EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EU Collaborative Framework for Patient Registries - Pilot Phase

Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP) joint meeting
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Problem statement

- Patient registries (PRs) are requested to MAHs in the context of risk management plans and as regulatory requirements for advanced therapies, medicinal products for paediatric use and orphan products.
- The current approach to PRs is sometimes suboptimal in scientific and resource terms:
  - lack of common protocols, scientific methods and data structures
  - lack of data sharing and transparency
  - lack of sustainability.
- Difficulty to assess the validity of results from individual PRs
- On-going national and EU initiatives on registries not well coordinated.

Example 1: The International Collaborative Gaucher Group (ICGG) Registry

- Commenced 1991 – on-going
- Sponsored by Genzyme – 62 countries- >6000 patients (2013)
- Registry open to all physicians caring for patients with all subtypes of Gaucher disease – broad range of data collected
- Registry provides a large amount of data on long-term treatment outcomes for enzyme replacement therapy

- Database for the International Collaborative Gaucher Group (ICGG) Gaucher Registry supported by Genzyme
- Logistical support for the ICGG Board, data analyses and publications provided by Genzyme.
- No access to data for regulators.
- Conflicts of interests ? Independence? Validity?

Neal J. Weinreb et al. Long-term clinical outcomes in type 1 Gaucher disease following 10 years of imiglucerase treatment. J Inherit Metab Dis. 2013; 36: 543–553.

Example 2: The Buproprion Pregnancy Registry

- Commenced 1997 – New enrolments stopped on Nov. 1, 2007- Follow-up through Mar 31, 2008
- Sponsored by GSK – 1,500 exposed pregnant women over 10 years

- Large percentage of cases lost to follow-up (35.8%)
- Under-/selective reporting of adverse reports
- Incomplete descriptions of reported cardiovascular effects
- Insufficient information to assess confounding factors
- Sample size inadequate
- "Credibility of data on potential signals impossible to assess" (Cole et al.)
- Advisory committee recommended discontinuation of the registry

- Inadequate methods – objectives not met – waste of resources

Cole JA et al. Bupropion in pregnancy and the prevalence of congenital malformations. Pharmacoepidemiol Drug Safety 2007;16:474-84.

Example 3: PSONET

- Investigator-initiated international scientific network of coordinated patient-based registries for the surveillance of psoriasis treatments and outcomes
- Aim: to monitor the long-term effectiveness and safety of systemic agents in the treatment of psoriasis
- Nine different registries across Europe
- Started in 2005 – supported by a grant from AIFA

- Common set of variables and procedures included and implemented in each registry (eg. inclusion criteria, clinical and sociodemographical characteristics, major outcomes, follow-up schedules)
- Data extracted from each registry and prepared in standardised form

- Analyses include comparative data on treatment strategies and biological products

- Data from multiple registries may be combined to provide large populations to study safety and effectiveness of outcomes and compare treatments.

http://www.psonet.eu

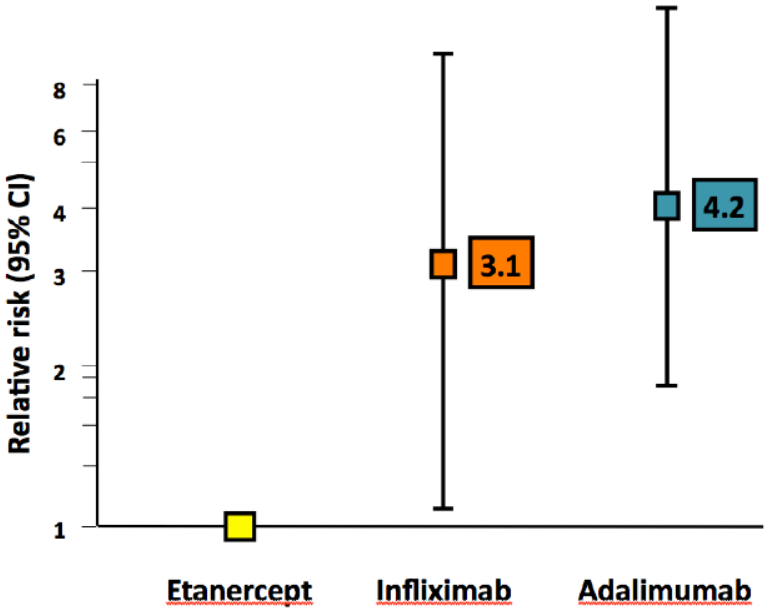
Example 4: BSR Biologics Register

Commenced in 2001

Prospective cohort of all UK patients **treated with anti-TNF therapy for RA**

Comparison of products within the register

- Differential risk of tuberculosis



Dixon et al.. *Ann Rheum Dis* **69**, 522-8 (2010)

Example 4: BSR Biologics Register

Time-wise comparisons

Impact of dietary advice

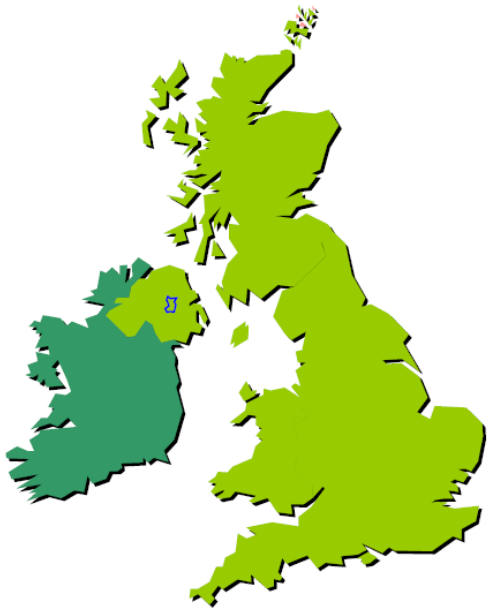
	Rates of infection during anti-TNF therapy	
Organism	Pre-2006	2006-
Listeria or salmonella	9 cases **5.1**/ 10,000 pyrs	6 cases **1.4**/ 10,000 pyrs

73% reduction

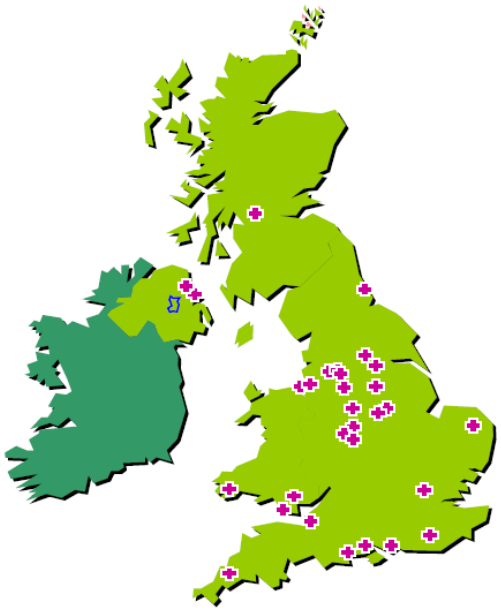
Example 4: BSR Biologics Register

Comparisons with other products from other registers

Incidence of serious adverse events



VS



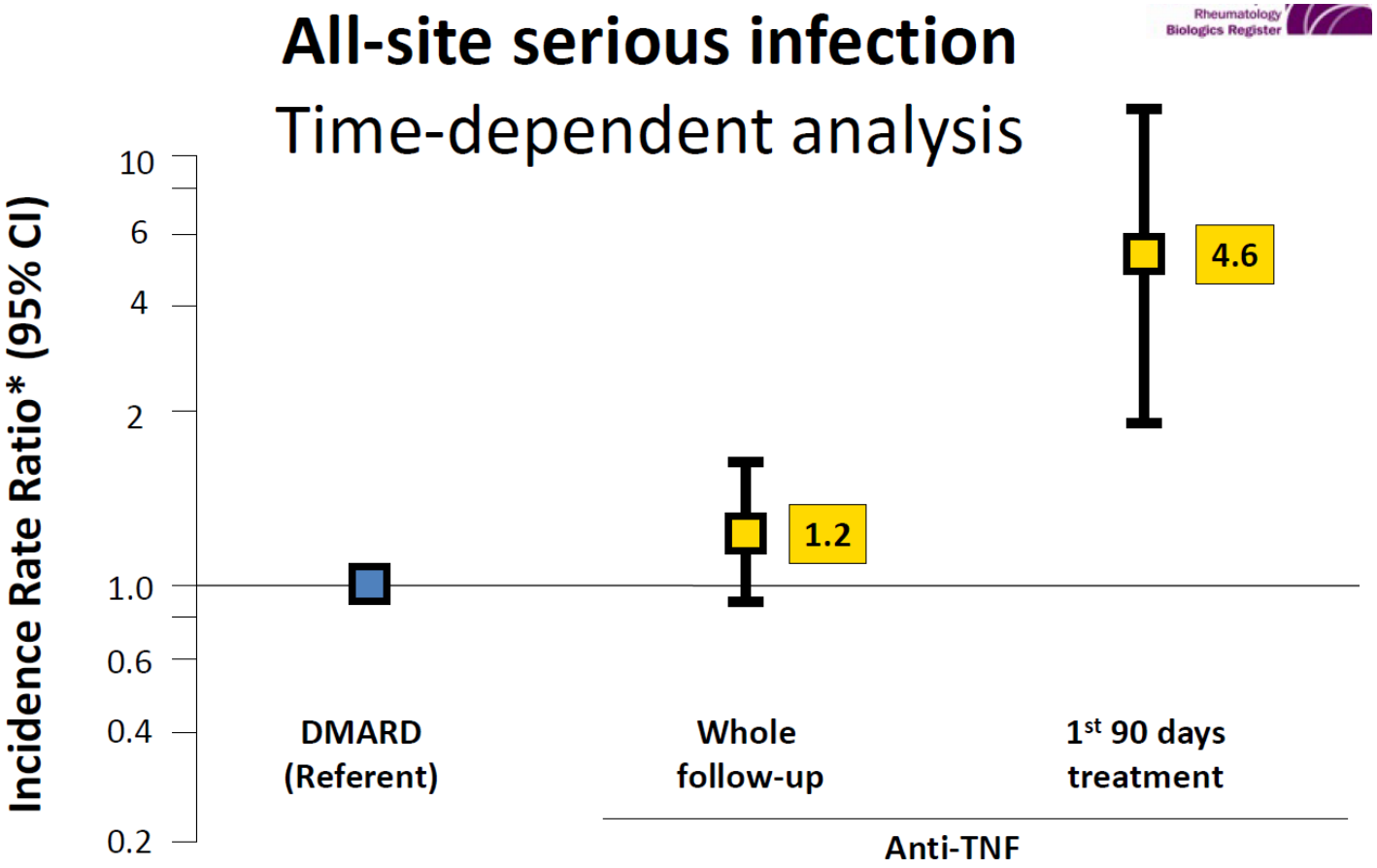
Anti-TNF treated RA cohort (n=4000)

- Infliximab
- Etanercept
- Adalimimab

Biologic-naïve active RA cohort (n=4000)

Example 4: BSR Biologics Register

Comparisons with other products from other registers (2)



* Adjusted for age, gender, disease severity, co-morbidity, extra-articular manifestations, baseline steroid use and smoking

Dixon et al. A&R, 2007, 56(9)

Objectives of the project

Primary objective

to develop and test an EU collaborative framework for patient registries that would facilitate the collection and analysis of high quality data on the efficacy and safety on medicinal products in the healthcare setting in order to confirm their benefit-risk profile.

Secondary objective

to test the feasibility of integrating registries in the adaptive licensing pilot, the one-stop shop strategy and the joint discussions between regulators and HTA bodies/payers.

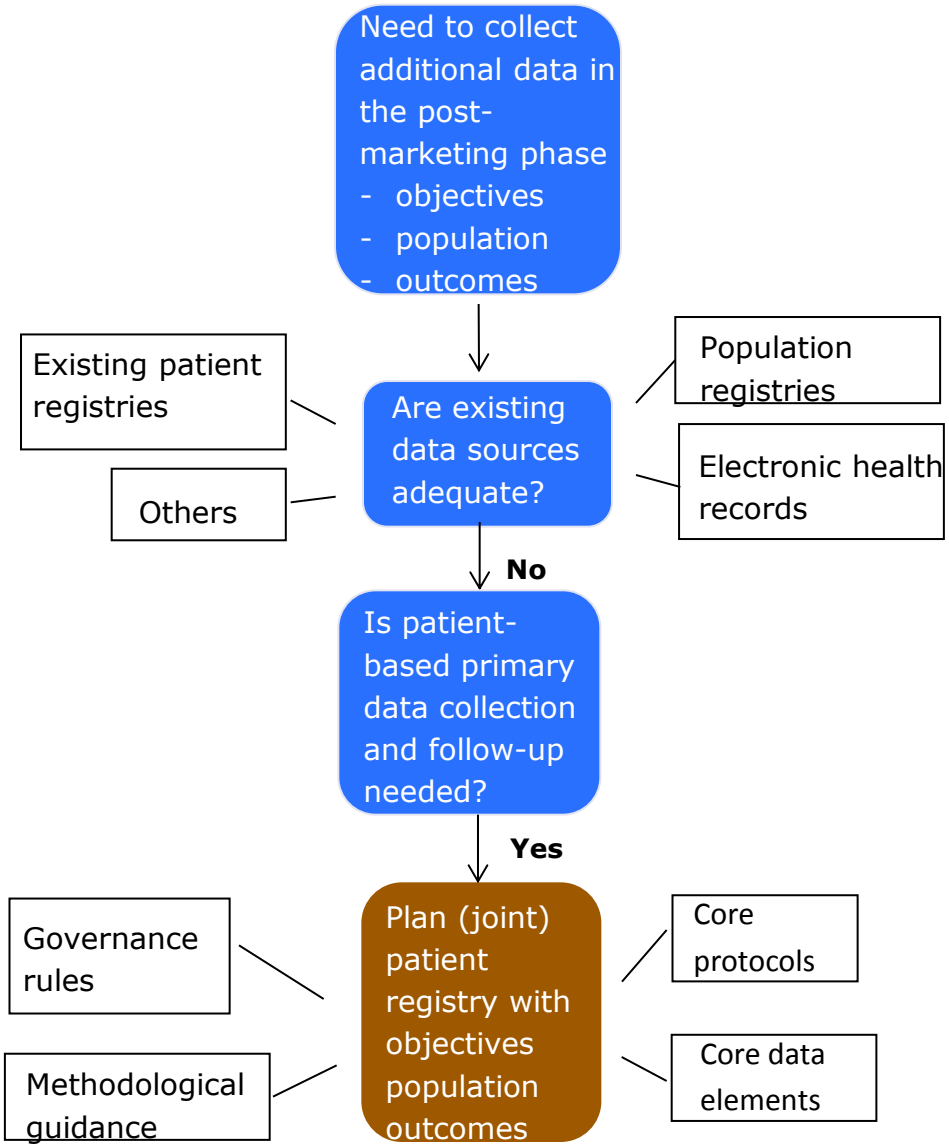
Opportunities

- New pharmacovigilance legislation provides legal mandate for EMA and NCAs to impose/support registries and encourage joint studies.
- Joint Action on Cross-Border Patient Registries iNiTiative (PARENT JA) and future Joint Action II on registries; it plans to deliver a draft methodological guidance and core data elements for registries in Q4 2014
- Other EU projects: European Reference Networks (ERN), RD CONECT (integrated platform for registries and biobank), European Research and Infrastructure Consortium (ERIC) platform for registries, JRC project for medical devices, European platform of rare disease registries, other disease registries (eg network of European cancer registries)
- National registries (e.g. AIFA)

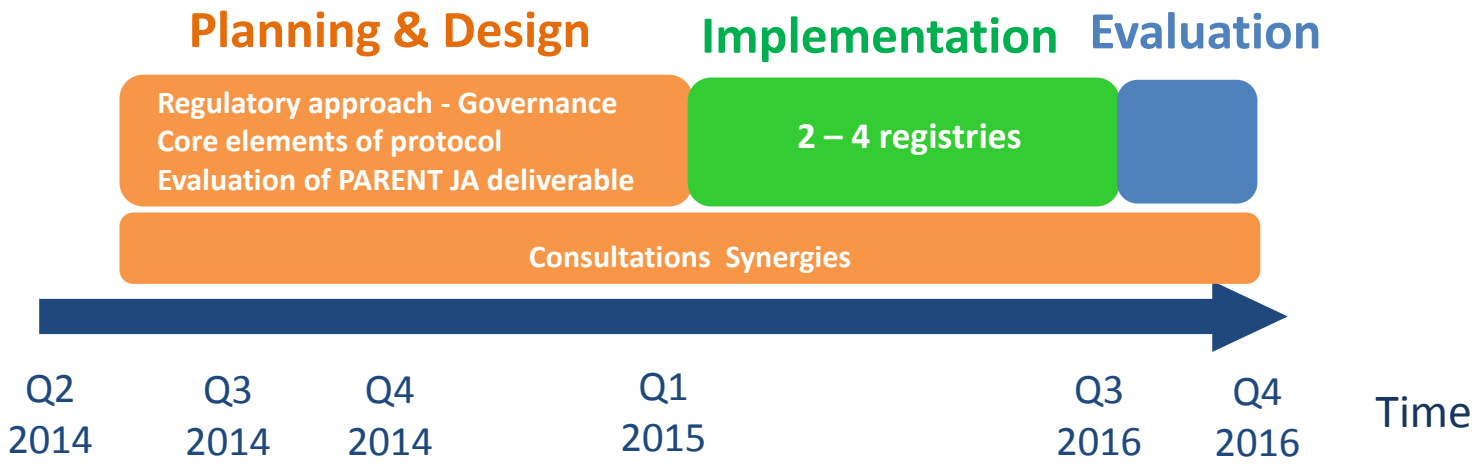
Approach

- Early effective dialogue between applicants, regulatory authorities, committees (CHMP, COMP, PDCO, PRAC) and other stakeholders in order to integrate their input into the design of the registry.
- Discussion on establishment, objectives, outcomes and methodology of registries pre-authorisation by Applicants through the EMA scientific advice procedure and in the context of pro-active preparation of a provisional risk management plan.
- Outcomes: broad range of outcomes can be collected (safety, efficacy, drug utilisation, economic outcomes,…); linkage to electronic health records.
- Development of a toolkit (core protocol, standard methodology, standard data elements , governance framework) based on PARENT JA deliverable

Approach (2)


Need to collect additional data in the post-marketing phase
- objectives
- population
- outcomes
Existing patient registries
Others
Are existing data sources adequate?
Population registries
Electronic health records
No
Is patient-based primary data collection and follow-up needed?
Yes
Governance rules
Methodological guidance
Plan (joint) patient registry with objectives population outcomes
Core protocols
Core data elements

Timetable (draft)



What will be delivered by the project?
(dates are tentative)

- Q4 2014: Strategy paper explaining the rationale, vision, methods and timelines for this pilot phase.
- Q1 2015: Technical specification including a suite of tools for patient registries, including:
  - core elements of a standard protocol
  - components of a standard methodology
  - common data elements
  - governance principles
  - guidance on data privacy rules applicable to the registry data and their access rights.
- Q4 2016: Results of the pilot phase on 2-4 patient registries, lessons learnt and areas for improvement.

Questions to the PCWP/HCPWP

- Do you agree with the general approach proposed to improve the quality/usefulness of patient registries (early dialogue with stakeholders, common suite of tools, governance rules, joint registries)?
- Could the PCWP/HCPWP support this project and nominate representatives to be consulted by the EMA Task Force?
- More generally, how could registry coordinators get support from health care professionals and patients for their participation in registries?