Switzerland - Cracking the medDRA Code: Medication Errors Hidden in a Spontaneous Reporting Database

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Disclosure statement

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

Disclaimer

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Content

- Legal obligation in Switzerland
- Medication errors spike in 2022
  - Paxlovid
  - Octenisept
- Pharmacovigilance Blog
- Counterfeit substances

⇓ Do medication errors, overdose, misuse and occupational or accidental exposure have to be reported?

Cases of medication error, overdose, misuse and occupational or accidental exposure without additional adverse drug reactions (ADRs) do not have to be reported individually in Switzerland. However, if these cases are reported to Swissmedic, they are entered in the national database. Cases with additional ADRs must be reported individually in accordance with Art. 59 TPA.

Therapeutic Products Act, TPA, Art. 59

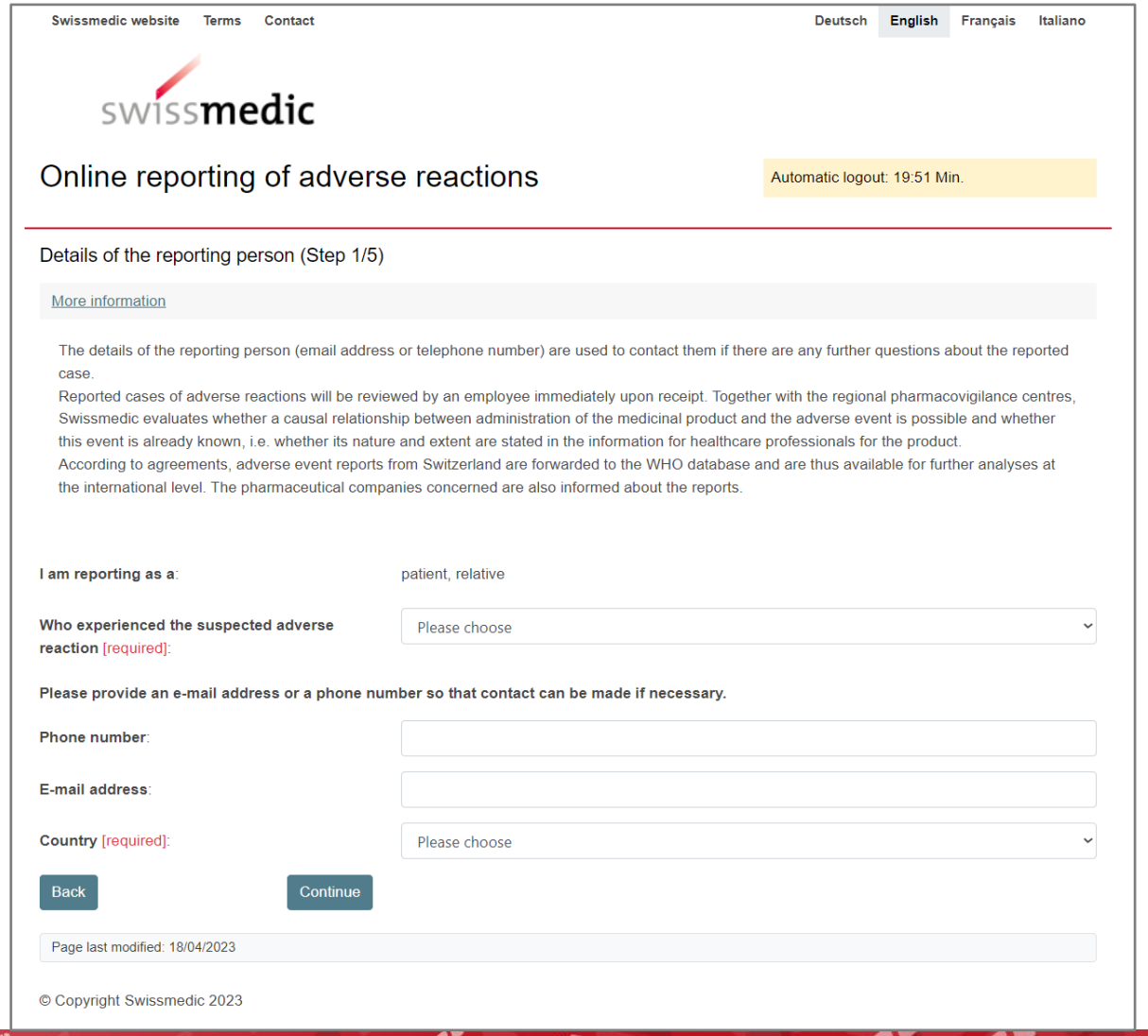
[3] Any person who professionally dispenses therapeutic products or administers them to humans or animals or who is entitled to do so as medical personnel must notify the Agency of any serious and previously unknown adverse effects and incidents, observations of other serious and previously unknown facts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

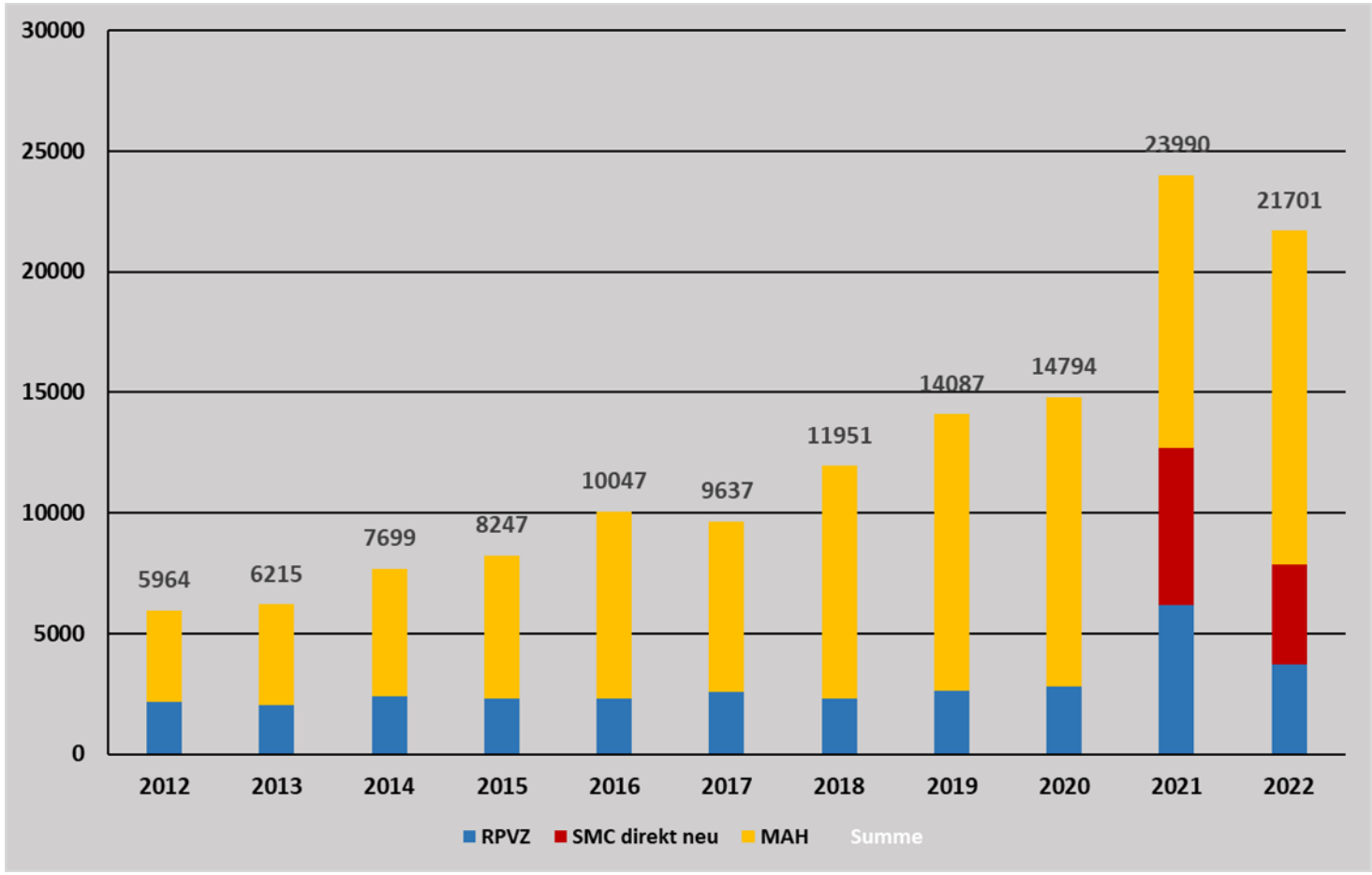
Direct patient reports webtool

- in total n=1129 reports between 13th of July 2022 - 20th of October 2023

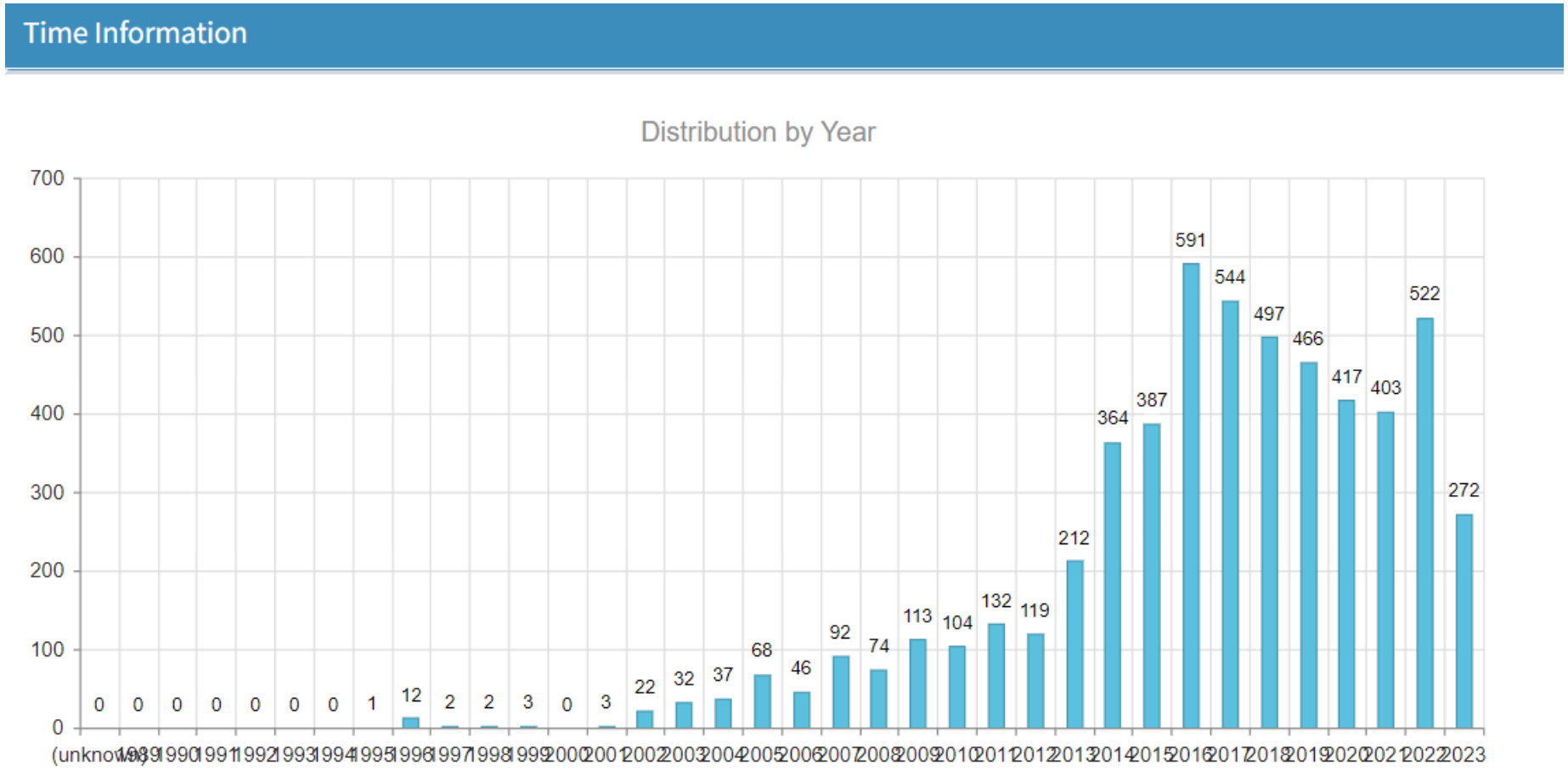
- N=3 reports related to SMQ medication error
  - wrong technique in product usage process *Spikevax vaccine*
  - prescribed underdose *Amoxicillin* (5 year old patient)
  - product packaging difficult to open *Procto-Glyvenol Supp.* (Lidocaine, Tribenosid)



Distribution of ICSRs 2012 - 2022



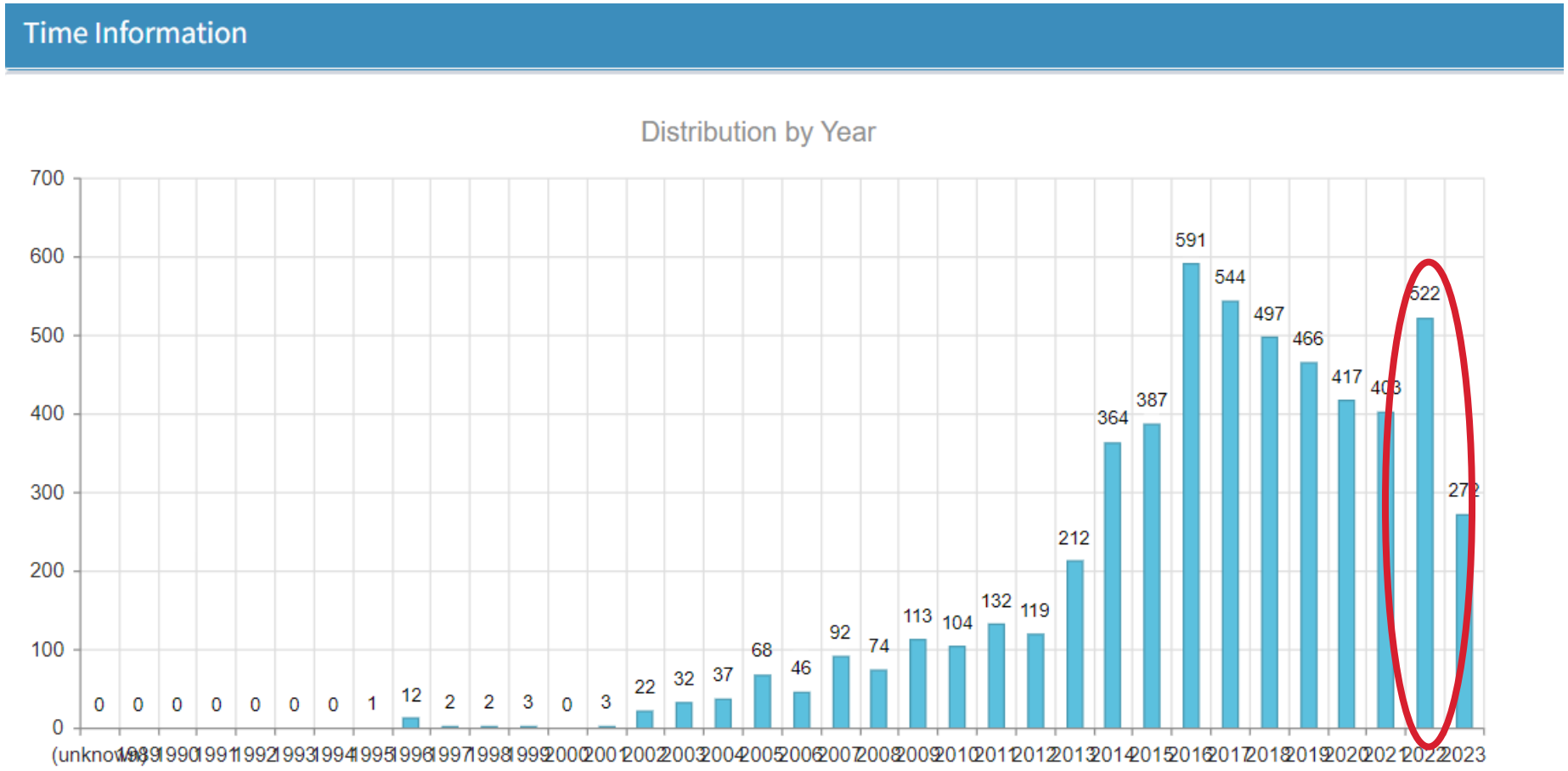
SMQ medication error in our database (N=5537, 3.5%)



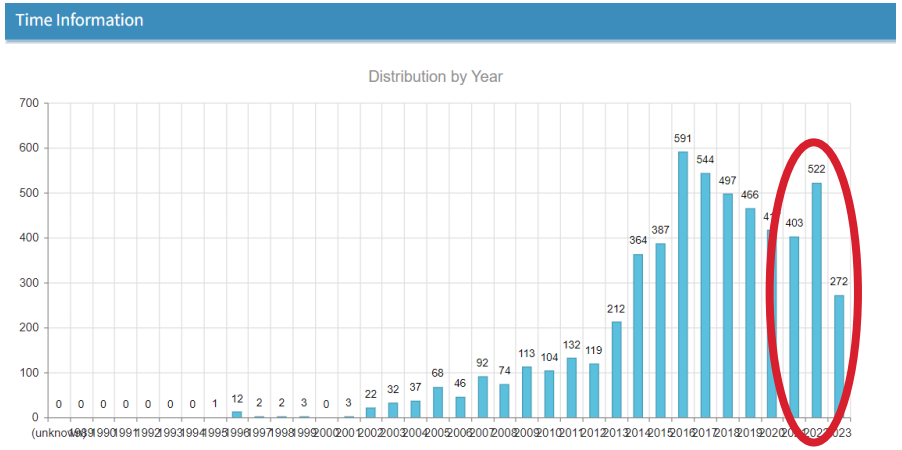
SMQ medication error in our database (N=5537, 3.5%)

Type of report	Primary reporter	Source
N= 5043 (91%) spontaneous report N=321 (6%) report from study N=173 (3%) other	N=4672 (84%) HCP N= 733 (13%) consumer N=4 (0.07%) lawyer	N= 4446 (80%) MAH N=1091 (20%) HCP/RPVC

SMQ medication error in our database (N=5537, 3.5%)

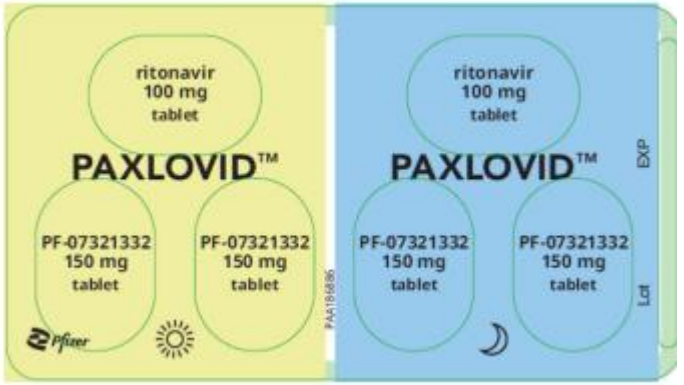


SMQ medication error in our database
2022 spike of reports (2022 n=522)
131 (25%) reports related to Covid-19



No. of reports	Product	Adverse events reported
117	Spikevax Bivalent Original/Omicron; Covid-19 vaccine Moderna	No adverse event, Product dispensing error / Product storage error / Product temperature excursion issue / Expired product administered / **Circumstance or information capable of leading to medication error**
7	Comirnaty (Pfizer vaccine)	Inappropriate schedule of product administration [*possibly intraarticular injection]* / wrong product administered
4	Paxlovid	Accidental overdose
1	Evusheld	Product administration error /Product preparation error [*dosage for preexposition & immune compromised*]
1	Vaxigrip Tetra (+ Spikevax vaccine)	Overdose [given twice]
1	Covid-19 vaccine Janssen	Product storage error [stored at lower temperature] / no adverse event

Paxlovid (Nirmatrelvir + Ritonavir)



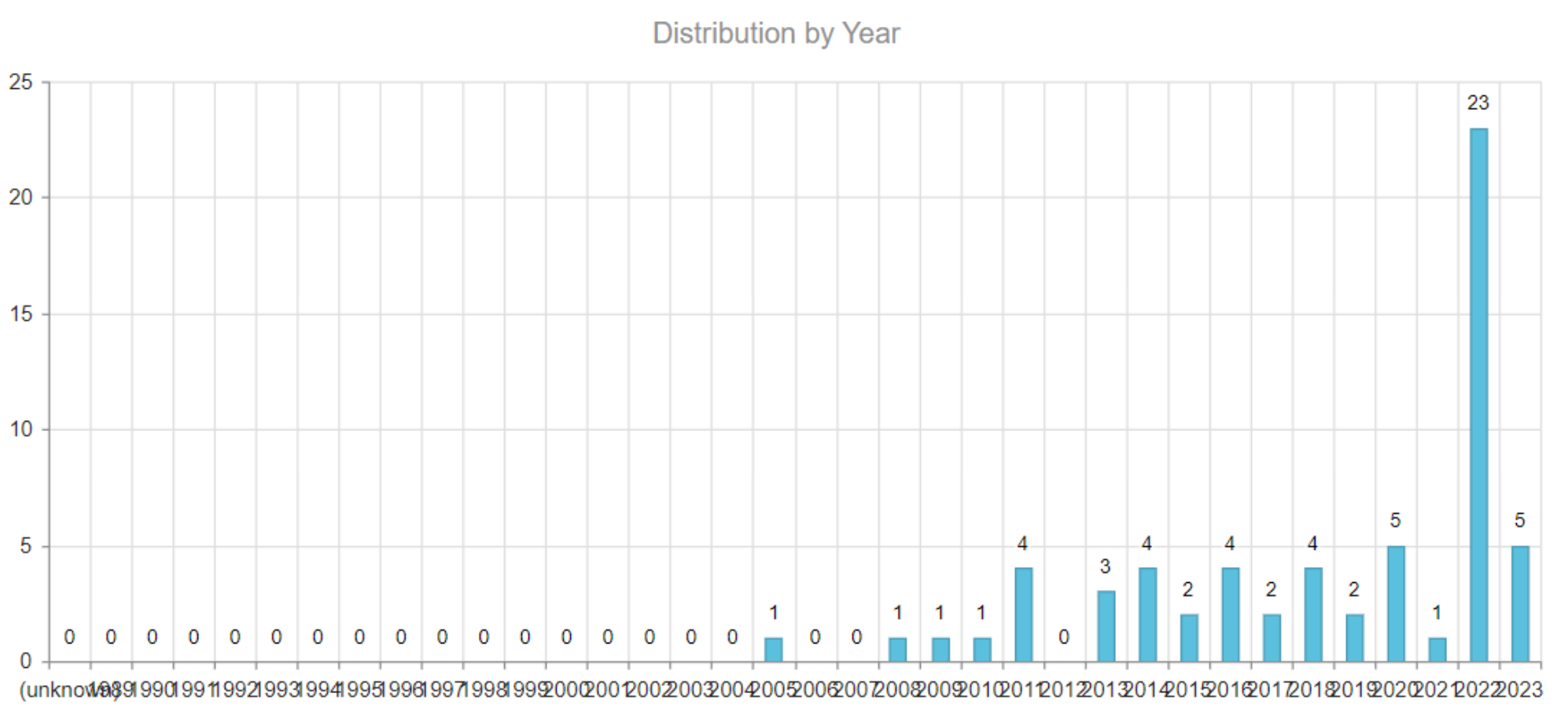
Picture:company information letter Pfizer, 2022

- Authorized in Switzerland in June 2022
- **Nirmatrelvir** is a novel active substance which inhibits a SARS-CoV-2 enzyme. The second substance, **Ritonavir**, is added to ensure that Nirmatrelvir is broken down more slowly in the liver and its antiviral efficacy lasts for longer.
- Warning from a regional Swiss hospital in **February 2023** regarding unclear information for renal impairment: On blister Nirmatrelvir was still referred to with the study name: **PF-07321332**
- Recommended dosage Nirmatrelvir 300mg (2 x150mg tablets) / Ritonavir 100mg (1 tablet) every 12 hours for 5 days
- **Renal impairment** (moderate; estimated GFR 30 to less than 60 mL/min):
  - Nirmatrelvir 150 mg (ONLY one of the two tablets) and Ritonavir 100 mg twice daily for 5 days

Paxlovid (Nirmatrelvir + Ritonavir)

- In total n=43 reports involving Paxlovid in CH-database (2022 - 17.10.2023)
  - N= 33 without medication error
  - N= 10 with medication error
    - N= 6 medication error coded appropriately
    - N= 4 medication errors not coded (labelled drug-drug interaction, prescribed overdose)

Octenisept disinfectant



Octenisept disinfectant

- Disinfectant octenidindihydrochlorid
- In our database N=60 cases with octenisept as suspected product between 26.06.2013-04.10.2023
- N=49 reports from health-care professionals, N=7 from consumers, N=4 unknown
- in N=46 cases there was a medication error, but only in N=21 (46%) a medication error is coded in the reports
- N=44 serious, N= 16 non-serious
- **In 2022 spike: 17 cases from the department of handsurgery local hospital**

Octenisept disinfectant

- 81 year old received aflibercept (Eylea®) intravitral injections for wet AMD
- Tobradex (dexamethasone + tobramycin) as a pre and post medication. Patient´s ocular surface was disinfected with octenisept.
- Patient experienced pseudoendophthalmitis, loss of vision.
- It was reported that the physician respected all the standard recommendations for the drug administration. **This was 2013.**
- Endopthalmitis is an inflammatory condition of the intraocular cavities (anterior and posterior segments) usually caused by infection. Intravitreal injections have been associated with endophthalmitis, which could be consequence of an improper aseptic injection technique and/or due to toxic intraocular exposure of suspect drug.
- Due to the temporal relationship the causal relationship between Eylea® injection and use of Octenisept as disinfectant and adverse event cannot be excluded.

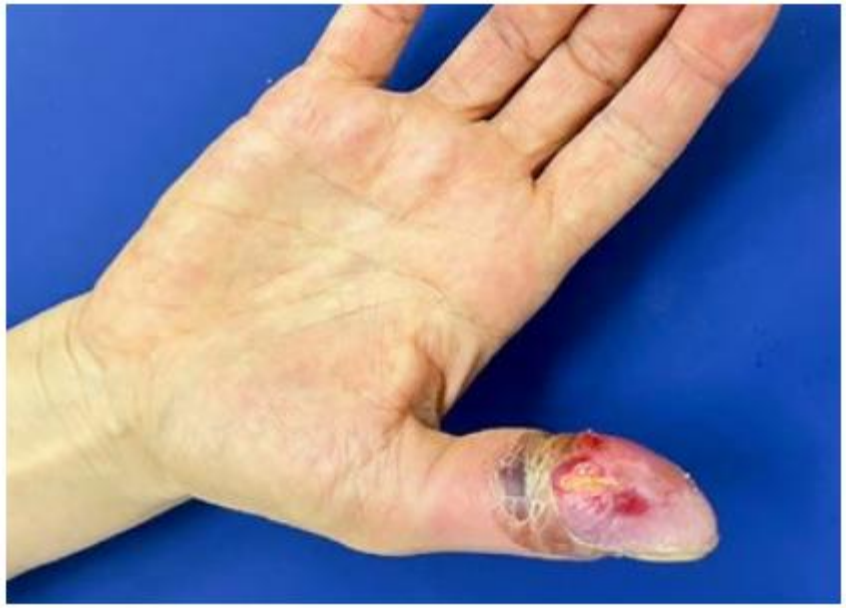
Octenisept disinfectant: Product information changing

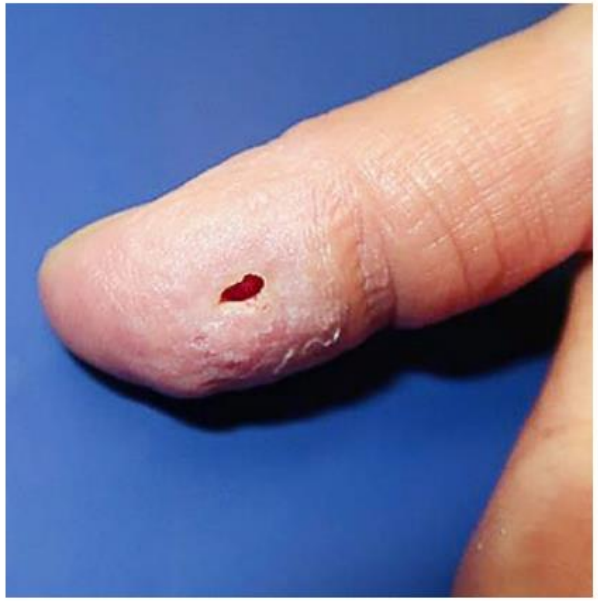
- Initially warning/contraindication of Octenisept use around the eye not included in product information.

- New contraindication:
- […] should not be applied around the eye

Octenisept disinfectant

- Patients suffered cat or dog bites and the wound was treated with an in depth tissue lavage with Octenisept
- Reports of the handsurgery department noticing a an increase in patients with necrotic skin lesions





Aktuelles aus den Regionalen Pharmacovigilance-Zentren

Lokale Gewebeschädigung nach Wundspülung unter Druck mit Antiseptikum

Dr. med. Lena Fuest[a], M. pharm. Sarah Banholzer[b], Prof. Dr. med. Manuel Haschke[b], Prof. Dr. med. Esther Vögelin[a], PD Dr. med. et phil. Stefan Weiler[b,c]
Inselspital, Universitätsspital Bern, Bern: [a] Universitätsklinik für Plastische- und Handchirurgie, [b] Klinische Pharmakologie & Toxikologie, Universitätsklinik für Allgemeine Innere Medizin; [c] Institut für Pharmazeutische Wissenschaften, Eidgenössische Technische Hochschule (ETH), Zürich

6 d and 43 d after Octenisept usage

Source: Lokale Gewebeschädigung nach Wundspülung unter Druck mit Antiseptikum, Fuest et al. 10.4414/smf.2023.09368 | 2023;23(37):1292–1294 | Swiss Medical Forum

Octenisept disinfectant: A safety problem in Switzerland and Germany

J Hand Surg Eur Vol. 2012 Jan;37(1):61-4. doi: 10.1177/1753193411414353. Epub 2011 Aug 4.

Aseptic tissue necrosis and chronic inflammation after irrigation of penetrating hand wounds using Octenisept®

T Franz [1], E Vögelin

Affiliations + expand

PMID: 21816890 DOI: 10.1177/1753193411414353

BUNDESÄRZTEKAMMER

Mitteilungen

ARZNEIMITTELKOMMISSION DER DEUTSCHEN ÄRZTESCHAFT

„Aus der UAW-Datenbank"

Schwere Gewebeschädigungen nach Spülung tiefer Wunden mit Octenisept®

Octenisept® ist ein wässriges Wund- und Schleimhautantiseptikum. Es enthält zwei Wirkstoffe: Octenidindihydrochlorid, das mit Zellwand- und Zellmembranbestandteilen der Mikrobenzelle reagiert und so zur Zerstörung der Zellfunktion führt, und Phenoxyethanol, das u. a. die Zellmembran durchlässiger für Kaliumionen macht und so antimikrobiell wirkt (1). Octenisept® ist zugelassen zur antiseptischen Behandlung von Schleimhaut und angrenzender Haut vor diagnostischen und operativen Maßnahmen im Ano-Genitalbereich und in der Mundhöhle sowie zur zeitlich begrenzten unterstützenden Therapie von Interdigitalmykosen und für adjuvante antiseptische Wundbehandlungen.

Ein 10-jähriges Mädchen war in einen langen rostigen Nagel getreten. Der Nagel hat ihren Turnschuh perforiert und war zwischen dem 2. und 3. Fußwurzelknochen durch die Fußsohle bis auf die Streckseite eingedrungen, ohne dort die Haut zu perforieren. Rettungssanitäter entfernten den Nagel. Im Krankenhaus wurde der Stichkanal in der Unfallnacht in Narkose kürettiert und mit Octenisept® gespült. Trotz Antibiotikatherapie mit Ampicillin/Sulbactam bildete sich eine zunächst als Phlegmone gedeutete Fußschwellung und Rötung aus, die operative Revisionen zwei und fünf Tage später nach sich zog. Dabei wurde eine Gegeninzision in der proximalen Fußsohle und am Fußrücken angelegt, die Stichkanäle kürettiert, Laschen eingelegt und jeweils mit Octenisept® gespült. Diese Spülungen wurden bei den Verbandswechseln auf Station fortgesetzt. Bakteriologische Abstriche blieben steril. Die Entzündungsparameter wa-

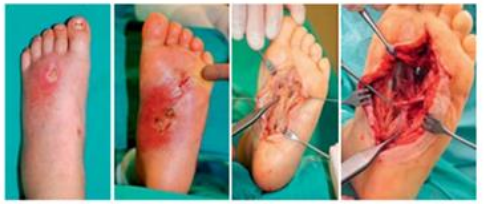


Abbildung 1: Die beiden Bilder links zeigen den Befund drei Wochen nach dem Unfall. Der Fuß war erheblich geschwollen und plantar und dorsal um die Stichkanäle herum großflächig gerötet. Der Stichkanal und die Gegeninzisionen waren schmierig belegt. Die beiden Bilder rechts zeigen den intraoperativen Befund: Ein Großteil der zentralen Fußmuskulatur war gläsern abgeblasst, brüchig und teils fettig, teils bindegewebig umgebaut. Der Musculus plantaris communis, die Lumbrikalismuskulatur, die Interosseusmukulatur und die mittleren oberflächlichen Zehenbeuger mussten reseziert werden.

Der dargestellte Fall zeigt typische Komplikationen, die nach Spülung von tiefen Wunden (z. B. Perforationswunden) mit Octenisept® auftreten können und sowohl in Literaturberichten (2–5) als auch in spontan gemeldeten Fällen immer wieder geschildert werden: Innerhalb von 24 Stunden tritt eine starke Schwellung und Rötung auf, die lange (über Monate) anhält und therapeutisch kaum zu beeinflussen ist. In den engen abgegrenzten Räumen von Händen und Füßen kann die Schwellung akut ein Kompartmentsyndrom verursachen, sodass notfallmäßig durch Kompartmentspaltung behandelt werden muss. Im Wundbereich und der näheren Umgebung können sich Fettgewebsnekrosen entwickeln und die betroffene Muskulatur erst fettig, dann fibrös umgebaut werden. Die frühen Reaktionen lassen an eine atypische oder protrahierte Phlegmone denken, ein Erregernachweis gelingt jedoch nicht. In der Fachinformation wird darauf hingewiesen, dass solche Reaktionen auftreten können, wenn tiefe Wunden mittels Spritze mit Octenisept® gespült werden. Ob die Wunde im dargestellten Fall während der initialen Operation tatsächlich auf diese Weise – also mittels Spritze – mit Octenisept® gespült wurde, lässt sich nicht mehr eruieren. Bei einer Spülung eines Kanals mit einer Spritze wird immer ein gewisser

Schwere Gewebeschädigungen nach Spülung tiefer Wunden mit Octenisept® („Aus der UAW-Datenbank")
Deutsches Ärzteblatt, Jg. 114, Heft 4, 27.01.2017

Octenisept disinfectant

- Warning has been changed to clearer state the superficial usage (wording like in German PI)
- - After irrigation of deep wounds by syringe, the occurrence of persistent edema, erythema and also tissue necrosis has been reported, some of which required surgical revision.
- To avoid tissue damage, the preparation must not be introduced into the depth of the tissue by means of a syringe. The preparation is intended for superficial application only (application by swab or spraying).
- ~~To avoid tissue necrosis, the preparation must therefore not be introduced or injected into the tissue under pressure. For usage in wounds, drainage must be ensured at all times (e.g. drainage, flap).~~

Octenisept disinfectant

- More ICSRs in 2022 regarding skin necrosis leading to an additional warning on product itself


octenisept®
farblos / incolore
Lösung zur Anwendung auf der Haut
Solution pour application cutanée

Zusammensetzung/composition: Octenidini dihydrochloridum 1 mg, Excipiens ad solutionem pro 1 ml.

DE Bitte lesen Sie die Packungsbeilage.
Bei Raumtemperatur (15 - 25°C) lagern und ausser Reichweite von Kindern aufbewahren.
Nicht einnehmen.

Um Gewebeschädigungen zu vermeiden, darf das Präparat nicht mittels Spritze in die Tiefe des Gewebes eingebracht werden. Das Präparat ist nur zur oberflächlichen Anwendung bestimmt (Auftragen mittels Tupfer oder Aufsprühen).

FR Veuillez lire la notice d'emballage.
Conserver à température ambiante (15 - 25°C) et hors de portée des enfants.
Ne pas avaler.

Pour éviter d'endommager les tissus, la préparation ne doit pas être appliquée en profondeur au moyen d'une seringue. La préparation n'est destinée qu'à une application superficielle (application au moyen d'un tampon ou d'une pulvérisation).

To avoid tissue damage the product should not be used with a syringe and introduced into the depth of the tissue. This product is only intended for the superficial usage by swap or spray

Old topics need new reminders
PV-Blog

Information for medical professionals from market surveillance of medicinal products

Pharmacovigilance in the spotlight

Learning from adverse reaction reports – cases from pharmacovigilance
The purpose of this new section is to use real-life case reports from Switzerland as a reminder of possible side effects that professionals should be aware of in day-to-day clinical practice. The only way to protect patients against undesirable effects is to take account of and report medicinal product risks.

Latest contributions

29.09.2023
Parenteral iron products and hypophosphataemia
iron products | ferric carboxymaltose | parenteral iron | hypophosphataemia.

11.08.2023
Tizanidine and clinically relevant interactions
Tizanidine | Sirdalud | pharmacokinetic interactions | drug interactions | muscle relaxant | antispasmodic agent | CYP1A2 inhibitors | fluvoxamine | ciprofloxacin

07.07.2023
Betaseptic and burns
Betaseptic | skin disinfection | burn | propanol | ethanol | povidone-iodine

Swissmedic Vigilance-News

Topical aspects of medicinal product risk assessment
Twice a year, the Safety of Medicines Division reports on current topics relating to adverse reaction surveillance and the evaluation of safety signals. Swissmedic's "Vigilance News" appears twice a year as an online resource.

Current Editions

30.05.2023
Swissmedic Vigilance-News Edition 30
In this edition:

- Checkpoint inhibitors: pregnancy-related outcomes
- JAK inhibitors: risk minimisation / dosage individualisation
- COVID-19 vaccines: myocarditis in elderly patients / adverse reactions after vaccination with bivalent vaccines
- Haemovigilance: incorrect blood component transfused and near misses

Previous issues

22.11.2022
Vigilance-News Edition 29
In this edition:

- Reports of urticaria after booster vaccination with Spikevax
- Contrast-induced neurotoxicity

Betaseptic and burns

In addition to the right choice of product, instruction and correct usage are important in preoperative skin disinfection with disinfectants containing alcohol to avoid burns caused by electrical devices (e.g. electrosurgical pencil) or irritation.

Key words: Betaseptic, skin disinfection, burn, propanol, ethanol, povidone-iodine

Incident data	Description
Case 2023 Age group: Adult (>/= 18 years) Sex: Male Medicinal product: Betaseptic® Active substances: Ethanol, propanol, povidone-iodine Indication: Preoperative skin disinfection ADR: Burn Outcome: recovering	Prior to abdominal surgery, the skin around the surgical site was disinfected. While an electrosurgical pencil was being used, the patient's skin ignited (flame) resulting in 2b degree burns to the right side of the neck and third degree burns to the right shoulder. The burns had to be excised by the plastic surgeon. A defect reconstruction was performed on the burn to the shoulder using bilateral advancement flaps.
Case 2009 Age: Adult (>/= 18 years) Sex: Male Medicinal product: Betaseptic® Active substances: Ethanol, propanol, povidone-iodine Indication: Preoperative skin disinfection ADR: Burn Outcome: recovered	During inguinal hernia surgery, the incision was made while the skin was still moist. When the surgical site was being prepared with an electrosurgical pencil, flames formed. The patient suffered second degree burns. The burns were treated locally with medical gauze. The burns healed without scar formation.

Summary and recommendation

Disinfectants such as Betaseptic®, Octeniderm® and Softasept® N are used in surgical and diagnostic interventions, and are highly flammable due to their high alcohol content. Burns can result if electrical devices are used before the disinfectant dries. In addition, accumulation of the substance in skin folds or underneath the recumbent patients can occur during preoperative skin disinfection.

The "Warnings" and "dosage/administration" sections of the relevant information for healthcare professionals mention that the solution must be completely dried and "pooling" under the recumbent patient must be avoided during preoperative skin disinfection and before use of electrical devices (particularly surgical high frequency devices).

Healthcare professionals are requested to report serious and/or previously unknown adverse drug reactions to Swissmedic. Please use the Electronic Vigilance Reporting Portal "ElViS" for this purpose.

Counterfeit substances

22 year old patient is delivered to the emergency room after injection of a blue injection pen

Soon after the injection the patient became unconsciousious and her relatives brought her to the ER

The injection pen has been purchased abroad and was supposed to contain Semaglutide

Swissmedic Medicrime department analysed the pen

Ozempic

The analysis of the content showed insulin glulisin and not semaglutide

Apidra (M-030636)

Counterfeit pen

Ozempic
Swissmedic issues warning about falsified Ozempic pens

Hospitalisations following use of falsified Ozempic pens – Swissmedic advises against purchasing medicinal products online and from unreliable sources abroad

07.07.2023

The latest generation of diabetes medications (GLP-1-agonists, e.g. Ozempic) are currently being widely discussed in the media. Since alongside their actual application, their use can also result in weight loss, they are often in demand as a slimming product. This can lead to supply shortages in some cases and to these products being purchased online or from unreliable sources (including sources abroad).

Due to high demand, falsifications of these products are increasingly appearing internationally. In Switzerland, reports have been submitted to Swissmedic concerning individuals who have obtained Ozempic from unreliable sources and been hospitalised after using it.

Swissmedic has recently received reports of hospitalisations in Switzerland in connection with Ozempic falsifications obtained outside of the legal Swiss distribution chain. The individuals affected were admitted with acute hypoglycaemia (low blood sugar). In one case, an insulin pen was identified in the package rather than an Ozempic pen. Hypoglycaemia triggered by an insulin overdose is acutely life-threatening and must be treated immediately.

Swissmedic emphasises that weight loss is not an officially authorised indication for Ozempic. This is what is known as an "off-label use". It must take place under medical supervision and can therefore only be prescribed by a doctor.

Confusing product appearance

Retrieval with the following MedDRA terms: n= 46 in our database

PT_CODE	PT_NAME
10080000	Product appearance confusion
10082712	Product confusion
10080827	Product design confusion
10069273	Product label confusion
10069332	Product name confusion
10074776	Product packaging confusion

Confusing product appearance

Retrieval with the following MedDRA terms: n= 46 in our database 2012 - 2023

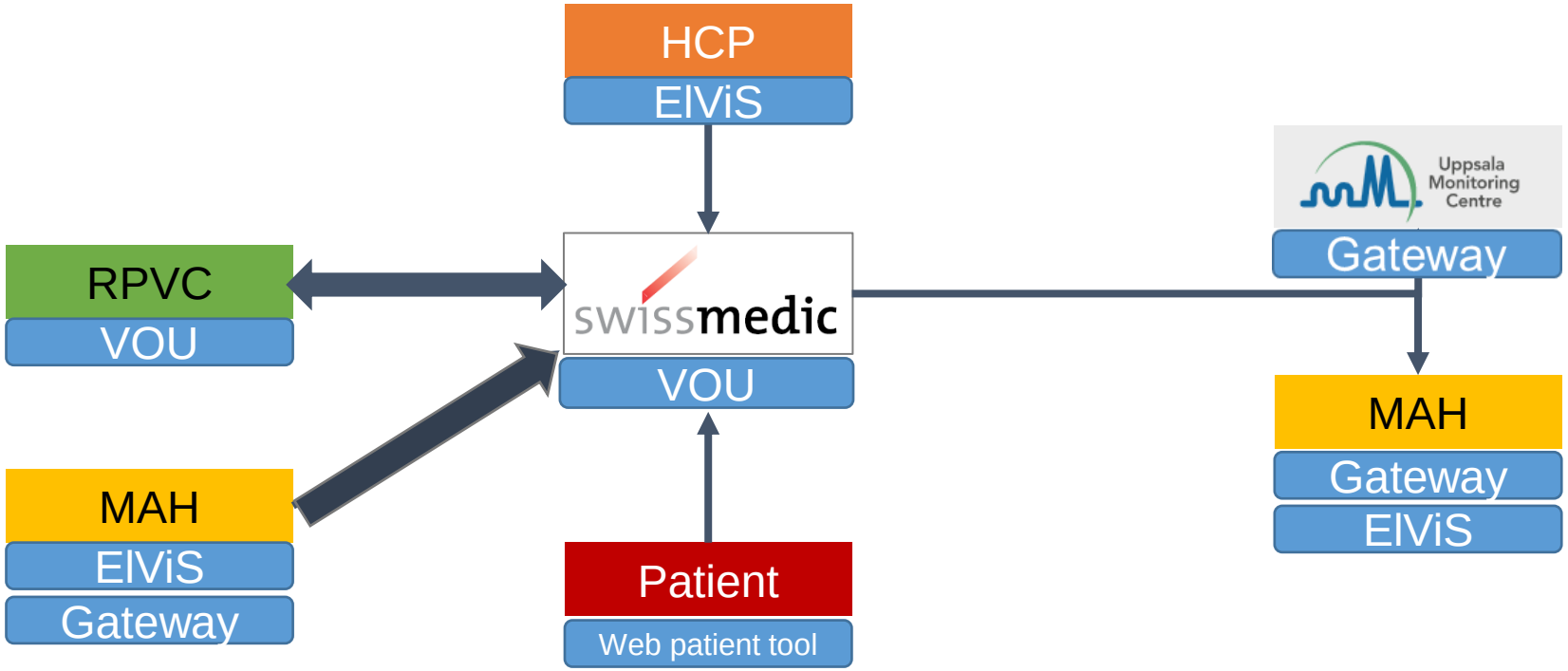
PT_CODE	PT_NAME
10080000	Product appearance confusion
10082712	Product confusion
10080827	Product design confusion
10069273	Product label confusion
10069332	Product name confusion
10074776	Product packaging confusion

- In 2022-2023 text search in case narrative «confusing product package», «confusing name», «unclear packaging», «misunderstanding packaging» in German (one of three national languages) led to finding of 164 possible cases -> 3.6x more than retrieval
- Future evaluation needed: how AI can be used

Please let me know if you have any questions:

Irene.scholz@swissmedic.ch

Processing of ICSRs from HCPs and non-HCPs: input channels



RPVC: regional pharmacovigilance center
MAH: market authorization holder
VOU: vigilance one ultimate (Swiss database)
ElViS: Electronic Vigilance System
HCP: health care professional