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

Vaccinovigilance 2018

Summary of adverse events following immunization reported in Switzerland during 2018

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Introduction
Executive summary

During 2018, the division Safety of Medicines of Swissmedic received 223 new case-reports of suspected adverse events following immunization (AEFI) from Switzerland. This is a slightly lower level as the number of cases submitted during 2017 (232 reports) but higher as compared to 2016 (209 reports).

AEFI-reports received during 2018 have been recorded and evaluated in the new pharmacovigilance database of Swissmedic - VigilanceONE Ultimate. There are no accurate data available regarding the total number of vaccines/doses administered during 2018 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.

Since 2010, important safety topics concerning vaccines – including potential risks - are being evaluated with participation of the Human Medicines Expert Committee (HMEC) of Swissmedic.

An increased AEFI reporting rate followed by a scientific evaluation of relevant cases can lead to risk minimisation measures in order to ensure vaccines safety, if necessary.

Figure 1
Number of AEFI reports per age group and gender, 2018

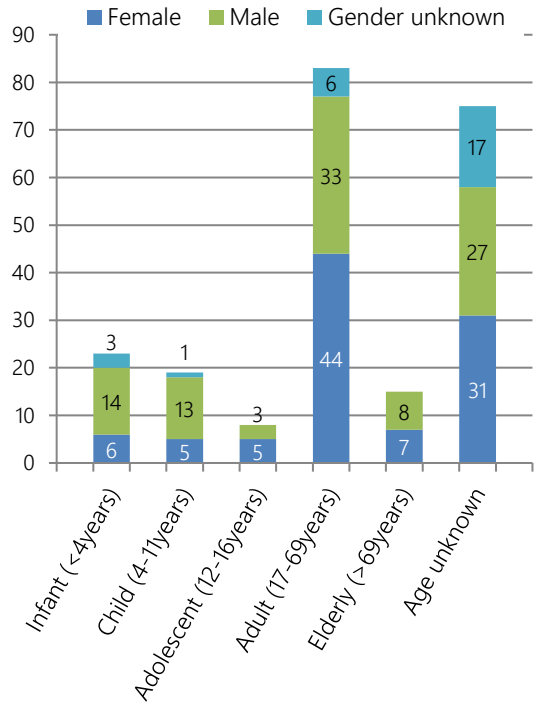

Figure 1 compares the number of reports per age group and gender. The largest number of AEFI reports involved adults (83 reports), followed by infants (23 reports), children (19 reports), elderly (15 reports) and adolescents (8 reports).

Throughout the year 2018, the number of reports concerning females was equal to the number of reports concerning males (98 reports in each group). In 27 AEFI reports, the gender of the persons remained unknown. In 75 case-reports, the age group of the patients was not reported.

Figure 2

Number of reports per vaccine group (ATC code) and seriousness, 2018

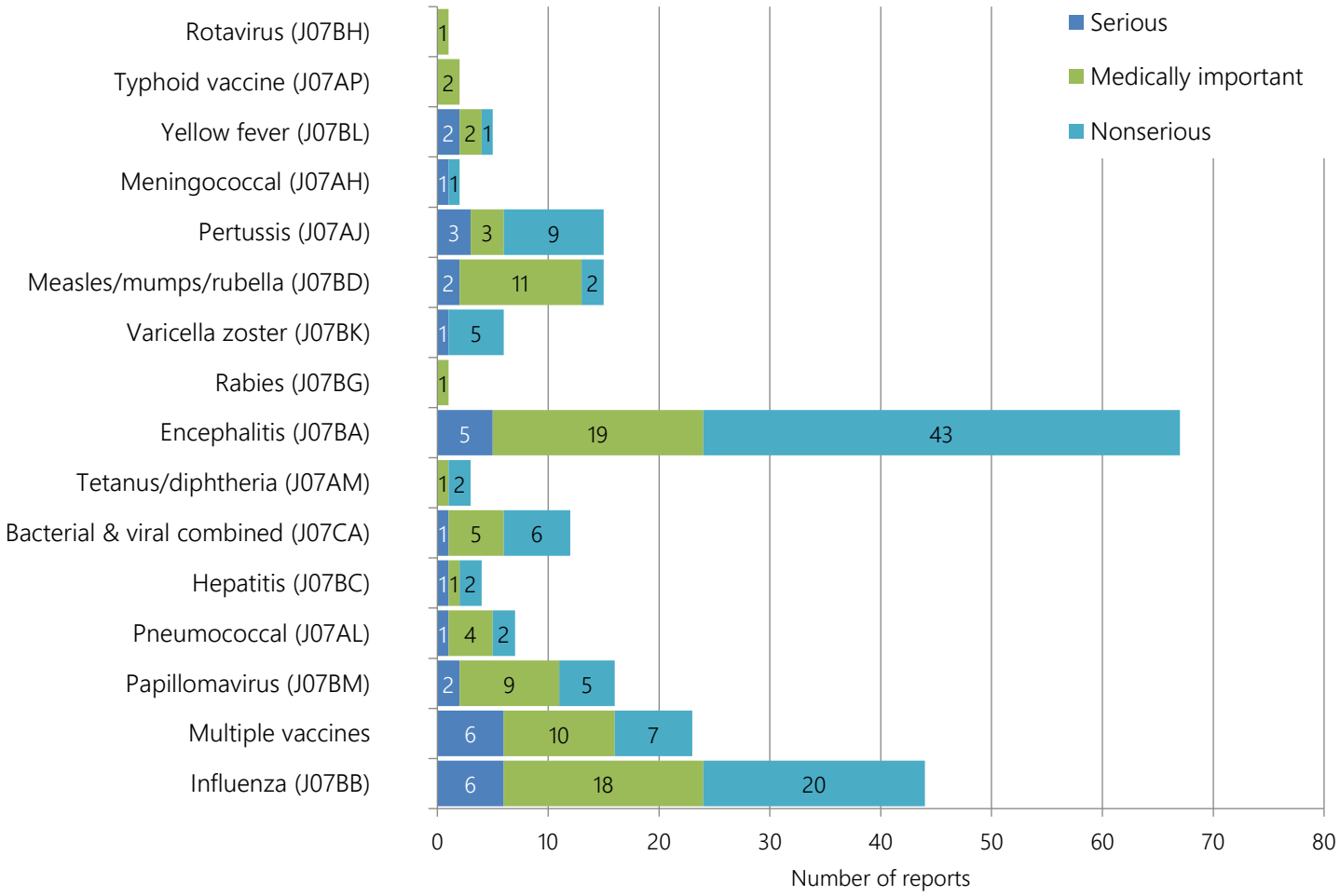

Figure 2 shows the number of spontaneous AEFI reports grouped per vaccine group (ATC code) and seriousness. There are no data available to Swissmedic regarding the number of doses administered in each particular vaccine group in 2018 and therefore this figure does not indicate which vaccine group displayed a higher AEFI rate (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 hence 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 223 spontaneous reports received in 2018, 105 (47.1%) were not-serious, 87 (39%) included medically important events and 31 (13.9%) of the reports involved AEFIs with serious consequences.

Generally, by considering all vaccines, the relative frequency (percentage) of 'serious' reports (i.e. reports containing AEFIs with serious consequences) decreased in 2018 as compared to those recorded during the previous year (13.9% in 2018 vs. 19.4% in 2017).

Figure 3

Number of AEFI reports per reporter qualification and seriousness, 2018

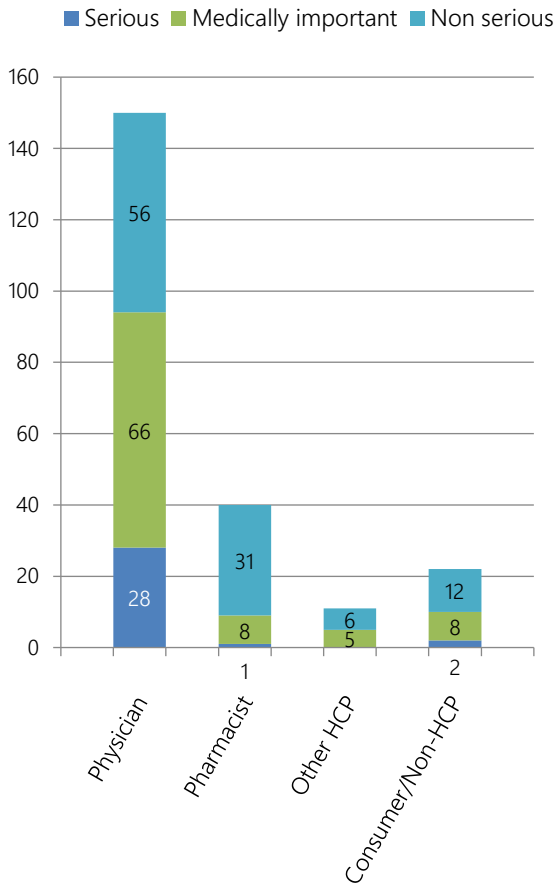

Figure 3 shows the number of Swiss AEFI reports in 2018 grouped by primary reporter and seriousness. Health care professionals - generally providing medically confirmed data and good quality of individual AEFI reports - have been primary reporters in the vast majority of cases.

Physicians reported the largest group of AEFI reports (150 of 223), comprising also a higher number of reports assessed as serious or medically important (94 of 150 reports).

Figure 4

Number of AEFI reports per age group and seriousness, 2018

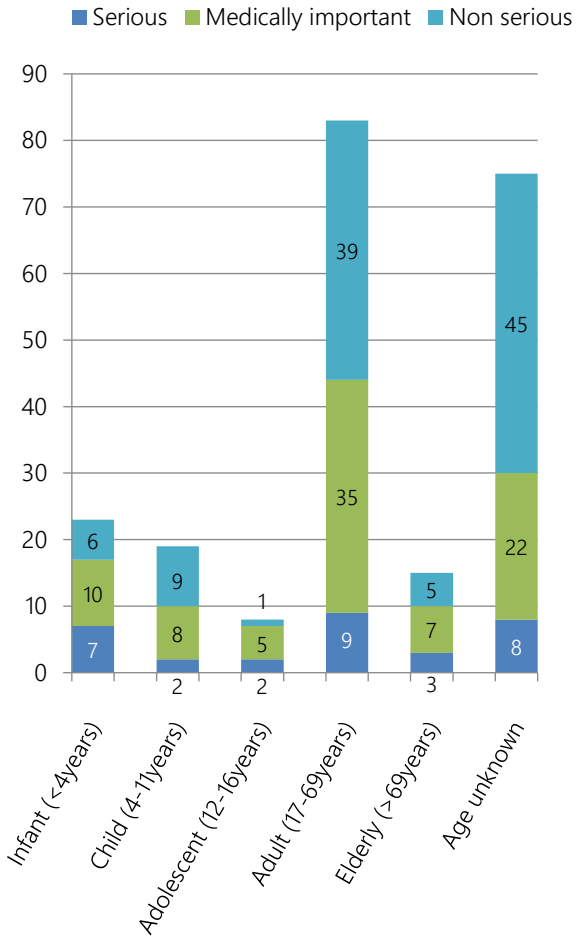

Figure 4 shows the number of spontaneous AEFI reports grouped by age group and seriousness. It becomes apparent that the highest numbers of 'serious' (9 reports) or 'medically important' (35 reports) have been recorded in the age group 'adults'.

However, during 2018, the age group adolescents totalises the highest percentage of 'serious' or 'medically important' cases taken together (7 of 8 reports, 87.5%) as compared with the other age groups analysed: 'infants' (17 of 23 reports, 69.6%), adults (44 of 83 reports, 53%) and children (10 of 19 reports, 52.6%).

Figure 5

Number of AEFI reports in Switzerland by System Organ Classes, 2018

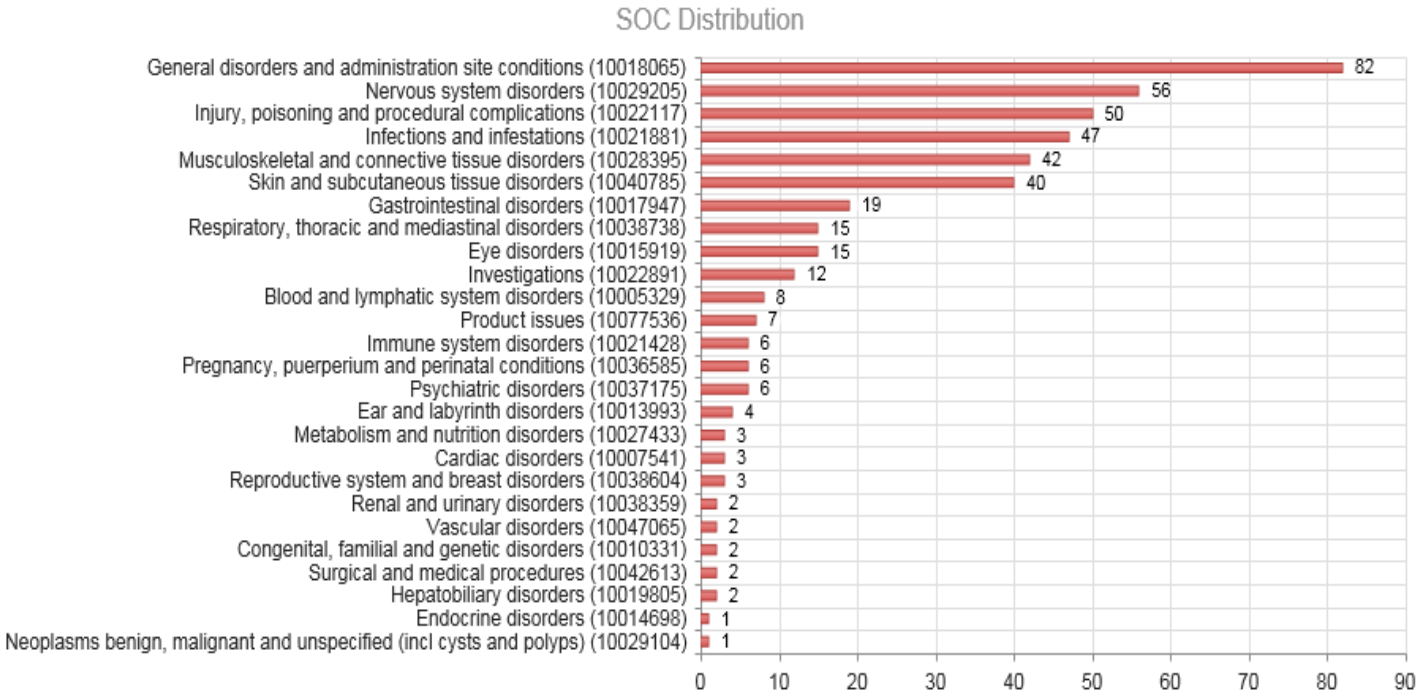

Figure 5 provides an overview on the AEFI reports received during 2018, as grouped by the MedDRA System Organ Classes (SOCs) concerned, i.e. regarding AEFIs of each report.

The following six organ classes were most frequently involved in reports after immunization:

- General disorders and administration site conditions (82 reports, 36.8%);
- Nervous system disorders (56 reports, 25.1%);
- Injury, poisoning and procedural complications (50 reports, 22.4%);
- Infections and infestations (47 reports, 21.1%);
- Musculoskeletal and connective tissue disorders (42 reports, 18.8%);
- Skin and subcutaneous tissue disorders (40 reports, 17.9%)

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Figure 6

AEFI reports by vaccine group (ATC code) and top 3 involved System Organ Classes, 2018

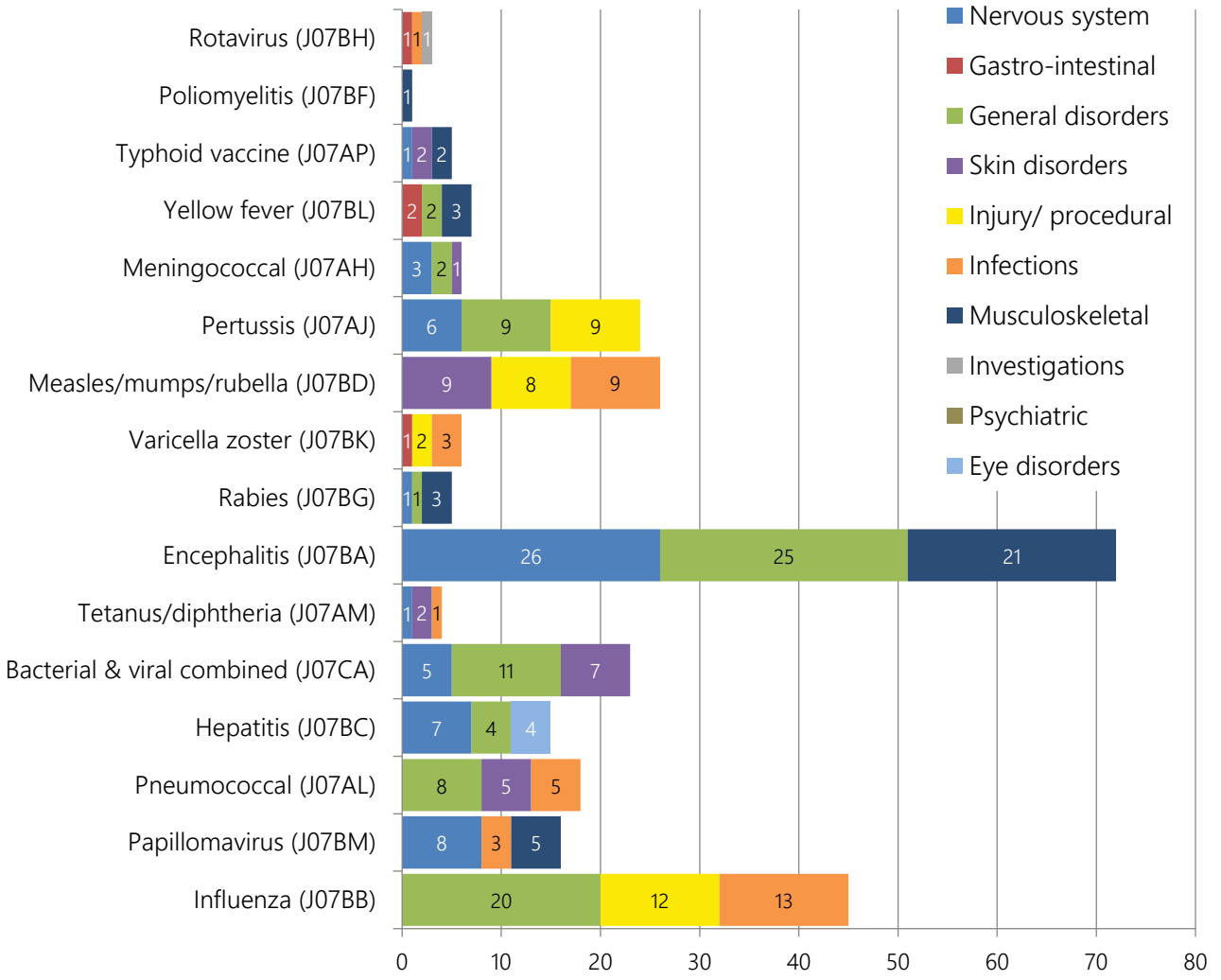

Figure 6 shows the AEFI reports by vaccine group (ATC code) and top 3 MedDRA system organ classes concerned.

Notably, most of the vaccines have a significant part of their frequently reported adverse events classified in the SOCs:

- General disorders and administration site conditions;
- Musculoskeletal and connective tissue disorders;
- Nervous system disorders;
- Skin and subcutaneous tissue disorders;
- Injury, poisoning and procedural complications.

Table 1

Overview on the most frequent AEFIs of all reports, 2018

Adverse event	System Organ Class	Number of reports
Injection site reactions	General disorders and administration site conditions	46
Erythema/ Rash/ Urticaria	Skin and subcutaneous tissue disorders	29
Headache	Nervous system disorders	26
Fever	General disorders and administration site conditions	24
Exposure during pregnancy	Injury, poisoning and procedural complications	17
Influenza	Infections and infestations	16
Vaccination failure	Injury, poisoning and procedural complications	16
Nausea/ Vomiting	Gastrointestinal disorders	13
Myalgia	Musculoskeletal and connective tissue disorders	12
Vertigo/ Dizziness	Nervous system disorders	11
Asthenia/Fatigue	General disorders and administration site conditions	10
Pain in extremity	Musculoskeletal and connective tissue disorders	10
Arthralgia	Musculoskeletal and connective tissue disorders	8
Paraesthesia	Nervous system disorders	7

Table 1 displays the most frequent AEFI as reported during 2018: injection site reactions; erythema/ rash/ urticaria; headache; fever; exposure during pregnancy; influenza; vaccination failure; nausea/ vomiting; myalgia; vertigo/ dizziness; asthenia/ fatigue; pain in extremity; arthralgia; paraesthesia.

Table 2

The most frequent AEFIs in 'serious' or 'medically important' reports, 2018

Adverse event	System Organ Class	Number of reports
Erythema/ Rash/ Urticaria	Skin and subcutaneous tissue disorders	17
Vaccination failure	Injury, poisoning and procedural complications	15
Headache	Nervous system disorders	14
Fever	General disorders and administration site conditions	13
Injection site reactions	General disorders and administration site conditions	12
Influenza	Infections and infestations	10
Nausea/ Vomiting	Gastrointestinal disorders	8
Asthenia/Fatigue	General disorders and administration site conditions	8
Arthralgia	Musculoskeletal and connective tissue disorders	7
Exposure during pregnancy	Injury, poisoning and procedural complications	7
Myalgia	Musculoskeletal and connective tissue disorders	6

Table 2 summarizes the most frequent AEFIs in reports assessed as 'serious' or 'medically important'. The two tables (Table 1 and Table 2) are displaying quite similar distributions of reported AEFIs. Furthermore, these tables contain well-known AEFIs, similar to those reported to Swissmedic during previous years. Reports of serious neurological AEFIs occurring in Switzerland during 2018 included:

- Two case-reports of 'encephalitis': one case of 'tick-borne viral encephalitis' occurring as result of vaccine ineffectiveness, in a 62-year-old female patient, 9 years after the basic immunization with tick-borne encephalitis vaccine. The second case – based on a literature article (see Ref. 1) - concerned a male patient of unspecified age with lung cancer and nivolumab-treatment who developed necrotizing encephalitis two months after receiving influenza vaccine. In each of these two cases, the outcome of the AEFI 'encephalitis' has not been reported.
- Three case-reports of 'meningoencephalitis': one case in a 4-year-old girl following the administration of influenza vaccine, with outcome reported as 'recovering/resolving'. The second case occurred in a 23-year-old male patient following tick-borne encephalitis vaccination, with outcome reported as 'recovered'. The third case occurred in a 56-year-old male patient following vaccination with two different vaccines: yellow fever vaccine and hepatitis A vaccine, with outcome of meningoencephalitis 'not recovered' at the time of reporting.

- One case reporting of 'hypotonic-hyporesponsive episode', 'tonic-clonic convulsions' and 'syncope', occurring in a 6-year-old girl following tick-borne encephalitis vaccination, with outcome of all AEFIs reported as 'recovered'.
- One case of 'viral meningitis' in a 6-year-old boy, following tick-borne encephalitis vaccination, with outcome reported as 'recovered with sequelae'.
- One case reporting a 'meningeal disorder' (meningeal irritation) in an 11-year-old boy, following administration of two different vaccines: meningococcal vaccine and HPV-vaccine, with outcome reported as 'recovered'.
- One case reporting of 'hallucinations' and 'somnolence' in a 16-year-old female following administration of multiple vaccines: typhoid vaccine/ HPV-vaccine and hepatitis A vaccine, with outcome 'unknown'.
- One case of 'facial paralysis' (Bell's palsy) in a 54-year-old man, following influenza vaccination, with outcome not reported.
- Two cases, each reporting of 'gaze palsy' and 'generalised tonic-clonic seizure': one case in a 15-year-old male, following hepatitis A/ hepatitis B vaccination, with outcome 'recovered'. The second case occurred in a 12-year-old female, following administration of multiple vaccines: tetanus vaccine/ diphtheria vaccine/ pertussis vaccine and hepatitis B vaccine. The outcome was 'recovered' at the time of reporting.

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This annual report was written by
Swissmedic
Safety of Medicines Department
Pharmacovigilance Unit
Hallerstrasse 7
3012 Berne, Switzerland
www.swissmedic.ch/pharmacovigilance

References

1. Heinz Laubli et al. Influenza vaccination of cancer patients during PD-1 blockade induces serological protection but may raise the risk for immune-related adverse events. Journal for Immunotherapy of cancer. 2018;6:40