Medicines & Healthcare products Regulatory Agency

3S – Smart Safety Surveillance

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CPRD NIBSC MHRA

Content

- Brexit
- Global PV regulatory systems – Smart Safety Surveillance
- Medical Device Regulations and “Operational Transormation” at MHRA
- Summary

Our vision

We protect and improve the health of millions of people every day through the effective regulation of medicines and medical devices, underpinned by science and research

UK Position on Brexit

- Position on medicines and medical devices regulation remains clear.
- We want to retain a close working partnership with the EU to ensure patients continue to have timely access to safe medicines and medical innovations.
- We are committed to continuing a close working relationship with the European Medicines Agency (EMA).
- Our vision is to ensure that patients remain front and centre in negotiations. The three principles that underpin negotiations for the UK's future relationship are that patients are not disadvantaged, industry is able to get their products into the UK market as quickly and simply as possible and the UK continues to play a leading role in promoting public health.

PV system at MHRA

- MHRA have always been leaders in Pharmacovigilance
  - Methodologies
  - Technologies

- We continue to enhance the UK system and innovate
  - Mobile Apps (WEB-RADR)
  - CPRD use
  - Direct Yellow card reporting from eHR systems
  - Yellow Card “Biobank”

PV as a global system

- MHRA already operate on a global level and this will continue
- We work closely with WHO, UMC, ICMRA and others
- Our PV expertise is often sought from EU and non EU NCAs
- We are delivering capacity building for other countries through 3S and other initiatives

TRIPLE-S (3S)

SMART SAFETY SURVEILLANCE

“Every person has the right to safe medical products”

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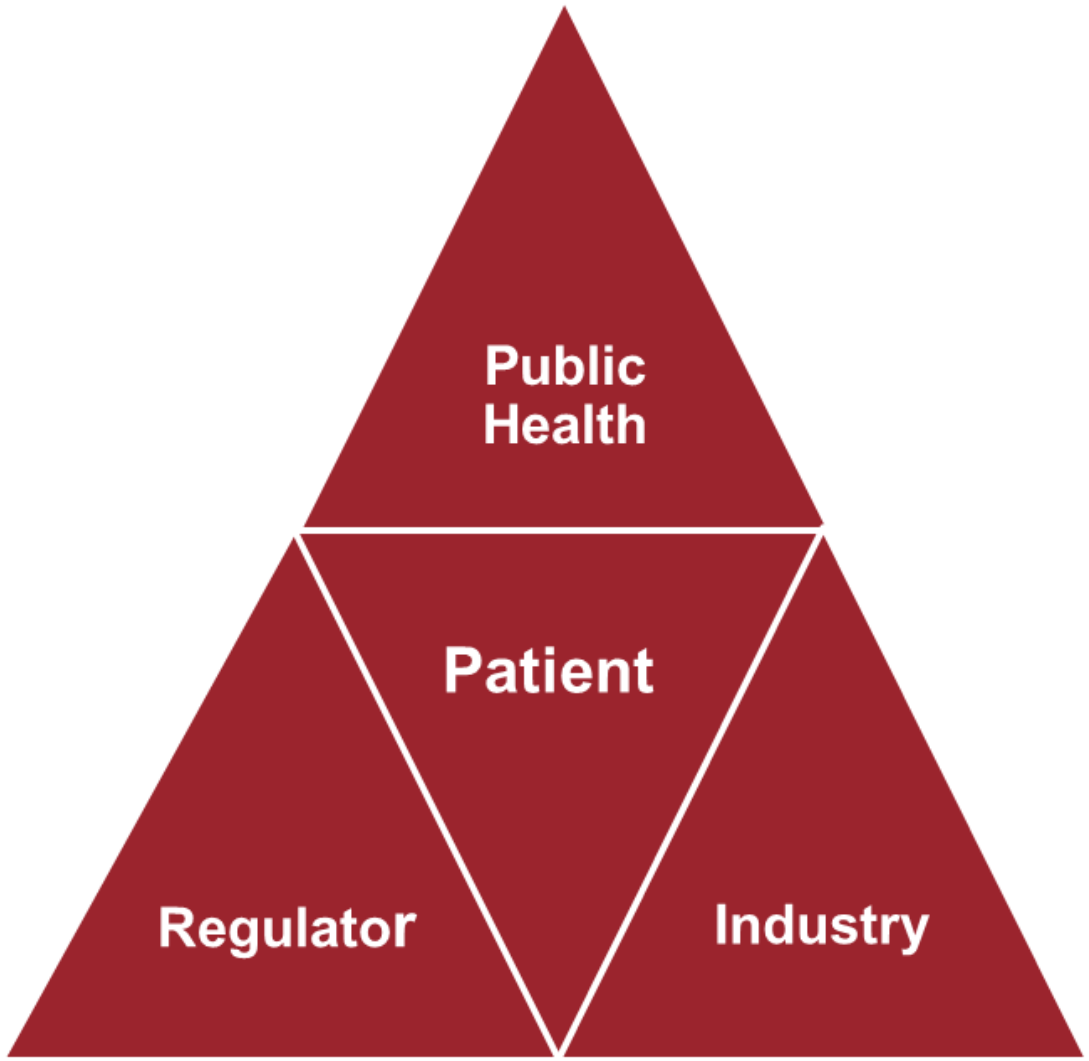
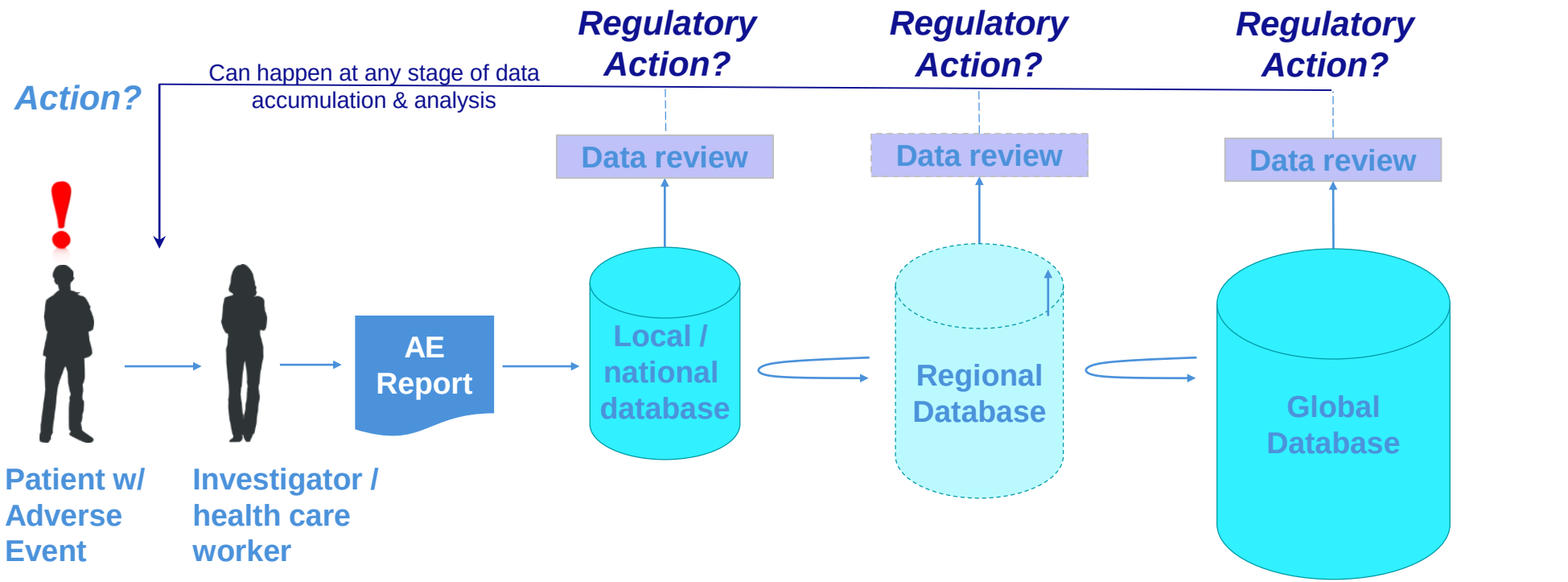


Overview of concept of an end to end safety surveillance system



Stakeholders

- Public Health System
- Sponsor / Manufacturer
- Regulator
- Regional Centers (e.g. WHO, African RECs)
- Global Facility (e.g. WHO, Continental)

Main challenges

A. Limited reporting

B. Limited local analysis

C. Limited action on signals impacting patients

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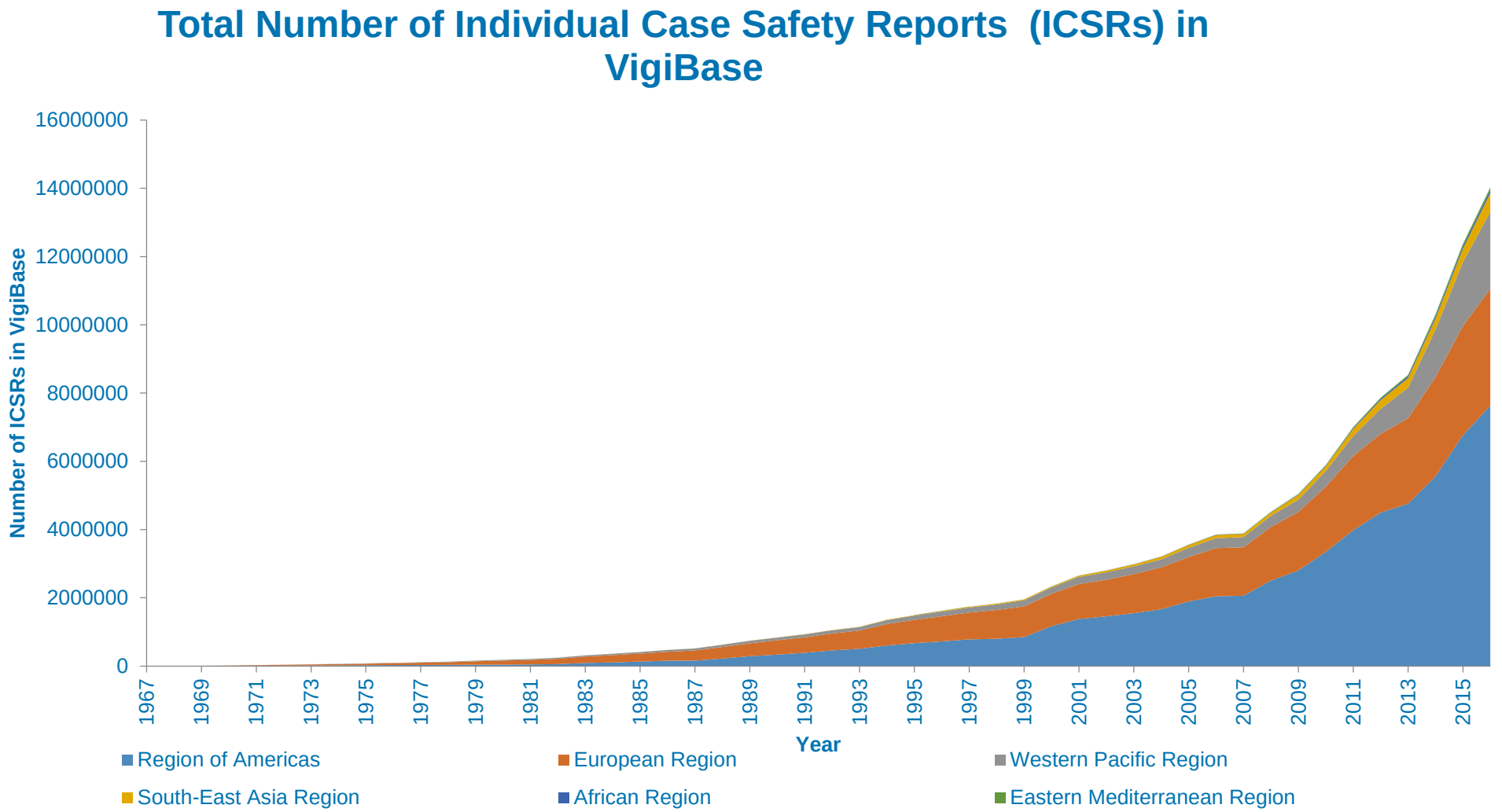
WHO ICSR Database (VigiBase)



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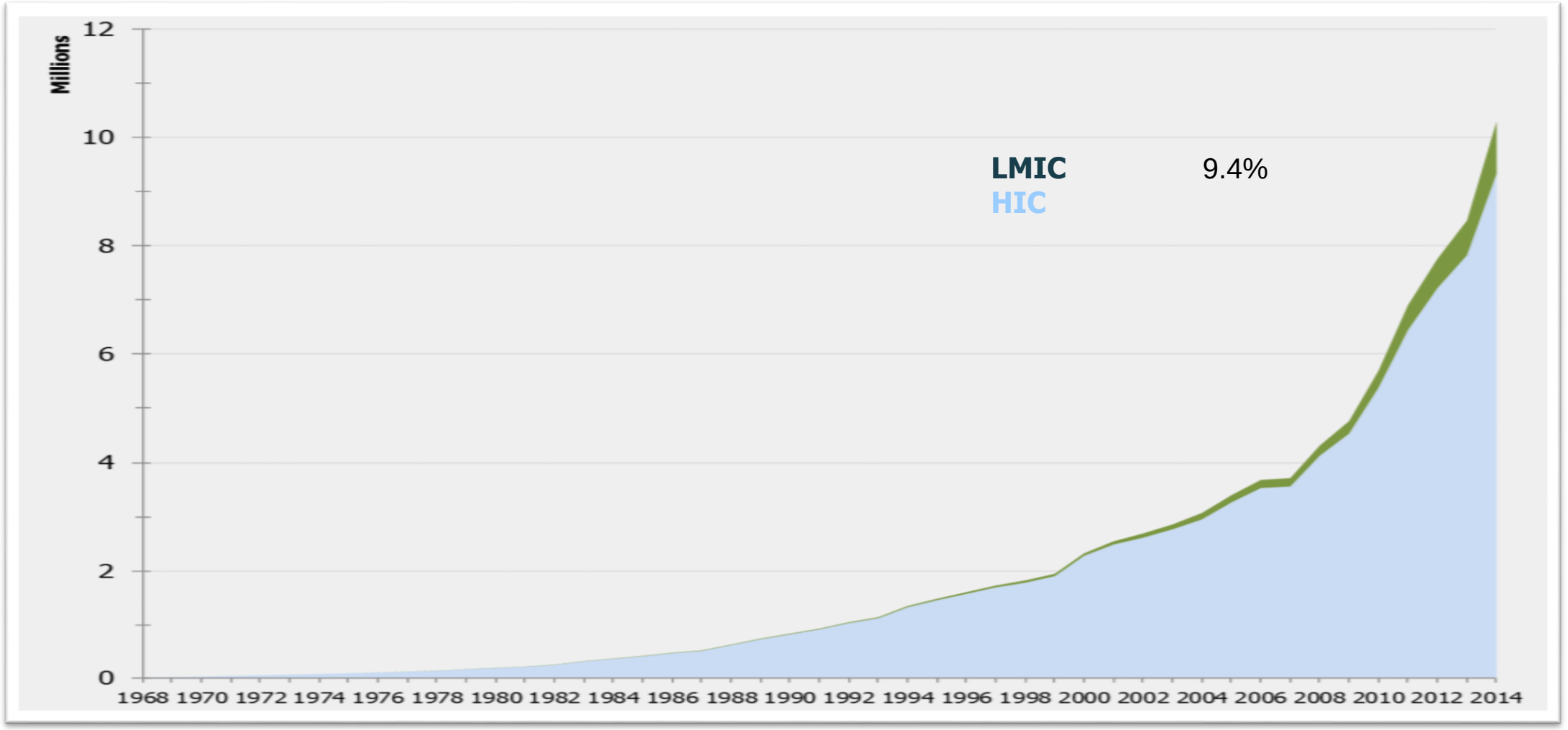
Very limited reporting from LMIC



Reporting statistics in LMIC

In some countries

- Average 0.106 reports/ physician in 5 years
  - Disease burden overwhelms
    - Less than 3 minutes per patient
      - ADR Reporting not a priority

Poor quality reports

- Less than 30% include 50% of essential information
  - Negative impact on analysis

Barriers to end-to-end Pharmacovigilance
Snapshot: 3 Main problems

Main challenges

Limitations

A. **Limited reporting**

B. **Low local capacity / capability to analyze data collected**

C. **Low NRA capacity / capability to take action from alert signals received**: Only a small fraction (3 in 55 according to 2010 survey by WHO) of the NRAs regularly take specific actions from signals received; most of these decisions are a replication of what was done by the SRAs

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3S Approach

Select pilot countries and products

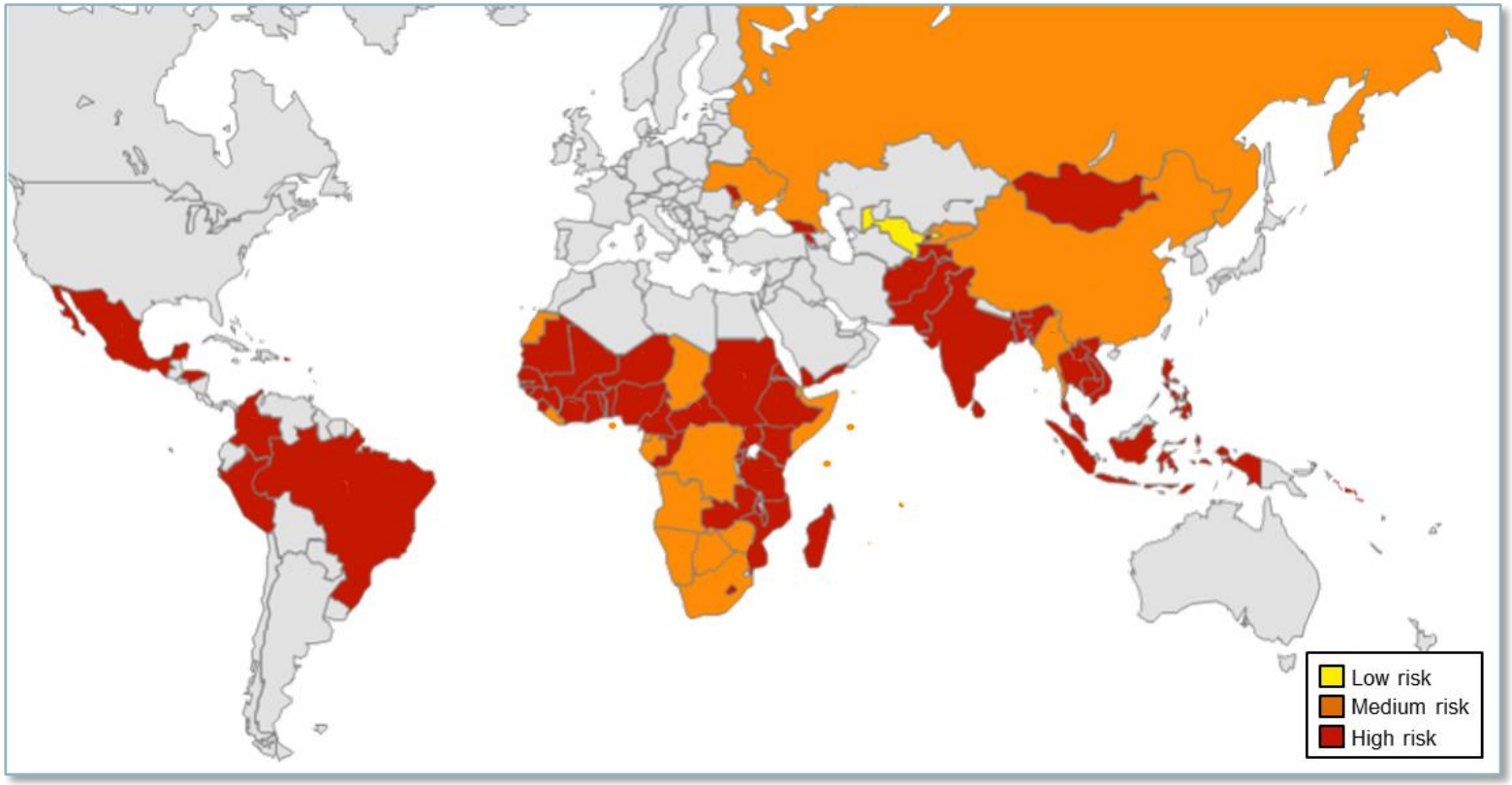
Develop action plans to build capacity in pharmacovigilance

Look at the regulatory system to support sustainability

Develop outcomes targets to measure against

Risk assessment – need for PV development

Geographic distribution of product launches, assessed by relative risk (2016-2018)



Source: SSWG Report, 2014

Risk-based assessment

1. Anticipated product pipeline
2. Anticipated or potential post-market safety risk
3. Pharmacovigilance capacity in launch country
4. Timing of product launch

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THE 3S VALUE PROPOSITION

Objectives

1. **System level:** Use the pilot products to build national pharmacovigilance systems that support regulatory decisions for all medicinal products and vaccines
2. **Product level:** Better characterize the safety profile of priority pilot products being used in public health programmes (PHPs) in LMIC settings

Sustainable Integrated PV Systems

- ✓ **Support informed benefit-risk decisions**, relevant to the local setting
- ✓ **Maintain public confidence** in medicines safety, supporting uptake of public health interventions
- ✓ **Enable access to innovative treatments**, tackling major public health challenges

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3S - CHALLENGES

- Lack of, or variable regulatory, legal and policy frameworks
- Difficulty getting adequate and appropriate staffing/resourcing, leading to significant delays
- Lack of project management, prioritisation, and commitment to timelines
- Lack of resources in-country
- Minimal supporting technology and infrastructure
- Where available, data is not integrated across stakeholders
- Limited regulator access to data

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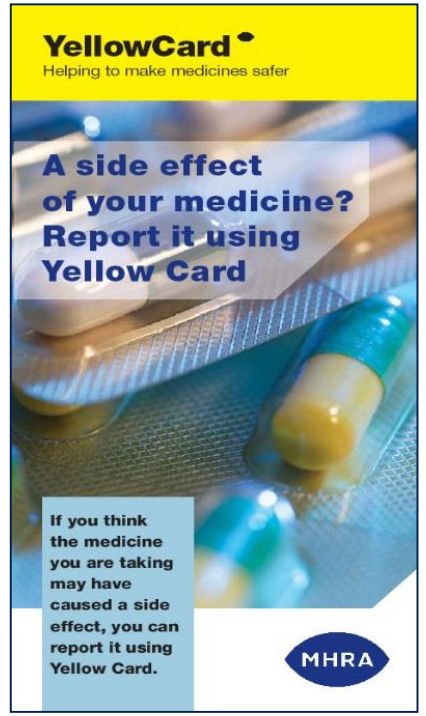
MHRA as a technical partner

- **Expertise in ADR systems**, signal management and assessment – pioneered database signal methodologies
- Advocate of **inclusive** PV involving all medicines users - benefits of patient reporting evaluated
- Introduced **risk management planning,** shifted PV from reactive to proactive evidence generation
- Proponent of scientific critical appraisal underpinning **benefit risk assessment**
- Experience in **regulatory aspects** including independent scientific committee advice, regulatory decision making
- Development of **guidelines** for all stakeholders eg GVP



3S - PILOTS

Product selection

- bedaquiline (BDQ) for multi-drug resistant (MDR) TB
- Rotavac – rotavirus vaccine
- tafenaquine (TFQ) for P.Vivax

Country selection

So far….

- Armenia (BDQ) – pilot underway
- India (Rotavac) – pilot underway
- Ethiopia (BDQ & TFQ) – scoping visit

- Discussions with potential others ongoing

3S BDQ in Armenia

- former Soviet republic in Eurasia
- population ~ 3 million
- official language - Armenian

3S BDQ in Armenia

High TB disease burden

- incidence 2016[1]: 44 new cases per 100,000

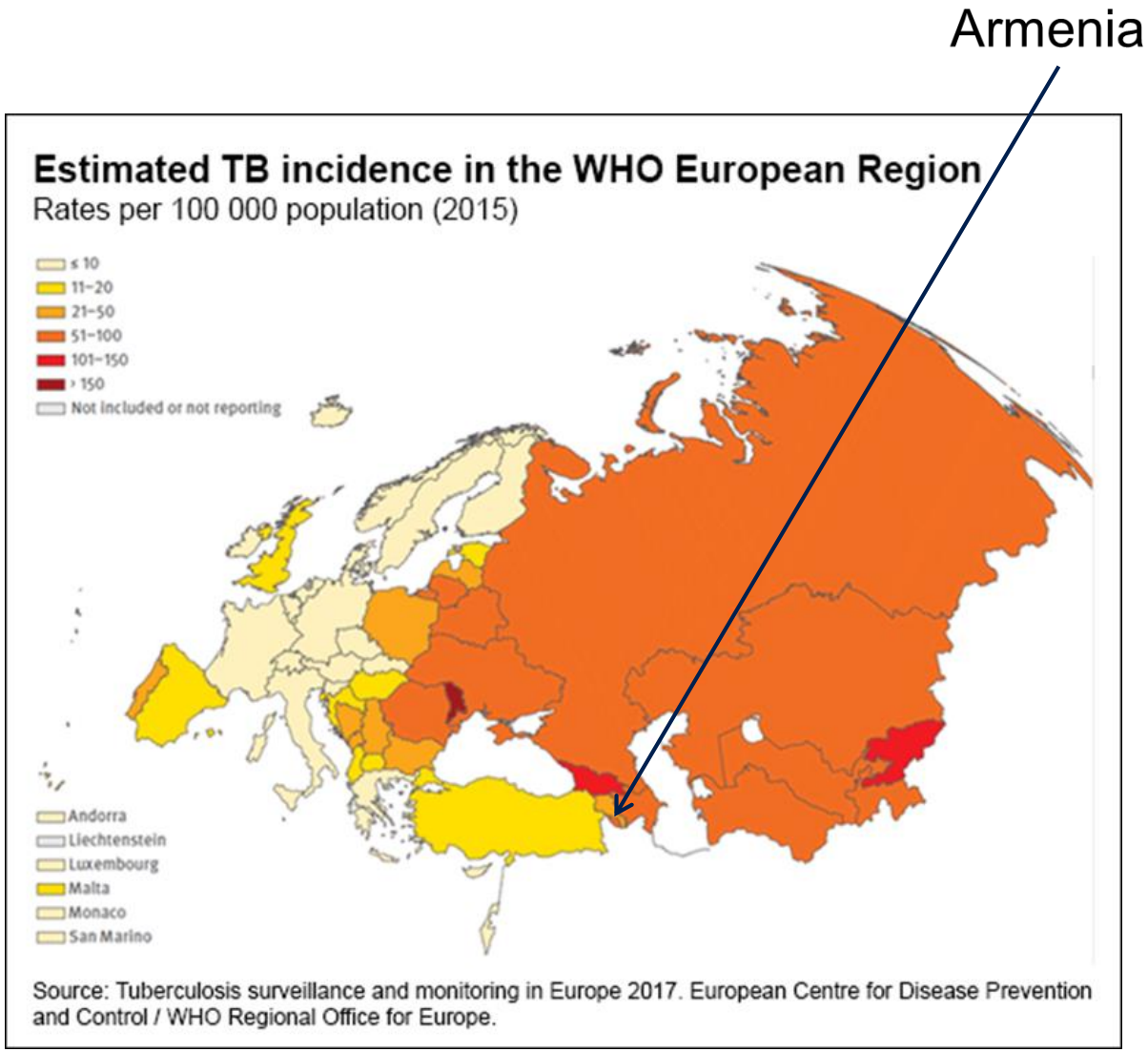
MDR-TB and XDR-TB serious problem

- prevalence 2016[1]: 11% amongst new cases; 46% amongst previously treated cases

One of the 1st countries to respond to XDR-TB challenge - implemented **compassionate use program** for access to BDQ (2013) and delamanid[2]

Has a national TB Control Centre and good network of TB clinics

[1] WHO, Global TB Report 2017; [2] EndTB.org



3S BDQ in Armenia

- Armenian Government support for 3S
- NRA fully committed
- Support and collaboration with pharmacists in the TB clinics

- Some PV specific legislation
- Medium functioning PV system
- Member of WHO PV Program
- Vigibase and Vigiflow connectivity
- ~ 500 ICSRs/year – 3,000 ever
- Data exchange with MSF[1] on adverse incidents for BDQ

Armenian Deputy Health Minister (centre, white dress) and TB Pharmacists join WHO, MHRA and NRA for 3S Kick-Off meeting in Yerevan, July 2018

[1] MSF – Médecins Sans Frontieres

3S BDQ in Armenia

Workplan – 12 months

- Strengthen ADR reporting
- Signal detection training
- Introduce PV evaluation to Armenian Pharmacy Committee
- Develop regulatory guidance for industry (RMP, PSUR etc)
- Critical analysis and risk assessment training
- Develop risk communication skills, including media handling

Bedaquiline/MDR-TB as the focus then extend to whole system

3S BDQ in Armenia – Strengthening ADR reporting

ADR Mobile App

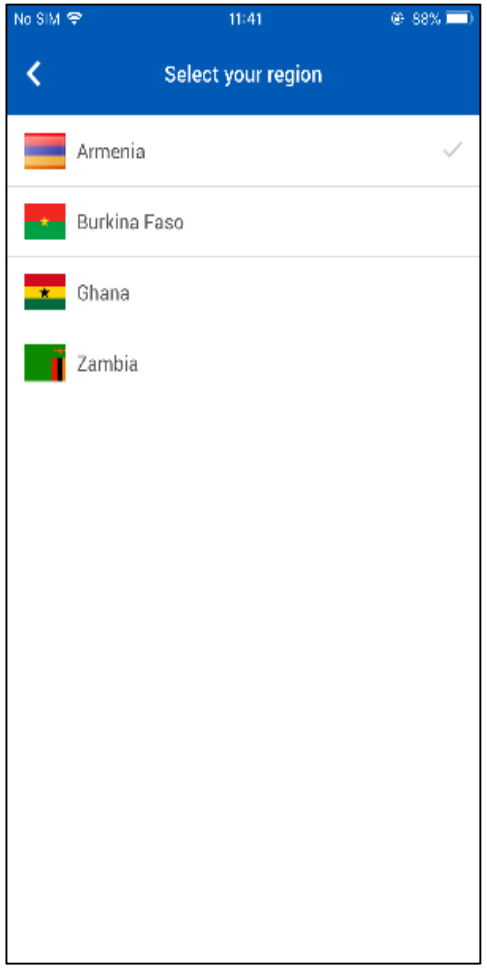
- Courtesy WEB-RADR project
- Convenient and easy to use alternative to paper or electronic ADR reporting forms
- For both android and iOS devices
- Adaptable for country needs (language, branding, drug database options)
- Instant access to medicines safety information

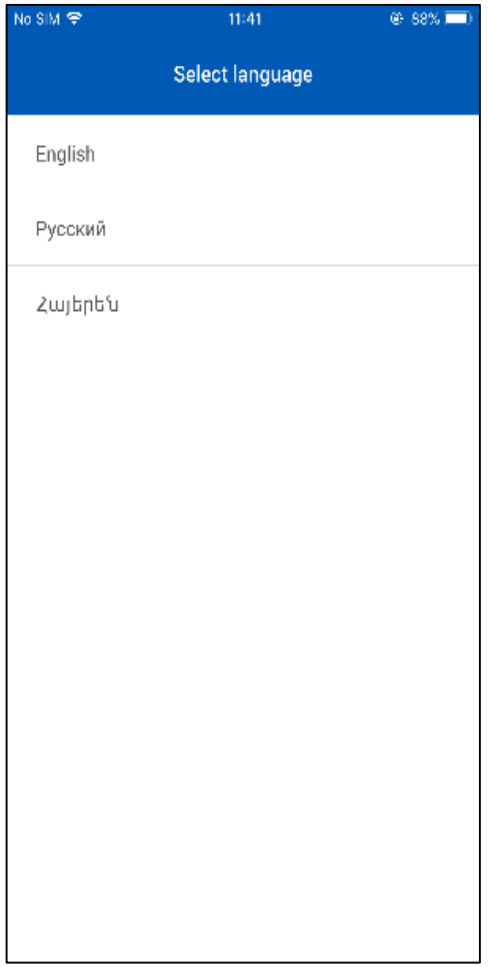
Use outside EU, LMIC Burkina Faso and Zambia in 2017
Eight more LMICs to roll-out in 2019, including Armenia

Med Safety mobile app

SMART SAFETY SURVEILLANCE

- ✓Facilitate ADR reporting
- ✓Free to download and use
- ✓Available for Android and iOS
- ✓Armenian, Russian and English languages
- ✓NRA news feed
- ✓Summaries of ADR data available in graph format





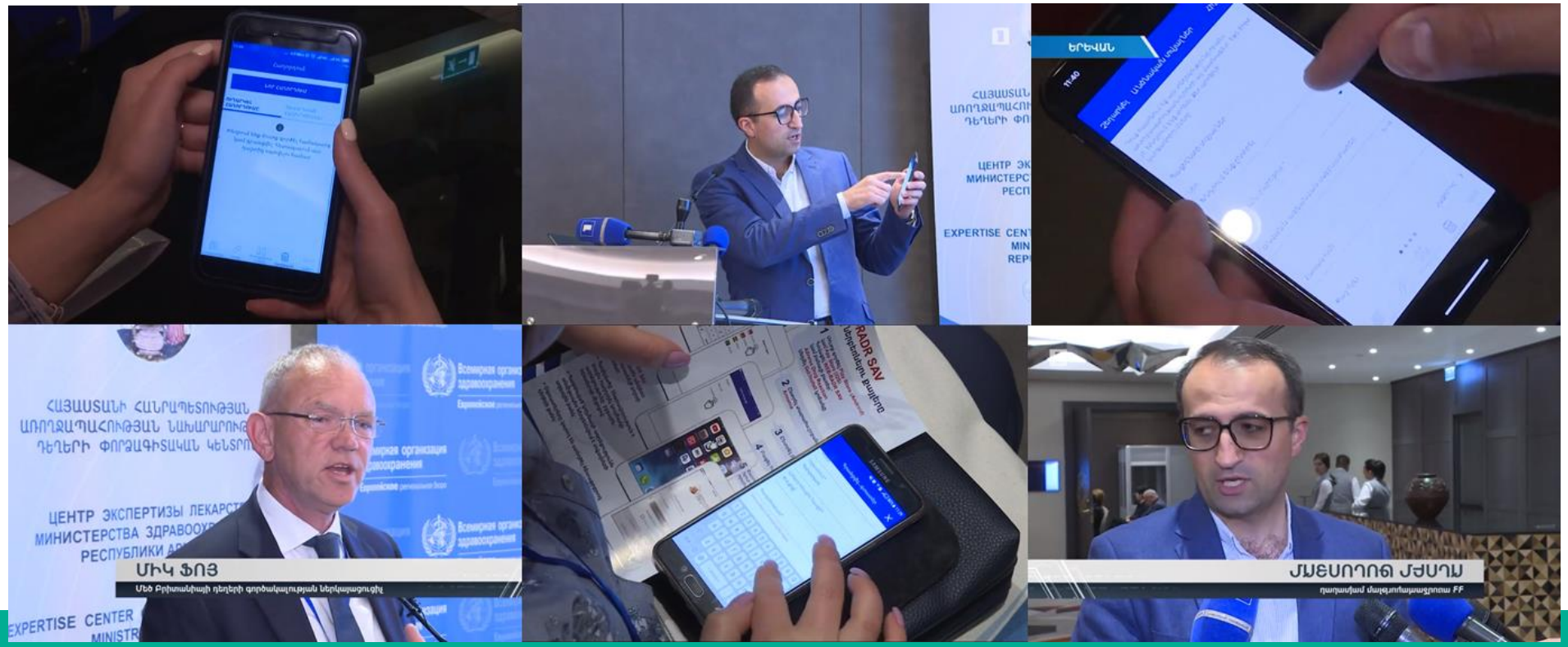
Med Safety mobile app launch

SMART SAFETY SURVEILLANCE

Launched 7 May 2019

Health Minister, Deputy Minister and Press

Wider social media activities



3S - Metrics

Product level

- Increased understanding of safety profile of product

  eg, confirm known safety profile, identify new signals - use in vulnerable populations (children, pregnancy), use in people living with HIV, ethnic/genetic susceptibilities, clinical practice issues

Country level (developed with country)

- Example:
  - Improved ADR reporting by district, reporter category etc
  - Improve quality of ADR reports
  - Capacity to collect, analyse, act
  - Improved visibility and trust in NRA and products

Some of what we've seen so far from a regulatory perspective

- Guidelines or regulations are variable when in place
- Ambition to follow EU or US regulations
- Not enough resource or expertise to monitor compliance or comply at NRA
- Ambition to be compliant ICH standards and aligned with major regulatory systems
  - i.e. 15 day reporting; signal detection; PSURs; and Risk Management Plans (country/region relevant and risk proportionate)
- Need to prioritise for areas of greatest risk

3S BDQ in Armenia – Challenges

- **RESOURCE!**
- Difficulty getting adequate and appropriate staffing/resourcing at NRA, leading to delays in project delivery
- Lack of resource, including expertise in-country, for delivery of goals
- Where available, data is not integrated across stakeholders
- Wants vs needs; short-term & long-term

Summary

The need for enhanced pharmacovigilance systems in LMICs is more pressing than ever

- to enable introduction of **innovative treatments** and vaccines, tackling the major public health challenges
- to promote **public confidence** in medicines safety and effectiveness, supporting uptake of public health interventions

must be sustainable, integrated locally and deliver decisions on benefit risk relevant to local healthcare

Registration introduces the product into the market
Safety keeps the product in the market throughout its life-cycle
– key enabler of ACCESS for PATIENTS

“Operational Transformation” - Medical Device Regulations and MHRA Future Vision

MDR comes into effect in May 2020

Safety features include the need for :

- New reporting timeframes
- Risk planning
- PSURs
- Signal detection
- Inspections

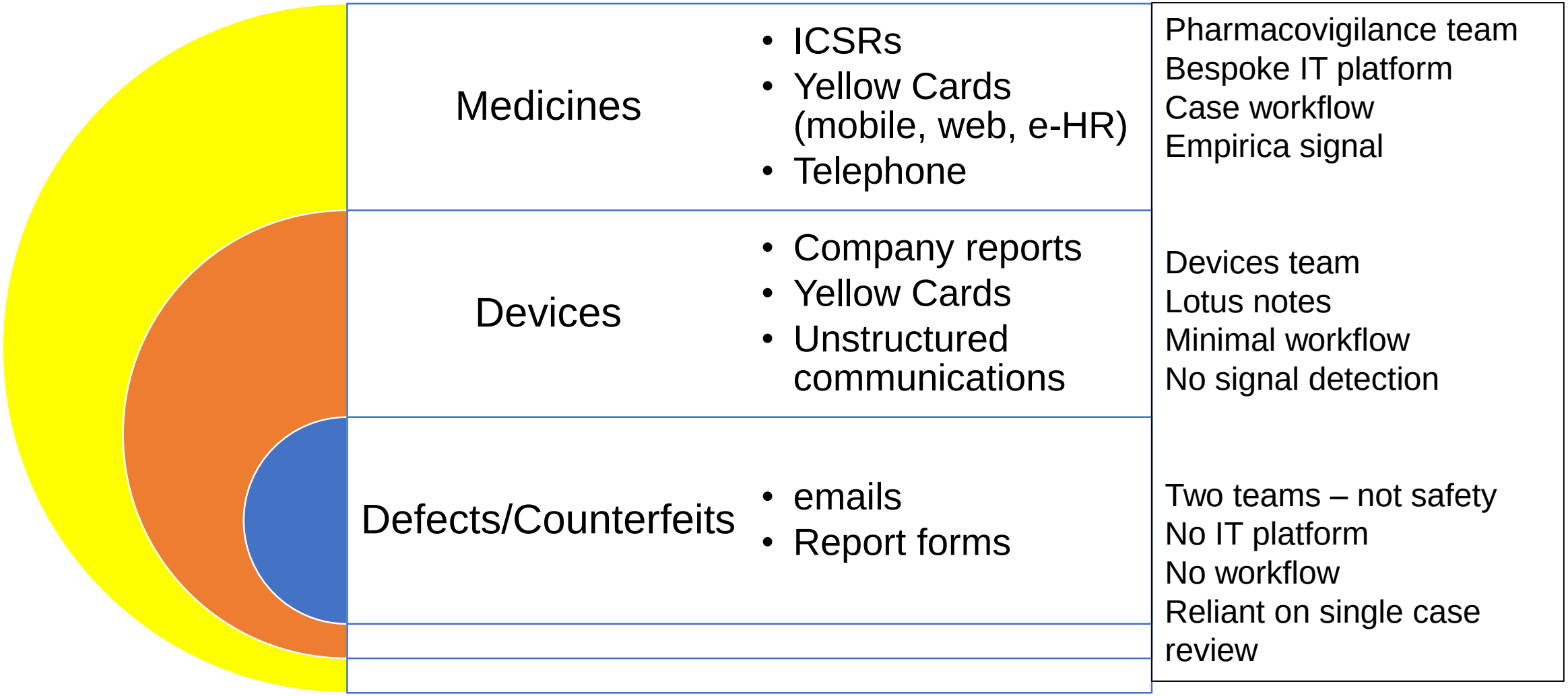
With a greater convergence of vigilance requirements and regulations of medicines and medical devices MHRA are moving toward a common single team for managing vigilance and signal detection with common approaches to risk management and risk communication

MHRA Vigilance Transformation - Vision

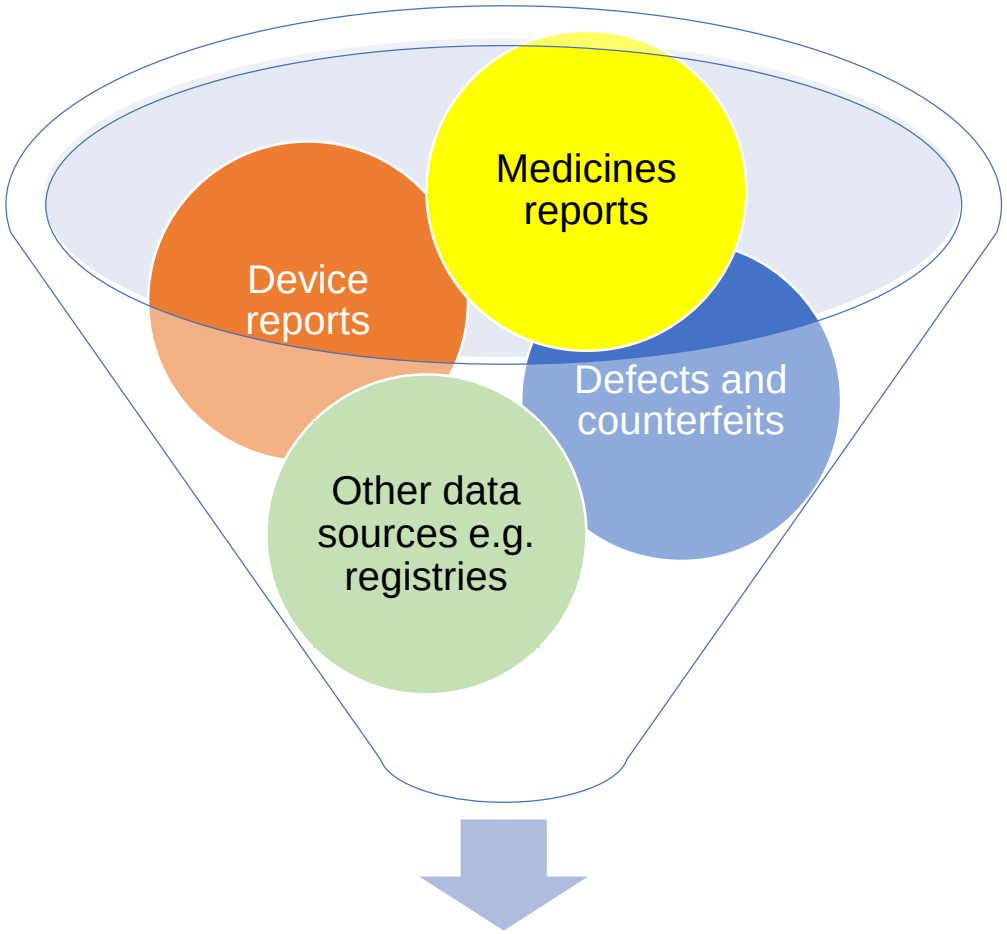
A world leading regulator proactively monitoring and acting on safety insights across the full product lifecycle, with measurable public health outcomes, through:

- Digital and connected data capture, analysis and sharing
- Rapid and robust safety decisions by prioritisation and smart collaboration
- Making the most of innovative vigilance approaches, our safety and surveillance expertise and expanding international capacity building

Current vigilance systems



Future vision



One common integrated vigilance platform

- One team with oversight of all safety issues on medicinal products
- Signal detection across all products
- Common approach to risk assessment and risk management
- Common communications

Summary

- The world is changing and safety is high on the agenda for all countries
- Low and middle income countries rely on help from stringent regulators to implement effective systems
- Patients and many healthcare professionals do not (should not need to) understand the differences between medicines and devices
- With MDR and other drivers for change MHRA are reviewing and changing how we do vigilance
- Brexit will change *how* we do vigilance but not *what* we do as we continue to put patient safety at the forefront of activities

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Any Questions?

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