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Vaccine adverse event monitoring systems across the European Union countries: Time for unifying efforts☆

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ABSTRACT

A survey conducted among 26 European Countries within the Vaccine European New Integrated Collaboration Effort (VENICE) project assessed the status of organization in prevention and management of adverse events following immunization (AEFI) and level of interconnection, with the aim at individuating points of strength and weakness. The emerging picture is for a strong political commitment to control AEFIs in Member States (MS), but with consistent heterogeneity in procedures, regulations and capacity of systems to collect, analyze and use data, although with great potentialities. Suggestions are posed by authors to promote actions for unifying strategies and policies among MS.

1. Introduction

Vaccinations prevent many deaths and diseases all over the world. Nevertheless, the prevention and control of adverse events following immunization (AEFI) remain a central aspect to improve safety and maintain public confidence in vaccines. Confidence is also crucial to reach optimal immunization coverage and reduction of the frequency of preventable diseases [1,2]. Although vaccines are required to have solid evidence of safety, public concerns are often raised and amplified by mass communication systems. Hence, immunization programs have the responsibility to address these concerns [3,4] being able to perform risk assessments and document the safety profile of products in use.

In complex surveillance systems as those in place in European Union (EU), AEFIs are managed in clinical settings and reported at regulatory level in national agencies dealing with pharmacovigilance. Therefore, the health staff responsible for vaccination may become less informed of the frequency and type of AEFI even in well established immunization programs. Since 1971 the World Health Organization (WHO) has set a Programme for International Drug Monitoring including AEFI reports across the World [5] and a system for monitoring events following the administration of EU licensed products by the European Medicines Agency EMEA [6].

Nonetheless, gaps in the AEFI reporting systems at world level, including many EU countries, have been evidenced as they appear to be heterogeneous, poorly coordinated and insufficiently funded [7–11]. We overview the ongoing practices and share of knowledge on immunization management and AEFI control among most European Member States (MS). Data were collected by the Vaccine European New Integrated Collaboration Effort (VENICE) project funded by EU DGSANCO [12,13].

2. Methods

All MSs, but Malta, and two EEA countries (IS, NO) participate to the VENICE project.[1]

☆ The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the opinion or policies of their organizations or of the participating project groups.

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[1] Participating Countries: Austria (AT), Belgium (BE), Bulgaria (BG), Czech Republic (CZ), Denmark (DK), Estonia (EE), Finland (FI), France (FR), Germany (DE), Greece

The AEFI survey has been conducted by asking each of the 26 national gatekeepers or appropriate contact points to fill in an online questionnaire, created by the authors and pre-tested in 5 MSs (BG, IE, IT, ES, NL). All MSs, but Cyprus and Luxembourg, participated to this survey (93%). The questionnaire included a majority of multiple choice questions, few open answer questions and some sub-related questions on 36 items, grouped as:

1. General organization of AEFI monitoring systems (3 questions including mass vaccination initiatives).
2. Political commitment on AEFIs (3 questions).
3. Detection system of AEFIs (15, here condensed in 5 main questions).
4. Investigation/Causality assessment (9, condensed in 6 questions).
5. Prevention and Treatment (2 questions).
6. Communication and Information (3 questions).
7. Training (1 question).

The proportion of answers provided in the results has been computed excluding missing values.

3. Results

3.1. General organization and juridical framework

AEFIs are reported in all the 26 responding MSs to a national regulatory authority for AEFI surveillance. The institutions/authorities in charge are the Drug Regulatory Agencies, including Pharmacovigilance in 15 MSs (58%), the Public Health Authorities in 5 (19%), while in 6 (23%) MSs the responsibility is shared by both. In 18 MSs a specific safety monitoring system for AEFIs is in place and 9 of them (FI, DE, HU, IS, LV, LT, NL, RO, SK) have this system in addition to Pharmacovigilance (35%). Six countries (23%: AT, FI, FR, IE, NL, UK) also organize special activities during extensive vaccination campaign, such as alerting physicians to report any adverse events (IE), or by establishing a Safety Working Group (UK). More than 80% (21/26) of countries have rules or laws to report and investigate AEFIs; in 18 MSs (69%), reporting is mandatory, with a frequency of 39% (7/18) for all events, of 28% (5/18) for serious events, and for both serious and "Other" or only "Other" events with the same rate of about 17% (3/18). Four countries have AEFI reporting as recommended and 3 as voluntary (Fig. 1). Twelve MSs (46%: AT, DK, FI, FR, DE, HU, IS, IT, NO, SI, SE, UK) put in place a compensation system for vaccine-related damage but only 3 (NO, RO, UK) reported the number of vaccine-related supported people (12%), even when not having specific rules for compensation (RO).

3.2. AEFI reporting, investigation and analysis

Sources of AEFI reports are: medical doctors (Public Health Physician, Primary Care Physician, Paediatrician and Hospital doctor) in 81% (21/26) of countries, including nurses in 45%, patient or parents in 8% (2/26) and others in 19% (5/26) of MSs. "Other" includes: manufacturer, pharmacist, public health officer, relatives, any person. In 9 countries (35%), only medical doctors fill in AEFI forms. Finally, in UK any person can report suspected side effects to vaccines and/or medicines. Adoption of specific forms for AEFI reporting was not uniformly set among MSs and was not strictly related to application of mandatory rules (Fig. 1). Ten countries (38%) have a formal procedure although with different reporting

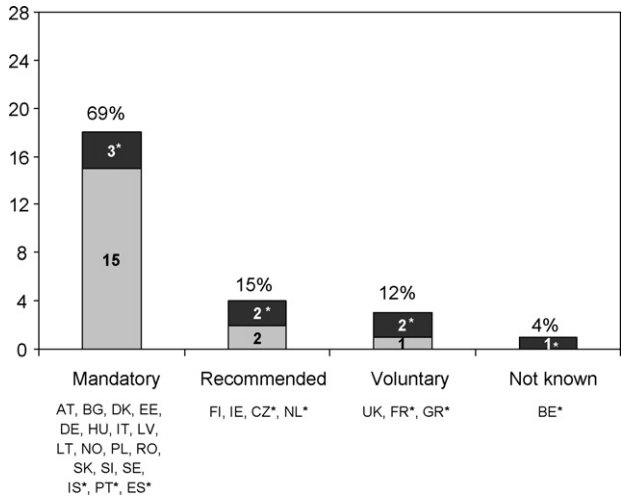

Fig. 1. Juridical framework of AEFI reporting in Member States. (▢) With a form; (■) without a form; (*) country/bar.

times in order to communicate an AEFI to the health authority. Eight of them (AT, BG, LV, LT, PL, RO, SI, SE) report within 24 h or less (31%), with 5 (BG, LV, LT, PL, RO) as mandatory for all events or events listed by a national authority (19%), and 3 (AT, SI, SE) as mandatory only for serious, new or unlisted events (12%). Over 65% (17/26) of countries adopt a classification for AEFIs. Six of them (AT, CZ, DE, HU, NO, PL) refer to WHO classification (23%) and 11 to others. Criteria of seriousness of event, type of vaccine and AEFI causality were mentioned by 18, 15 and 10 MSs, respectively. Nine countries (35%) adopted case definitions for AEFIs. Seven of them (AT, BG, CZ, IT, LV, LT, RO) refer to WHO definitions (27%) and 2 (NL, SE) to a combination of Brighton Collaboration's and other not specified (8%). AEFI reports are analysed at national level at different time intervals (Fig. 2). All but 3 countries (BE, DK, GR) report the number of AEFIs for at least one of the requested years (2003–2005) with a considerable difference in absolute numbers and seriousness of reactions (Table 1). Most (22/26) European countries communicate AEFI reports to EMEA (85%). A lower proportion (17/26 – 65%) has connections with one or more EU networks for AEFI surveillance and/or Pharmacovigilance: 13 countries (50%) referred to EUDRA, 11 countries (42%) to WHO and one referred to the Brighton Collaboration. Eight out of 26 (31%) of MSs have a connection with both EUDRA and WHO. Twenty countries (77%) investigate their AEFIs to

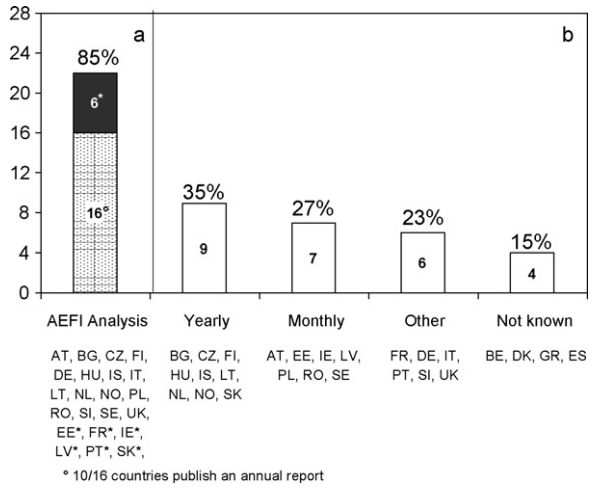

Fig. 2. AEFI analysis and timing in Member States. a: (▨) With classification; (■) without classification; (*) country/bar.

(GR), Hungary (HU), Iceland (IS), Ireland (IE), Italy (IT), Latvia (LV), Lithuania (LT), The Netherlands (NL), Norway (NO), Poland (PL), Portugal (PT), Romania (RO), Slovakia (SK), Slovenia (SI), Spain (ES), Sweden (SE), United Kingdom (UK).

Table 1
AEFIs reported in participating countries (years 2003–2005).

Countries	AEFIs													
	2003					2004					2005				
	Total N.	Serious N.	Serious with sequelae N.	Serious rate/10^5	Doses administered/ sold N.	Total N.	Serious N.	Serious with sequelae N.	Serious rate/10^5	Doses administered/ sold N.	Total N.	Serious N.	Serious with sequelae N.	Serious rate/10^5	Doses administered/ sold N.
AT	115	15	4	–	2,382,514	137	10	1	–	2,384,608	96	12	3	–	2,356,283
BE	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
BG	–	–	–	–	1,971,764	30	1	1	–	2,043,398	49	37	1	–	–
CZ	–	–	–	–	1,651,318	785	785	–	–	1,699,457	814	814	–	–	1,370,619
DK	–	–	–	–	579,052	–	–	–	–	518,520	–	–	–	–	509,995
EE	10	4	0	–	–	15	8	0	–	–	22	13	0	–	–
FI	963	70	–	2.8	2,467,000	1,046	66	–	3.5	2,699,000	996	35	5	1.4	2,429,000
FR	712	363	–	–	–	665	348	–	–	–	682	313	–	–	–
DE	1,199	884	–	–	41,800,000	1,237	858	30	–	41,500,000	1,393	919	34	–	44,500,000
GR	–		–	–	–	–	–	–	–	–	–	–	–	–	–
HU	92	2	2	–	2,000,000	242	7	7	–	2,000,000	38	1	1	–	2,000,000
IS	3	0	0	0	127,447	2	0	0	0	118,583	2	0	0	0	135,106
IE	250	245	–	–	–	275	259	–	–	–	401	381	–	–	1,383,687
IT	933		–	–	–	2,010	241	–	–	–	1,842	221	–	–	–
LV	57	57	–	–	–	21	21	–	–	–	29	29	–	–	–
LT	39	39	7	–	910,000	16	15	5	–	910,000	28	28	2	–	780,000
NL	1,372	91	0	4.8	1,900,000	2,141	92	0	4.8	1,900,000	1,036	48	0	2.5	1,900,000
NO	346	19	0	–	1,519,000	367	13	1	–	1,702,000	359	9	1	–	1,880,000
PL	521	169	–	–	–	746	204	–	–	–	878	229	–	–	–
PT	72	20	–	–	–	97	48	–	–	–	60	27	–	–	–
RO	–	0	0	–	7,000,000	–	0	0	–	8,000,000	63	0	0	–	8,000,000
SK	128	30	–	2.8	1,083,433	124	41	–	3.8	1,065,985	292	15	–	1.5	1,012,560
SI	202	4	0	–	854,825	235	2	0	–	726,324	200	0	0	–	746,885
ES	446	–	–	–	–	571	236	–	–	–	628	172	–	–	–
SE	587	85	–	–	3,563,700	725	84	–	–	4,199,600	923	63	–	–	4,573,000
UK	2,052	1009		–	–	1,757	869	–	–	–	2,205	1069	–	–	–
Total	10,099	3106	27	–	66,246,353	13,244	4208	59	–	67,267,875	13,036	4435	61	–	69,004,135

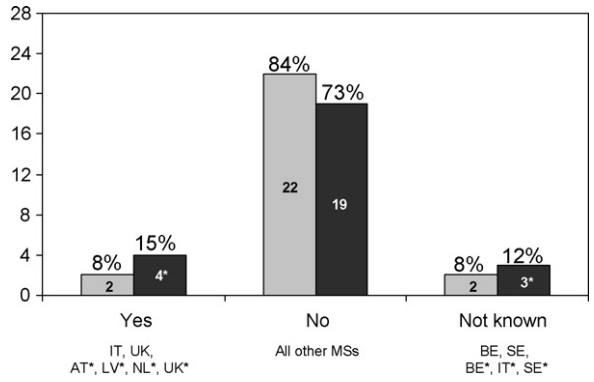

Fig. 3. Countries with a national/local protocol to reduce frequency and management of AEFIs. (▢) With a national/local protocol to reduce frequency; (■) with a national/local protocol for management; (*) country/bar.

establish a causal relationship, although with different procedures. In particular, 15 MSs (58%: AT, BG, FI, DE, HU, IT, LV, LT, NL, NO, PT, RO, ES, SE, UK) investigate AEFI systematically, and 5 countries (FR, IS, PL, SK, SI) on need (19%). In 12/20 MSs the investigation is mandatory (60%). In 7 countries (FI, HU, IS, IT, NL, PT, SE), a national health authority (27%) is in charge of investigating and assessing causality, while a local health authority is in charge in 4 countries (FR, LV, RO, SK) (15%). In 6 countries (31%) the responsibility of investigating AEFIs is shared among authorities at different levels (national, local and/or other) with 2 MSs (BG, DE) having responsibilities at all levels.

Thirteen countries that systematically investigate AEFIs (AT, BG, FI, HU, IT, LV, LT, NL, NO, RO, ES, SE, UK), and 2 (EE, FR) not performing systematic investigation have put in place a system/network for identification and analysis of AEFIs. Eleven countries (AT, BG, EE, FI, FR, HU, LV, NL, ES, SE, UK) have a centralized system, supported by a group of experts (42%). At local level AEFIs are identified and analyzed by a group of experts in 3 countries (LV, NO, ES), through the network of pharmacovigilance (8%) in 2 countries (FR, IT), and in 3 MSs (12%) with other (UK by a "AEFI" reporter; LT and BG by a Public Health Centre).

Only 5 countries (19%: AT, FR, NL, NO, UK) have a procedure for clinical and laboratory investigation for AEFIs identification and follow-up. Nine countries (35%: DK, FI, HU, LV, LT, NL, NO, SK, SI) have a counselling service for pre- and post-vaccination AEFI prevention. Four countries (15%) have protocols for AEFI management and 2 MSs (8%) have protocols for reducing AEFI frequency (Fig. 3). Two countries (LV, NL) have both protocols. Nine countries (35%) have large-linked databases (AT, DK, FI, FR, IS, NO, PL, SE, UK) suitable for vaccine safety studies, but only 6 (AT, DK, FR, PL, SE, UK) use these databases for safety purposes (23%) and 8 countries have performed case studies (31%: DE, DK, FI, IE, NL, PL, PT, UK).

3.3. Communication

All but 3 countries (BE, GR, PT) (12%), give information on AEFIs to a wide spectrum of targets. Of MSs sharing different targets (23/26), 10 (38%) give communication to patient or parents and 21 (81%) to vaccine personnel. Public opinion is informed in 10 countries: in 3 of them communication is given also to movements against vaccines (12%). Seven countries (27%) give information also to "Others": AEFI reporters, health professionals, web-site communication, State Agency of Medicine, health care professional, marketing authorisation holder, physicians and pharmacists (Fig. 4). In 6 countries (EE, ES, IT, NO, RO, SK) communication on AEFI is given only to vaccine personnel (23%). Finally, communication is also available through web sites in 3 countries (SI, NL, SE). As for the authorities in charge of communication on AEFIs, 25/26 MSs (96%)

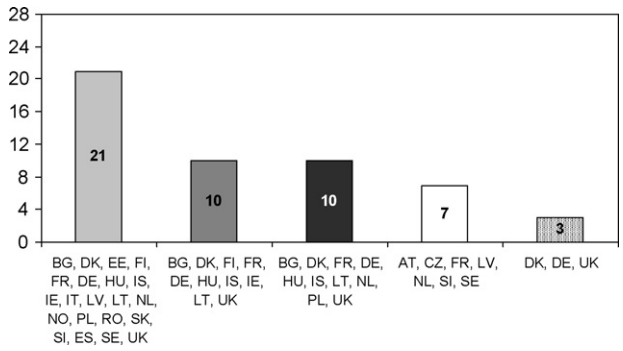

Fig. 4. Categories to which communication of AEFIs is given. (▢) Vaccine personnel; (▢) public opinion; (■) parent/patient; (□) other; (▨) movements against vaccines.

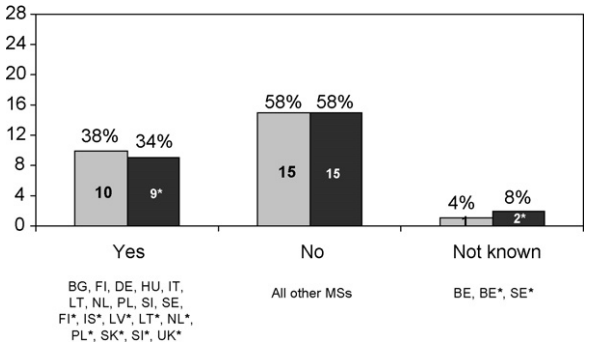

Fig. 5. Countries with training and annual reporting for health staff on AEFIs. (▢) Annual report; (■) training program/manual; (*) country/bar.

have a national authority for communication to media: 7 (27%) of them include also local health personnel (DE, DK, IE, LT, LV, NO, RO) and 2 (8%) include other categories (vaccine manufacturers in DK; epidemiologists/medical officers at regional level in HU).

3.4. Training

Only a minority of countries have established systems to inform and update personnel on AEFIs surveillance. In particular, 9 countries (35%) developed a training program/manual for health staff on prevention, identification and treatment of AEFIs and 10 countries (38%) release a AEFI annual report making it available also to the public (Fig. 5).

4. Discussion

The increasing spread of vaccination and the consequent reduction of vaccine preventable diseases, together with the continuous introduction of new vaccines, have raised more attention on occurrence of AEFIs at global level. Their prevention and control remains a crucial activity to increase safety and maintain public confidence in vaccines and optimal immunization coverage.

In 2005 the WHO Global Advisory Committee on Vaccine Safety underlined the need for improved monitoring and analysis of AEFI at international level. From the analysis of the WHO Adverse Reactions Database of the Uppsala Monitoring Centre reports from only 3 countries accounted for 82% of all the recorded AEFI [10]. The current free circulation of persons and goods across EU would ultimately lead to common strategies also for controlling vaccine preventable infections. Different countries use the same vaccines in similar target population groups and the availability of comparable data on AEFI surveillance is clearly desirable. To improve international collaboration and disseminate information on vaccine issues among MSs, including AEFIs, the VENICE project was

launched [13]. The present analysis was conducted in western and eastern Europe to provide an overview on state regulations and performances in 26 EU countries. The large participation to this survey indicates the interest in improving the AEFI monitoring systems from most countries and in sharing experiences and programmes. A previous survey conducted in 1999–2000 in western European countries already identified some problems of vaccinovigilance, such as insufficient funding and personnel, lack of denominators, of proper analysis and feedback [7].

Our results show that relevant and articulated surveillance systems are active in all the countries. However, variability in reporting procedures, regulations, and analysis performances was found. Although a strong political commitment at national level clearly emerges, AEFIs are mostly monitored only by the pharmacovigilance reporting system. However, immunisation is certainly different from drug treatment for many issues [11], the major difference being their offer to healthy subjects. Therefore, AEFI monitoring with the involvement of health authorities dealing with vaccine administration, as already performed in 11 countries, should be encouraged in all MSs. There is a great potentiality of surveillance systems to collect and analyse data in most countries (85%), but with a limited use and share of such data on a general scale. In fact, although some MSs stated to have large linked databases (LLDBs), only in a few countries use them for safety studies. The use of case definitions is also limited to 35% countries and should be extended to all MSs. Connections with one or more EU surveillance networks cover only part of the MSs (65%) and refer to different organizations, suggesting the need for a more homogeneous adoption. There are special activities in some countries/regions, such as pre- and post-vaccination counselling (35%), which could be thoroughly analyzed as potential best practice model. Although most MSs perform AEFI analysis and some kind of classification, only 10 MSs publish reports, which are an important feedback for personnel that should be an objective of all MSs. Health staff training programmes are practically neglected in most MSs. Taking into consideration the current knowledge of vaccinees and the rate of growing information and disinformation in this field, continue education and updating of personnel is recommended.

The overall picture suggests that particular efforts should be put on encouraging prompt and regular transmission of reports, in particular of serious events. A crucial additional need is related to AEFI data sharing and use among all MSs. This could be facilitated by creating one LLDB at European level, to track vaccinations and clinical outcomes. Countries with noteworthy models should share their know-how and experience with others to reach a shared gold standard. In fact, due to present differences in organization evidenced by this study between MSs, priority should be given to identify a platform of minimal requirements for qualified AEFI surveillance systems to be adopted. Strong efforts should be made to unify action and information among personnel in charge of vaccination with those in charge of surveillance. Finally, it is necessary to focus the institutional attention on the relevance of the health staff training and on the availability of suitable training tools for preventing, identifying and treating AEFIs. This fundamental aspect resulted largely underestimated, with most MSs (65%) not having programmes for continuous updating personnel on vaccine issues. This is an important issue where WHO, ECDC and other European organizations could be helpful and effective. Information for citizens also needs to be implemented on a more regular basis.

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Appendix A

See Table A.1.

Table A.1
Synopsis of collected data from countries participating to the survey.

Question	AT	BE	BG	CZ	DK	EE	FI	FR	DE	GR	HU	IS	IE
1. Presence of specific AEFI monitoring system	Y	N	Y	N	Y	N	Y	N	Y	N	Y	Y	N
2. System in addition to pharmacovigilance	N	N	N	N	N	N	Y	N	Y	N	Y	Y	N
3. Authority responsible for AEFI surveillance	PV	PV	PV, PH	PV	PV	PV	PV, PH	PV	PV, PH	PV	PH	PH	PV
4. Mandatory rules or laws for reporting and investigation	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y
5. Compensation System – n. of compensations (2004–2005)	Y – NK	N	N	N	Y – NK	N	Y – NK	Y – NK	Y – NK	N	Y – NK	Y – NK	N
6. Form for AEFI reporting	Y	N	Y	N	Y	Y	Y	N	Y	N	Y	N	Y
7. Personnel in charge of reporting	a–d, f	NA	a, c, d	b, c, d	a–f	a, c, d	a–d	NA	a, c, d, f	NAP	a, c, d	a–d	a, c, d
8. Juridical framework	man	NA	man	rec	man	man	rec	vol	man	vol	man	man	rec
9. Type of AEFIs with mandatory report	o	se	ae	se	o	se	NA	o	se	NAP	ae	se	ae
10. Formal procedure and reporting time	Y – o	N	Y – h	Y – d	N	N	N	N	N	N	N	N	N
11. N. of AEFIs/year (2003–2005) for at least 1 year	Y	NA	Y	Y	NK	Y	Y	Y	Y	NA	Y	Y	Y
12. Communication to EU organizations	E	NA	E	NK	E	E	E	E, o	E	E	E	E	E
13. Frequency of analysis	m	NA	y	y	NK	m	y	o	o	NK	y	y	m
14. Classification of AEFIs	Y	NA	Y	Y	Y	N	Y	N	Y	NA	Y	Y	N
15. Type of classification	c, s, v	NA	s, v	s, v	o	NAP	c, s, v	NA	c, s, v	NA	s, v	s, v	NA
16. List of case definitions	Y – WHO	NA	Y – WHO	Y – WHO	N	N	N	N	N	NA	N	N	N
17. Case studies	N	NA	N	N	Y	N	Y	N	Y	N	N	N	Y
18. Connection with EU networks	E, EU, ED	NA	ED, WHO	WHO	ED	ED, WHO	E, WHO	ED, WHO	ED, WHO	NA	Y	E	ED
19. Counselling service	N	NA	N	N	Y	N	Y	N	N	N	Y	N	N
20. Flow chart of flux for reporting	x		x						x		x		
21. Investigation for causality	Y – WHO	NA	Y – WHO	N	N	N	Y – WHO	on-o	Y – WHO	N	Y – WHO	on	N
22. Mandatory investigation	ae	NA	se	N	N	N	ae	N	N	N	ae	N	N
23. Authority in charge of investigation	o	NA	l, n, o	NAP	NAP	NA	n	l	l, n, o	NA	n	n	NAP
24. Network for identification and analysis	Y – n	NA	Y – l, n	N	NK	Y – n	Y – n	Y – l, n	N	N	Y – n	N	N
25. Procedure for clin/lab investigation and follow-up	Y	NA	N	N	N	N	N	Y	N	N	N	N	N
26. Large-linked databases	Y	NA	N	N	Y	N	Y	Y	N	N	N	Y	N
27. N. of serious AEFIs/year (2003–2005) for at least 1 year	Y	NA	Y	Y	NK	Y	Y	Y	Y	NA	Y	Y	Y
28. N. of serious AEFI/year with sequelae for at least 1 year	Y	NA	Y	NK	NK	Y	Y	NK	Y	NA	Y	Y	NK
29. Vaccine doses administered-sold/year for at least 1 year	Y	NA	Y	Y	Y	NK	Y	NK	Y	NA	Y	Y	Y
30. Protocol for AEFI prevention	N	NA	N	N	N	N	N	N	N	N	N	N	N
31. Protocol for AEFI management	Y	NA	N	N	N	N	N	N	N	N	N	N	N
32. Communication on AEFI (addressee)	e	None	a–c	e	a–d	b	b, c	a–c, e	a–d	None	a–c	a–c	b, c
33. Authority in charge of informing media	o[a]	NA	n	n	n, l, o	n	n	n	n, l	o[a]	n, o	n	n, l

Table A.1 (*Continued*)

Question	AT	BE	BG	CZ	DK	EE	FI	FR	DE	GR	HU	IS	IE
34. Publication of annual report	N	NA	Y	N	N	N	Y	N	Y	N	Y	N	N
35. Specific surveillance during campaigns	Y	NA	N	N	N	N	Y	Y	N	N	N	N	Y
36. Health staff training	N	NK	N	N	N	N	Y	N	N	N	N	Y	N

Question	IT	LV	LT	NL	NO	PL	PT	RO	SK	SI	ES	SE	UK
1. Presence of specific AEFI monitoring system	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	N
2. System in addition to pharmacovigilance	N	Y	Y	Y	N	N	N	Y	Y	N	N	N	N
3. Authority responsible for AEFI surveillance	PV	PV, PH	PV, PH	PH	PV	PH	PV	PV	PH	PV, PH	PV	PV	PV
4. Mandatory rules or laws for reporting and investigation	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	N
5. System – n. of compensations (2004–2005)	Y – NK	N	N	N	Y – 0 (04) 1 (05)	N	N	N – 1 (05)	N	Y – NK	N	Y – NK	Y – 5 (04) 5 (05)
6. Form for AEFI reporting	Y	Y	Y	N	Y	Y	N	Y	Y	Y	N	Y	Y
7. Personnel in charge of reporting	a–d	c, d	c, d	NAP	a–d	a, b, d, f	a–d	c	c, d	a, c, d	a–d	a–d	a–f
8. Juridical framework	man	man	man	rec	man	man	man	man	man	man	man	man	vol
9. Type of AEFIs with mandatory report	ae	o	o	NAP	se	ae	o	ae	se	ae	ae	o	ae
10. Formal procedure and reporting time	NA	Y – h	Y – o	N	N	Y – h	N	Y – h	N	Y – o	NA	Y – h	Y – d
11. N. of AEFIs/year (2003–2005) for at least 1 year	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12. Communication to EU organizations	E	E	E	E	E	E	E	None	E	NK	E	E	E
13. Frequency of analysis	o	m	y	y	y	m	o	m	y	o	NK	m	o
14. Classification of AEFIs	Y	N	Y	Y	Y	Y	N	Y	N	Y	N	Y	Y
15. Type of classification	s, v	NAP	c, v	c, s, v	c, s, v	s, v	s, c	s	c, s, v	s	c, s, v	c, s, v, o	s
16. List of case definitions	Y – WHO	Y – WHO	Y – WHO	Y – BC, o	N	N	N	Y – WHO	N	N	N	Y – BC, o	N
17. Case studies	N	N	N	Y	NK	Y	Y	N	N	N	N	NK	Y
18. Connection with EU networks	ED, WHO	E, ED	ED, WHO	BC	E	N	N	N	WHO	N	ED, WHO	ED, WHO	E, ED
19. Counselling service	N	Y	Y	Y	Y	N	N	N	Y	Y	N	N	N
20. Flow chart of flux for reporting	x	x	x		x	x	x				x		x
21. Investigation for causality	Y – WHO	Y – WHO	Y – WHO	Y – WHO	Y – o	on-WHO	Y – WHO	Y – WHO	on-WHO	on	Y – o	Y – WHO	Y – o
22. Mandatory investigation	N	ae	o	N	N	se	o	ae	N	se	N	o	ae
23. Authority in charge of investigation	n, o	l	l, n	n	o	l, n	n	l	l	NAP	l, n	n	l, n
24. Network for identification and analysis	Y – l, n	Y – l, n	Y – l, n	Y – n	Y – l, n	N	N	Y	N	N	Y – l, n	Y – n	Y – l, n
25. Procedure for clin/lab investigation and follow-up	N	N	N	Y	Y	N	N	N	N	N	N	N	Y
26. Large-linked databases	NA	N	N	N	Y	Y	N	N	N	N	NA	Y	Y
27. N. of serious AEFIs/year (2003–2005) for at least 1 year	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
28. N. of serious AEFI/year with sequelae for at least 1 year	NK	NK	Y	Y	Y	NK	NK	Y	NK	Y	NK	NK	NK
29. Vaccine doses administered-sold/year for at least 1 year	NK	NK	Y	Y	Y	NK	NK	Y	Y	Y	NK	NK	NK
30. Protocol for AEFI prevention	Y	N	N	N	N	N	N	N	N	N	N	NK	Y
31. Protocol for AEFI management	NK	Y	N	Y	N	N	N	N	N	N	N	NK	Y
32. Communication on AEFI (addressee)	b	b, e	a–c	a, b, e	b	a, b	None	b	b	b, e	b	b, e	a–d
33. Authority in charge of informing media	n	n, l	n, l	n	n, l	n	n	n, l	n	n	n	n	n

Table A.1 (*Continued*)

Question	AT	BE	BG	CZ	DK	EE	FI	FR	DE	GR	HU	IS	IE
34. Publication of annual report	Y	N	Y	Y	N	Y	N	N	N	Y	N	Y	N
35. Specific surveillance during campaigns	N	N	N	Y	N	N	N	N	N	N	N	N	Y
36. Health staff training	N	Y	Y	Y	N	Y	N	N	Y	Y	N	NK	Y

Y = yes.
N = no.
NA = no answer.
NK = not known.
NAP = not applicable.
Question 3: PV = pharmacovigilance; PH = public health.
Question 7: a = public health physician; b = nurse; c = physician/paediatrician; d = hospital doctor; e = patient/parent; f = other (manufacturer, holder of marketing authorization, physicians, pharmacists, public health officer, relatives, any person).
Question 8: man = mandatory; vol = voluntary; rec = recommended.
Question 9: ae = all events; se = serious events; o = other.
Question 10: h = within 24 h; d = days; o = other (as soon as possible, not known).
Question 11: see Table 1.
Question 12: E = EMEA; o = other; none.
Question 13: m = monthly; y = yearly; o = other (on need, weekly, every 3 months, every 2 years, continuously on web database basis with open access).
Question 15: c = causality; s = seriousness; v = type of vaccine; o = other.
Question 16: WHO = World Health Organization; BC = Brighton Collaboration; o = other.
Question 18: E = EMEA; EU = European Union; ED = EUDRA; WHO = World Health Organization; BC = Brighton Collaboration.
Question 21: WHO = World Health Organization; o = other; on = on need.
Question 22: ae = all events; se = serious events; o = other.
Question 23: l = local health authority; n = national health authority; o = other (Bundesamt fur Sicherheit im Gesundheitwesen, regional epidemiologists and Members of National expert committee, physicians, manufacturer, Regional Centers for PharmacoVigilance, Staff at NIPH).
Question 24: l = at local level; n = at national level.
Question 27–29: see Table 1.
Question 32: a = parent/patient; b = vaccine personnel; c = public opinion; d = movements against vaccines; e = other (AEFI reporters, health professionals, web-site communication, report available on home page, SAM-State Agency of Medicine, marketing authorisation holder, physicians, pharmacists).
Question 33: l = local health personnel; n = national authority; o = other (Agency for Health and Food Safety, Ministry of Health, vaccine manufacturers, regional health authority: epidemiologists, medical officers).
[a] Marked in the "other" box, but referring to national organizations.

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