Pharmacovigilance: Some basics of drug safety and special aspects for oncologists/hematologists

Swiss Oncology & Hematology Congress SOHC

23 November 2023

Thomas Stammschulte
Leiter Pharmakovigilanz

Schweizerisches Heilmittelinstitut
Institut suisse des produits thérapeutiques
Istituto svizzero per gli agenti terapeutici
Swiss Agency for Therapeutic Products

Hallerstrasse 7, 3012 Bern
www.swissmedic.ch

Disclosure statement

- Full-time employee at Swissmedic, Bern, Switzerland
- No relationships to disclose.

Disclaimer

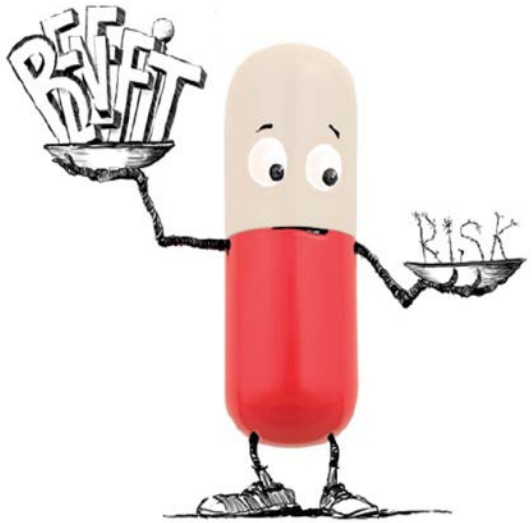
The information within this presentation represents the views of the presenter, not necessarily those of Swissmedic or any other referenced organization.

Definition of Pharmacovigilance

WHO:

Pharmacovigilance (PV) is defined as the science and activities relating to the **detection**, **assessment**, **understanding** and **prevention** of **adverse effects** or any other drug-related problems.

→ Pharmacovigilance aims to ensure that all available medicines have a favourable benefit-risk profile



Benefit-risk(harm)-assessment of medicines

Data sources

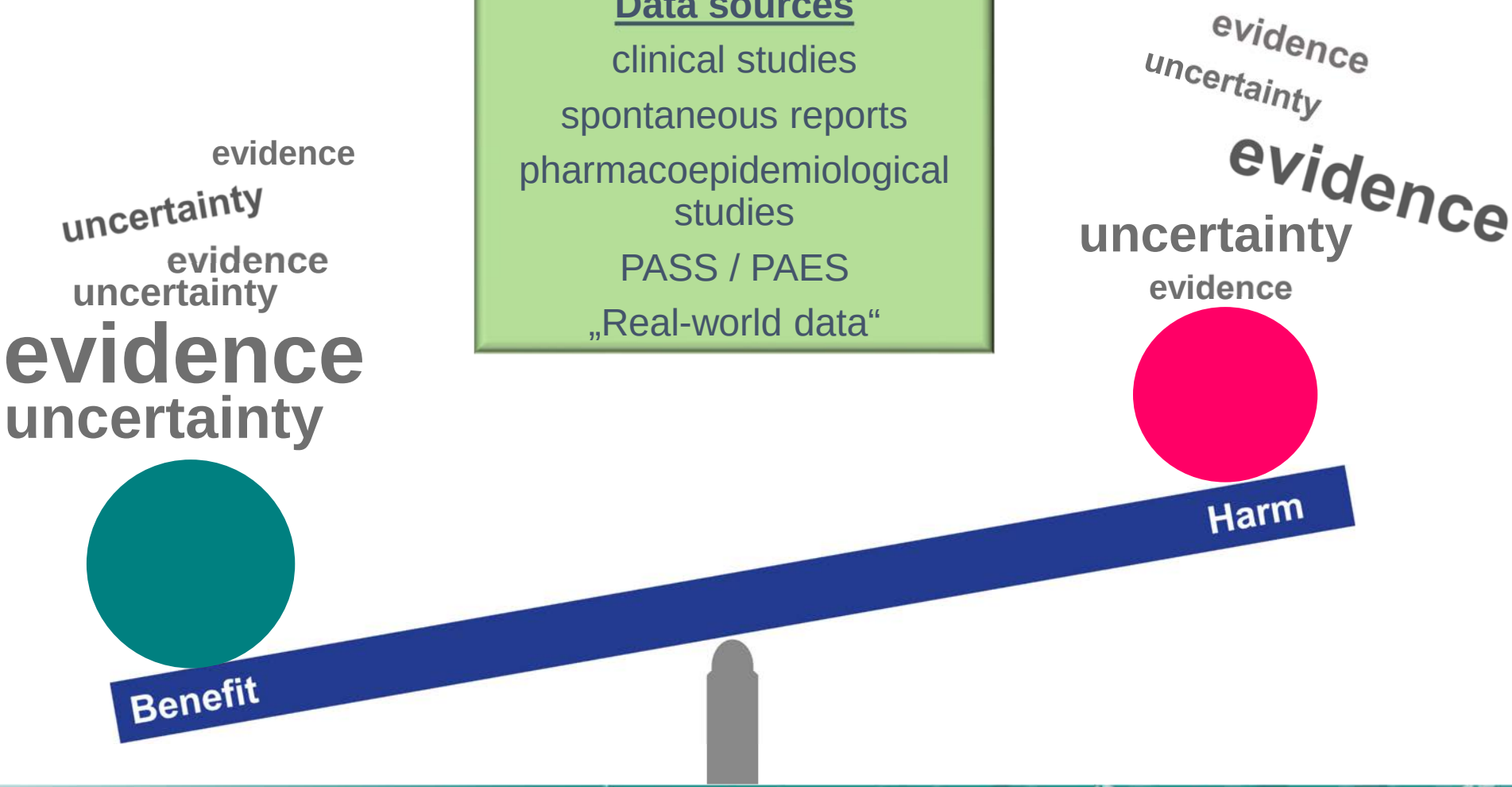
clinical studies

spontaneous reports

pharmacoepidemiological studies

PASS / PAES

„Real-world data“



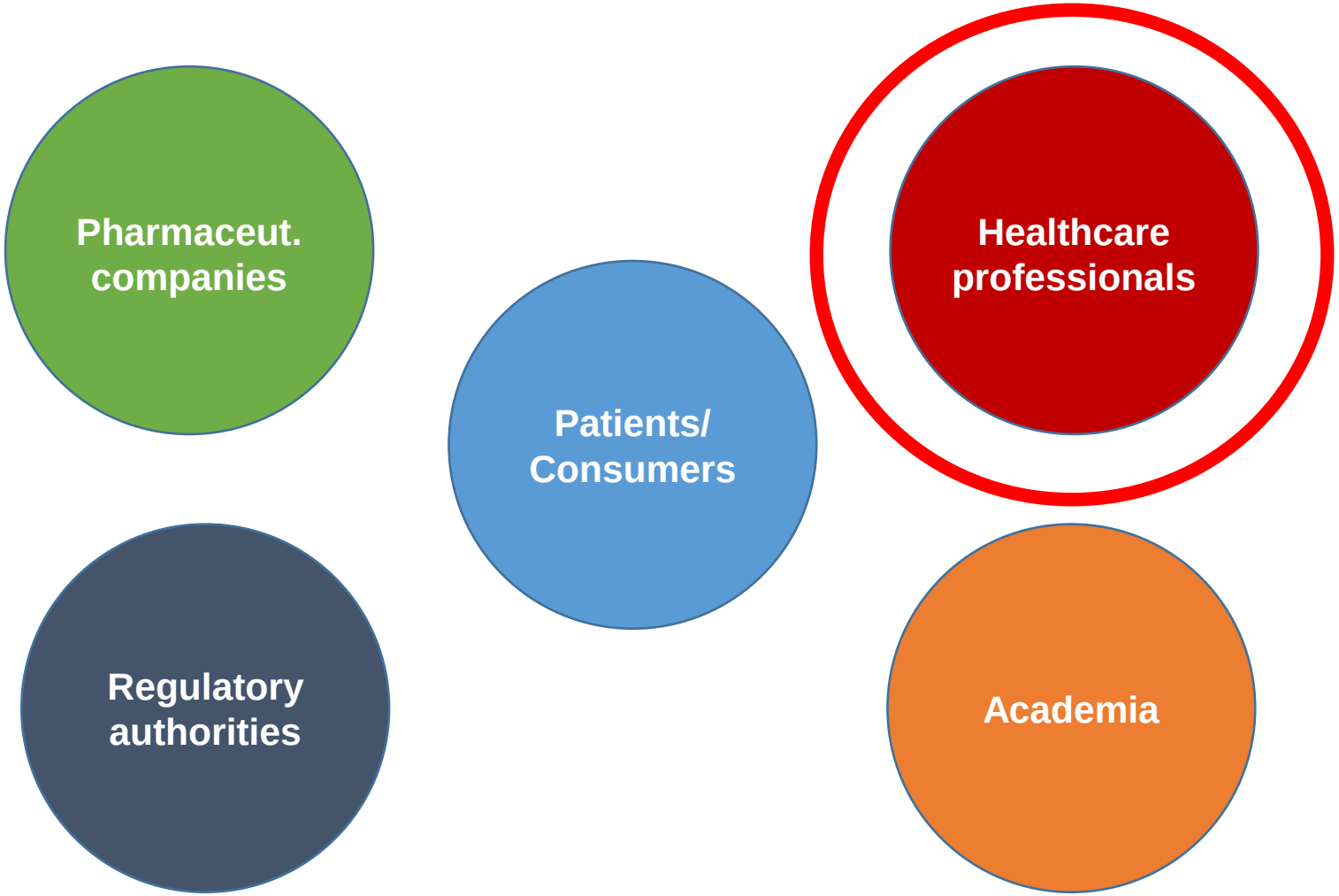
Definition «Adverse drug reaction» (ADR)

A response to a medicinal product which is **noxious** and **unintended**. Adverse reactions may arise from use of the product within or outside the terms of the marketing authorisation… .

Use outside the marketing authorisation includes **off-label use**, **overdose**, **misuse**, **abuse** and **medication errors**.

(Definition EMA GVP)

Parties involved in pharmacovigilance



Potential knowledge gaps at market approval of medicines

- rare / very rare ADRs (< 0.1%)
- Long-term use / late effects
- specific populations (e.g. children, pregnant women, elderly, polymorbid patients)
- drug interactions
- off-label-use, misuse
- usage in daily practice
- monitoring

► surveillance following market launch necessary for the identification of potential risks

How many study participants are needed to detect an ADR?

Incidence of ADR		Number of exposed participants
1 : 10	very common	30
1 : 100	common	300
1 : 1000	uncommon	3.000
1 : 10.000	rare	30.000
1 : 100.000	very rare	300.000

→ **rare and very rare ADRs are usually not detected before approval**

Example: mRNA vaccines / anaphylaxis

Table 1
Characteristics, components, and clinical trials of the vaccines BNT162b2, mRNA-1273, and AZD1222 for COVID-19 prevention.

	BNT162b2	mRNA-1273
Type of vaccine	mRNA vaccine	mRNA vaccine
Active component	mRNA encoding the viral spike (S) glycoprotein of SARS-Cov-2	mRNA encoding the viral spike (S) glycoprotein of SARS-Cov-2
Carrier or vector	PEGylated lipid nanoparticle	PEGylated lipid nanoparticle
Excipients[†]	• ALC-0315 = (4-hydroxybutyl) azanediyl) bis (hexane-6,1-diyl) bis(2-hexyldecanoate) • ALC-0159 = 2-[(**polyethylene glycol**) **2000**] –N,N-ditetradecylacetamide • 1,2-distearoyl-sn-glycero-3-phosphocholine • Cholesterol • Potassium chloride • Potassium dihydrogen phosphate • Sodium chloride • Disodium hydrogen phosphate dihydrate • Sucrose • Water for injections	• SM-102 • 1,2- dimyristoyl-rac-glycero-3-**methoxy polyethylene glycol-2000 [PEG2000** -DMG] • 1,2-distearoyl-sn-glycero-3-phosphocholine • Cholesterol • **Tromethamine** • **Tromethamine hydrochloride** • Acetic acid • Sodium acetate • Sucrose
Phase-III-trials		
Number of participants	44,000	30,000
Randomization (vaccine:placebo)	1:1	1:1
Regimen	Two doses	Two doses
Effectiveness after second dose (%)	95	94.1

[†] Potential triggers of allergic reactions are highlighted in bold in the excipient lists of the vaccines.

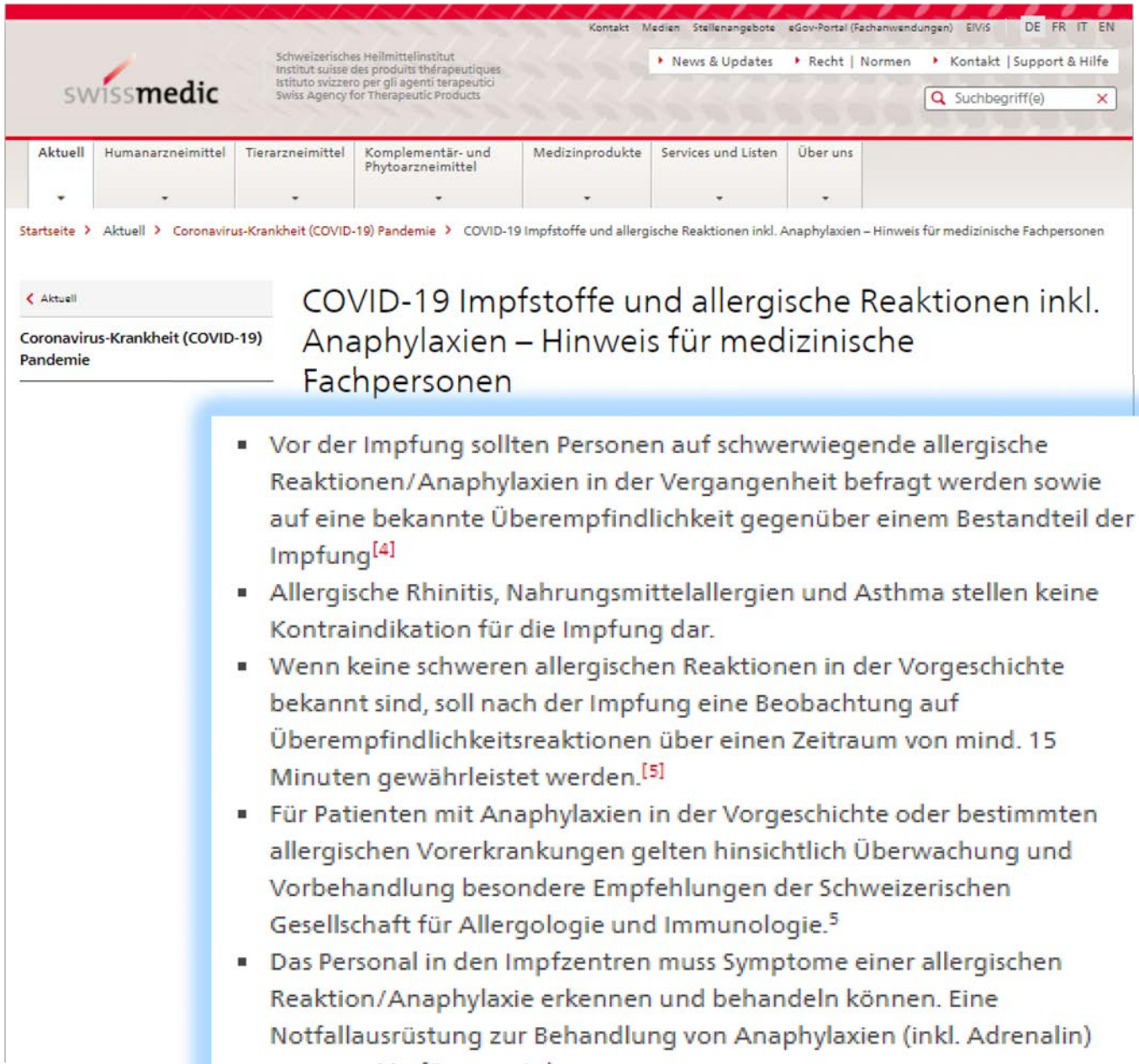
Cabanillas, Novak. Allergology International 70 (2021) 313-318.

Example: mRNA vaccines / anaphylaxis

Table 2
Summary of the reports from the Center for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA) regarding the anaphylactic reactions to the COVID-19 vaccines BNT162b2 and mRNA-1273.

	BNT162b2 Comirnaty	mRNA-1273 Spikevax
Time period evaluated	December 14, 2020 – December 23, 2020	December 21, 2020 – January 10, 2021
Doses administrated (first dose)	1,893,360	4,041,396
Cases of adverse reactions reviewed	175	108
Cases of anaphylaxis (Brighton Collaboration case definition criteria)	21	10
Females (%) among anaphylaxis cases	90	100
Anaphylactic cases per million vaccine doses	11.1	2.5

Cabanillas, Novak. Allergology International 70 (2021) 313-318.


Kontakt Medien Stellenangebote eGov-Portal (Fachanwendungen) EIVis
DE FR IT EN
swissmedic
Schweizerisches Heilmittelinstitut
Institut suisse des produits thérapeutiques
Istituto svizzero per gli agenti terapeutici
Swiss Agency for Therapeutic Products
News & Updates
Recht | Normen
Kontakt | Support & Hilfe
Suchbegriff(e)
Aktuell
Humanarzneimittel
Tierarzneimittel
Komplementär- und Phytoarzneimittel
Medizinprodukte
Services und Listen
Über uns
Startseite › Aktuell › Coronavirus-Krankheit (COVID-19) Pandemie › COVID-19 Impfstoffe und allergische Reaktionen inkl. Anaphylaxien – Hinweis für medizinische Fachpersonen
Aktuell
Coronavirus-Krankheit (COVID-19) Pandemie
COVID-19 Impfstoffe und allergische Reaktionen inkl. Anaphylaxien – Hinweis für medizinische Fachpersonen
Vor der Impfung sollten Personen auf schwerwiegende allergische Reaktionen/Anaphylaxien in der Vergangenheit befragt werden sowie auf eine bekannte Überempfindlichkeit gegenüber einem Bestandteil der Impfung[4]
Allergische Rhinitis, Nahrungsmittelallergien und Asthma stellen keine Kontraindikation für die Impfung dar.
Wenn keine schweren allergischen Reaktionen in der Vorgeschichte bekannt sind, soll nach der Impfung eine Beobachtung auf Überempfindlichkeitsreaktionen über einen Zeitraum von mind. 15 Minuten gewährleistet werden.[5]
Für Patienten mit Anaphylaxien in der Vorgeschichte oder bestimmten allergischen Vorerkrankungen gelten hinsichtlich Überwachung und Vorbehandlung besondere Empfehlungen der Schweizerischen Gesellschaft für Allergologie und Immunologie.5
Das Personal in den Impfzentren muss Symptome einer allergischen Reaktion/Anaphylaxie erkennen und behandeln können. Eine Notfallausrüstung zur Behandlung von Anaphylaxien (inkl. Adrenalin) muss zur Verfügung stehen.

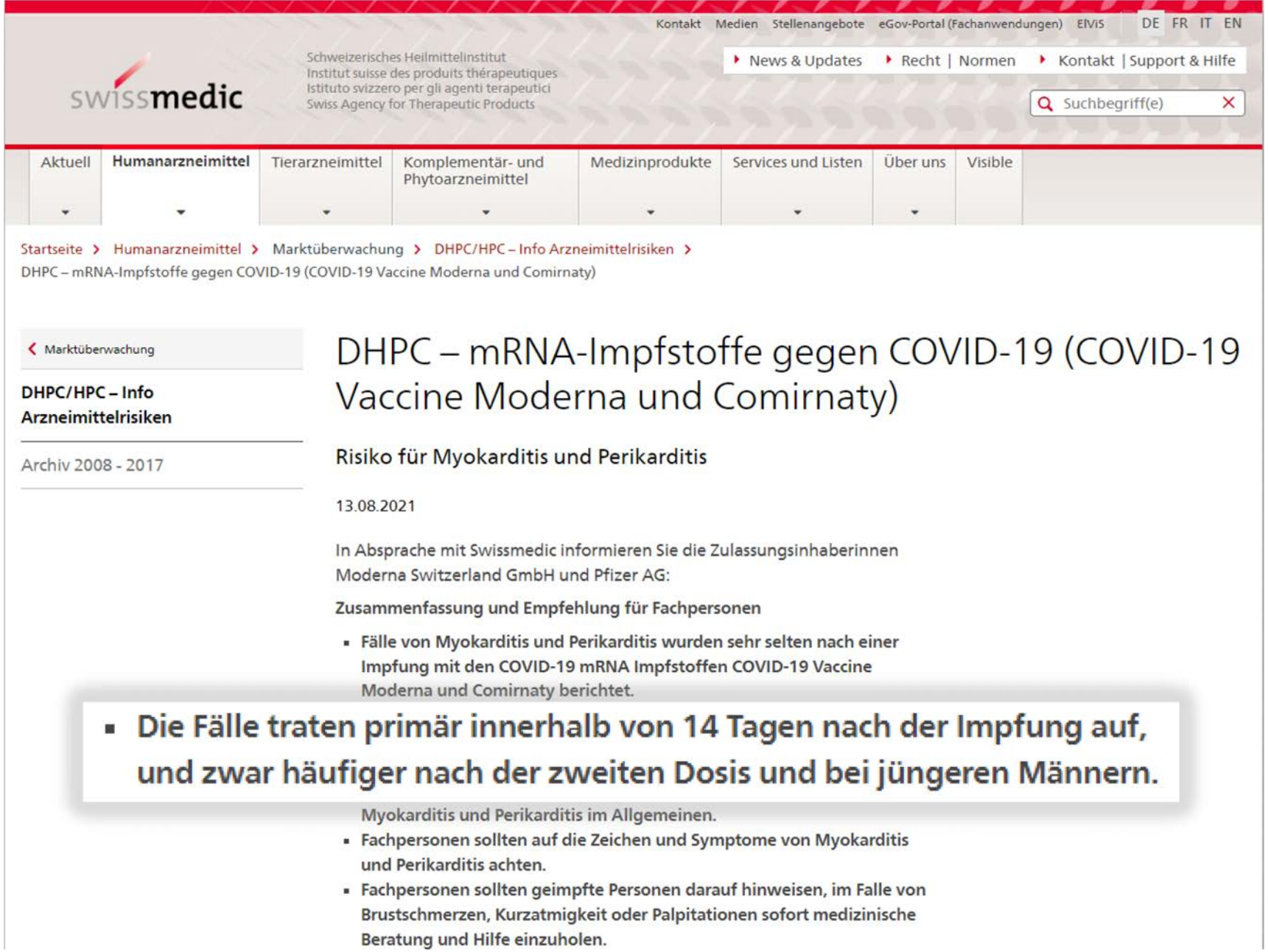
Frequencies of ADRs are defined as...

very common	(≥ 1/10)
common	(≥ 1/100 to < 1/10)
uncommon	(≥ 1/1,000 to < 1/100)
rare	(≥ 1/10,000 to < 1/1,000)
very rare	(< 1/10,000)
not known	(cannot be estimated from the available data)

Potential knowledge gaps at market approval of medicines

- rare / very rare ADRs (< 0.1%)
- Long-term use / late effects
- specific populations (e.g. children, pregnant women, elderly, polymorbid patients)
- drug interactions
- off-label-use, misuse
- usage in daily practice
- monitoring

► surveillance following market launch necessary for the identification of potential risks



Kontakt Medien Stellenangebote eGov-Portal (Fachanwendungen) EIViS DE FR IT EN

swissmedic

Schweizerisches Heilmittelinstitut
Institut suisse des produits thérapeutiques
Istituto svizzero per gli agenti terapeutici
Swiss Agency for Therapeutic Products

News & Updates | Recht | Normen | Kontakt | Support & Hilfe

Suchbegriff(e)

Aktuell | Humanarzneimittel | Tierarzneimittel | Komplementär- und Phytoarzneimittel | Medizinprodukte | Services und Listen | Über uns | Visible

Startseite > Humanarzneimittel > Marktüberwachung > DHPC/HPC – Info Arzneimittelrisiken >
DHPC – mRNA-Impfstoffe gegen COVID-19 (COVID-19 Vaccine Moderna und Comirnaty)

Marktüberwachung

DHPC/HPC – Info Arzneimittelrisiken

Archiv 2008 - 2017

DHPC – mRNA-Impfstoffe gegen COVID-19 (COVID-19 Vaccine Moderna und Comirnaty)

Risiko für Myokarditis und Perikarditis

13.08.2021

In Absprache mit Swissmedic informieren Sie die Zulassungsinhaberinnen Moderna Switzerland GmbH und Pfizer AG:

Zusammenfassung und Empfehlung für Fachpersonen

- **Fälle von Myokarditis und Perikarditis wurden sehr selten nach einer Impfung mit den COVID-19 mRNA Impfstoffen COVID-19 Vaccine Moderna und Comirnaty berichtet.**
- **Die Fälle traten primär innerhalb von 14 Tagen nach der Impfung auf, und zwar häufiger nach der zweiten Dosis und bei jüngeren Männern.**

Myokarditis und Perikarditis im Allgemeinen.

- **Fachpersonen sollten auf die Zeichen und Symptome von Myokarditis und Perikarditis achten.**
- **Fachpersonen sollten geimpfte Personen darauf hinweisen, im Falle von Brustschmerzen, Kurzatmigkeit oder Palpitationen sofort medizinische Beratung und Hilfe einzuholen.**

Potential knowledge gaps at market approval of medicines

- rare / very rare ADRs (< 0.1%)
- Long-term use / late effects
- specific populations (e.g. children, pregnant women, elderly, polymorbid patients)
- drug interactions
- off-label-use, misuse
- usage in daily practice
- monitoring

► surveillance following market launch necessary for the identification of potential risks

WICHTIGE MITTEILUNG

Juli 2016

Low-Dose Methotrexat bei rheumatoider Arthritis und Psoriasis: ANWENDUNG NUR 1 MAL WÖCHENTLICH Massnahmen, um akzidentelle Überdosierungen durch tägliche Anwendung zu verhindern

Zusammenfassung

- Trotz Warnhinweisen in den Arzneimittelinformationen und wiederholter Fachpublikationen ereignen sich weiterhin schwerwiegende akzidentelle Überdosierungen von Low-Dose Methotrexat durch tägliche Fehlanwendung bei Patienten mit rheumatoider Arthritis oder Psoriasis.
- Das vorgeschriebene wöchentliche Intervall widerspricht der Gewohnheit, Medikamente, besonders Tabletten, täglich anzuwenden.
- Gemeinsam mit Swissmedic, der Stiftung für Patientensicherheit und den betroffenen Patientenorganisationen wurden nun weitere Massnahmen erarbeitet, damit die korrekte, 1x wöchentliche Gabe von Low-Dose Methotrexat allen Beteiligten bekannt gemacht und im Alltag eingehalten wird. **Ihr Erfolg hängt von der konsequenten Umsetzung durch alle Betroffenen im Alltag ab. Bitte unterstützen Sie uns dabei.**

Spontaneous reporting:
early warning system for the detection of drug-safety problems

- systematic collection and evaluation of suspected ADRs reported spontaneously (= outside of studies) by healthcare professionals of patients/consumers
  - ➢ detection of unknown and/or rare ADRs
  - ➢ detection of ADRs in association with new medicines (< 5 years on the market)
  - ➢ ongoing surveillance of well-established medicines
  - ➢ inclusion of the total exposed population / all medicines («real-world»)
  - ➢ generation of signals: starting point for additional studies / evaluation

Some shortcomings of spontaneous reporting

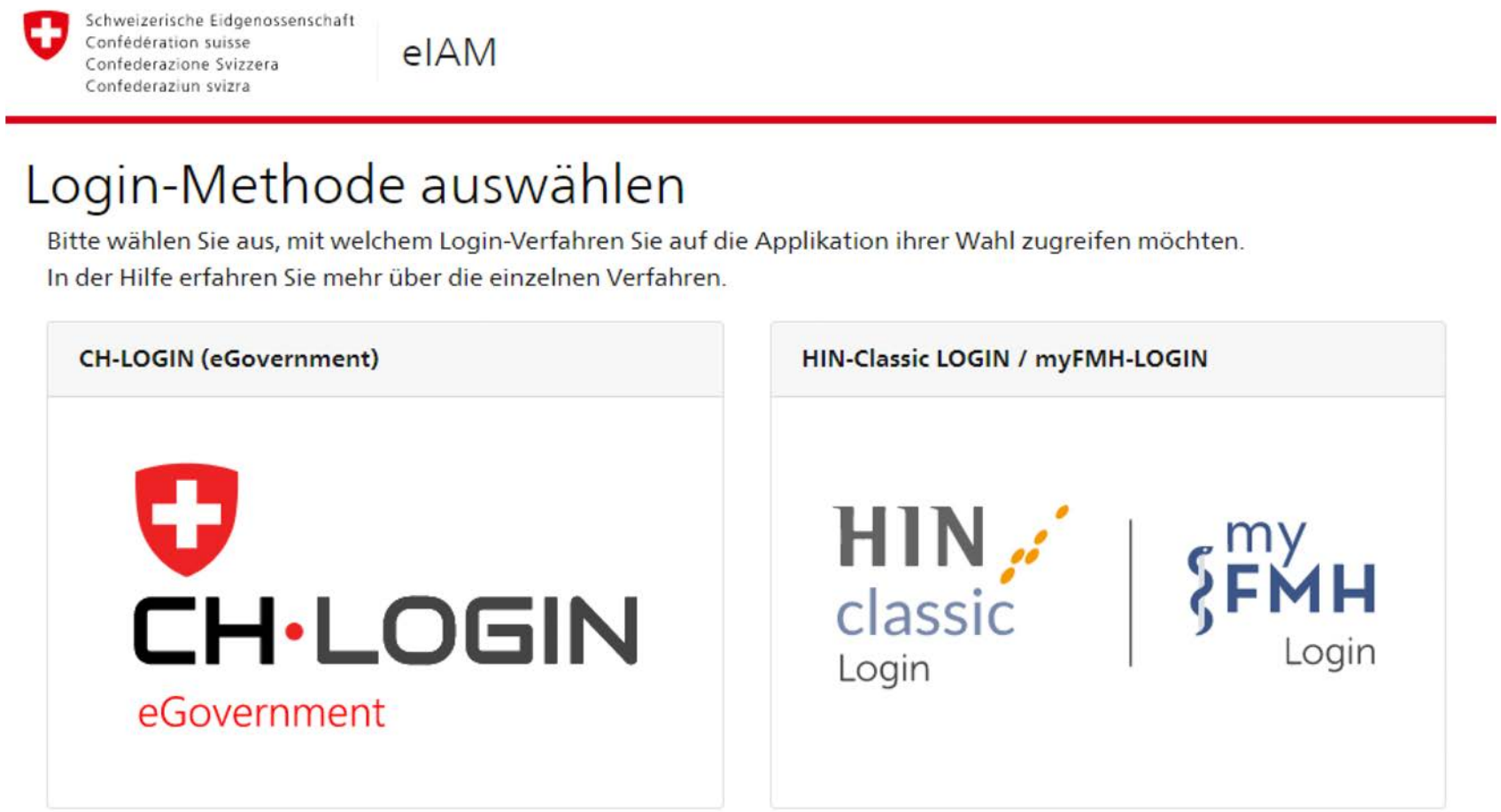
- no calculation of ADR incidences possible
- no valid drug-drug comparisons possible
- poorly documented reports are common
- high underreporting rate
- reporting can be biased by media / publication
- Weber effect (peak in reporting within the first two years after approval followed by a decline of reports)

Therapeutic Products Act, TPA, Art. 59

[3] Any person who professionally dispenses therapeutic products or administers them to humans or animals or who is entitled to do so as medical personnel must notify the Agency of any serious and previously unknown adverse effects and incidents, observations of other serious and previously unknown facts or quality defects that are of significance for drug safety.[138]

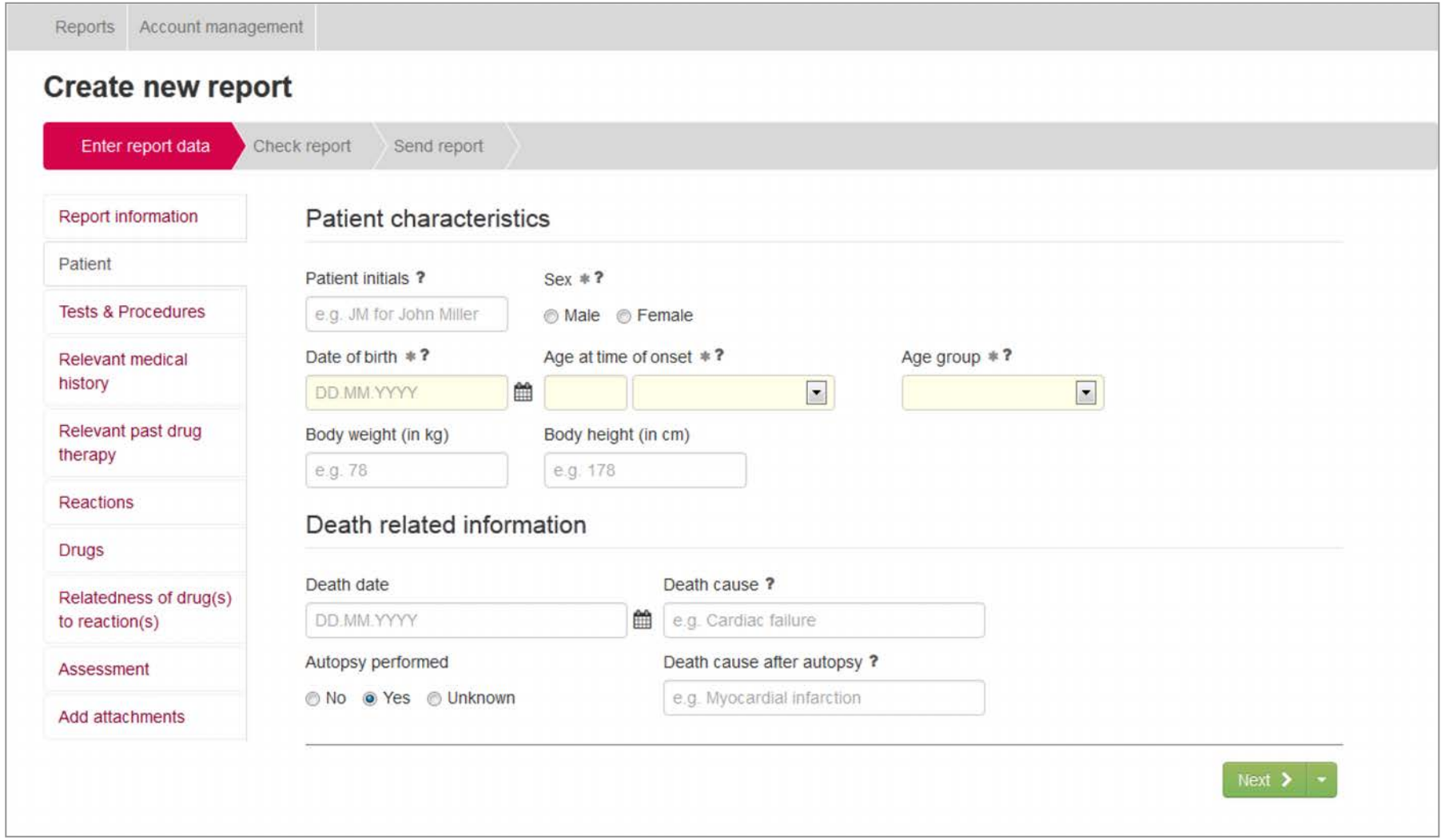
4 Consumers, patients and their organisations as well as interested third parties, may notify the Agency for adverse events and reactions with therapeutic products.

ElViS: Electronic Vigilance Reporting System

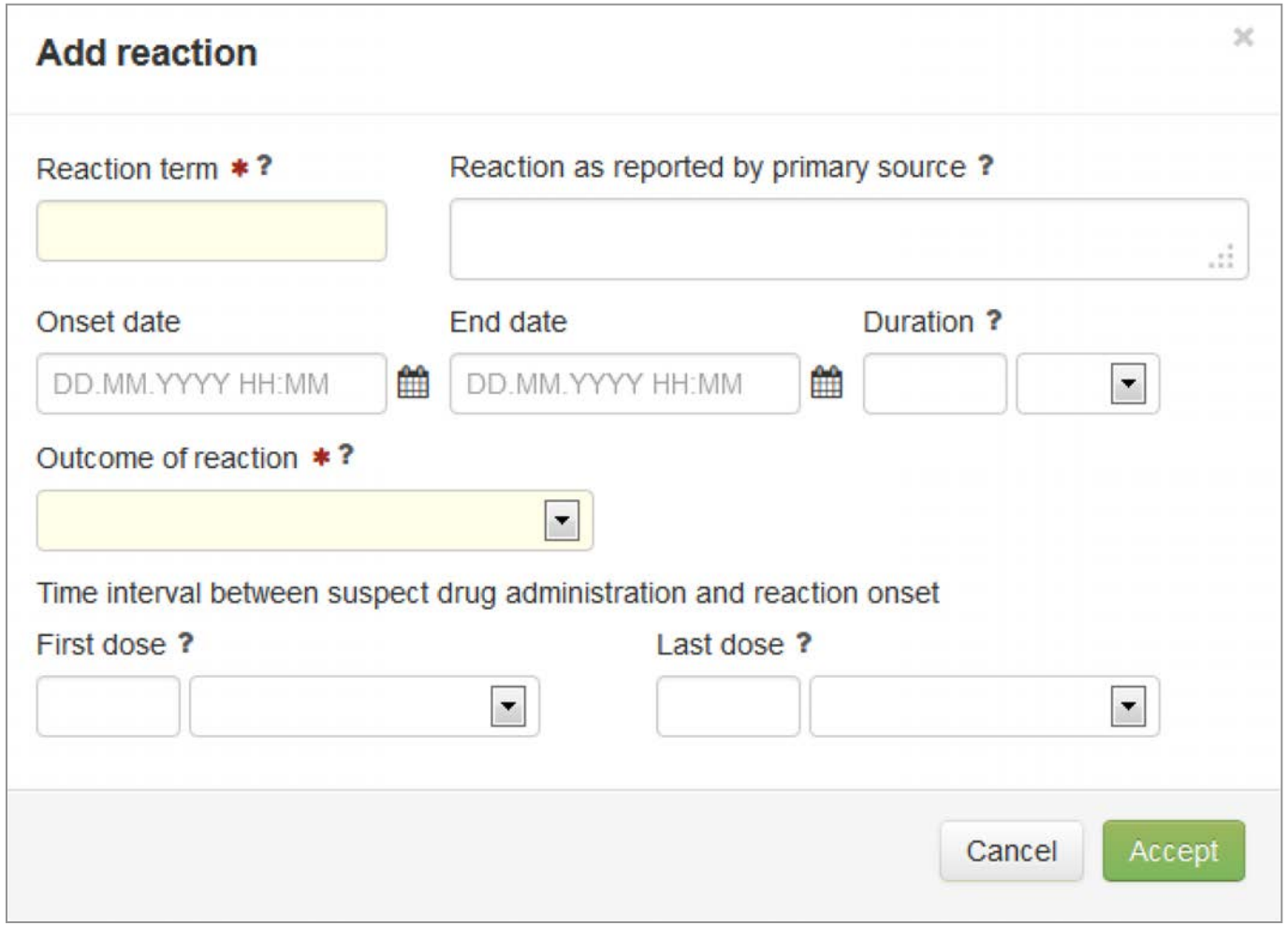


https://www.swissmedic.ch/swissmedic/de/home/services/egov-services/elvis.html

ElViS: Electronic Vigilance Reporting System



ElViS: Electronic Vigilance Reporting System



Drug Safety
https://doi.org/10.1007/s40264-023-01319-y

ORIGINAL RESEARCH ARTICLE

Hospitalisations Related to Adverse Drug Reactions in Switzerland in 2012–2019: Characteristics, In-Hospital Mortality, and Spontaneous Reporting Rate

Patrick E. Beeler[1,2] · Thomas Stammschulte[3] · Holger Dressel[1]

Accepted: 9 May 2023

Approximately 2.3% of admissions are caused by ADRs, and the related in-hospital mortality is 2.2%. The estimated reporting rate is 5% and 12%, respectively, which emphasises the need for improved ADR reporting in hospitals.

Abstract

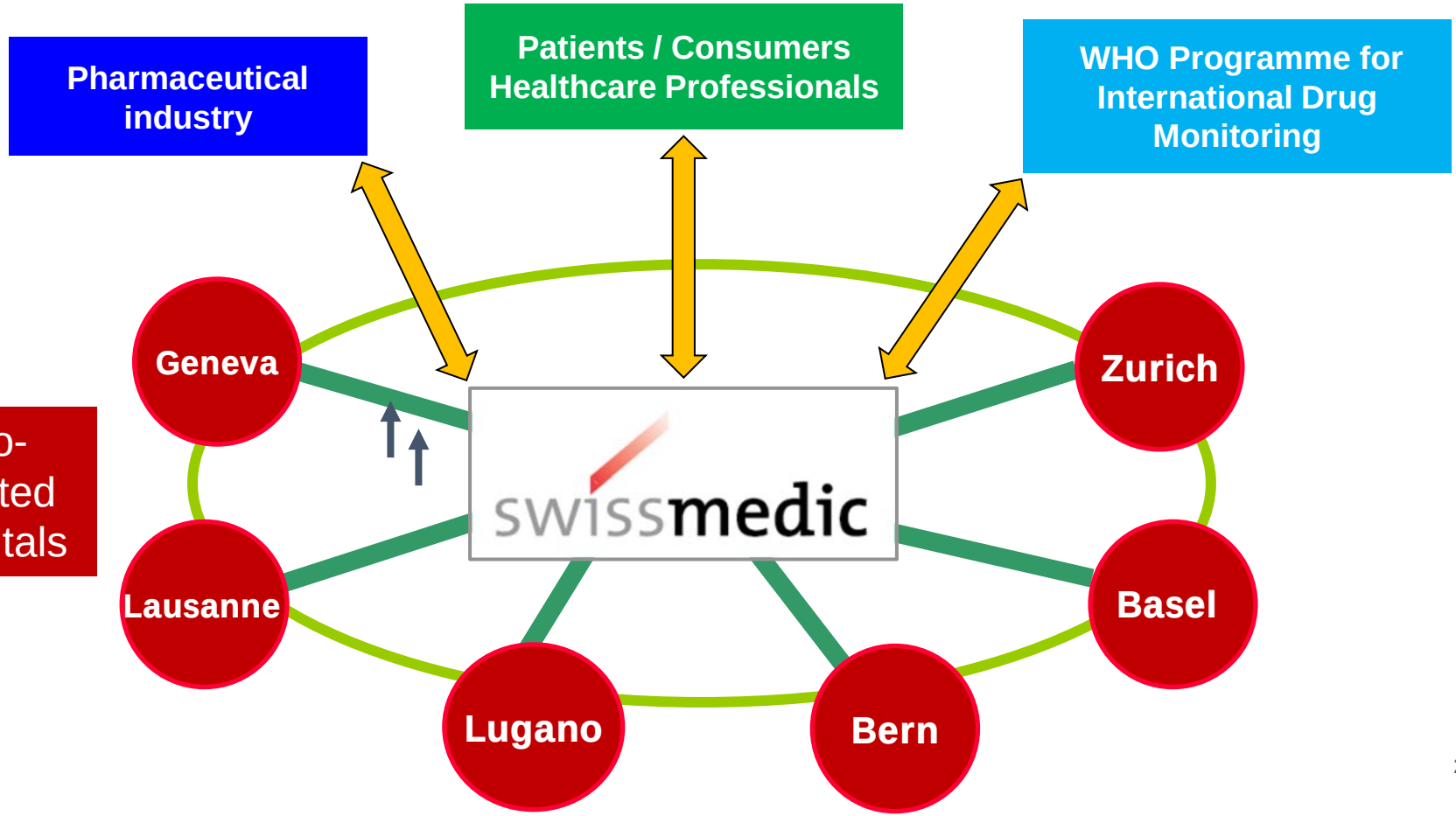
Introduction ...lisation and death. This s... ...nd estimates the spontane... ...ally obliged to report AD...

Methods Th... ...tical Office. ICD-10 codi... ...afety reports (ICSRs) collected in the Swiss spontaneous reporting system during the same period were considered.

Results Among 11,240,562 inpatients, 256,550 (2.3%) were admitted for ADRs, 132,320 (51.6%) were female, 120,405 (46.9%) were aged ≥ 65 (median of three comorbidities, interquartile range [IQR] 2–4), and 16,754 (6.5%) were children/teenagers (0 comorbidities, IQR 0-1). Frequent comorbidities were hypertension (89,938 [35.1%]), fluid/electrolyte disorders (54,447 [21.2%]), renal failure (45,866 [17.9%]), cardiac arrhythmias (37,906 [14.8%]), and depression (35,759 [13.9%]). Physicians initiated 113,028 (44.1%) of hospital referrals, and patients/relatives 73,494 (28.6%). Frequently ADR-affected were the digestive system (48,219 [18.8%], e.g. noninfective gastroenteritis and colitis), the genitourinary system (39,727 [15.5%], e.g. acute renal failure), and the mental/behavioural state (39,578 [15.4%], e.g. opioid dependence). In-hospital mortality was 2.2% (5669). Since ICSRs indicated 14,109 hospitalisations and 700 in-hospital deaths, estimated reporting rates were 5% and 12%, respectively.

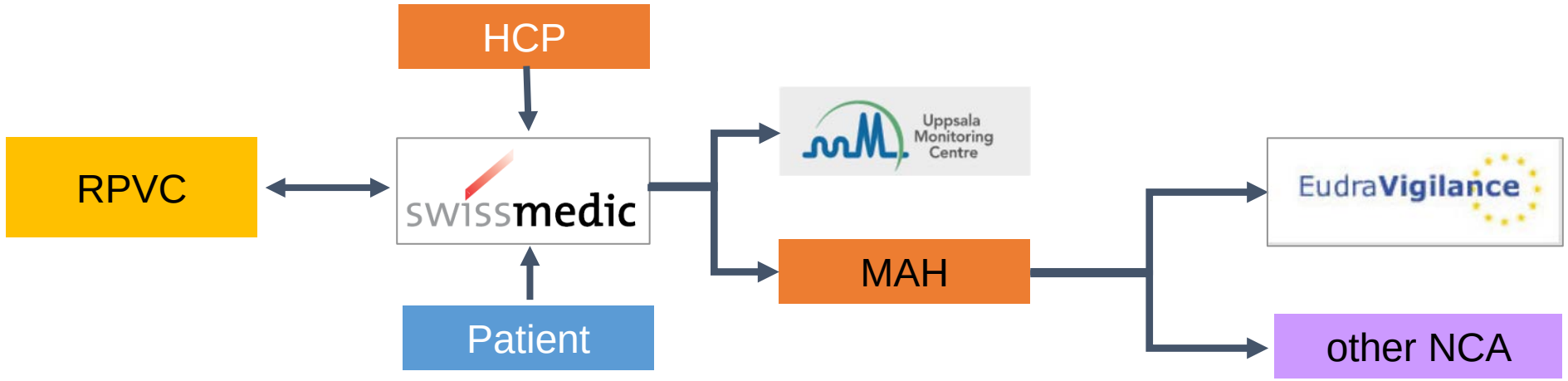
Conclusions This 8-year observation in Switzerland revealed that 2.3%, or roughly 32,000 admissions per year, were caused by ADRs. The majority of ADR-related admissions were not reported to the regulatory authorities, despite legal obligations.

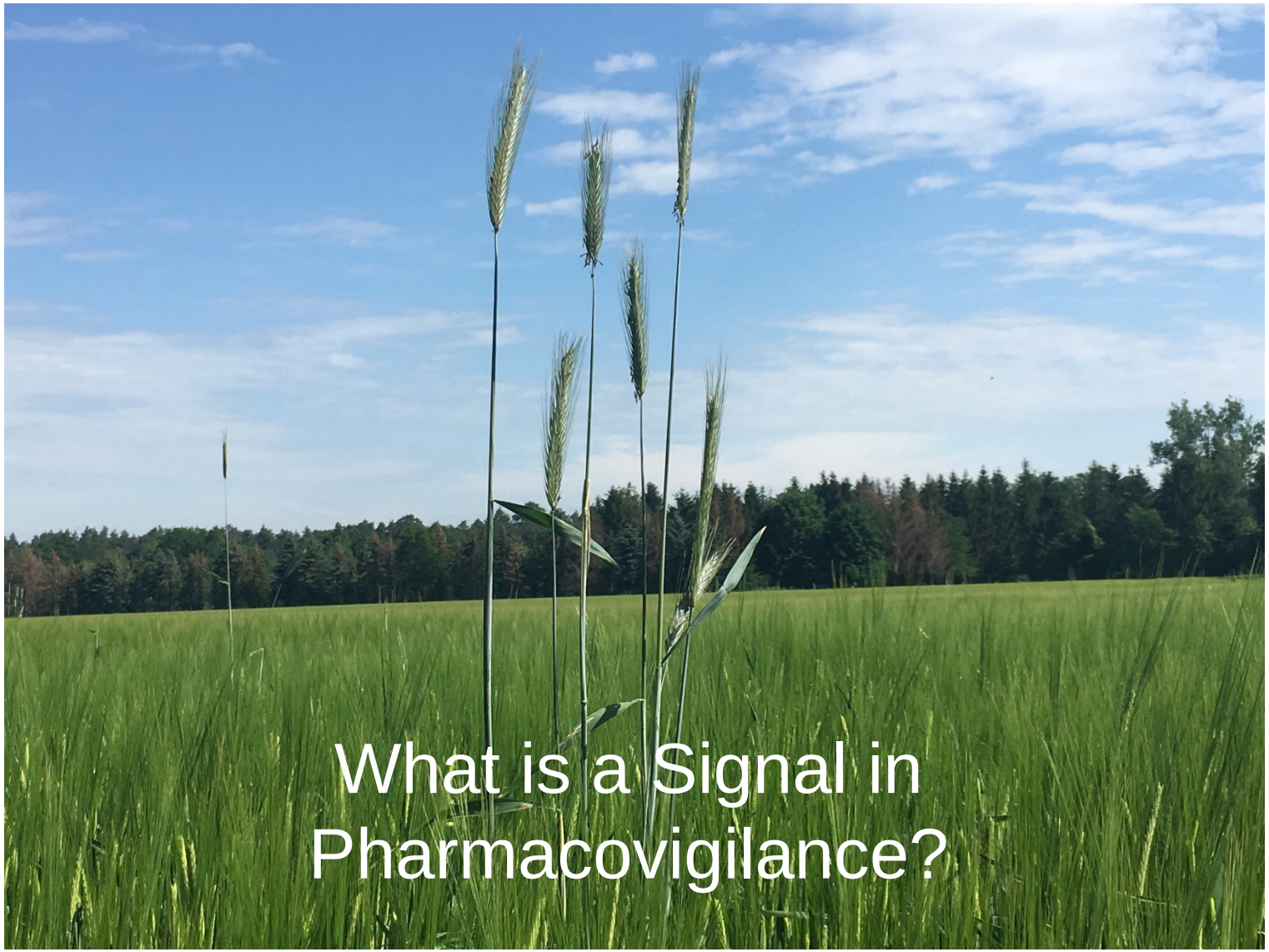
The Swiss Pharmacovigilance Network



Six regional pharmaco-vigilance centers located at the university hospitals

Processing ICSRs from HCPs and patients and their global journey




What is a Signal in Pharmacovigilance?

Signal in Pharmacovigilance: Definitions

- *Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending on the seriousness of the event and the quality of the information.*

  (The classic WHO definition)

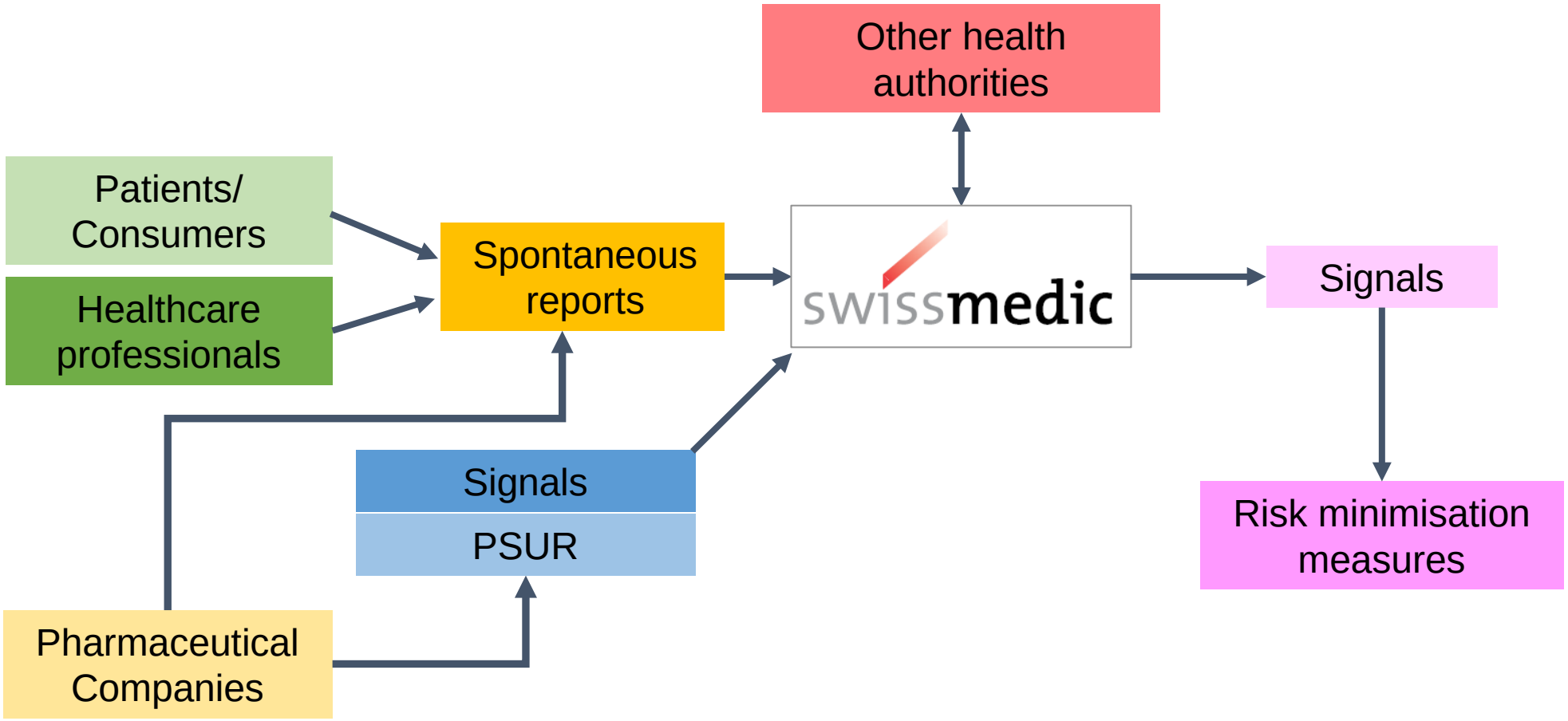
- *Information that arises from one or multiple sources (including observation and experiments), which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, which would command regulatory, societal or clinical attention, and is judged to be of sufficient likelihood to justify verificatory and, when necessary, remedial actions.*

  Hauben and Aronson. Defining 'Signal' and its Subtypes in Pharmacovigilance Based on a Systematic Review of Previous Definitions. *Drug Safety*, 2009, 32 (2), 99-110.

Signals may derive from…

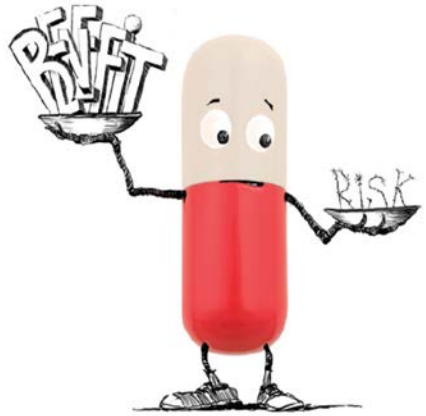
- Individual case safety reports (ICSRs)
- Information from marketing authorisation holder
  (Risk Management Plan, Periodic Safety Update Report)
- WHO International Drug Monitoring Programme
- Information from other regulatory authorities
- Scientific literature
- Scientific meetings / congresses
- Media
- Social Media

Drug Safety: From case reports to confirmed signals

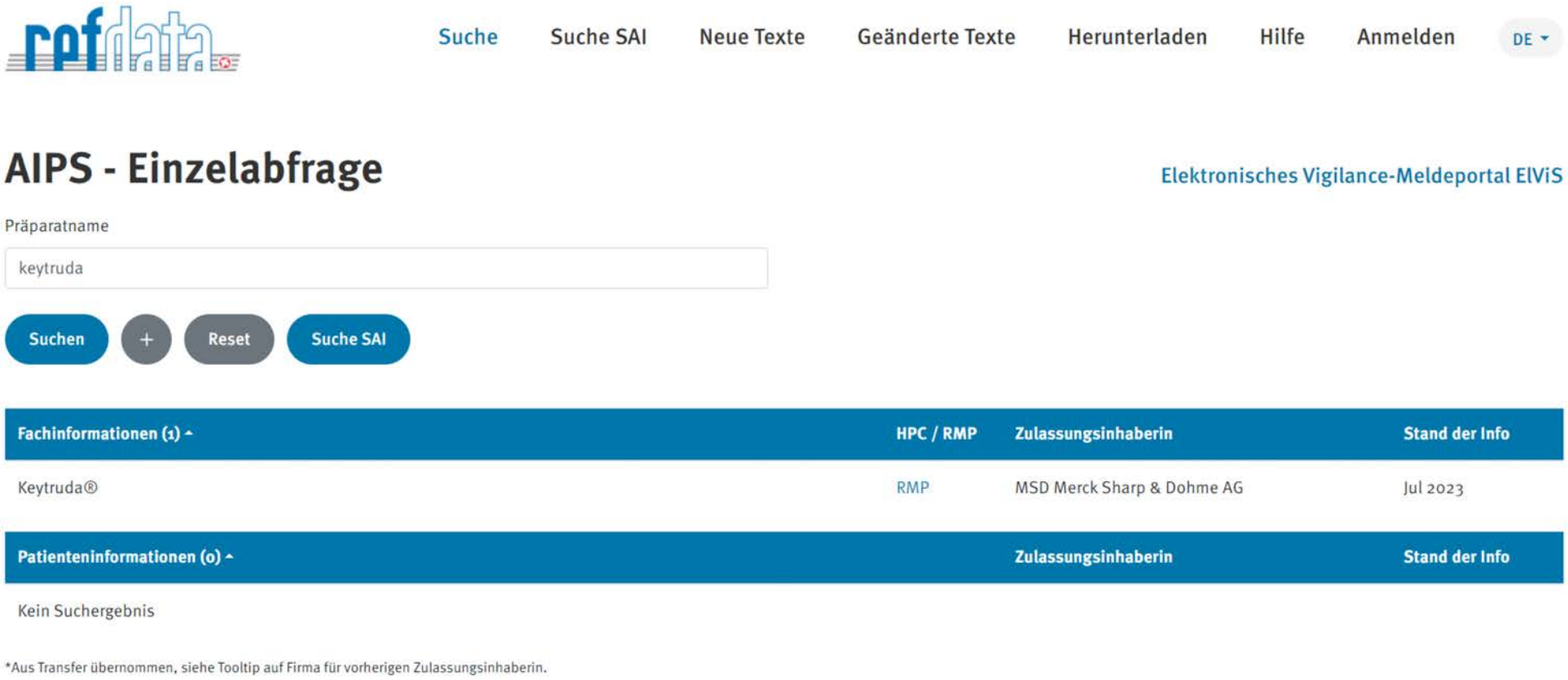


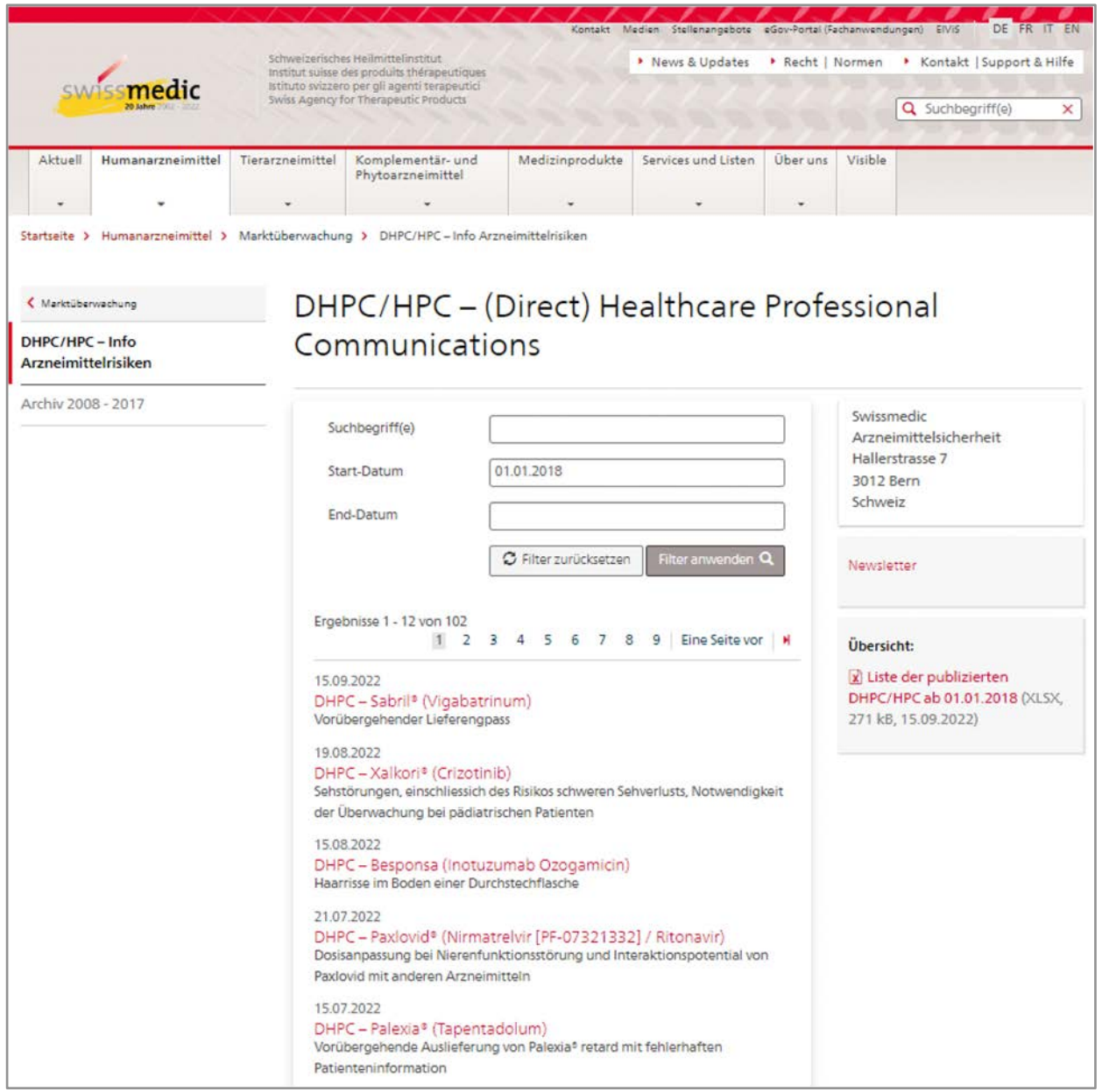
Risk minimisation measures

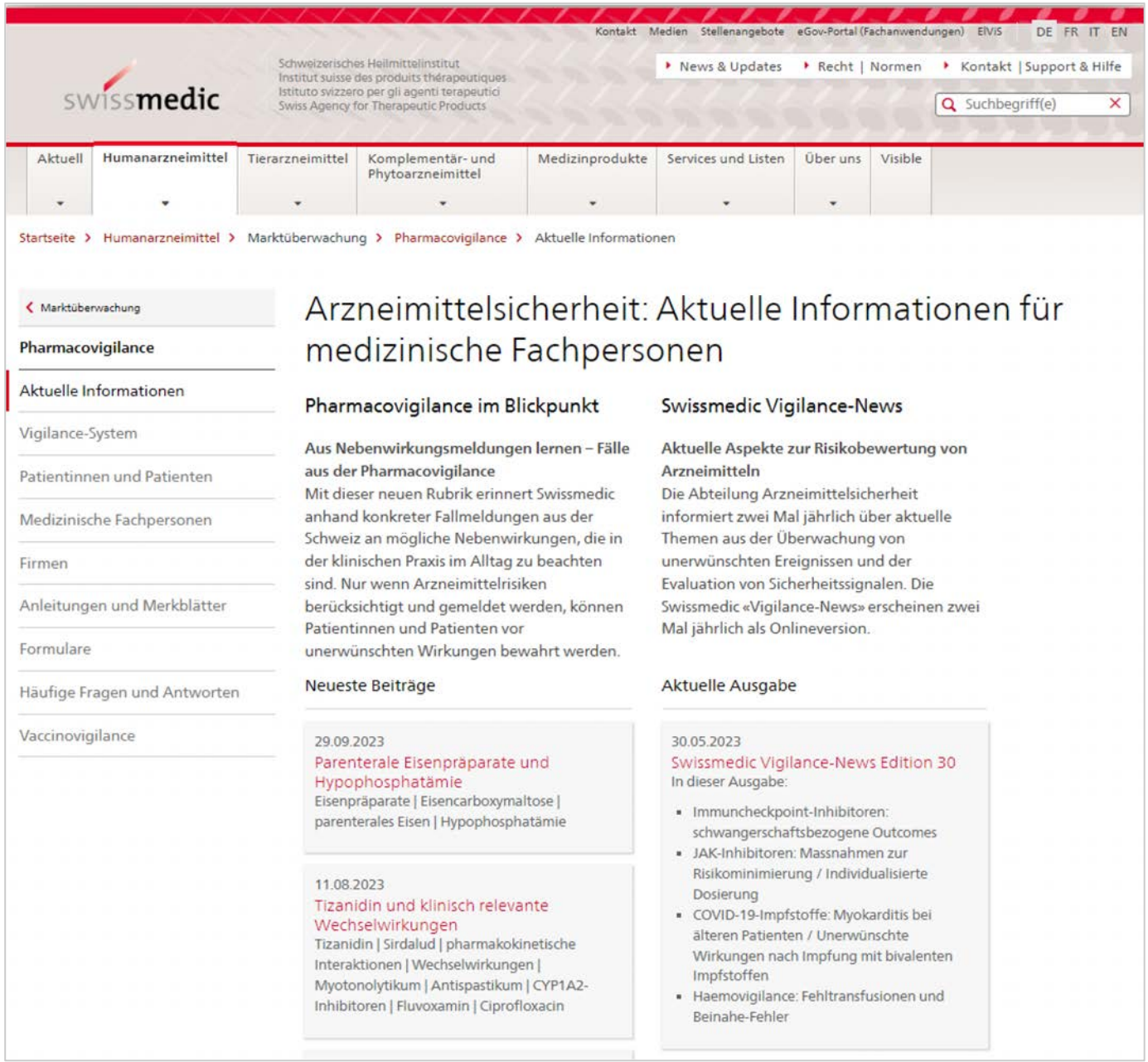
- Adaptation of the drug information (e.g. new adverse effects, warnings or precautions...)
- Restrictions of use (e.g. indication, population, dosage, package size)
- DHPC (Direct Healthcare Professional Communication)
- Educational materials for healthcare professionals / patients
- Post Authorisation Safety Studies (PASS)
- Recall
- Suspension of marketing authorisation / withdrawal



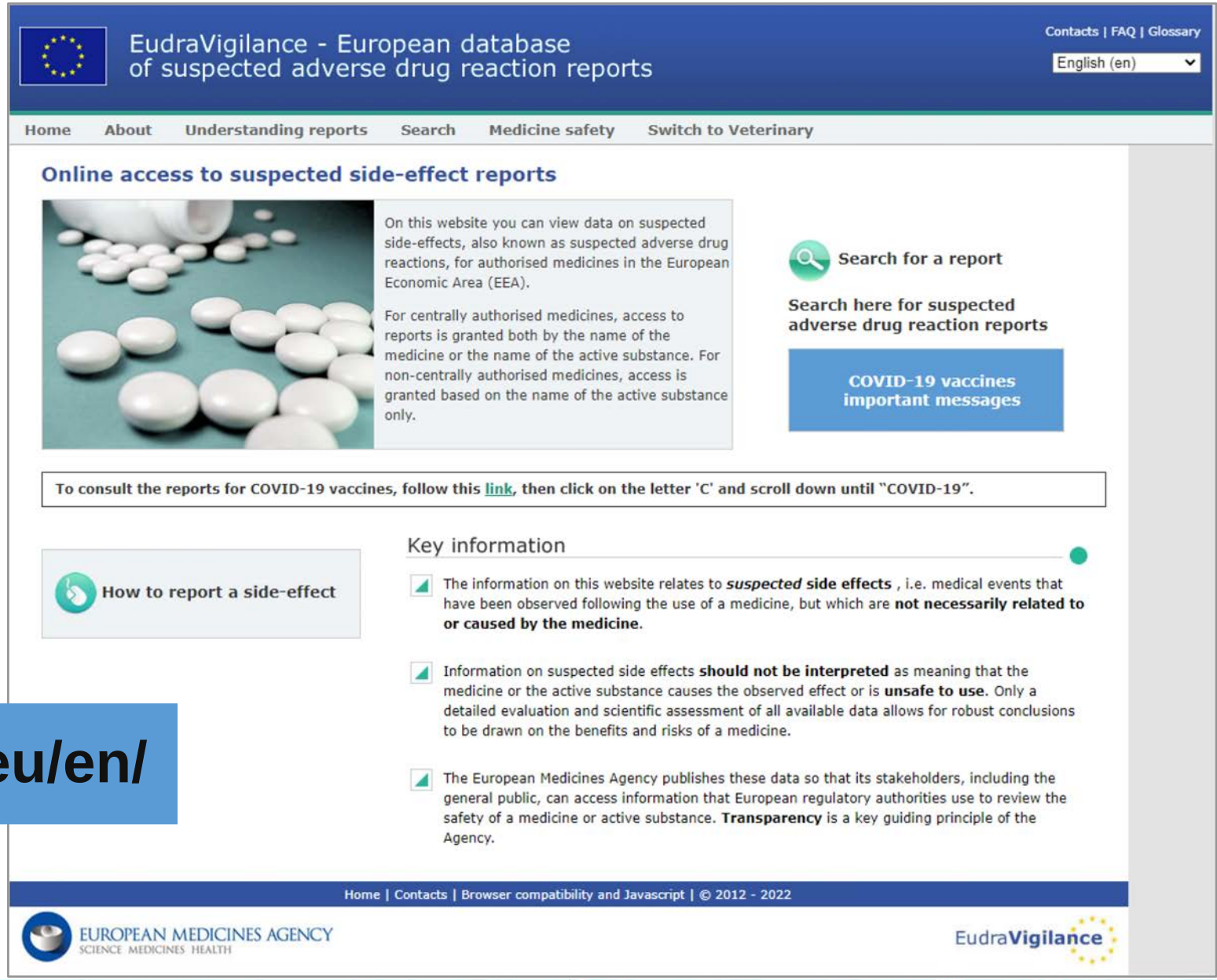
Information on safety and adverse reactions of medicines




Kontakt Medien Stellenangebote eGov-Portal (Fachanwendungen) EIVIS
DE FR IT EN
swissmedic
Schweizerisches Heilmittelinstitut
Institut suisse des produits thérapeutiques
Istituto svizzero per gli agenti terapeutici
Swiss Agency for Therapeutic Products
News & Updates
Recht | Normen
Kontakt | Support & Hilfe
Suchbegriff(e)
Aktuell
Humanarzneimittel
Tierarzneimittel
Komplementär- und Phytoarzneimittel
Medizinprodukte
Services und Listen
Über uns
Visible
Startseite > Humanarzneimittel > Marktüberwachung > DHPC/HPC – Info Arzneimittelrisiken
Marktüberwachung
DHPC/HPC – Info Arzneimittelrisiken
Archiv 2008 - 2017
DHPC/HPC – (Direct) Healthcare Professional Communications
Suchbegriff(e)
Start-Datum
01.01.2018
End-Datum
Filter zurücksetzen
Filter anwenden
Ergebnisse 1 - 12 von 102
1 2 3 4 5 6 7 8 9 Eine Seite vor
15.09.2022
DHPC – Sabril® (Vigabatrinum)
Vorübergehender Lieferengpass
19.08.2022
DHPC – Xalkori® (Crizotinib)
Sehstörungen, einschliessich des Risikos schweren Sehverlusts, Notwendigkeit der Überwachung bei pädiatrischen Patienten
15.08.2022
DHPC – Besponsa (Inotuzumab Ozogamicin)
Haarrisse im Boden einer Durchstechflasche
21.07.2022
DHPC – Paxlovid® (Nirmatrelvir [PF-07321332] / Ritonavir)
Dosisanpassung bei Nierenfunktionsstörung und Interaktionspotential von Paxlovid mit anderen Arzneimitteln
15.07.2022
DHPC – Palexia® (Tapentadolum)
Vorübergehende Auslieferung von Palexia® retard mit fehlerhaften Patienteninformation
Swissmedic
Arzneimittelsicherheit
Hallerstrasse 7
3012 Bern
Schweiz
Newsletter
Übersicht:
Liste der publizierten DHPC/HPC ab 01.01.2018 (XLSX, 271 kB, 15.09.2022)


Kontakt Medien Stellenangebote eGov-Portal (Fachanwendungen) ElViS
DE FR IT EN
swissmedic
Schweizerisches Heilmittelinstitut
Institut suisse des produits thérapeutiques
Istituto svizzero per gli agenti terapeutici
Swiss Agency for Therapeutic Products
News & Updates
Recht | Normen
Kontakt | Support & Hilfe
Suchbegriff(e)
Aktuell
Humanarzneimittel
Tierarzneimittel
Komplementär- und Phytoarzneimittel
Medizinprodukte
Services und Listen
Über uns
Visible
Startseite > Humanarzneimittel > Marktüberwachung > Pharmacovigilance > Aktuelle Informationen
Marktüberwachung
Pharmacovigilance
Aktuelle Informationen
Vigilance-System
Patientinnen und Patienten
Medizinische Fachpersonen
Firmen
Anleitungen und Merkblätter
Formulare
Häufige Fragen und Antworten
Vaccinovigilance
Arzneimittelsicherheit: Aktuelle Informationen für medizinische Fachpersonen
Pharmacovigilance im Blickpunkt
Aus Nebenwirkungsmeldungen lernen – Fälle aus der Pharmacovigilance
Mit dieser neuen Rubrik erinnert Swissmedic anhand konkreter Fallmeldungen aus der Schweiz an mögliche Nebenwirkungen, die in der klinischen Praxis im Alltag zu beachten sind. Nur wenn Arzneimittelrisiken berücksichtigt und gemeldet werden, können Patientinnen und Patienten vor unerwünschten Wirkungen bewahrt werden.
Swissmedic Vigilance-News
Aktuelle Aspekte zur Risikobewertung von Arzneimitteln
Die Abteilung Arzneimittelsicherheit informiert zwei Mal jährlich über aktuelle Themen aus der Überwachung von unerwünschten Ereignissen und der Evaluation von Sicherheitssignalen. Die Swissmedic «Vigilance-News» erscheinen zwei Mal jährlich als Onlineversion.
Neueste Beiträge
29.09.2023
Parenterale Eisenpräparate und Hypophosphatämie
Eisenpräparate | Eisencarboxymaltose | parenterales Eisen | Hypophosphatämie
11.08.2023
Tizanidin und klinisch relevante Wechselwirkungen
Tizanidin | Sirdalud | pharmakokinetische Interaktionen | Wechselwirkungen | Myotonolytikum | Antispastikum | CYP1A2-Inhibitoren | Fluvoxamin | Ciprofloxacin
Aktuelle Ausgabe
30.05.2023
Swissmedic Vigilance-News Edition 30
In dieser Ausgabe:
Immuncheckpoint-Inhibitoren: schwangerschaftsbezogene Outcomes
JAK-Inhibitoren: Massnahmen zur Risikominimierung / Individualisierte Dosierung
COVID-19-Impfstoffe: Myokarditis bei älteren Patienten / Unerwünschte Wirkungen nach Impfung mit bivalenten Impfstoffen
Haemovigilance: Fehltransfusionen und Beinahe-Fehler

https://www.adrreports.eu/en/



Thank you for your attention!

thomas.stammschulte@swissmedic.ch