Patients @ EMA

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Eurordis Summer School 2012, Barcelona

EURORDIS
Rare Diseases Europe

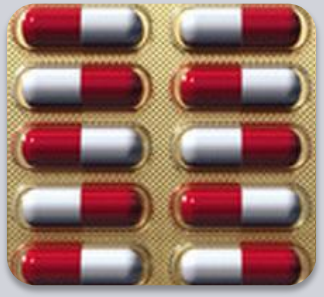
Please comment (fictitious case)

- A pulmonary hypertension patients' organisation collects information from its members, annually.
- Information includes contact details, health status evolution disease history, treatments and co-medications
- From 2002 to 2009, out of 160 new members, 7 had been exposed to Mediator®

Are you prepared? How would your organisation respond to:

- Quantitative data you have on the use of the medicine
- And also qualitative data (by MS…)
- Whether patients are aware of the increased risks
- Whether they are reporting benefits & which ones
- How pts would react to a market withdrawal
- Which off-label uses are reported by patients

The benefit-risk is a matter of



Constrains and ease of use

Frequency of side effects

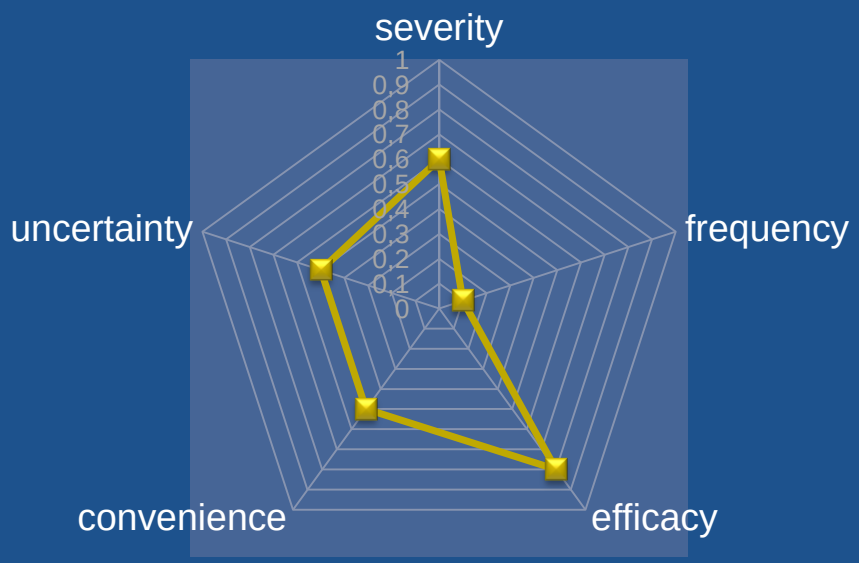
Efficacy including quality of life

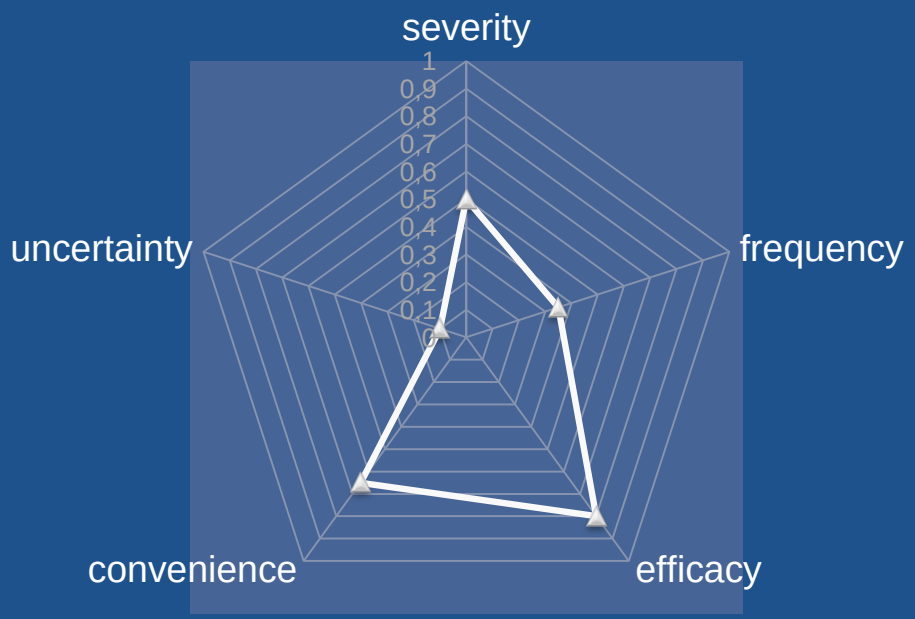
Severity of side effects

Uncertainty what is unknown as of today?

EURORDIS
Rare Diseases Europe

In fact a 5D balance model





Agencies and Democratisation workshop, Liege, 2007

European Governance: Transparency and democracy in European Agencies

- Horizontal decentralisation involves the delegation of some tasks to **agencies**.
- Which guarantees do we need in terms of
  - transparent decision-making,
  - high-quality expert advice,
  - unbiased consultations,
  - independence,
  - legitimacy,
  - accountability

Transparency: legal basis

- EU Treaty (Declaration 17 of the Annex)
  - "(…) Transparency of the decision-making process strengthens the democratic nature of the institutions and the public's confidence in the administration."
- Council Regulation (EEC) No. 2309/93
- Public assessment reports
- Information on experts/declaration of interests

Transparency: limitations

- confidentiality constraints
  - protection of commercial and industrial secrecy,
  - protection of individuals and of privacy

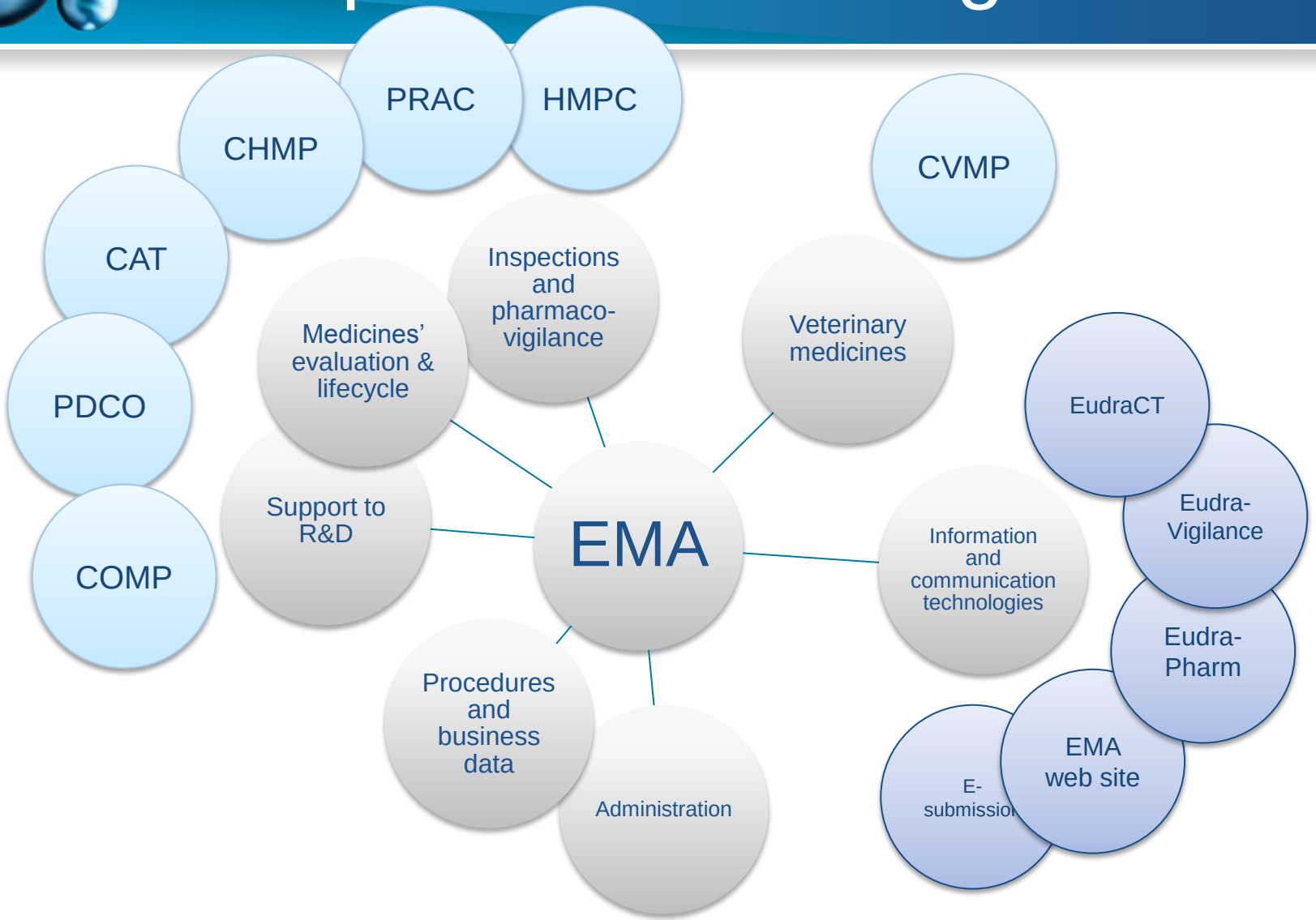
Identified stakeholders

- patients / patients' groups / public
- healthcare professionals
- pharmaceutical companies
- Academia (e.g. IMI projects, ENCEPP…)
- regulatory authorities
- Health technology assessment bodies
- scientific media
- lay media

Available tools

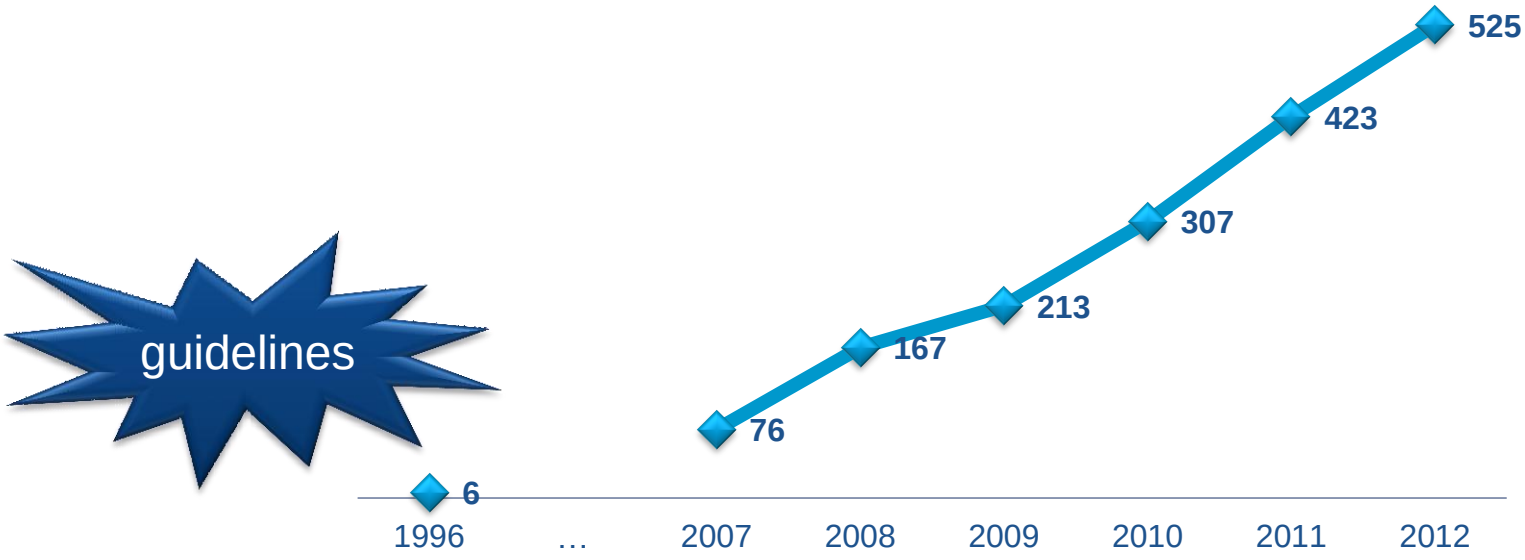
- EMA press releases
- Scientific committees agendas and monthly reports
- Summaries of CHMP & COMP opinions
- EPARs (European Public Assessment Report) with SmPC
- EMA/CHMP public statements
- Annual reports
- Work programmes
- SOPs
- Committees guidance documents
- Dialogue with stakeholders
- Workshop reports
- …

Simplified EMA reorganisation



A constant progress

Overall occasions when patients/consumers are involved in EMA activities, pey year



From EMA Sixth report on the progress of the interaction with patients' and consumers' organisations (2012)

The PCWP

- Basically: the platform of exchange where we discuss together “how do we work with such an agency?”
- Dialogue between patients, consumers and all scientific committees at EMA
- Established 2007 (working group 2004-2007)
- Chaired by Isabelle Moulon (EMA) & Lise Murphy (EURORDIS)
- With Juan Garcia, Nathalie Bere and other colleagues
- New membership in progress (up to 20)
  - new co-chair election September 2013

All 34

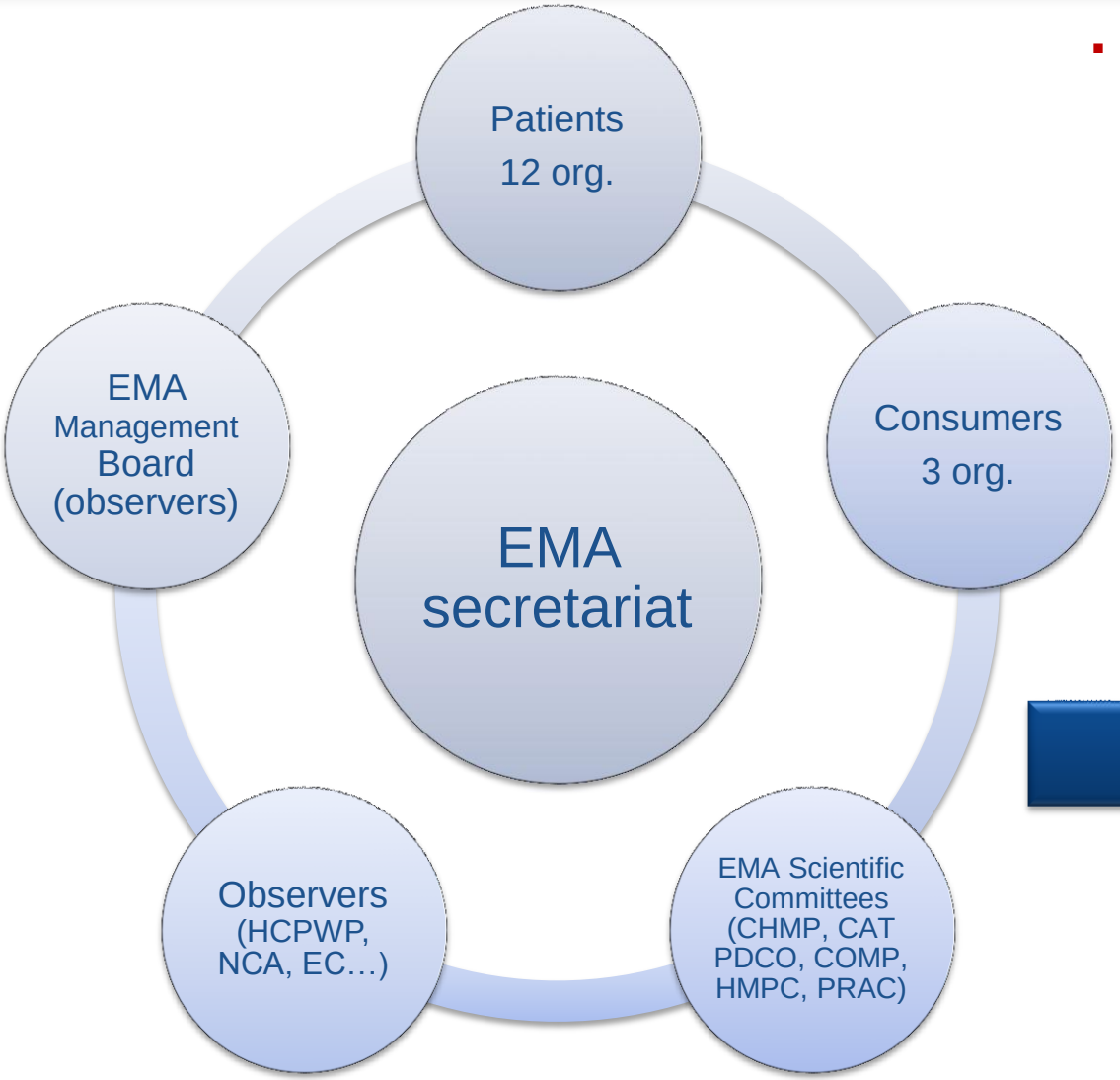
PCWP

Patients as representatives/experts

As representatives (e.g. PCWP)	As experts
Consulted on issues of general interest: the opinion of the organisation e.g. on the new logo for additional monitoring of medicines ▼	Consulted on product or disease specific issues e.g. guidelines for the evaluation criteria, scientific advice for benefit/risk evaluation
Can liaise with their organisation in order to deliver the position of the organisation, or give their own	Invited as individual expert Does not represent the organisation Personal expertise
Usually no confidential matter, but it the case: MAH will be informed, and can agree or not to disclose confidential data	Should inform EMA if consulted by applicant/sponsor/MAH
	Confidentiality undertaking
	Conditions to consult with other patient experts
	Adheres to same rules as all other experts
Personal view: should have a mandate and a decision making capacity	Name entered in the EMA EU experts' database

The patients' and consumers' working party (PCWP) is made up of:

- Committee for Medicinal Products for Human Use (CHMP),
- Pharmacovigilance and Risk Assessment Committee (PRAC),
- Committee for Orphan Medicinal Products (COMP),
- Committee for Advanced Therapies (CAT),
- Co-ordination Group for Mutual Recognition and Decentralised Procedures–Human (CMD(h)),
- Healthcare Professionals' Working Party (HCPWP),
- Paediatric Committee PDCO),
- Committee on Herbal Medicinal Products (HMPC)



- Number of patients/consumers organisations will increase to 20 as of September 2013

The patients' and consumers' working party (PCWP) addresses:

- How to best work with the EMA
- Expectations from each other working together
- Transparency of the regulatory process
- Including the patient's views in EMA processes
- Training needs
- Information to the public

PCWP @ EMA

- 34 patients' and consumers' organisations eligible to work with EMA (eligibility criteria)
  - 8 for rare diseases, including EURORDIS
  - 15 are member of the PCWP
    - Meet 4 times a year with representatives of all EMA scientific committees
    - Mandate
    - Action plan
    - Evaluation and report

EURORDIS and PCWP

- We have a task force: Drug Information, Transparency and Access (DITA)
- Follows the PCWP work flow
  - Plus off-label use, NATC products, QofL, members' own issues, working with national authorities…
- Currently 13 members
- Meets 2x / year, and conference call
- 4-5 new members expected among you!

Our activities (summarised)

Interaction	• Rules for the involvement of patients • Policy on conflicts of interest
Pharmacovigilance	• Pilot self-reporting • Implementation of new legislation
Information	• EPAR summary for the public, package leaflets • Risk communication • Information on benefit/risk
Transparency	• Dissemination of EMA decisions and documents • Public hearings • Medicine Supply shortages

Example 1: a comment to PL

1. What X is and what it is used for

X contains the active substance Z. X is
Therapy and is given to adults with Gau

How X works

Signs of this disease are one or more o

- spleen or liver enlargement
- a low number of red blood cell
- a tendency to bleed easily cau
  platelet count. (Platelets stop b
  plug in a hole in a vessel)
- bone disease

Comment:
Why are neurological or dermatological symptoms not mentioned? It gives the impression that X is only for type I Gaucher disease.
A bullet point "sometimes other signs such as yellowish-brown skin colour or neurological symptoms exist" should be added.

Example 2: Consultation Pharmacovigilance & Additional monitoring

Selection of the black symbol
Outcome consultation with the stakeholders

(3) Would you have any **other suggestions** for the 'black symbol'?

Black triangle with an eye inside	
Traffic lights	
Capsule behind magnifying glass	
Non-inverted triangle with capsule inside	
Vigilant eye with capsule inside	
Banner (indicating 'work in progress')	
Traffic cone (indicating 'work in progress')	
Video surveillance	
Hand icon	

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Example 3: Joint EMA / university of Groningen study on disease outcome preferences

- EMA Project on Benefit-Risk Methodology
- Values and Preferences for Health States Among Patients (efficacy and safety)
- 3 therapeutic areas (research phase)
  - Cardiovascular, central nervous system, oncology
  - Study launched with UK MS society – November 2011
- Presented by: Andrea Beyer, EMA/UMCG Collaboration

Treatment attributes and levels in MS study

Treatment attribute	Levels
Number of relapses during next 5 years	No relapse
	1 relapse
	3 relapses
	4 relapses
Time (from today) until your disease worsens	8 years
	5 years
	3 years
	1 year
Chance of dying from liver failure within 10 years	None would die
	5 patients out 1000
	20 patients out 1000
	50 patients out 1000
Chance of dying or severe disability from PLM within 10 years	None would die
	5 patients out 1000
	20 patients out 1000
	50 patients out 1000
Chance of dying from leukaemia within 10 years	None would die
	5 patients out 1000
	20 patients out 1000
	50 patients out 1000

Johnson Reed F. Multiple Sclerosis patients' benefit-risk preferences: Serious adverse event risks versus treatment efficacy. JNeurol 2009 256:554-62

Example of comparing treatment option

Treatment features	Treatment A	Treatment B
Number of relapses during the next 5 years	4 relapses	2 relapses
Time (from today) until your MS gets worse	3 years	3 years
Chance of dying from liver failure within 10 years	None would die	20 patients out of 1000 (2%) would die
Chance of dying or severe disability from PML within 10 years	5 patients out of 1000 (0,5%) would die	None would die
Chance of dying from leukaemia within 10 years	None would die	None would die
Which treatment would you choose?	Treatment A?	Treatment B?
	50%	50%

CHMP consultation with POS

- Pilot phase
  - Can't be systematic: too many products, too many regulatory decisions
  - First identify topics where CHMP will consult with POs
- E.g. benefit/risk re-evaluation
  - benefit not fully demonstrated with increasing risks
    - Onsenal®/celecoxib for Familial Adenomatous Polyposis
  - CHMP may ask which quantitative/qualitative data we have regarding the use of the medicine
  - Whether patients are aware of the increased risks
  - Whether patients are reporting benefits and which ones
  - How patients would react to a possible market withdrawal
- Are we prepared?

Other activities

- To communicate on the risks and benefits of medicines together
  - With equal emphasis on efficacy than on risks
- To follow-up the implementation of the legislation on pharmacovigilance
- User testing for all EMA IT projects
- All EMA workshops (medication errors, patient support programmes…)
- Clinical trial data and transparency
- Newly: medicines supply shortages

Some cases

- **Supply shortage**
  - Myozyme® - March 09
  - Thyrogen – March 2011- continues
  - Cerezyme® and Fabrazyme® June 09 – continues
  - Increlex – April 2013 – continues
- **Product defect** (with or without supply shortage)
  - Norvir® capsules - October 98
  - Viracept® 2007
  - All products Ben Venue Laboratories since December 2011 (Angiox, Busilvex, Caelyx, Cayston, Ceplene, Ecalta, Luminity, Mepact, Soliris, Torisel, Velcade,Vibativ, Vidaza and Vistide)
- **Adverse drug reaction**
  - Cox 2 inhibitors 2005
  - Biphosphonates/ osteonecrosis of jaw 10/2010
- **Sudden market withdrawal**
  - Dextropropoxyphene September 09

To help you:

- Is a medicine designated as orphan?
- When is a MAA submitted?
- New safety alerts
- Safety referrals
- EudraVigilance
- EudraCT register
- New PASS/PAES
- Trainings