EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance in 2018

24 September 2018

Twelfth Pharmacovigilance Stakeholder Forum

Dr Peter Arlett
Head of Pharmacovigilance and Epidemiology Department
EMA

Headlines

1. EU pharmacovigilance supports safe and effective use of medicines
2. EU pharmacovigilance supports patients to get new products
3. EU pharmacovigilance legislation fully implemented
4. New EudraVigilance system launched November 2017: detects safety issues earlier
5. Robust assessment supports rapid effective action on safety issues
6. Enhanced engagement with users of medicines
7. Driving process improvement through regulatory science
8. Starting to realise the potential of real world evidence
9. Challenges: new data, new technology
10. Challenges: making an impact through change in healthcare practice

In this presentation……

- Reminder: our shared objective
- Focus on product benefit risk
- Focus on public engagement
- Focus on pharmacovigilance processes
- Focus on new data and new science
- Don’t forget the people
- Challenges and opportunities

Reminder: our shared objective.....

To promote the health and wellbeing of EU citizens, through optimisation of the safe and effective use of medicines

- Underpinned by robust science, efficient processes and excellent people
- Manage benefit risk through the lifecycle of products
- Go beyond regulation: bringing together stakeholders to deliver innovation safely

…..to understand how the pharmacovigilance system works…..

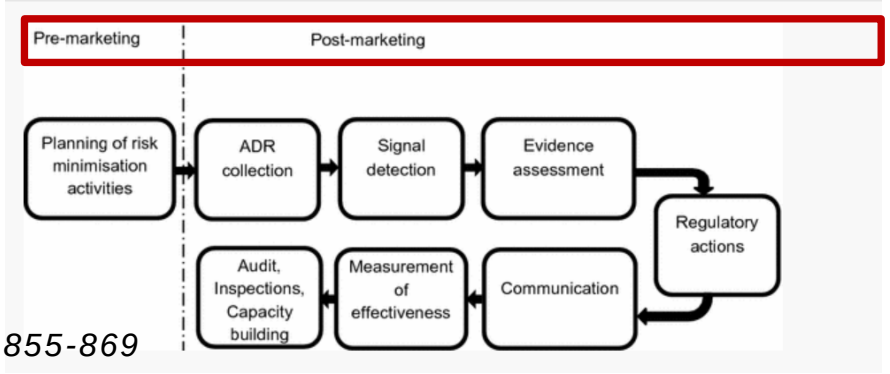
Drug Saf (2017) 40:855–869
DOI 10.1007/s40264-017-0572-8

CrossMark

LEADING ARTICLE

Promoting and Protecting Public Health: How the European Union Pharmacovigilance System Works

Aniello Santoro[1] · Georgy Genov[1] · Almath Spooner[2,3] · June Raine[3,4] · Peter Arlett[1]



Santoro et al 2017 Drug safety 40:855-869

Focus on product benefit risk

A few examples of benefit risk action taken at EU level……

CAR-T cell products Kymriah and Yescarta authorised for leukaemia / lymphoma: intensive PRIME support including registry

First two CAR-T cell medicines recommended for approval in the European Union

Press release

29/06/2018

First two CAR-T cell medicines recommended for approval in the European Union

Development of Kymriah and Yescarta supported through PRIME

The European Medicines Agency (EMA) has recommended the first two marketing authorisations for chimeric antigen receptors (CAR) T-cells medicines in the European Union (EU). Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel) are advanced therapies for blood cancer. They belong to a new generation of personalised cancer immunotherapies that are based on collecting and modifying patients' own immune cells to treat their cancer.

Kymriah and Yescarta are also the first medicines supported through EMA's PRIority MEdicines (PRIME) scheme to receive positive opinions from the Committee for Medicinal Products for Human Use (CHMP). The voluntary scheme provides early and enhanced scientific and regulatory support to medicines that have the potential to address, to a significant extent, patients' unmet medical needs. Kymriah was granted eligibility to PRIME on 23 June 2016, for the treatment of acute lymphoblastic leukaemia (ALL). Yescarta was granted eligibility to PRIME on 26 May 2016 for the treatment of diffuse large B-cell lymphoma (DLBCL).

"CAR-T cells transform the fight against serious and often fatal diseases in the EU," said Dr Martina Schüssler-Lenz, chair of the Committee for Advanced Therapies (CAT). "Kymriah and Yescarta offer an innovative approach where patients' cells are reprogrammed and reinjected to attack the cancer."

Because Kymriah and Yescarta are advanced-therapy medicinal products (ATMPs), they were assessed by the CHMP and the CAT, the Agency's expert committee for cell-, gene- or tissue-based medicines which is responsible for the evaluation of these products. The CAT adopts an advisory opinion, which is taken into account by the CHMP when giving its recommendation regarding the authorisation of the medicine concerned.

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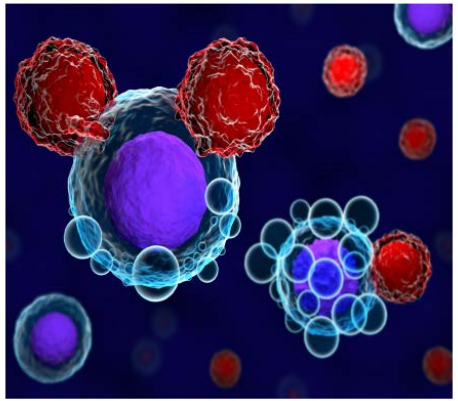
15 May 2018
EMA/204454/2018

Pharmacovigilance and Epidemiology Department
Inspections, Human Medicines, Pharmacovigilance and Committees Division

Report on CAR T-cell therapy Registries
Workshop 9 February 2018

Patient Registries Initiative



September PRAC - 4 signals required letters to healthcare professionals

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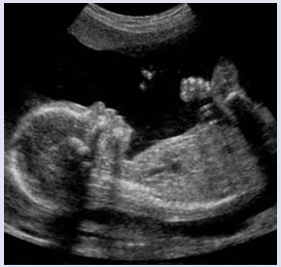


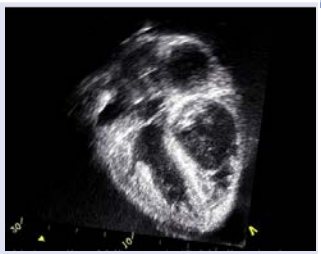
Sildenafil (REVATIO, VIAGRA)

- Pulmonary hypertension & death in infants exposed in utero
- Clinical trial in growth retardation (off label)

27/07/2018 - EMA notified that trial suspended
05/09/2018 – PRAC agrees letter warning to professionals

Rivaroxaban (XARELTO)

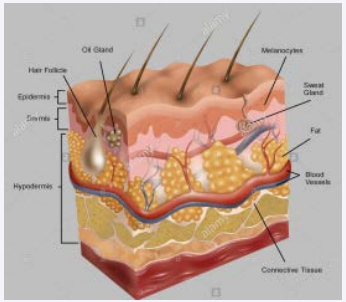
- Increased mortality, bleeding and clots in patients treated for trans-catheter aortic valve replacement (off label)



13/08/2018 - EMA notified that trial suspended
14/08/2018 – EU Incident Management Network teleconference
05/09/2018 – PRAC agrees letter warning to professionals

Hydrochlorothiazide

- Risk of lip and non-melanoma skin cancer

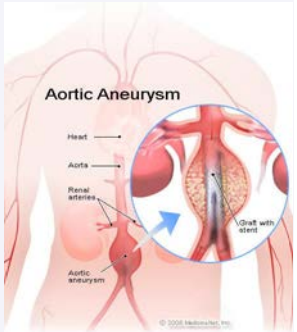


12/2017 - Two Danish epidemiological studies published
Q1 2018 EMA epidemiological study
05/09/2018 – PRAC agrees letter warning to professionals

Fluoroquinolones

Risk of aortic aneurysm and dissection

2015-2018 - Epidemiological and non-clinical studies
05/09/2018 – PRAC agrees letter warning to professionals



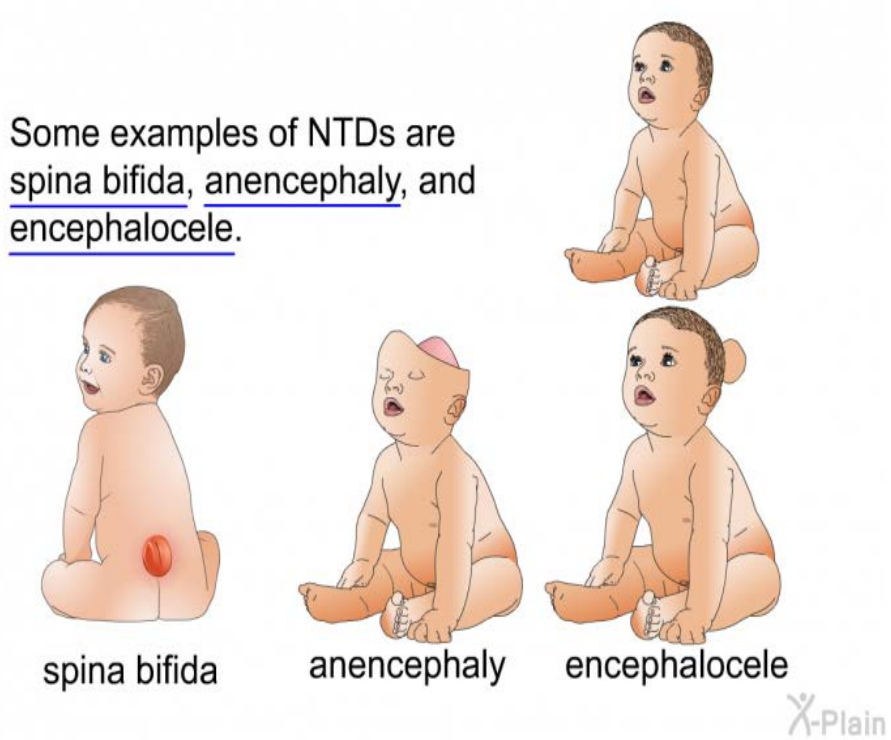
Dolutegravir (Tivicay): treatment for HIV infection

Cases of neural tube defects from observational study of use in Botswana

7/5/18 EMA informed of study result by WHO and company

17/5/18 PRAC agreed letter warning professionals not to use dolutegravir in women planning a pregnancy and that women of child bearing potential who take dolutegravir should use effective contraception

18/5/18 Coordinated press-releases from EMA, FDA and WHO with consistent warnings



Daclizumab beta (Zinbryta): treatment for multiple sclerosis

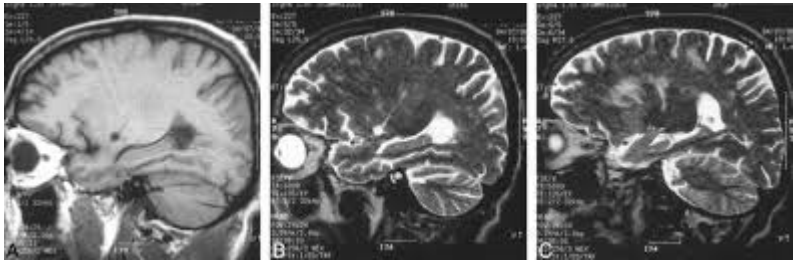
Spontaneous reports from a neurology centre in Germany of encephalitis and death

20/2/18 EMA informed by PEI

23/2/18 EU Incident Review Network teleconference recommends referral to PRAC

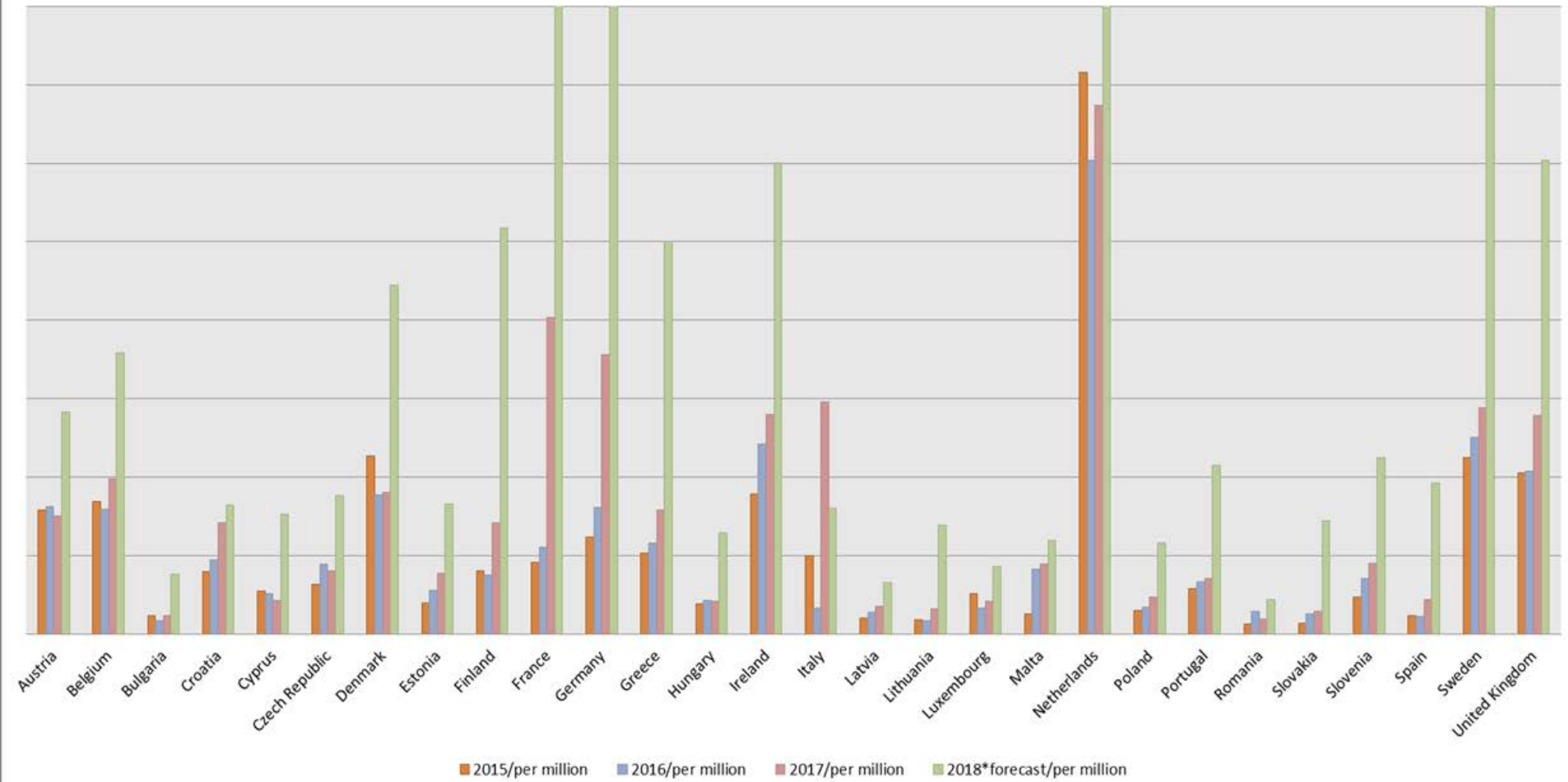
1/3/18 MAH informs of intention withdraw the marketing authorisations

6/3/18 PRAC recommends benefit risk negative with suspension of the product and recall to pharmacy and hospital level + letter to warn professionals



Focus on public engagement
...core of this mornings sessions....

Patient reporting in EudraVigilance



Public Hearing: quinolone and fluoroquinolone medicines

Quinolone- and fluoroquinolone-containing medicinal products

Summary | Key facts | **Public hearing** | All documents

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) held a public hearing on this topic on 13 June 2018 at the Agency's premises in London:

- Agenda and list of speakers
- Written interventions

- Summary report - available in all EU languages below

bg - balgarski,
cs - čeština,
da - dansk,
de - Deutsch,
el - ελληνικά,
es - español,
et - eesti keel,
lt - lietuvių kalba,
fr - français,
hr - Hrvatski,
hu - magyar,
it - italiano,
lv - latviešu valoda,
mt - Malti,
nl - Dutch,
pl - polski,
pt - português,
ro - romana,
sk - slovenčina,
sl - slovenščina,
fi - suomi,
sv - svenska.

The hearing was broadcast live on 13 June from 13:00 - 18:00 (UK time).

The **video recording** is available.

01 Issue 1 - 2018
July 2018

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SCIENCE MEDICINES HEALTH

What's new in Pharmacovigilance?

QPPV UPDATE

Published by the European Medicines Agency

An agency of the European Union

IN THIS ISSUE

Pharmacovigilance IT systems 2
Pharmacovigilance processes 4
Pharmacovigilance guidance 5
Pharmacovigilance dialogue 5

QPPV Update

This QPPV Update provides Qualified Persons responsible for Pharmacovigilance (QPPVs) and all other people working in pharmacovigilance with an update on EU Pharmacovigilance, relating to medicines for human use.
We would welcome your feedback as well as any suggestions on topics you think would be of interest to colleagues. Your feedback should be sent via ASK EMA online form.

Guidance for pharmaceutical companies to prepare for UK withdrawal from the EU

On 19 June 2018 the European Medicines Agency (EMA) and the European Commission updated their guidance to help pharmaceutical companies prepare for the United Kingdom's (UK) withdrawal from the European Union (EU).

Updates to the questions-and-answers document are marked 'NEW' and include new information on back-up arrangements for QPPVs. The Agency has also published an updated version of its practical guidance for industry which outlines the steps that companies should follow to make sure that necessary changes to their marketing authorisation are made by the end of March 2019. The document should be read in conjunction with the updated Q+A document. Further information can be found here .

Need more information?

Further information about the work of the European Medicines Agency is available on our website

Research: listening to the public

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The aim of this study was to evaluate whether prospective real-time media monitoring for specific medicinal products has the potential to enhance communication in terms of proactivity and preparedness for information provision to the public, in particular by a regulatory body.

Bahri *et al. BMC Medicine* (2017) 15:91
DOI 10.1186/s12916-017-0850-4

BMC Medicine

RESEARCH ARTICLE Open Access

Application of real-time global media monitoring and 'derived questions' for enhancing communication by regulatory bodies: the case of human papillomavirus vaccines

Priya Bahri[1,2*], Julianna Fogd[2], Daniel Morales[2,3], Xavier Kurz[2] and on behalf of the ADVANCE consortium

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2018) **84** 1696–1705 1696

REVIEW

Listen to the public and fulfil their information interests – translating vaccine communication research findings into guidance for regulators

Priya Bahri and Mireia Castillon Melero

Surveillance & Epidemiology Service, Pharmacovigilance Department, European Medicines Agency,

The objectives of the present article were therefore to respond to stakeholders and support awareness of the guidance in EU-GVP, its implementation and training activities through:

- Providing insights into the triggers and methods for developing the guidance;
- Sharing the evidence base for its recommendations; and
- Indicating how this guidance and recent other guides add value for regulators inside and outside the EU in a complementary manner.

Focus on pharmacovigilance processes

News and press releases
Events
What's new
Committee highlights
Therapeutic areas: latest updates
Medicine evaluation figures
Publications
Press and social media

New EudraVigilance system is live

News

22/11/2017

New EudraVigilance system is live

Better safety monitoring for patients across Europe

The European Medicines Agency (EMA) has launched today a new and improved version of EudraVigilance, the European information system of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the European Economic Area (EEA). The new system makes it easier for marketing authorisation holders and sponsors of clinical trials to report suspected adverse reactions and allows for better analysis of this information for the benefit of patient safety in Europe.

A landmark paper on EudraVigilance …

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Around 50% signals derive from Eudravigilance ICSRs

Other sources
- PSURs
- RMPs
- post-authorisation safety studies
- published literature

>54% serious safety issues detected earlier if EV used in addition to other resources

Alvarez Y et al 2010

Drug Safety 33(6) 475 -87

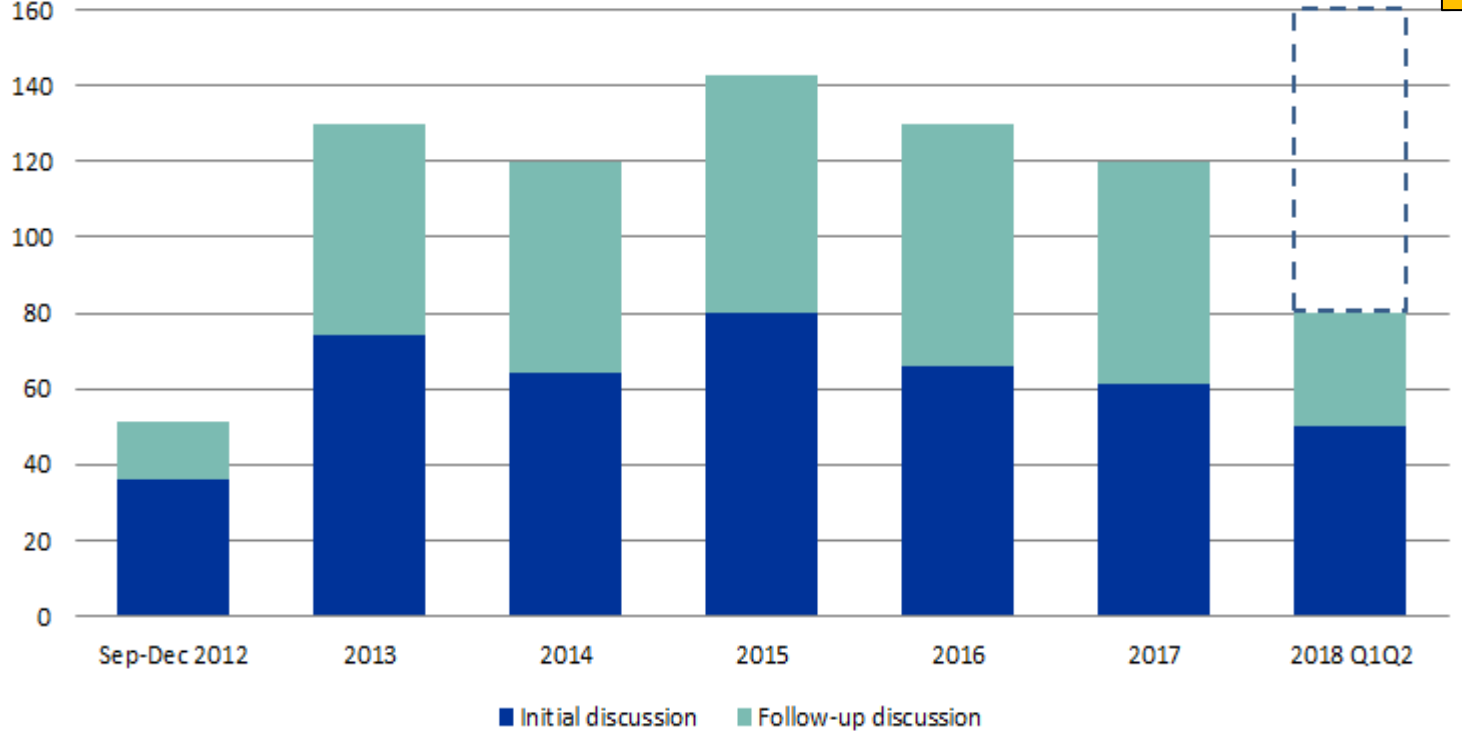
Table II. Detection of drug-event pairs using standard proportional reporting ratio (PRR) signal criteria defining a signal of disproportionate reporting (SDR) with synonymous Medical Dictionary for Regulatory Activities (MedDRA®) terms restricted to important medical events

Outcome measure	SDR from PRR within study		No SDR during study
	PRR first	standard pharmacovigilance first	
Safety issues [n (%)]	217 (53.6)	79 (19.5)	109 (26.9)
Mean time gain (y)	2.45	–1.07	
Maximum time gain (y)	8.34		

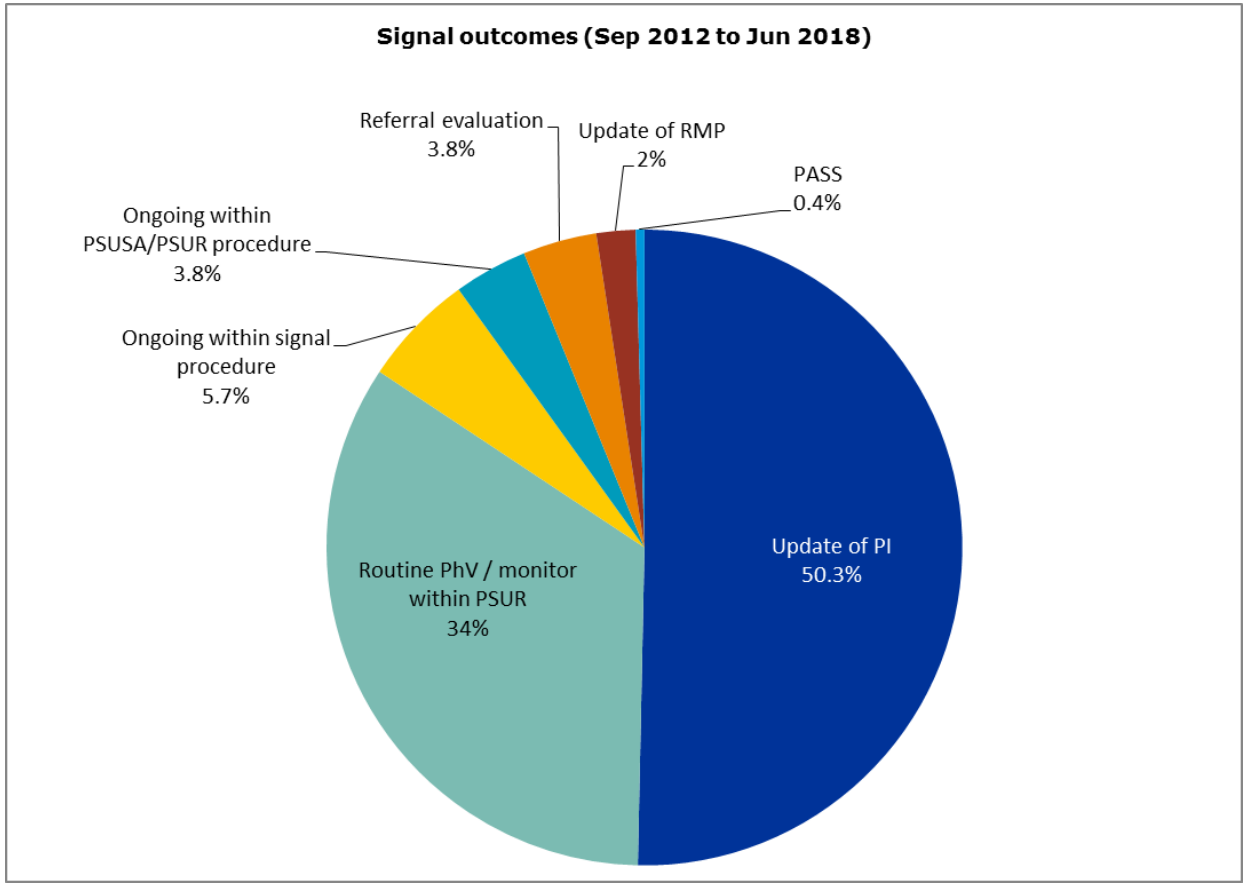
Median: 12 per month

Number of signal discussions at PRAC per year (2012-2018 Q1Q2)

Sep 2012 – Jun 2018
774 signal discussions
453 signals



*Dashed line – 2018 estimate based on Q1Q2


Signal outcomes (Sep 2012 to Jun 2018)
Referral evaluation
3.8%
Update of RMP
2%
PASS
0.4%
Ongoing within
PSUSA/PSUR procedure
3.8%
Ongoing within signal
procedure
5.7%
Routine PhV / monitor
within PSUR
34%
Update of PI
50.3%

Signal detection pilot – extension of the pilot through 2019

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SCIENCE MEDICINES HEALTH

To: Industry Stakeholders Associations (Human)

31 August 2018
EMA/592946/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Dear Industry Stakeholders,

Subject: Extension of the period of the pilot of signal detection in EudraVigilance by marketing authorisation holders

Background

The EU pharmacovigilance legislation[1] requires marketing authorisation holders (MAHs) to continuously monitor data in EudraVigilance to the extent of their access to the database and to inform forthwith the Agency and National Competent Authorities (NCAs) of validated signals detected in the database. The extended access to EudraVigilance allowing MAHs to fulfil their obligations came into effect on 22 November 2017. Regulatory guidance on the detection and reporting of signals from EudraVigilance is provided in the Good Pharmacovigilance Practices (GVP) Module IX on Signal Management.

In July 2017, in order to streamline this new process, the European Commission (EC) agreed to a phased implementation of the above legal requirements. The initial phase of the implementation started on 22 February 2018 for a period of one year and concerns a limited number of active substances[2] selected based on the list of medicinal products subject to additional monitoring.

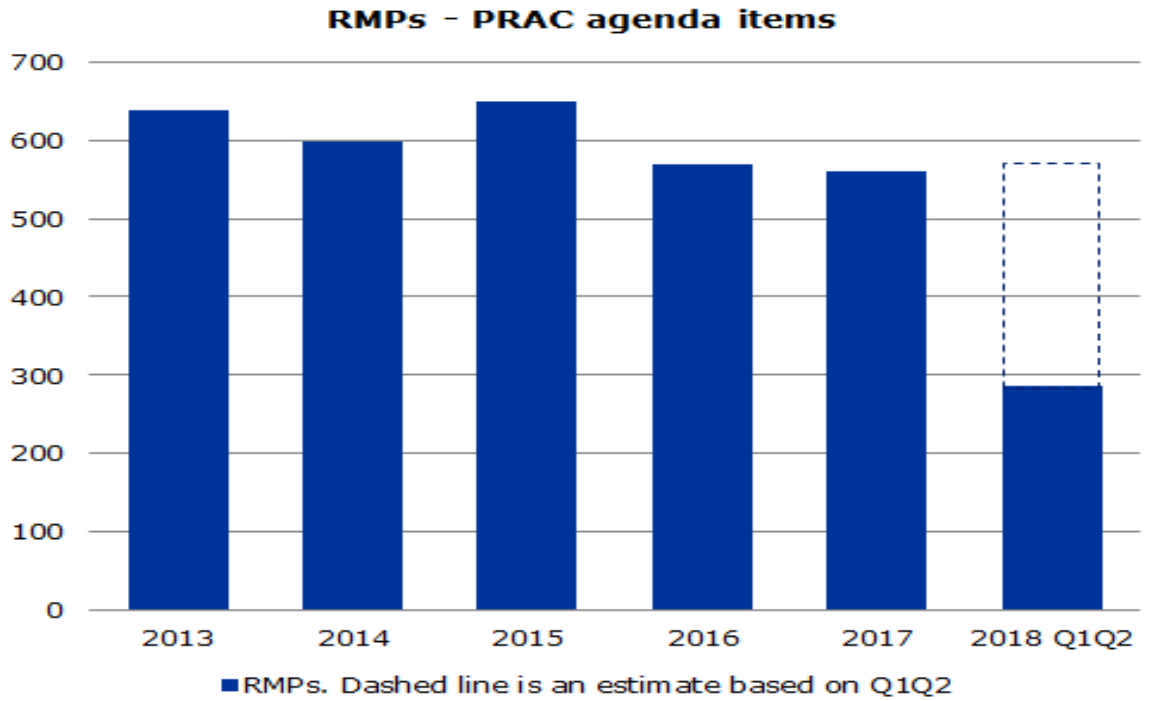
Extension of the pilot period

It is considered that more experience is needed during the pilot phase. Therefore a prolongation of the pilot period beyond 22 February 2019 has been agreed with EC. This means that after this date, only those MAHs with an active substance or combination included on the 'pilot list'[2] will have to continue performing signal detection in EudraVigilance for these substances.

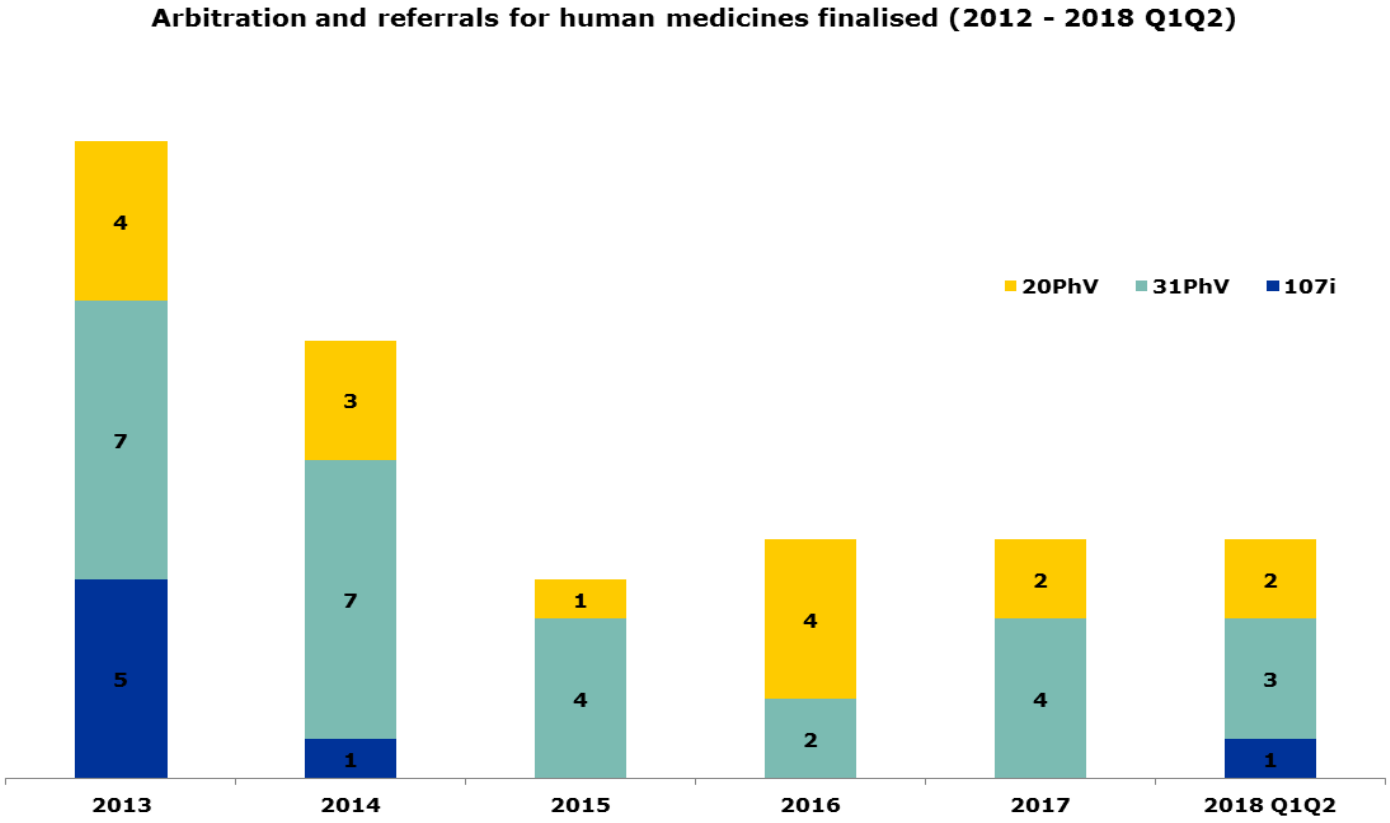
Next steps

By September 2019, the Agency will finalise a report outlining the first year of experience (February 2018 - February 2019), including both workload and process aspects. In that context, please note that EMA intends to survey MAHs involved in the pilot on their experience, including signals reported within PSURs or safety variations in line with the process outlined in GVP IX. Therefore, MAHs are encouraged to prospectively record such information.

RMPs: deliver proactive planning of risk minimisation and data collection



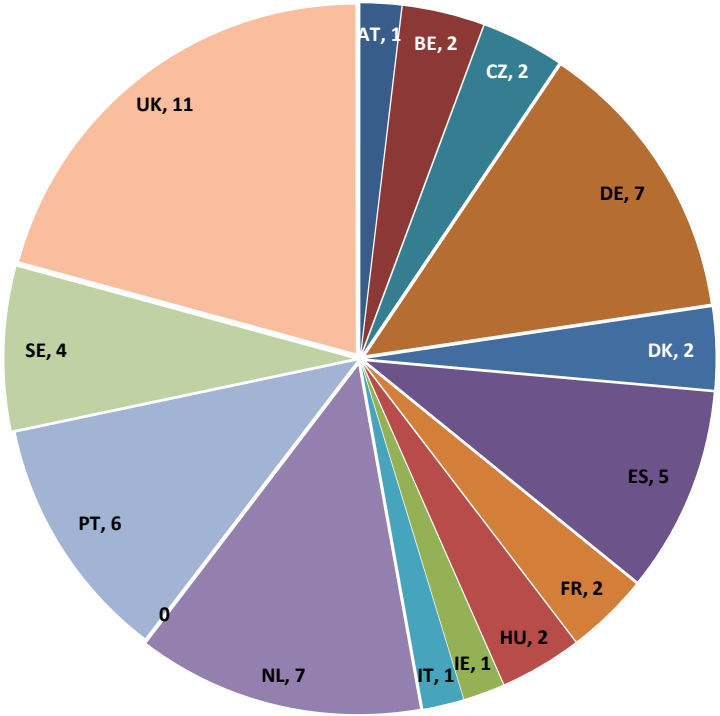
Pharmacovigilance referrals



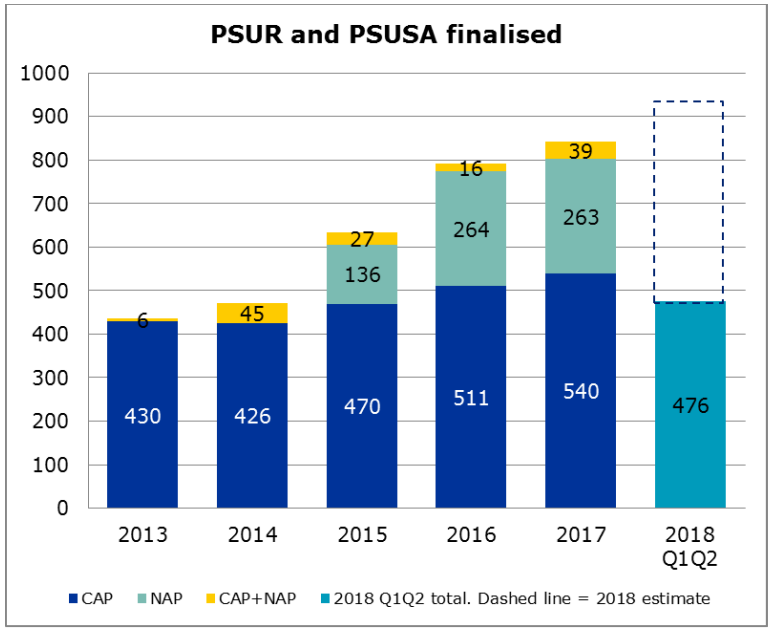
Finalised and ongoing pharmacovigilance referrals 2018 YTD

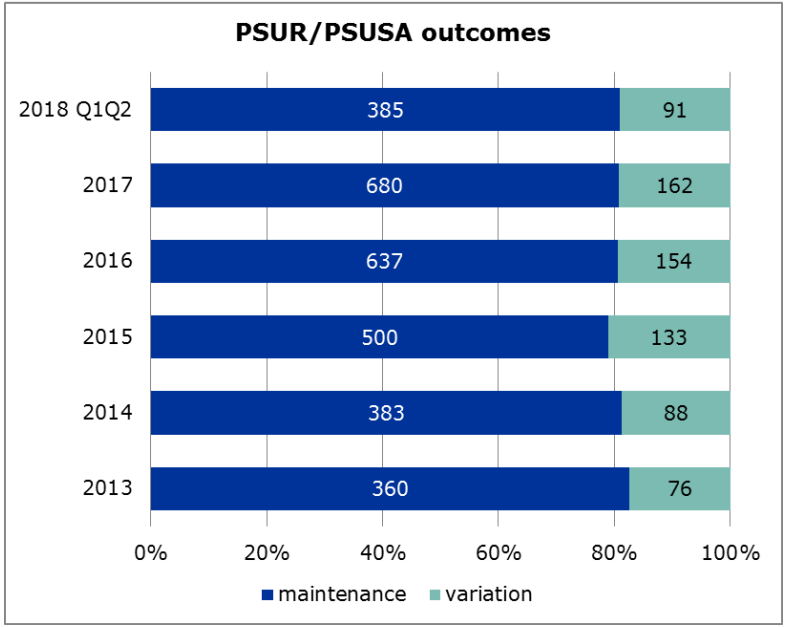
Procedure name	INN	Article	Start date	Finalised
Retinoids	acitretin, adapalene, alitretinoin, bexarotene, isotretinoin, tretinoin, tazarotene	31PhV	Jul-16	Mar-18
Quinolone and fluoroquinolone	nalidixic acid, pipemidic acid, cinoxacin, enoxacin, pefloxacin, lomefloxacin, ciprofloxacin, levofloxacin, ofloxacin, moxifloxacin, norfloxacin, prulifloxacin, rufloxacin, flumequin	31PhV	Feb-17	**Ongoing**
Valproate	valproate	31PhV	Mar-17	Mar-18
Flupirtine	flupirtine	31PhV	Oct-17	Mar-18
Hydroxyethyl starch (HES)	hydroxyethyl starch	107i	Oct-17	Jun-18
Xofigo	radium Ra223 dichloride	20PhV	Dec-17	Jul-18
Esmya	ulipristal acetate	20PhV	Dec-17	May-18
Zinbryta	daclizumab	20PhV	Mar-18	May-18
Methotrexate oral formulations	methotrexate	31PhV	Apri-18	**Ongoing**

Rapporteurs appointed on referrals from Jul. 2012– End Jun 2018

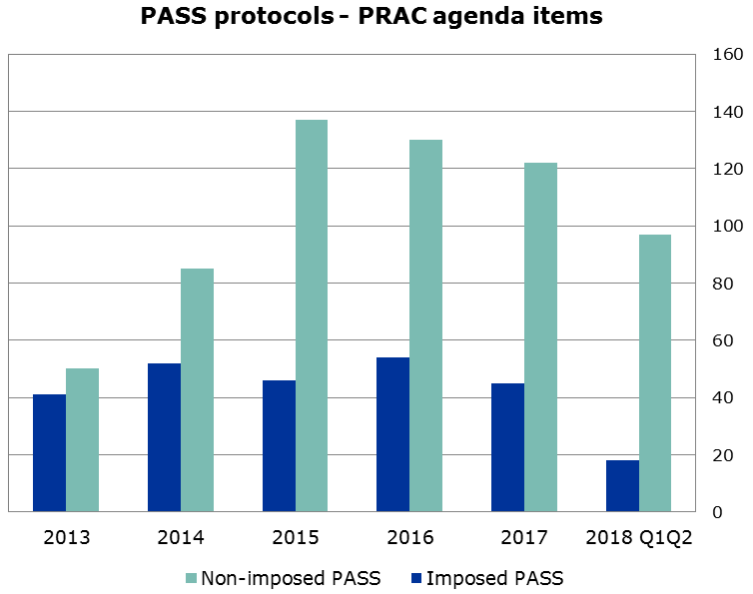


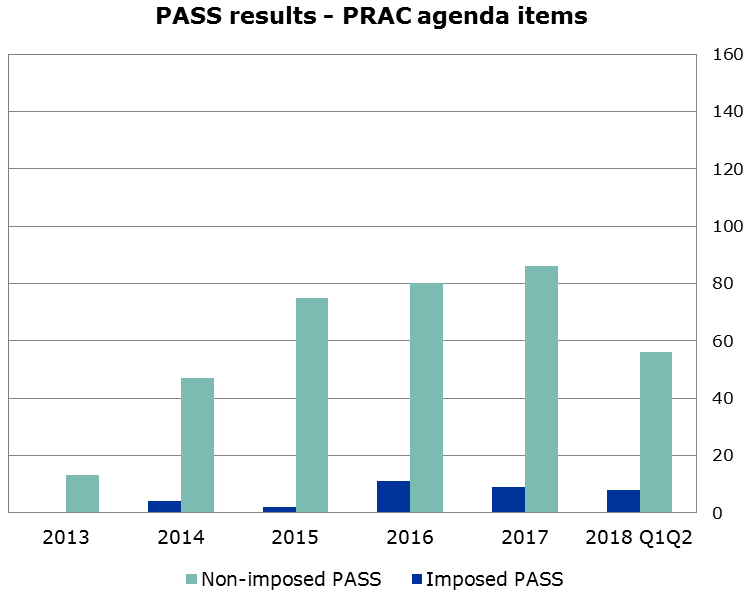
PSURs: benefit risk assessments result in direct updates to product information – faster warnings to patients





PASS: delivering high quality evidence on the safety of medicines





Focus on new data and new science

Regulators in-house studies

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2013-2017 multiple EMA in-house RWD studies to support Committees (mainly PRAC)

46 – THIN (UK EHRs)

29 - IMS FR/DE

Association between systemic fluoroquinolone exposure and tendon rupture: population-based nested case-control study

Association between hydrochlorothiazide exposure and skin cancer: a series of population-based case-control studies

Antidepressant use during pregnancy and risk of autism spectrum disorder and attention deficit hyperactivity disorder: systematic review of observational studies and methodological considerations

Cohort Study of Psychiatric Adverse Events Following Exposure to Levonorgestrel-Containing Intrauterine Devices in UK General Practice

EMA-funded studies

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External RWD studies to support EMA Committees (2010-2017)

15 – EMA externally contracted studies

EMA-funded studies	N databases	N countries
A/H1N1 pandemic vaccines and pregnancy outcomes	1	1
Impact of risk minimisation in patients treated with rosiglitazone-containing products	2	2
Isotretinoin and the effectiveness of the Pregnancy Prevention Programme in Europe	5	3
Patterns and determinants of use of oral contraceptives in the EU	5	3
Monitoring the effectiveness of risk minimisation in patients treated with pioglitazone-containing products	3	3
Risk of cardiac valve disorders associated with the use of biphosphonates	6	3
Association between anxiolytic or hypnotic drugs and total mortality	2	2
Metformin use in renal impairment	2	2
Study of regulatory communication and risk awareness following the Article 31 referral of Combined Hormonal Contraceptives in relation to thromboembolism	n/a	6
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	9	6
Study of utilisation of Combined Hormonal Contraceptives in Europe	3	3
Anti-microbial resistance: choice of therapeutic interventions and outcomes for the treatment of infections caused by MDR Gram negative pathogens	4	1
Methods and data sources for determining long-term effects of drug exposure during pregnancy, with application to antiepileptic medicines	n/a	28
Impact of EU label changes for systemic diclofenac products: post-referral prescribing trends	4	3
Impact of EU label changes for hydroxyzine products: post-referral prescribing trends	4	3

EU healthcare databases: 2018 characterisation

BMJ Open

Electronic healthcare databases in Europe: descriptive analysis of characteristics and potential for use in medicines regulation

Alexandra Pacurariu,[1] Kelly Plueschke,[1] Patricia McGettigan,[1,2] Daniel R Morales,[1,3] Jim Slattery,[1] Dagmar Vogl,[1] Thomas Goedecke,[1] Xavier Kurz,[1] Alison Cave[1]

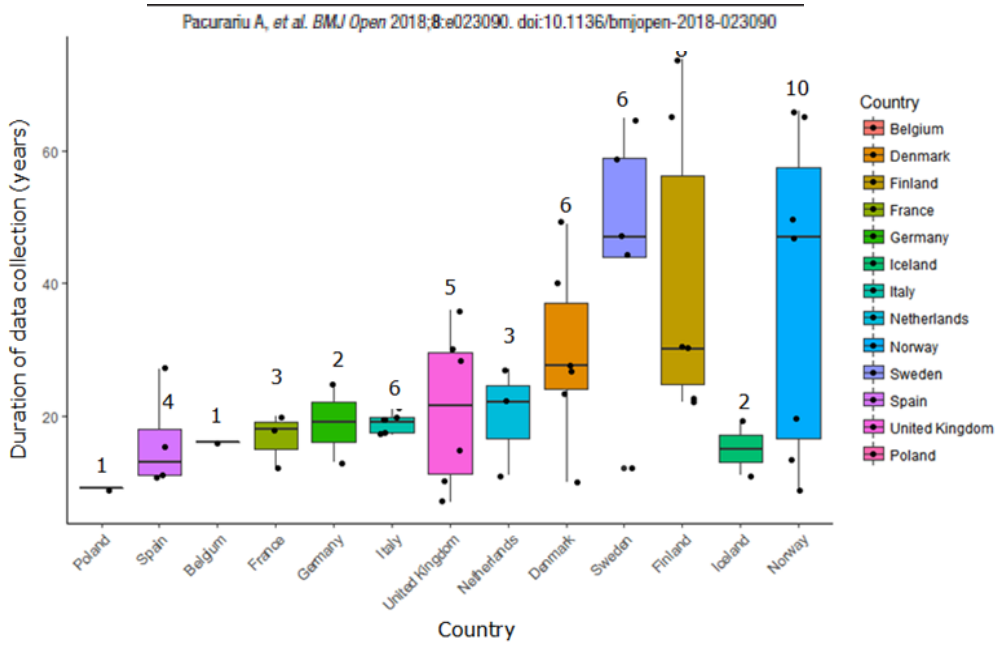


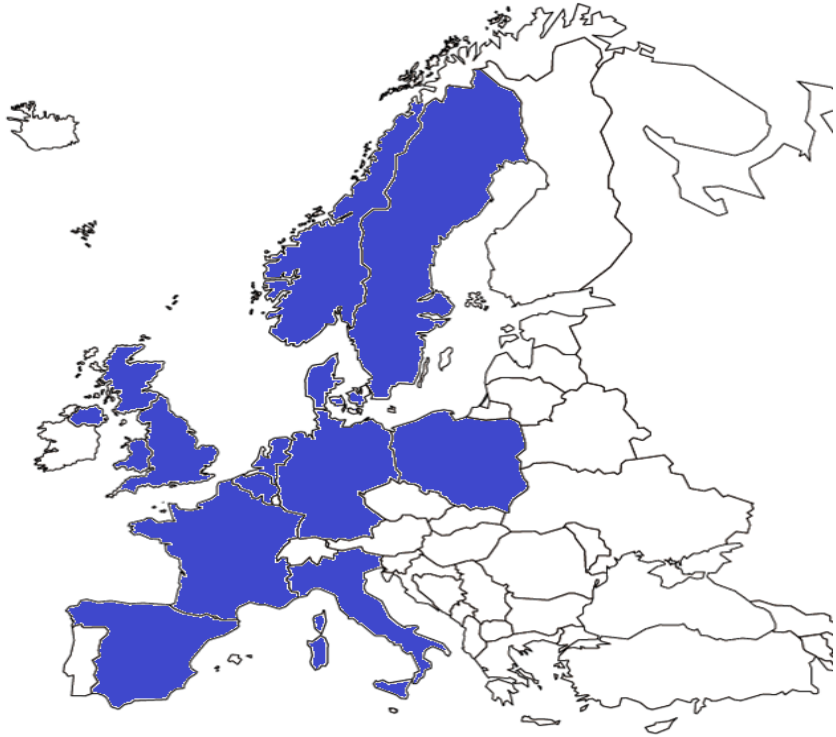
Figure 3 European data sources and duration of data collection. Box plots indicate the median (horizontal black line) data collection time by country while the margins of the box plot represent the IQR, the vertical lines indicate the minimum and maximum values. The number of databases per country are provided above the box plots.

Only 13 member states have electronic health databases considered suitable for regulatory decision making

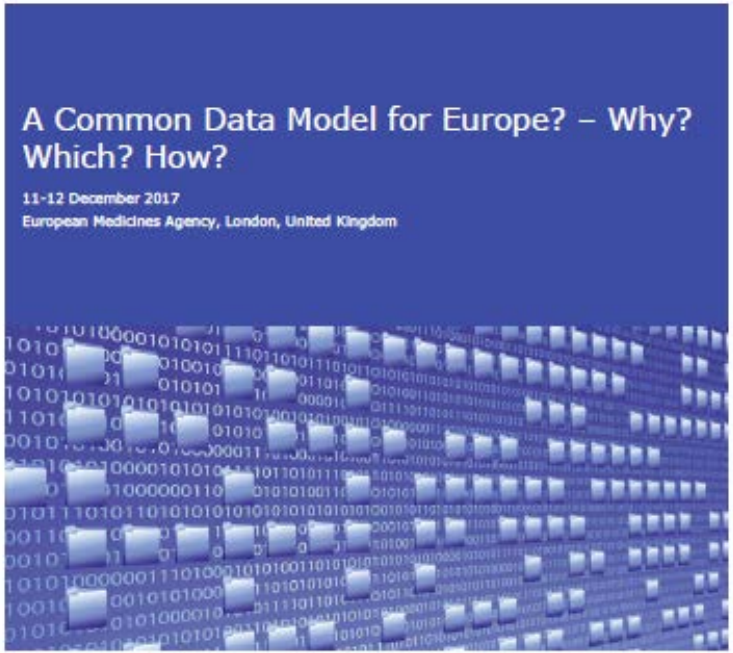
High heterogeneity in data collected or available through linkages and in data quality

New EMA framework contracts for real world data and qualitative research: to deliver evidence for decision-making

- Lot 1: Use of innovative methods to optimise the utility of sparse data to support benefit/risk assessment
- Lot 2: Qualitative research
- Lot 3: Pharmacoepidemiology research – rapid descriptive studies
- Lot 4: Pharmacoepidemiology research – association studies, including pregnancy and breastfeeding research



Steps to support future real world data use



Objectives:

To define the **opportunities and challenges** around implementation of a common data model in Europe to support regulatory decision making.

Output:

To **propose guiding principles** for the development of Common Data model in Europe including **key criteria for validation** in the context of regulatory decision making.

Activities in Big Data

HMA-EMA Joint Big Data Taskforce

Characterisation, usability and applicability, gap analysis.

Recommendations

Q3-4 2018

EMA Big Data Workshop – November 2016

- Define the Big Data landscape from a regulatory perspective
- Clarify the opportunities and the challenges
- Identify what is needed for Big Data to be exploited to support medicines development and regulatory decision making

Mandate HMA / EMA Joint Task Force Big Data

Priority: Reinforce the scientific and regulatory capacity and capability of the network, Innovation and access to new medicines, Optimisation of the regulatory operations

Patient Registries

EUROPEAN MEDICINES AGENCY

Cystic Fibrosis Registries Workshop: 14th June 2017

Multiple-Sclerosis Registries Workshop: 7th July 2017

CAR T-Cell therapies Registries Workshop: 9th February 2018

Haemophilia Registries Workshop: 8th June 2018

Participants: regulators, companies, registry holders, health technology assessment bodies, patient and health care representatives

Diseases selection?

- ✓ Products recently authorised or authorisation process ongoing
- ✓ New products - business pipeline
- ✓ EU disease registries have requested support for harmonisation
- ✓ On-going qualification procedures for two EU-wide registry platforms

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 September 2018
EMA/578123/2018

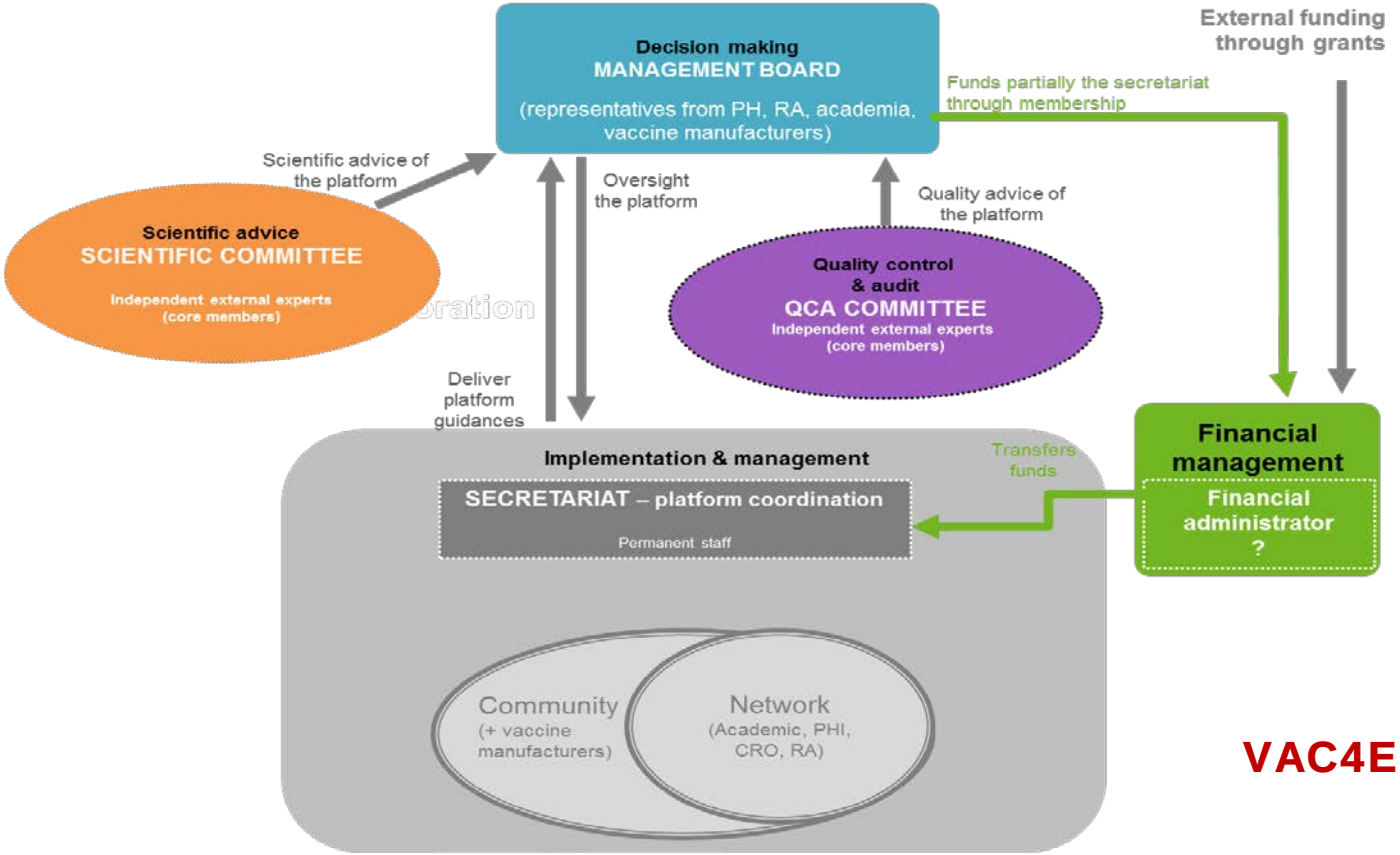
Draft reflection paper

Use of patient registries for regulatory purposes – methodological considerations

DRAFT V1.1

ADVANCE: vaccine benefit risk monitoring

EUROPEAN MEDICINES AGENCY



VAC4EU platform

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2018) 84 419–433 419

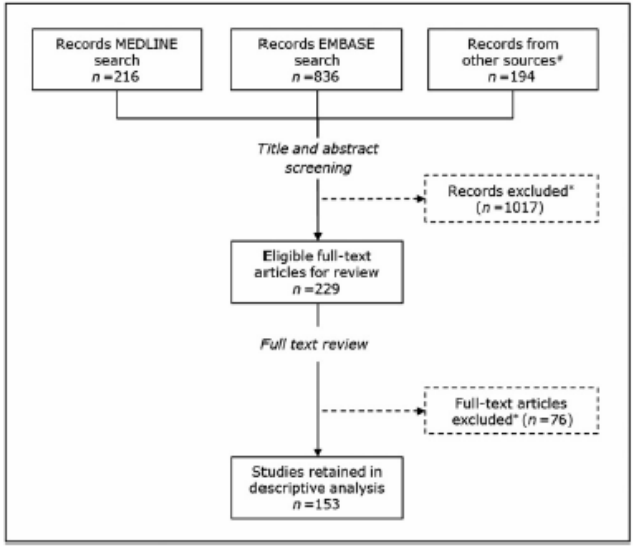
SYSTEMATIC REVIEW AND META-ANALYSIS

Measuring the impact of medicines regulatory interventions – Systematic review and methodological considerations

Thomas Goedecke[1], Daniel R. Morales[1,2], Alexandra Pacurariu[1,3] and Xavier Kurz[1]

Conclusion

Despite their potential global impact, the effects of pharmacovigilance regulatory interventions remain largely unquantified. A collaborative effort is required among regulators, health technology assessment bodies, academia and industry to help define measurable public health outcomes including intended and unintended consequences of regulatory decisions at the population level. Guidelines on the reporting of such studies and research to establish the best methods to evaluate such interventions are required. Results of impact research should be systematically disseminated to increase knowledge on the effectiveness of regulatory interventions. The EU PAS Register®, a publicly accessible platform for observational post-authorization research, could be used for this purpose.



Don’t forget the people

New PRAC composition – as of September 2018

EUROPEAN MEDICINES AGENCY

PRAC chair

Sabine Straus - Medicines Evaluation Board (NL)

PRAC vice chair

Martin Huber - Federal Institute for Drugs and Medical Devices (DE)

Independent scientific experts nominated by the European Commission

- Birgitta Grundmark - Uppsala Monitoring Centre (WHO)
- Antoine Pariente - Université de Bordeaux (FR)
- Livia Puljak - University of Split School of Medicine (HR)
- Stefan Weiler - University of Zurich (CH)
- Hedvig Marie Egeland Nordeng - University of Oslo (NO)
- Daniel Morales - University of Dundee (UK)

Members representing patients' organisations nominated by the European Commission

- Marco Greco – European Federation of Crohn's & Ulcerative Colitis Associations
- Albert van der Zeijden – International Alliance of Patients' Organizations

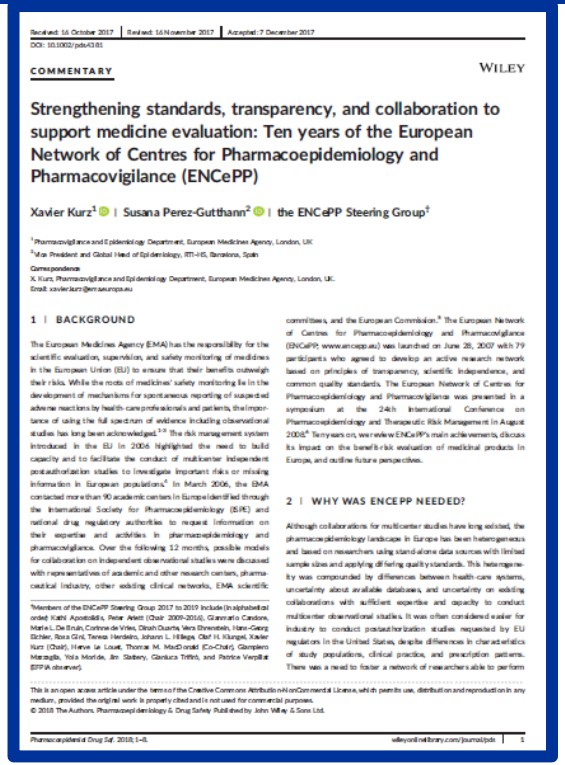
Members representing healthcare professionals nominated by the European Commission

- Raymond Anderson - Pharmaceutical Group of the European Union
- Kirsten Myhr - Health Action International-Europe

Members nominated by the Member States

10 years of ENCePP

EUROPEAN MEDICINES AGENCY



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DOI: 10.1002/pds.4181

COMMENTARY

WILEY

Strengthening standards, transparency, and collaboration to support medicine evaluation: Ten years of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

Xavier Kurz[1] | Susana Perez-Gutthann[2] | the ENCePP Steering Group[†]

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1 | BACKGROUND

The European Medicines Agency (EMA) has the responsibility for the scientific evaluation, supervision, and safety monitoring of medicines in the European Union (EU) to ensure that their benefits outweigh their risks. While the roots of medicines' safety monitoring lie in the development of mechanisms for spontaneous reporting of suspected adverse reactions by health-care professionals and patients, the importance of using the full spectrum of evidence including observational studies has long been acknowledged.[1,2] The risk management system introduced in the EU in 2006 highlighted the need to build capacity and to facilitate the conduct of multicenter independent postauthorization studies to investigate important risks or missing information in European populations.[3] In March 2006, the EMA contacted more than 90 academic centers in Europe identified through the International Society for Pharmacoepidemiology (ISPE) and national drug regulatory authorities to request information on their expertise and activities in pharmacoepidemiology and pharmacovigilance. Over the following 12 months, possible models for collaboration on independent observational studies were discussed with representatives of academic and other research centers, pharmaceutical industry, other existing clinical networks, EMA scientific committees, and the European Commission.[4] The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP; www.encepp.eu) was launched on June 28, 2007 with 79 participants who agreed to develop an active research network based on principles of transparency, scientific independence, and common quality standards. The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance was presented in a symposium at the 24th International Conference on Pharmacoepidemiology and Therapeutic Risk Management in August 2008.[4] Ten years on, we review ENCePP's main achievements, discuss its impact on the benefit-risk evaluation of medicinal products in Europe, and outline future perspectives.

2 | WHY WAS ENCEPP NEEDED?

Although collaborations for multicenter studies have long existed, the pharmacoepidemiology landscape in Europe has been heterogeneous and based on researchers using stand-alone data sources with limited sample sizes and applying differing quality standards. This heterogeneity was compounded by differences between health-care systems, uncertainty about available databases, and uncertainty on existing collaborations with sufficient expertise and capacity to conduct multicenter observational studies. It was often considered easier for industry to conduct postauthorization studies requested by EU regulators in the United States, despite differences in characteristics of study populations, clinical practice, and prescription patterns. There was a need to foster a network of researchers able to perform

[†]Members of the ENCePP Steering Group 2017 to 2019 include (in alphabetical order) Kathi Apostolidis, Peter Arlett (Chair 2009-2016), Gianvalo Candore, Maria L. De Bruin, Corinne de Vries, Dinah Duarte, Vera Ehrenstein, Hans-Georg Eichler, Sara Gini, Teresa Herdeiro, Johann L. Hillege, Olaf H. Klungel, Xavier Kurz (Chair), Herve le Louet, Thomas M. MacDonald (Co-Chair), Giampiero Mazzaglia, Yola Moride, Jim Slattery, Gianluca Trifirò, and Patrice Verpillat (EFPIA observer).

Centres (>150)

Networks (>20)

Data sources (>120)

ENCePP

Transparency

EU PAS Register

Independence

Registration of studies

Publication of protocols and results

Roles and responsibilities of all parties

Code of conduct

Standards

Methodological Guide on Research Standards

Challenges and opportunities

- Realising the potential of real world data to support decision-making and better public health:
  - New data sources
  - New technology
  - New analytical approaches
- Process improvement: greater efficiency and effectiveness through evidenced-based process improvement
- Better engagement with the public
- Making an impact: change healthcare deliver to benefit public health

Headlines

1. EU pharmacovigilance supports safe and effective use of medicines
2. EU pharmacovigilance supports patients to get new products
3. EU pharmacovigilance legislation fully implemented
4. New EudraVigilance system launched November 2017: detects safety issues earlier
5. Robust assessment support rapid effective action on safety issues
6. Enhanced engagement with users of medicines
7. Driving process improvement through regulatory science
8. Starting to realise the potential of real world evidence
9. Challenges: new data, new technology
10. Challenges: making an impact through change in healthcare practice