Safeguarding public health

The New PV Legislation

Perspective from a Member State

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Reinforcing patient safety in Europe, Zagreb June 2011

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Background

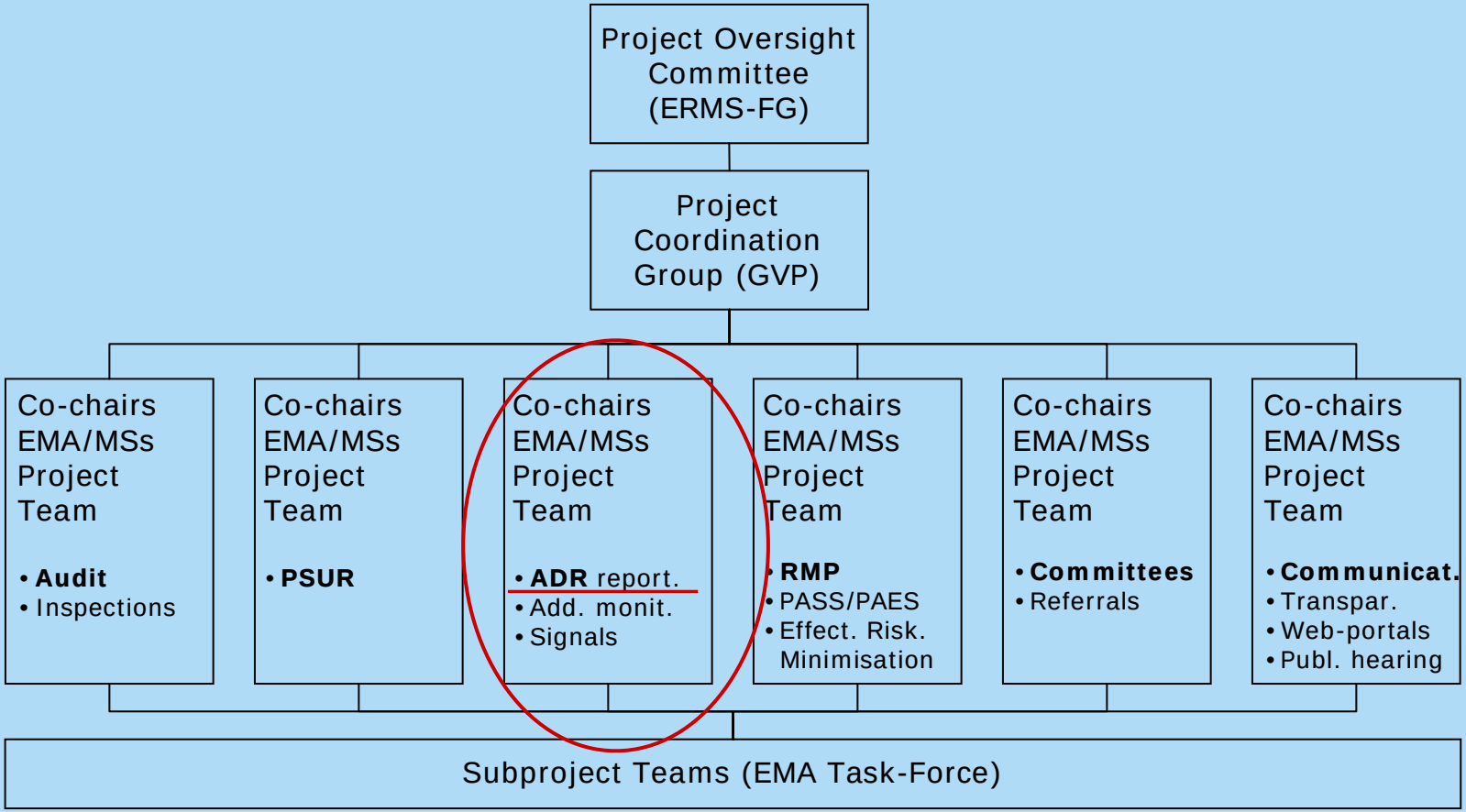
A lack of clear roles and responsibilities for the key responsible parties and a lack of clear obligations against which they perform their roles (resulting in poor compliance);
Slow EU decision-making on drug safety issues particularly for nationally authorised products and frequent disharmony in action taken by the Member States;
Low levels of transparency relating to pharmacovigilance and relatively limited EU coordination of communication about the safety of medicines, plus complex product information with poor penetration of key warnings;
Cumbersome oversight of companies' pharmacovigilance systems by the authorities;
A lack of proactive and proportionate monitoring including a lack of risk management and structured data collection in the form of post authorisation safety studies and duplicative reporting rules for the industry and authorities relating to both 15-day, literature and periodic (PSUR) reporting of ADRs;
Lack of inclusiveness of stakeholders including a lack of direct patient reporting of ADRs and their virtual absence from decision-making.

At least 591 lives and €237 Million saved

Process

- Positive vote in EU parliament Sept 2010
- Formal adoption and publication 31 December 2010
- Transposition over 18 months
  - Development of guidelines
  - Development of systems
  - National regulation changes
  - Implementing measures
- Effective from July 2012

Governance of the Implementation of the New Pharmacovigilance Legislation



ADR Reporting
Definitions:

Directive 2010/84/EU

Article 1

Article 1 is amended as follows:

(a)Point 11 is replaced by the following

11. Adverse reaction: A response to a medicinal product which is noxious and unintended

ADR Reporting
Definitions:

Directive 2010/84/EU

(Chapter 5) For the sake of clarity, the definition of the term 'adverse reaction' should be amended to ensure that it covers noxious and unintended effects resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse of the medicinal product.

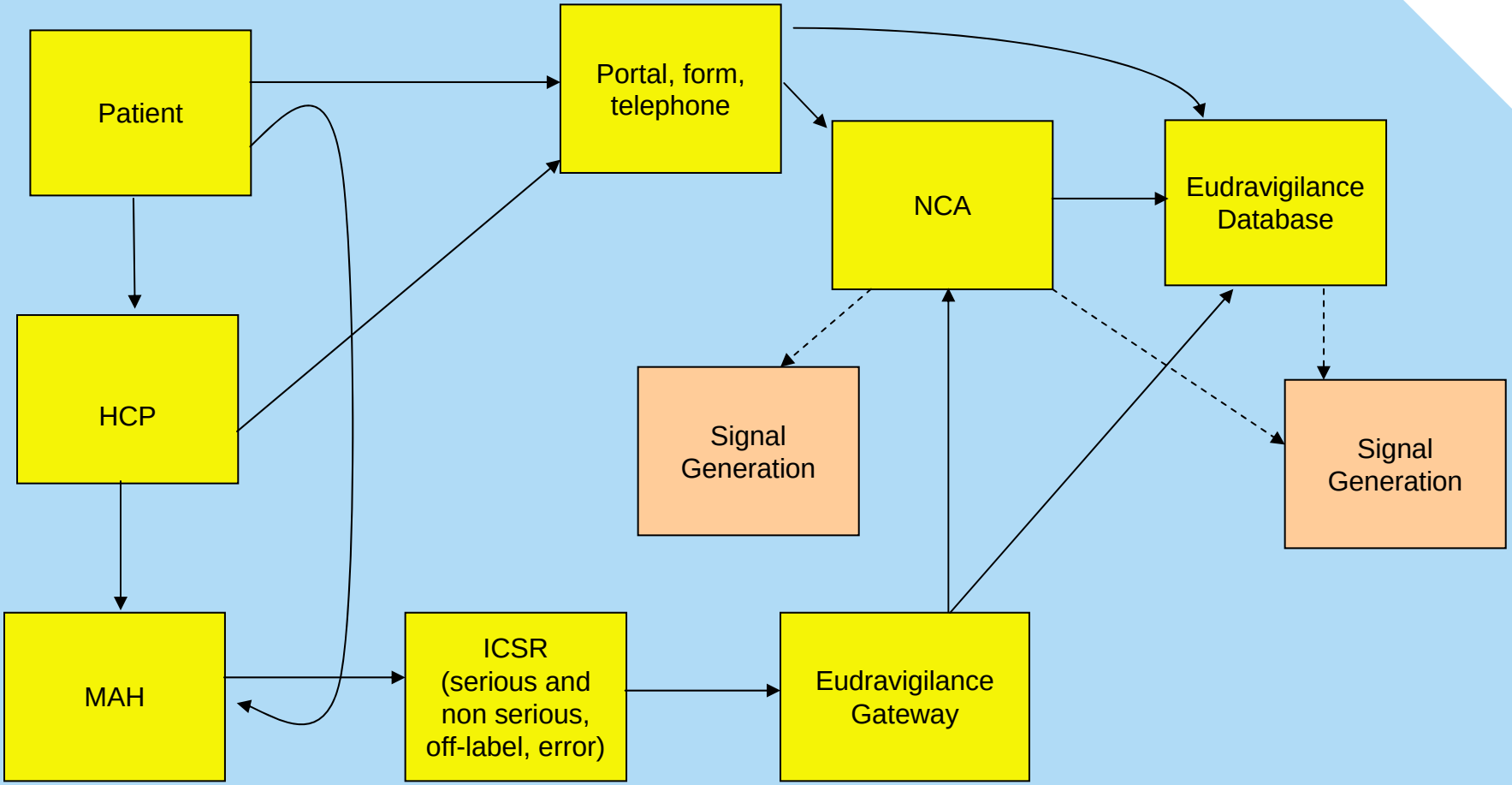
ADR Reporting:

Directive 2010/84/EU
Article 107(3)

MAHs shall submit to Eudravigilance:
all Serious 15 days
All non-serious 90 days

Note: includes error, off-label, expected, patient, *and worldwide?*

ICSR Reporting – Future Vision



ADR Reporting: However…..

Directive 2010/84/EU

Article 2 – Transitional Provisions

- Eudravigilance functionality to be met first
- Functional requirements to be drawn up by MSs and Agency
- Functionalities to be audited
- Article 107(3) applies 6 months after audit

Latest position EV ready for audit late 2014

In the Interim…

- Format of the ICSR – E2B(R3)
- Drug/Product Dictionary – IDMP,
- Routing of ICSRs via gateway
- Data cleansing project

Some questions

ADR Reporting by NCAs

- Are NCAs expected to implement new rules from July 2012 without EV functionality?
- Will Non-serious be reportable?
- Will patient reports be reportable?
- Will error be reportable?
- What should be sent to EV?
- How will I cope with volumes?

PSURs

The requirements for PSURs have been significantly amended i.e.

- **For many generic and traditional herbal medicinal products, PSURs will no longer be required**. However, competent authorities can request PSURs for these products on the basis of pharmacovigilance concerns.

- MAHs shall submit **to EMA** *(after the repository has been established)* PSURs containing:

  - Summaries of data relevant to the benefits and risks of the product ***(line listings will no longer be routinely required)***.

PSURs

- The frequency with which PSURs are to be submitted shall be specified in the MA.
- For MAs granted prior to the implementation of this legislation, in general, the frequency will be as stated in current legislation.
- For MAs containing the same active substance the frequency may be amended and harmonised to facilitate a single assessment in the context of work-sharing. The single frequency will be made public by EMA. MAHs may submit requests to adjust the submission frequency e.g. to aid harmonisation.
- EMA shall send PSUR assessment reports to the MAH (*after the new repository has been implemented*).

What do Member States need to do?

PSURs

- Establish which products are exempt
- Harmonise dates
- Establish work-sharing procedures
- Agree e-forms
- Establish repository
- Develop guidance and SOPs

Literature Searching

- EMA shall monitor selected medical literature for reports of adverse reactions to medicinal products containing certain active substances. It shall publish the list of active substances being monitored and the publications subject to this monitoring.

- For products containing the active substances referred to in the list of publications monitored by the EMA, MAHs shall not be required to expedite reports from these sources to the Eudravigilance database, but they shall monitor *all other medical literature* and report any adverse reactions, as required.

  Literature searching will still need to be conducted for the purpose of PSUR production and ongoing safety review.

What do Member States need to do?

Literature reporting

- Work with EMA to develop list of products
  - and the journals to be monitored

- Develop guidance and SOPs

Additional Monitoring

- Similar to UK Black Triangle Scheme
- List to be maintained by EMA and include:
  - all new active substances
  - any biological product
  - others subject to consultation with PRAC
- Removal from list reviewed at 5years – can be extended subject to PRAC agreement
- Black symbol – exact details agreed by EC following PRAC recommendation

Additional Monitoring

- List to be published on web-portals
- Awareness of new medicines/monitoring
- Information on PIL and statement about ADR reporting
- One system throughout the community
- Inclusion to be selected by PRAC

What do Member States need to do?

Additional Monitoring

- Work with EMA to develop list of products
- Agree symbol to be used
- Develop guidance for inclusion in PIL and SPC
- Engage with HCPs and patients
- Transition from Black Triangle (UK)

Pharmacovigilance Master File

- Replaces the need for individual detailed descriptions (DDPS)
- Only summary of system required
- Must be permanently available for inspection
- Must be provided within 7 days of request

What do Member States need to do?

PV Master File

- Develop guidance for industry
  - How to move existing MAs, through variations?
  - Internal audits
  - Submissions

- Train inspectors

Signal Detection

- First time signals have been in legislation
- Member States will use Eudravigilance tools to detect signals
- PRAC will prioritise and track progress
- EPITT will be used as the repository for signals

What do Member States need to do?

Signals

- Train in EV tools for signal detection
- Feed in to PRAC on signals detected
- Develop guidance and SOPs
- Decide what to do with current systems

Transparency

- Legislation – Article 102:
  - *'The Member States shall: (1) take all appropriate measures to encourage patients, doctors, pharmacists and other health-care professionals to report suspected adverse reactions to the national competent authority*'

- New requirements for member states
  - Web portal for reporting

Web-Portals (1)

- European portal to be established containing:
  - Committee members information
  - Agendas and minutes
  - Summary Risk Management Plans
  - List of substances under additional monitoring
  - Locations for PV System Master Files
  - Information on how to report and links to national web-portals
  - Dates and frequency for PSUR submission
  - Protocols and public abstracts for PASS
  - Initiation of procedures under 107i – 107l
  - Assessment conclusions, recommendations, opinions and decisions by committees

Web-Portals (2)

- National web-portal to be established containing:
  - Public assessment Reports and Summaries
  - SPCs and PILs
  - Summary Risk Management Plans
  - List of substances under additional monitoring
  - Information on how to report and electronic reporting forms
  - *Important information for the public*

What do Member States need to do?

Web Portals

- Invest in IT
- Develop reporting forms
- Engage with HCPs and patients
- Develop communication messages
- Ensure quality control is in place

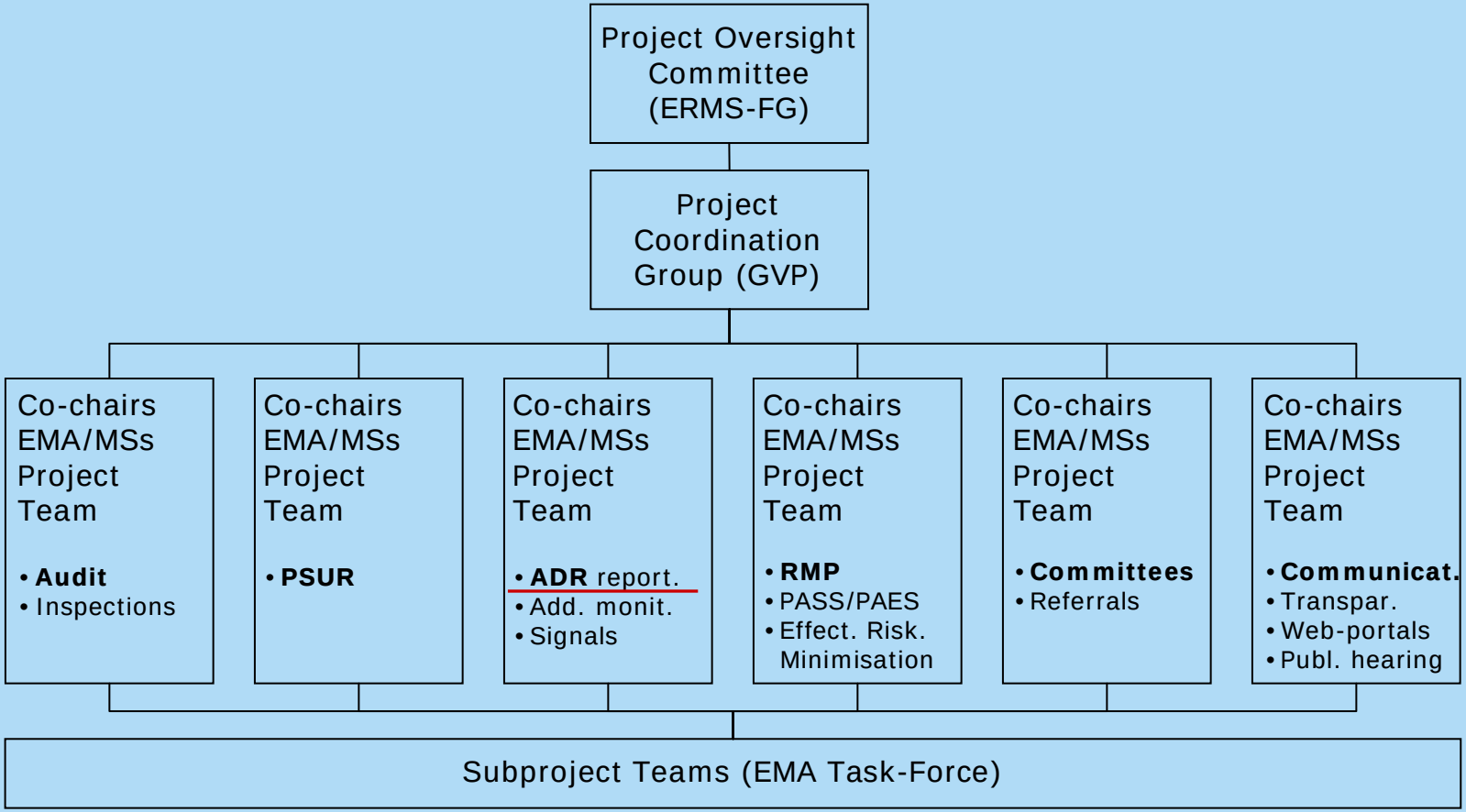
Conclusions

- The new PV package provides an opportunity to greatly improve the European system for the benefit of public health
- Duplication of work will be much reduced for resource savings for industry and regulators
- Patients will be involved in the system from beginning to end
- Information provision will be much improved but with this comes higher expectations
- Signal detection – assessment - action needs to be the main beneficiary
- There is much to do in the coming years to ensure success
- Member States need to start preparing

Hope and Aims

- That the benefits can be realised as soon as possible.
- PSURs, literature are inclusive and deliver early saving
- Patient reporting can be introduced across the community on time
- There is a consistent adoption in all territories
- EV functionality is delivered on time
- Signal detection – assessment - action is the main beneficiary

The Challenge



The Challenge

- Ensure transition is as smooth as possible.
- That all Member States are in a position to adopt new rules at the same time
- To deliver a consistent comprehensive GVP
- That all stakeholders have a say and buy-in to new system

Thank You!

Questions?