Summary of adverse events following immunization reported in Switzerland during 2013

Executive summary

During 2013, Swissmedic received 138 case reports of suspected adverse events following immunization (AEFI) in Switzerland. This is a lower number of reported cases as compared to 2012, which might reflect a decreased incidence of adverse reactions following vaccinations. However, since there are no accurate data available regarding the total number of vaccines/doses administered during 2013 a straightforward conclusion cannot be drawn. In addition, a slightly decreased primary reporting rate due to the absence of new major safety issues concerning vaccines (locally and internationally) and therefore less general focus on this subject last year should be considered. As previously, Swissmedic continues to actively encourage spontaneous reporting of AEFIs in good quality. Since 2010, important topics with regard to AEFIs are evaluated and discussed with experts of the Swissmedic Human Medicines Expert Committee.

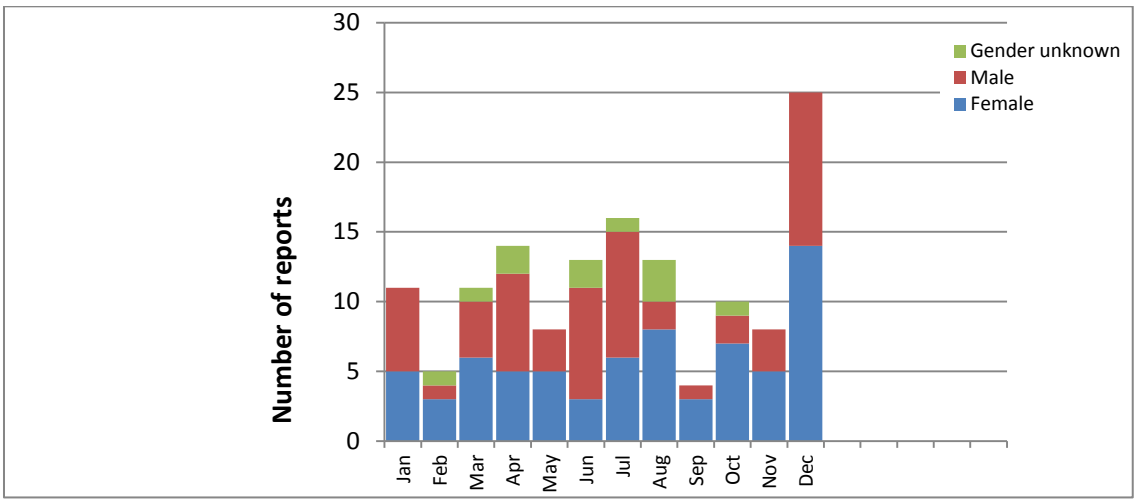

Figure 1 shows the number of AEFI reports received in 2013, as grouped by calendar months and compared by gender. The months with the highest numbers of AEFIs reported were December (25 reports received), July (16 reports) and April (14 reports). Throughout the year, the number of reports concerning females (70 reports) was higher as the number of reports regarding males (57 reports). In 11 AEFI reports, the gender of the persons remained unknown.

Figure 2. Number of AEFI reports per age group and gender, 2013

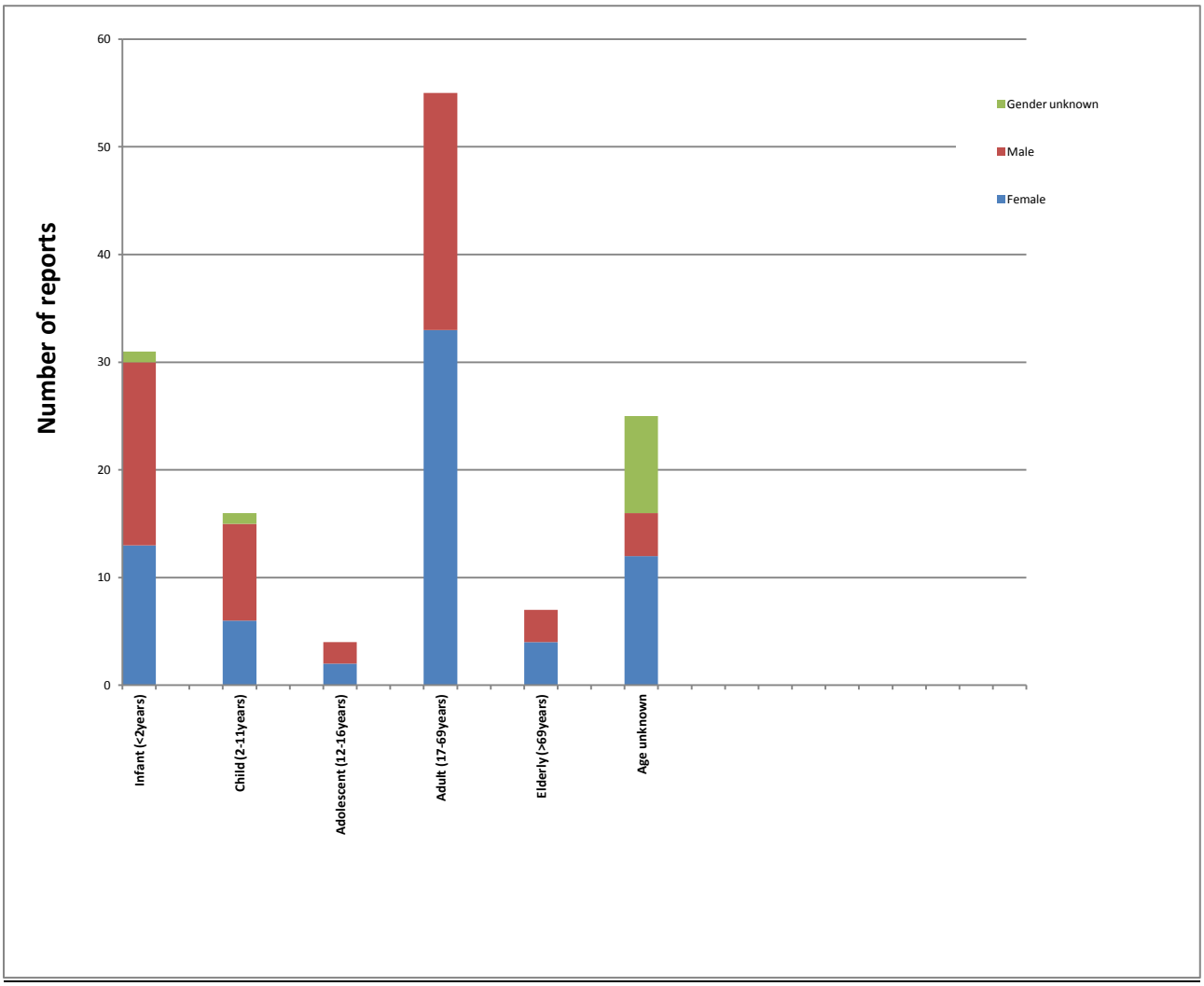

Figure 2 compares the number of reports per age group and gender. The largest number of AEFI reports involved adults (55 reports), followed by infants (31 reports) and children (16 reports). A higher difference in gender is recorded in the adults group (33 reports of females vs. 22 males). In 25 cases (reports), the age of the patients was not recorded.

Figure 3. Number of reports per vaccine group (ATC code) and seriousness, 2013

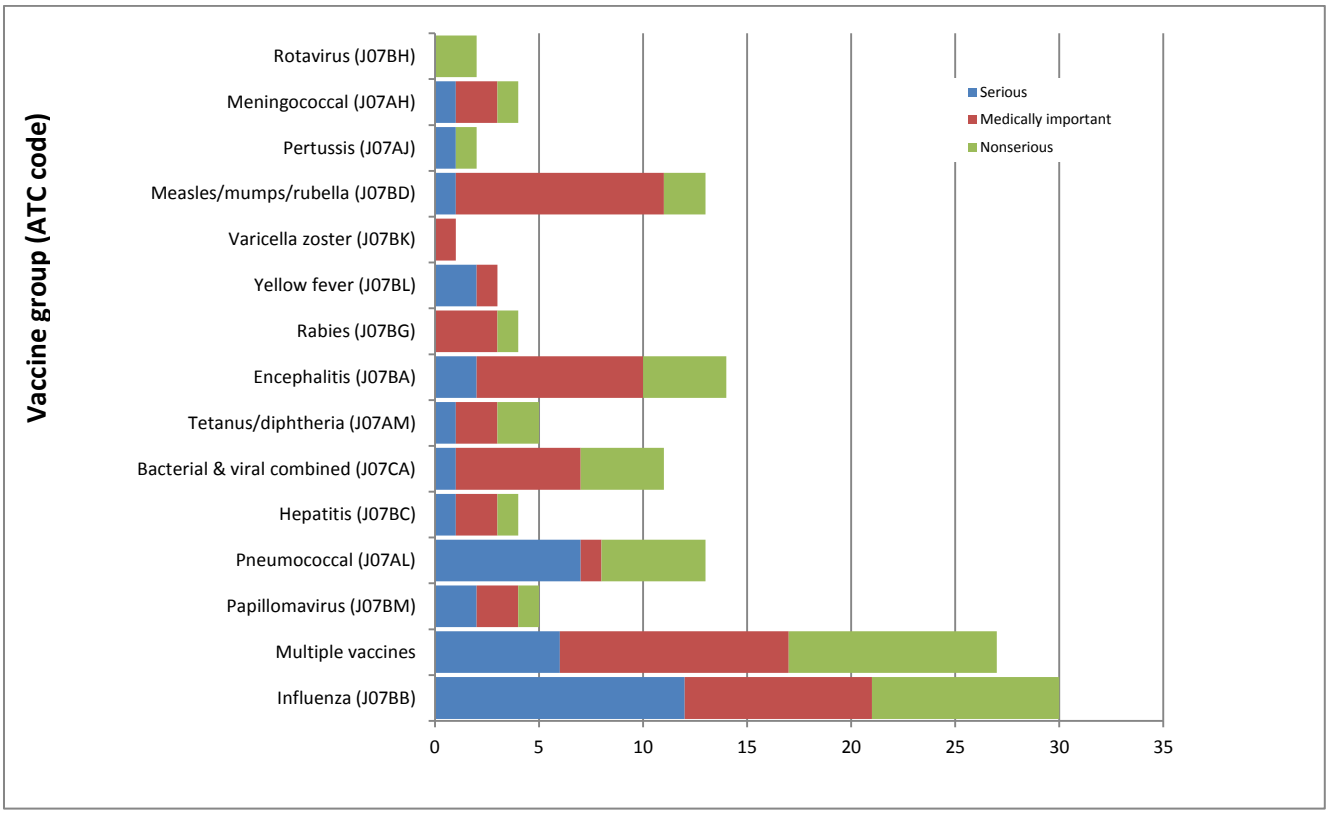

Figure 3 shows the number of spontaneous AEFI reports grouped per vaccine group (ATC code) and seriousness. There are no data available regarding the number of doses administered in each vaccine group and therefore this figure does not show which vaccine group displayed a higher AEFI rate (as number 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. A report is assessed as 'medically important' if it does not fulfil the criteria for 'seriousness' mentioned but it involves an event considered to be medically significant. All other reports are assessed as 'not serious' (e.g. self-limiting adverse events with good recovering). Of the 138 spontaneous reports, 43 (31.2%) were not-serious, 58 (42%) were medically important events and 37 (26.8%) of the AEFIs included events with serious consequences. The relative frequencies (percentages) of serious and medically important reports were close to those recorded during previous year 2012.

Figure 4 provides an overview on the AEFI reports received during 2013, grouped by the primary System Organ Classes (SOCs) concerned (i.e. regarding the leading AE of each report). Following four organ classes were most frequently involved in reports after immunization: Central and peripheral nervous system disorders (28 reports, 20.2%); Body as a whole – general disorders (26 reports, 18.8%); Application site disorders (15 reports, 10.8%); Foetal disorders (14 reports, 10.1%).

Figure 4. Number of AEFI reports in Switzerland by System Organ Classes, 2013

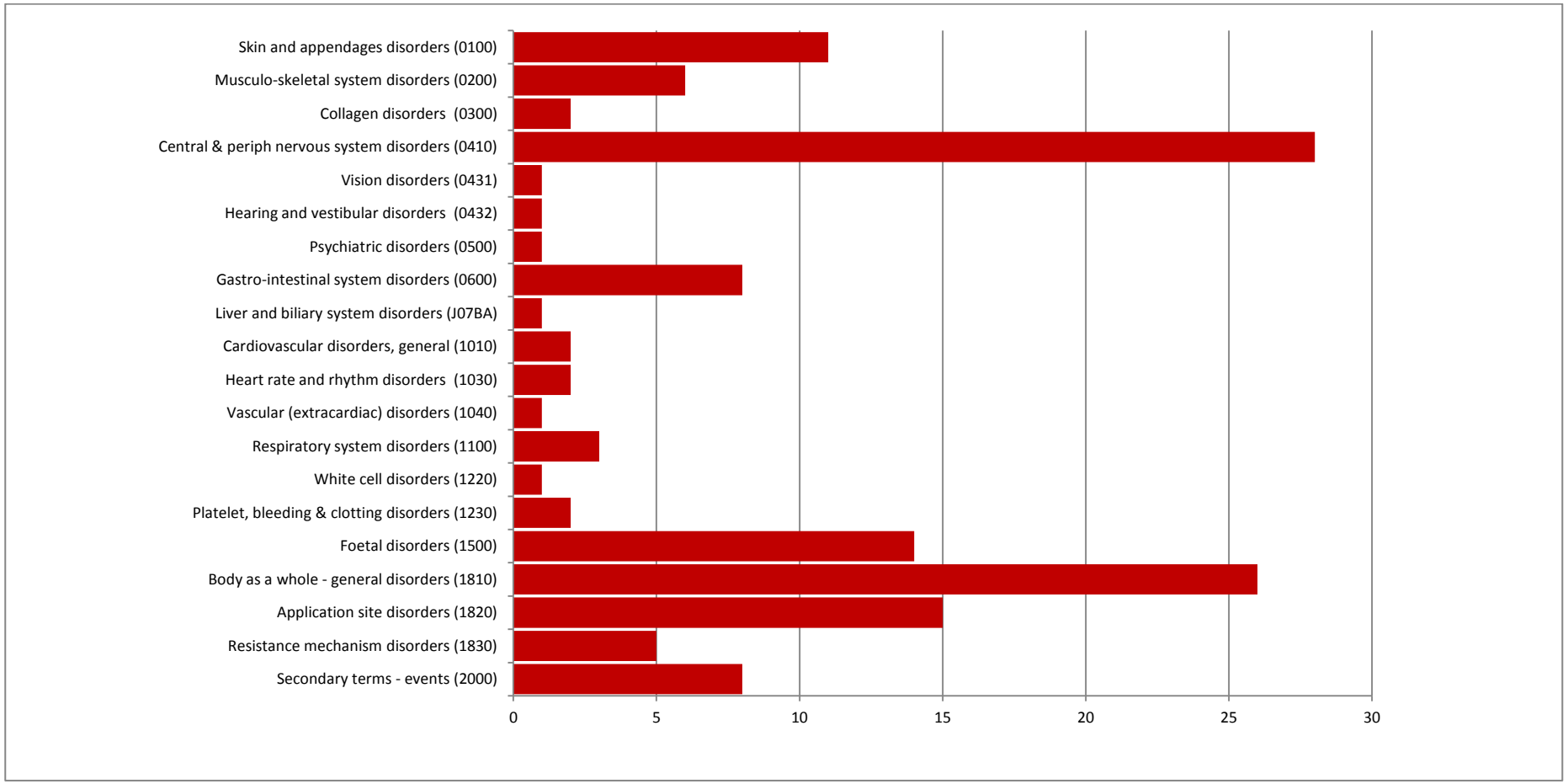

Figure 5. AEFI reports by vaccine group (ATC code) and top 3 involved System Organ Classes, 2013

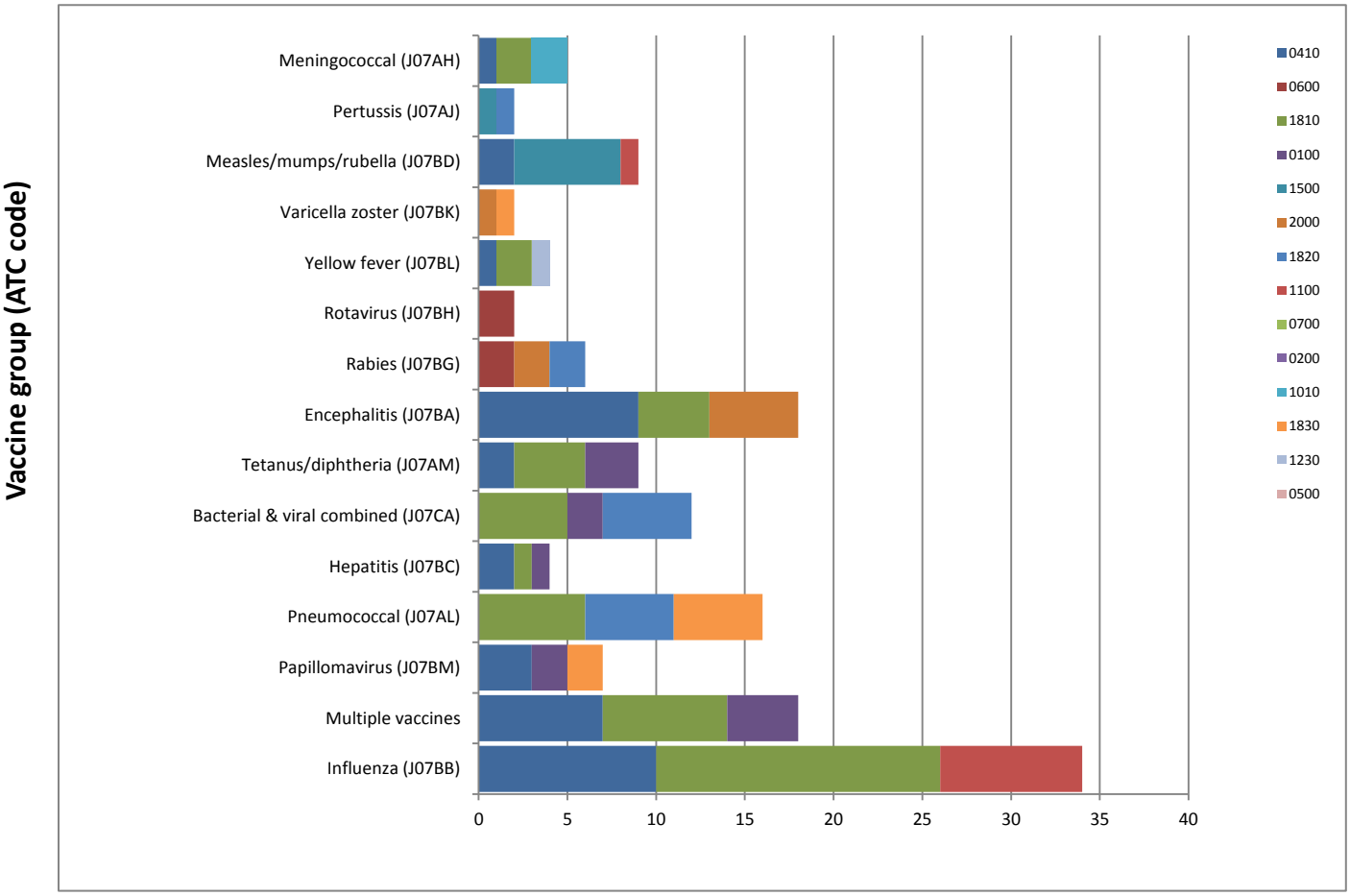

Figure 5 shows the AEFI reports by vaccine group (ATC code) and top 3 system organ classes. Notably, in the WHO-Art coding system drug exposures during pregnancy or before pregnancy are coded and counted under Foetal disorders (1500), which explains the higher number of reports in this organ class. Thus, in figure 4 and figure 5 they are 9 exposures in pregnancy classified under Foetal disorders (3 with measles/mumps/rubella vaccine, 1with hepatitis A vaccine, 1 with yellow fever vaccine, 4 with multiple vaccines) and 5 cases of vaccine exposure before pregnancy (all with measles/mumps/rubella vaccine and 3 of them with multiple vaccines). All these cases remained without any significant medical consequences and no congenital anomalies were reported/recorded following immunization in 2013.

Figure 6. Number of reports per vaccine group (ATC code) and labelling, 2013

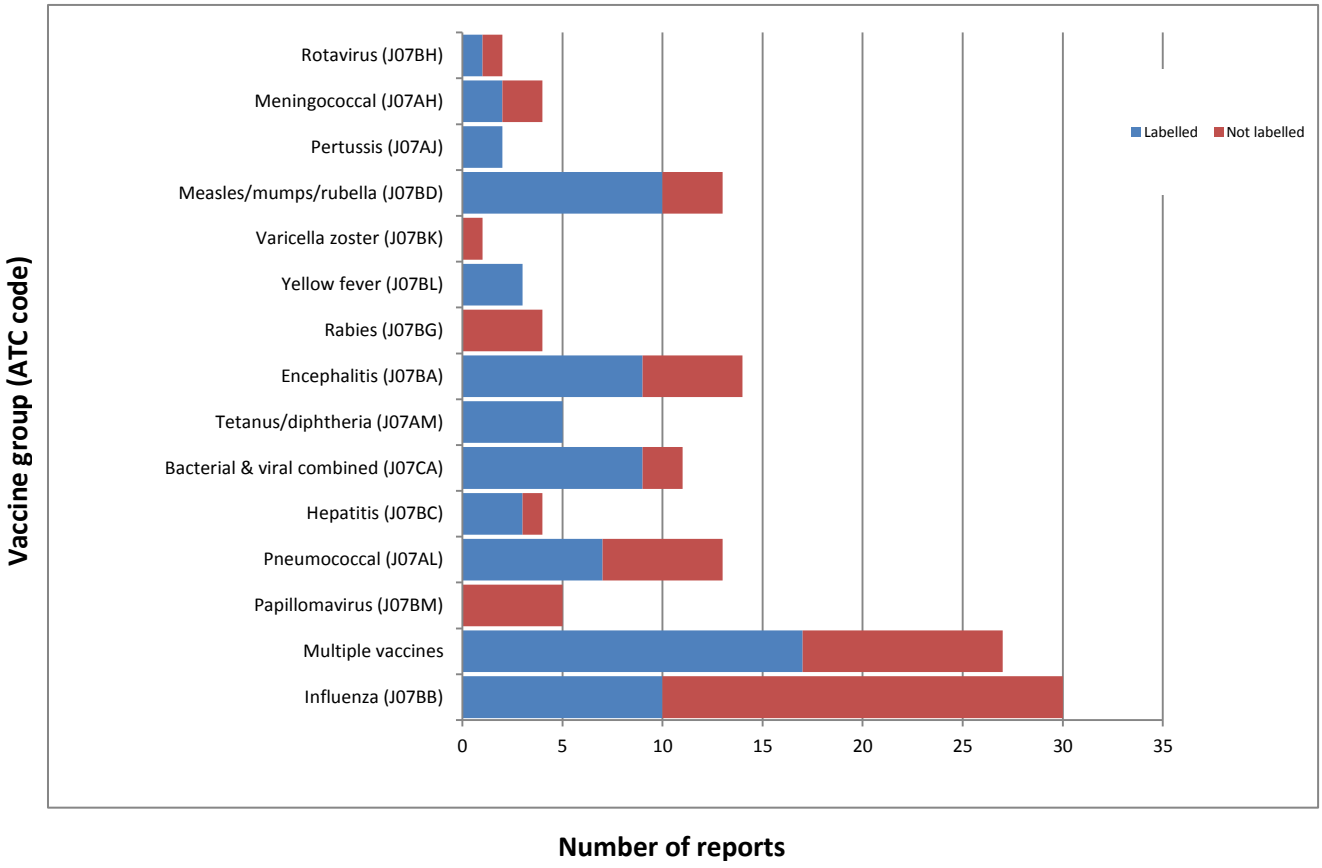

Figure 6 shows the number of AEFI reports per vaccine group (ATC code) and labelling status. Vaccine groups with higher numbers of reports containing unlabelled AEFIs were influenza (20 of 30 reports), pneumococcal (6 of 13 reports) and the group regarding immunizations with multiple vaccines (10 of 27 reports with unlabelled AEs).

Table 1. Overview on the most frequent AEFIs of all reports, 2013

Adverse event	System Organ Class	Number of reports
Injection site reactions	Application site disorders	41
Exanthema (Rash)	Skin and Appendages	13
Fever	Body as a whole	12
Drug exposure in pregnancy	Foetal disorders	9
Headache	Central and Peripheral Nervous System	9
Vertigo/Dizziness	Central and Peripheral Nervous System	7
Nausea/ Vomiting	Gastrointestinal System	7
Dyspnoea	Respiratory system	5
Convulsions	Central and Peripheral Nervous System	5
Drug exposure before pregnancy	Foetal disorders	5
Medicine ineffective	Body as a whole	5

Table 1 displays the most frequently AEFI as reported during 2013 (at least 5 reports): injection site reactions; exanthema (rash); fever; drug exposure in pregnancy; headache; vertigo/dizziness; nausea/vomiting; dyspnoea; convulsions; drug exposure before pregnancy; medicine ineffective.

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

Adverse event	System Organ Class	Number of reports
Injection site reactions	Application site disorders	10
Drug exposure in pregnancy	Foetal disorders	9
Fever	Body as a whole	6
Headache	Central and Peripheral Nervous System	5
Medicine ineffective	Body as a whole	5
Convulsions	Central and Peripheral Nervous System	5
Influenza-like symptoms	Body as a whole	4
Drug exposure before pregnancy	Foetal disorders	4
Vertigo/Dizziness	Central and Peripheral Nervous System	4
Septicaemia pneumococcal	Resistance mechanisms disorders	4

Table 2 summarizes the most frequent AEFIs assessed as 'serious' or 'medically important' (at least 4 reports). The two tables are displaying similar distributions of reported AEFIs, and additionally 4 case reports with pneumococcal septicaemia are apparent in the table with serious AEFIs.

In all these 4 cases of pneumococcal septicaemia a pneumococcal immunization had been performed. In 2 of the cases, 'drug ineffective' was also reported as AEFI, considering that the severe pneumococcal infection should have been prevented by the vaccine. In one case, a 2 year-old female patient had been vaccinated with 13-valent vaccine and developed pneumococcal septicaemia, pneumonia and pleurisy with the pneumococcal serotype 3, which is covered by the 13-valent vaccine. The child was hospitalised and finally recovered from the events completely. In the second case-report, a 6-year-old female patient had been previously immunized with the 13-valent pneumococcal vaccine. She developed an invasive pneumococcal infection, was hospitalized and recovered completely after treatment. The pneumococcal serotype involved in this case was not known by the primary reporter and therefore a lack of efficacy with the 13-valent vaccine in this patient could not be excluded. The other two cases of septicaemia were both received as literature reports as published during 2013 (Reference 1). This literature article mentions a total of 3 cases of invasive pneumococcal infection - two of them of pneumococcal sepsis and one case of pneumococcal meningoencephalitis – all 3 cases occurring after immunization with pneumococcal 7-valent conjugate vaccine. Two of these 3 literature cases (one with meningoencephalitis in a 2-year old male child and the other one with pneumococcal septicaemia and meningoencephalitis in a 11-month-old girl) had a fatal outcome despite intensive therapy in the hospital. However, in all these literature cases the serious pneumococcal infections were produced by pneumococcal serotypes which are not covered

by the the 7-valent conjugated vaccine, i.e. by serotype 1 or serotype 7. Therefore, these cases were not due to lack of efficacy of pneumococcal 7-valent conjugate vaccine, but represent concurrently occurring bacterial infections, assessed as not related to pneumococcal 7-valent conjugate vaccine.

Another fatal case reported after immunization concerned a 6-week-old male infant, who was immunized in Switzerland with multiple vaccines (including 13-valent pneumococcal vaccine, DTP – HepB – IPV + Hib) and then travelled abroad and died soon thereafter. According to scarce information provided by the family and not medically confirmed, the child had a severe pneumonia in Mozambique and probably an infection with H1N1 influenza virus. It was transferred to a hospital in Johannesburg (South Africa) but died there shortly after, despite intensive care treatment. Since medically confirmed data, including medical records from South Africa (e.g. final diagnoses, treatments, autopsy report) could not be obtained even with repeated follow-up attempts, the final evaluation of this case remains difficult. Taking into account the limited data transmitted by the family and the concurrent H1N1 infection which provides a probable alternative explanation, the causality of this AEFI report and its fatal outcome has been assessed as unlikely related to the vaccinations.

Among other serious or medically important AEFIs during 2013, 4 cases of convulsions were reported (all recovered) and also one case of fever convulsions after immunization of a young child (also recovered).

Further suspected neurological AEFIs reported as serious were:

- one case of encephalitis in a 79 year-old male following immunization with influenza vaccine, outcome ‘recovered’
- one case of encephalomyelitis and polyradiculitis in a 68 year-old male after influenza vaccine, outcome ‘recovering’
- one case of facial palsy in a 13 year-old female following human papilloma vaccine, outcome ‘not recovered’ at the time of reporting
- one case of meningitis in an adult male after tick-borne encephalitis vaccine, outcome ‘recovered’
- one case of myelitis in a 38 year-old adult male following immunization with multiple vaccines (tick-borne encephalitis, DTP vaccine), outcome ‘recovered’
- one case of multiple sclerosis in a 18 year-old female following human papilloma vaccine, outcome not recovered. This case occurring during 2009 was reported retrospectively by the family and documented with medically confirmed data.
- one case of facial paralysis in a 26 year-old female after influenza vaccination, outcome ‘not recovered’
- one case of hemiparesis and sensory disturbance in a 18 year-old male following immunization with multiple vaccines (Tick-borne encephalitis vaccine, Tetanus vaccine, Diphtheria vaccine, Hepatitis A vaccine and Hepatitis b vaccine) outcome ‘recovered’

- one case of suspected upper motor neuron lesion in a 36 year-old women following tick-borne encephalitis immunization, outcome ‘not recovered’

- 3 cases of Guillain-Barré syndrome: 2 cases in relation with influenza vaccines (1 of these with outcome ‘recovered’, 1 case with outcome ‘not recovered’ at the time of reporting); 1 further case following the immunization against tick-borne encephalitis, outcome reported as ‘unknown’

Reference

1. Invasive pneumococcal infection despite 7-valent conjugated vaccine. Sebastien Joye, Anja Gao, Simon Kayemba-Kay’s, Jacques Cotting, Marie-Hélène Perez. Clinics and Practice 2013; 3:e1; p.27.