

Pharmacovigilance requirements for Member States



Member States requirements MHRA

- **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 MHRA

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
MODULE X	Additional Monitoring
MODULE XV	Safety Communications
MODULE XVI	Risk Minimisation Measures

PRODUCT- AND POPULATION-SPECIFIC CONSIDERATIONS
ANNEXES

Collecting ADRs



Helping to make medicines safer

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Welcome to the on-line reporting site for the Yellow Card Scheme

You can report suspected side effects (also known as adverse drug reactions) to a medicine, vaccine, herbal or complementary remedy by clicking "Report Side Effect" below.

The Yellow Card Scheme, run by the MHRA and the Commission on Human Medicines, is used to collect information from both health professionals and the general public on suspected side effects.

Report Side Effect

Important information about side effects

All medicines can cause side effects. Some may not yet be known so that's why it's important for people to report to the Yellow Card Scheme. Many side effects are mild, but some can be serious and even life-threatening. Others appear after taking a medicine for a long time or even after stopping a medicine.

It is important for people to report as these are used to identify side effects and other problems which might not have been known about before. If a new side effect is found, the MHRA will review the way that the medicine can be used, and the warnings that are given to people taking it to minimise risk and maximise benefit to the patient. Further information can be found under our [FAQ section](#).

If you would like to report an adverse incident involving a medical device, an adverse blood reaction/event or a suspected counterfeit product, see [reporting other problems](#).

Please note we cannot provide medical advice. If you are worried about a symptom you think may be a side effect:

1. Check the patient information leaflet supplied with the medicine. This lists the known side effects and advises you what to do.
2. Talk to your doctor or pharmacist.
3. Call NHS Direct in England and Wales on 0845 46 47 (telephone 0845 005 46 47) or call NHS24 in Scotland on 08454 24 24 24 (telephone 1800).

Already Registered?

If you have already registered with this site, please login.

Email Address:

Password:

[Forgotten your Password?](#)

Welcome to our new website

We have recently updated our website and would appreciate your feedback. The information we receive will help us to improve the website further.

If you would like to comment on our website or report a technical problem please [contact us](#).

[Information in other Languages](#)

[Cymraeg](#)
[عربي](#)
[हिन्दी](#)
[Punjabi](#)

Helping to make medicines safer

A side effect of your medicine? Report it using Yellow Card

If you think the medicine you are taking may have caused a side effect, you can report it using Yellow Card.

Helping to make medicines safer

SUSPECTED ADVERSE DRUG REACTIONS

If you are suspicious that an adverse reaction may be related to a drug or combination of drugs please complete this Yellow Card. For reporting advice please visit [www.mhra.gov.uk/yellowcard](#). Do not be put off reporting because some details are not known.

PATIENT DETAILS

Patient Initials: Sex: ☐ M ☐ F Weight (if known (kg):

Age (at time of reaction): Identification number (Your Practice / Hospital Ref):

SUSPECTED DRUG(S)

Give brand name of drug and batch number if known

Route	Dosage	Date started	Date stopped	Prescribed for
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

SUSPECTED REACTION(S)

Please describe the reaction(s) and any treatment given:

Date reaction(s) started: Date reaction(s) stopped:

Do you consider the reaction to be serious? ☐ Yes ☐ No

If yes, please indicate why the reaction is considered to be serious (please tick all that apply):

Patient died due to reaction: ☐ Involved or prolonged important hospitalisation: ☐

Life threatening: ☐ Involved persistent or significant disability or incapacity: ☐

Consequential abnormality: ☐ Medically significant abnormality please give details:

OTHER DRUGS (including self-medication & herbal remedies)

Did the patient take any other drugs in the last 3 months prior to the reaction? ☐ Yes ☐ No

If yes, please give the following information if known:

Drug (Brand, if known)	Route	Dosage	Date started	Date stopped	Prescribed for
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Additional relevant information e.g. medical history, test results, known allergies, rechallenge (if performed), suspect drug interactions. For congenital abnormalities please state all other drugs taken during pregnancy and the last menstrual period.

REPORTER DETAILS

Name and Professional Address:

Post code: Tel No:

Speciality: Signature: Date:

CLINICIAN (if not the reporter)

Name and Professional Address:

Post code: Tel No:

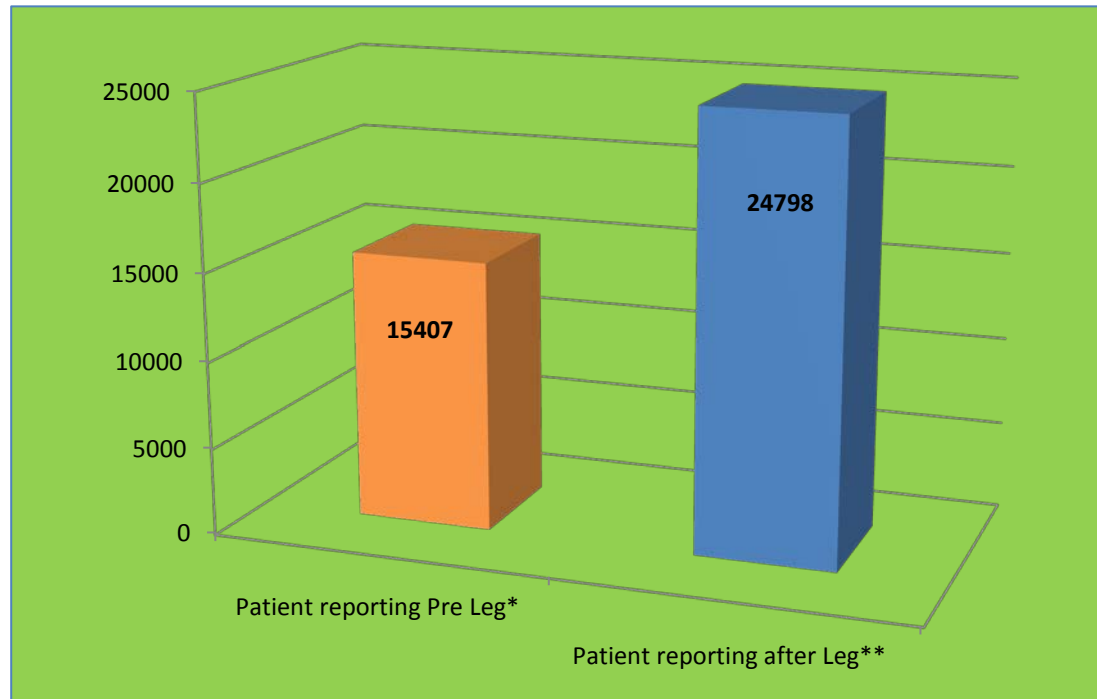
Speciality:

*This is to enable you to identify the patient in any future correspondence concerning this report. Please attach additional pages if necessary.

Report a side effect with a medicine or vaccine

Yellow Card

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



As a patient, you have the right to report unwanted side effects of medicines 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.

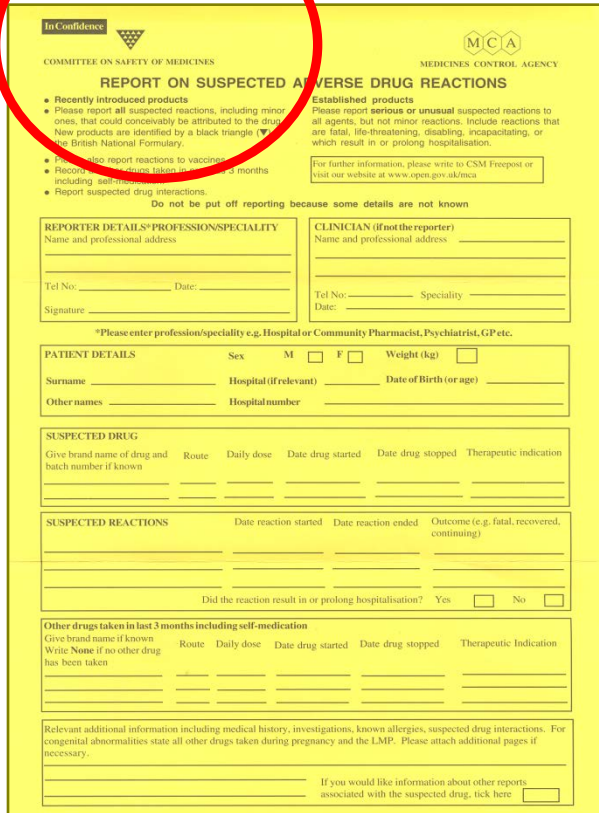


▼ Additional monitoring

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



The image shows a yellow form titled "REPORT ON SUSPECTED ADVERSE DRUG REACTIONS" from the Medicines Control Agency (MCA). A red circle highlights the top left corner of the form, which contains the "In Confidence" label and the black triangle symbol. The form is divided into several sections: "REPORTER DETAILS", "CLINICIAN (if not the reporter)", "PATIENT DETAILS", "SUSPECTED DRUG", "SUSPECTED REACTIONS", and "Other drugs taken in last 3 months". It includes fields for name, address, telephone number, date, sex, weight, hospital, date of birth, and date of reaction. There are also checkboxes for "Did the reaction result in or prolong hospitalisation?" and "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



**Patient Safety Alert**

Stage Three: Directive
Improving medication error incident reporting and learning
20 March 2014

Alert reference number: NHS/PSAD/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)

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

2 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;

3 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,

4 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.

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

6 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.

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

8 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,

9 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 be 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: pharmacovigilance@mhra.gsi.gov.uk

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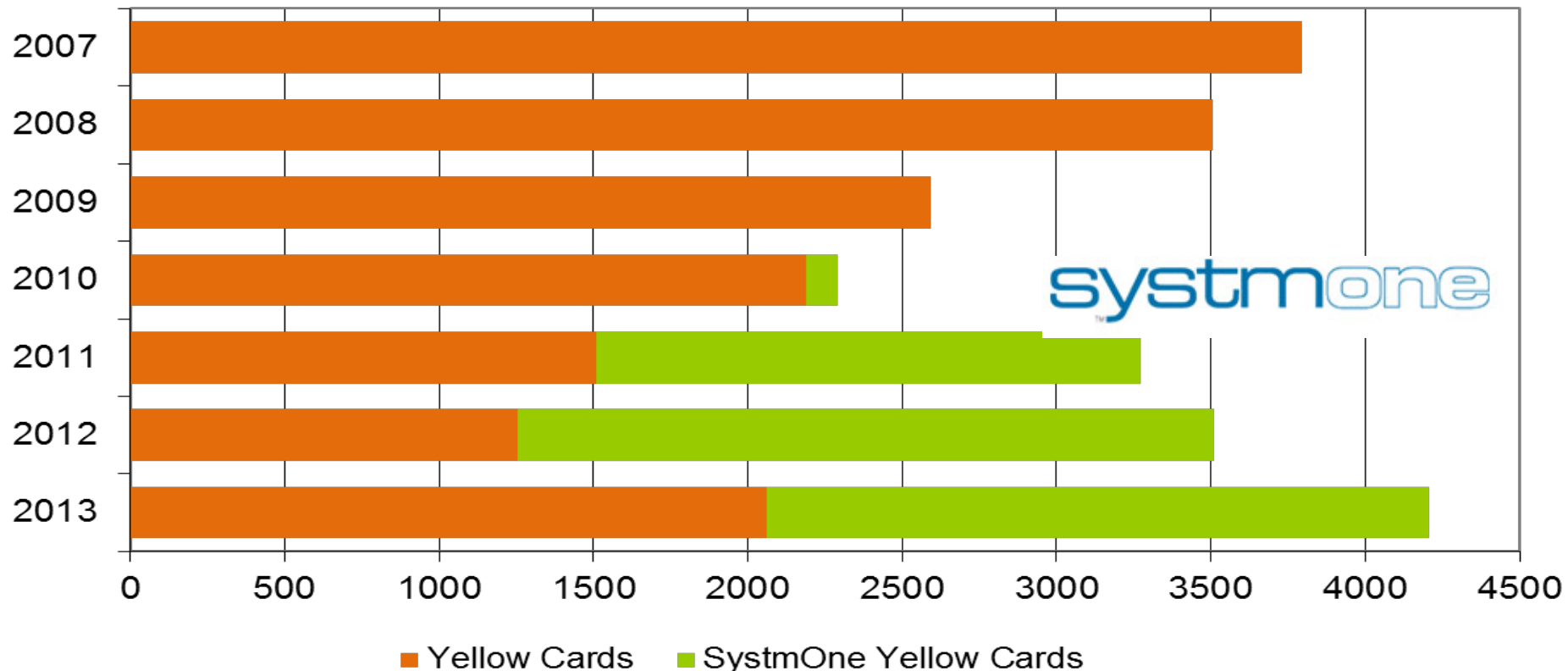
© NHS England March 2014

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

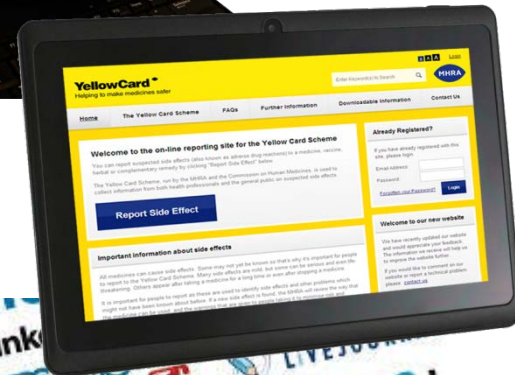
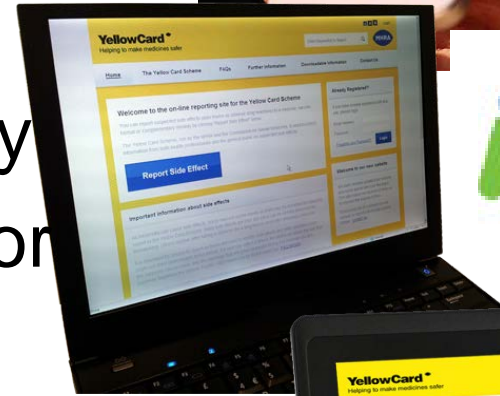
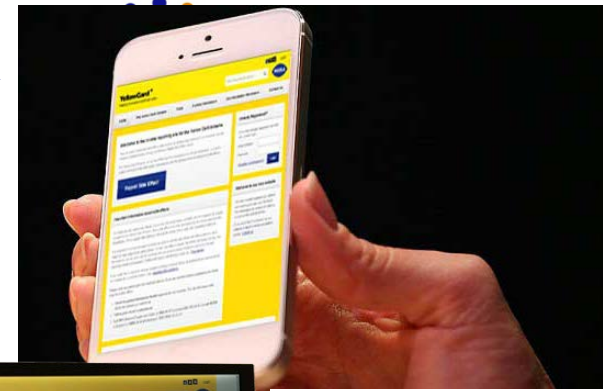
Innovative medicines initiative

Collaboration between
regulators, academia & industry

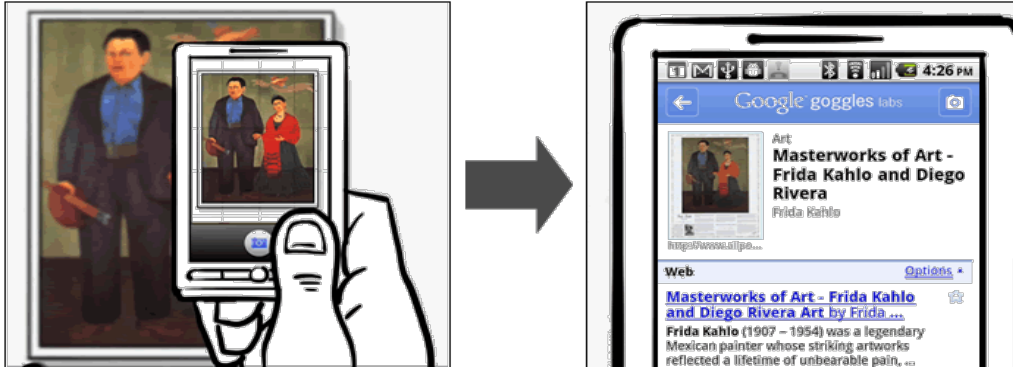
Development of a **mobile app** for

- 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



Eudravigilance – 3419 substances

420 CAPs on URD
(signals monitored by
EMA)

~3000 on existing
signals monitoring
list e-RMR

~ 1750 to be
allocated to a
lead member
state for
signals

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

Methodologies for signals MHRA

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, Raphaëlle Beau-Lejdstrom, Bridget King, Suzie Seabroke, Andrew Thomson, Philip Bryan  

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

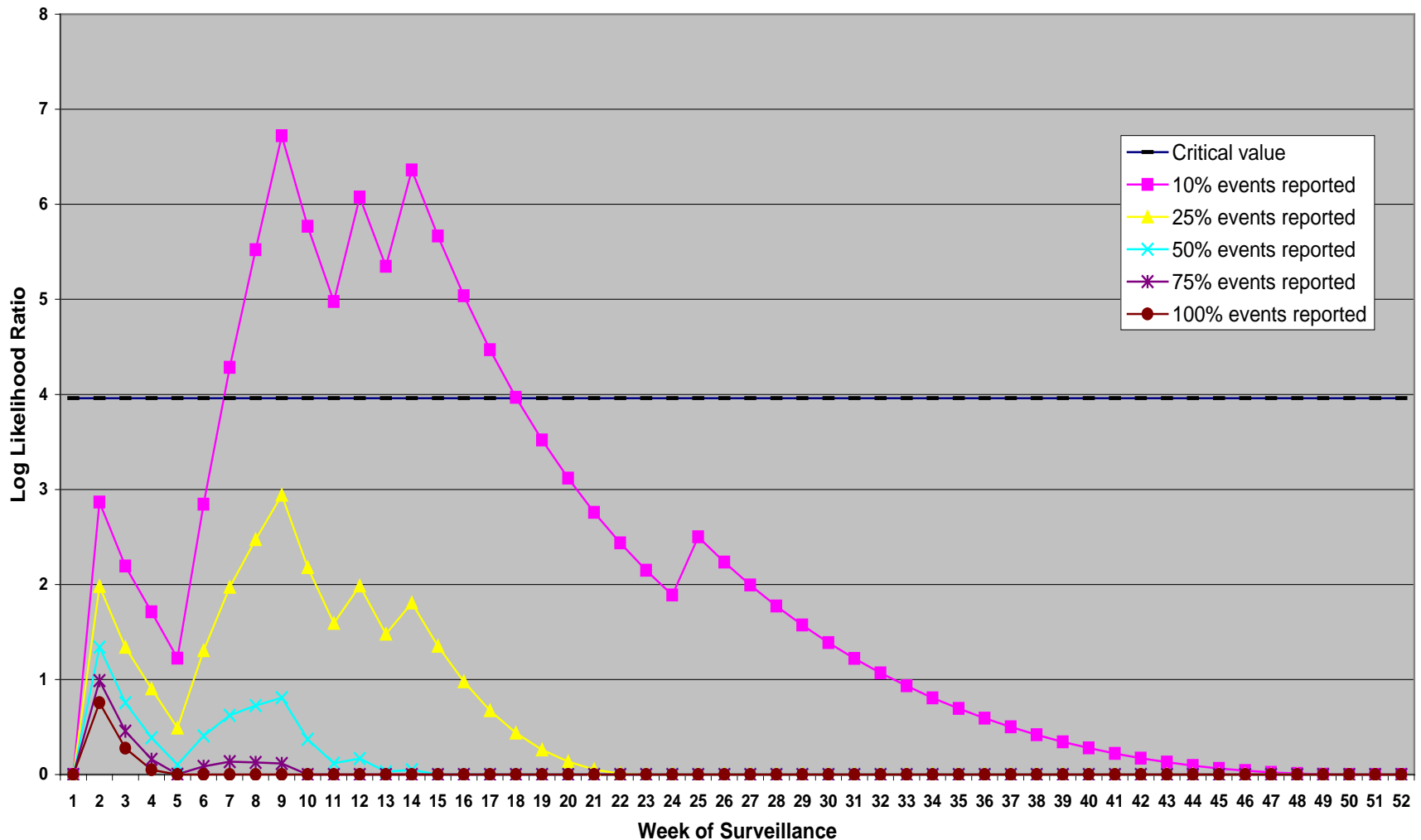
Maximised sequential probability ratio testing
for observed vs expected signals

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



© bruce adams

Maximised SPRT for ME/Chronic Fatigue Syndrome for girls aged 12/13 years (2008-2009)



Assessment responsibilities

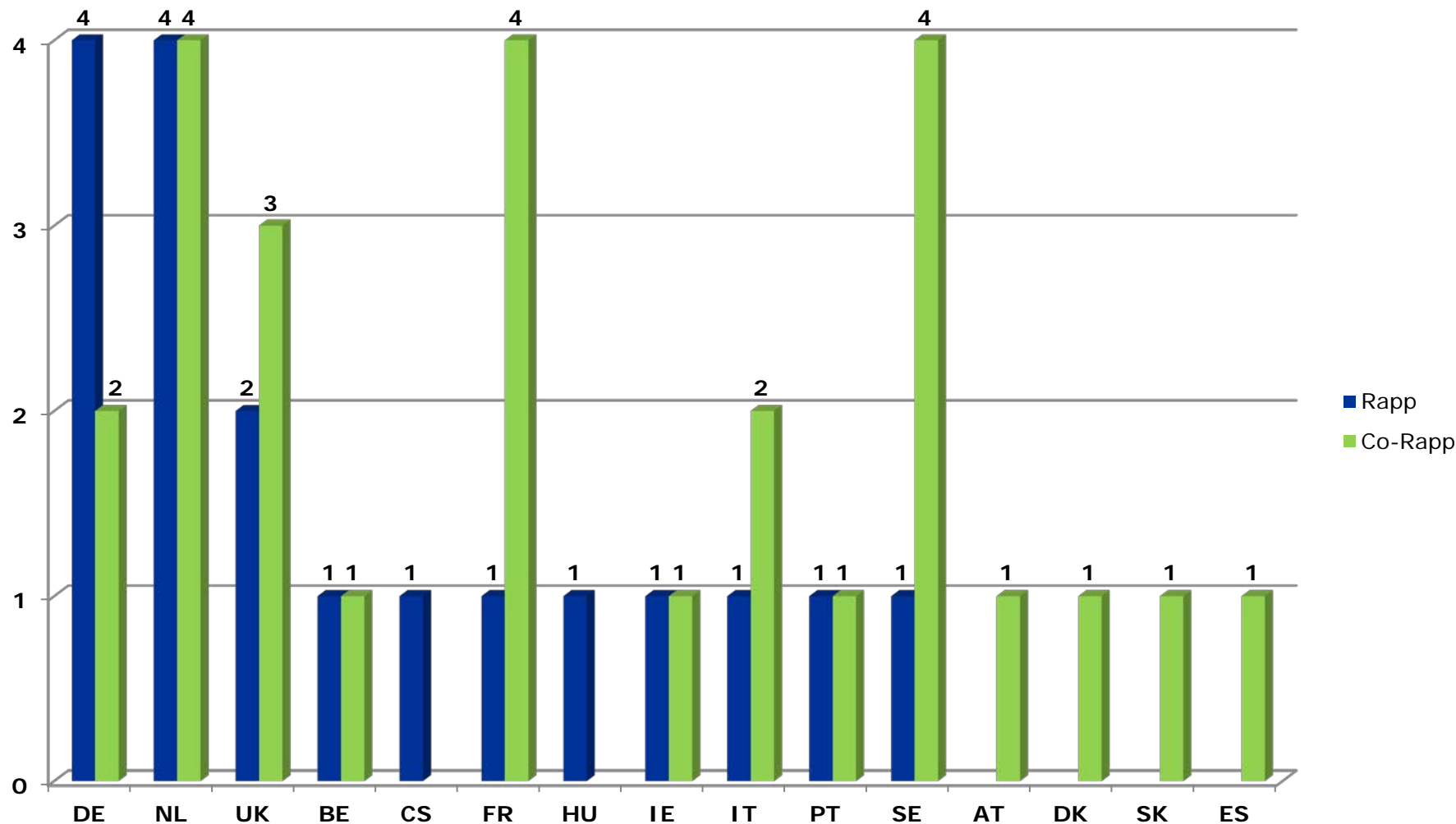


- **Risk Management Plans** for all medicines
- Moving towards **single assessments for periodic safety update reports**
- Increased activities with **PASS & in future PAES**
- Using **all available data** sources including patient registries, and pharmacoepidemiological approaches



Taking lead role in Referral

Rapporteurship and Co-Rap referral procedures initiated at PRAC in 2013



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

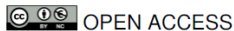
Single assessments of PSURs started
with centrally authorised medicines in 2013,
expanded to active substances contained in
in **both centrally and nationally
authorised** medicines in April 2013



RESEARCH

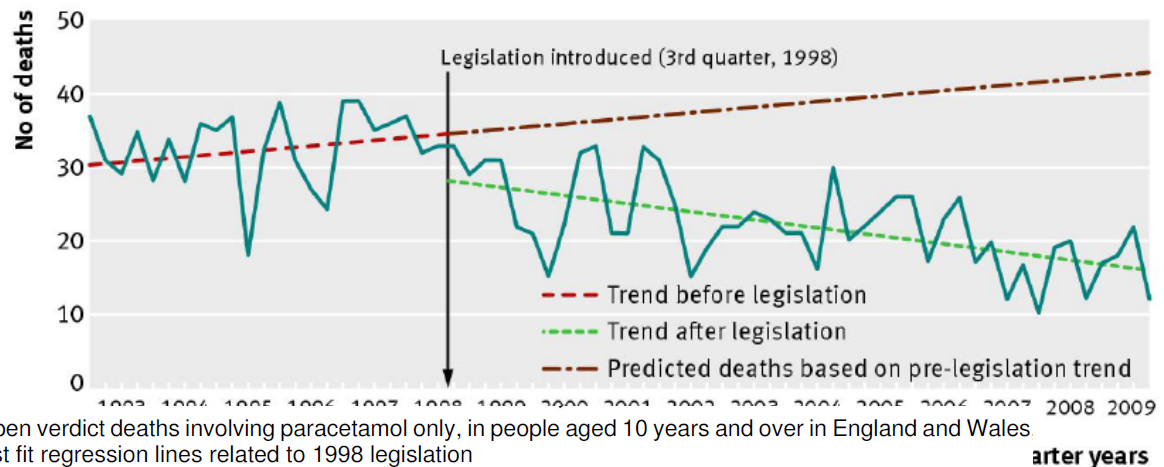
Impact of new warnings and reduced pack sizes for paracetamol in UK

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 Dodd *statistician*³, William Bernal *reader in hepatology*, Navneet Kapur *professor of psychiatry and pop*



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



Overall Aims of SCOPE



www.scopejointaction.eu

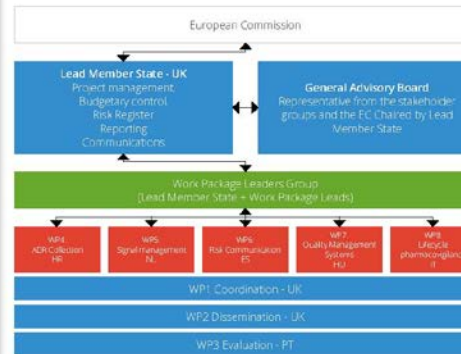
Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) Joint Action

The SCOPE Joint Action has received funding from the European Union

Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action was established to maximise the effective implementation of the European Pharmacovigilance Directive into effect in June 2012 by the National Competent Authorities (NCAs) in EU member states. The project is funded by The Consumers, Health and Food Executive Agency (CHAFEA), with the member state partners. SCOPE aims to provide practical tools and guidance to improve their pharmacovigilance systems and also ensure that those developments are sustainable in the future. This Joint Action will enable coordinated pharmacovigilance operations in the future which will lead to a consistent approach across all member states.

The project is made up of eight work packages, three of which are 'horizontal', and carry out the core areas of the project. The other five work packages are 'vertical'; these will deliver specific objectives, ranging from improvements in Adverse Drug Reaction reporting to quality management systems. SCOPE will use the benefits of a central cross-cutting structure to bring noticeable improvements to the pharmacovigilance systems of all member states. A key aim is to help lesser resourced NCAs develop skills and capacity in order to benefit citizens in their territory and the whole network.

Project Structure



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**