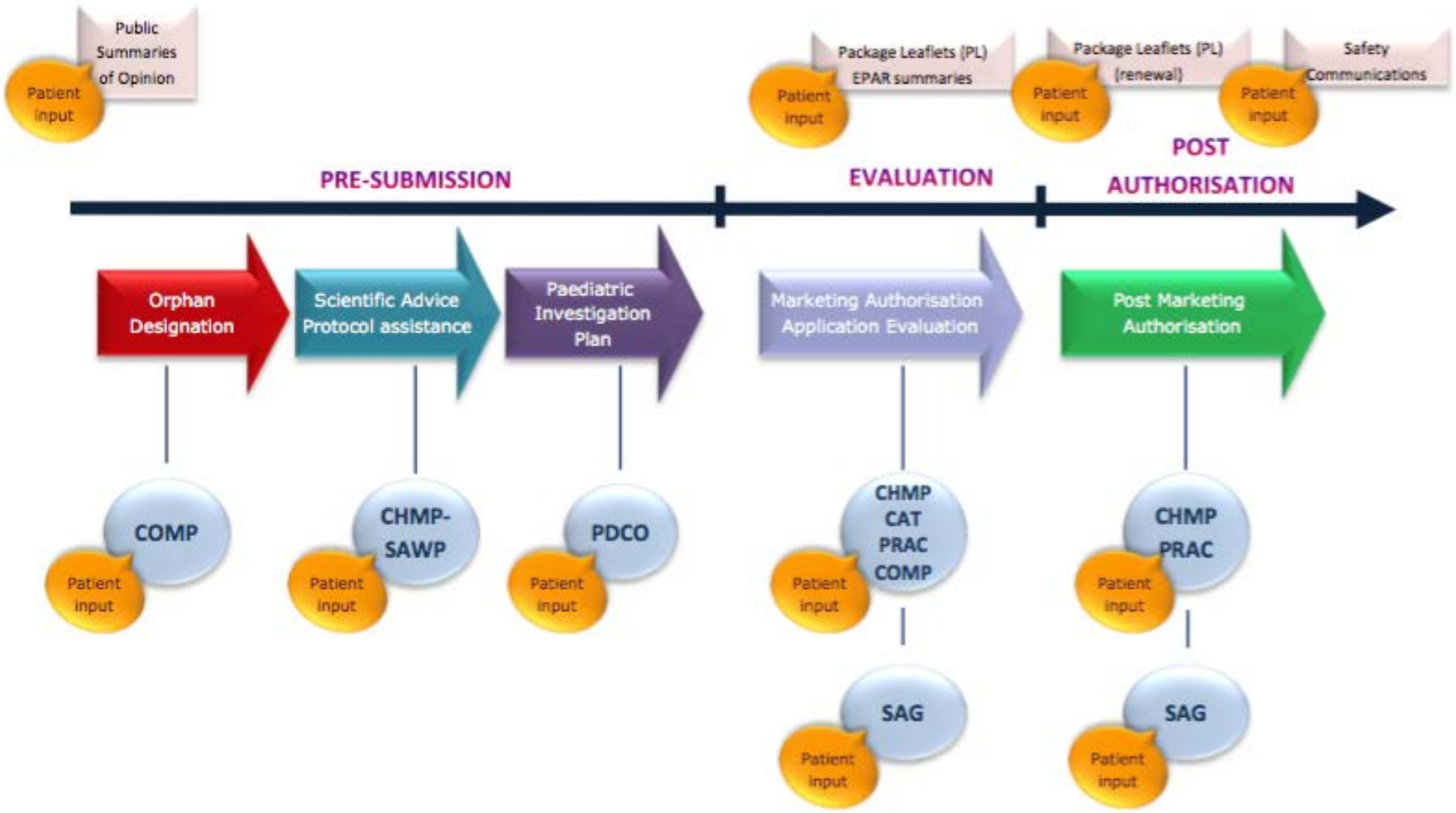
- PCWP is consulted by EMA, Committees and WPs on a range of topics (e.g. draft guidelines; EMA policies)
  - If topic relevant to majority of members, WP provides common position
  - Otherwise, relevant WP members respond individually
- PCWP members can also be contacted to identify appropriate experts for inclusion within topic or working groups, or workshops, etc
  - Depending on nature of activity experts may need to complete DoI and can be involved as individuals
- All working party representative members are asked to complete a DOI for transparency purposes

Patient & consumer involvement over years



Slide courtesy EMA

Opportunities for involvement along the medicine lifecycle at EMA



Categories of patient participation:

Patients representing *patients'* organisations	• Management Board • EMA Scientific Committee(s)
Patients representing *their* organisations	• Patients' and Consumers' Working Party (PCWP) • EMA consultations • Workshops
Patients as *individual* experts	• Scientific Advice / Protocol Assistance Procedures • Scientific Advisory / *ad hoc* expert Groups • Scientific committee consultations • Review of documents

What are PCWP members doing?

- Representative: coordinates all requests from EMA (experts, SAG requests, input to agenda, input to EMA workshops, EPAR & PL review feedback, participation in topic groups, represent PCWP in other EMA groups & workshops)
- Alternate: replaces rep when needed, but: training camp for future representatives
- PCWP is a network where collaboration with representatives of other patient groups & health care professionals is happening
- Continuity is key for success
- Examples: Code of conduct, medicines shortages
- SAG: Scientific Advisory Group; EPAR: European Public Assessment Report; PL: Package leaflet

Thanks

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