Vaccinovigilance in Europe — need for timeliness, standardization and resources

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Objective To identify gaps in the systems for reporting adverse events following immunization (AEFI) in Europe by means of an interactive database constructed using a standardized approach.

Methods A comparative survey was conducted in 1999–2000, using structured questionnaires addressed to the government authorities responsible for national immunization programmes and drug safety surveillance in all European Union (EU) Member States and in Norway and Switzerland.

Findings The reporting of adverse vaccine reactions (AVRs) is covered by regulations in 13 of the 17 countries. Four countries have a specialized expert group with responsibility for vaccine safety. Only six professionals work full-time on vaccine safety in the 17 countries; in four of these countries the person is medically qualified. Fourteen countries have centralized reporting systems; in 14 countries the responsible authority is the drug regulatory agency. AEFI are reported using the procedure used for adverse drug reactions (ADRs) in all except four countries. The reporting form is not usually designed for vaccines and important details may therefore not be requested. Clinical definitions for vaccine reactions are not available. Twelve countries have appropriate official definitions for events or reactions, but the list of reportable events varies considerably between countries. The assessment of adverse vaccine reactions (AVRs) is hampered by lack of exact denominator data. Feedback to the rapporteurs was provided in 13 countries, but its quality was highly variable.

Conclusion The database facilitated a simple comparison of vaccinovigilance systems across participating countries. Most of the problems identified related to the reporting and analysis of AEFI could be solved through standardization and intensified international collaboration. On a national level, functional vaccinovigilance systems should be the shared responsibility of the drug regulatory authority and the national immunization programme. The resources for development and management of vaccine safety systems should be urgently improved.

Keywords Vaccines/adverse effects; Adverse drug reaction reporting systems/organization and administration; Product surveillance, Postmarketing/organization and administration; Legislation, Drug; Databases, Factual/standards; International cooperation; Comparative study; European Union; Norway; Switzerland (*source: MeSH, NLM*).

Mots clés Vaccins/effets indésirables; Services données effets secondaires médicaments/organisation et administration; Vigilance produits de santé; Législation pharmaceutique; Base données factuelles/normes; Coopération internationale; Etude comparative; Communaute économique européenne; Norvège; Suisse (*source: MeSH, INSERM*).

Palabras clave Vacunas/efectos adversos; Sistemas de registro de reacción adversa a medicamentos/organización y administración; Vigilancia de productos comercializados; Legislación de medicamentos; Bases de datos factuales/normas; Estudio comparativo; Cooperación internacional; Unión Europea; Noruega; Suiza (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: التأثيرات الضائرة للقاحات؛ تنظيم وإدارة نُظم التبليغ عن التفاعلات الضائرة للأدوية؛ ترصد المنتوجات؛ تنظيم وإدارة المنتوجات بعد التسويق؛ تشريعات الأدوية؛ قواعد المعطيات الواقعية؛ معايير قواعد المعطيات؛ التعاون الدولي؛ دراسة مقارنة؛ الاتحاد الأوروبي؛ سويسرا (**المصدر: رؤوس الموضوعات الطبية – المكتب الإقليمي لشرق المتوسط**)

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Voir page 833 le résumé en français. En la página 834 figura un resumen en español. يمكن الاطلاع على الملخص بالعربية في صفحة **834**.

Introduction

The benefits of immunization have been evident ever since vaccination was introduced by Jenner in the late eighteenth century. In international health forums, the pivotal role of immunizations in solving global health problems was acknowledged in 1993 when The World Bank highlighted the cost-effectiveness of immunizations in The World Development Report (*1*).

Immunization has become a victim of its own success. As the incidence of diseases preventable by vaccination steadily decreases, the advances made are being undermined by vaccine scares. For example, the measles–mumps–rubella vaccine and its suggested connection with chronic bowel disease or autism in the United Kingdom (*2*) and hepatitis B vaccine with multiple sclerosis in France (*3*) have had serious repercussions in other countries. The situation has been aggravated by the inability of authorities to provide a timely and accurate research-based response to the alleged adverse vaccine reactions (AVRs), or more generally, to adverse events following immunization (AEFI).

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During the past decade a number of initiatives have been taken to improve vaccine safety. Canada and the United States have developed and invested in national surveillance systems for AEFI, the responsibility for which is shared by both the drug regulatory agency and the national immunization programme, and staff are appropriately trained (*4*–*6*). The North American systems are continuously assessed and upgraded, and additional features such as targeted active surveillance have been added (*7*, *8*). Australia was one of the first countries to introduce an immunization register for childhood vaccines to improve assessment of immunization coverage and reports of AEFI (*9*). WHO has also made immunization safety a priority project (*10*), in which improved national surveillance systems for adverse events are key elements (*11*). In Europe the development of vaccine safety systems has been heterogeneous. A few countries such as the Netherlands (*12*) and Denmark (*13*) have surveillance systems that permit analysis of suspected events. Targeted surveillance programmes have been conducted in the United Kingdom (*14*, *15*).

Vaccines are very different from other pharmaceuticals: if there is a problem with certain drugs, the health professional reporting adverse events usually just changes to an alternative treatment. For vaccines, the critical questions following reports of AEFI are how to proceed with primary immunization series or with boosters. The assessment of individual situations requires a specialized knowledge of vaccines, of adverse reactions and of clinical medicine, most often paediatrics (*4*). The fact that vaccines are generally given to healthy people decreases the threshold for tolerance of adverse events: an incidence of only 1:100 000 may be only just acceptable for vaccines, whereas for adverse reactions to drugs an incidence as high as 1:1–1:100 may be accepted (*16*, *17*).

The example of intussusception following oral rotavirus vaccine demonstrates how important it is to have reliable data on prior background incidence, readiness to detect signals for unexpected reactions and good denominator data on vaccine use (*18*, *19*). Analysis of the clinical significance and causal assessment of a signal also require supplementary studies by competent staff (*19*–*22*). Drawing on current international experience, the likely essential components of a system for surveillance of adverse events after vaccination, vaccinovigilance (*23*), are given in Box 1.

The European Commission (EC) has started several initiatives intended to provide a comprehensive picture of public health programmes in the European Union (EU). The Scientific and Technical Evaluation of Vaccination Programmes in the European Union (EUVAX project), was part of a series of inventory projects on communicable diseases commissioned by the EC (*24*–*26*). The immediate objective of the EUVAX project was to create an interactive database on all aspects of immunization programmes, including programme planning, administration, funding and monitoring, for public health specialists (*26*). The long-term development objective is to facilitate comparisons between countries and to provide a possibility for sharing experiences to identify strengths and weaknesses in the national policies and programmes so that the assembled database could serve as a planning tool for future recommendations. Based on the findings of the EUVAX project, the present paper provides a critical appraisal of the existing vaccine safety surveillance or vaccinovigilance systems in Europe.

Box 1. **Features of a functional vaccinovigilance system**[a]

- Clear organization and regulatory framework
- Awareness of the reporting system among professionals
- Appropriate reporting form
  - general adverse drug reaction form that is adaptable to all pharmaceuticals, or a special form for reporting adverse events following immunization
- Collaboration between the drug regulatory agency and the national immunization programme
- Sufficient funding
- Competent full-time staff
- Availability of expertise in vaccinology
  - full-time or through consultancy arrangements
  - support from a group of experts
- Unambiguous case definitions
- Availability of reliable information on the actual number of immunizations
- Regular analysis of reports
- Timely follow-up of signals
- Supplementary targeted causality analyses
- Appropriate and timely feedback to rapporteurs
- Written standard operating procedures for all actions

[a] Vaccinovigilance is defined as all methods of assessment and prevention of adverse events following immunizations.

Methods

In addition to all EU Member States, Norway and Switzerland agreed to participate in the study.[b]

We always obtained ministry-level approval for the review process and for the proposed list of contact persons for each particular sector. The data were collected using structured face-to-face interviews based on a questionnaire mailed in advance, to minimize non-response and different interpretations of questions. The pre-tested questionnaire was distributed to the interviewees 2–4 weeks before the interview took place. We also requested that background statistics, regulations, guidelines and other documentation be made available for the actual review. International definitions for adverse events and reactions were used (Box 2). In 16 of the participating countries, the data were collected in interview sessions with the contacts and a representative of the EUVAX Project Team. The authorities in Norway submitted their response by post and unclear items were discussed by telephone; the quality of the Norwegian data did not differ from those of other countries. The collection of data began in January 1999 and was completed in January 2000, although subsequent attempts were made to recover missing data. After the data had been entered into the database, requests were sent to the collaborators to verify data accuracy. The final project report was published in 2001 (*26*).

The database was constructed by Vineyard International Ltd. The database server utilized Microsoft Windows NT 4.0,

[b] The following ISO 3166 country codes have been used in this report: Austria (AT); Belgium, Flemish (BE-Fle); Belgium, French (BE-Fre); Switzerland (CH); Germany (DE); Denmark (DK); Spain (ES); Finland (FI); France (FR); Great Britain (GB); Greece (GR); Ireland (IE); Italy (IT); Luxembourg (LU); Netherlands (NL); Norway (NO); Portugal (PT); Sweden (SE).

Oracle Workgroup Server 7.3.4 and Vineyard Manager 3.1 applications. The web server was built on Microsoft Windows NT 4.0, Microsoft Internet Information Server 4.0 and Vineyard Web Gateway 2.0.31. The open database is accessible with Standard Query Language (SQL) tools. The output is currently organized in summary tables and country profiles.

Results

Regulatory aspects

In most European countries, reporting of AEFI is covered by law or other regulations, often supplemented by guidelines or other official recommendations. The responsible authority is the drug regulatory agency in all countries except Austria (*Bundesministerium für soziale Sicherheit, Generationen und Konsumentenschultz*), Switzerland (Swiss Federal Office of Public Health) and Luxembourg (*Direction de la Santé*). In Finland and the Netherlands the regulatory authorities have delegated the practical management of the reporting system to other organizations (FI: National Public Health Institute (KTL); and NL: The Netherlands Pharmacovigilance Foundation (LAREB) (adults) and the National Institute of Public Health and the Environment (RIVM) (children)). Collaboration between different authorities mainly comprises consultations and sharing of information.

International reporting is the responsibility of the drug regulatory agency in all countries except Austria (*Bundesministerium*) and Luxembourg (*Direction de la Santé*). All EU Member States report to the European Medicines Evaluation Agency (EMEA). All countries except Germany, Italy and Switzerland collaborate with the Uppsala Monitoring Centre in Sweden, which runs the adverse drug reactions database for the WHO Programme for International Drug Monitoring.

Organization

Vaccinovigilance was managed regionally in France, Spain and Sweden. Switzerland operates both centralized and regional systems. All other countries had centralized reporting systems. In all countries, vaccine safety surveillance relied on passive reporting of suspected AEFI. Reporting was voluntary at the local level in five countries (BE, GB, IE, NL and PT). At the regional level, reporting was voluntary in Germany, Ireland and the Netherlands (Table 1).

Resources

Resources for vaccine safety activities were scarce (Table 1). Only six out of the 17 countries had one professional working full-time on vaccine safety. In four countries (DE, FI, NL and PT) this person was medically qualified. An additional four personnel spent more than 50% of their working time on vaccine safety, and 68 personnel spent less than 50%. No regional surveillance system except that of Sweden (which had five nurses) employed personnel dedicated to vaccinovigilance.

Expert groups

Expert groups working in pharmacovigilance have been charged with reviewing issues of vaccine safety in ten countries, but in only four of these countries is this a specialized vaccinovigilance group (Table 1). The groups are appointed by the Ministry of Health or the Minister of Health, except in Finland (appointed by the Head of Department of Vaccines at KTL) and in the Netherlands (appointed by the *Gezondheidsraat*). The frequency with which these expert groups meet ranges from one to two meetings per month (GR) to one meeting every 3 months (AT, NL and SE).

The groups in different countries have differing responsibilities relating to the indications and contraindications for vaccines, and the overall reporting system for AEFI. The groups in Denmark, Finland and Sweden deal only with AEFI.

Reporting of adverse events following immunization

Reporting follows the same route and uses the same forms as are used for adverse drug reactions (ADRs) in all except four countries (CH, FI, NO and NL (children)). Thus the reporting form is usually not designed for vaccines and important details may not be asked for. For example the trade name is not requested on forms used in Norway and the lot number is

Box 2. **Definitions of adverse events and reactions**[a]

Adverse drug reaction (ADR)

In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as therapeutic dose(s) may not be established, all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

When considering already marketed medicinal products, an adverse drug reaction is a response to a drug that is noxious and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.

Adverse event (AE)

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).[a]

Serious adverse event (SAE) or serious adverse drug reaction (serious ADR)

Any untoward medical occurrence that at any dose: 1) results in death; 2) is life-threatening; 3) requires inpatient hospitalization or prolongation of existing hospitalization; 4) results in persistent or significant disability or incapacity; or 5) is a congenital anomaly or birth defect.

Unexpected adverse drug reaction (UADR)

An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. "Investigator's brochure" for an unapproved investigational product or the package insert/summary of product characteristics for an approved product).

[a] From: ICH guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (www.emea.eu.int).

Table 1. **Findings on the organization of vaccine safety activities in 17 European countries**[a]

	AT	BE-Fle	BE-Fre	CH	DE	DK	ES	FI	FR	GB	GR	IE	IT	LU	NL	NO	PT	SE	No. of countries
AEFI[b] covered by law or other regulations	X	X	X	X	X		X	X	X	X		X	X	X	X	X		X	13
Passive reporting of suspected AEFI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	17
Reporting is voluntary at the local level		X	X							X		X		X	X		X		7
Reporting is voluntary at the regional level					X							X			X				3
Full-time staff					X		X	X							X		X		5
Medically qualified staff					X			X							X		X		4
An expert group on vaccine safety	X	X	X			X		X	X	X	X	X			X			X	10
Expert group of vaccine specialists						X		X							X			X	4

[a] ISO 3166 country codes: Austria (AT); Belgium, Flemish (BE-Fle); Belgium, French (BE-Fre); Switzerland (CH), Germany (DE); Denmark (DK); Spain (ES); Finland (FI); France (FR); Great Britain (GB); Greece (GR); Ireland (IE); Italy (IT); Luxembourg (LU); Netherlands (NL); Norway (NO); Portugal (PT); Sweden (SE).
[b] AEFI = adverse events following immunization.
X indicates a positive answer.

not requested on forms used in five countries (BE, DK, GR, LU and SE) (this information is essential to detect signals of problems with vaccine quality), and there is no question on dose in the immunization schedule in seven countries (DK, ES, FR, GB, GR, IE and SE) (essential for evaluation of allergic reactions). Furthermore, details on the injection site are not sought in ten countries. National case definitions specific for vaccine reactions do not exist.

Reports are sent electronically in Spain and the United Kingdom, and on paper in all other countries. Reporting is supplemented by personal phone calls in five countries (CH, ES, IE, LU and NL).

Reporting personnel

The reporting personnel in all countries are physicians. Public health nurses are also authorized to report in five countries, and nurses in eight countries. The feedback is given by pharmacists in nine countries, including Austria and Greece, where physicians are not involved at all in evaluating or responding to the reports.

Events to be reported

There is considerable variation in the list of reportable events (Table 2) and not all countries have appropriate definitions for events or reactions (Table 3). Sweden and the United Kingdom have stipulated that all suspected reactions to new drugs including vaccines should be reported, and the Austrian and Swedish authorities request reports on increasing frequencies of known reactions.

Only France and the Netherlands used information on the number of vaccinated persons for denominator data and to allow for reliable estimation of coverage. Data collected in Finland and Switzerland relate to the number of distributed vaccine doses, which is obviously not the same as the number of doses actually administered. No denominators are used in ten countries (AT, BE, DK, GR, IE, IT, LU, NO, PT and SE).

Table 2. **Reportable adverse events following immunization**

Reaction or event[a]	Yes	No	Countries[b]
SAVR	16	2	BE-Fle, BE-Fre
UAVR	16	2	BE-Fle, BE-Fre
All AVR	8	10	AT, BE-Fle, BE-Fre, CH, FI, FR, NL, NO, PT, SE
SAE	10	8	AT, BE-Fle, BE-Fre, DE, DK, GB, IE, SE
UAE	10	8	AT, BE-Fle, BE-Fre, DE, DK, GB, IE, SE
All AEs	5	13	BE-Fle, BE-Fre, ES, GR, LU

[a] AVR = adverse vaccine reaction; SAVR = serious adverse vaccine reaction; UAVR = unexpected adverse vaccine reaction; AE = adverse event; SAE = serious adverse event; UAE = unexpected adverse event. Definitions as for all drugs (Box 2).
[b] ISO 3166 country codes: Austria (AT); Belgium, Flemish (BE-Fle); Belgium, French (BE-Fre); Switzerland (CH); Germany (DE); Denmark (DK); Spain (ES); Finland (FI); France (FR); Great Britain (GB); Greece (GR); Ireland (IE); Luxembourg (LU); Netherlands (NL); Norway (NO); Portugal (PT); Sweden (SE).

Feedback

Feedback to the rapporteurs is provided in 13 countries, but the quality of the response is very variable, and may be no more than an acknowledgement of the receipt of the report. The type of reaction is not classified in six countries (AT, BE, ES, FR, GB and SE) and there is no assessment made of causality in four countries (AT, ES, IE and SE). Advice on future immunizations is given in ten countries. In many cases, the feedback to the vaccinator is given by professionals other than physicians.

Analysis of reports

Analysis of reports is irregular in four countries (AT, CH, ES and SE). At least the total number of all received AEFI reports is reported in all countries except Switzerland. Serious AEFI are

Table 3. **Definitions for adverse events and reactions**

Definition for	No definition available:[a]
Adverse event	AT, NO
Adverse drug reaction	IT, LU, NO, PT
Adverse vaccine reaction	AT, BE, DK, FR, GR, LU, NO

[a] ISO 3166 country codes: Austria (AT); Belgium, Flemish (BE-Fle); Belgium, French (BE-Fre); (Denmark (DK); France (FR); Greece (GR); Italy (IT); Luxembourg (LU); Norway (NO); Portugal (PT).

analysed separately in all but four countries (BE, CH, GR and SE). Events are summarized by vaccine in all countries except Greece and Norway, and by sex and/or age in nine countries. Analyses by batch numbers are performed in Austria, Germany and Ireland. Vaccine and immunization registers were kept only in Belgium and Norway.

Vaccine-related injuries

Vaccine-related injuries have received very little attention in the countries surveyed. Only incidental information could be obtained on the compensation paid, and no analyses of the cases were available. The compensation systems range from no-fault compensations to compensation through legal action and court cases. Statistics for vaccine-related injuries are lacking or limited in most countries. During 1989–99 concerns about vaccine safety led to very few regulatory actions in Europe. Batch withdrawals were ordered in five countries (AT, BE, DE, GR and PT) because of quality concerns. Other regulatory actions included changes in the product-specific texts of the "Summary of product characteristics".

Discussion

This study is the first to provide a comprehensive picture of the organization of vaccinovigilance in western Europe. Several major problems were identified: lack of full-time staff and funding, lack of definitions, lack of denominators and, as a consequence, lack of proper analyses, and inappropriate or non-existent feedback.

The importance of immunizations in the global battle against infectious diseases is constantly growing (*27*). It is vital to maintain the positive image of immunization by producing reliable information on adverse effects of vaccines at a national level and distributing it transparently and effectively.

Improving vaccinovigilance in Europe

The problem of resources for vaccinovigilance should be solved urgently as both staff and funding are insufficient in most countries. Appropriate management and evaluation of reports of AEFI needs specialized personnel with an in-depth knowledge of vaccinology and often of paediatrics (*11*). An increase in the number of staff may be unjustified if based only on the number of incoming reports, but should also be assessed against the response required to deal with evolving public health concerns, vaccine scares and contacts from the media (*28*). The development of vaccinovigilance activities and policies also needs resources (*28*).

Vaccinovigilance systems should be steered by specialized national expert groups. The vaccinovigilance activities should be coordinated between the drug regulatory agencies, the authority responsible for the immunization programmes and institutes of public health. There should be clearly defined responsibilities and transparent procedures in place.

The ADR reporting forms used in several countries are poorly applicable to reporting AEFI, because much of the information essential for studying reactions to vaccines is not required for studying reactions to other drugs. To obtain comparable data, minimum requirements for reporting AEFI should be established, including case description, age, patient history, time interval (i.e. time between vaccination and occurrence of the event), trade name, lot number, number of doses given, date, vaccination site, concomitant vaccines, other drugs in use, re-challenge data and outcome information. Case definitions and standard operating procedures for case investigation and follow-up are needed (*29*, *30*).

The usefulness of reporting of adverse reactions depends strongly on the timeliness and quality of the feedback sent to the rapporteurs. If physicians never receive a reply to their queries or concerns, their interest in further reporting will soon wane. An acknowledgement of receipt is insufficient: practitioners often need advice on how the immunization regimen should continue. If sufficient expertise is not available in the drug regulatory authority, alternative arrangements should be made to make expert consultation possible in academic or public health institutes.

The accumulating data on AEFI should be analysed regularly, using appropriate methods, and these data should be related to a relevant denominator. Possible denominators include potential or actual vaccinees, all vaccine doses distributed or administered, doses of a vaccine type and doses of a particular product. Linking data on AEFI with immunization registers is emerging as a major advance in vaccine safety research (*6*, *9*). Ad hoc analyses should be performed as required. The results should be disseminated widely to both professionals and the general public.

The management of reports of AEFI should be based on standard operating procedures, and strategic plans should be drafted for the development of national vaccinovigilance activities. Regional systems within countries may be functional, but if reporting to the central level is voluntary, some of the relevant data may never reach the national statistics.

Although probably an uncommon problem, vaccine-related injuries should receive more attention. Readily available statistics would provide welcome reassurance to both professionals and the general public on the safety of injections. The consideration of this aspect should begin by defining vaccine-related injuries, and reviewing the compensation systems.

The purpose of the passive surveillance systems is mainly to give alarm signals (*15*). The system should be able to recognize any potential increase in the incidence of previously known adverse reactions, and also be able to detect novel, rare adverse events that may be causally related to immunization. This has been shown to be feasible (*7*, *19*, *20*, *31*), but cannot be accomplished without regular, systematic review of the data on AEFI.

Once a potential problem has been identified, further investigation and epidemiological studies are needed. Computerized linkage of immunization and medical outcome records is one of the methods that should be considered for such further evaluations (*15*, *32*). Efficient passive reporting systems complemented by ad hoc active surveys should be the basis for improved post-licensing vaccine safety surveillance in Europe in the future.

International collaboration

The Uppsala Monitoring Centre is the WHO Collaborating Centre for International Drug Monitoring. Currently, more than 70 countries participate in the programme and there are almost 3 million spontaneous ADR case reports in the database (*22*). Unfortunately, these data are not very useful for solving vaccine-related questions because the WHO Adverse Reaction Terminology (WHO-ART) coding system is not optimal for typical AEFI. Sharing of data on reactions is nevertheless very important, and the communication should be channelled through interdisciplinary networks that include vaccinologists and experts on pharmacovigilance and epidemiology. Immunization records are useful at both the individual and population levels to facilitate data linkage studies (*9*, *14*, *32*).

WHO has launched a global initiative to enable national immunization programmes to prevent, detect early, and respond quickly to adverse events so as to minimize their negative impact on health and on national immunization programmes (*27*). The Immunization Safety Priority Project focuses on vaccine quality, injection safety, and surveillance and management of adverse events following immunization. The project has many elements that European countries could utilize when drafting their strategic plans for vaccine safety activities. Such plans are currently non-existent.

Another important initiative is the global activity for developing guidelines and standardized case definitions for AEFI within the Brighton Collaboration, and the European Research Programme for Improved Vaccine Safety Surveillance (EUSAFEVAC project) (*29*, *30*). Based on voluntary contributions, it serves as a model for international collaboration in pivotal public health issues.

The study showed that a standardized international database is a major resource for comparative research on health systems, and a practical tool for identifying gaps and weaknesses in national administrative systems. It also indicated that most of the problems related to reporting and analysis of AEFI that were identified could be solved through standardization and intensified international collaboration. Once the database has been set up, data from new countries can be added easily. To maintain its usefulness, it should be updated regularly, as with the database on surveillance systems for communicable diseases.

Unfortunately, the European Commission has not yet launched the EUVAX database for public access. The current plan is to integrate the database into the European Public Health Information Network (EUPHIN) platform, which is already being widely utilized by European professionals working in public health, and which should be fully functional within the next few years. Several databases are already accessible at http://hsscd.euphin.org. The EUSAFEVAC Project is now focusing on a number of problems identified in the EUVAX Project. ■

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Résumé

Vaccinovigilance en Europe - nécessité d'agir en temps utile, de façon standardisée et avec des ressources suffisantes

Objectif Identifier les lacunes des systèmes de notification des manifestations postvaccinales indésirables en Europe au moyen d'une base de données interactive construite selon une approche standardisée.

Méthodes Une enquête comparative a été réalisée en 1999-2000 au moyen de questionnaires structurés adressés aux services responsables des programmes nationaux de vaccination et de pharmacovigilance dans tous les Etats Membres de l'Union européenne ainsi qu'en Norvège et en Suisse.

Résultats La notification des réactions postvaccinales indésirables est prévue par la réglementation de 13 des 17 pays considérés. Quatre pays disposent d'un groupe d'experts spécialement chargé de la sécurité vaccinale. Sur l'ensemble des 17 pays, seuls six professionnels travaillent à plein temps sur la sécurité vaccinale ; dans quatre pays, il s'agit de médecins. Quatorze pays possèdent un système de notification centralisé, et dans 14 pays également l'autorité responsable est l'agence de réglementation pharmaceutique. Les manifestations postvaccinales indésirables sont notifiées selon la procédure de pharmacovigilance dans tous les pays sauf quatre. Le formulaire de notification n'étant en général pas conçu pour les vaccins, des détails importants risquent d'être omis. Il n'est pas prévu de définition clinique des réactions postvaccinales. Dans 12 pays il existe des définitions officielles appropriées pour les incidents ou réactions, mais la liste des incidents soumis à notification varie considérablement d'un pays à l'autre. L'évaluation des réactions postvaccinales indésirables est rendue difficile par l'absence de dénominateur exact. Un retour d'information est prévu à l'intention des services notificateurs dans 13 pays, mais il est de qualité très variable.

Conclusion La base de données a facilité la comparaison entre les systèmes de vaccinovigilance des pays participants. La plupart des problèmes liés à la notification et à l'analyse des manifestations postvaccinales indésirables pourraient être résolus par une standardisation des définitions de cas et une intensification de la collaboration internationale. Au niveau national, la responsabilité d'un système de vaccinovigilance fonctionnel devrait incomber à la fois à l'agence de réglementation pharmaceutique et au programme national de vaccination. Il est urgent de renforcer les moyens consacrés au développement et à la gestion des systèmes de sécurité vaccinale.

Resumen

Vigilancia de las vacunas en Europa - necesidad de acción rápida, normalización y recursos

Objetivo Identificar las lagunas de los sistemas empleados para informar sobre los eventos adversos postinmunización (EAPI) en Europa por medio de una base de datos interactiva desarrollada con arreglo a un método normalizado.

Métodos En 1999–2000 se realizó un estudio comparativo basado en cuestionarios estructurados dirigidos a las autoridades públicas responsables de los programas nacionales de inmunización y la farmacovigilancia en todos los Estados Miembros de la Unión Europea (UE) y en Noruega y Suiza.

Resultados La notificación de las reacciones adversas a las vacunas (RAV) es objeto de regulación en 13 de los 17 países estudiados. Cuatro países disponen de un grupo de expertos encargados de garantizar la seguridad de las vacunas. Sólo seis profesionales trabajan con dedicación exclusiva en la seguridad vacunal en 17 países; en cuatro de esos países el responsable tiene algún tipo de calificación médica. Catorce países han centralizado los sistemas de notificación; en 14 países la autoridad responsable es el organismo de reglamentación farmacéutica . En todos los países salvo en cuatro, los AEPI se notifican siguiendo el mismo procedimiento usado para las reacciones adversas a los medicamentos (RAM). Por lo general el formulario de notificación no está diseñado pensando en las vacunas, lo que implica la omisión de detalles importantes; por ejemplo, no se facilitan definiciones clínicas de las reacciones a las vacunas. Doce países suministran definiciones oficiales apropiadas de los eventos o reacciones, pero la lista de eventos notificables varía considerablemente de un país a otro. La evaluación de las reacciones adversas a las vacunas (RAV) se ve obstaculizada por la falta de datos exactos sobre el denominador. En 13 países los encargados de informar recibieron sugerencias, cuya calidad fue no obstante muy variable.

Conclusión La base de datos ayudó a comparar de manera sencilla los sistemas de vigilancia de las vacunas en los países participantes. La mayoría de los problemas identificados en relación con la notificación y el análisis de los EAPI podrían resolverse mediante actividades de normalización y de intensificación de la colaboración internacional. A nivel nacional, el buen funcionamiento de los sistemas de vigilancia vacunal debe ser una responsabilidad compartida del organismo de reglamentación farmacéutica y el programa nacional de inmunización. Es preciso mejorar urgentemente los recursos necesarios para el desarrollo y gestión de sistemas de vigilancia de la seguridad de las vacunas.

ملخص

التيقظ للقاحات في أوروبا: ضمان القيام به في الوقت المناسب، ووضع معايير لإجراءاته وتوفير موارده

الغرض: التعرُّف على الفجوات الموجودة في نُظُم التبليغ عن الأحداث الضائرة بعد التمنيع في أوروبا عن طريق وضع قاعدة معطيات تفاعلية باستخدام أسلوب يستند على معايير.

الطريقة: تم إجراء مسح مقارن في الفترة من ١٩٩٩ إلى ٢٠٠٠ استخدمت فيها استبيانات أعدت مسبقاً ووجهت للسلطات الحكومية المسؤولة عن برامج التمنيع الوطنية وعن ترصد سلامة الأدوية في جميع الدول الأعضاء في الاتحاد الأوروبي إضافةً إلى النرويج وسويسرا.

الموجودات: يخضع التبليغ عن التفاعلات الضائرة للقاحات لقواعد تنظيمية في ١٣ بلداً من البلدان السبعة عشر التي شملتها الدراسة. أما البلدان الأربعة الباقية فتوجد بها مجموعة خبراء متخصصة مسؤولة عن سلامة اللقاحات. ويعمل ستة مهنيين فقط طوال الوقت لمراقبة سلامة الأدوية في البلدان السبعة عشر؛ وفي أربعة فقط من هذه البلدان يكون الشخص المسؤول عن مراقبة سلامة الأدوية حاصلاً على مؤهل طبي. وقد تبين أن أربعة عشر بلداً بها نظام تبليغ مركزي، وأن السلطة المسؤولة في ١٤ بلداً هي الهيئة المعنية بتنظيم الأدوية. ويتم التبليغ عن الأحداث الضائرة التي تقع بعد التمنيع باتباع الإجراءات المستخدمة لرصد التفاعلات الضائرة للأدوية في جميع البلدان، باستثناء أربعة بلدان فقط. وفي بعض الأحيان لا يكون نموذج التبليغ مصمما للتبليغ عن اللقاحات، ومن ثم قد لا تُطلب بعض التفاصيل المهمة. ولا تتاح تعريفات سريرية لتفاعلات اللقاحات. وهناك ١٢ بلداً لديها تعريفات رسمية مناسبة للأحداث أو التفاعلات، غير أن قائمة الأحداث التي يجب التبليغ عنها تختلف اختلافاً كبيراً من بلد لآخر. ويؤدي نقص المعطيات الأساسية الدقيقة إلى إعاقة تقييم التفاعلات الضائرة للقاح. وقد تم تقديم معلومات ارتجاعية لمقرري اللجان في ١٣ بلداً، ولكن جودتها كانت متفاوتة تفاوتاً كبيراً.

الحصيلة: أدت قاعدة المعطيات إلى تيسير إجراء مقارنة مبسطة بين نُظُم التيقظ للقاحات في البلدان المشاركة في الدراسة. ومن الممكن حل معظم المشكلات التي تم التعرف عليها والمتعلقة بالتبليغ عن الأحداث الضائرة بعد التمنيع وتحليلها، عن طريق وضع المعايير والتعاون الدولي المكثف. وعلى أي مستوى وطني، ينبغي أن تتقاسم السلطة المعنية بتنظيم الأدوية والبرنامج الوطني للتمنيع المسؤولية عن نظم التيقظ الفعالة للقاحات. وينبغي أيضاً الإسراع بتنمية الموارد اللازمة لتطوير وإدارة نُظُم سلامة اللقاحات.

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