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# Consultancy and surveillance of post-immunization adverse events in the Veneto region of Italy for 1992–2008

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**Key words:** AEFI (adverse events following immunization), immunization, consultancy, surveillance, vaccine safety

**Abbreviations:** ADR, adverse drug reaction; AEFI, adverse events following immunization; AIFA, national drug agency; CI, contraindications; HHE, hypotonic-hyporesponsive episode; PH, public health; PHU, public health unit; PV, pharmacovigilance; aP, acellular pertussis vaccine; BCG, tubercolosis vaccine; DT, diphteria-tetanus vaccine; DTaP, diphtheria-tetanus-acellular pertussis vaccine; DTP, diphtheria-tetanus-whole cell pertussis vaccine; DTaPHB, diphtheria-tetanus-acellular pertussis-hepatitis B vaccine; HB, hepatitis B vaccine; HA, hepatitis A vaccine; Hexavalent (DTaPIPVHBHiB), diphtheria-tetanus-acellular pertussis-inactivated polio-hepatitis B-*Haemophilus influenzae* type b vaccine; Hib, *Haemophilus influenzae* type b vaccine; HPV, human papilloma virus vaccine; INF, influenza vaccine; IPV, inactivated polio vaccine; MMR, measles-mumps-rubella vaccine; Men C, meningococcal C vaccine; MMRV, measles-mumps-rubella-varicella vaccine; OPV, oral polio vaccine; PCV, pneumococcal conjugate vaccine; PV 23 valent, 23-valent pneumococcal polysaccharide vaccine; TBE, tick-borne encephalitis;TT, tetanus vaccine



Prevention and control of adverse events following immunization (AEFI) are fundamental activities of successful immunization programs. AEFI reporting, investigation and analysis, integrated by consultancy for subjects needing a specialized evaluation, represent an ideal model for vaccine safety surveillance.

In the Veneto Region of Italy the Green Channel Centre has been created by the local Public Health authority, to offer a consultancy activity for vaccinations at risk of adverse events and to ensure an efficient AEFI surveillance system with regular feedback data for vaccine personnel.

This report updates the overall activity provided by the Green Channel between 1992 and 2008, concerning consultations for previous AEFI and contraindications to vaccinations and analysis of AEFI reports.

After 1,280 consultancy cases, 998 (78%) subjects were found eligible for vaccination, with personalized precautions suggested in 42% of cases. Of a total of 724 patients actually vaccinated as per the Green Channel instructions, only 55 subjects (7.6%) reported mild symptoms and one (0.3%) a moderate allergic reaction. Since 1993, a total of 5,006 AEFI reports have been collected and evaluated by the Green Channel against more than 20 millions of vaccine doses administered with an estimate mean AEFI rate of 2.3 x 10,000 doses per year. The majority of them (94%) were found in causal relationship with vaccines; of these, 267 reports (5.6% - 0.1/10,000 doses) were serious and 9 of these subjects, affected by a neurological event, were not recovered or were still on therapy at follow up.

This regional activity has proven efficacious in evaluating and managing individual cases at potential risk of AEFI and integrating the national passive surveillance system.

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## Introduction

Prevention and control of adverse events following immunization (AEFI) is a central aspect to improving safety and maintaining public confidence in vaccines, particularly in areas where some preventable diseases are uncommon and/or the risk-benefit perception of immunization has changed. Therefore, advanced immunization programs must include activities to monitor vaccine safety and improve risk assessment and communication to assure optimal immunization coverage.[1] In addition to passive reporting, AEFI investigation and analysis, thorough consultancy by experts from different disciplines should be performed on a regular basis.[2,3] Moreover, in some countries specialized consultancy activities for pre- and post-vaccination AEFI prevention and evaluation have been organized at regional and national levels.[4,5]

In Italy, AEFI surveillance is mandatory and since 2003 the responsibility of adverse events to both drugs and vaccines has been reorganized and assigned to the National Drug Agency (AIFA). At the regional level, in 1992 the Green Channel Centre was created by the local Public Health (PH) Authority of the Veneto Region, Italy, to offer a consultancy activity for individuals at risk of adverse events and to ensure a more efficient AEFI surveillance system with regular feedback data for vaccine personnel.[6]

This report updates the overall activity supplied by the Green Channel between 1992 and 2008.

**Table 1.** Green channel consultations: referral reason and vaccine groups involved

| Submitted vaccine groups | Previous AEFI N. | Suspected CI/precaution N. | Total | |
|---|---|---|---|---|
| | | | N. | % |
| 1st year series° | 339 | 207 | 546 | 42.7 |
| HB | 131 | 154 | 285 | 22.3 |
| MMR/MMRV and/or Varicella | 44 | 128 | 172 | 13.4 |
| TT/DT/DTaP booster | 81 | 13 | 94 | 7.3 |
| INF | 10 | 17 | 27 | 2.1 |
| OPV/IPV (booster) | 10 | 14 | 24 | 1.9 |
| Other vaccines* | 43 | 89 | 132 | 10.3 |
| Total | 658 | 622 | 1,280 | 100 |

AEFI, adverse events following immunization; CI, contraindication. °1st year series: one or more mandatory/recommended vaccines administered in children aged <1 year (diphtheria-tetanus-pertussis whole cell/acellular pertussis vaccine, *Haemophilus influenzae* type b vaccine, HB, oral or inactivated polio vaccine); *Other. Influenza, yellow fever, varicella, BCG, HA, HPV, PCV, Men C, TBE, typhoid oral or different combinations.

**Table 2.** Green channel consultations: detailed referral reasons

| Previous adverse events | Number of cases | Suspected contraindication | Number of cases |
|---|---|---|---|
| injection site reaction | 55 | Personal history of: | |
| | | neurological disease | 113 |
| systemic event: | | allergic disease | 76 |
| skin reaction | 271 | vaccine hypersensitivity[b] | 82 |
| neurological symptoms | 86 | immunodeficiency | 53 |
| fever + other mild symptoms | 62 | autoimmune disease | 51 |
| HHE/persistent screaming | 55 | specific organ disease[a] | 38 |
| specific organ disease[a] | 32 | congenital disease | 29 |
| cephalalgia | 22 | cutaneous disease | 21 |
| thrombocytopenia | 13 | cephalalgia | 11 |
| arthralgia/arthritis | 12 | adverse drug reaction | 11 |
| vasculitis | 10 | Kawasaki syndrome | 9 |
| anaphylaxis | 6 | other | 37 |
| other | 34 | Family history of AEFIs or disease[c] | 58 |
| | | Fear of risk of AEFI | 33 |
| Total | 658 | Total | 622 |

[a]Specific organ disease: hepatic, hematologic, respiratory, cardiovascular, kidney, gastrointestinal disorder. [b]To the vaccine or its components (i.e., preservative, contaminant, adjuvant). [c]Severe allergic disease, immunodeficiency, neurological disorder.

## Results

**Green Channel consultations.** A total of 1,280 patients were referred to the Green Channel for evaluation of previous AEFI (658-51%) or suspected contraindications (CI) (622-49%) to mandatory or recommended vaccines. Seventy-six percent of all cases involved children up to 13 years of age. A direct clinical examination at the Centre was done in 462 (36%) cases, while in 64%, consultation was based on a record review. Allergy testing with vaccines and their components was performed in 240 (19%) of the subjects.

The vaccines of main concern for previous AEFI or suspected CI to their administration are listed in **Table 1**; most of them (546-43%) included the immunization series administered in the first year of age, followed by HB vaccine, mandatory in Italy for infants and adolescents since 1991; live attenuated vaccines and toxoid boosters were also frequently implicated.

In **Table 2**, detailed referral reasons according to clinical data submitted are reported. In regard to the nature of the AEFIs, the most frequent adverse events involved skin and neurological manifestations; also the majority of suspected CI were due to underlying neurological disease or allergic and immunologic disorders.

After consultation, 998 (78%) of the submitted cases were found eligible for vaccination: individualized precautions for safer administration were indicated for 424 (42%) subjects, including temporally separated single injections (114 cases), administration in hospital with full strength or graded doses (109); alternative brand of vaccine (85), modified schedule with specific component suspension (86), anti-allergic premedication (30). Temporary suspension or exemption was requested in 82

(6.4%) and 74 (5.8%) cases, respectively, due to consistent CI to individual vaccines or severe AEFI with earlier doses or already acquired protection (5 cases). Seventy-six (5.9%) subjects were recommended for further exams or specialistic consultation. A group of 50 (3.9%) not needing further doses of vaccines was given alternative advice or information (on causal relation, immunization not due, etc.).

The vaccination was actually administered as per the Green Channel instructions to 724 (73%) subjects, 345 with suspected CI and 379 with previous AEFI; administration in hospital was organized for 74 of them. Fifty-five (7.6%) subjects vaccinated reported mild and short-lasting adverse effects; only one patient (0.3%), affected by severe food and respiratory allergy, developed urticaria and broncospasm after MMR vaccination in hospital; the subject recovered one hour after appropriate treatment.

A total of 127 (13%) cases refused to continue the recommended vaccination; immunization was postponed or not done in another 85 (8.5%) patients, due to varying decisions taken by vaccine personnel. There is no outcome of vaccine administration after consultation reported for 36 subjects (3.6%).

In the study period, electronic consultation (by fax or e-mail) was also provided in 2,614 cases of suspected CI or AEFIs and 396 general issues. The main users were Public Health Unit (PHU) personnel (66%), followed by pediatricians or other specialists (20%) and citizens (14%).

**AEFI surveillance.** During the 16 year surveillance period and with more than 20 millions vaccine doses administered, the Green Channel received and evaluated 5,006 AEFI report forms, resulting in a mean reporting rate of 2.3 per 10,000 doses per year and 70 reports per million of population per year, although with significant differences among different PHUs. Distribution of data by type of vaccine administered is shown in **Table 3**. Although the highest AEFI reported frequencies were for diphtheria-tetanus (DT) and tetanus toxoid (TT) vaccines, as previously observed in this Region,[6] these data are influenced by periodical changes in the recommended regional immunization schedule, in particular by the introduction of new or combined vaccines. Taking into account the number of administered doses, the highest specific reporting rate per 10,000 doses was found for MMRV vaccine (23.1), followed by varicella (10.5), tetravalent DTaPHB (9.4), BCG (8.6) and hexavalent (8.5) vaccine. The most administered product was influenza vaccine (>8 million of doses), although it showed the lowest AEFI reporting rate (0.2 per 10,000 doses). The high reporting rate calculated for the recently introduced MMRV vaccine, in 14 (19% of reports) cases associated with serious events, needs to be further confirmed because of the low number of administered doses.

The age groups more frequently involved were adolescents and adults aged ≥13 (32%), followed by children 1–5 years old (28%), infant <1 year old (22%) and children 6–12 (16%). In 74 (1.5%) reports age of patient was not indicated. With regard to the time of onset of symptoms, 62% of the reports concerned events that appeared within 24 hours after administration and 26% after 1–7 days, as previously described.

The nature of the 9,596 reported single or combined events described in 5,006 reports is summarized in **Table 4**, with injection site reactions and fever as the most frequently reported events. On the whole, 50% of forms reported systemic events, 29% local reactions, about a half due to toxoids, and 21% both local and general events. According to system organ disease classification, the most frequent categories were administration site conditions (30%), general disorders (27%) skin manifestations (12%) and nervous system disorders (9%). After causality assessment, AEFI forms were judged as follows: definite in 54% of reports, probable in 35%, possible in 5% and unrelated in 4%. An additional 2% was unclassifiable for insufficient essential information.

**Table 3.** Distribution of AEFI reports by vaccines administered

| Vaccine | N° | % |
|---|---|---|
| TT | 675 | 13.48 |
| DT | 633 | 12.64 |
| Hexavalent | 571 | 11.41 |
| HB | 416 | 8.31 |
| MMR | 414 | 8.27 |
| DTaP | 354 | 7.07 |
| DTP | 256 | 5.11 |
| INF | 225 | 4.49 |
| Hexavalent + PCV | 114 | 2.28 |
| Men C | 88 | 1.76 |
| PV 23valent | 87 | 1.74 |
| MMRV | 71 | 1.41 |
| Varicella | 64 | 1.28 |
| DTaPHB | 63 | 1.26 |
| DTP + OPV + HB | 60 | 1.20 |
| Hexavalent + Men C | 55 | 1.10 |
| PCV | 53 | 1.06 |
| Hib | 49 | 0.98 |
| MMR + Varicella | 43 | 0.86 |
| DTaP + MMR | 40 | 0.80 |
| DTaPHB + OPV + Hib | 39 | 0.78 |
| IPV | 35 | 0.70 |
| Hexavalent + MMR | 34 | 0.68 |
| DTaP + Men C | 32 | 0.64 |
| HPV | 31 | 0.62 |
| Typhoid oral | 31 | 0.62 |
| DTaPHB + IPV | 26 | 0.52 |
| Yellow fever | 25 | 0.50 |
| BCG | 23 | 0.46 |
| Measles | 22 | 0.44 |
| aP | 21 | 0.42 |
| DTaPHB + IPV + Hib | 20 | 0.40 |
| MMR + HB | 19 | 0.38 |
| OPV | 16 | 0.32 |
| Other single or combined (n. < 16) | 301 | 6.01 |
| Total | 5006 | 100 |

**Table 4.** Frequently reported adverse events

| Event | N. | % |
|---|---|---|
| Injection site reaction | 2,498 | 26 |
| Fever <39.5°C | 1,139 | 11.9 |
| Fever ≥39.5°C | 498 | 5.2 |
| Headache | 322 | 3.4 |
| Urticaria | 318 | 3.3 |
| Persistent crying | 281 | 2.9 |
| Irritability | 277 | 2.9 |
| Exanthema | 259 | 2.7 |
| Arthralgia | 232 | 2.4 |
| Pruritus | 184 | 1.9 |
| Vomiting | 190 | 2 |
| Erythema | 156 | 1.6 |
| HHE | 138 | 1.4 |
| Pallor | 123 | 1.3 |
| Asthenia | 118 | 1.2 |
| Lymphadenopathy | 105 | 1.1 |
| Diarrhoea | 100 | 1 |
| Nausea | 91 | 0.9 |
| Rash | 88 | 0.9 |
| Faintness | 87 | 0.9 |
| Fever not specified | 82 | 0.8 |
| Somnolence | 79 | 0.8 |
| Anorexia | 76 | 0.8 |
| Hypotonia | 73 | 0.8 |
| Myalgia | 70 | 0.7 |
| Dizziness | 70 | 0.7 |
| Febrile convulsion | 65 | 0.7 |
| Abdominal pain | 62 | 0.6 |
| Malaise | 61 | 0.6 |
| Parotid enlargement | 61 | 0.6 |
| Others (<50 events) | 1,693 | 17.6 |
| Total | 9,596[a] | 100 |

[a]In 5,006 AEFI report sheets.

The 4,719 reports of causally related manifestations were classified according to their seriousness into mild (64%), moderate (30%) and serious (5.6%). All the 267 reports of serious events (**Table 5**) were evaluated through a complete record examination and followed up to recovery or stabilization of the disease. These events included 71 local reactions and 196 systemic events, 32% judged certain, 44% probable and 24% possible, i.e., in temporal relationship to vaccination but possibly due to other unidentified causes. Among serious systemic events, the most frequent were central nervous system disorders such as convulsions and ataxic manifestations. Thrombocytopenia was described in 18 reports, and it was associated with live attenuated vaccines in most cases. There were 11 cases of anaphylaxis, 9 of them sufficiently described to meet the Brighton Collaboration case definition.[9] All cases of serious AEFIs recovered completely except nine patients (3.4%), who still had neurological symptoms or were currently on therapy. In 5 cases, updated follow up information was not available. The mean overall serious event reporting rate was 0.1 reports per 10,000 administered doses per year; as regards vaccine administered, the highest reporting rate was found for BCG vaccine with 6.1 reports per 10,000 doses administered, although 90% were local reactions, and MMRV with a reporting rate of 4.5 per 10,000 doses.

In addition to the described events, 50 serious events were judged unrelated to vaccination; they included 4 cases of death, due to haemolytic-uremic syndrome, cardiac arrest, sudden death from mitral prolapse and viral interstitial pneumonitis. On the basis of available data they were not judged causally related to vaccination.

During this long period of AEFI surveillance activity in collaboration with Pharmacovigilance (PV) and PH personnel, safety signals have been detected and evaluated. In particular, two clusters of abscesses due to specific lots of BCG vaccine and 28 cases of allergic reactions to a brand of MMR vaccine containing dextran as residual component have been analyzed.[10] The last signal, regarding cases of serious neurological and haematological manifestations after live viral vaccines, is still under evaluation.

## Discussion

Prevention and surveillance of AEFI is an essential activity in assuring a high standard of vaccine safety and confidence in current immunization programs, particularly in countries where preventable diseases have been mostly eliminated. In addition to passive AEFI surveillance systems now in place in most countries, specialist immunization clinics, competent in assessing AEFIs, evaluating potential contraindications and managing subsequent vaccinations are needed to deal with potential risks at the individual level. In some European countries and in the United States such consultancy centres have been created.[4,5] In an ideal model, in fact, both activities for AEFI surveillance and consultancy should be part of a comprehensive system for vaccine safety control. With this intent, a reference Centre, named the Green Channel, was created in 1992 in the Veneto Region of Italy to support PHU personnel and pediatricians in the management of cases of increased risk of AEFI, and to improve the national AEFI passive surveillance system of analysis and investigation.[6] The Centre also has training and updating functions, by participating in regional initiatives to improve the competency of vaccine personnel (courses, booklets).

The overall activity of a 16 year period shows that this Regional Centre is efficacious in the prevention and control of AEFIs. Because of this organization of vaccinovigilance and the high quality standard of immunization activities and optimal vaccine coverage, the Veneto Region has recently obtained the authorization to make all vaccinations recommended and is exempt from national mandatory immunization laws.

The specialized consultancy activity shown to be particularly useful in the management of immunization for individuals at risk of reactions and the selection of subjects needing a suspension or exemption. From the entire study population the majority of

**Table 5.** Serious causally related events reported in the surveillance period

| Event | N. | Event | N. |
|---|---|---|---|
| Injection site reaction | 71[a] | Myopathy | 2 |
| Fever convulsion | 62 | Brachial neuritis | 2 |
| Febrile convulsion | 26 | Strabismus | 2 |
| Ataxia | 19 | Schoenlein-Henoch purpura | 2 |
| Thrombocytopenia | 18 | Uveitis | 2 |
| Anaphylaxis | 11 | Transverse myelitis | 1 |
| Encephalopathy | 7 | Dizziness | 1 |
| Facial paralysis | 7 | Left cardiac failure | 1 |
| Vasculitis | 5 | Respiratory insufficiency | 1 |
| Guillain Barrè syndrome | 4 | Hepatitis | 1 |
| Acute disseminated encephalomyelitis | 2 | Optical neuritis | 1 |
| Arthritis | 2 | Taste and smell disorders | 1 |
| Herpes Zoster | 2 | Proteinuria | 1 |
| Meningitis | 2 | Subclavian thrombosis | 1 |
| Hypertonia | 2 | Other neurological events | 6 |
| Serum sickness | 2 | Total | 267 |

[a]Including 34 sterile abscesses, 7 septic abscesses, 17 abscesses not specified and 13 cellulitis.



subjects evaluated were found eligible for vaccination and were successfully immunized; however, a significant portion of cases needed personalized investigation and hospitalized treatment which allowed them to receive the benefit of vaccination reducing the risk of AEFI. Finally, a significant number of refusals to immunization or further testing, although not relevant to maintenance of high immunization coverage, suggests the need for improved risk communication. In comparison with the very first years of activity, current personnel training and availability of tools such as guidelines and Internet access to in-depth CI and AEFI issues have resulted in a better selection of cases for consultancy and, for example, decreasing inappropriate referrals for well-known situations such as MMR administration in egg allergic subjects; these facilities have also improved AEFI reporting.

The Veneto AEFI surveillance system represents an important source of data for monitoring the safety of old and new vaccines and for signal detection of events to be further investigated, as previously reported in reference 10. Although the problem of underreporting in this country is evident when comparing national data with other states such as the Netherlands, Finland and Czech Republic,[5,13] the Veneto region has better AEFI reporting rates than the mean national data; moreover, the easy availability of the number of administered doses, which is a more reliable denominator than distributed ones, improves the quality of analysis.

The results of AEFI surveillance show that the majority of the Veneto region reports include mild and transient events, confirming the positive benefit-risk balance of immunization as reported by other monitoring systems.[11-14] All AEFI reports have been investigated and, in case of serious or unexpected events, followed up to recovery or stabilization. This is a gold standard of any surveillance system, although not adopted by all European countries, according to the results of a survey conducted in 2007.[5] This activity has been facilitated in Veneto by the recent change in the flux of reporting data on a computerized basis and improved collaboration with the local PV centre. Another strength of this activity is the international collaboration established and carried on through many years of activity, through sharing of expertise with safety experts all over the world.

In recent years, an increase in serious AEFI reports has been observed by the Green Channel, suggesting greater attention and accuracy in notification of these events by the PH officials. The current proportion of serious events is similar to that reported in Finland and Australia,[12,14] and significantly lower than the one observed in Switzerland.[11] Unfortunately, limited diagnostic procedures are still performed in the acute phase of some of these events, resulting in an incomplete differential diagnosis and identification of other potential etiologic factors. This represents an important limitation that raises the number of cases with a possible causal relationship with vaccination in the absence of other causes identified. Therefore efforts are needed to improve differential diagnosis of serious AEFI, for example by applying case definitions and using standardized protocols for investigations during the acute phase. Another objective to achieve is to create and use the infrastructure for large linked databases already working in some countries, which is essential for collaborative studies on vaccine safety as reviewed in reference 15 and 16.

## Methods

**Consultancy activity.** The Green Channel consultancy activity is aimed at preventing adverse reactions for subjects needing a special examination for suspected AEFI or CI to start or continue vaccination, as revealed by a standardized anamnesis used at the PHU level, as previously described in reference 6. Briefly, each of the 1,280 submitted cases was evaluated by clinical and/or

detailed record examination. When indicated, in vivo/in vitro allergy or immunology testing was performed, in order to identify specific sensitizations to vaccine components, according to recommended procedures.[7,8] Finally, a conclusive report was released to the PHU physician, containing indications for subsequent vaccination, with standard procedure or individualized precautions such as premedication, temporally separated single injections, alternative brand, and/or administration in hospital with full strength or graded doses according to published protocols. In cases of serious AEFI or CI, indicating temporary suspension or exemption, vaccination was not recommended.

Wire consultation activity, initially carried out biweekly by telephone, and later on by e-mail and fax, was also offered to PHU personnel and pediatricians in order to respond to simple general and specific and/or urgent questions on CI and AEFIs and risk communication.

**Regional AEFI surveillance system.** The Green Channel Centre was created in 1992 to ensure an efficient regional AEFI surveillance system with regular feedback of analyzed data to vaccine personnel. At the national level, AEFI reporting in Italy is mandatory and, until 2002, reports were forwarded both to PH and PV Authorities by two different forms and procedures. Since 2003, AEFI flux data has been unified with the drug PV and is the responsibility of the National Drug Agency. This change has improved regional activities, simplified bureaucratic procedures and led to quicker transmission of data to the Green Channel Centre.

AEFI are currently reported to the local PV Unit by a standardized form that is sent to the national ADR database. According to local regulation, in the Veneto Region AEFI reports are also forwarded to the Green Channel for specialistic analysis, classification and follow up of serious events.

At the Green Channel, 5,006 AEFI reports from 1993–2008 have been examined, classified and computerized into a specific database; reported adverse events were coded using WHO Adverse Reaction Terminology. Unusual and serious cases were thoroughly studied and followed up to recovery or stabilization of the manifestation. Data were classified as per PHU reporting the AEFI, vaccines administered, date of vaccination, age group (0–11 months, 1–5 years, 6–12 years, ≥13 years) of the subject, number of doses, time interval between administration and onset of reaction, nature of reaction, system organ classes, extent (local injection site versus systemic reactions) and degree of causality (*definite, probable, possible, unlikely, unrelated* and *unclassifiable)* according to WHO classification, using all but one categories: "unlikely" was not used because it was considered insufficiently informative; thus, events plausibly explained by underlying disease or drug intake have been included in the group "unrelated" or coincidental events. Reports causally related to vaccination were further classified as per their seriousness into *common*, *relevant* (clinically significant although resolved spontaneously or after treatment within a few hours/days), and *serious*, as defined by the onset of life-threatening reactions, residual disability, neurological symptoms, hospitalization or death. Population-based and vaccine administered reporting rates were calculated; in the latter case if two or more vaccines were administered, the reported AEFI was attributed to the vaccine which most likely caused the event; otherwise the event was attributed to each administered vaccine. Data are summarized and discussed in annual reports which are sent to the Public Health Authority and then forwarded to vaccine personnel. Reports are available on the Green Channel's web site (http://www.ospedaleuniverona.it/Servizi/Canale-Verde/Canale-Verde-inglese/).



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