MHRA
Regulating Medicines and Medical Devices

Pharmacovigilance requirements for Member States

Medicines and Healthcare Products Regulatory Agency

Member States requirements

- **Collecting reports of ADRs** from health professionals and patients – & encouraging this
- **Notifying signals** to EMA
- **Benefit risk assessment** as Rapporteur/ lead Member State
- **Communicating safety** information
- **Monitoring effectiveness** of risk minimisation
- Operating **quality systems**

Good Vigilance Practices GVP

INTRODUCTION Legal Basis and Structure of Pharmacovigilance Guidance

MODULE **I**	Pharmacovigilance Systems and their Quality Systems
MODULE **II**	Pharmacovigilance System Master File
MODULE **III**	Pharmacovigilance Inspections
MODULE **IV**	Audits
MODULE **V**	Risk Management Systems
MODULE **VI**	Management and Reporting of ADRs
MODULE **VII**	Periodic Safety Update Reports
MODULE **VIII**	Post-Authorisation Safety Studies
MODULE **IX**	Signal Management
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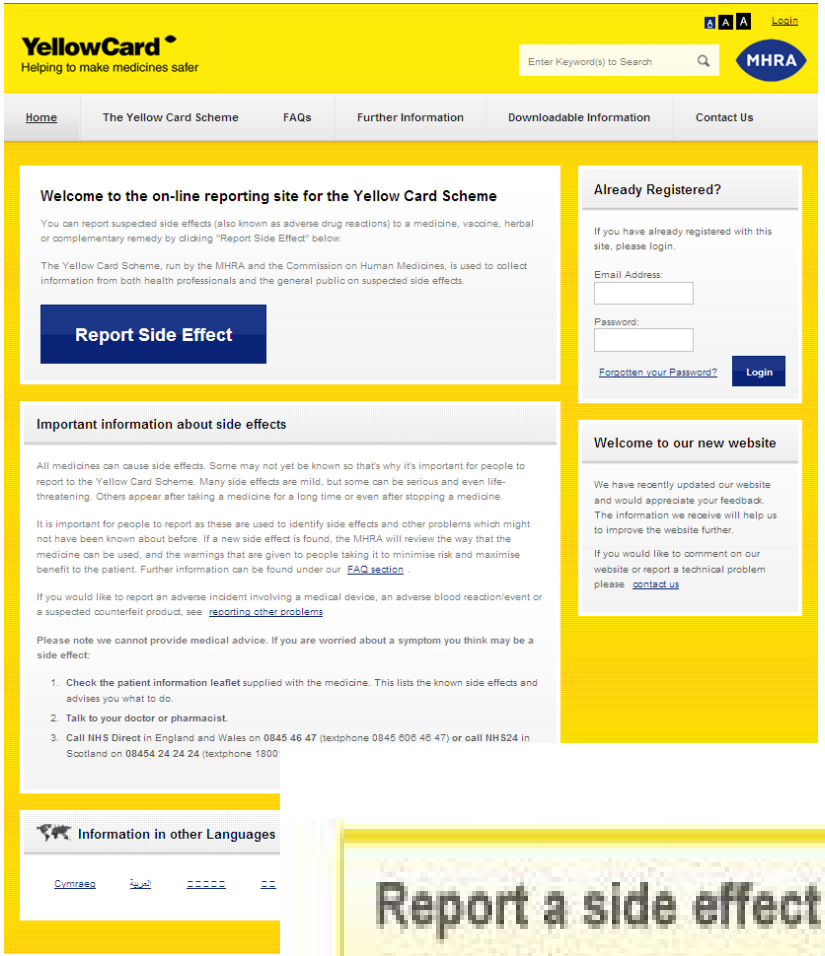
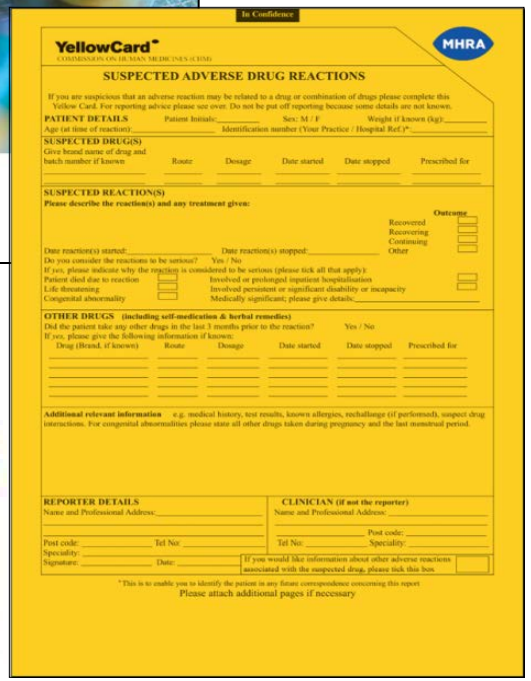
MODULE **XV**	Safety Communications
MODULE **XVI**	Risk Minimisation Measures

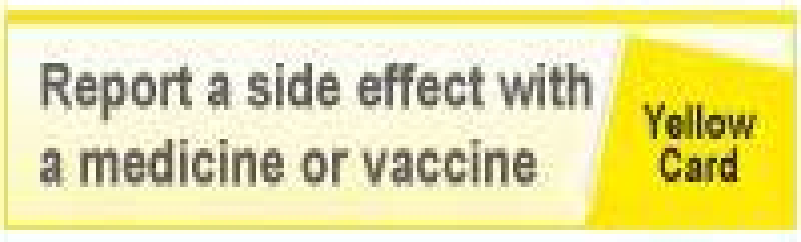
PRODUCT- AND POPULATION-SPECIFIC CONSIDERATIONS

ANNEXES

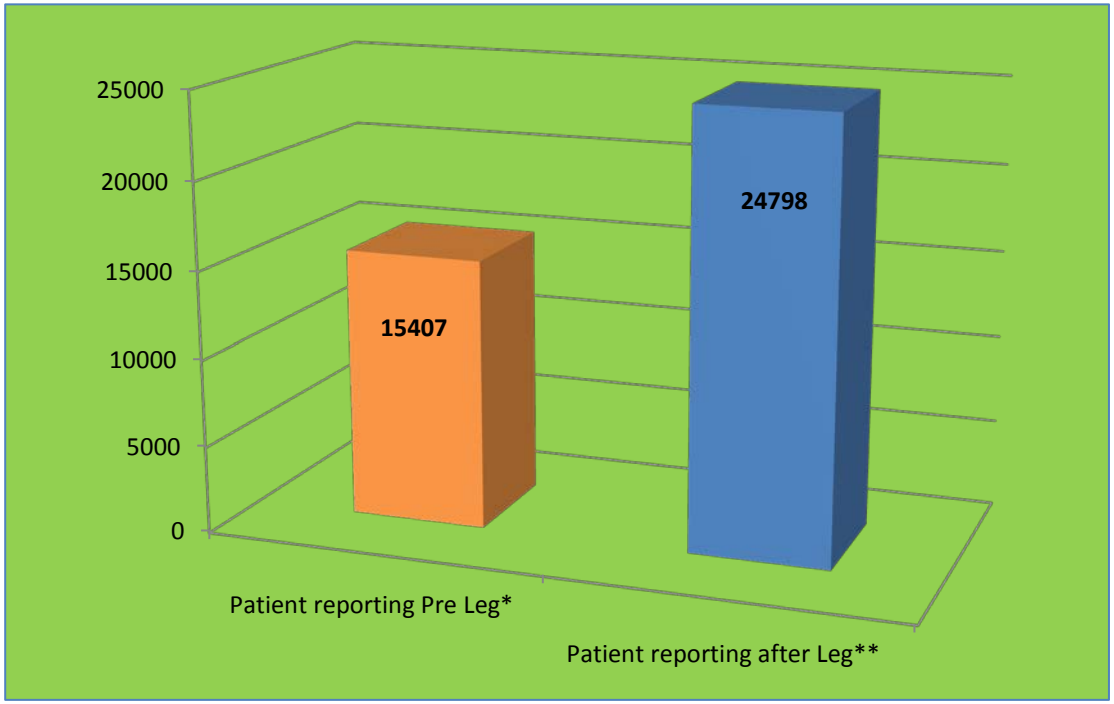
Collecting ADRs







Patients' contribution to ADR reporting



* Pre legislation data period - 02/07/2011 - 01/07/2012

** Post legislation data period -02/07/2012 - 01/07/2013

Encouraging ADR reporting

MHRA

As a patient, you have the right to report unwanted side effects of medicine directly to the authorities. You can also report a side effect on behalf of someone in your care, such as a child or relative.

Remember to speak to your doctor or pharmacist if you are worried about any suspected side effects.

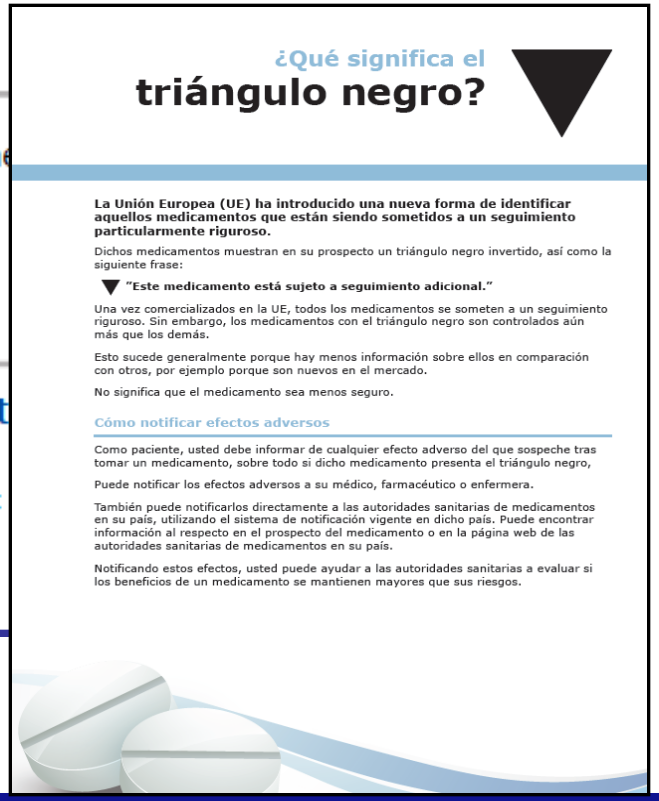
Why report a side effect?

We are always learning more about medicines.

Although they are tested extensively in clinical trials before they are authorised, not everything can be known about their side

How do I report a side effect

If you think a medicine has caused a side effect, please check the package leaflet that comes with the medicine for information on how to report it.



¿Qué significa el

triángulo negro?

La Unión Europea (UE) ha introducido una nueva forma de identificar aquellos medicamentos que están siendo sometidos a un seguimiento particularmente riguroso.

Dichos medicamentos muestran en su prospecto un triángulo negro invertido, así como la siguiente frase:

▼ **"Este medicamento está sujeto a seguimiento adicional."**

Una vez comercializados en la UE, todos los medicamentos se someten a un seguimiento riguroso. Sin embargo, los medicamentos con el triángulo negro son controlados aún más que los demás.

Esto sucede generalmente porque hay menos información sobre ellos en comparación con otros, por ejemplo porque son nuevos en el mercado.

No significa que el medicamento sea menos seguro.

Cómo notificar efectos adversos

Como paciente, usted debe informar de cualquier efecto adverso del que sospeche tras tomar un medicamento, sobre todo si dicho medicamento presenta el triángulo negro,

Puede notificar los efectos adversos a su médico, farmacéutico o enfermera.

También puede notificarlos directamente a las autoridades sanitarias de medicamentos en su país, utilizando el sistema de notificación vigente en dicho país. Puede encontrar información al respecto en el prospecto del medicamento o en la página web de las autoridades sanitarias de medicamentos en su país.

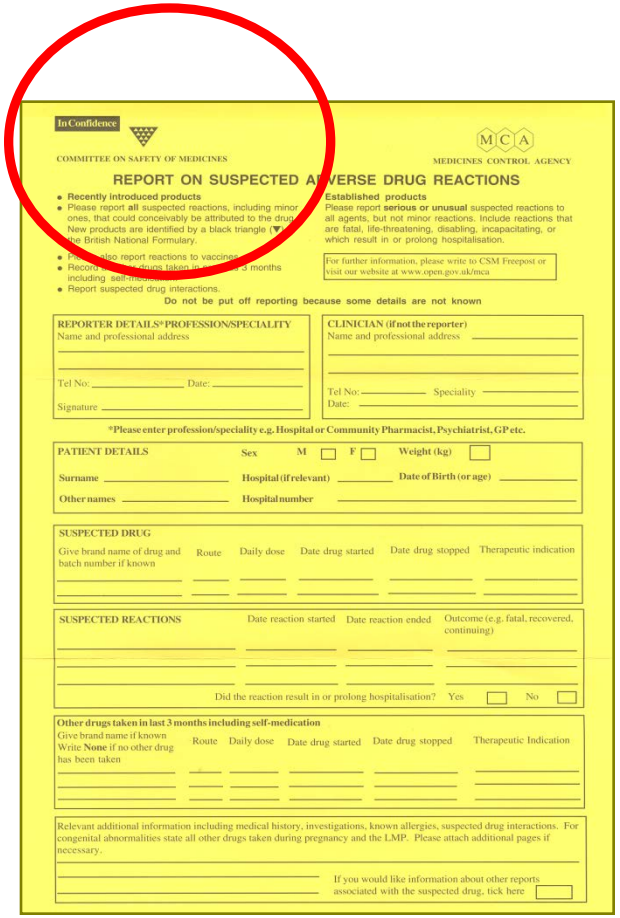
Notificando estos efectos, usted puede ayudar a las autoridades sanitarias a evaluar si los beneficios de un medicamento se mantienen mayores que sus riesgos.

▼ Additional monitoring

Black triangle ▼ assigned to new active substances and certain other categories

Printed next to product name in professional advertisements and drug formularies

Tells health professionals to report all reactions
- around 70 - 80% UK reports are black triangle drugs



In Confidence

COMMITTEE ON SAFETY OF MEDICINES — MEDICINES CONTROL AGENCY

REPORT ON SUSPECTED ADVERSE DRUG REACTIONS

- Recently introduced products
- Please report **all** suspected reactions, including minor ones, that could conceivably be attributed to the drug. New products are identified by a black triangle (▼) in the British National Formulary.
- Please also report reactions to vaccines
- Record medicines taken in the last 3 months including self-medication
- Report suspected drug interactions.

Established products
Please report **serious or unusual** suspected reactions to all agents, but not minor reactions. Include reactions that are fatal, life-threatening, disabling, incapacitating, or which result in or prolong hospitalisation.

For further information, please write to CSM Freepost or visit our website at www.open.gov.uk/mca

Do not be put off reporting because some details are not known

REPORTER DETAILS* PROFESSION/SPECIALITY
Name and professional address
Tel No: Date:
Signature

CLINICIAN (if not the reporter)
Name and professional address
Tel No: Speciality
Date:

*Please enter profession/speciality e.g. Hospital or Community Pharmacist, Psychiatrist, GP etc.

PATIENT DETAILS — Sex M F — Weight (kg)
Surname — Hospital (if relevant) — Date of Birth (or age)
Other names — Hospital number

SUSPECTED DRUG
Give brand name of drug and batch number if known | Route | Daily dose | Date drug started | Date drug stopped | Therapeutic indication

SUSPECTED REACTIONS | Date reaction started | Date reaction ended | Outcome (e.g. fatal, recovered, continuing)

Did the reaction result in or prolong hospitalisation? Yes No

Other drugs taken in last 3 months including self-medication
Give brand name if known. Write **None** if no other drug has been taken | Route | Daily dose | Date drug started | Date drug stopped | Therapeutic Indication

Relevant additional information including medical history, investigations, known allergies, suspected drug interactions. For congenital abnormalities state all other drugs taken during pregnancy and the LMP. Please attach additional pages if necessary.

If you would like information about other reports associated with the suspected drug, tick here

UK Strengthening reporting in National Health Service

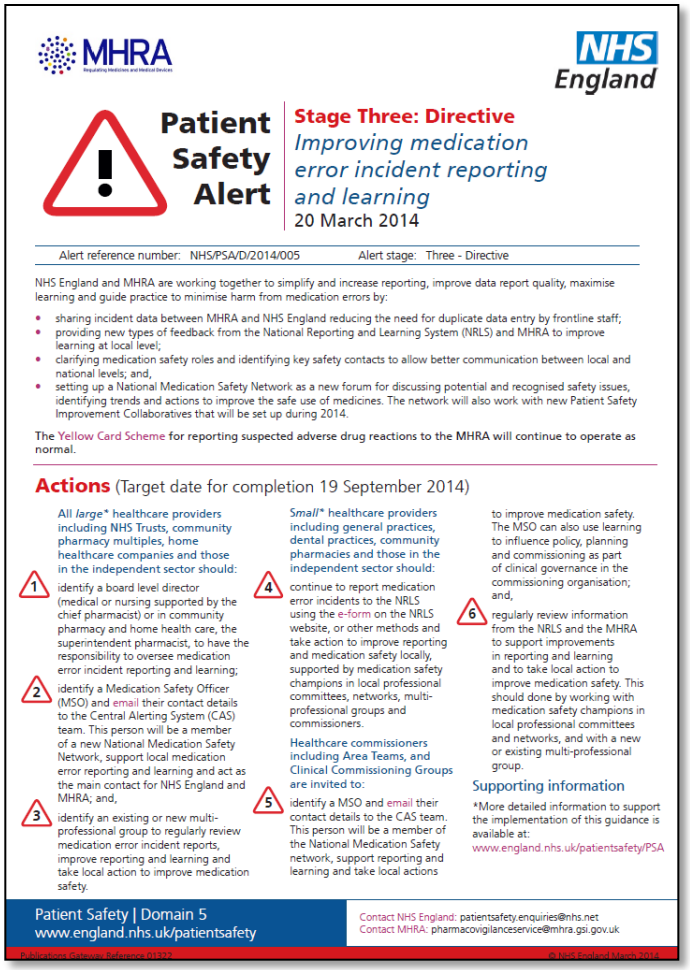
Integrated reporting route

Medication Safety Officers

Local multidisciplinary groups

National Medication Safety Network

Oversight by medical or nursing directors with support of pharmacists



MHRA

NHS England

Patient Safety Alert

Stage Three: Directive

Improving medication error incident reporting and learning

20 March 2014

Alert reference number: NHS/PSA/D/2014/005 Alert stage: Three - Directive

NHS England and MHRA are working together to simplify and increase reporting, improve data report quality, maximise learning and guide practice to minimise harm from medication errors by:

- sharing incident data between MHRA and NHS England reducing the need for duplicate data entry by frontline staff;
- providing new types of feedback from the National Reporting and Learning System (NRLS) and MHRA to improve learning at local level;
- clarifying medication safety roles and identifying key safety contacts to allow better communication between local and national levels; and,
- setting up a National Medication Safety Network as a new forum for discussing potential and recognised safety issues, identifying trends and actions to improve the safe use of medicines. The network will also work with new Patient Safety Improvement Collaboratives that will be set up during 2014.

The Yellow Card Scheme for reporting suspected adverse drug reactions to the MHRA will continue to operate as normal.

Actions (Target date for completion 19 September 2014)

All *large** healthcare providers including NHS Trusts, community pharmacy multiples, home healthcare companies and those in the independent sector should:

1. identify a board level director (medical or nursing supported by the chief pharmacist) or in community pharmacy and home health care, the superintendent pharmacist, to have the responsibility to oversee medication error incident reporting and learning;
2. identify a Medication Safety Officer (MSO) and email their contact details to the Central Alerting System (CAS) team. This person will be a member of a new National Medication Safety Network, support local medication error reporting and learning and act as the main contact for NHS England and MHRA; and,
3. identify an existing or new multi-professional group to regularly review medication error incident reports, improve reporting and learning and take local action to improve medication safety.

*Small** healthcare providers including general practices, dental practices, community pharmacies and those in the independent sector should:

4. continue to report medication error incidents to the NRLS using the e-form on the NRLS website, or other methods and take action to improve reporting and medication safety locally, supported by medication safety champions in local professional committees, networks, multi-professional groups and commissioners.

Healthcare commissioners including Area Teams, and Clinical Commissioning Groups are invited to:

5. identify a MSO and email their contact details to the CAS team. This person will be a member of the National Medication Safety network, support reporting and learning and take local actions to improve medication safety. The MSO can also use learning to influence policy, planning and commissioning as part of clinical governance in the commissioning organisation; and,
6. regularly review information from the NRLS and the MHRA to support improvements in reporting and learning and to take local action to improve medication safety. This should done by working with medication safety champions in local professional committees and networks, and with a new or existing multi-professional group.

Supporting information

*More detailed information to support the implementation of this guidance is available at: www.england.nhs.uk/patientsafety/PSA

Patient Safety | Domain 5
www.england.nhs.uk/patientsafety

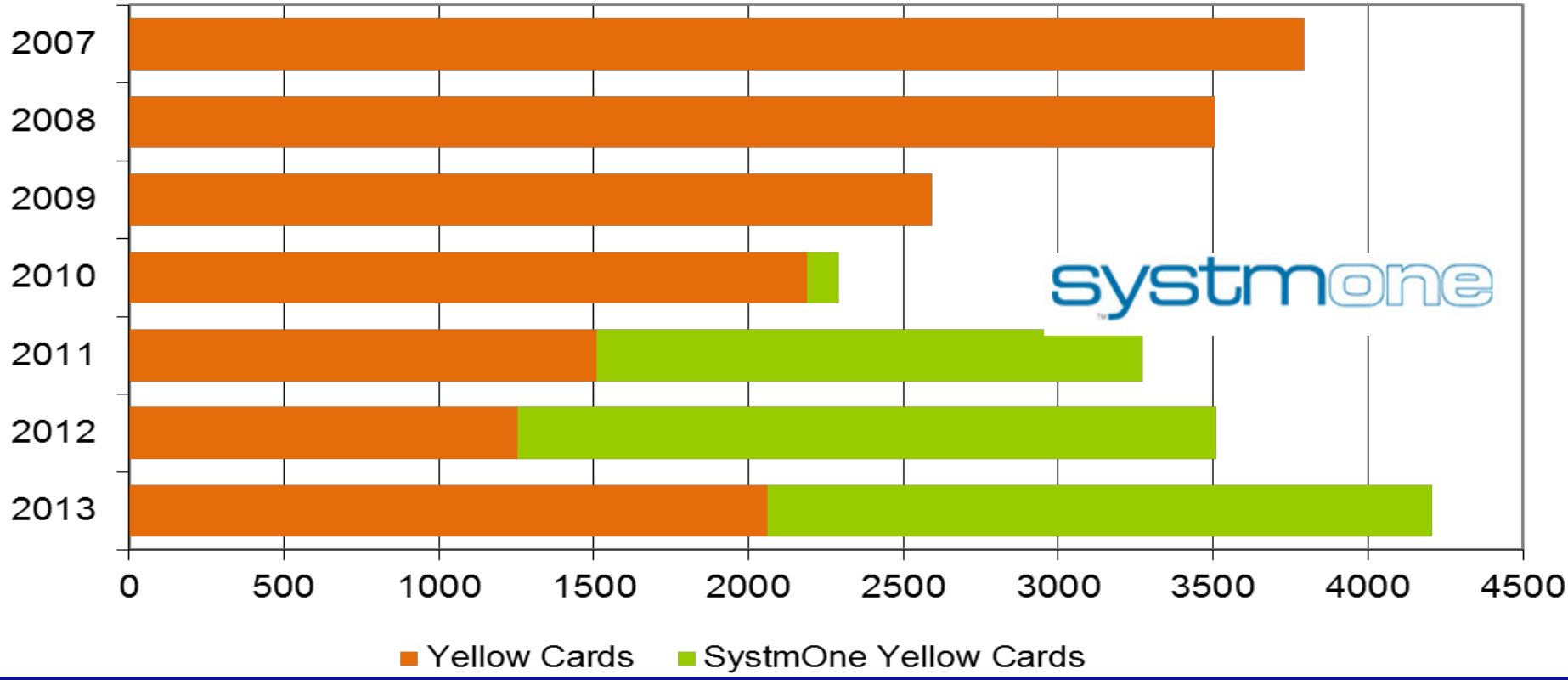
Contact NHS England: patientsafety.enquiries@nhs.net
Contact MHRA: pharmacovigilanceservice@mhra.gsi.gov.uk

Publications Gateway Reference 01372 © NHS England, March 2014

Reporting ADRs direct from doctor's clinical systems

Electronic Yellow Card reporting introduced in clinical systems

SystmOne GP system - 20% of GP practices
In 2013 - 51% GP reports from SystmOne



Using mobile technology

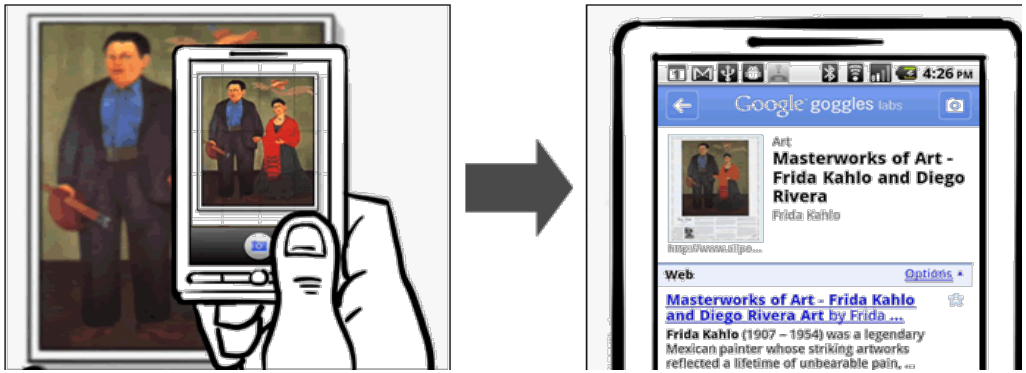
Innovative medicines initiative
Collaboration between regulators, academia & industry

Development of a **mobile app** for

- ADR reporting
- Provision of information to users

Evaluation of using **social media** data to identify ADRs

Use of new IT for ADRs



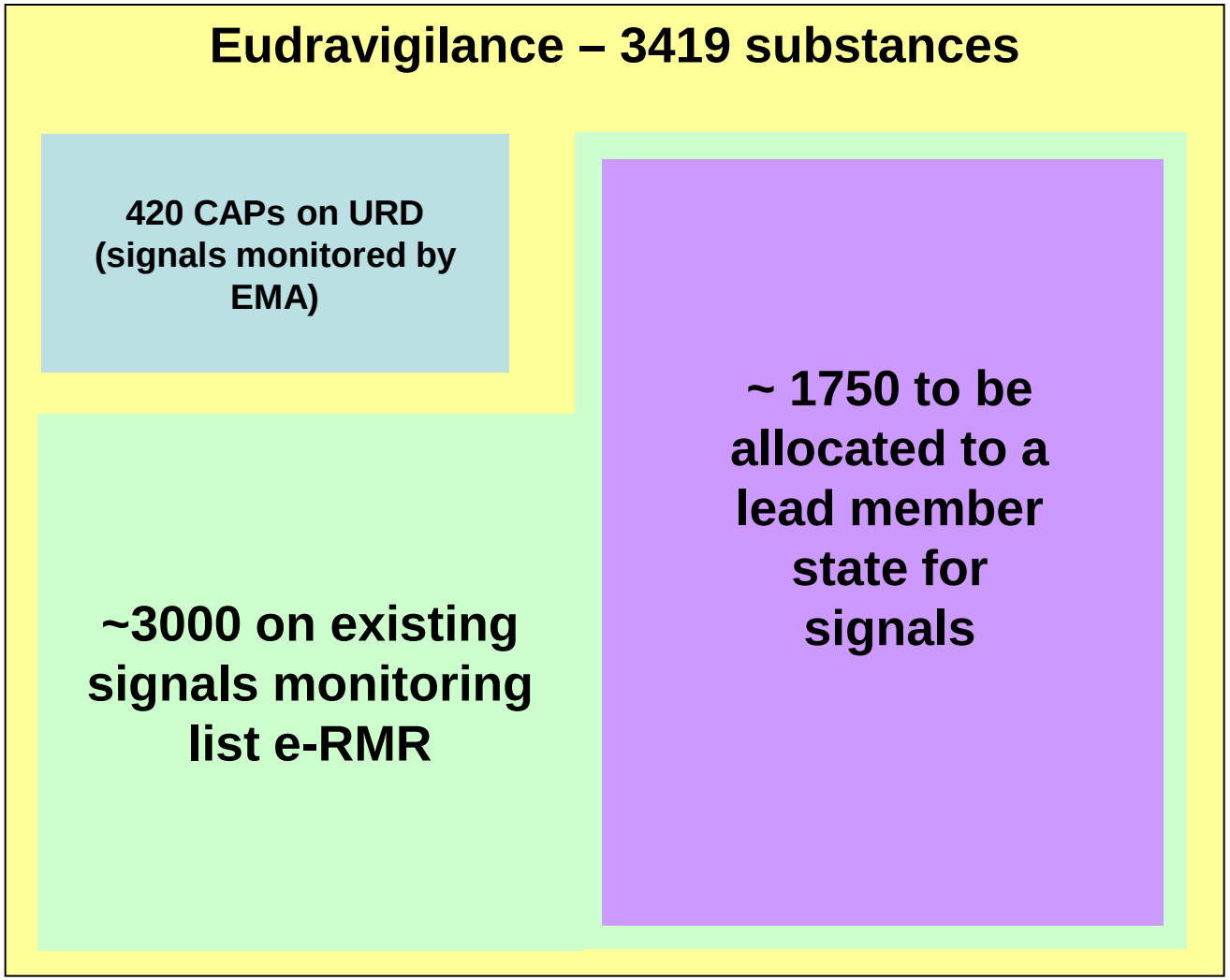
Med App checks skin lesion, transmits image

Adverse drug reaction data management

Member States decide whether to maintain in house data management systems or solely use EudraVigilance

EudraVigilance full functionality by 2016

Signal detection by MS for EV substances



- Member States take lead role for monitoring substances on EV
- List kept under review

Methodologies for signals

example HPV vaccine

Vaccine

Volume 31, Issue 43, 9 October 2013, Pages 4961–4967

14273||

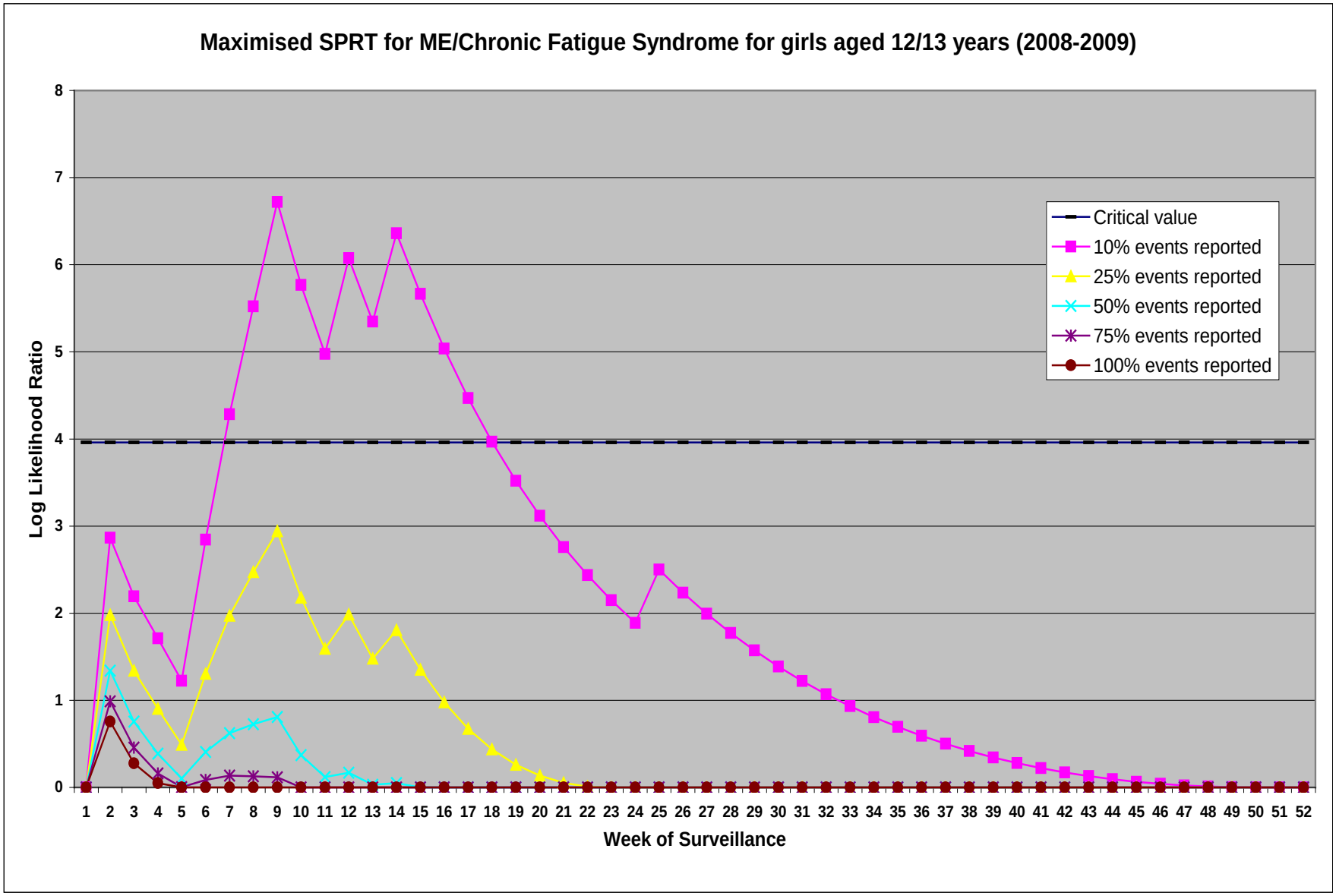
Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK

Katherine Donegan, Raphaelle Beau-Lejdstrom, Bridget King, Suzie Seabroke, Andrew Thomson, Philip Bryan

Vigilance and Risk Management of Medicines, Medicines and Healthcare products Regulatory Agency, London, UK

Maximised sequential probability ratio testing for observed vs expected signals

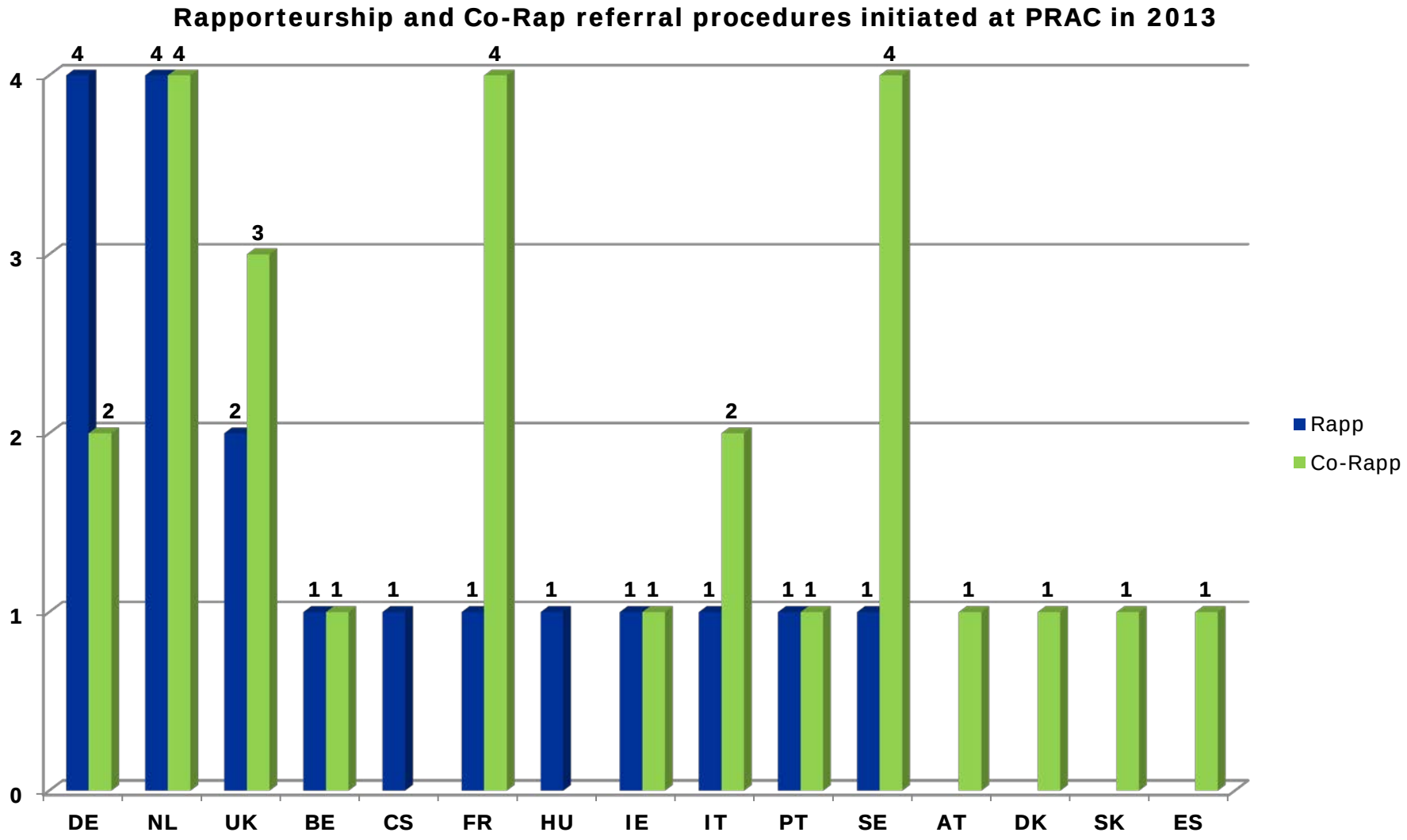
Donegan et al 2013, Vaccine 31, 43, 4961-7


Maximised SPRT for ME/Chronic Fatigue Syndrome for girls aged 12/13 years (2008-2009)
Log Likelihood Ratio
Week of Surveillance
Critical value
10% events reported
25% events reported
50% events reported
75% events reported
100% events reported

Assessment responsibilities

- **Risk Management Plans** for all medicines
- Moving towards **single assessments for periodic safety update reports**
- Increased activities with **PASS & in future PAES**
- Using **all available da**ta sources including patient registries, and pharmacoepidemiological approaches

Taking lead role in Referral



Assessment of PSURs

EURD list facilitates **harmonisation** of data lock points & submission frequency for PSURs for medicines containing **same active substances or combinations** subject to different MAs authorised in >1 MS

Allows **single assessment of related PSURs** to strengthen benefit-risk

Single assessments of PSURs started with centrally authorised medicines in 2013, expanded to active substances contained in in **both centrally and nationally authorised** medicines in April 2013

Monitoring impact of action in MS

BMJ

BMJ 2013;346:f403 doi: 10.1136/bmj.f403 Page 1 of 9

RESEARCH

Long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses

OPEN ACCESS

Keith Hawton *professor of psychiatry and direct*
researcher[1], Sue Simkin *researcher*[1], Sue Dodc
statistician[3], William Bernal *reader in hepatolog*
Navneet Kapur *professor of psychiatry and popu*

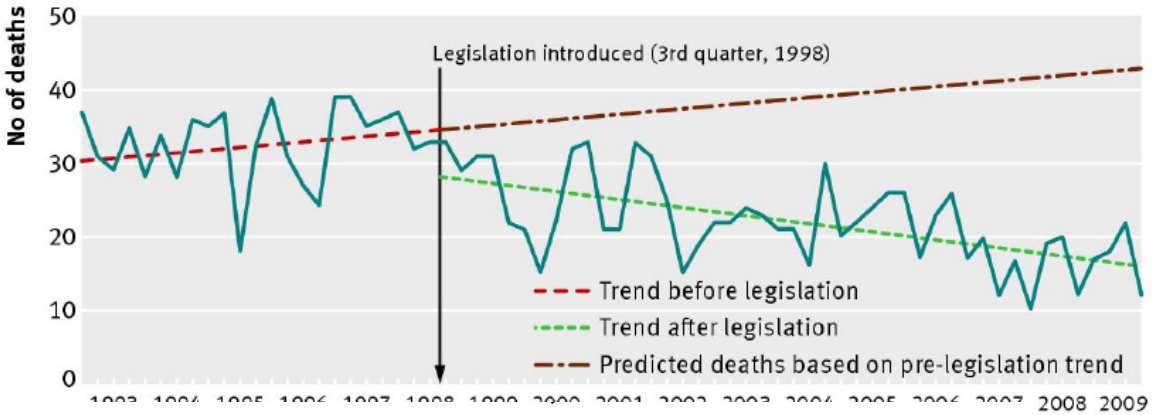


Fig 1 Suicide and open verdict deaths involving paracetamol only, in people aged 10 years and over in England and Wales 1993-2009, and best fit regression lines related to 1998 legislation

Impact of new warnings and reduced pack sizes for paracetamol in UK

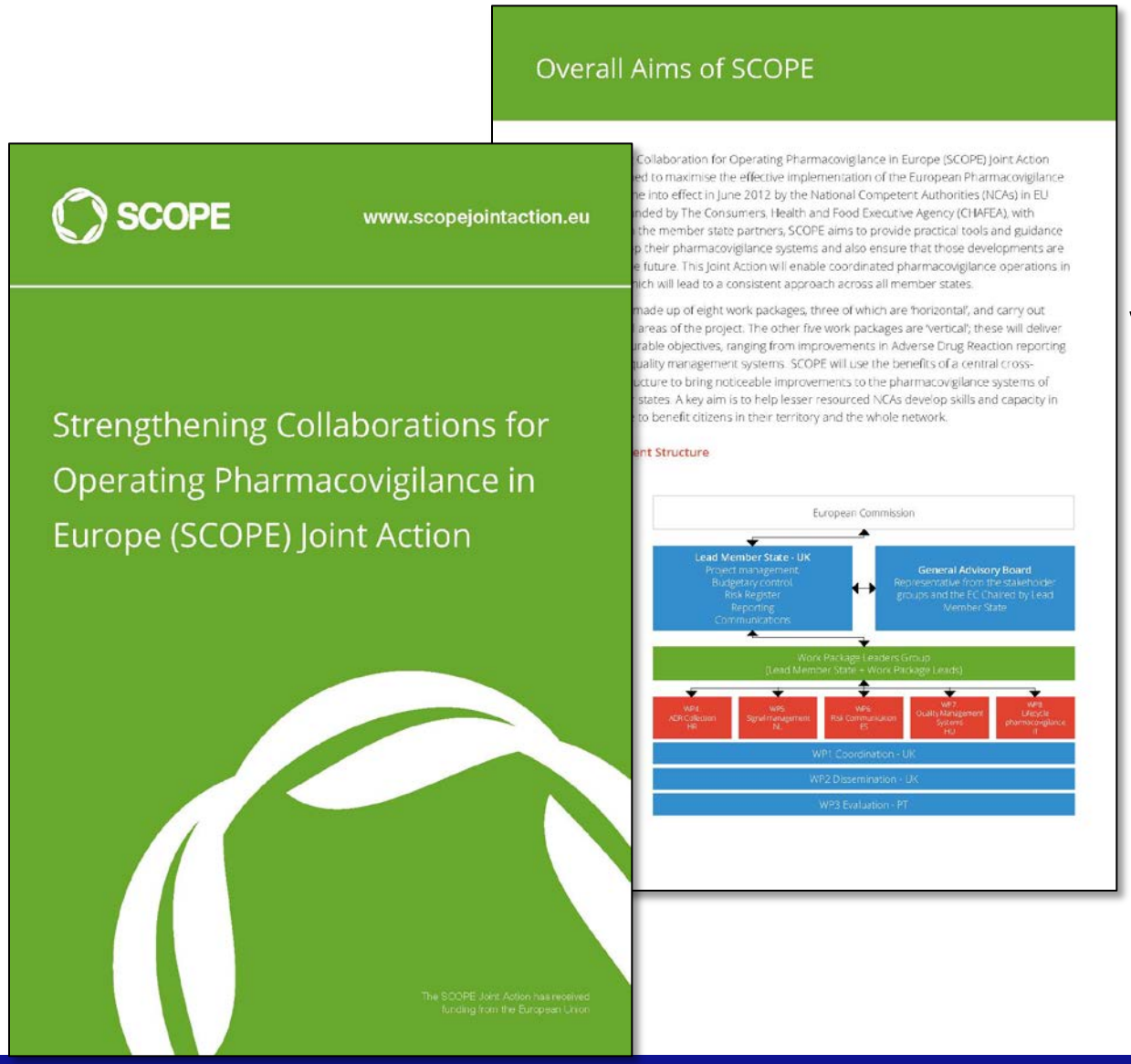
Operating Quality Systems

- Requirement for Quality Management Systems
- Independent audits must be conducted

- Audit reports need to be submitted to the EC
  - Assessment of systems
  - Resources
  - SOPs
  - Etc etc.

- System runs alongside benchmarking initiative

Strengthening Member States pharmacovigilance capability



EU Commission Joint Action

Project started November 2013

Conclusion

- EU pharmacovigilance system depends on strong **national surveillance systems** embedded in MS
- National diversity is good for the EU network eg some member states have **regional monitoring centres**, some are strong in pharmacoepidemiology
- Pharmacovigilance continues to evolve in **methodologies** and **technological capability**
- **Not in question – the central role of vigilant healthcare professionals & patient engagement**