Summary of adverse events following immunization reported in Switzerland during 2015

Executive summary

During 2015, Swissmedic received 278 case reports of suspected adverse events following immunization (AEFI) from Switzerland. This is nearly on the same level as the number of reported cases during 2014 (296 reports) and a significantly higher number as compared to 2013 (138 reports). Notably, there are no accurate data available regarding the total number of vaccines/doses administered during 2015 and therefore a straightforward conclusion regarding AEFI reporting rates cannot be drawn. Similarly to 2014, during 2015 a substantial number of AEFI cases (80 reports in 2015 vs. 106 reports in 2014) occurring in previous years have been submitted retrospectively to Swissmedic and have also been considered in this evaluation. However, no new safety signals have emerged from these older retrospective AEFI-reports received during 2015. 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 are being discussed and evaluated by experts of the Swissmedic Human Medicines Expert Committee (HMEC). 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, 2015

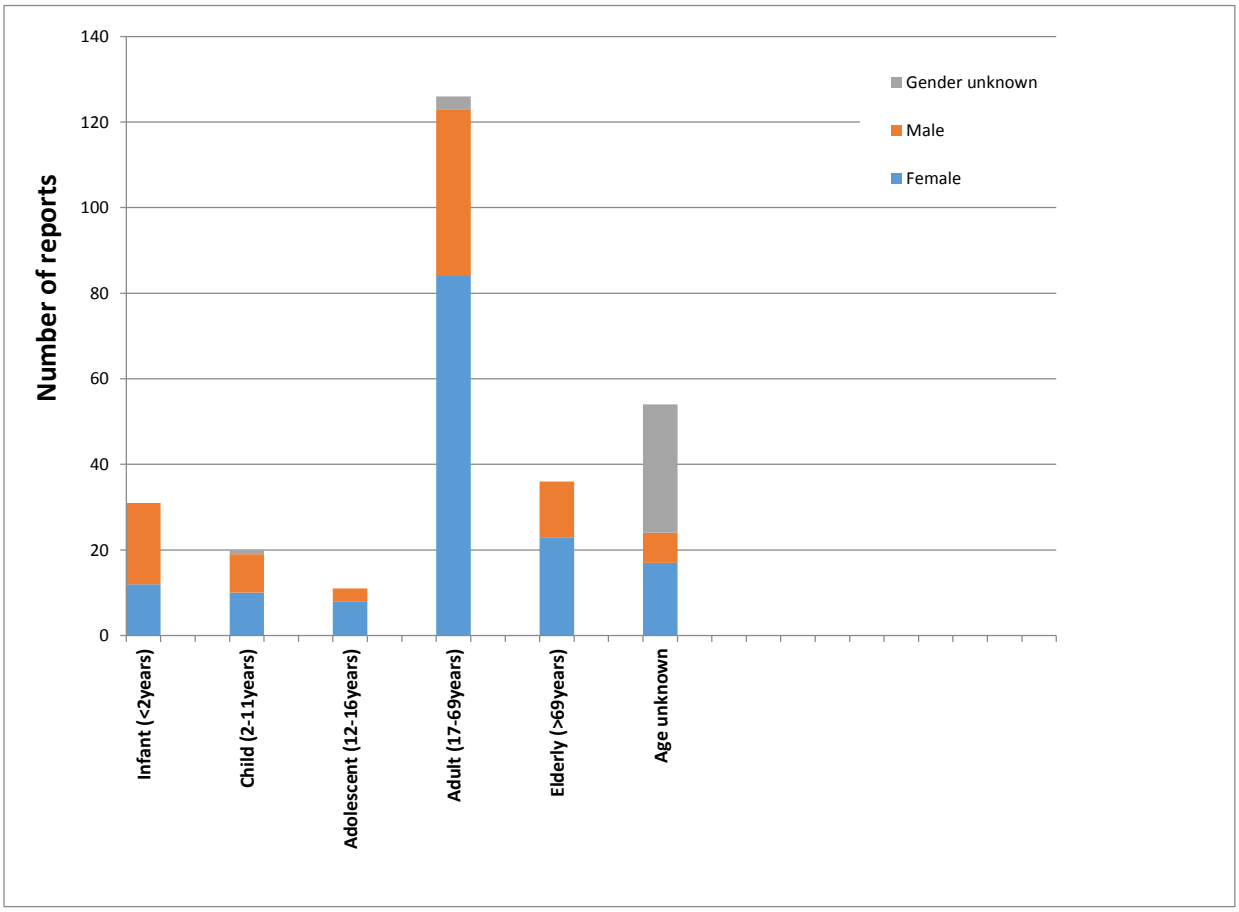

Figure 1 compares the number of reports per age group and gender. The largest number of AEFI reports involved adults (126 reports), followed by elderly (36 reports) and infants (31 reports). Throughout the year, the number of reports concerning females (154 reports) was significantly higher than the number of reports regarding males (90 reports). In 34 AEFI reports, the gender of the persons remained unknown. A higher difference in gender is apparent in the group 'adults' (84 reports of females vs. 39 males). In 54 case-reports, the age of the patients was not recorded.

Figure 2. Number of reports per vaccine group (ATC code) and seriousness, 2015

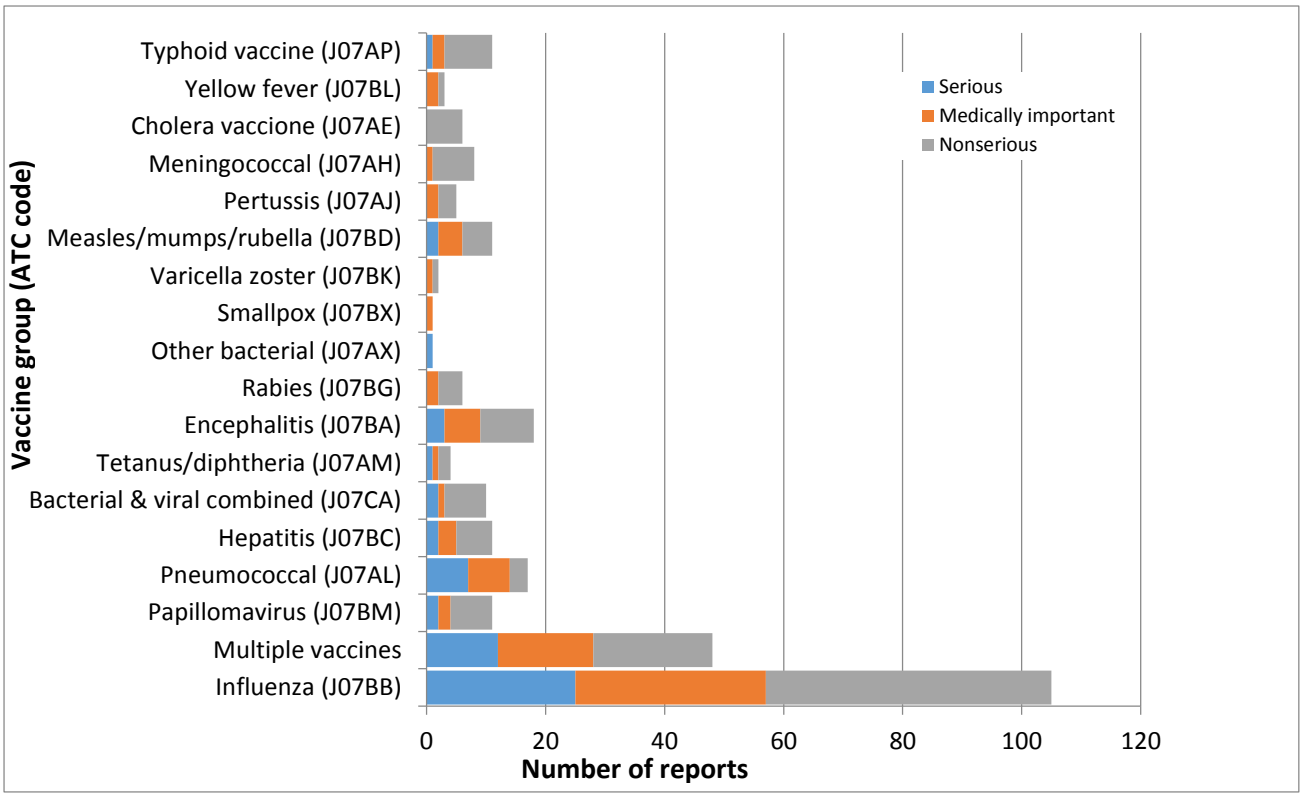

Figure 2 shows the number of spontaneous AEFI reports grouped per vaccine group (ATC code) and seriousness. There are no data available regarding the number of doses administered in each particular vaccine group and therefore this figure does not indicate which vaccine group displayed a higher AEFI rate (as number per 100'000 doses). Generally, a safety report is assessed as 'serious' if it involves an adverse event leading to death, to hospitalization or to prolongation of an existing hospitalization, if it was life threatening or resulted in a significant or persistent disability or a congenital anomaly. Additionally, a report is assessed as 'medically important' (and therefore serious) 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 278 spontaneous reports received in 2015, 138 (49.5%) were not-serious, 83 (30%) included medically important events and 57 (20%) of the reports involved AEFIs with serious consequences. The relative frequency (percentage) of 'not serious' reports (i.e. without serious consequences) was higher as compared to those recorded during the previous year (49.5% in 2015 vs. 31.1% in 2014).

Figure 3. Number of AEFI reports per reporter qualification and seriousness, 2015

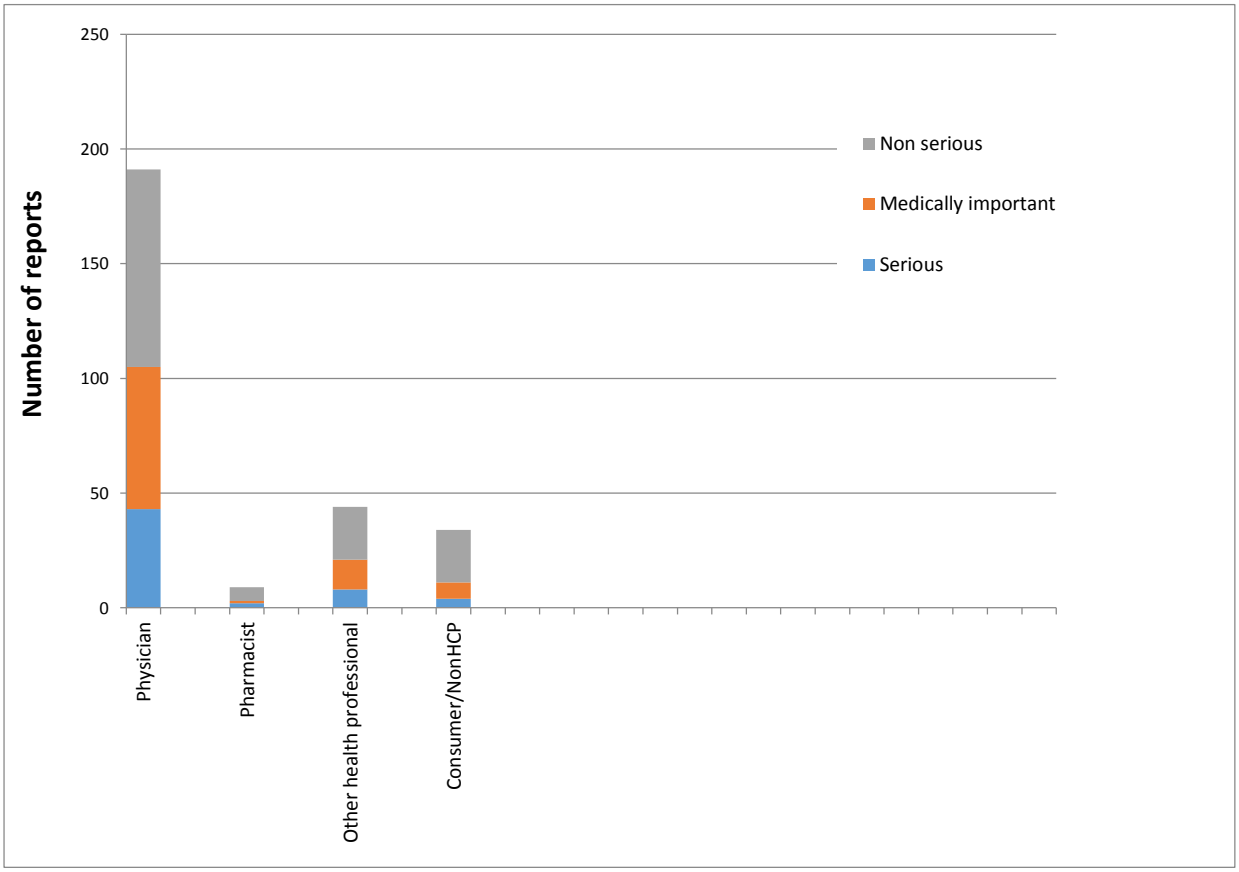

Figure 3 shows the number of Swiss AEFI reports in 2015 grouped by primary reporter and seriousness. Health care professionals, mostly providing medically confirmed data and good quality of individual AEFI reports, primarily reported the vast majority of cases. Physicians reported the largest group of AEFI cases (191 of 278), including also a higher number of reports assessed as serious or medically important (105 of 191 reports).

Figure 4. Number of AEFI reports per age group and seriousness, 2015

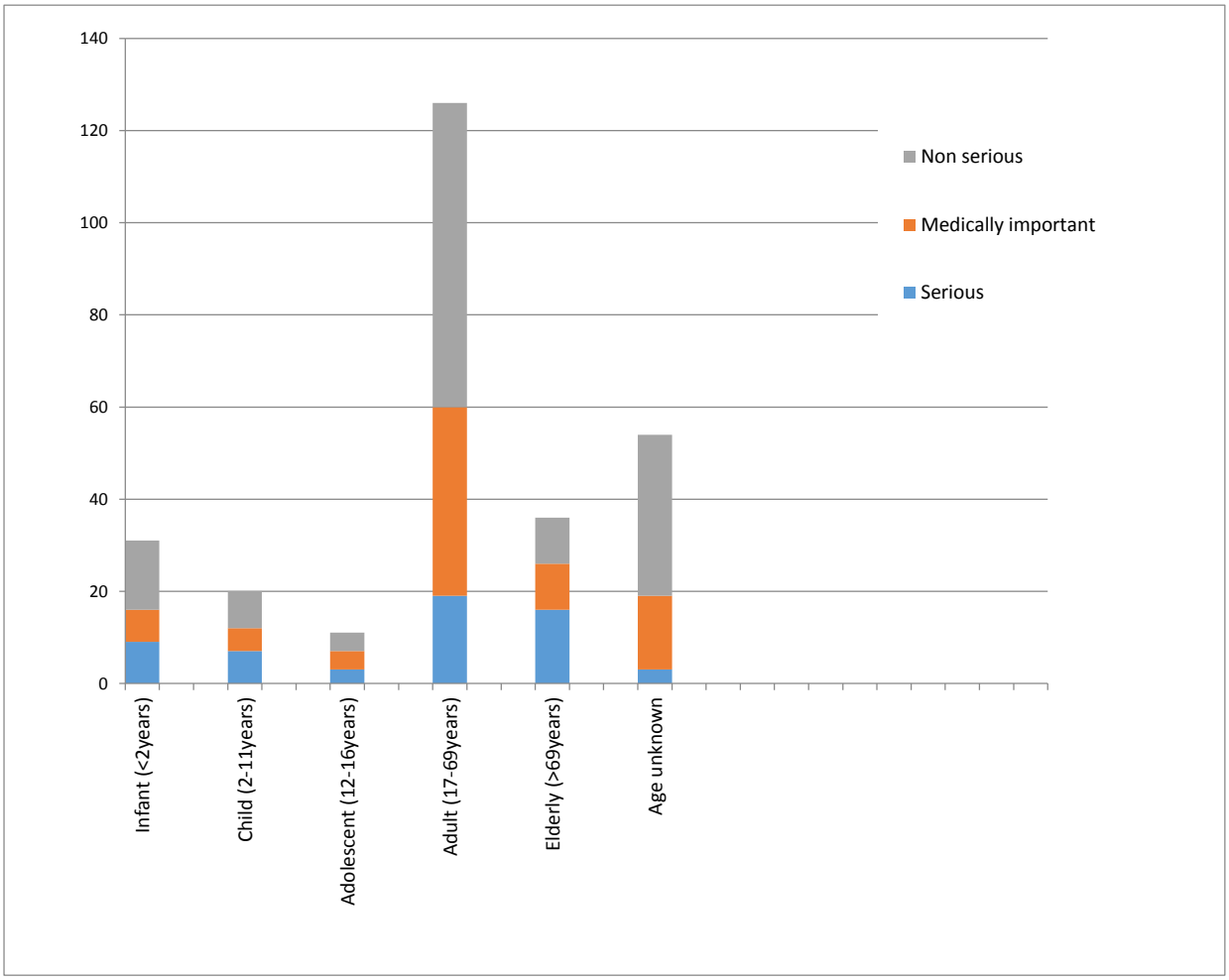

Figure 4 shows the number of spontaneous AEFI reports grouped by age group and seriousness. It becomes apparent that the highest numbers of 'serious' (19 reports) or 'medically important' (41 reports) have been recorded in the age group 'adults'. However, the age group 'adults' totalises the lowest percentage of 'serious' or 'medically important' cases taken together (60 of 126 reports, 47.6%) as compared with the other age groups analysed: infants (16 of 31 reports, 54.8%); children (12 of 20 reports, 60%); adolescents (7 of 11 reports, 63.6%) and elderly (26 of 36 reports, 72%).

Figure 5 provides an overview on the AEFI reports received during 2015, as grouped by the primary MedDRA System Organ Classes (SOCs) concerned (i.e. regarding the leading AEFI of each report). The following five organ classes were most frequently involved in reports after immunization: General disorders and administration site conditions (119 reports, 43.1%); Nervous system disorders (87 reports, 31.5%); Musculoskeletal and connective tissue disorders (53 reports, 19.2%); Skin and subcutaneous tissue disorders (52 reports, 18.8%); Injury, poisoning and procedural complications (40 reports, 14.5%).

Figure 5. Number of AEFI reports in Switzerland by System Organ Classes, 2015

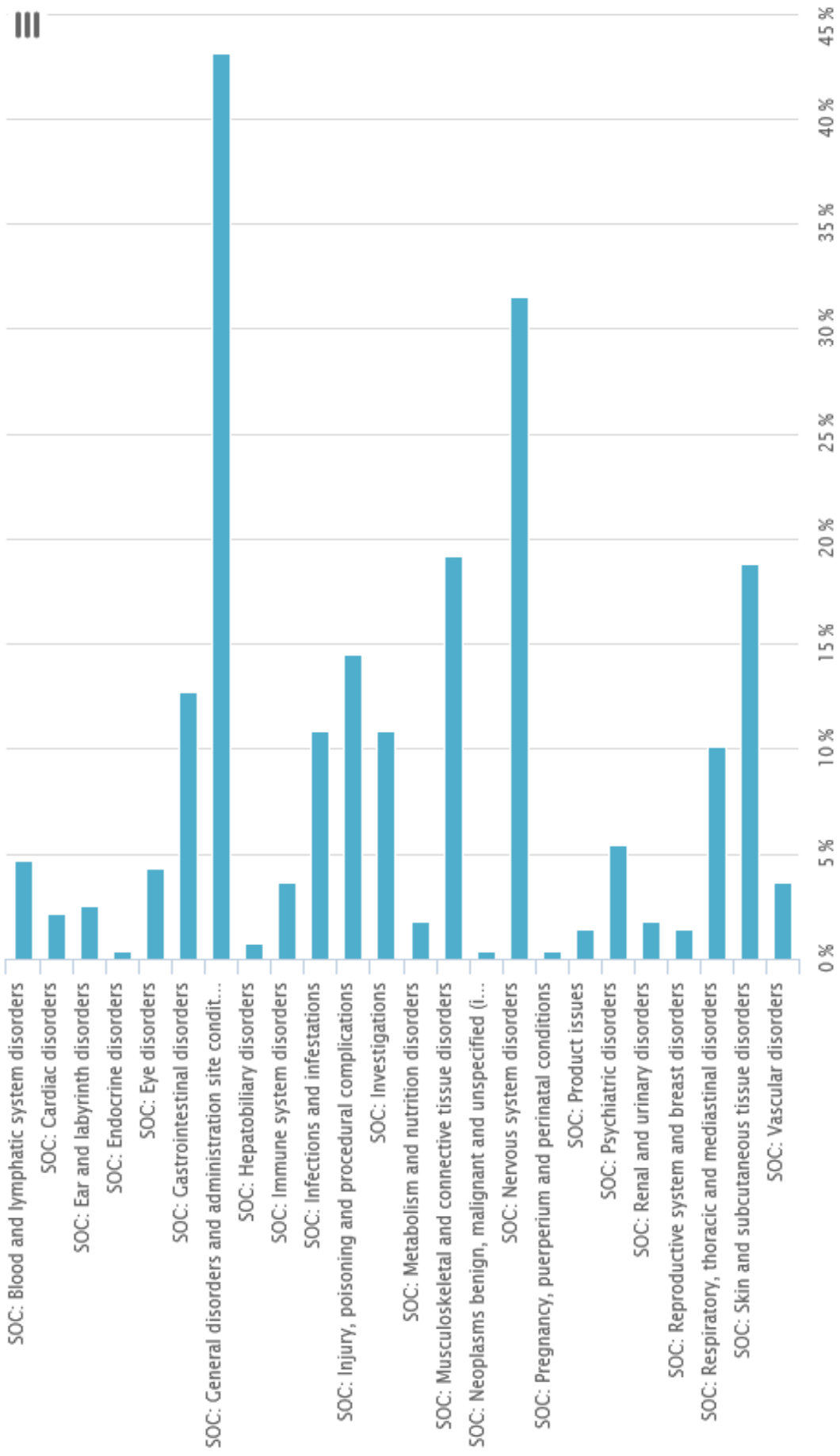

Figure 6. AEFI reports by vaccine group (ATC code) and top 3 involved System Organ Classes, 2015

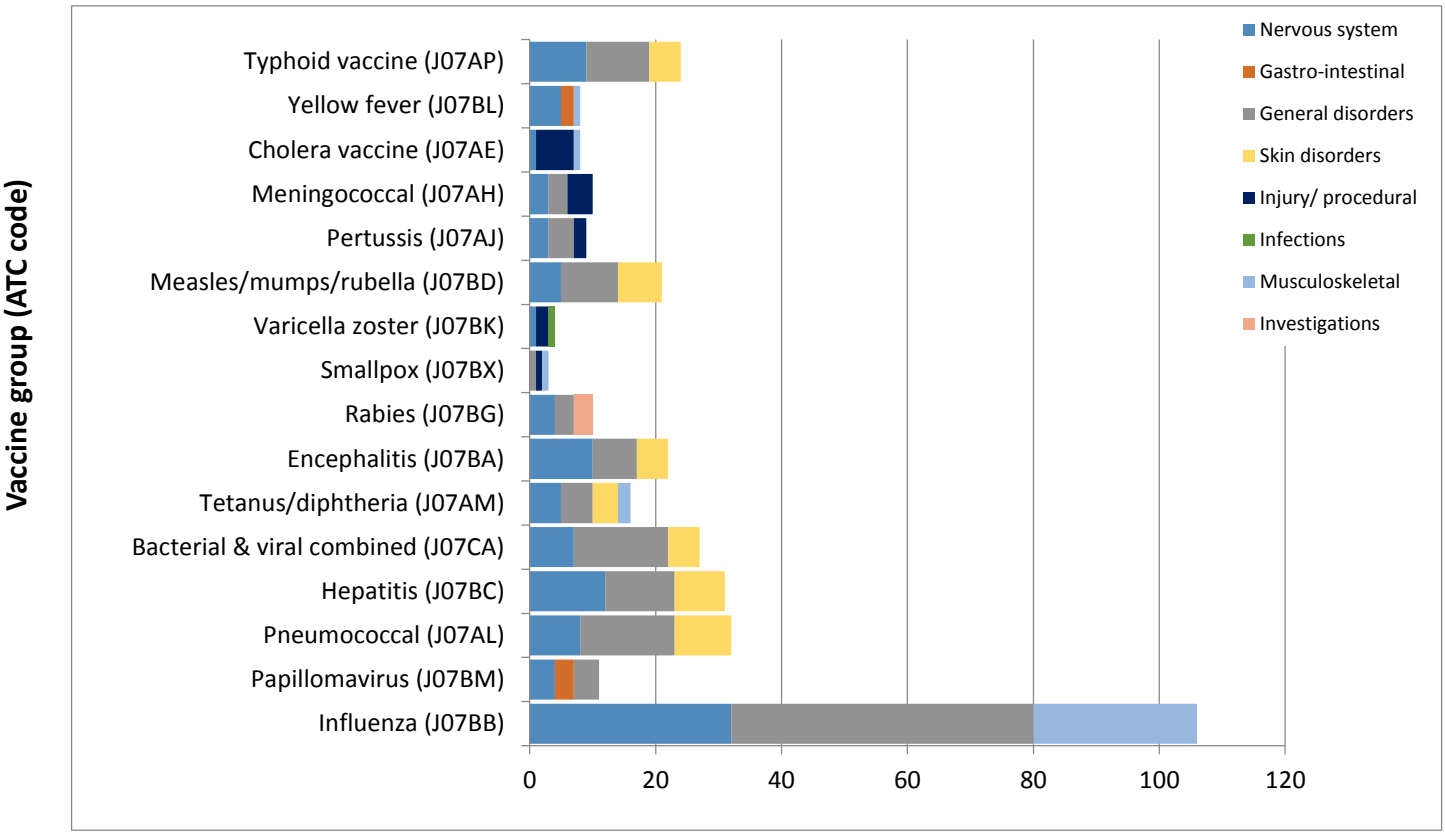

Figure 6 shows the AEFI reports by vaccine group (ATC code) and top 3 MedDRA system organ classes concerned. Notably, most of the vaccines have a significant part of their frequently reported adverse events classified in the SOCs: General disorders and administration site conditions; Musculoskeletal and connective tissue disorders; Skin and subcutaneous tissue disorders.

Table 1. Overview on the most frequent AEFIs of all reports, 2015

Adverse event	System Organ Class	Number of reports
Injection site reactions	General disorders and administration site conditions	66
Fever	General disorders and administration site conditions	49
Erythema/ Rash/ Urticaria	Skin and subcutaneous tissue disorders	38
Headache	Nervous system disorders	26
Nausea/ Vomiting	Gastrointestinal disorders	26
Asthenia/Fatigue	General disorders and administration site conditions	22
Influenza like illness	General disorders and administration site conditions	15
Chills	General disorders and administration site conditions	13
Arthralgia	Musculoskeletal and connective tissue disorders	12
Myalgia	Musculoskeletal and connective tissue disorders	11
Abdominal pain	Gastrointestinal disorders	11

Table 1 displays the most frequent AEFI as reported during 2015 (>10 reports): injection site reactions; fever; exanthema/ rash/ urticaria; headache; nausea/ vomiting; asthenia/ fatigue; influenza like illness; chills; arthralgia; myalgia; abdominal pain.

Table 2. The most frequent AEFIs classified as 'serious' or 'medically important', 2015

Adverse event	System Organ Class	Number of reports
Injection site reactions	General disorders and administration site conditions	24
Fever	General disorders and administration site conditions	17
Erythema/ Rash/ Urticaria	Skin and subcutaneous tissue disorders	14
Nausea/ Vomiting	Gastrointestinal disorders	14
Asthenia/ Fatigue	General disorders and administration site conditions	12
Headache	Nervous system disorders	10
Influenza like illness	General disorders and administration site conditions	7
Abdominal pain	Gastrointestinal disorders	6
Arthralgia	Musculoskeletal and connective tissue disorders	6

Table 2 summarizes the most frequent AEFIs assessed as 'serious' or 'medically important' (>5 reports). The two tables (Table 1 and Table 2) are displaying similar distributions of reported AEFIs. New AEFI appearing in these two tables as compared with previous year 2014 are 'asthenia/ fatigue', 'influenza like illness' and 'arthralgia', possibly also in relation with the high number of AEFI following influenza vaccination reported during 2015.

Medically confirmed neurological AEFIs reported as serious during 2015 included:

- 2 cases of 'hypotonic-hyporesponsive episode': One case in a 4 months old male infant following the administration of several different vaccines: tetanus vaccine/ diphtheria vaccine/ hepatitis b vaccine/ pertussis vaccine/ polio vaccine/ haemophilus influenza type B vaccine and pneumococcal vaccine, outcome 'recovered'. The second case occurred in a 2-month-old male infant, also following the administration of several different vaccines: tetanus vaccine /diphtheria vaccine/ pertussis vaccine/ polio vaccine/ haemophilus influenza type B vaccine and pneumococcal vaccine, with outcome also 'recovered'.

- One case reported an 'apparent life threatening event' in a 2-month-old female after immunization with tetanus vaccine/ diphtheria vaccine/ hepatitis b vaccine/ pertussis vaccine/ polio vaccine/ haemophilus influenza type B vaccine and pneumococcal vaccine. Symptoms included dystonia, gaze palsy, cyanosis and tongue movement disturbance. The duration of the entire event was ca. 5 minutes and the outcome was reported as 'recovered'.
- 2 case-reports of 'multiple sclerosis': one case in a 23-year-old female after tick-borne encephalitis vaccine and hepatitis A vaccine (outcome reported as 'not recovered'); one case in a 29 year old male following A/H1N1 influenza pandemic vaccine (outcome reported as 'not recovered').

- 2 cases of ‘optic neuritis’: one case in a 6-year-old female after tick-borne encephalitis vaccination (outcome reported as ‘recovering’); the second case occurred in a 35 years old women following influenza vaccine (outcome ‘recovered with sequelae’).

- 3 cases of ‘narcolepsy’ following tick-borne encephalitis vaccine as received as literature reports (Reference 1). The authors present 3 cases with rapid onset of narcolepsy-cataplexy after tick-borne encephalitis vaccination, occurring similarly to narcolepsy post H1N1 influenza vaccination: one case in a 19-year-old male (outcome ‘unknown’ at the time of reporting); one case concerning a 32-year-old male (with outcome reported also as ‘unknown’); and one case occurring in a 13-year-old male (outcome reported also as ‘unknown’). The authors concluded that TBE vaccination should also be considered as possible trigger for narcolepsy-cataplexy in predisposed individuals. However, to date Swissmedic has received no further reports of narcolepsy following TBE vaccination.

- 3 cases of Guillain-Barré syndrome: one case in a 62-year-old men after hepatitis A /hepatitis B vaccine (outcome ‘not recovered’); one case in a 12 months old female following tetanus vaccine (outcome ‘recovered with sequelae’); one in a patient of unknown age and gender after influenza vaccine, hepatitis b vaccine and typhoid vaccine (outcome reported also as ‘unknown’).

- One case-report of ‘facial paresis’ in a 77-year-old male following influenza vaccination (with outcome ‘recovering’).

- 4 cases of ‘syncope’: one case in a 13-year-old female after HPV vaccination (outcome ‘unknown’); one case in a 81 year old male following influenza vaccination (outcome ‘unknown’); one case in a 32-year-old female after influenza vaccine (outcome ‘recovered’); one case in an 8-year-old male after TBE vaccine (outcome reported as ‘recovered’).

Fatal case-report received by Swissmedic in 2015:

An AEFI-report describes the occurrence of sudden death in a 72-year-old female suffering from a severe mitral valve defect, with left-sided cardiac insufficiency, atrial fibrillation and enlargement of the left ventricle, after immunization with influenza vaccine. On the day of vaccination, the patient was in a stable general condition under her regular cardiac medication. However, five hours after the vaccination she was found dead at home, apparently without any prior signs of cardiac decompensation. Considering the alternative more probable explanations for sudden death due to her severe cardiac comorbidities, the causal relation with the influenza vaccination was assessed as ‘unlikely’.

References

1. Pareja HH, Mathis J, Bassetti C, Kallweit U. Post tick-borne encephalitis (TBE) vaccination narcolepsy-cataplexy. European Journal of Neurology. 2015;22 (Suppl. 1):54