EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

# Opportunities for public health and pharmacogenomics from the new pharmacovigilance legislation

EMA Pharmacogenomics Workshop
8 October 2012

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Head, Pharmacovigilance and Risk Management, EMA
Patient Health Protection

# Agenda

- Opportunities for public health and PGM:
  - Need to strengthen the system
  - Objectives and measures in the new legislation
  - Implementation
  - impact

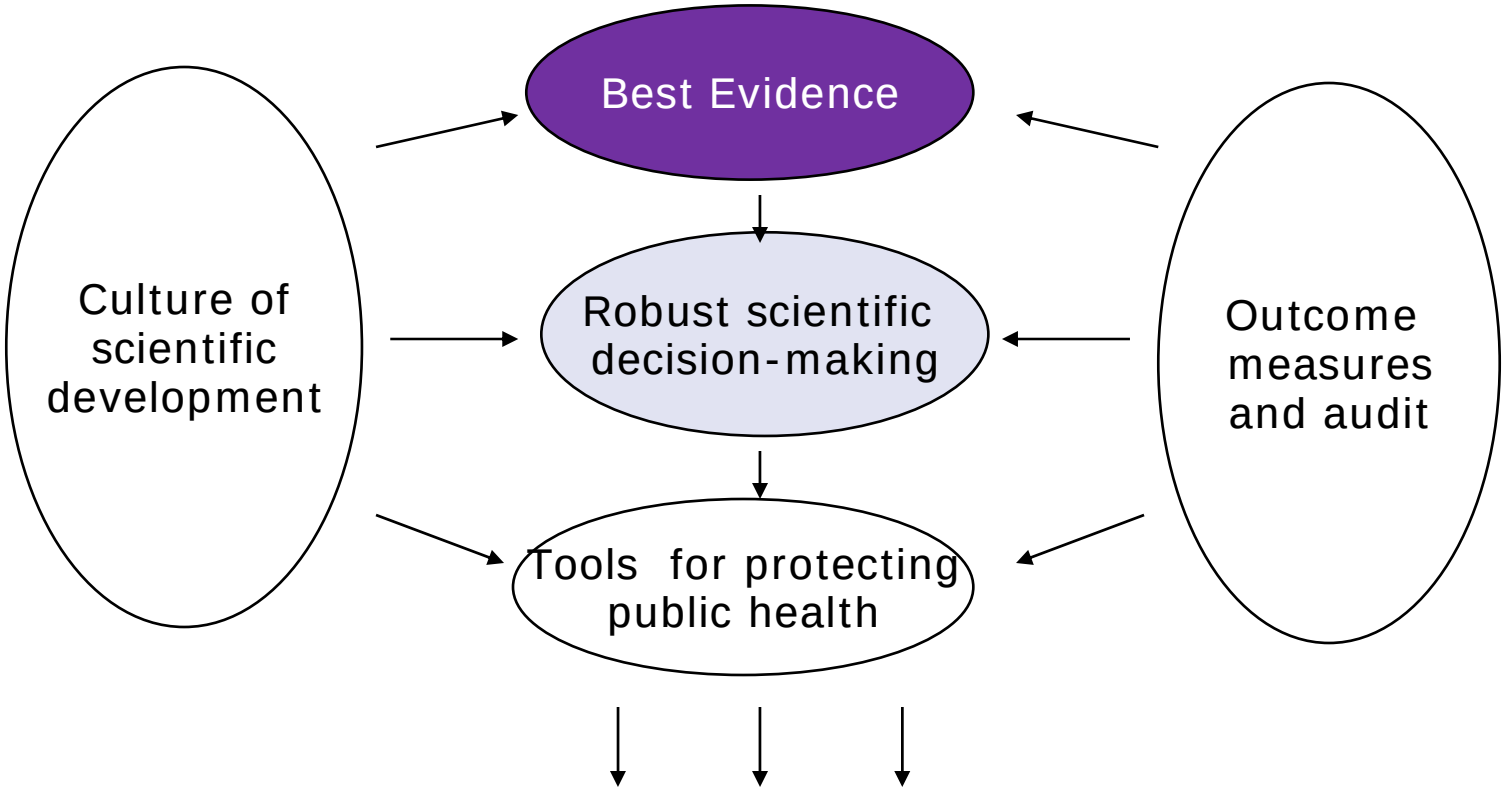
# Regulatory framework

- Steps in the PV process:
  - Collect and manage data
  - Detect and manage signals
  - Evaluate safety issues
  - Benefit risk assessment
  - Regulatory action / risk minimsation
  - Communication
  - Audit

# Regulatory framework

- Steps in the PV process:
  - Risk management planning
  - Collect and manage data
  - Detect and manage signals
  - Evaluate safety issues
  - Benefit risk assessment
  - Regulatory action / risk minimsation
  - Communication
  - Audit

# Established ‘best practice’ model in pharmacovigilance

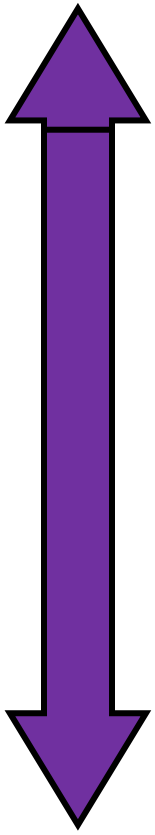



**Measurable excellence in terms of public health benefit**

Waller & Evans. Pharmacoepidemiology & Drug Safety 2003;12:17

# We should be embracing the entire spectrum of evidence.....

**Variable degree of certainty (e.g. causality, incidence)**



- **Meta-analysis**
- **Clinical trial**
- **Prospective cohort (with controls)**
- **Case control study**
- **Observational cohort (no controls)**
- **Individual case report / case series**

# Opportunities for public health and PGM

- Opportunities from the new PV legislation
  - Opportunities for improvement
  - 9-years in the making
  - Objectives and measures
  - impact

# Burden of adverse drug reactions

Medicines save lives and relieve suffering, but:

- 5% of all hospital admissions are for ADRs,
- 5% of all hospital patients suffer an ADR,
- ADRs are the 5$^{th}$ most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU Societal cost of ADRs Euro 79 Billion / year

# Opportunities for improvement: Need To Strengthen Pharmacovigilance

Current EU system recognised as one of the most robust in the world. However, improvements can be made due to:

- Insufficient clarity on roles and responsibilities
- For nationally authorised products, lack of rapid EU decision-making
- Patients and healthcare professionals not included
- Risk and benefit assessed separately
- Need for more EU capacity for post-authorisation studies / monitoring
- Lack of funding for EU pharmacovigilance
- Some duplication of effort
- Need for more planning of safety monitoring
- Limited transparency

# New EU Pharmacovigilance Legislation – 9-years in the making

- 2004: Commission launches independent study into the strengths and weaknesses of the EU PhV system
- 2007: Commission launches strategy to strengthen
- 2008: Commission proposal for new legislation
- Council of Ministers and European Parliament adopt new legislation Autumn 2010 and both **Regulation (EC) 1235/2010** and **Directive 2010/84/EC** published on 31 December 2010
- July 2012: new legislation applies
- Some provisions become effective later, e.g:
  - ADR reporting to EMA only,
  - PSUR reporting to EMA only.

# 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
- Science based - integrate benefit and risk
- Risk based/proportionate
- Increased proactivity/planning
- Reduced duplication/redundancy
- Increase transparency and provide better information on medicines

# 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 / PRAC / decision-making
- Transparency and communication
- Coordination of inspections
- Pharmacovigilance Audits
- Fees charged and payments for assessments / services

# Understanding the measures

Coordination / create lists of medicines:

- Create controlled lists of all EU products and substances to:
  - Support EU medicines databases (e.g. EudraVigilance)
  - Support coordination of safety monitoring (e.g. identifying all products impacted by a decision on a safety concern)

*What this means for you:*

- *the reports of suspected side effects sent in will be more effective at identifying safety issues*
- *When safety issues, warnings will go in the right leaflets*
- *In future, dictionaries available for the EU regulatory network, industry, researchers, healthcare professionals and the public*

# Understanding the measures

Authorisation requirements:

- The marketing authorisation dossiers submitted to EMA and National agencies will change, e.g.
  - Pharmacovigilance system description will be reduced in the authorisation
  - Pharmacovigilance System Master File (PSMF) maintained by all companies in their offices (can be requested or inspected)

  *What this means for you:*

  - *Less variations to the authorisation (reduced burden for industry and regulators)*
  - *Responsibility to maintain an accurate file on-site*

# Understanding the measures

Risk Management Plans and Post-authorisation studies:

- All new products will have a risk management plan
  - The post-authorisation studies will be legally binding
  - Studies in plans will cover safety and efficacy
  - New oversight for these studies to ensure they are of high quality

  *What this means for you:*

  - *Patients and health professionals may be asked to participate in studies of authorised medicines*
  - *High quality information on the benefits and risks of medicines will be generated post-authorisation*
  - *Studies may cover PGM endpoints / collect PGM data*

# Understanding the measures

Effectiveness of risk minimisation:

- Monitoring of effectiveness is a new legal obligation for industry and regulators.

*What this means for you:*

*–For the most important safety issues specific studies will be done for products on the market to ensure:*

- *Safety messages are understood*
- *Safety messages change prescribing and dispensing behaviour of health professionals*
- *Adverse reactions are reduced (health outcomes)*

# Understanding the measures

Reporting of suspected side effects (suspected ADRs):

- We all, as patients, are now able to report suspected side effects
- from 2016 (if budget) all ADR reports will come from industry and national agencies to EudraVigilance only

*What this means for you:*

- *From July 2012 all patients can report a suspected side effect*
- *From 2016, industry will be able to reinvest the savings from simpler reporting of ADRs into safety studies*

# Understanding the measures

Detecting new or changing safety issues (“signal detection”)

- New legal obligation to analyse data to detect new safety issues, for EMA and national regulatory agencies, and for industry

*What this means for you:*

- *New or changing safety issues should be detected more quickly*
- *New advice and warnings will go in leaflets more rapidly*
- *Adverse reactions should be minimised*

# Understanding the measures

Periodic Safety Update Reports:

- Content changes to Benefit Risk Evaluation Report
- No-longer routine reports for generic products / timing of submission will be risk proportionate
- In time EMA will process all reports for the EU and all assessments will come through the EMA Committees (including all the nationally authorised products)
- Binding legal outcomes e.g. variation, suspension, revocation

*What this means for you:*

*–More risk proportionate use of resource by industry and regulators*

*–For important products benefits and risks are re-examined regularly after market entry*

*–Assessments will rapidly lead to changes to warnings*

# Understanding the measures

Scientific Committee / Decision making

- New Committee: Pharmacovigilance Risk Assessment Committee
- All key safety issues to pass through this committee

*What this means for you:*

*–High quality benefit risk assessment, including dedicated PGM expertise*

*–Legally binding outputs for product reviews – fast efficient updates to all product information*

# Understanding the measures

Transparency and communication

- Major increase in documents publically available
- Public hearings for referrals
- EMA communication coordination for issues on nationally authorised products
- EU and National medicines 'web-portals': agendas, minutes, recommendations, opinions
- Companies to keep their product info up to date with the web-portal

*What this means for you:*

–*More (and better) information on benefits and risks of medicines*

–*Faster information on new safety issues and new advice*

–*Coordination of information between Member States*

–*Faster updates of product information*

# Understanding the measures

Inspections and audits:

- Strengthened EU coordination of inspection
- Regular audits: for EMA, for national authorities, for industry

*What this means for you:*

*–Greater assurance of the quality of pharmacovigilance performed by industry and regulators*

# Understanding the measures

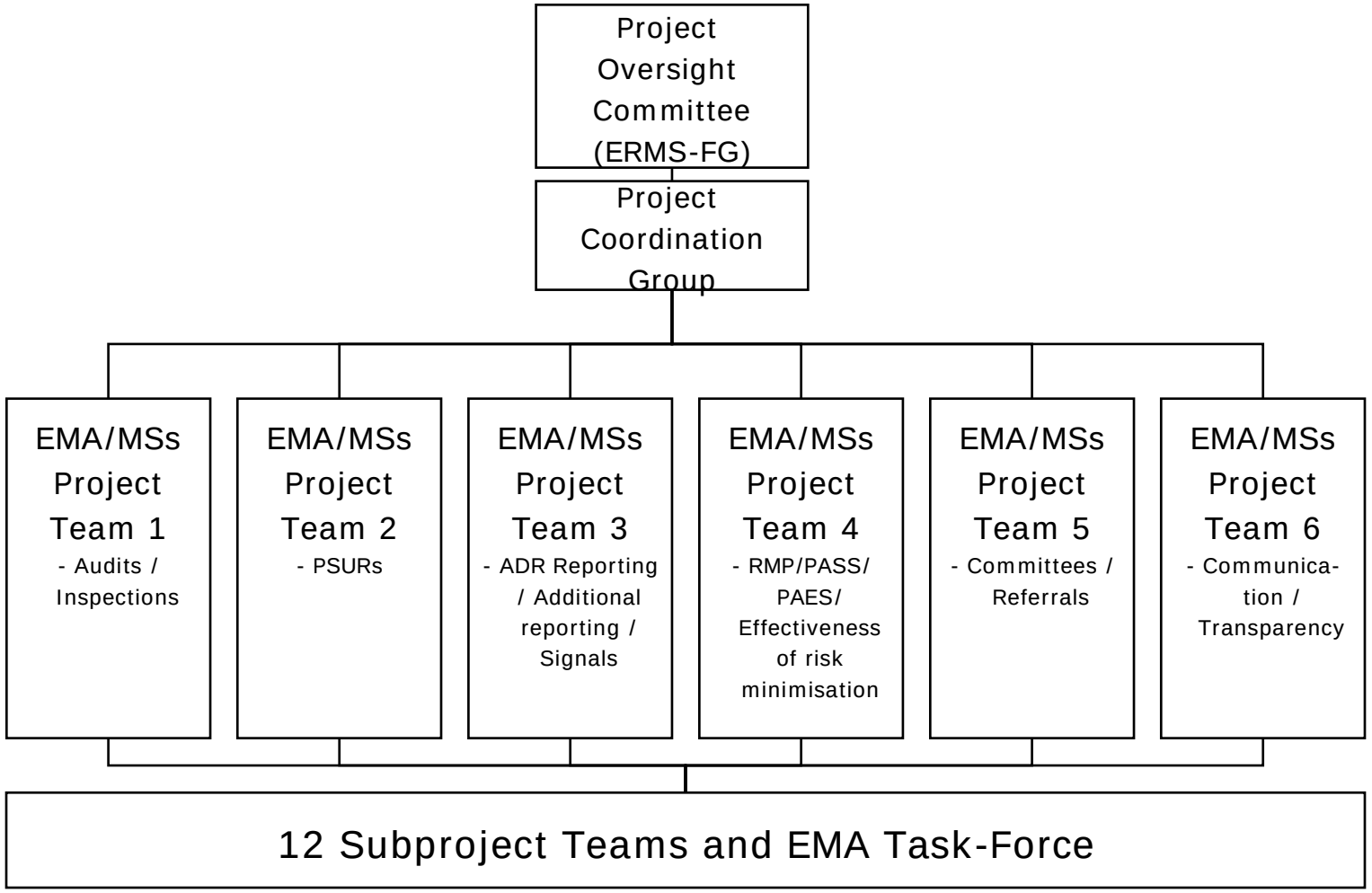
Fees charged for pharmacovigilance:

- New fees charged to industry – European Commission consultation recently closed

  *What this means for you:*

  *–Adequate resources should be available to ensure robust public health protection.*

# Governance of the Implementation of the New Pharmacovigilance Legislation for EU Tasks



EUROPEAN MEDICINES AGENCY
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5 September 2012
EMA/PRAC/520121/2012
Patient Health Protection

# Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of the inaugural plenary meeting 19-20 July 2012

Centre Albert Borschette, Conference Room AB-0C

Rue Froissart 36, 1040 Brussels, Belgium

## 1. Introduction

### *1.1. Welcome and keynote address by the EMA, Executive Director*

Speaker: Guido Rasi

The EMA Executive Director welcomed all participants to the inaugural meeting of the PRAC and thanked the European Commission for hosting it in Brussels.

He explained that the first meeting of the PRAC would focus mainly on addressing aspects relating to the mandate of the PRAC and on adopting its Rules of Procedures.

Prof Rasi reminded the PRAC that the European Medicine Agency (EMA) has a strict policy on the handling of conflicts of interests for its staff, scientific experts including committee members and Management Board representatives. Further details are provided under item 2.4.

Regarding the role of the new Committee, the Executive Director underlined that the PRAC will deliver outcomes which will be turned into binding regulatory decisions. This is why it is particularly important that outcomes are clear, scientifically robust and provide the public and stakeholders with a full rationale.

The PRAC will focus on the processes outlined in the legislation. In this regard, the agenda of the PRAC will be designed to show the adherence of PRAC discussions with the tasks outlined by the new pharmacovigilance legislation.

Finally the EMA Executive Director concluded announcing that the election of the Chair and vice-Chair

EUROPEAN MEDICINES AGENCY
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3 September 2012
EMA/PRAC/432046/2012
Patient Health Protection

# Pharmacovigilance Risk Assessment Committee (PRAC)

## Draft agenda of meeting 3-5 September 2012

### Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda

**EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures**
(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

**Signals assessment and prioritisation**
(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
In most cases, the evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

**Risk Management Plans (RMPs)**
(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.
RMPs are continually modified and updated throughout the lifetime of the medicine as new information

# New legislation impact:

- Biggest change to the legal framework for human medicines since 1995
- Entire product life-cycle impacted
- Major change project that will take a few years to fully implement
- Establishment of the PRAC is key milestone
- Opportunity to better collect and better analyse PGM data for public health

# New legislation impact:

- Full implementation estimated to save between:
  - –500 and
  - –5,000 lives per year
- Savings to society between:
  - –250 Million Euros and
  - –2.5 Billion Euros per year

Ref: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=SEC:2008:2671:FIN:en:PDF