EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PROTECT

imi

Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

Post Approval Summit 2010

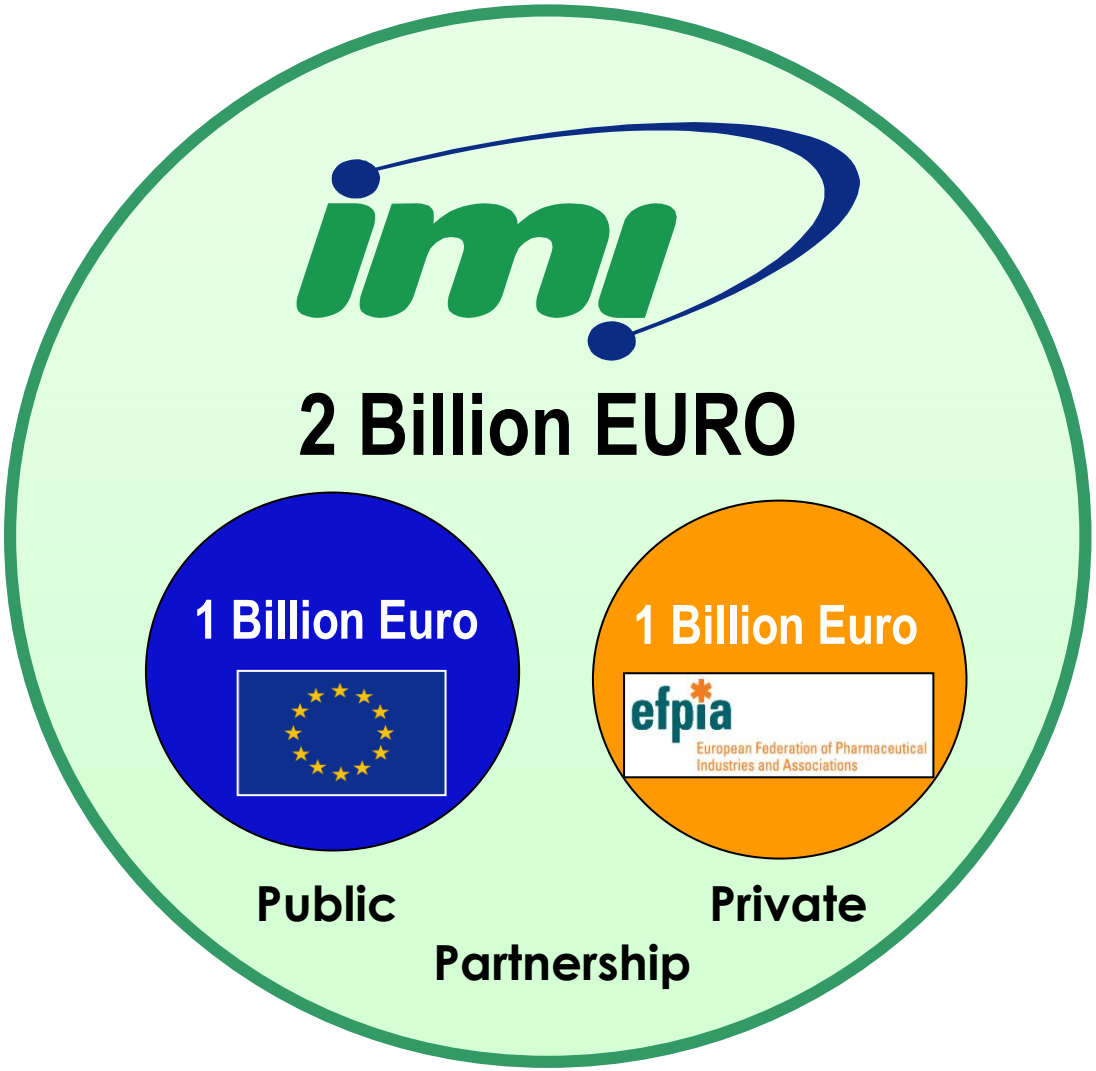
Presented by: Dr Stella Blackburn

Innovative Medicines Initiative

IMI grew out of the European Technology Platform on Innovative Medicines

In 2004. vision document, produced by EFPIA, identified the key research bottlenecks that hamper the drug development process:

Innovative Medicines Initiative



Designed to bring together large and small biopharmaceutical and healthcare companies, regulators, academia and patients to work together to tackle common goals, the Innovative Medicines Initiative (IMI) it is the largest Public Private Partnership in the world

2008 Call for research projects on 18 topics

2009 Call for research projects on 9 topics

2010 Scientific priorities identified

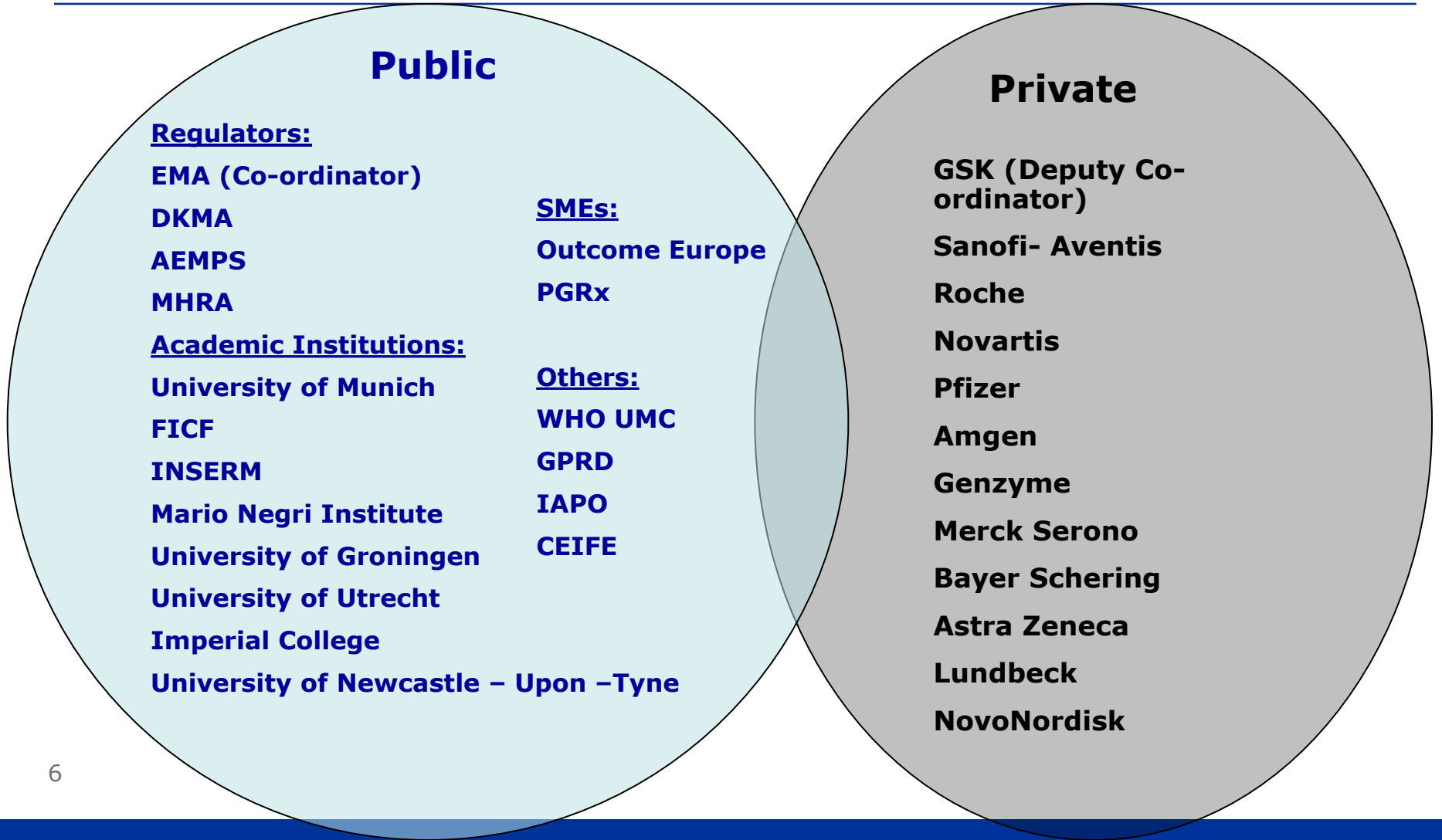
Call No. 6:

Strengthening the monitoring of Benefit and Risk

PROTECT

Pharmacoepidemiological **R**esearch on **O**utcomes of **T**herapeutics by a **E**uropean **C**onsor**t**ium

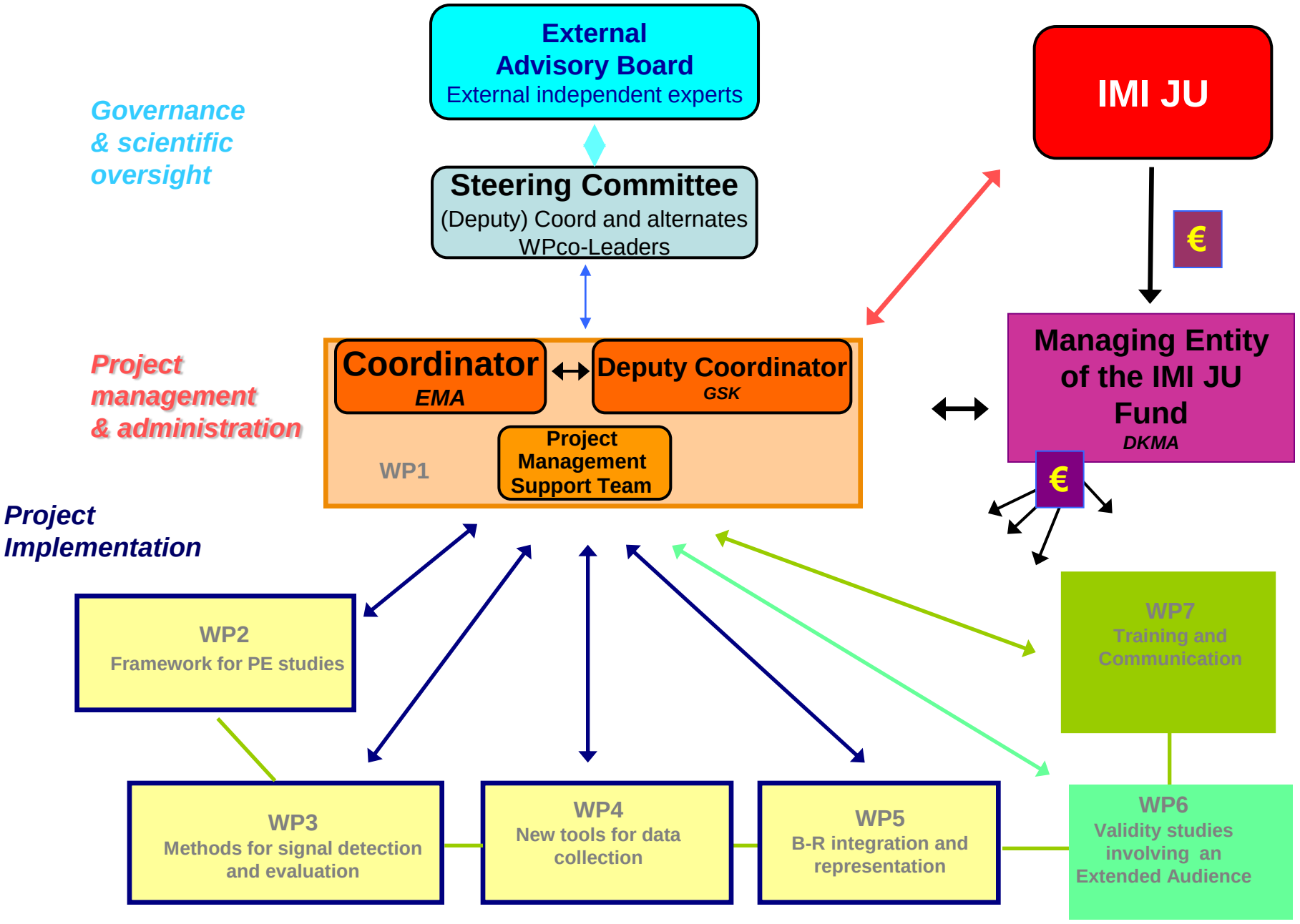
PROTECT: Key participants



PROTECT Goal

The goal of PROTECT is to strengthen the monitoring of benefit-risk of medicines in Europe by developing innovative methods that will:

- enhance the early detection and assessment of adverse drug reactions from different data sources (clinical trials, spontaneous reporting, and observational studies)
- enable the integration and presentation of data on benefits and risks


External
Advisory Board
External independent experts
IMI JU
Governance
& scientific
oversight
Steering Committee
(Deputy) Coord and alternates
WPco-Leaders
€
Project
management
& administration
Coordinator
EMA
Deputy Coordinator
GSK
Managing Entity
of the IMI JU
Fund
DKMA
WP1
Project
Management
Support Team
€
Project
Implementation
WP2
Framework for PE studies
WP7
Training and
Communication
WP3
Methods for signal detection
and evaluation
WP4
New tools for data
collection
WP5
B-R integration and
representation
WP6
Validity studies
involving an
Extended Audience

Members of the External Advisory Board

Name	Affiliation	Expertise
Corinne De Vries, PhD	Department of Pharmacy and Phamacology, University of Bath, UK	Pharmacoepidemiology
Trevor Gibbs, MD	Former Head of Global Pharmacovigilance and Product Safety, GSK, UK; Chief Medical Officer at ii4sm	Pharmacovigilance, Health Outcomes, Public Health
David Haerry	European AIDS Treatment Group (EATG), Brussels, Belgium	Public Health Patients' preference
Vicky Hogan, MSc	Associate Director General, Marketed Health Products Directorate (MHPD), Health Canada, Canada	Benefit-risk assessment
Michael Lewis, MD	EPES Epidemiology, Pharmcoepidemiology and Systems Research GmbH, Berlin, Germany	Pharmacoepidemiology
Allen Mitchell, MD	Slone Epidemiology Center, Boston, USA	Perinatal epidemiology Pharmacoepidemiology
Marcus Müllner, MD	Head of AGES PharmMed (Austrian Medicines and Medical Devices Agency), Austria	Benefit-risk assessment Clinical epidemiology Pharmacovigilance
Gerald Dal Pan, MD, M.H.S.	Director, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research (CDER), Food and Drug Administration (FDA), USA	Pharmacovigilance, Drug development, Public Health & Risk management
Munir Pirmohamed, MD	Department of Pharmacology and Therapeutics, University of Liverpool, UK	Pharmacology Pharmacovigilance
Samy Suissa, PhD	Department of Epidemiology/Biostatistics, McGill University, Montreal, Canada	Biostatistics Pharmacoepidemiology

Work Packages

1. Project management and administration
2. Framework for pharmacoepidemiological studies
3. Methods for signal detection
4. New tools for data collection from consumers
5. Benefit-risk integration and representation
6. Validation studies involving an Extended Audience
7. Training and Communication

WP2: Framework for Pharmacoepidemiological Studies

Objective

To develop, test and disseminate methodological standards for the design, conduct and analysis of pharmacoepidemiological studies, applicable to different safety issues using different data

Example

To develop study protocols between selected drugs and key AEs

To provide guidelines on how to identify public health impact of AEs

To investigate discrepancies in results between databases and explore differences with other data sources

To evaluate identified signal from signal detection strategies in electronic health databases

Work Package 2 : **Work plan**

Three Working Groups

- WG 1: Databases
- WG 2: Confounding
- WG 3: Drug Utilisation

Work Package 2 : WG1 Databases

Conduct of 5 Adverse Event-Drug pair studies in different EU databases

- Selection of 5 key AE-drug pairs
- Identification of key characteristics of databases
- Development of study protocols for all 5 AE-drug pairs
- Compare results of studies

Work Package 2 : **WG 2 plan (Confounding)**

Objective

- To enhance the practical use of innovative methods to control confounding

Method

- Creation of simulated cohorts
- Use of methods to adjust for observed and unobserved confounding

  e.g. time-dependent exposure, propensity scores, instrumental variables, PERR adjustment

Work Package 2 : **WG 3 plan (Drug Utilisation data)**

WG 3 plan

- Use of national drug utilisation data
  - ✓ To describe and update the main characteristics of multinational European working groups on drug utilisation monitoring and research
  - ✓ Explore use of IMS data by companies
- Evaluation and dissemination of methodologies for drug utilisation studies in order to estimate the potential public health impact of ADRs

Work Package 2 : **WG 1 progress status**

Selection of 5 Key AEs and drugs

Selection criteria:

- AEs that caused regulatory decisions
- Public health impact (seriousness of the event, prevalence of drug exposure, etiologic fraction)
- Feasibility
- Range of relevant methodological issues

Work Package 2 : **WG 1 progress status**

Initial selection of 5 Key AEs and drugs

- Initial list of 55 events and >55 drugs

- Finalisation of selection based on literature review and consensus meeting

Hip Fracture and antidepressants (taking benzodiazepines into account)

Acute liver injury and antibiotics (class to be determined, e.g. macrolides)

Myocardial infarction and antipsychotics, HRT, antiasthmatic drugs (beta2 agonists, anticholinergics, inhaled corticosteroids)

Suicide/depression and antiepileptics

Cancer and calcium channel blockers

Work Package 2 : **WG 1 progress status**

Inventory of databases

Database	Country	Source	Cum Population	Active
GPRD	UK	GP	11 M	3.6 M
Mondriaan	NL	Multisource	1.4 M (GP)	0.6 M (GP), 13.5 (Pharmacy), 1.2 M
Bifap	SP	GP	3.2 M	1.6 M
Danish registries	Denmark	Multisource	5.2 M (All DBs)	5.2 M (All DBs)
THIN	UK	GP	7.8 M	3.1 M
Mediplus	Germany	GP	10	?
Bavarian Claims	Germany	Claims	10.5 M	9.5 M
PGRx	France	Case-referent	10,000	10,000

Work Package 3 : **Objective**

To develop new methods, and assess existing ones, for signal detection from spontaneous reports, electronic health records and clinical trials.

Scope

- To develop new methods for signal detection
- To implement and examine the value of screening methods in electronic health records
- To provide advice on good signal detection practices

Work Package 3 : **Sub-projects**

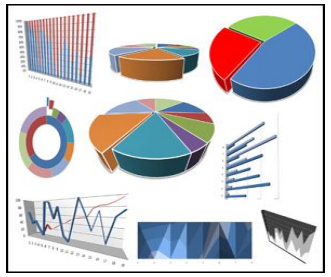
1. Merits of disproportionality analysis
2. Structured database of known ADRs
3. Risk estimates from trials
4. Signal detection recommendations
5. Better use of existing ADR terminologies
6. Novel tools for grouping ADRs
7. Other information to enhance signal detection
8. Signal detection based on SUSARs
9. Subgroups and risk factors
10. Signal detection in Electronic Health Records
11. Drug-drug interaction detection
12. Duplicate detection

WP4: New Tools for Data Collection from Consumers

Objective

To develop modern methods of data collection directly from consumers in their natural language in several EU countries, including using web-based screens, text messaging and computerised telephone interviews

Work Package 5 : **Objectives**



- To investigate methods of collating data on benefits and risks
- To develop novel modelling approaches allowing continuous benefit-risk modelling along the lifecycle of products
- To build an easy-to-use and understand graphical representations of benefits and risks of medicinal products for use by patients, healthcare prescribers, regulatory agencies, and drug manufacturers, along the lifecycle of the products

Work Package 6 : **Work plan**

1. To apply tools and methods developed in WP2,3,4

- Feasibility in other types of data sources, eg. disease registries
- Elements to be considered for the choice of methods and data sources:
  - usefulness
  - potentiality for high quality studies
  - impact of results
- Transfer to other population and diseases

Work Package 7 : Training and Communication

1. Identify PROTECT deliverables that could be introduced in undergraduate and continuous education, and liaise with IMI pharmacovigilance and pharmacoepidemiology training consortium (EU2P)

2. Identify best tools for disseminating the project results and increasing expertise outside the consortium

3. Identify training opportunities from within the consortium that may be offered to consortium partners and possibly to PhD students (eg. EU2P)

The research presented here is being conducted as part of the PROTECT consortium (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium) which is a public-private partnership coordinated by the European Medicines Agency

It has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) for the Innovative Medicine Initiative under *Grant Agreement* n° 1150004.

More information ?

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