

Enhancing Pharmacovigilance

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Navigating Compliance and Value for Future

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Outline

- What
- Why
- When
- Stakeholders
- Pharmacoeconomics & Pharmacoepidemiology
- FAERS
- Why PV still matters
- What lies ahead
- Our duty



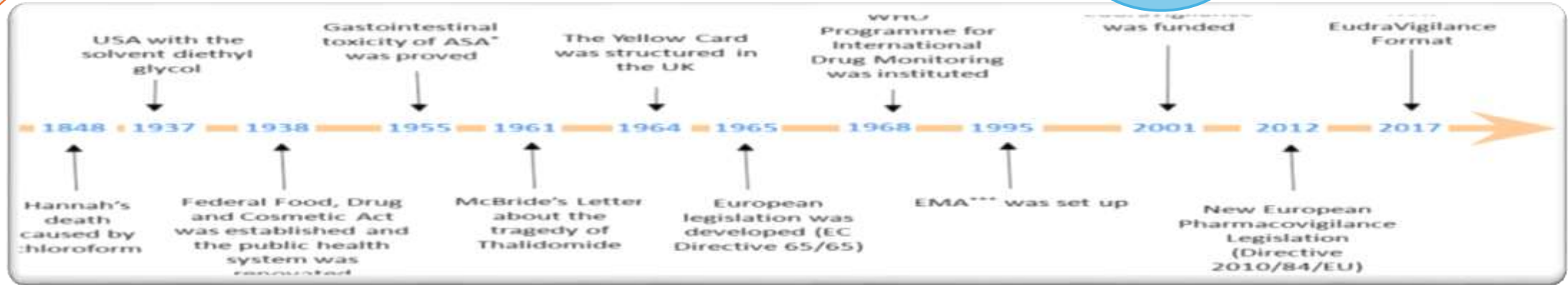
What?

- Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.
 - Throughout the lifecycle
 - Herbals, traditional and complementary medicines, blood products, biologicals, vaccines, *medical devices, digital therapeutics*
 - LoE, counterfeit, off-label, abuse, misuse, overuse, medication errors, interactions with
 - Not just prevention but also mitigation

**Complex interlinked subject
which requires adequate
expertise and technologies**

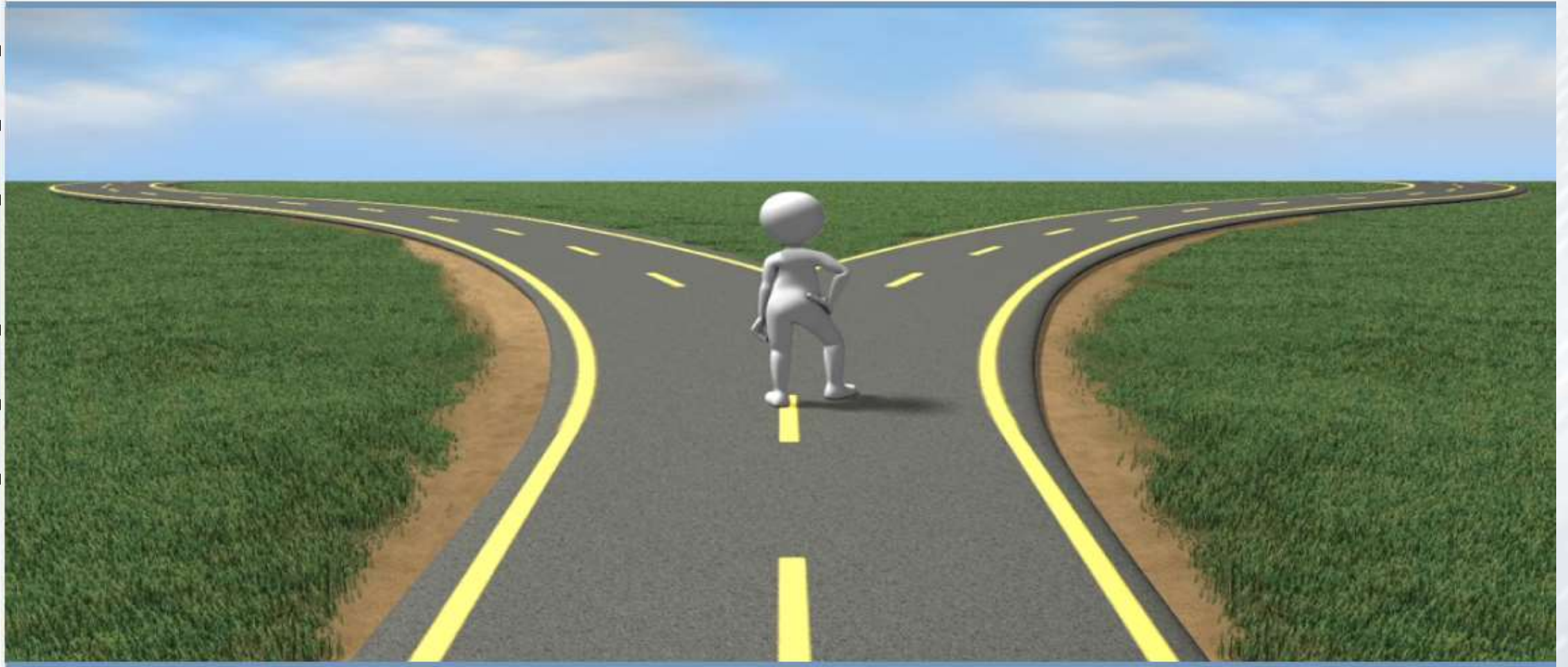
When?

175 Years Young



International Journal of Clinical Pharmacy (2018) 40:744–747

Why?

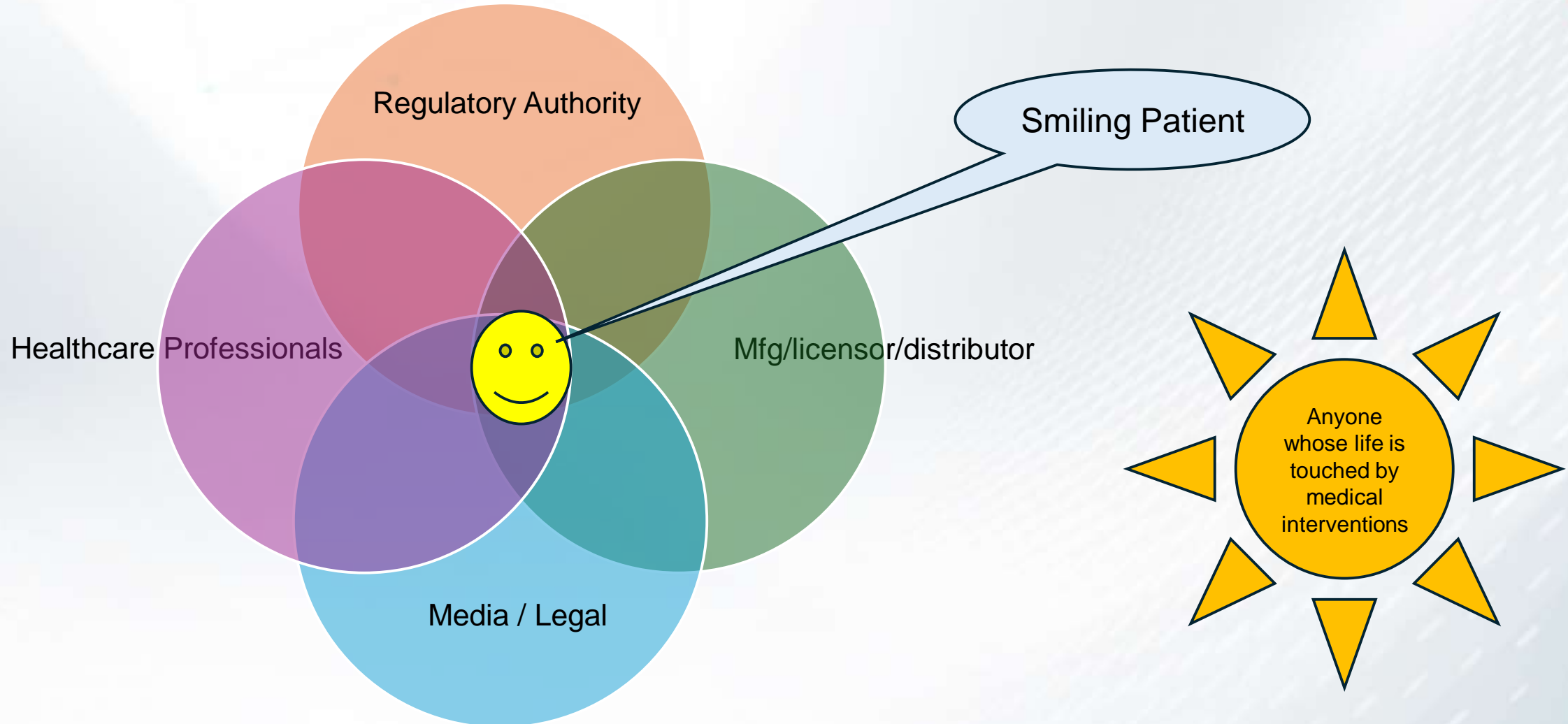


Drug name	Withdrawn	Country	Remarks
Oxyphenisatin (Phenisatin)		Australia, France, Germany, UK, US	Hepatotoxicity. ^[3]
Secobarbital		France, Norway, others.	
Lysergic acid diethylamide (LSD)	1950s–1960s		
Thalidomide			
			hepatotoxicity. ^[12]
			Lack of efficacy as shown by PROWESS-SHOCK study ^{[17][18][19]}
			Serious cutaneous reactions. ^[57]
Ranitidine (Zantac)	2020	Worldwide	Found to spontaneously break down into the carcinogen <i>N</i> -nitrosodimethylamine.

FDA removes Boxed Warning about risk of leg and foot amputations for the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR)

FDA Drug Safety Podcast

Stakeholders



Pharmacoeconomics & Pharmacoepidemiology

Setting ¹	Preventable ADRs	
	Cost	Hospital Stay
Inpatient	€2,851 to €9,015	6.1 ± 2.3 days
Outpatient	€174 to €8,515	9.2 ± 0.2 days

- ADRs were 4th topmost cause of death in USA² But in 2023, not even in top 10
- Median rate of hospital admissions attributable to ADRs in individuals aged ≥ 65 years is ~10%³
- Fatal ADRs represent 1.34% of total ADRs⁴.
 - Top 3 class - Antineoplastic/immunomodulating, neurological and cardiovascular
 - Top 3 individual drugs - denosumab, lenalidomide and thalidomide
- ADRs are significantly underreported worldwide, with estimates of up to 94% not reported by healthcare professionals⁵

1. *Expert Opinion on Drug Safety*, 17(7), 681–695. <https://doi.org/10.1080/14740338.2018.1491547>

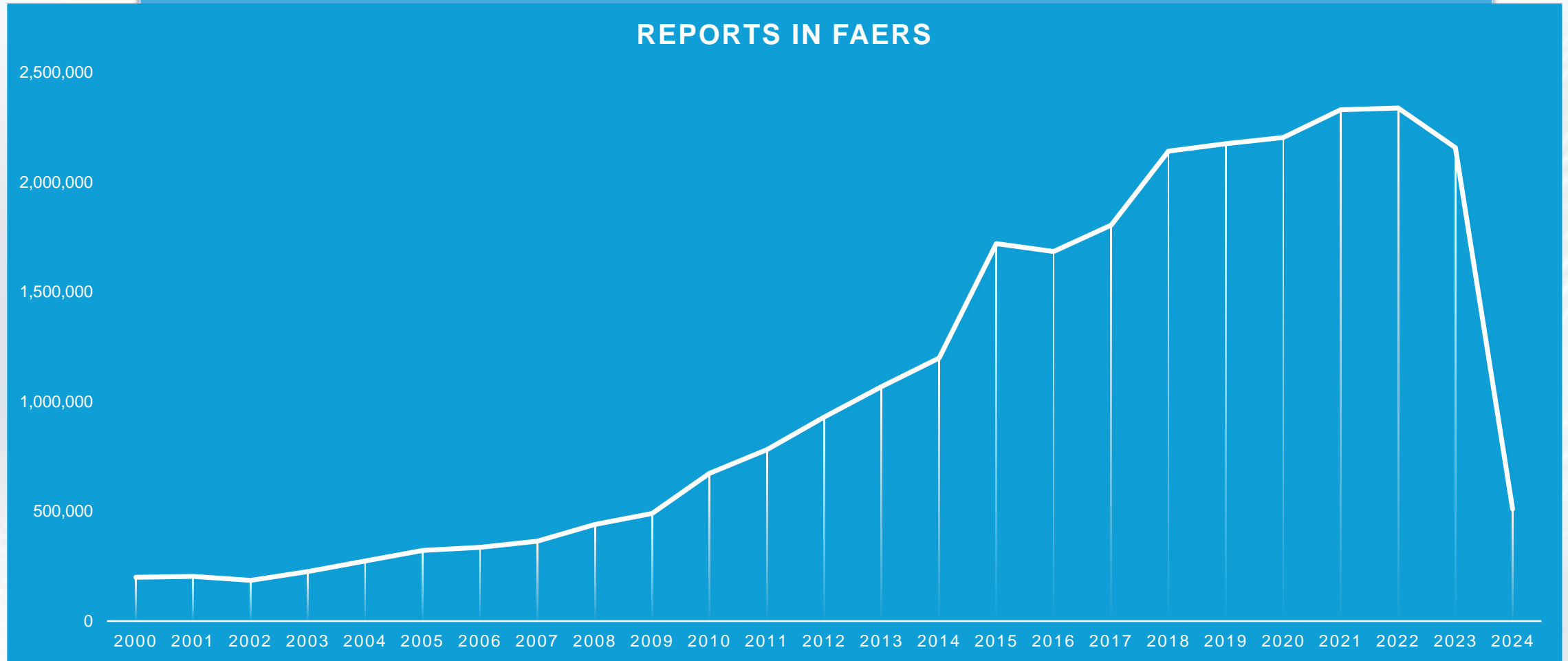
2. *Lancet* 1998 Apr 18;351(9110):1183. doi: 10.1016/S0140-6736(98)23016-9.

3. *Pharmacoepidemiology* **2024**, 3(2), 208-222; <https://doi.org/10.3390/pharma3020013>

4. *British Journal of Clinical Pharmacology*; Volume87, Issue11 November 2021, 4334-4340

5. *Drug Saf.* **2006**, 29, 385–396.

FAERS Data



Cardiac Disorders	16,799
Renal And Urinary Disorders	15,239
Psychiatric Disorders	12,581

Why PV still matters?

- Health Hazard Assessments – deciding class of recall (could/might/unlikely)
- Due diligence
- Product selection
- Ongoing signal detection
- Patient engagement

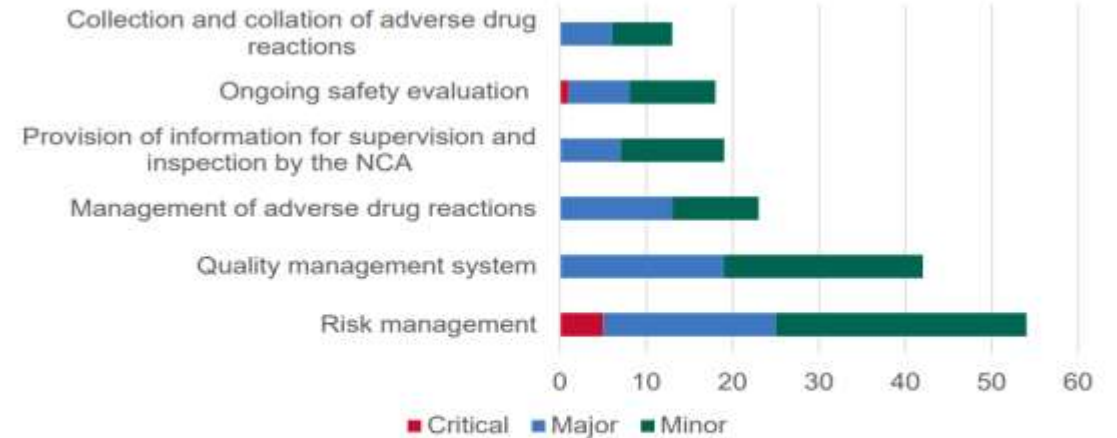
MHRA Findings Report 04Sep2023

4. Inspections over time

The number of inspections per reporting period and the average time spent on inspection since 2012/13 is displayed in Figure 10.



Figure 5 - Findings by topic area



Since 01 April 2012, a total of 94 critical findings have been reported. For the current reporting period, six critical findings were identified from six inspections. This is consistent with previous reporting periods. The number and distribution of critical findings across inspection topics is presented in Figure 6.

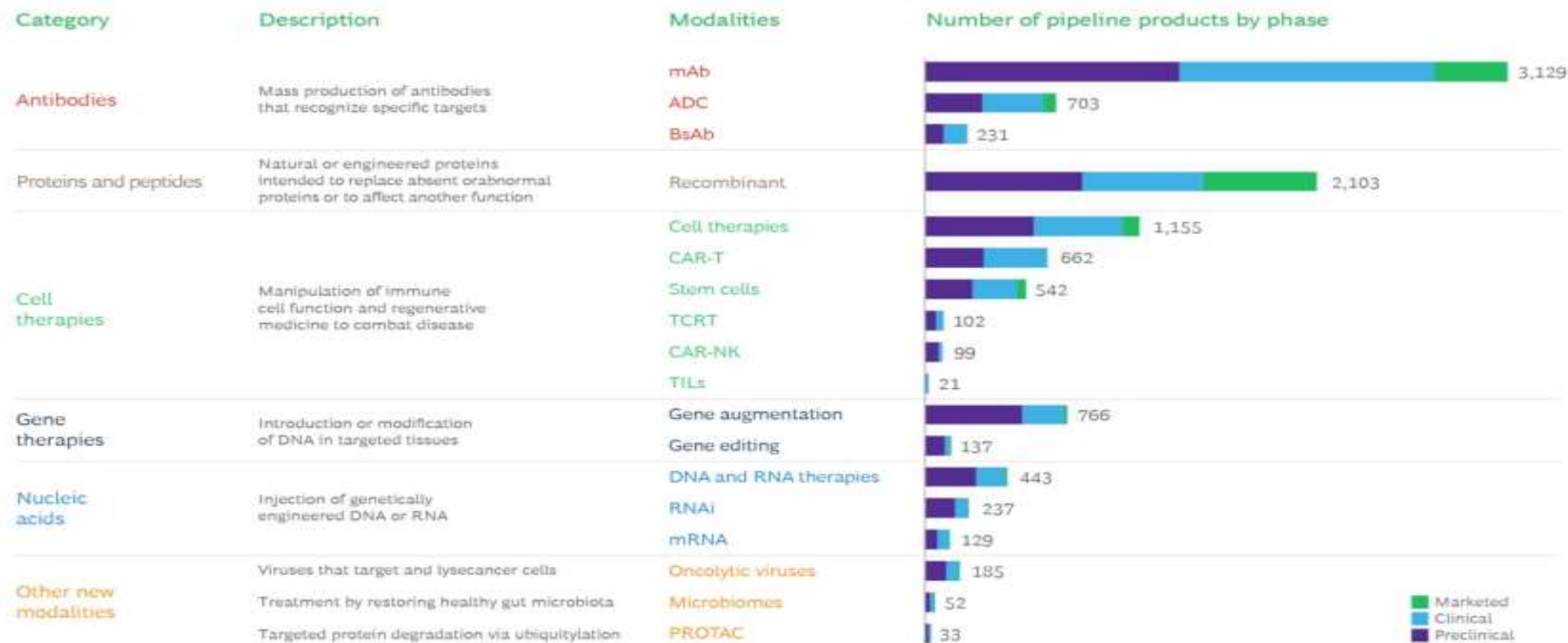
Few critical/major findings

- Inadequate aRMM implementation
- Incomplete/inaccurate signal management
- Deviation and CAPA management
- Delay in providing documents during inspection
- Lack of oversight on MRPs/PSPs
- Delay in filing safety variations

Potential safety issues July 2019–June 2020

Medication	Safety alert
Fluoroquinolones	Concomitant use with ACEI or ARBs contraindicated in patients with moderate to severe renal impairment (CrCl 30 mL/min) and in older patients
Monteluast	Monitor for neuropsychiatric reactions, e.g., nightmares, depression, anxiety, change in behavior, speech impairment (stuttering), and obsessive-compulsive symptoms for all age groups
Hydroxychloroquine	Risk of serious and life-threatening QT prolongation, torsades de pointes, syncope, cardiac arrest, and sudden death, particularly in combination with other medications known to prolong QT interval
Denosumab	Risk of multiple vertebral fractures after stopping, to consider benefits and risks before initiating treatment with denosumab, to cover with an alternative bone sparing agents when stopping denosumab
Methotrexate	Risk of fatal overdose due to inadvertent daily instead of weekly dosing
Empagliflozin	Risk of peri- and postoperative diabetic ketoacidosis in surgical patients with SGLT2 inhibitors, recommend temporary discontinuation before scheduled surgery
Domperidone	No longer licensed or indicated for use in children younger than 12 years old or those weighing less than 35 kg due to lack of efficacy
Ticagrelor	Safety signal of severe cutaneous adverse reactions

Exhibit 3 - Definition and Pipeline Snapshot by Modality



Sources: Evaluate Pharma; BCG analysis.

Note: ADC = antibody-drug conjugate; BsAb = bispecific antibody; CAR-NK = chimeric antigen receptor-transduced natural killer cell; CAR-T = chimeric antigen receptor T cell; mAb = monoclonal antibody; PROTAC = proteolysis-targeting chimera; TCRT = T-cell receptor therapy; TIL = tumor-infiltrating lymphocyte.

What lies ahead?

- Ecopharmacovigilance
 - Science and activities concerning detection, assessment, understanding and prevention of *adverse effects or other problems related to the presence of pharmaceuticals in the environment*, which affect both human and the other animal species
- Artificial Intelligence/Machine Learning/Automation
 - CIOMS Working Group XIV – Artificial Intelligence in Pharmacovigilance – by 2027
 - AE detection
 - Triage and QC
 - Literature review
 - Automated reporting
 - Signal detection
- Social Media

Collaboration b/w regulatory agencies & pharmaceutical companies to establish the standard guidelines and safeguard the ethical and responsible use of AI technology in pharmacovigilance.

Our duty

- Create Awareness
- Change Attitude/Perception towards Benefit & Risk
- More proactive approach to PV
- PV as more of a science, less of a compliance

Communicate, Communicate & Communicate

Medicine, the only profession that labors incessantly to destroy the reason for its existence - James Bryce



THANK YOU