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SCIENCE MEDICINES HEALTH

ENCePP Anniversary 2007-2017

10 years of collaboration in the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

ENCePP Plenary meeting, 21 November 2017

Presented by Susana Perez-Gutthann
Member of ENCePP Steering Group and Deputy Chair 2012-2016

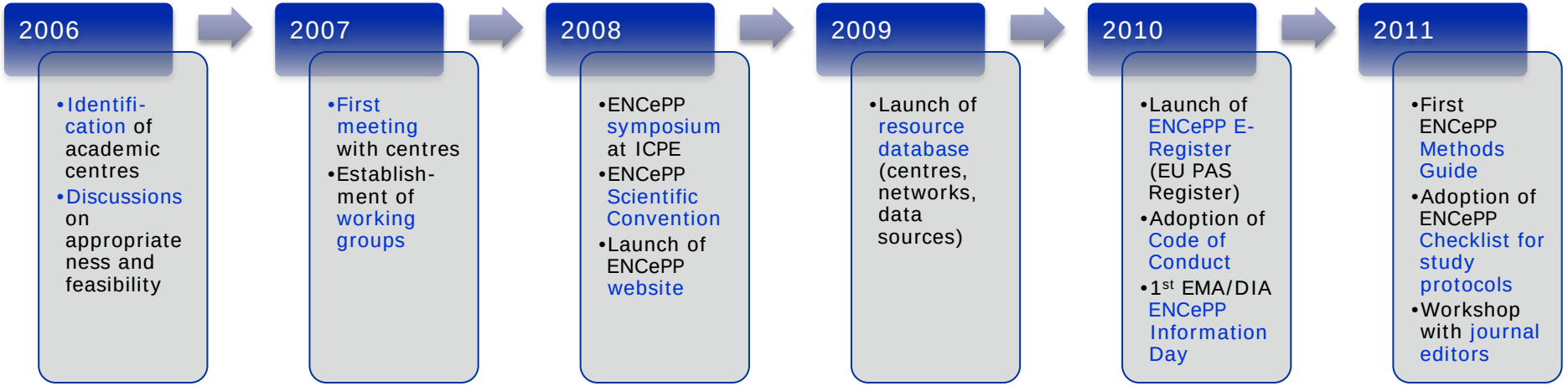
Then: Why ENCePP?

- Inherent fragmentation of research, information (e.g Databases, Registries) and knowledge in Europe
- Consequently, many PASS performed in the US
  - May not reflect EU clinical experience
  - Does not support research in the EU
- Need to establish new tools for the monitoring of the benefit-risk balance of medicinal products in Europe

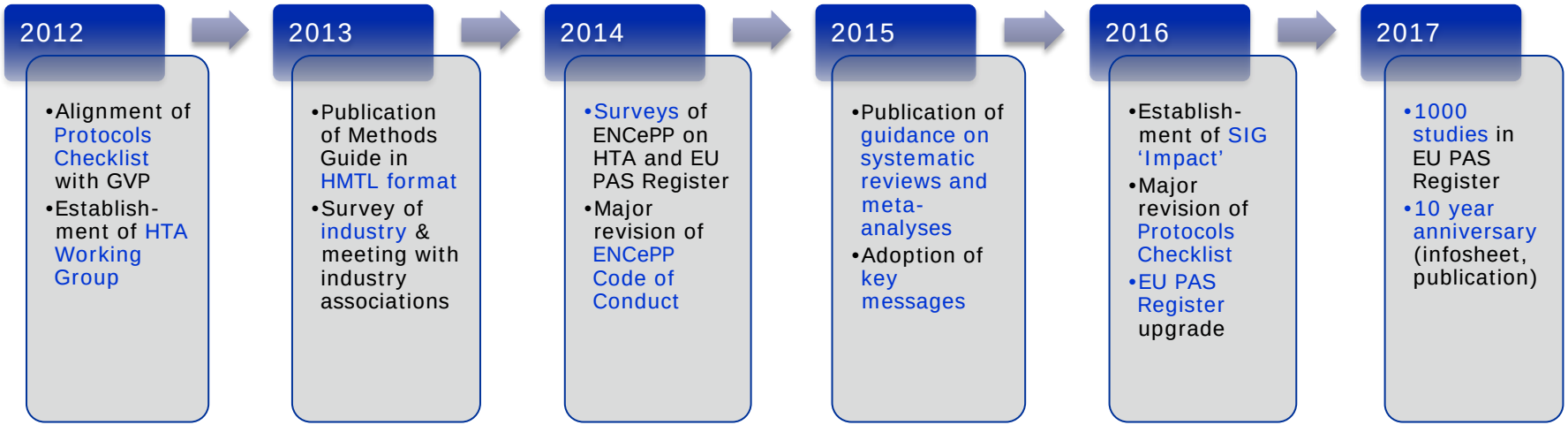
Now: What is ENCePP?

- An initiative that **brings together expertise and resources** in pharmacoepidemiology and pharmacovigilance across Europe
- Aims to **strengthen the monitoring of the benefit:risk balance of medicinal products**
- Comprises research centres and networks referred to as '**ENCePP partners**'
- **Globally acknowledged** for its expertise and outputs

Some important milestones



Milestones cont.



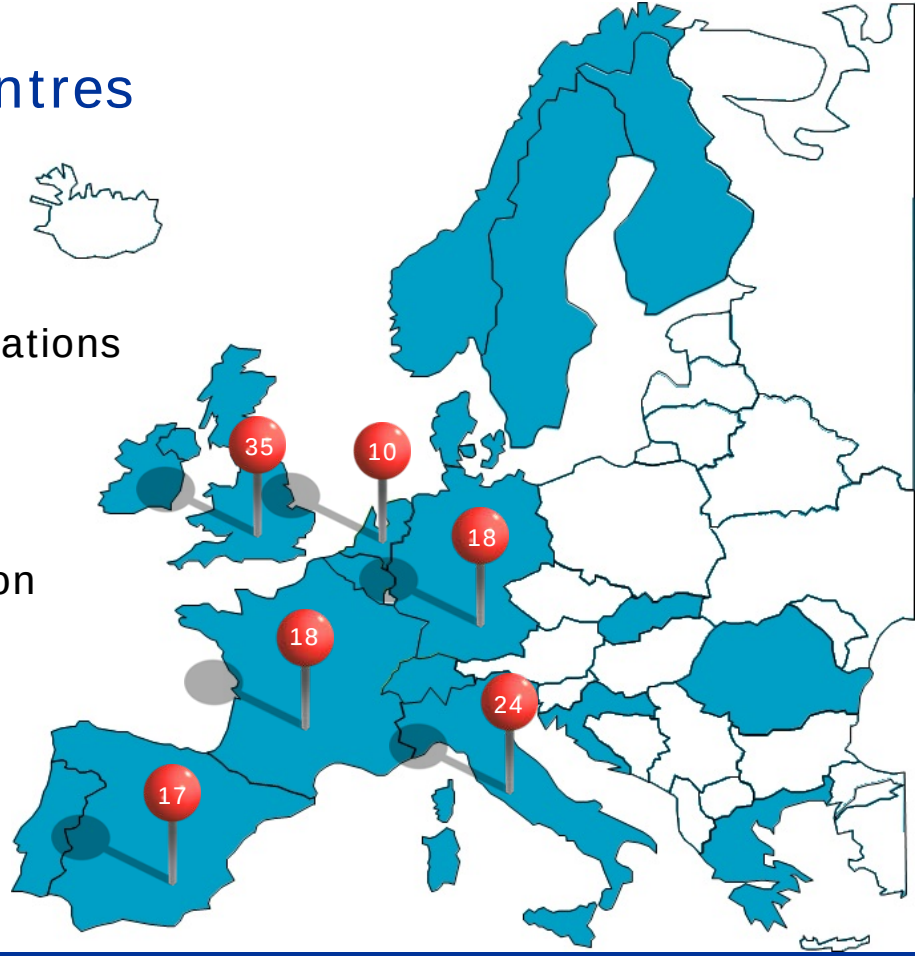
ENCePP inventory of research centres

168 public institutions and research organisations

18 European countries

Room for improvement ➔ Under-representation from new Member States

countries with largest representation



10 years of collaboration

- 16 **plenary meetings**
  - ~1400 participants
    - Meeting minutes and presentations: http://www.encepp.eu/publications/PlenaryMeetingReports.shtml
- 7 **working groups**, 2 **Special Interest Groups**, 2 **Task Forces**
  - 132 meetings of WGs, SIGs, TFs
- 5 **Steering Groups**
  - 42 Steering Group meetings
    - Meeting minutes: http://www.encepp.eu/publications/SGMeetingReports.shtml
- 6 **work plans**

…. And counting….

EMA Support team

Xavier Kurz, EMA lead Working Group 1 and Acting Chair of Steering Group

Jim Slattery, EMA lead Working Group 3 and Statistical adviser to the Steering Group

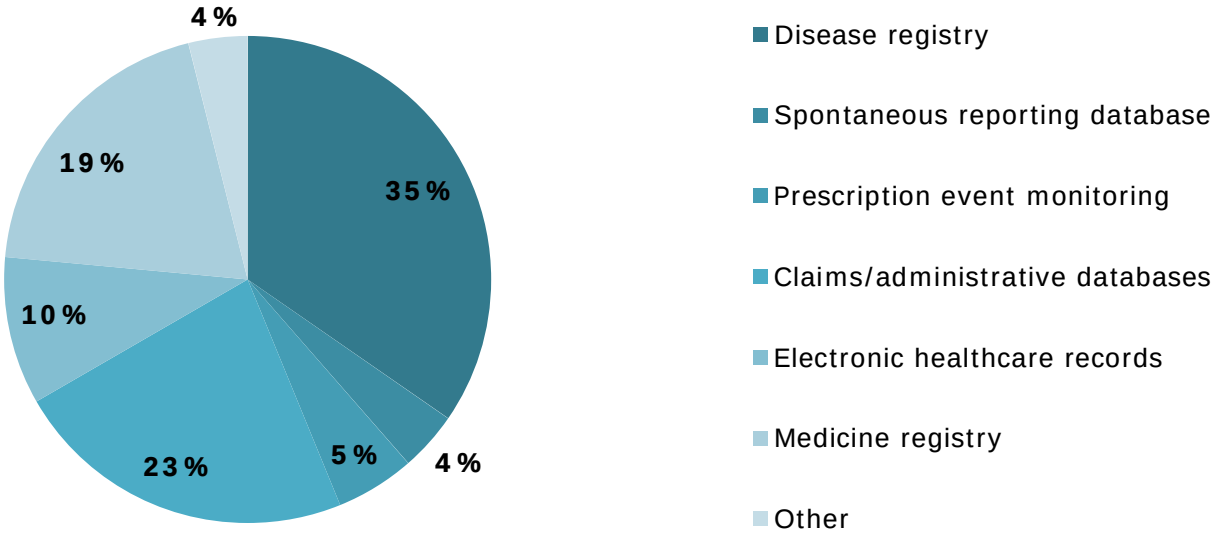
Thomas Goedecke, EMA lead Working Group 2 and SIG Impact

Dagmar Vogl, ENCePP Secretariat

Eeva Rossi, ENCePP Secretariat

ENCePP inventory of data sources

104 Data sources (Sep 2017)



Methodological guidance

ENCePP Guide on Methodological Standards in Pharmacoepidemiology

- A single web resource for methodological English language guidance (6th revision published in July 2017)

  - 5000 views on average per month in 2017
  - 850 downloads on average per month in 2017
  - 424 references selected, commented and updated
  - 31 authors

Governance principles

ENCePP Checklist for Study Protocols

- Supporting best practice in study design
- Promoting transparency on study methods

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ENCePP Checklist for Study Protocols (Revision 3)

Adopted by the ENCePP Steering Group on 01/07/2016

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) welcomes innovative designs and new methods of research. This Checklist has been developed by ENCePP to stimulate consideration of important principles when designing and writing a pharmacoepidemiological or pharmacovigilance study protocol. The Checklist is intended to promote the quality of such studies, not their uniformity. The user is also referred to the ENCePP Guide on Methodological Standards in Pharmacoepidemiology, which reviews and gives direct electronic access to guidance for research in pharmacoepidemiology and pharmacovigilance.

For each question of the Checklist, the investigator should indicate whether or not it has been addressed in the study protocol. If the answer is "Yes", the section number of the protocol where this issue has been discussed should be specified. It is possible that some questions do not apply to a particular study (for example, in the case of an innovative study design). In this case, the answer 'N/A' (Not Applicable) can be checked and the "Comments" field included for each section should be used to explain why. The "Comments" field can also be used to elaborate on a "No" answer.

This Checklist should be included as an Annex by marketing authorisation holders when submitting the protocol of a non-interventional post-authorisation safety study (PASS) to a regulatory authority (see the Guidance on the format and content of the protocol of non-interventional post-authorisation safety studies). The Checklist is a supporting document and does not replace the format of the protocol for PASS as recommended in the Guidance and Module VIII of the Good pharmacovigilance practices (GVP).

Study title:

Study reference number:

Section 1: Milestones	Yes	No	N/A	Section Number
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[1]	☐	☐	☐	
1.1.2 End of data collection[2]	☐	☐	☐	
1.1.3 Study progress report(s)	☐	☐	☐	
1.1.4 Interim progress report(s)	☐	☐	☐	
1.1.5 Registration in the EU PAS register	☐	☐	☐	
1.1.6 Final report of study results	☐	☐	☐	

[1] Data from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the data from which data extraction starts.
[2] Data from which the analytical dataset is completely available.

ENCePP Checklist for Study Protocols (Revision 3)

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London, 14 July 2016
EMA/929208/2011

The ENCePP Code of Conduct

FOR SCIENTIFIC INDEPENDENCE AND TRANSPARENCY IN THE CONDUCT OF PHARMACOEPIDEMIOLOGICAL AND PHARMACOVIGILANCE STUDIES

The ENCePP Code of Conduct was adopted on 7 May 2010 by the Steering Group of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). The terms of the Code of Conduct are reviewed by the ENCePP Steering Group periodically after its adoption.

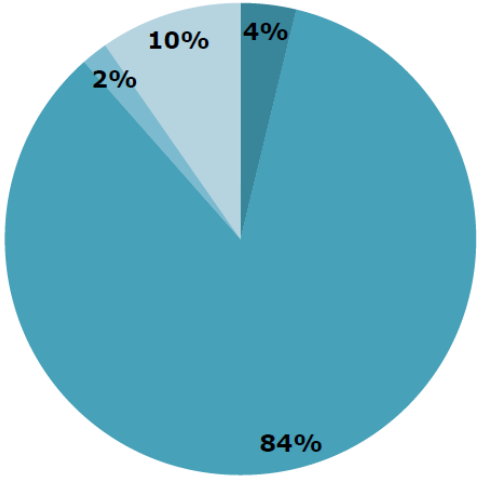
Steps taken	Date
Adoption	7 May 2010
Revision 1	12 September 2010
Revision 2	21 November 2011
Revision 3	21 February 2014
Revision 3 editorial amendment	14 July 2016

ENCePP Code of Conduct

- Promoting transparency and scientific independence throughout the research process

EU PAS Register® (formerly ENCePP E-Register of Studies)

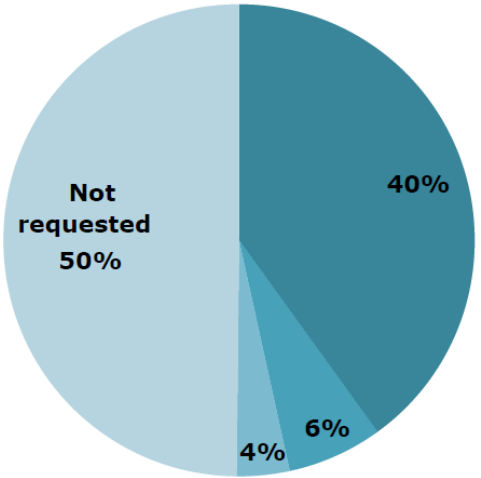
Increased transparency in high quality, multi-centre, independent non-interventional post-authorisation studies (PAS)



1145

PAS registered
(By type, July 2017)

- Active surveillance
- Observational study
- Clinical trial
- Other



50%

of registered studies were requested by a regulator:

- Europe
- United States
- Rest of the World

ENCePP and regulatory decision-making / regulatory science

- ENCePP members provide data and publications occasionally to EMA that could support drug safety reviews
- EMA funded studies (through public procurement)
- European Commission FP7 Drug Safety programme
- IMI public-private partnerships

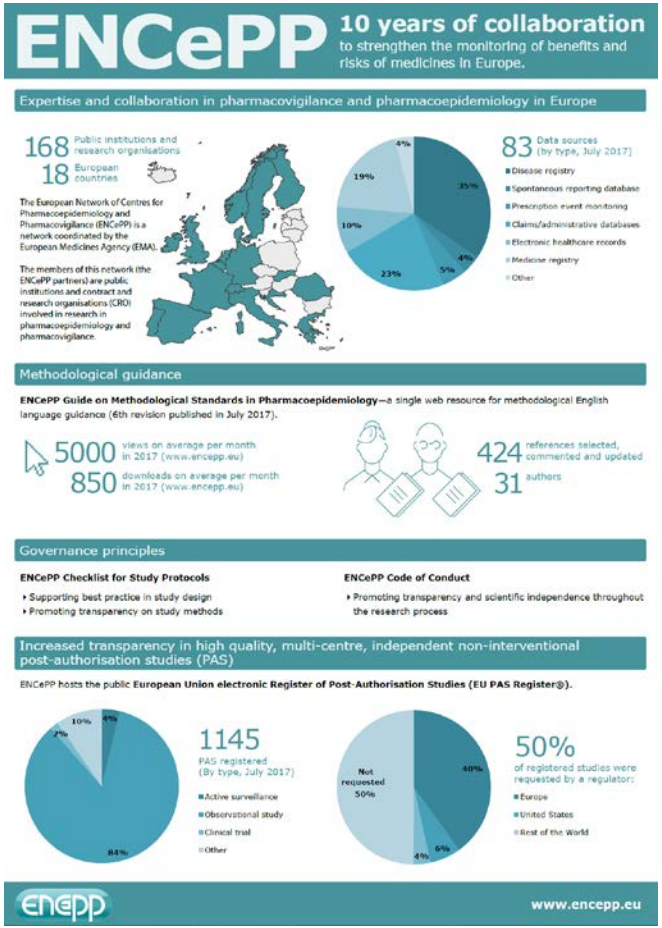
Difficult to determine the impact of one study on the regulatory decision, as any decision is based on a body of evidence

What next?

- Collaborate to strengthen the capacity for multi-centre studies including work on innovative methods to access and analyse data from electronic databases, e.g. use of common data models
- Further promote transparency and independency through revision of the Code of Conduct
- Ensure the network remains focussed on public health and relevant to the decisions taken by regulators, Health Technology Assessment and other bodies
- Ensure the network includes new experts and centres and embraces relevant new areas of activity e.g. use of patient registries, social media information and big data
- Increase the number, breadth and depth of collaboration between ENCePP and non-European researchers and health decision-makers
- Further develop the “pharmacovigilance” component of ENCePP through collaborations with other groups.

Promotional material

- Anniversary manuscript:
  Strengthening standards and collaborations to support medicines evaluation: Ten years of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)
  - *For publication in PDS open access*
- Anniversary leaflet:
  ENCePP: 10 years of collaboration to strengthen the monitoring of benefits and risks of medicines in Europe
  - *Available for download on ENCePP website (http://www.encepp.eu/publications/documents/ENCePP.pdf)*



Thank you for your attention

Further information

encepp_secretariat@ema.europa.eu
www.encepp.eu

List of studies funded by EMA to support the benefit-risk evaluation of medicinal products (2010-2017)

Study title	EUPAS Register number	Link to publication of results
A/H1N1 pandemic vaccines and pregnancy outcomes	5304	Link to study report included in EU PAS Register
Impact of risk minimisation in patients treated with rosiglitazone-containing products	2236	https://www.ncbi.nlm.nih.gov/pubmed/24068766
Isotretinoin and the effectiveness of the Pregnancy Prevention Programme in Europe	4654	Link to study report included in EU PAS Register
Patterns and determinants of use of oral contraceptives in the EU	11085	https://www.ncbi.nlm.nih.gov/pubmed/26492444
Monitoring the effectiveness of risk minimisation in patients treated with pioglitazone-containing products	3221	Link to study report included in EU PAS Register
Risk of cardiac valve disorders associated with the use of biphosphonates	7967	https://www.ncbi.nlm.nih.gov/pubmed/26694594
Association between anxiolytic or hypnotic drugs and total mortality	10626	https://www.ncbi.nlm.nih.gov/pubmed/26256008
Metformin use in renal impairment	7492	http://bmjopen.bmj.com/content/5/9/e008531.full https://www.ncbi.nlm.nih.gov/pubmed/27504911
Study of regulatory communication and risk awareness following the Article 31 referral of Combined Hormonal Contraceptives in relation to thromboembolism	21357	Study on-going
Characterising the risk of major bleeding in patients with Non-Valvular Atrial Fibrillation: non-interventional study of patients taking Direct Oral Anticoagulants in the EU	21042	Study on-going
Study of utilisation of Combined Hormonal Contraceptives in Europe	21353	Study on-going
Anti-microbial resistance: choice of therapeutic interventions and outcomes for the treatment of infections caused by MDR Gram negative pathogens	21360	Study on-going
Methods and data sources for determining long-term effects of drug exposure during pregnancy, with application to antiepileptic medicines	21172	Study on-going
Impact of EU label changes for systemic diclofenac products: post-referral prescribing trends	Study planned	
Impact of EU label changes for hydroxyzine products: post-referral prescribing trends	Study planned	

List of studies funded by the European Commission's 7th Framework programme for drug safety studies to support the benefit-risk evaluation of medicinal products (2007-2013)

Study title	EUPAS Register number	Link to CORDIS website [2]
SOS: Safety Of non-Steroidal anti-inflammatory drugs		http://cordis.europa.eu/project/rcn/89349_en.html
ARITMO: Arrhythmogenic potential of drugs	20755	http://cordis.europa.eu/project/rcn/94061_en.html
ADDUCE: Attention Deficit Hyperactivity Disorder Drugs Chronic Effects	6902, 3986	http://cordis.europa.eu/project/rcn/96780_en.html
EUROmediCAT: Safety of Medication use in Pregnancy in Relation to Risk of Congenital Malformations	2222	http://cordis.europa.eu/project/rcn/98223_en.html
PHARMACHILD: Long-term Pharmacovigilance for Adverse effects in Childhood Arthritis focussing on Immuno-modulatory drugs	19359	http://cordis.europa.eu/project/rcn/96819_en.html
STOP: Suicidality: Treatment Occurring in Paediatrics		http://cordis.europa.eu/project/rcn/97369_en.html
CARING: Cancer risks and insulin analogues	11823	http://cordis.europa.eu/project/rcn/100436_en.html
SAFEGUARD: Safety Evaluation of Adverse Reactions in Diabetes	20761, 20765	http://cordis.europa.eu/project/rcn/100121_en.html
Astro-Lab: Assessment of safety of LABAs in asthma in routine care by combining healthcare databases and direct patient follow-up	14482	http://cordis.europa.eu/project/rcn/101108_en.html
EpoCan: Assessing long term risks and advancing towards better Epoetin driven treatment modalities		http://cordis.europa.eu/project/rcn/100286_en.html
PREDICTION-ADR: Personalisation of treatment In Cardiovascular disease through next generation sequencing in Adverse Drug Reactions		http://cordis.europa.eu/project/rcn/109336_en.html