PROTECT

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Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

Innovation through Consortia: The IMI PROTECT Project

A Public-Private Partnership for New Methodologies in Pharmacovigilance and Pharmacoepidemiology

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Personalised Medicine

The concept of personalised medicines aims at identifying better those individuals who will respond to and benefit from a medicine, and avoid those who will not benefit or even suffer harm as a result of treatment

What are the needs ?

- **Data collection**
  - efficient and simple methods for early data collection directly from patients
  - non-prescribed medicines
  - linkage to health event databases

- **Signal detection**
  - spontaneous reports: in-depth analysis of methods and good practice recommendations
  - better use of electronic health records and clinical trials

What are the needs?

- **Signal evaluation**
  - understanding the variability in results of studies of a same safety issue in different data sources
  - detailed guidance and standards regarding design, conduct and analysis of pharmacoepidemiological studies

- **Benefit-risk assessment**
  - Need for widely accepted method for integrating data on benefits and risks from clinical trials, observational studies and drug reaction reports
  - benefit-risk assessment for patients, prescribers, regulators...

PROTECT Goal

To strengthen the monitoring of benefit-risk of medicines in Europe by developing innovative methods

to enhance early detection and assessment of adverse drug reactions from different data sources (clinical trials, spontaneous reporting and observational studies)

to enable the integration and presentation of data on benefits and risks

These methods will be tested in real-life situations.

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PROTECT

Partners

Public

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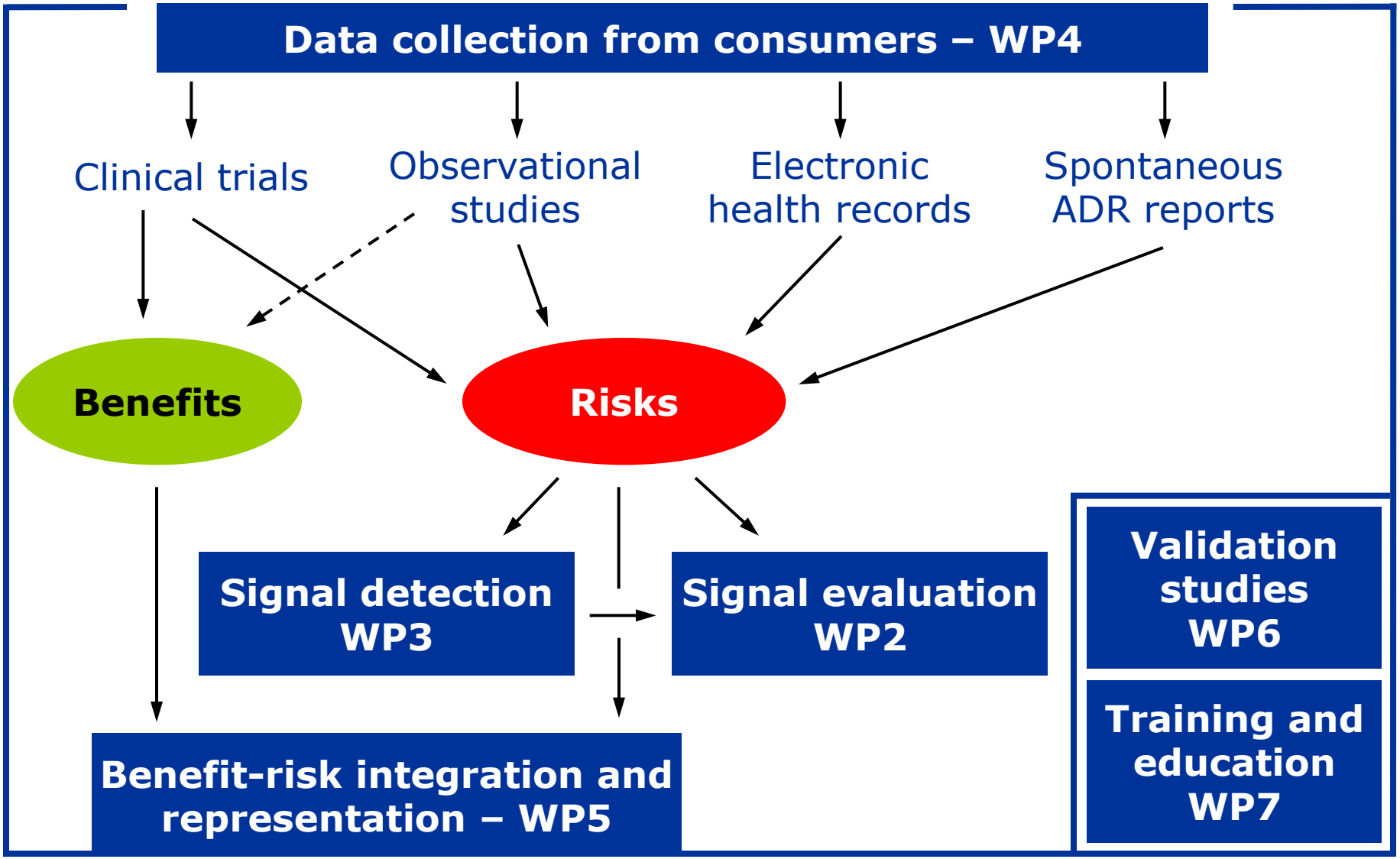

Data collection from consumers – WP4
Clinical trials
Observational studies
Electronic health records
Spontaneous ADR reports
Benefits
Risks
Signal detection WP3
Signal evaluation WP2
Validation studies WP6
Training and education WP7
Benefit-risk integration and representation – WP5

WP 2: Framework for pharmacoepidemiological studies

Objectives:

To:

- develop
- test
- disseminate

methodological standards for the:

- design
- conduct
- analysis

of pharmacoepidemiological studies applicable to:

- different safety issues
- using different data sources

Work Package 2

Work plan

- Three Working Groups (WG1-WG3)
  - Databases
  - Confounding
  - Drug Utilisation

Work Package 3: Signal Detection

Objective:

To improve early and proactive signal detection from spontaneous reports, electronic health records, and clinical trials.

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

Work Package 4: Data collection from consumers

Objectives:

To assess the feasibility, efficiency and usefulness of modern methods of data collection including using web-based data collection and computerised, interactive voice responsive systems (IVRS) by telephone

Work Package 4 - Project Definition

- Prospective, non interventional study which recruits pregnant women directly without intervention of health care professional
- Collect data from them throughout pregnancy using either web based or interactive voice response systems (IVRS):
  - medication usage, lifestyle and risk factors for congenital malformation
- Compare data with that from other sources and explore differences
- Assess strengths and weaknesses of data collection and transferability to other populations

Work Package 4 - Issues with current methods

Using health care professionals to capture data

- Expensive and data capture relatively infrequent
- Will miss drug exposure before comes to attention of HCP
- Patients may not tell truth about “sensitive” issues

Work Package 5: Benefit-risk Integration and Representation

Objectives:

- To assess and test methodologies for the benefit-risk assessment of medicines
- To develop tools for the visualisation of benefits and risks of medicinal products

➔ Perspectives of patients, healthcare prescribers, regulatory agencies and drug manufacturers

➔ From pre-approval through lifecycle of products

Work Package 5: Workstreams

Workstreams	
A	Develop framework for benefit-risk analysis
B	Review of methodologies used, elicitation of preferences and integrating effects and preferences
C	Criteria for case study selection & case study selection
D	Determine data to be gathered from case studies and format required
E	Develop software to support application of methodology and graphical representation
F	Application of methodology and graphical methodology to case studies wave 1

Work Package 5: Work Plan

1. Review of methodologies used to model effects of medicines, elucidation of patients' preferences and integrating effects and preferences.

   Review of methodologies for graphical representation and visualisation techniques.

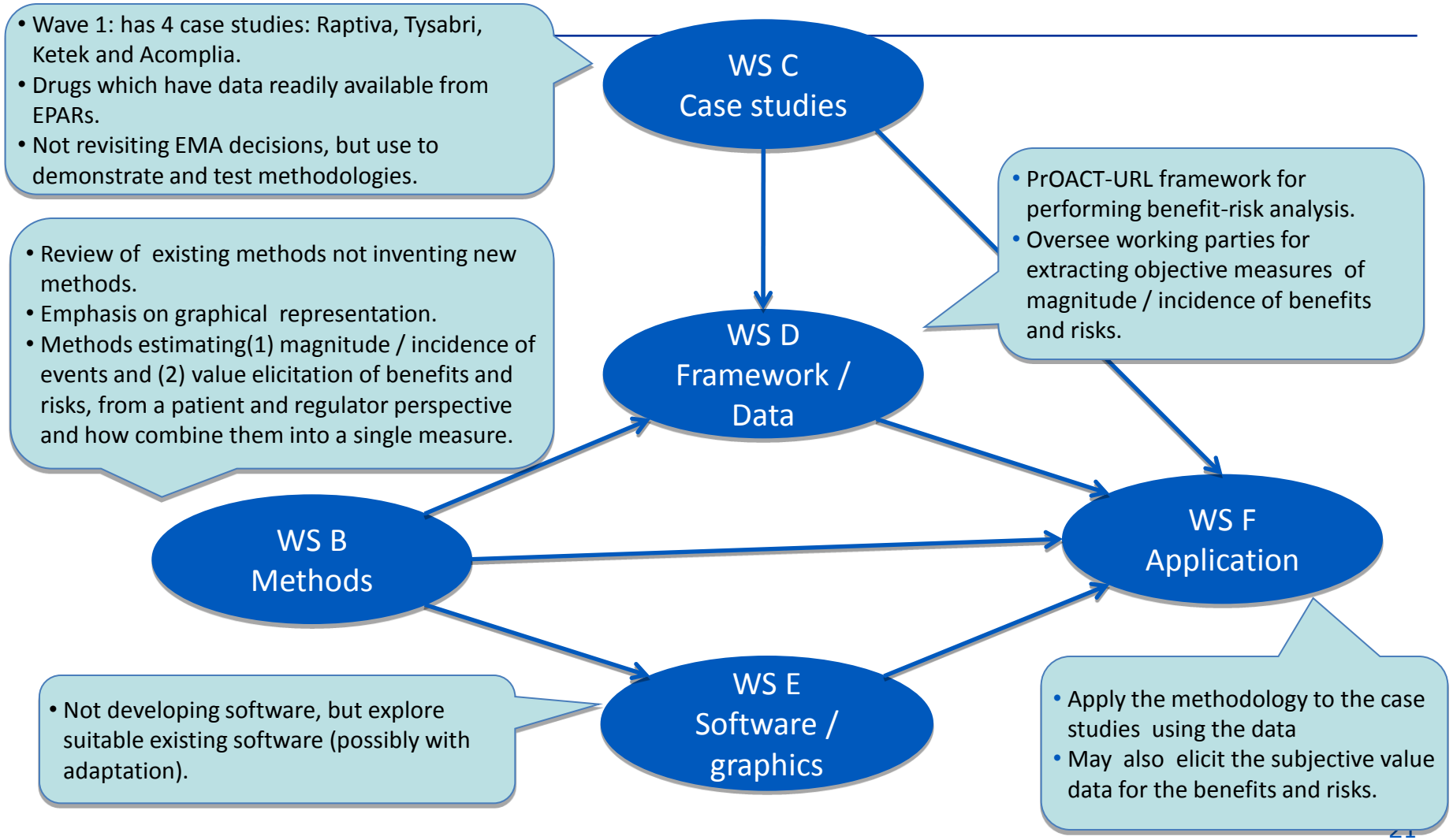
2. Selection of case studies (waves 1 and 2)
3. Data selection/requirements for case studies
   - Wave 1: Raptiva, Tysabri, Ketek and Acomplia
   - Identification/development of software for B/R
4. Application of methodology, recommendations, finalisation of tools, protocols for validation studies.

Work Package 5: Workstream A - completed

- **Framework for B-R analysis**: achieved through a **Charter**

  - Large scope covering principally post-approval setting, individual and population-based decision making, ***various perspectives*** (patients, prescriber, regulators, industry)
  - Address possible interdependencies with other PROTECT WPs
  - Review of B-R methodologies and ***graphical representation tools***
  - Selection of candidate methodologies based on specified criteria
  - Process for selection of case studies, according to selection criteria
  - Implementation of case studies using relevant methodologies and ***including preferences of various stakeholders***
  - Test available representation technologies applied to above mentionned case studies and B-R methodologies
  - ***Publication and presentation*** of case studies in various settings

Work Package 5: Overview



Work Package 6: Validation

Objective:

To validate and test the transferability and feasibility of methods developed in PROTECT to other data sources and population groups.

Work Package 6 - Inventory of data sources

- Creating a comprehensive list of data sources
  - Review of European databases (EHC, cohorts, registries)
  - ENCePP
  - EFPIA
- Outcomes will be evaluated in light of the inventory of data sources (e.g. type of data, covariate information, mode of collection, type of prescription data, etc)

Work Package 7: Training & communication

Objective:

To identify training opportunities and support training programmes to disseminate the results achieved in PROTECT.

Key Deliverables

- Methodological standards for the design, conduct and analysis of pharmacoepidemiology studies applicable to different safety issues using different data
- Recommendations on current signal detection methods as tools
- New methods for signal detection from spontaneous reports, electronic health records and clinical trials
- New methods of data collection directly from consumers using web-based screens ,text messaging and computer interviews
- An assessment of the methodologies for benefit risk analysis and recommendation for use
- Approaches for benefit risk modelling throughout product lifecycle
- Tools for graphical expression for the benefit and risks of medicinal products

In Summary

- Sets up a framework which should readily incorporate personal perspectives

  - If there is data on personalized baseline risk of outcomes, that directly impinges on risk benefit

  - If treatment effects differ by group, that impacts on the risk benefit for members of that group

  - If individuals have different preferences/ utilities that also impacts on risk-benefit and therefore personalises it.

- Graphical displays can be interactive, and would therefore potentially allow for adjustment of baseline risk (perhaps based on age, family history etc) and allow a patient to adjust their preferences for different outcomes/ side-effect etc.

More information?

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