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Vaccinovigilance
Annual report 2021

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Annual report 2021

Summary of adverse events following immunization reported in Switzerland during 2021

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Executive summary

During 2021, the Pharmacovigilance Unit of Swissmedic received a massively increased number of case-reports of suspected adverse events following immunization (AEFI) from Switzerland, as compared to previous years. The vast majority of these reports were submitted in relation with the new Covid-19 vaccines during the nation-wide vaccination campaign which was underway throughout the year 2021. In addition to that, 159 AEFI-reports have been submitted in Switzerland for non-Covid vaccines during 2021, which is a significantly lower number as compared with previous years 2020 (271 reports) or 2019 (273 reports). However, this difference is not unexpected and is probably a consequence of the large scale new Covid-19 vaccination and information campaign, resulting in a shift of awareness and focus towards the new Covid-vaccines within the general population and also amongst healthcare professionals. Firstly, the high number of reports concerning Covid-19 vaccines can be attributed to the unprecedented high exposure to these vaccines. Additionally, it illustrates the strong association between public attention and the quantity of spontaneous reports. The number could be misinterpreted as a false signal for safety concerns in association with the Covid-19 vaccines. However, most of these reports describe well-known reactions following Covid-19 immunization such as fever, chills or administration site reactions. This summary-report has its main focus on non-Covid vaccine AEFI, since several Covid-19 vaccine safety reports have been regularly published as cumulative updates on Swissmedic's website and further similar reports will follow in future. Nevertheless, a brief summary of Covid-19 AEFI reports received during 2021 is presented in the final section of this document.

Similar to previous year, AEFI-reports submitted during 2021 have been recorded, assessed and analysed in the pharmacovigilance database of Swissmedic. However, no accurate data was available regarding the number of vaccine doses administered in Switzerland during 2021 for different non-Covid vaccine groups and therefore a straightforward conclusion regarding AEFI reporting rates cannot be drawn. As previously, Swissmedic is encouraging spontaneous reporting of AEFIs in high quality, which enables early detection of new safety signals. Important safety issues concerning vaccines are being evaluated in international collaboration with other foreign agencies and/or with participation of the Human Medicines Expert Committee (HMEC) of Swissmedic, if necessary. An increased AEFI reporting rate within the Swiss database, followed by an assessment of relevant cases can lead to risk minimisation measures in order to ensure vaccines safety.

Figure 1
Number of AEFI reports per age group and gender, 2021

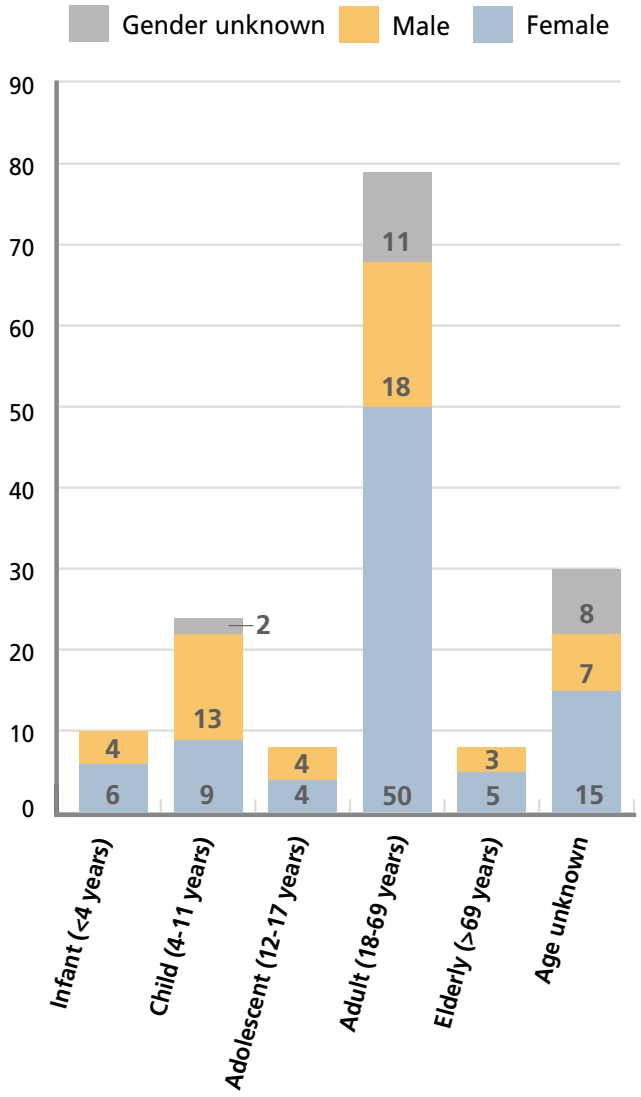

Figure 1 compares the number of reports per age group and gender. The largest number of AEFI reports involved adults (79 reports), followed by children (24 reports), infants (10 reports), adolescent (8 reports), elderly (8 reports). Throughout the year 2021, the number of reports concerning females (89 reports; 56%) exceeded the number of reports concerning males (49 reports; 30.8%). In 21 AEFI reports 13.2%), the gender of the persons remained unknown. In 30 case-reports (18.8%), the age-group of the patients was not recorded.

Figure 2
Number of reports vaccine group (ATC code) and seriousness, 2021

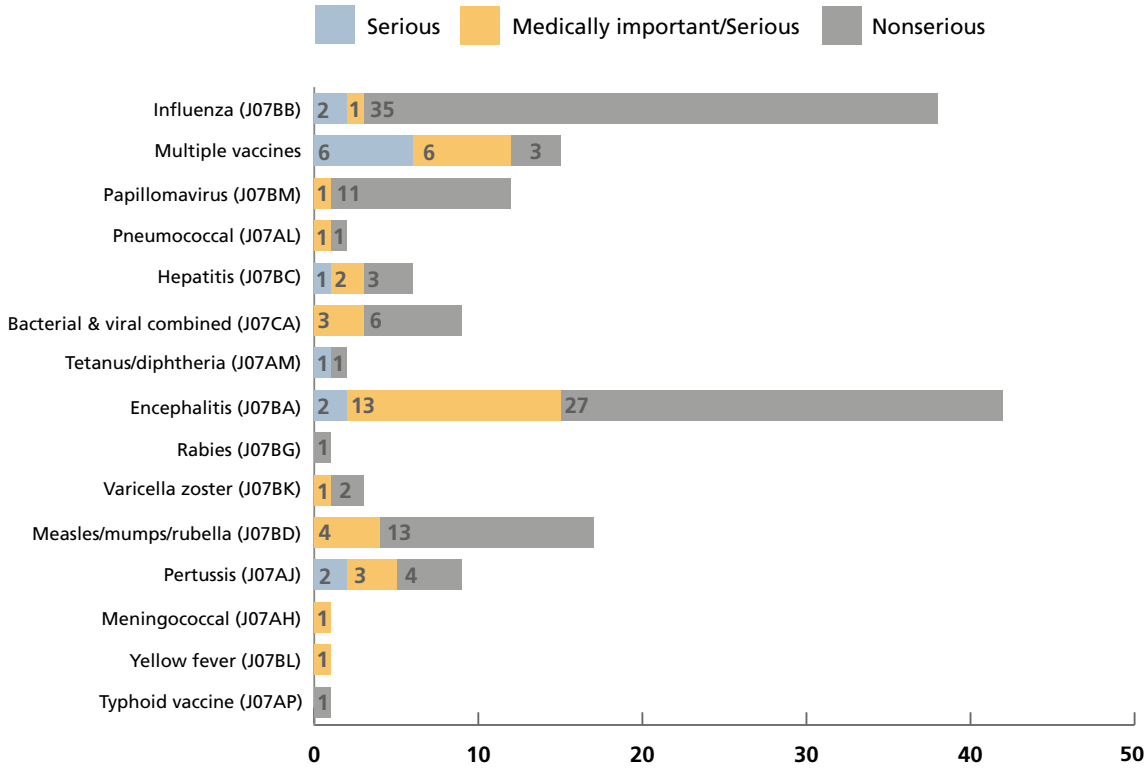

Figure 2 shows the number of spontaneous AEFI reports grouped per vaccine group (ATC code) and seriousness. There are no accurate data available to Swissmedic regarding the number of doses administered in each particular non-Covid 19 vaccine group in 2021 and therefore this figure does not indicate which vaccine group displayed a higher AEFI rate (e.g. as number per 100'000 doses).

Generally, a safety report is assessed as 'serious' if it involves an adverse event leading to death, to hospitalisation or to prolongation of an existing hospitalisation, if it was life threatening or resulted in a significant or persistent disability or a congenital anomaly. Furthermore, a report is assessed as 'medically important' (and therefore, also as 'serious') even if it does not fulfil the criteria for 'seriousness' mentioned, but it involves an event considered to be significant by medical judgement. All other reports are assessed as 'not serious' (e.g. self-limiting adverse events with good recovering). Of the 159 spontaneous reports received in 2021, 108 (67.9%) were not-serious, 37 (23.3%) included only medically important events and 14 (8.8%) of the reports involved AEFIs with serious consequences.

Generally, by considering all vaccines in 2021, the relative frequency (percentage) of 'serious' including 'medically important' cases taken together (51 reports, i.e. 29.9%) was equal to that recorded in the previous year 2020 (29.9%) and lower as compared to 2019 (35.2%).

Case-reports where several (n>1) different vaccines have been administrated and have been reported in relation with suspected AEFI, are shown in Figure 2 as 'Multiple vaccines'.

During 2021, a higher number of cases was submitted in relation with the tick-borne encephalitis vaccination and are shown in Figure 2 as ATC code 'Encephalitis (J07BA)'. However, the majority of these case-reports were assessed as 'non-serious', whereas the number of 'serious' and/or 'medically important' cases regarding encephalitis vaccines (n=15) was comparable with those received for other vaccine groups. Among the serious/medically important reports, some few cases of 'vaccination failure'/'drug ineffective' and consecutive 'tick-borne viral encephalitis' or 'meningitis' have been received for this vaccine-group (see also further below).

Figure 3
Number of AEFI reports by reporter qualification and seriousness, 2021

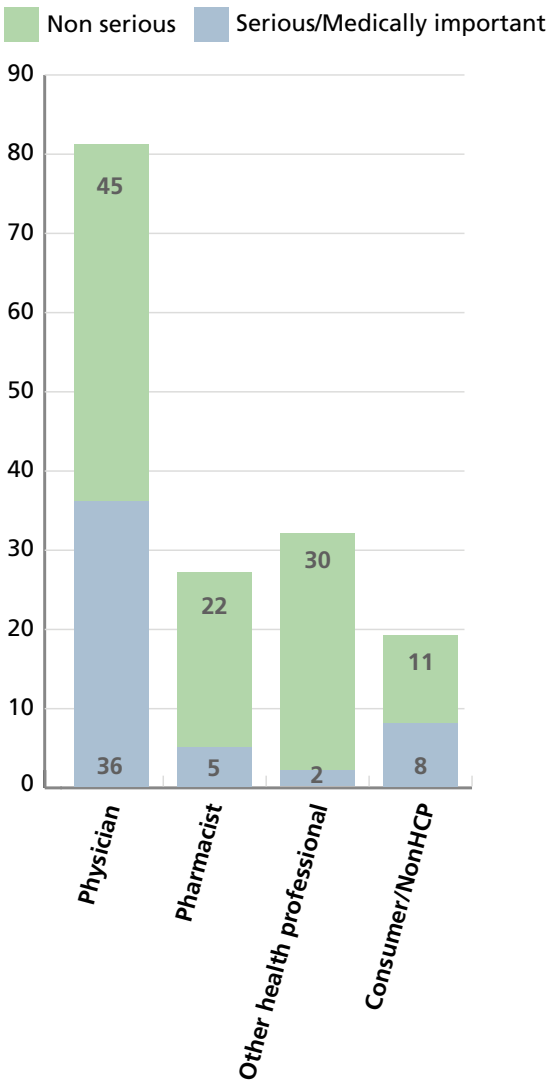

Figure 4
Number of AEFI reports by age group and seriousness, 2021

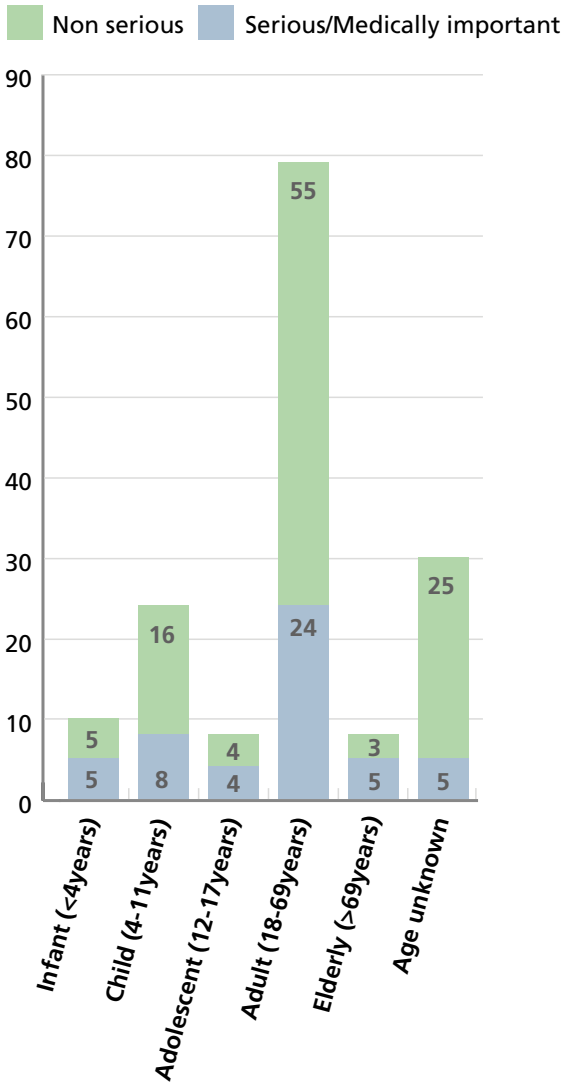

Figure 3 shows the number of Swiss AEFI reports in 2021 grouped by primary reporter and seriousness. Health care professionals - generally providing medically confirmed data and good quality of individual AEFI reports - have been primary reporters in the vast majority of cases. Physicians reported the largest group of AEFI reports (81 of 159), also comprising a higher number of reports assessed as serious or medically important (36 of 81 reports). Notably, consumers/patients submitted to Swissmedic the lowest number (19) of non-Covid AEFI reports during 2021.

Figure 4 shows the number of spontaneous AEFI reports grouped by age group and seriousness. It becomes apparent that the highest number of 'serious' or 'medically important' (24 AEFI-reports in total) have been recorded in the age group 'adults'. However, during 2021 the age groups 'elderly' totalises the highest percentage of 'serious' or 'medically important' cases taken together (with 5 of 8 reports, 62.5%) as compared with the other age groups specifically recorded: 'infants' (5 of 10 reports, 50%), 'adolescents' (4 of 8 reports, 50%), 'children' (8 of 24 reports, 33.3%) and 'adults' (24 of 79 reports, 30.4%).

Figure 5
Number of AEFI reports in Switzerland by Sytem Organ Classes, 2021

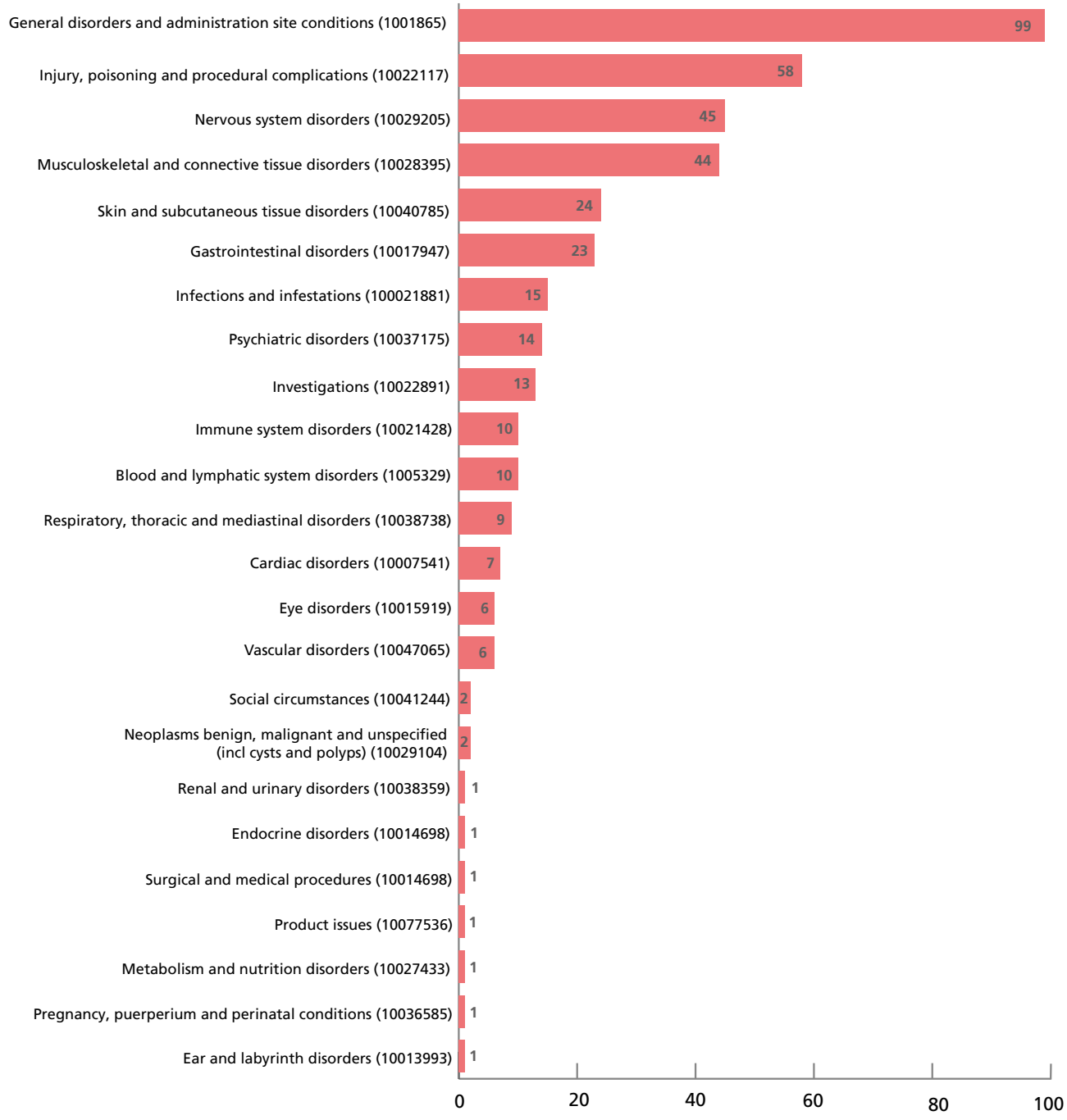

Figure 5 provides an overview on the AEFI reports received during 2021, as grouped by the MedDRA System Organ Classes (SOCs) concerned, i.e. regarding all AEFIs of each report. The following six organ classes were most frequently involved: General disorders and administration site conditions (in 99 reports); Injury, poisoning and procedural complications (58 reports); Nervous system disorders (in 45 reports); Musculoskeletal and connective tissue disorders (44 reports); Skin and subcutaneous tissue disorders (24 reports); Gastrointestinal disorders (23 reports).

Figure 6
Overview on the most frequent AEFIs of all reports, 2021

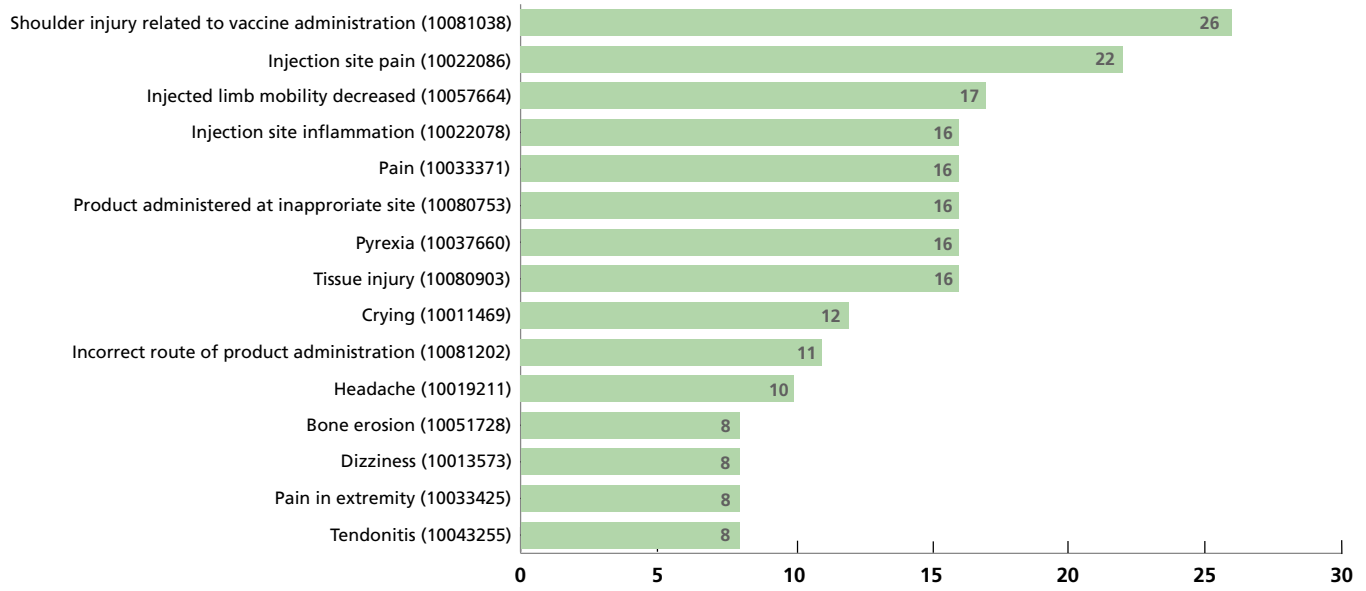

Figure 6 displays the most frequent AEFI reported during 2021 as MedDRA Preferred Terms, such as: shoulder injury related to vaccine administration; different injection/vaccination site reactions; pain; pyrexia; crying; incorrect vaccine administration (site or route); headache; dizziness, pain in extremity.

A number of 26 case-reports with "shoulder injury related to vaccine administration" have been received in 2021, in association with "incorrect route of product administration", "product administered at inappropriate site", or other additional AEFI. Some of these cases were submitted to Swissmedic by different reporters and are originating from a literature publication of a case series occurring following incorrect peri-articular vaccine administration during the seasonal influenza immunization campaign in 2017 (Ref. 1). Notably, all these reports have been submitted as non-serious cases.

Figure 7
The most frequent AEFIs in «serious» reports, 2021

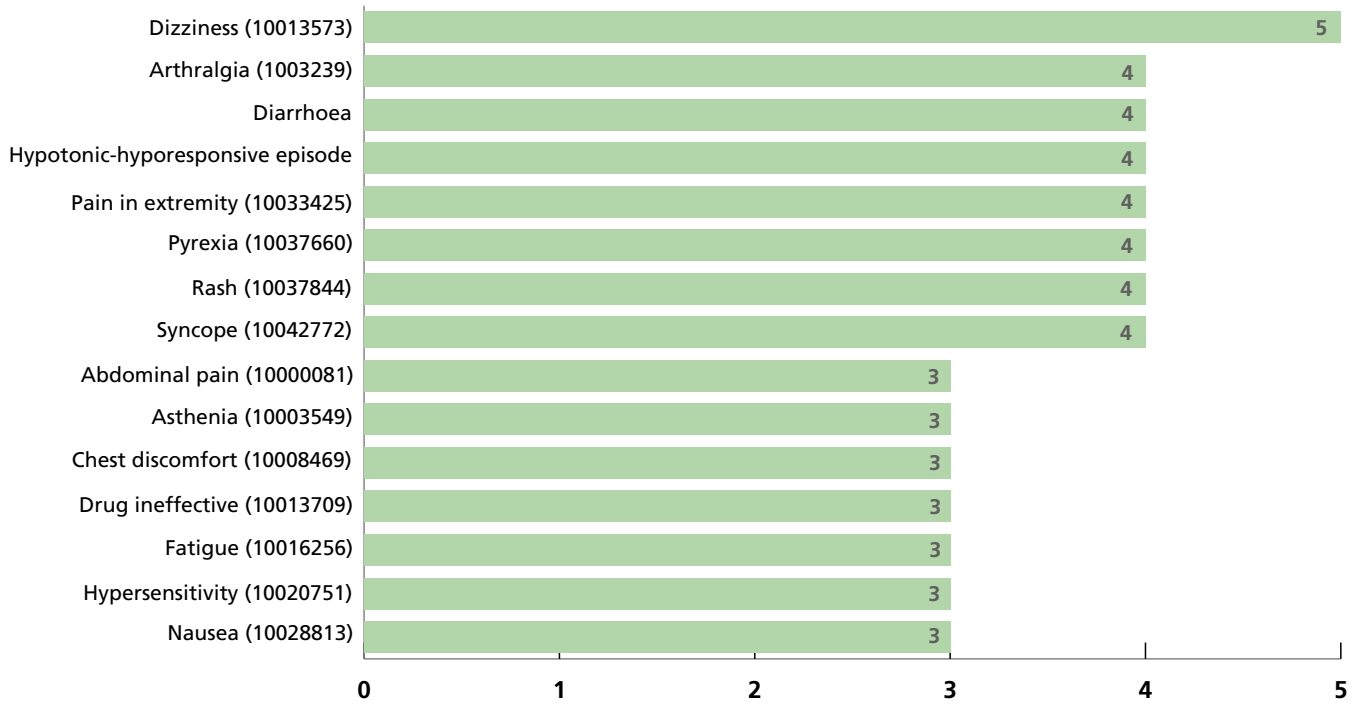

Figure 7 summarizes the most frequent AEFIs submitted as MedDRA Preferred Terms in reports assessed as 'serious' or 'medically important', such as: dizziness; arthralgia; diarrhoea; hypotonic-hyporesponsive episode; pain in extremity; pyrexia; rash; syncope.

Three case-reports of 'vaccination failure' were reported in 2021 following tick-borne encephalitis vaccination (one case, serious, of TBE-meningoencephalitis, outcome 'recovered'); varicella virus vaccination (one case, non-serious, with 'Herpes zoster', outcome 'unknown'); and human papilloma virus immunization (one case, non-serious, with anogenital warts, outcome 'unknown').

Reports of serious neurological AEFIs occurring in Switzerland during 2021 included:

- Four case-reports of 'hypotonic-hyporesponsive episode' (three of them occurring in infants, one with patient age not reported). Each of the four cases occurred following administration of multiple vaccines and the outcome of the episode was always reported as 'recovered'.

- Three cases-reports of encephalitis/encephalopathy: one case with a 'missed booster dose' of tick-borne encephalitis vaccination and consecutive 'tick-borne viral encephalitis' in a 5-year-old male child, with outcome reported as 'recovered'. The second case of 'encephalitis' occurred in a 36-year-old male following a combined diphtheria/ pertussis/ tetanus vaccination, with outcome 'recovering' at the time of reporting. One case of 'encephalopathy' occurred in a male of unknown age following tick-borne encephalitis vaccination, with outcome 'not recovered'.

- Two cases-reports of 'transverse myelitis': one case in a 17-year-old female adolescent flowing tick-borne encephalitis vaccination; the second case occurred in a 73-year-old elderly woman following influenza vaccination. In both cases, the outcome was reported as 'ongoing'.

- Two cases-reports of meningitis: one case of 'aseptic meningitis' occurred in a 26-year-old male following concomitant administration of multiple different vaccines, with outcome reported as 'recovered', however with a residual 'neuralgia'; the second case of 'meningitis' occurred in a 43-year-old women following tick-borne encephalitis vaccination, with outcome 'unknown'.

- Two case-reports of 'loss of consciousness': one case in a 8-year-old child following measles/ mumps/ rubella vaccine, with outcome 'recovered'; the second case in a 41-year-old male following tick-borne encephalitis vaccination, with outcome also 'recovered'.

- One case-report of 'altered state of consciousness' in an 86-year-old woman following pneumococcal vaccination, with outcome 'unknown'.

- One case-report of 'catatonia' and 'confusional state' in a 14-year-old male adolescent following vaccination against HPV and hepatitis a/ hepatitis b, with outcome 'not recovered' at the time of reporting.

- One case-report of 'cataplexy and 'narcolepsy' in a 13-year-old male patient following tick-borne encephalitis vaccination, with outcome 'unknown'.

- One case-report of 'epilepsy' in a 72-year-old woman following influenza vaccination, with outcome reported as 'recovered'.

- One case-report of 'brachial plexopathy' occurring in a 61-year-old woman following diphtheria/polio/tetanus vaccination, with outcome 'not recovered' at the time of reporting.

No case-reports with fatal outcome have been received by Swissmedic in 2021 for non-Covid 19 vaccines.

AEFI reports received by Swissmedic in 2021 following Covid-19 vaccinations

In Switzerland, the Covid-19 vaccine rollout and vaccination campaign were started in late December 2020 and only a single AEFI-report was submitted in 2020 for these new vaccines. Hence, AEFI reports received in 2021 are reflecting the spontaneous safety reporting on Covid-19 vaccines during the first year of the nation-wide immunization campaign.

As published by Swissmedic in "Update 20 - Reports of suspected adverse reactions to COVID-19 vaccines in Switzerland" (Ref. 2), up to 14 December 2021 Swissmedic evaluated 10,842 reports on suspected adverse drug reactions to COVID-19 vaccinations that occurred with a temporal link to the vaccinations. At 6,915 (64%), most of the reports were classified as not serious, while 3,927 (36%) reports were classified as serious. About half of the reports were submitted by medical professionals, while 5,478 or 50.5% came directly from those affected, i.e. the patients. The average age of those affected was 52 years, with 13.1% aged 75 or over. In the cases classified as serious, the average age was 54.5 years, and for reports temporally linked to a death it was 79.7 years. The majority of the reports concerned women (64%) and there were a few cases where no gender was specified.

In 178 serious cases, the people concerned died at different time-intervals after receiving the vaccine. Despite a chronological association, there is no concrete evidence indicating that the Covid-19 vaccination was the cause of death.

7,426 (68.5%) reports involved Modernas COVID-19 vaccine Spikevax® (for approx. 64% of the vaccine doses administered – this was the most widely used COVID-19 vaccine in Switzerland), while 3,141 (29%) were associated with Pfizer/BioNTech's Comirnaty® (with approx. 36% administered vaccine doses).

The reports of adverse reactions received and analysed by 14.12.2021 did not alter the positive benefit-risk profile of the COVID-19 vaccines used in Switzerland, largely confirming their known side effects profile. Known side effects of COVID-19 vaccines are listed in the continually updated Swiss product information texts published (Ref. 3).

As important safety topic, 'myocarditis/pericarditis' was particularly addressed in this 'Update 20', since very rare cases of myocarditis and pericarditis have been reported following vaccination with the COVID-19 mRNA vaccines. These cases generally occurred within 14 days of vaccination and more frequently after the second dose and in younger men. By 14.12.2021, 267 cases of myocarditis and/or pericarditis with a suspected relation to vaccinations had been reported and evaluated out of a total of more than 12.75 million vaccine doses administered in Switzerland. Of these, 52 were linked with Comirnaty and 206 with Spikevax. The large majority of cases involved males (n = 199, 74.5%) and the mean age was 37 years (median: 51, range: 14 to 88 years). The persons affected received medical treatment and most have recovered by the time of reporting. Considering the national safety data and available international study results, the Swiss Federal Commission for Vaccination (FCV) has made the vaccination recommendation for persons under 30 years of age more specific.

Further cumulative Safety Updates on Covid-19 vaccines have been published by Swissmedic on the Website on a regular basis, the most recent on 26 August 2022 (Ref. 4).

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