EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

New Pharmacovigilance Legislation: Update on implementation

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In this talk:

- Objectives
- Key measures
- Implementation
- What to expect 2012
- Conclusions

Why? - To Further Strengthen Pharmacovigilance

- 5% of all hospital admissions are for Adverse Drug Reactions (ADRs)
- 5% of all hospital patients suffer an ADR
- ADRs are the 5th most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU societal cost of ADRs amounts to Euro 79 Billion per year

Why? - Background

- Opportunities identified to strengthen and rationalise EU PhV to better protect public health
- Excellent public health protection and promotion requires:
  - Science
  - Law
  - Resources
- Much good work ongoing prior to the new legislation e.g:
  - IMI Protect – regulatory science
  - EudraVigilance – key resouce
  - ENCePP – research capacity building

How? - Making of New Legislation by the European Commission

- 2003: EC decision to undertake an assessment of the Community system of pharmacovigilance
- Both **Regulation (EC) 1235/2010** and **Directive 2010/84/EC** have been published on 31 December 2010
- July 2012: new legislation will apply
- Some transitional provisions:
  - ADR reporting to EMA only,
  - PSUR reporting to EMA only,
  - Pharmacovigilance System Master File

Why? High Level Objectives

Promote and protect public health by reducing burden of ADRs and optimising the use of medicines:

- Clear roles and responsibilities / robust and rapid EU decision-making
- Engage patients and healthcare professionals (involve + empower)
- Science based
- Integrate benefit and risk
- Risk based/proportionate
- Increased proactivity/planning
- Reduced duplication/redundancy - Strengthen the EU Network
- Increase transparency and provide better information on medicines

What? - Scope of Changes

- Coordination / lists of medicines
- Authorisation requirements
- Risk Management Plans
- Post-Authorisation Studies (Safety and Efficacy)
- Effectiveness of risk minimisation
- Adverse Drug Reactions reporting
- Signal detection
- Periodic Safety Update Reports
- Scientific Committees / decision-making
- Transparency and communication
- Coordination of inspections
- Pharmacovigilance Audits
- Fees charged and payments for assessments / services

Impact

Biggest change to the legal framework for human medicines since 1995

Implementation – key risks

• For EMA: the lack of human and financial resources is the biggest risk to the implementation and operation of the new legislation → Scenario planning and prioritisation exercise ongoing

•Commission bridging budget 2012? Critical for success

•Commission proposal in 2012 for a fee regulation revision (effective 2014?) Critical for success

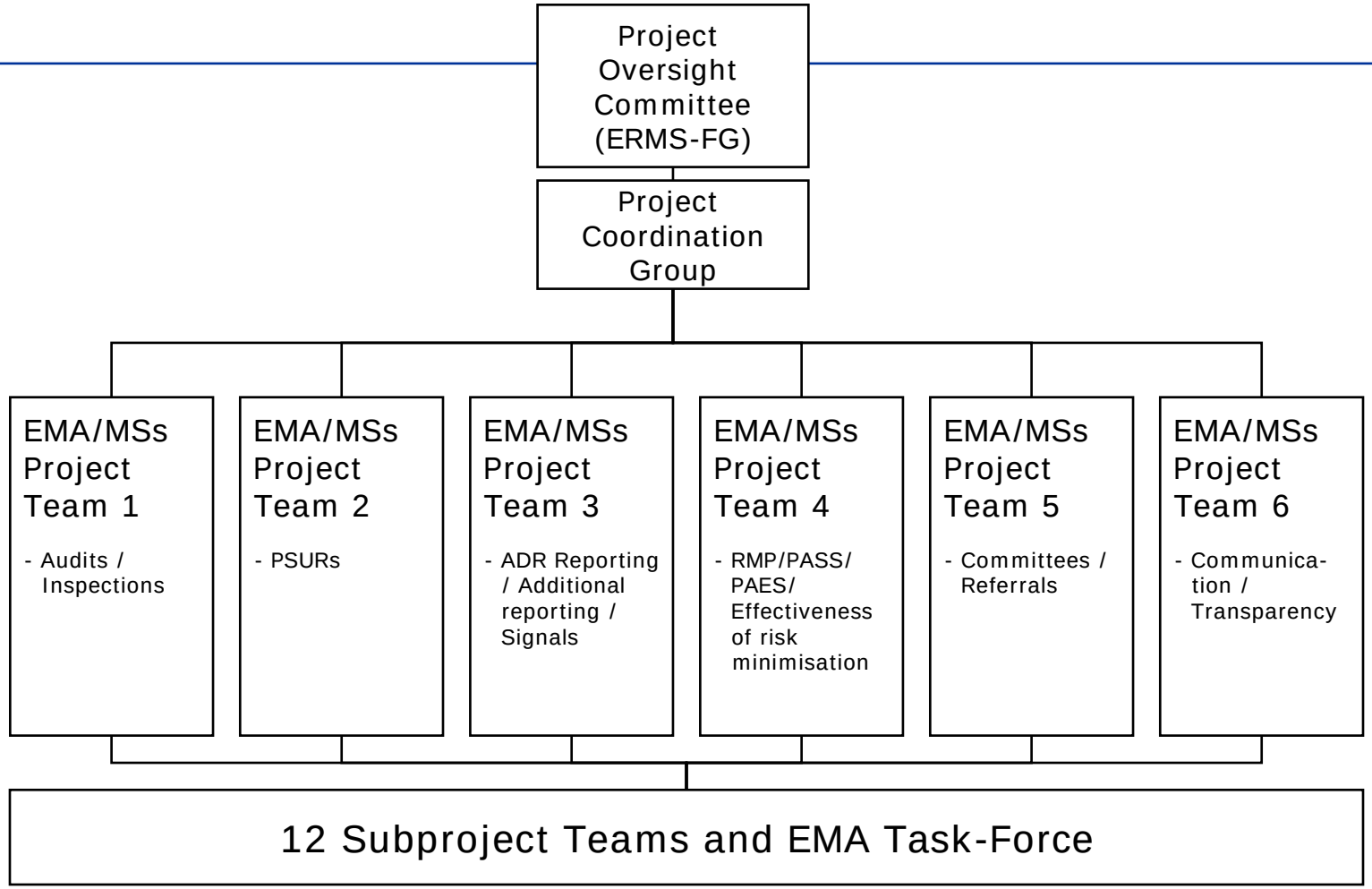
• For all Stakeholders: lack of involvement (i.e. information, consultation) in the implementation

•For all Stakeholders: manage expectations

How to implement?

- Dedicated governance structure
- 6 Member States / EMA Project Teams
- 12 EMA Subproject Teams
- Stakeholders meetings involving EMA, Member States, EC, Industry, Patients and Healthcare Professionals representatives:
  - Three meetings held on 15th April, 17th June and 20th October 2011 (presentation and videos on EMA website)
  - 2012 dates: 27 February; 25 May; 1 October

How to implement? – Governance structure



Pharmacovigilance and Risk Assessment Committee (PRAC)

Key new committee for the benefits and risks on medicines

Membership:

- Member State experts
- Additional Commission appointed experts
- Patient representative and alternate
- Healthcare professional representative and alternate

Commission deadline 1 December

(http://ec.europa.eu/health/human-use/latest_updates/index_en.htm)

Transparency / web-portal

The new legislation and the Internet

- Key element of the legislation: **to publish online** new information for the general public
- Spirit is of **openness and transparency**
- To **promote the safe use of medicines**

Internet use in the EU27

- 70% of households in the EU27 have internet access
- More than half of individuals in the EU27 used the internet **daily** in 2010
- Approx half of internet users in the EU27 looked for information on the websites of **public authorities**

Eurostat, Data in focus, Internet usage, 2010

What the legislation says

- EMA to publish considerable amounts of new data and documents (agendas, minutes, PASS protocols, PASS study abstracts, RMP summaries, etc.)
- EMA to launch a European medicines web portal
- National authorities to launch national medicines web portals (ADRs, SPCs, PILs, reporting forms for ADRs)

Vision for pharmacovigilance online

- **Network of websites** (European medicines web portal and national web portals) with the aim of:
  - Highlighting information on medicines
  - Highlighting safety issues with medicines
  - Promoting patient reporting through linking to online forms
  - Promoting transparency on regulatory procedures associated with safety of medicines
  - Announcing public hearings on medicine safety issues (live broadcast?)

Vision for the European medicines web portal

- Static website ‘signposting’ (directing) users to relevant information on other websites (NCAs, national portals, EU clinical trials register, EMA etc.)
- Available in 23 official EU languages
- Designed for the European public: consumer-facing
- NCAs and Commission involved closely in design
- Spirit of the implementation: start simple and focus on the user

Profound increase in transparency

Public:

- Names and qualifications and declared interests of the committee members
- All agendas and minutes of the committees
- Summaries of all risk management plans
- List of medicinal products
- Locations of the company Pharmacovigilance systems and contacts points
- Reporting information
- PSUR submission dates
- Protocols and results of post-authorisation studies
- Announcement of referrals and public hearings
- All conclusions of assessments, recommendations, opinions, approvals and decisions

Companies keep products up to date with web-portal

"The marketing authorisation holder [company] shall ensure that product information is kept up to date with current scientific knowledge, including the conclusions of assessments and recommendations made public by means of the European medicines web-portal...."

Responsibility shift to the companies!

Coordination of safety announcements

EMA responsibility:

"*For active substances contained in medicinal products authorised in more than one Member State, the Agency shall be responsible for the coordination between national competent authorities of safety announcements and shall provide timetables for the information being made public.*

Under the coordination of the Agency, the Member States shall make all reasonable efforts to agree on common safety messages and the timetables for their distribution. The Pharmacovigilance Risk Assessment Committee shall, at the request of the Agency, provide advice on those safety announcements."

Public hearings

Written consultation of all stakeholders for all referrals

For important risk and benefit risk referrals – oral 'hearings'

Plan to start for targeted referrals in Autumn 2012

How to organise – still under discussion

Key opportunity to engage in medicines regulation and patient safety

Article 57(2), second subparagraph of Regulation (EC) No. 1235/2010 – Legal requirements

Article 57(2), second subparagraph of Regulation (EC) No. 1235/2010 requires:

- **The Agency** to publish the format for the electronic submission of information on medicinal products for human use by 2 July 2011
- **The marketing-authorisation holders** to submit information to the Agency electronically on all medicinal products for human use authorised or registered in the European Union by 2 July 2012, using this format
- **The marketing-authorisation holders** to inform the Agency of any new or varied marketing authorisations granted in the EU as of 2 July 2012, using this format

Article 57(2), second subparagraph of Regulation (EC) No. 726/2004 – Benefits

This information will help the Agency to:

- Create a list of all medicines authorised and registered in the EU, including medicines authorised centrally via the Agency and medicines authorised by regulatory authorities in EU Member States

This information will help the Agency and Stakeholders to:

- Identify medicines (including biologics/biosimilars) accurately, especially medicines included in reports of suspected adverse reactions
- Coordinate the regulation and safety-monitoring of medicines across the EU
- Facilitate the international harmonisation activities (ICH E2B and M5)

Eudravigilance development

- Publication of anonymised data for centrally authorised products early 2012
- Publication of anonymised data for common substances end 2012 (to be confirmed)
- Patient reporting to (remaining) Member States July 2012
- Member States and companies report to EudraVigilance only (following EudraVigilance audit) in 2015 based on new EudraVigilance functional specifications.

Key achievements: Concept paper on implementing measures published by the European Commission

'Those measures supplement essential aspects of the new pharmacovigilance system with the more technical details that have to be observed by marketing authorisation holders, national competent authorities and EMA in the daily practice of applying the new legislation.

It is therefore important that they are fit for purpose and strike the necessary balance between the fundamental objective of the current legislative framework for medicinal products, i.e. to safeguard public health, and general internal market requirements.'

Deadline for public consultation: 7 November 2011

Development of Good Vigilance Practices

- GVP will be developed in a **modular approach** in order to facilitate its maintenance
- Roles and responsibilities are clearly defined for GVP development:
  - Module Rapporteur
  - Module Co-Rapporteur
  - Regulatory reviewers
  - Editors
  - Language reviewers
  - Technical terms reviewer
  - Assistant Editor

Development of Good Vigilance Practices

- GVP will be drafted at EMA/MSs Project Team level, following a **phased approach**
- Formal public consultation (8 weeks)
- Agreement at ERMS-FG level
- Endorsement by CHMP, PRAC/PhVWP, Coordination Group and relevant experts groups
- Adoption by EMA Executive Director

Development of Good Vigilance Practices

- **First 'wave' of modules to be published <u>in July 2012</u>**
  - Module I: Pharmacovigilance Systems and their Quality Systems
  - Module II: Pharmacovigilance System Master File
  - Module V: Risk Management Systems
  - Module VI: Data Management of Individual Case Safety Reports
  - Module VII: Periodic Safety Update Reports
  - Module VIII: Post-Authorisation Safety Studies
  - Module X: Detection and Management of Signals and information

Development of Good Vigilance Practices

- **Second 'wave' of modules to be published <u>in December 2012</u>**
  - Module III: Pharmacovigilance Inspections
  - Module IV: Audits
  - Module IX: Post-Authorisation Efficacy Studies
  - Module XI: Public Participation in Pharmacovigilance
  - Module XII: Continuous Pharmacovigilance, Ongoing Benefit-Risk Evaluation, Regulatory Action and Planning of Public Communication
  - Module XIII: Incident Management
  - Module XIV: Educational and Communication Tools and Materials for Pharmacovigilance and Risk Minimisation
  - Module XV: Effectiveness of risk Minimisation
  - Module NR: Referral Procedures for Safety Reasons

In 2012 – watch out for:

Patient reporting to MSs

Access to (some) EudraVigilance data

New committee (PRAC) – including patients and healthcare professionals

New referrals including public hearings

Publication of recommendations, conclusions, opinions

Conclusions

- **Excellent public health protection requires:**
  - **Science**
  - **Law**
  - **Resources**
- **New law: prioritisation and planning critical + Collaboration,**

For better pharmacovigilance and better health protection and promotion