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Are vaccines safe?

2017

Vaccine **A**dvice for **C**lini**C**ians **S**ervice (VACCSline)

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Learning objectives

- Explain the stages of clinical trials
- Describe how vaccine safety continues to be monitored post-licensure
- List possible adverse events post vaccination

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- What questions may you expect a parent or patient to ask you relating to vaccine safety?

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How do we know vaccines are safe?

- Clinical trails prior to licencing – safety, identify expected adverse events
- Post-licensing surveillance
- Protocols and Stand Operating Procedures for their storage and administration

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Phases of Clinical Trials

Phase I:

Small group of people (20-80)

Safety – safe dose and identifying side effects

Phase II:

Large group (100-300)

Effectiveness & Safety

Phase III:

Larger group (1,000-3,000)

Effectiveness, monitor side effects

Compare to commonly used treatment

Phase IV:

Post marketing

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Post licensure "studies"

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- Vaccine effectiveness – reduction in disease, herd immunity

- Adverse events (phase 4 surveillance)
  - Larger number of people vaccinated
  - Diverse range of people vaccinated
  - Manufacturing problems (*National Institute for Biological Standards and Control* (*NIBSC*)

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Vaccine Production

- *National Institute for Biological Standards and Control* (*NIBSC*) routinely batch test vaccines
- Manufacturing problems - withdraw batches

NIBSC
Confidence in Biological Medicines

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Adverse events

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Medications

- Given to sick people
- Predominantly to elderly
- Influence on immune system, if any, inhibitory
- Designed to have short lived
- influence
- Minor AE's likely to be tolerated
- Individually prescribed

Vaccines

- Given to healthy people
- Given to young people
- Stimulating immune system
- Designed to have long lasting effect after single or few doses
- Minor adverse effects may not be tolerated
- Universally recommended

For vaccines;

- **Increased likelihood of coincidental association**
- **Increased difficulty in establishing association**

(Slide courtesy of Dr. Matthew Snape)

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WHO classifications of AEFIs

- programme-related
- vaccine-induced
- coincidental
- unknown.

Causality assessment of adverse events following immunization. WER 2001;76:85-89

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wrong intervals

expired vaccine

wrong route

Contraindications ignored

Programme related

too much, too little or no diluents

wrong dose

prepared incorrectly

incorrect storage

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Common vaccine induced AEFIs

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Local adverse reactions

- Usually early, mild and self limiting
- Pain, swelling and redness at the injection site
- Common with DTaP containing vaccines (5-25%)
- Less common with MenC, flu, pneumococcal

Systemic reactions:

- Fever, malaise, myalgia, irritability, headache and loss of appetite
- Hours (usually within 48 hours) with inactivated vaccines
- Later with live vaccines – dependent on viral replication
- Fever/rash 7-10 days; parotitis 3 + weeks post MMR

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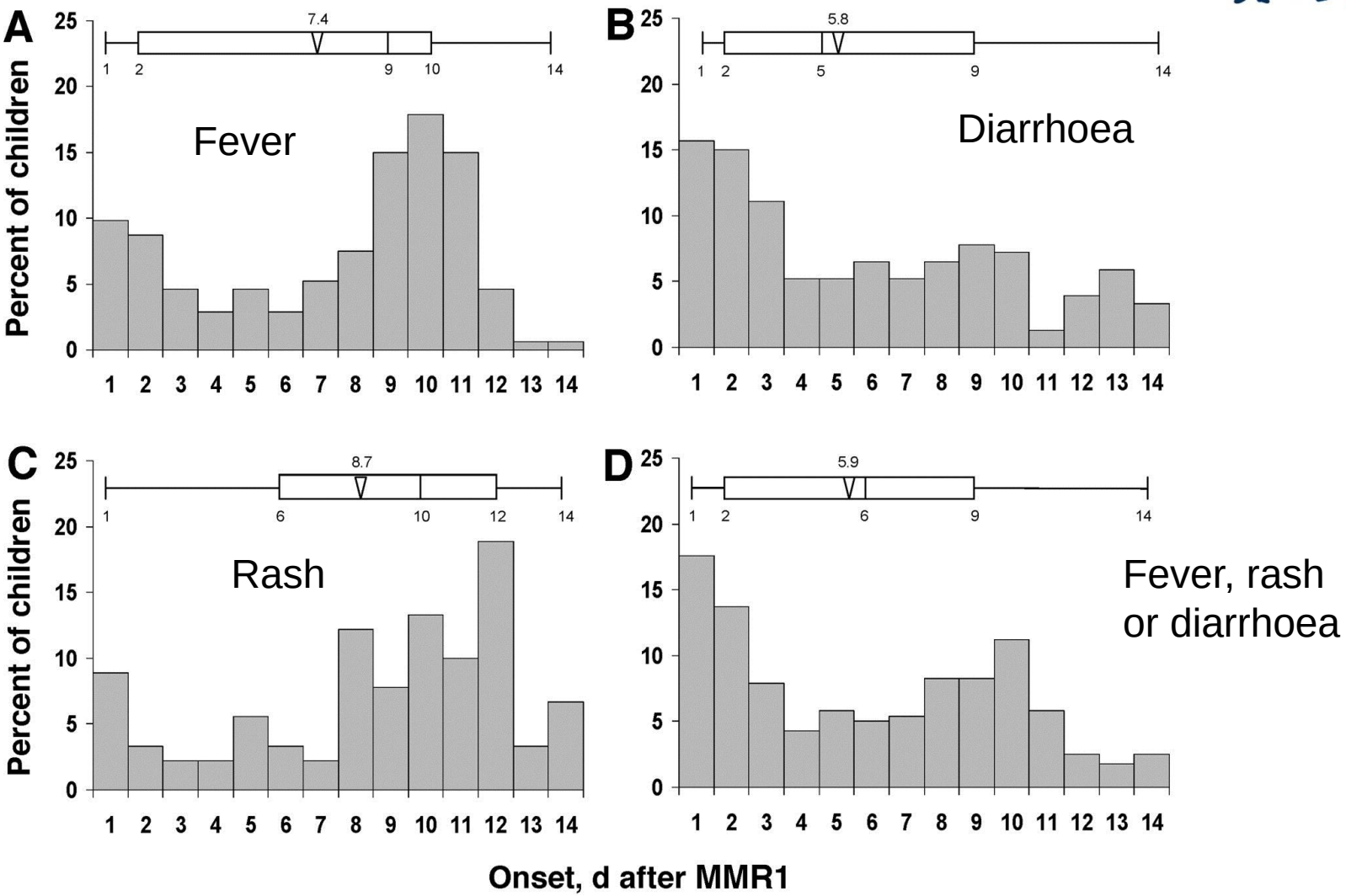
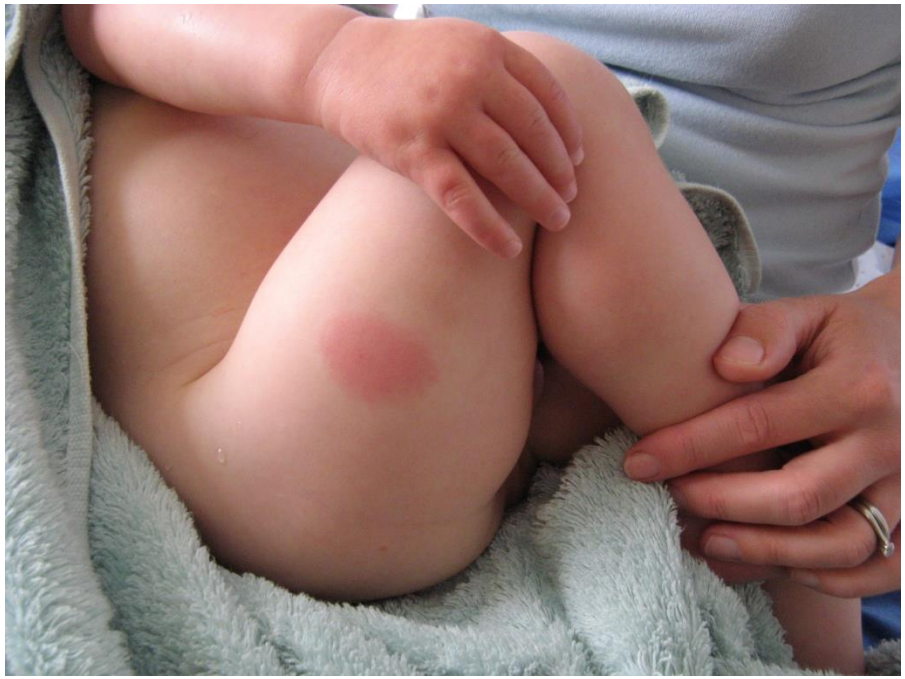
FIGURE 5 Symptom onset

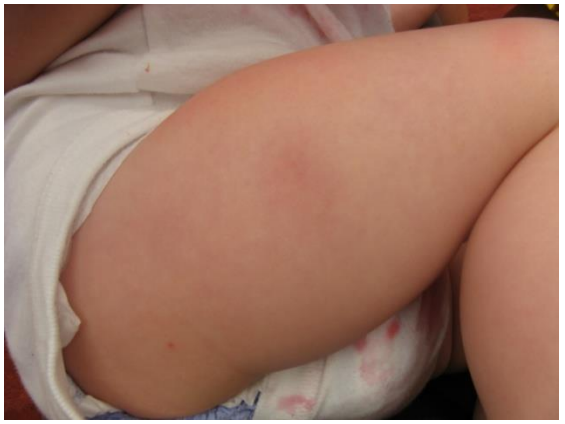


LeBaron, C. W. et al. Pediatrics 2006;118:1422-1430

(Slide courtesy of Dr. Matthew Snape)



Local redness 24 hours after immunisation



Day 4 post immunisation

How would you advise a parent if they asked you about this reaction? Could it happen again?

Photos courtesy Karen Ford

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Routine use of antipyretics

Managing common vaccine-induced AEFIs

Whilst paracetamol and ibuprofen can lower the duration of fever and reduce distress, there is no evidence that they prevent febrile convulsions. It is not therefore recommended that these drugs are used routinely to prevent fever following vaccination as there is some evidence that prophylactic administration of antipyretic drugs around the time of vaccination may lower antibody responses to some vaccines (Prymula *et al.*, 2009).

From online green book
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/147868/Green-Book-Chapter-8-v4_0.pdf

Exception: Men B if given with primary immunisations under one year of age give prophylactic paracetamol

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Men B & paracetamol use

- Routinely when Men B is given with other infants immunisations up to one year of age
- Give 2.5 ml of paracetamol (120mg/5ml):
  - With or shortly after vaccination
  - 2 further doses spaced 4-6 hours apart

Aim: to decrease occurrence of high fever rates > 38 degrees following administration of MenB with other routine infants imms

(50-80% - around 2 out of 3 infants)

Prophylactic paracetamol reduced fever rates without affecting the immune response to Men B or the other routine infant immunisations when given together

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Men B and paracetmol

- https://www.gov.uk/government/publications/menb-vaccine-and-paracetamol
- **MenB and Paracetamol mock consultation**

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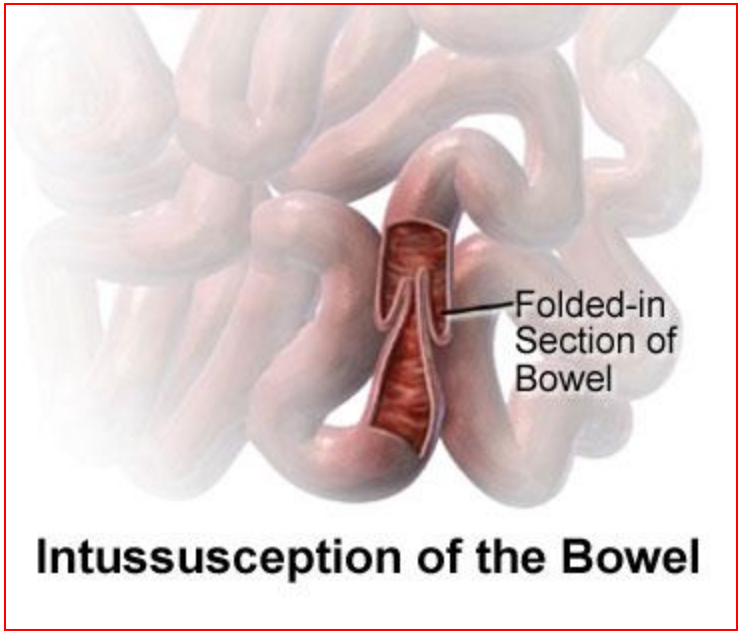
Vaccine specific AEFI



Intussusception of the Bowel

- Intussusception is a naturally occurring condition of the intestines
- Incidence begins to rise after 6 months of age

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Vaccine specific AEFI: Intussusception

- Research from some countries suggests that Rotarix® may be associated with a very small increased risk of intussusception

- ***Data from observational safety studies performed in several countries indicate that rotavirus vaccines carry an increased risk of intussusception, mostly within 7 days of vaccination. Up to 6 additional cases per 100,000 infants have been observed in the US and Australia against a background incidence of 33 to 101 per 100,000 infants (less than one year of age) per year, respectively*. (Rotarix SPC https://www.medicines.org.uk/emc/medicine/17840)**

Even with this small potential risk, the benefits of vaccination in preventing the consequences of rotavirus infection outweigh any possible side effects

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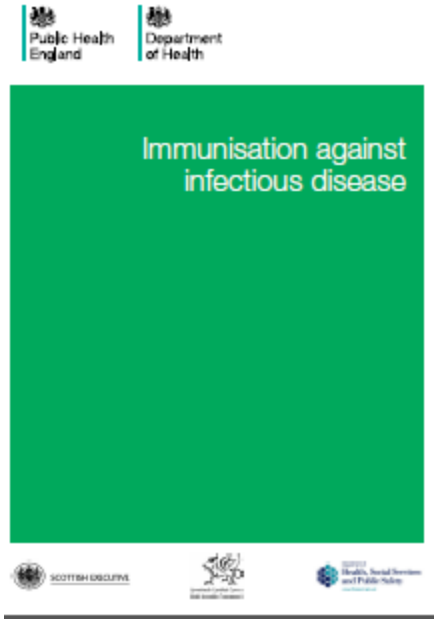
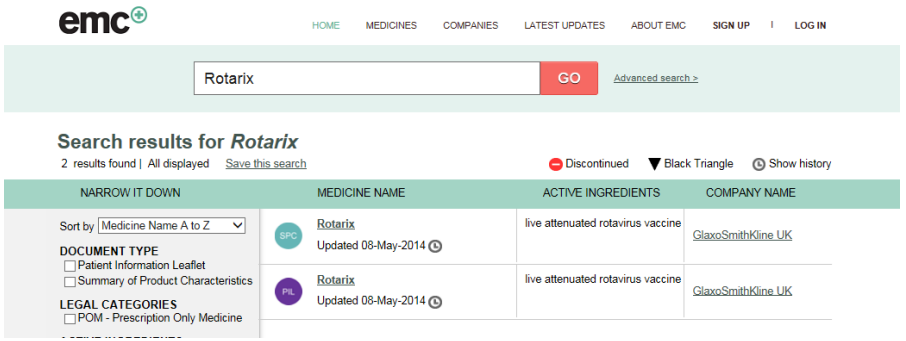
Details of Vaccine Specific AEFI's





http://www.medicines.org.uk/emc/search

Summary of Product Characteristics

https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book#the-green-book

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Allergic reactions; Anaphylaxis

- Very rare

  1997 – 2003 – 130 reports to MHRA (no deaths)
  117 million doses of all vaccines

- 0.65 per million immunisations

- Potentially life threatening

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Distinguishing anaphylaxis from other reactions

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Syncope (Faint)	*Anxiety attack*	*Breath holding episode*	*Anaphylaxis*
Good central pulses but may be bradycardic Respiration continues Pallor Warm skin Unusual in pre-school children No upper airway oedema No itching Patient regains consciousness when lying down	May appear fearful Usually tachycardic Hyperventilation Pallor Complain of tingling of face and extremities Complain of feeling light-headed, dizzy or numb	Mainly in young children Generally distressed/ crying prior to episode Facial flushing and perioral cynosis Can briefly become unconscious during which breathing returns	Poor central pulses, usually sinus tachycardia Possible apnoea, especially in children Upper airway oedema, sneezing Bronchospasm, may be audible expiratory wheeze or stridor Urticarial lesions Itching Sense of impending doom Flushing/sweating Cold skin Patient does not revive when lying down

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Potential triggers to anaphylaxis

- Egg proteins (yellow fever, Epaxal (Hep A) and influenza vaccines)
- Thiomersal (some flu in the past seasons and hep B vaccines)
- Antibiotics (neomycin, streptomycin and polymixin B)
- Stabilisers and other vaccine components (yeast, gelatin)
- Toxoid (DTaP, Td)

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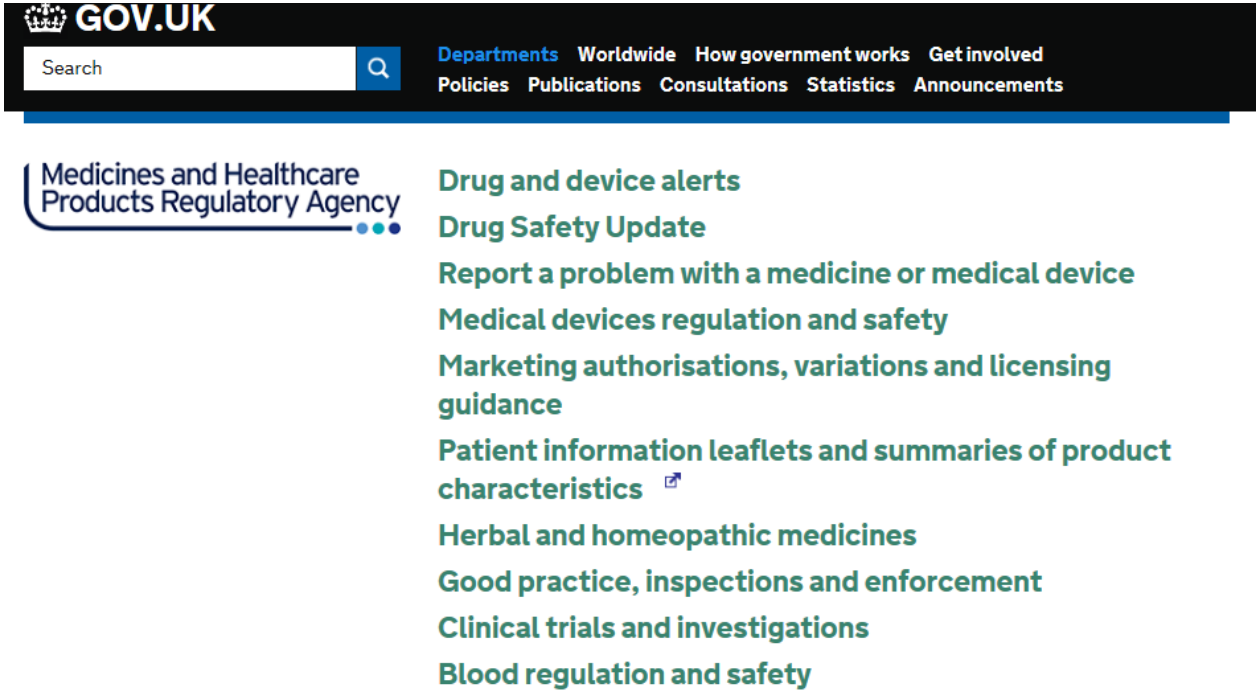
Reporting AEFI's



https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

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GOV.UK

Search

Departments Worldwide How government works Get involved
Policies Publications Consultations Statistics Announcements

Medicines, medical devices and blood regulation and safety – guidance

The Yellow Card Scheme: guidance for healthcare professionals

What to report

Medicines

For established medicines and vaccines you should report all serious suspected ADRs, even if the effect is well recognised.

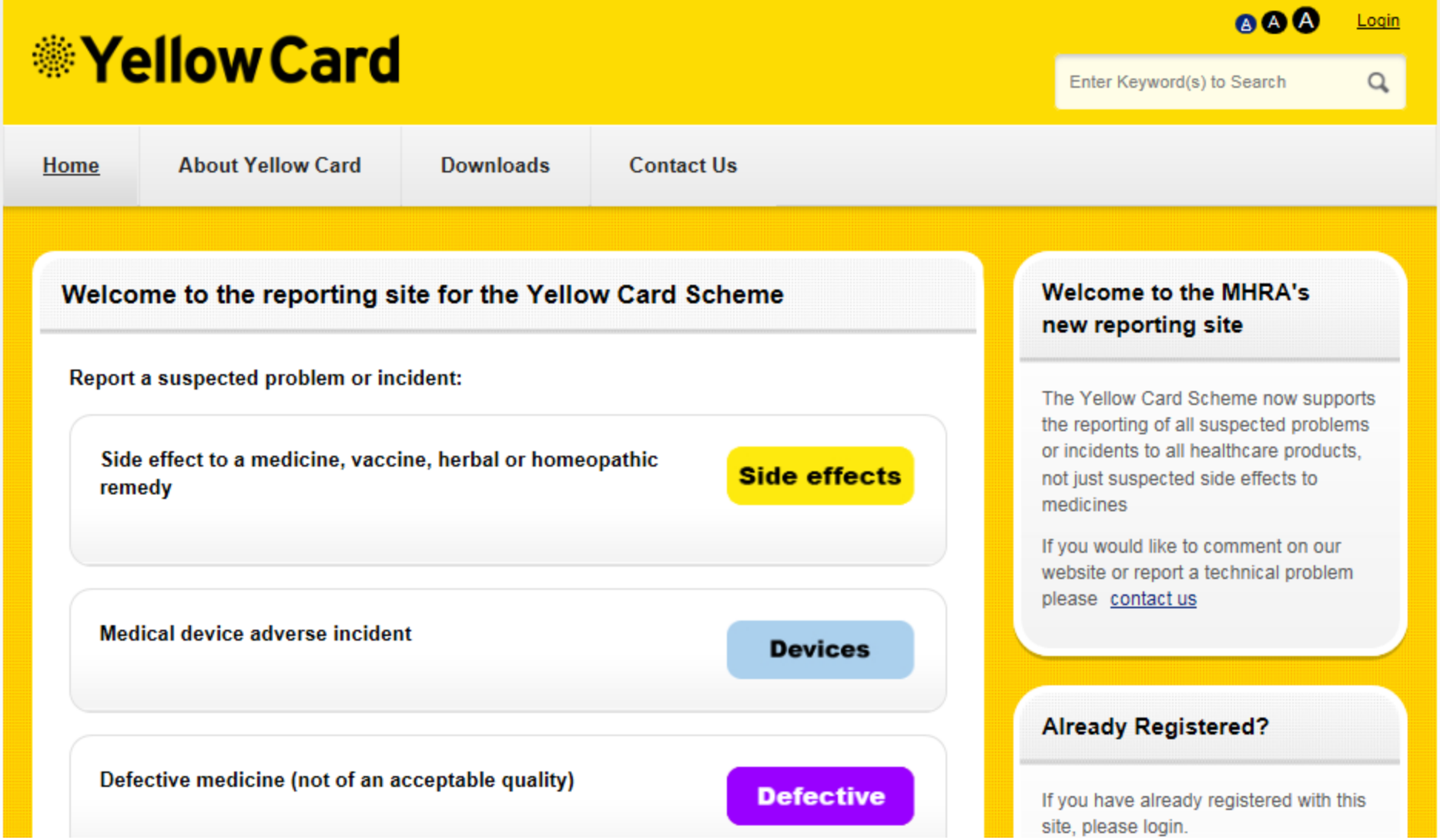
We are particularly interested in receiving Yellow Card reports of suspected ADRs:

- in children
- in patients that are over 65
- to biological medicines and vaccines
- associated with delayed drug effects and interactions
- to complimentary remedies such as homeopathic and herbal products

See what to include in your Yellow Card of an adverse drug reaction (PDF, 73.8KB, 3 pages) .

See specific areas of interest for adverse drug reactions reporting (PDF, 65.8KB, 2 pages) .

https://www.gov.uk/the-yellow-card-scheme-guidance-for-healthcare-professionals#how-to-report



https://yellowcard.mhra.gov.uk/

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What is the MHRA?

The **Medicines and Healthcare products Regulatory Agency (MHRA)** is the government agency responsible for ensuring that medicines and medical devices work and are acceptably safe. When any possible problem is found, the MHRA takes prompt action to protect the public and reduce risk.

For more information about the MHRA:

Visit: **www.mhra.gov.uk**
Email: **info@mhra.gsi.gov.uk**
Tel: **020 3080 6000**

Reporting Adverse Drug Reactions to the Yellow Card Scheme

Healthcare professionals are asked to help improve medicines safety by reporting suspected Adverse Drug Reactions (ADRs) to the Yellow Card Scheme. Please support the scheme by following the these reporting guidelines.

- Please report **all** suspected ADRs **for new medicines** (identified by the black triangle ▼ symbol)
- Please report **all serious** suspected ADRs for established vaccines and medicines, including unlicensed medicines, herbal remedies, and medicines used off-label
- **If you are unsure, please report anyway.**

Help make medicines safer for everyone

www.mhra.gov.uk/yellowcard MHRA

▼	All **Suspected** ADRs
Other medicines/vaccines	All **Serious** ADRs

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Continuous safety review

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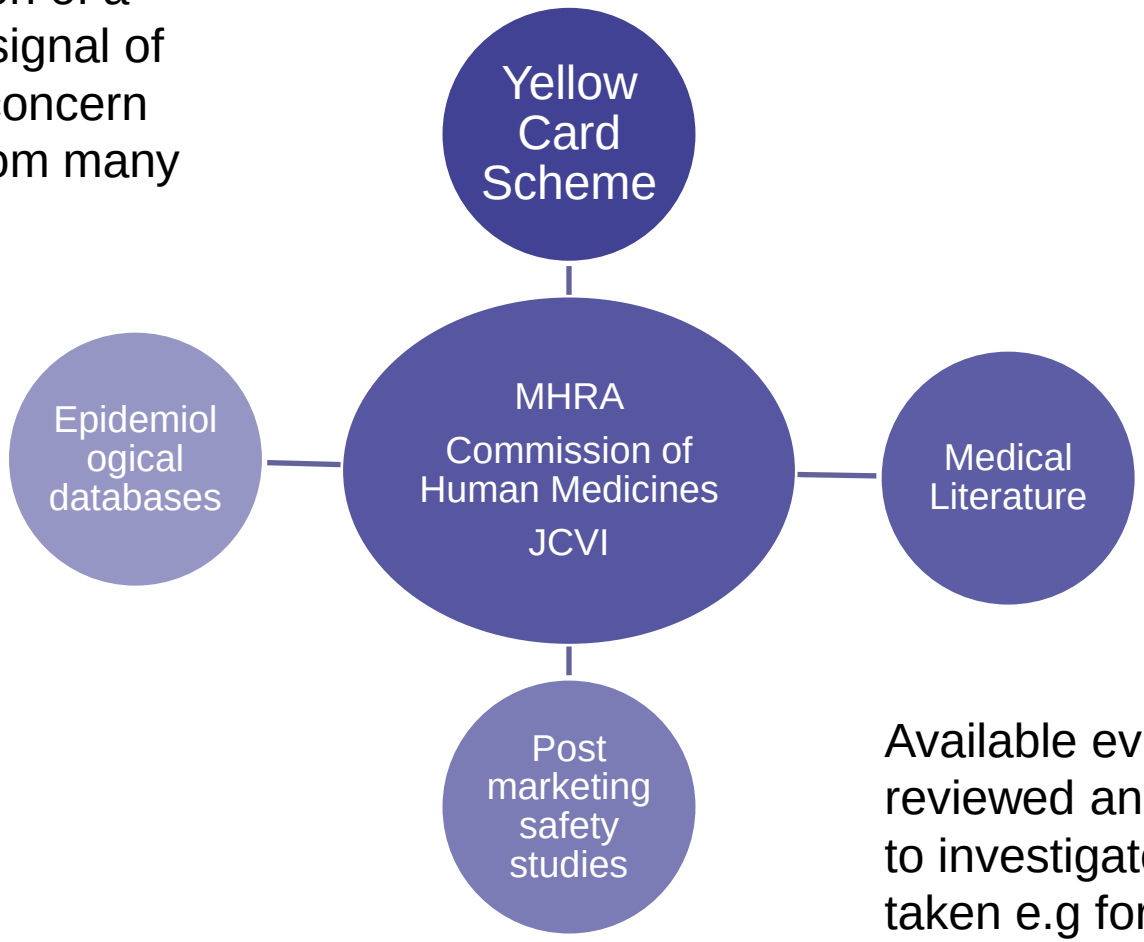
Information of a possible signal of a safety concern pooled from many sources



Available evidence reviewed and action to investigate further taken e.g formal epidemiological studies

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Reassure parents/patient about vaccine safety…

- Rigorous safety system for vaccines that continues post –licensure and after their introduction in to the routine schedule