Continuous dialogue from product development throughout product life cycle

Tomas Salmonson

Vice chair CHMP

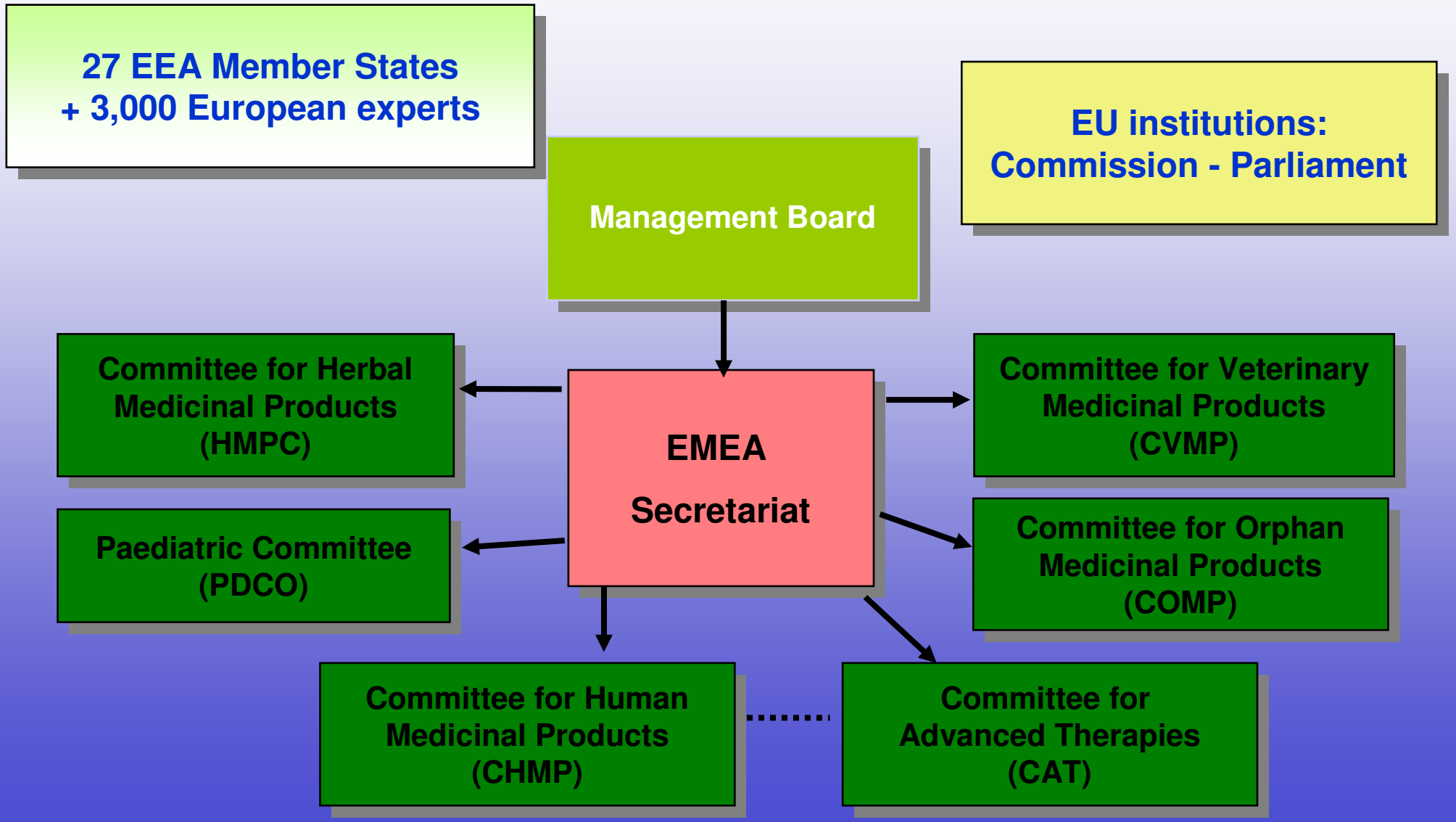
Outline of presentation

- The network of EMEA committees and working parties
- Statistics on SA/PA
- Rapporteur /Co-Rapporteur Appointment
- Interaction with Rapporteurs
- Post authorisation dialogue

Outline of presentation

- The network of EMEA committees and working parties

Interaction between Committees



Interactions between Committees

- PDCO-CHMP: regular meetings of Chairs, "informal", CHMP members at PDCO
- COMP-CHMP: regular meetings of Chairs, "informal", CHMP members at COMP
- SAWP: members from COMP
- SAWP-PDCO: being developed
- PDCO-other CHMP WP: being developed, coordination on overlapping topics, joint WP, PDCO to provide input into CHMP guidelines
- CAT-CHMP: being developed

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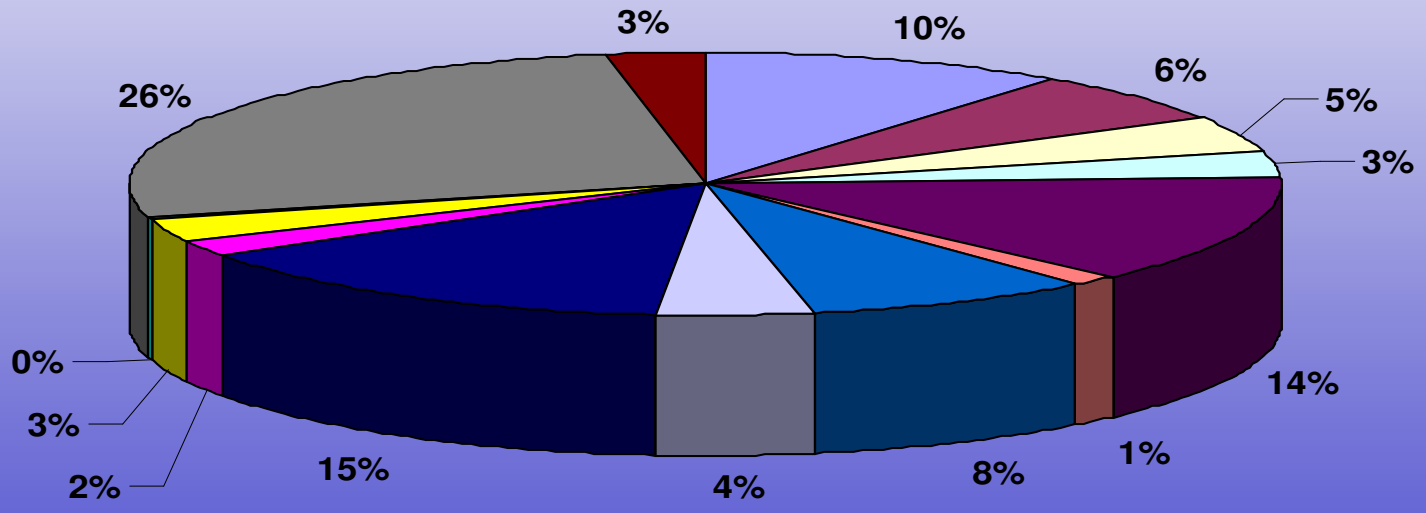
- Statistics on SA/PA

Scientific Advice and Protocol Assistance 2002-2008

	2002	2003	2004	2005	2006	2007	2008
Total SA/PA	86	97	122	194	259	288	321
Protocol Assistance	11	17	29	44	50	41	45

Scientific Advice and Protocol Assistance 2002-2008
By ATC codes



Scientific Advice

SAWP Chair → presents ~6 advices at CHMP meeting

CHMP members → ≥1 thorough peer-review / each main advice

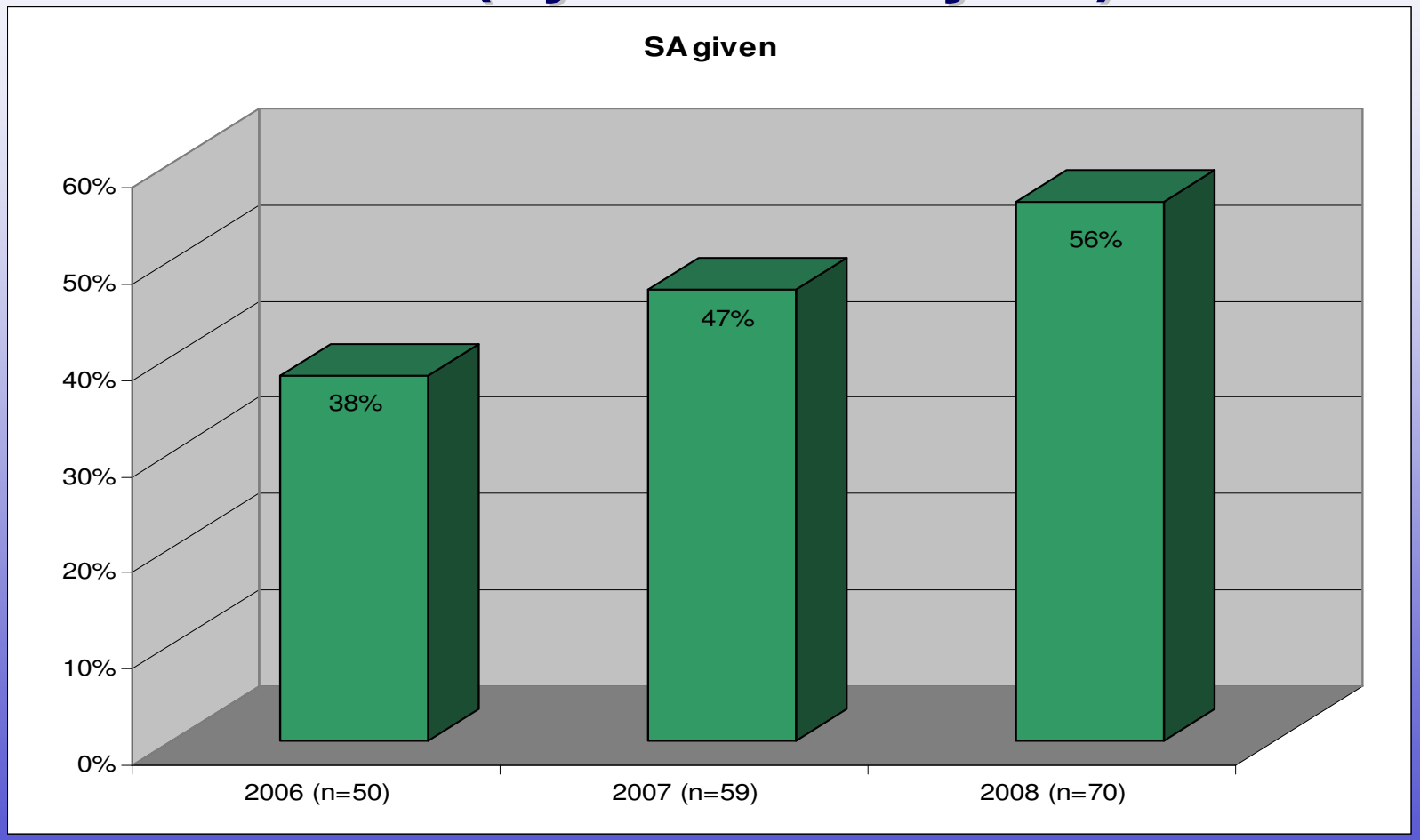
comment during SAWP presentation at CHMP meeting

CHMP / EWP Chairs → attend SAWP meeting to summarize CHMP decisions with ciritical impact on SA's

SAWP secretariat → liaise with PDCO for paediatic SA's / PA's

PDCO Chair or representative → informs CHMP of critical PDCO decisions

Proportion of MAAs that received SA (by outcome year)



Does compliance with SA influence the outcome?

MAAs between 2004-2007

192 MAAs with an outcome

- Positive opinion – 140 (72.9%)
- Negative opinion – 10 (5.2%)

} **52 (27.1%)**

- Withdrawal – 42 (21.9%)

- Non-orphans drugs – 141 (73.4%)
- Orphan drugs – 51 (26.6%)

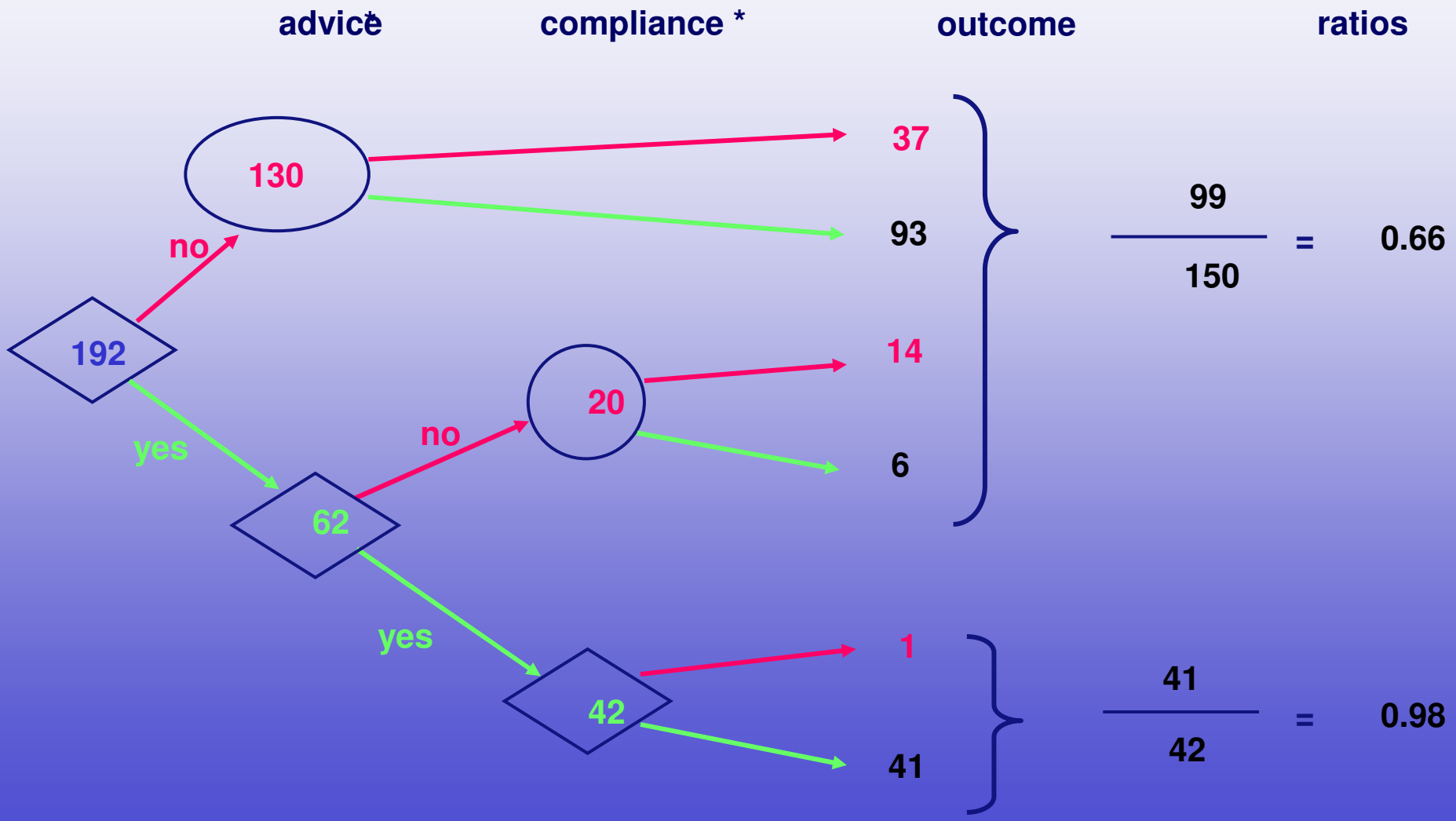
Does compliance with SA influence the outcome?

The 72 MAA outcomes with SA (2004-2007) were assessed concerning compliance with:

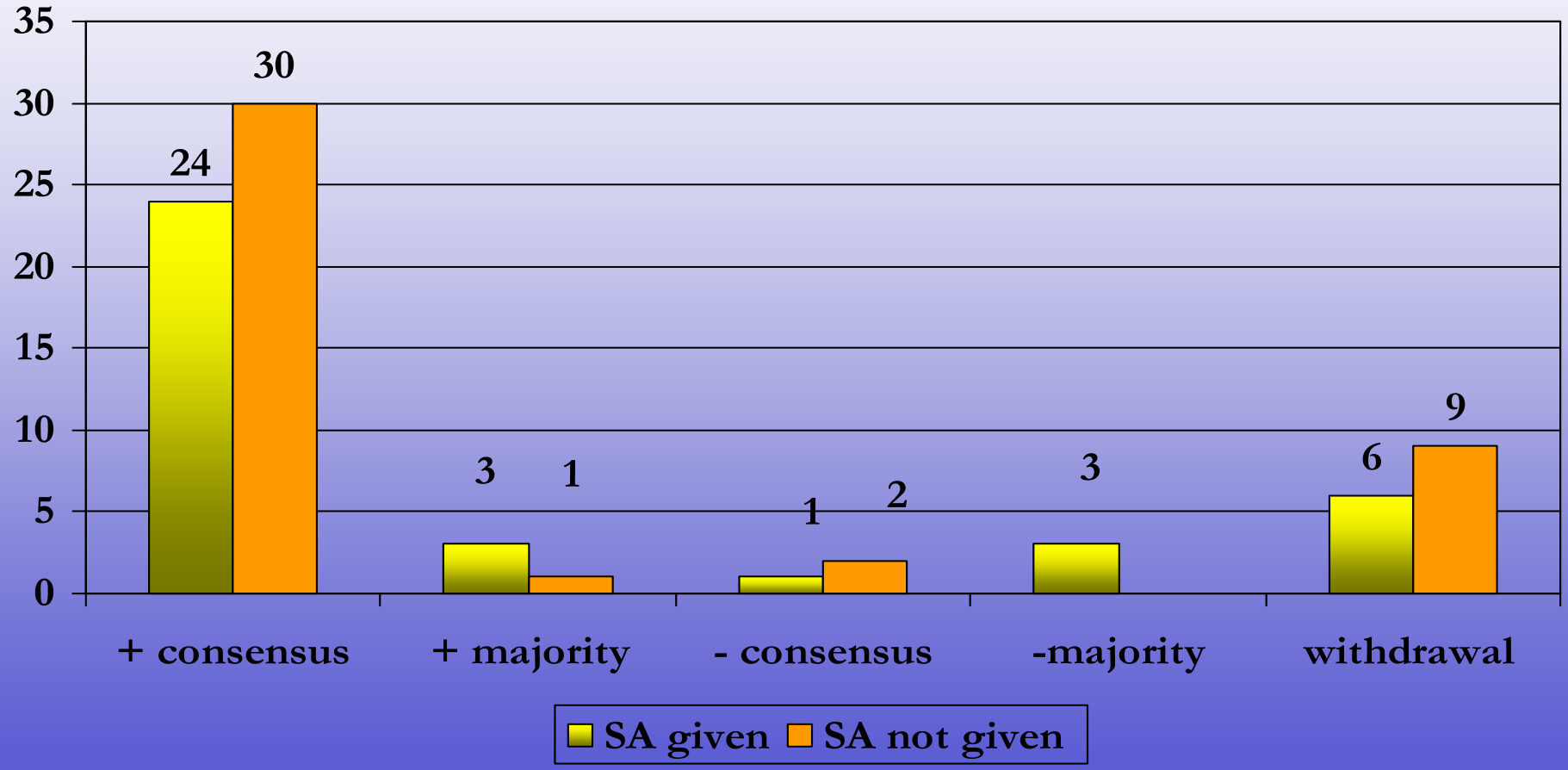
- Choice of primary endpoint
- Choice of comparator
- Statistical analyses

- Non-compliance defined as not adhering to one or more of the 3 variables
- 10 MAAs did not include questions concerning any of the 3 variables
- 62 MAA outcomes with SA analysed

SA compliance and MAA outcome



MAAs: outcome 2008 (jan – nov)



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→ Members still state relative priority

→ Collated by EMEA Secretariat

→ Proposal made by CHMP Chair

→ best available scientific expertise

→ highly subjective judgement

→ experience over time

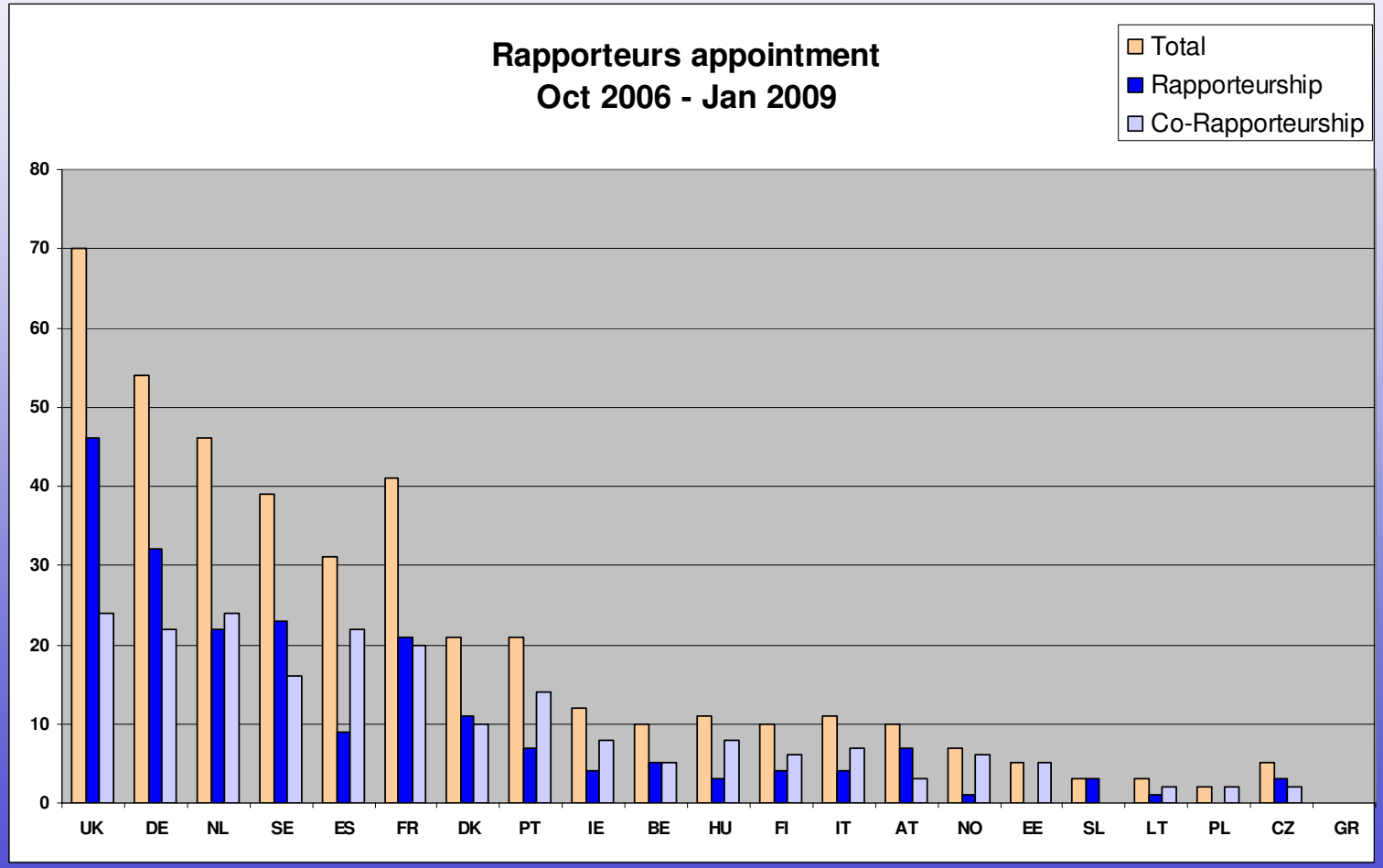
Rapporteurship appointment

- Once eligibility confirmed and if submission within 6-months, appointment of Rapporteurs and their assessment teams take place
- CHMP Secretariat sends list of products requiring Rapporteurs appointment at the next CHMP meeting to all CHMP members
- Within 2 weeks CHMP members asked to express their interest and provide details regarding their proposed assessment team
  - ✓ Quality, non-clinical, clinical, environmental assessment, pharmacovigilance…
  - ✓ Experience with similar therapeutic area, similar products
  - ✓ Regulatory experience

Rapporteurship appointment (2)

- EMEA internal review of the nominations received
- Filter information received and propose draft outcome
- No linkage/exclusion due to role as Scientific Advice Co-ordinator
- Discussion of draft outcome with CHMP Chair on Monday CHMP week
- CHMP Chair makes final proposal according to objective criteria in line with best available scientific expertise (http://www.emea.europa.eu/pdfs/human/regaffair/12406605en.pdf)
- Adoption of Rapporteurs appointment by the Committee
- Outcome letters sent to applicants during the week following CHMP meeting

Rapporteurship appointment



Role of the Peer Reviewer

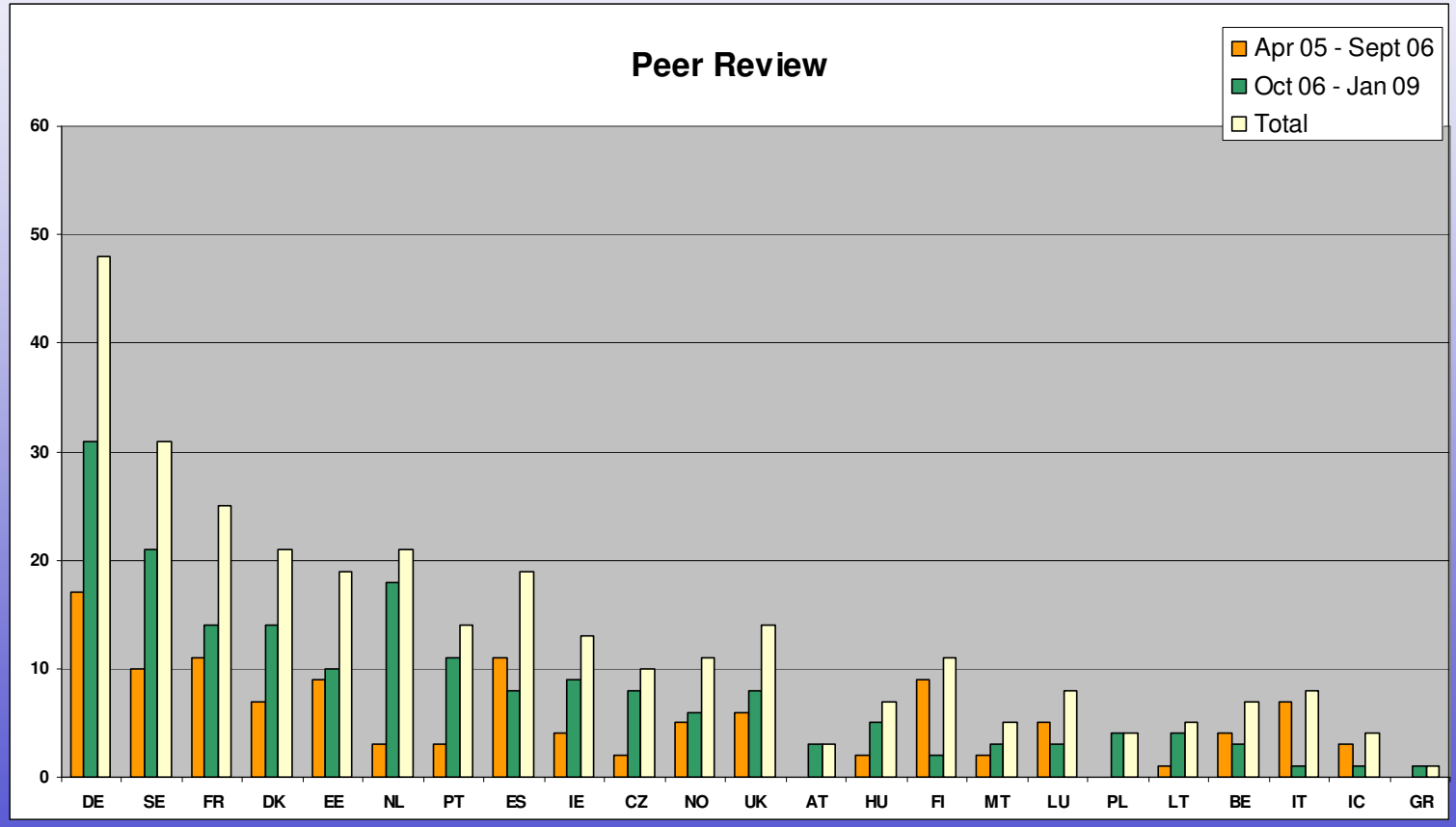
- Appointed at the same time of Rapporteurs but detail not shared with applicants
- To contribute to quality assurance of the List of Questions
- Peer Review may encompass whole or part of Q / S / E
- Peer Reviewer systematically address
  - ✓ Extent to which scientific argumentation supports proposed LoQs
  - ✓ Consistency issues raised LoQs and CHMP guidelines / Scientific Advice and similar issues seen with products same class / indication
- EMEA Peer Review Team also appointed
- CHMP members also contribute to review system

What is the CHMP Peer Review?

80 Reports	80-100 Peer Review	100 Comments	107 Draft LOQ	112 Tele-conference	115 Draft LOQ	120 CHMP Adopts LOQ

- CHMP members and scientific secretariat review the rapporteurs' reports
  - Content, consistency, format
  - Peer reviewer's comments are not made available to applicants
- Purpose
  - Improve day 120 List of Questions (LoQ)

Peer review appointment



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Interaction with Rapporteurs

- Pre-submission
  - national advice
  - after appointment
- Day 0-120
- Post Day 120 LoQ
  - "clarification" meetings
  - pre-submission meetings
- Before OE
- Post OE (after trend vote)

A few thoughts….

- when (during CHMP week?)
- "clarification" meetings
- advice before OE
- interpretation of trend votes

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Review and Learning Project on RMP

- Objectives
  - To learn from experience to remedy problems:
    - Quality/completeness of RMP
    - Post-authorisation Safety Studies
    - overall usefulness of RMPs

- Actions proposed to meet the objectives
  - *EMEA Risk Management team* to take the lead for revisit of EU RMP guideline and template, to map RMP implementation in Member States, and to arrange interactive workshop with Industry.
  - *A joint CHMP, PhVWP, CMD(h) and EMEA drafting group* to be established and to draft recommendations on procedures, best practices, training etc and on approaches for involvement of expertise, advice, etc.
  - *Department of Clinical Epidemiology of the Utrecht University* to finalise analysis of scientific quality of the PASS in RMPs and to propose improved procedures, and to progress with a review the outcomes of RMP implementations.
  - *The Review and Learning project group* to propose approaches to evaluate the short- and long-term overall usefulness of Risk Management, including better knowledge of life-time safety, safer/more effective use in real life and positive impact on drug related Public Health at large.

Risk minimisation Plan

If additional risk minimisation activities is needed

- Should list safety concerns for which risk minimisation activities is needed
- Should include both routine and additional risk minimisation activities

Additional Risk Minimisation Activities

- Controlled distribution
- Educational information for physicians
  - Particular serious risks associated with medicine
  - Existence of surveillance programme
  - Pregnancy prevention plans
- Patient information
- Patient alert card
- Patient monitoring card
- Training programme

Risk Management Plans

from 01/09/2005 – 31/10/2008

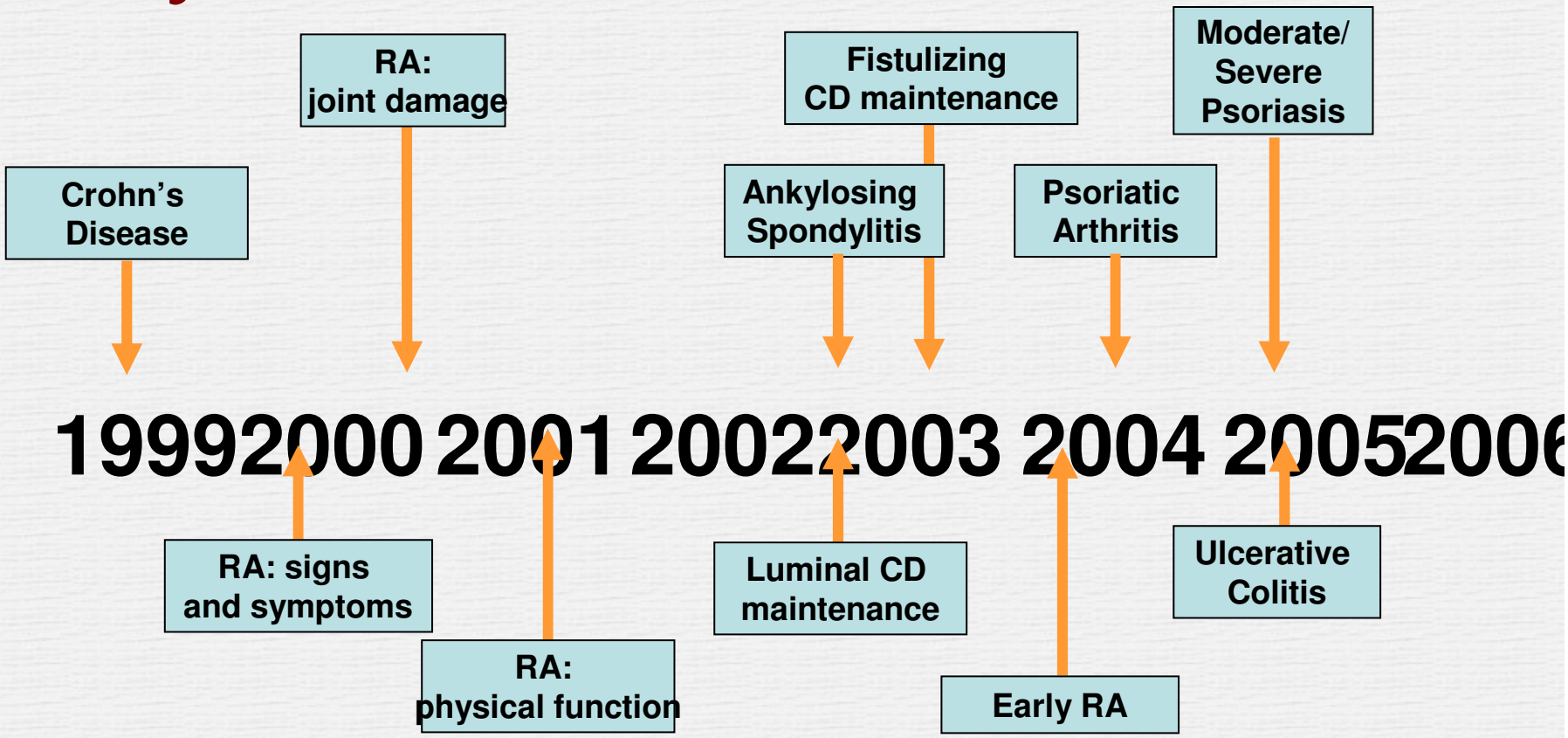
	Positive Opinions	RMP	Additional Risk min activities
New Marketing Authorisations	170	143	20

Update to the EU-RMP

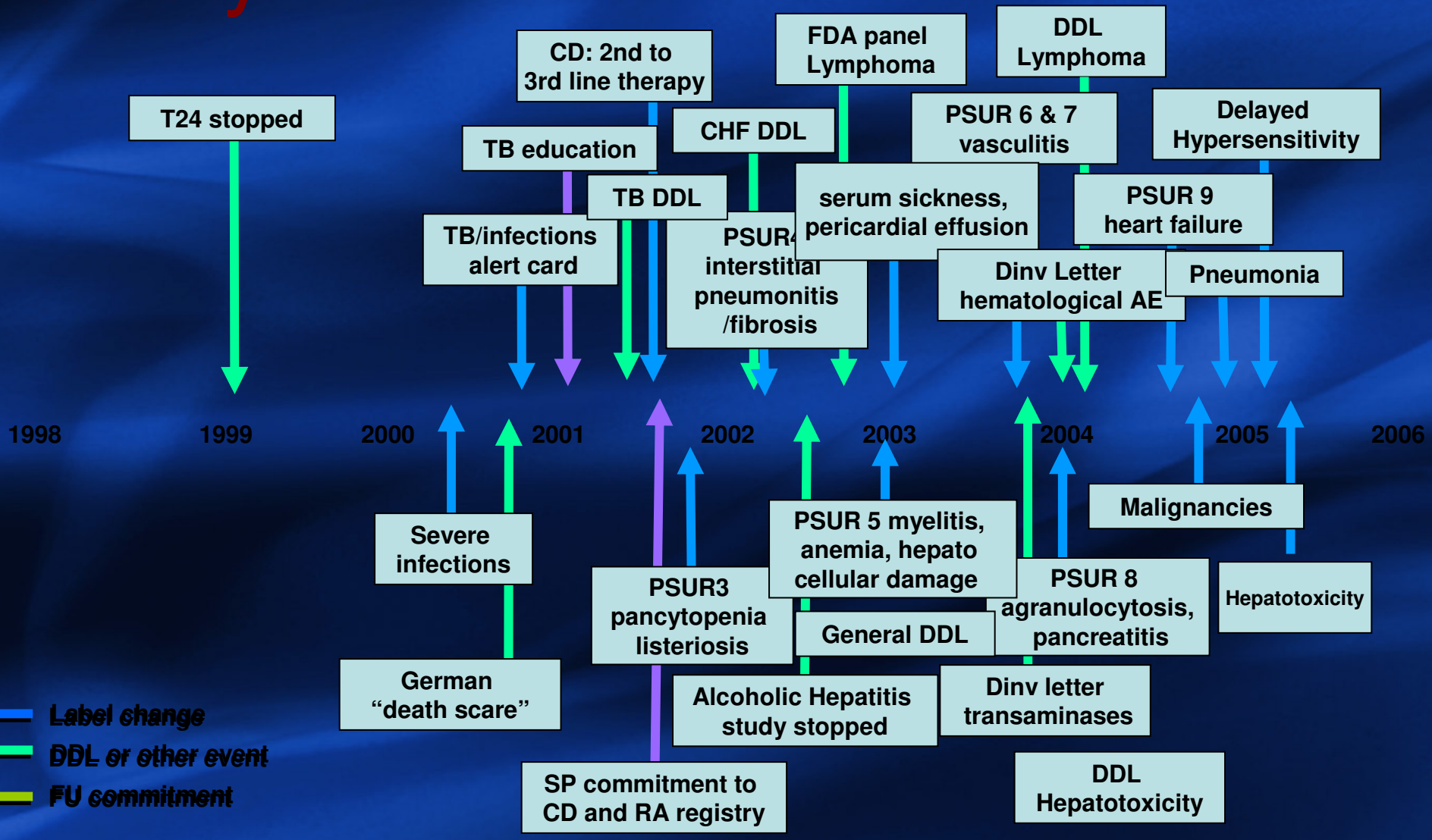
The EU-RMP is a living document

- updated throughout the lifecycle of the product
- safety specification will change over time
  - results from other clinical trials
  - results from studies in PhV Plan
  - spontaneous reports and literature
- PhV Plan and Risk Min Plan will also change over time

Evolution of Remicade (EU): Efficacy



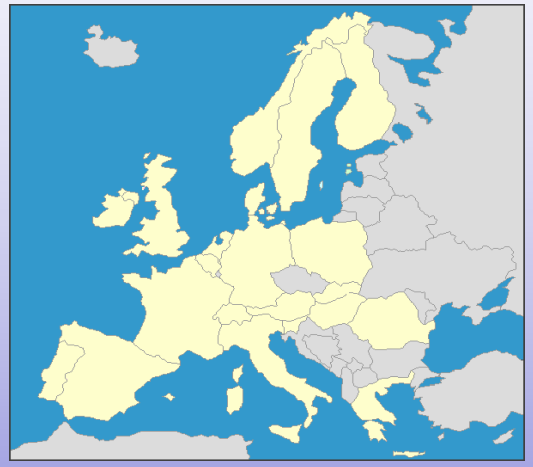
Evolution of Remicade (EU): Safety



ENCePP project

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

- **87** partner organisations (56 partners in 2007)
- in **21** European countries



- 2 **Plenary Meetings** in 2007 and 2008 with more than 70 participants (research centres, database & registry owners, learned societies, NCAs, observers from Industry & patients' and health care professionals' organisations, etc)

ENCePP project

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

- **ENCePP Implementation Advisory Group (ENCIAG):** Advisory Group of 11 experts from academia, regulators (NCAs, CHMP, PhVWP) and learned societies
- **4 ENCePP Working Groups (WG)**

Core Objectives 2009:

- Progress & implementation of first results of ENCePP WGs

  incl. the publication of a **Set of guidance & standards**, the **ENCePP Code of Conduct** and **Inventories of the existing European resources for PEpi research**
- Start to commission first studies through the network

Web page: http://www.encepp.eu/

Thank you for your attention