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Improving Global Monitoring of Vaccine Safety

A Survey of National Centres Participating in the WHO Programme for International Drug Monitoring

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Abstract

Background: The WHO Programme for International Drug Monitoring (PIDM) was established in 1968 following the thalidomide disaster. The PIDM has had considerable success in analyzing drug-related adverse event reports, but more limited progress has been made in analyzing vaccine-related reports. In June 2005, the Global Advisory Committee on Vaccine Safety, acknowledging these limitations, called for a global consultation to address the need for improved monitoring and analysis of vaccine-related adverse event reports on an international level.

Objective: In preparation for this consultation and as part of a larger study designed to evaluate the PIDM, a survey of the National Pharmacovigilance Centres of all 76 countries participating in the PIDM at the time the survey was conducted.

Results: Thirty-six countries (47%) responded. Of the 36 responding countries, 16 (44%) reported having a separate surveillance system for adverse events following immunizations (AEFIs) and 30 (83%) reported forwarding AEFI reports to the PIDM. Seven of the 36 countries (19%) indicated that one or more population subgroups are systematically excluded from their country's AEFI surveillance system. Five of the seven countries exclude reports concerning recipients of travellers' vaccines; three exclude recipients of vaccines administered by private physicians outside the national immunization programme and supply scheme; and five exclude reports from the military sector. Only half of the respondents knew of the Brighton Collaboration, a major international initiative aimed at the standardization of AEFI definitions.

Conclusion: The survey identified critical elements that should be addressed quickly to improve global vaccine safety monitoring. Communication between national adverse drug reaction and AEFI surveillance authorities, ability to pay for advancing technology in developing countries, and proper use of services and terminologies are issues of concern.

Background

The WHO Programme for International Drug Monitoring (PIDM) is an international adverse event monitoring system developed following the thalidomide disaster of 1961.[1] An adverse drug reaction (ADR) is usually defined as "an undesirable response associated with use of a drug that either compromises therapeutic efficacy, enhances toxicity, or both".[2] In general, the laws governing ADRs do not cover medication errors, as these are usually covered by other programmes, such as medication error reporting systems in hospitals or reports to professional licensing bodies. Pharmaceutical companies will not report medication errors unless there is a legal requirement. Administration of the PIDM is the joint responsibility of the WHO Collaborating Centre for International Drug Monitoring, more commonly referred to as the Uppsala Monitoring Centre (UMC), and the WHO Headquarters (WHO/HQ).[3]

Countries participating in the PIDM submit ADR reports, including adverse events following immunization (AEFI) reports, to the UMC through their National Pharmacovigilance Centre (NPC). Once received by the UMC, reports are stored in the WHO Adverse Reaction Database. Participation in the PIDM has increased since its inception in 1968. Canada was one of the 10 founding members. As of September 2007, the PIDM had grown to include 83 countries with full membership (76 countries at the time of the survey) and 20 countries with associate member status out of 193 WHO Member States. The WHO database now contains over 3.7 million case reports,[4] of which about 8% are vaccine related.

The UMC uses the WHO Drug Dictionary to identify drugs and vaccines.[5] The Anatomical Therapeutic Chemical (ATC) classification system is used to divide drugs and vaccines into groups "according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties".[6]

There are several terminologies for describing adverse events. The WHO Adverse Reaction Terminology (WHO-ART), the Medical Dictionary for Regulatory Affairs (MedDRA) and the Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART) are used by countries of the PIDM. The UMC is able to link these terminologies so that reports coded with different terminologies are comparable.

The Brighton Collaboration is an international voluntary collaboration of professionals and organizations aiming to develop standardized, widely disseminated and globally accepted AEFI definitions and AEFI monitoring guidelines for data collection, analysis and presentation.[7] The CIOMS/WHO Working Group on Vaccine Pharmacovigilance, a recent collaboration of the CIOMS and the WHO, aims to (i) propose standardized definitions relevant for monitoring the safety of vaccines (e.g. 'AEFI', 'vaccine failure'); (ii) contribute to the efforts of the Brighton Collaboration by assisting in the development, review, evaluation and approval of AEFI definitions; and (iii) collaborate with the CIOMS Working Group on Standardized MedDRA Queries to ensure that proposed queries will be applicable to vaccines.[8] The CIOMS/WHO Working Group on Vaccine Pharmacovigilance and the Brighton Collaboration are expected to lead to significant progress in the standardization of AEFI definitions and vaccine safety terminology.

Participating countries have access to various internet services provided by the UMC, including VigiFlow (an online adverse event report management system, previously referred to as Vigibase Online at the time of the survey), Vigisearch (an online search facility for searching the database) and Vigimed (an e-mail conferencing facility exclusively for PIDM countries).[1,9] These services are intended to improve adverse event reporting, both within a country and to the UMC, allow NPCs to search the WHO database, and facilitate discussion among NPCs. Signals identified by the PIDM are included in the UMC's publication *SIGNAL*. This is a restricted access document made available to NPCs of countries participating in the PIDM and, when appropriate, to product manufacturers.

Except for a few biological products, most drugs are chemical products. Vaccines are biological drug products. Despite the many differences between

vaccines and drugs, vaccines are commonly thought of as being similar to drugs. While some vaccines may be used in the treatment of disease (e.g. Baçille Calmette-Guérin [BCG] vaccine in the treatment of bladder cancer) and are therefore somewhat akin to drugs, most vaccines are intended to prevent and control disease. Some of the special characteristics that differentiate vaccines used for disease prevention from drugs are:

- vaccines are usually administered to large populations of healthy individuals and nearly entire birth cohorts, in view of the universal nature of most vaccination programmes;
- most vaccines are administered to infants and children;
- vaccine administration is often promoted or even made mandatory by governments;
- a main issue in the safety and efficacy of vaccines is maintaining an adequate 'cold chain' (i.e. a system for keeping vaccines at the appropriate temperature, from the start of manufacture until the time of use, in order to maintain vaccine quality and potency);
- potential variation between different brands and lots of a vaccine necessitates lot-by-lot surveillance of vaccines at the postmarketing stage;
- the public is, in general, less willing to accept the risks associated with vaccines.

A country wishing to join the PIDM must have an NPC responsible for national ADR surveillance, national AEFI surveillance, or both. The NPC must adhere to the criteria set out in the UMC publication 'Joining the WHO Programme for International Drug Monitoring'.[3] Generally, the UMC communicates with only one national surveillance authority in each country. If two surveillance authorities exist, for example where ADR and AEFI surveillance are conducted by separate authorities, the UMC usually communicates with the authority designated as the NPC. It is the responsibility of the NPC to communicate with any other national surveillance authorities in the country. All national surveillance authorities may submit adverse event reports to the UMC.

Pharmacovigilance centres, whether for drugs or vaccines, differ greatly in their relationship with governments. For example, the centre can be within a government department, a medical college (e.g. a college of pharmacists), a university, a non-governmental organization, an institute (e.g. an institute of pharmacy) or an agency. They can cover a whole country, a province or state, a region or a smaller geographical unit. The responsibility for AEFI surveillance may rest with a pharmacovigilance centre, the regulatory authority or the national immunization programme. In some countries the responsibility is shared. For example, in the US responsibility is shared between the National Immunization Program (part of the Centers for Disease Control and Prevention) and the regulatory authority (i.e. the US FDA) with a jointly administered system.[10] In other countries AEFI surveillance is conducted by different organizations, depending on the source of vaccines (e.g. privately administered vaccines versus vaccines administered in the public sector as part of a national immunization scheme).

The PIDM was developed initially for chemical rather than biological products. Very little has changed since its inception to take account of unique characteristics of vaccines. In particular, the same drug classification system is used to categorize drugs and vaccines, adverse reaction terminologies have not been expanded to include all symptoms of AEFIs, and ADR and AEFI reports are analysed in the same way. Considering the differences in characteristics between drugs and vaccines, the ability of the PIDM to meet the needs of vaccine safety is of great international public health importance.[11,12]

A survey of authorities responsible for AEFI surveillance in all countries participating in the PIDM was conducted as part of a larger evaluation of the PIDM on how it serves the needs of vaccine safety. Two other components of the evaluation included an analysis of the WHO Adverse Reaction Database and a systematic review to identify and compare Bayesian methods used in drug and vaccine signalling. These parts of the evaluation will be reported in separate publications.[13,14] The objective of this survey was to gather evidence on (i) the process and the product of national AEFI surveillance; (ii) the level of communication between na-

tional ADR and AEFI surveillance authorities; and (iii) the acceptability and usefulness of the PIDM, the Brighton Collaboration's AEFI definitions and the various Internet-based services provided by the UMC.

Methods

At the time of the survey in July 2005, 76 countries were participating as full members in the PIDM. These included five countries from the WHO African Region, 13 countries from the WHO Americas Region, six countries from the WHO Eastern Mediterranean Region, 38 countries from the WHO European Region, four countries from the WHO South-east Asian Region and 10 countries from the WHO Western Pacific Region.

A questionnaire was developed in collaboration with interested parties, including the WHO, the UMC and the Public Health Agency of Canada. The questionnaire was mailed to the UMC's contact person at the NPC in each of the 76 countries during the fourth week of July 2005. Contact persons were asked to forward the questionnaire and its accompanying cover letter to the authority most responsible for AEFI surveillance within their country, if this was not the NPC. A reminder was sent out during the second week of October 2005 following a presentation of preliminary survey results at the 28th Annual Meeting of Representatives of the National Centres participating in the WHO Programme for International Drug Monitoring, Geneva, Switzerland, September 2005.

The questionnaire included 25 questions addressing:

- if countries are forwarding AEFI reports to the UMC;
- how AEFI reports are forwarded to the UMC;
- what types of AEFI reports are forwarded to the UMC;
- which terminologies are used to code AEFI reports;
- the usefulness of the communication services provided by the UMC;
- overall impressions of the PIDM and WHO database with respect to AEFI surveillance and vaccine safety.

In addition to questions about reporting practices, respondents were asked a question about the Brighton Collaboration designed to assess global awareness and acceptability of the Brighton Collaboration's AEFI definitions. Descriptive statistics including counts and percentages were calculated. Frequency distributions were prepared where appropriate.

Ethical approval was obtained from the Ottawa Hospital Research Ethics Board.

Results

A summary of responses to the questions is presented in table I. Responses to open questions and additional results are presented in the text below. For open-ended questions, where more than two respondents gave a response, the number giving the response is presented in the text.

Response Rate

Thirty-six of 76 (47%) countries responded to the survey, a response rate consistent with previous surveys of NPCs (Sten Olsson, UMC, personal communication). Responses were received from 20 (53%) of the 38 countries in the WHO European Region, three (23%) of the 13 countries in the WHO Americas Region and 50–60% of countries in each of the remaining four WHO Regions (figure 1).

Forwarding AEFI Reports to the UMC

Four of the six countries that do not forward AEFI reports to the UMC have separate surveillance systems for ADRs and AEFIs (one country did not indicate whether its ADR and AEFI surveillance systems are separate). Two survey respondents made it clear that there was a lack of communication and collaboration between their ADR and AEFI surveillance authorities. One respondent was from a country's national AEFI surveillance authority and indicated that the AEFI surveillance authority did not know about the UMC. The other respondent was

Table I. Survey responses to closed questions

Question	n[a]	Yes (%)	No (%)	Missing
Practices for forwarding AEFI reports				
Does your country have separate surveillance systems for reporting ADRs and AEFIs?	34	15 (44)	19 (56)	2
Does your country forward AEFI reports to the UMC?	36	30 (83)	6 (17)	0
Are there financial or other considerations that hinder or limit reporting of AEFIs to the UMC?	35	7 (20)	28 (80)	1
Are the UMC's instructions for AEFI reporting clear?	21	20 (95)	1 (5)	9
Are the UMC's instructions for AEFI adequate?	23	21 (91)	2 (9)	7
Does reporting to the UMC occur at regular intervals?	27	20 (74)	7 (26)	3
Is the workload associated with AEFI reporting to the UMC manageable?	28	26 (93)	2 (7)	2
Types of AEFI reports forwarded to the UMC				
Are vaccine programme errors (i.e. 'medication errors') reported to the UMC?	30	14 (47)	16 (53)	0
Are vaccine failures reported to the UMC?	29	18 (62)	11 (38)	1
Are individual AEFI reports ever screened, ruled-out as cases and not submitted to the UMC?	28	9 (32)	19 (68)	2
Does any assessment and classification (e.g. definite, probable, possible) of causality for the relationship between a reported AEFI and vaccine administration take place at the national level before AEFI reports are forwarded to the UMC?	30	25 (83)	5 (17)	0
Terminologies used to code AEFI reports				
Are you planning to switch to MedDRA?	25	11[b] (44)	14 (56)	4
Are there specific terms that cause problems for classifying AEFIs?	30	7 (23)	23 (77)	6
Are there terms missing from the coding terminology you are using?	28	5 (18)	23 (82)	8
Have you heard of the Brighton Collaboration?	35	18 (51)	17 (49)	1
Will you be applying the definitions proposed by the Brighton Collaboration to your national AEFI surveillance system?	20[c]	15 (75)	5 (25)	1
Utility of communication services provided by the UMC				
Have you heard of Vigibase Online?	36	30 (83)	6 (17)	0
Are you planning to switch to Vigibase Online?	27	11[d] (41)	16 (59)	3
Have you used Vigimed for your vaccine-related queries?	36	16 (44)	20 (56)	0
Are you satisfied with the number of responses you have received to your queries?	16	15 (94)	1 (6)	0
Have you used Vigisearch to find vaccine-related data in the WHO database?	36	19 (53)	17 (47)	0

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Table I. Contd

Question	n[a]	Yes (%)	No (%)	Missing
Are you satisfied with the results of your search?	18	16 (89)	2 (11)	1
Do you receive the UMC's *SIGNAL* publication?	36	29 (81)	7 (19)	0
Is the *SIGNAL* publication useful?	30[e]	30 (100)	0 (0)	1

a The total (n) is the sum of the 'yes' and 'no' responses. Totals differ because of skipping patterns: the number of respondents 'eligible' to respond to each question varied depending on each respondent's response to earlier questions.

b Seven countries were already using MedDRA at the time of survey. These countries were considered a 'yes' to the question "Are you planning to switch to MedDRA?"

c Two respondents who indicated that they had not heard of the Brighton Collaboration answered this question in addition to those 18 respondents who were aware of the Brighton Collaboration definitions. Respondents were referred to the Brighton Collaboration's website[7] in the questionnaire. Both of these respondents indicated that they would be applying the Brighton Collaboration's AEFI definitions.

d Five countries were already using Vigibase Online at the time of the survey. These countries were considered a 'yes' to the question "Are you planning to switch to Vigibase Online?"

e Two respondents indicated that they did not regularly receive the *SIGNAL* publication but that they have received some issues. Based on the issues they had received, both respondents indicated that the publication was useful.

ADR = adverse drug reaction; **AEFI** = adverse events following immunization; **MedDRA** = Medical Dictionary for Regulatory Affairs; **UMC** = Uppsala Monitoring Centre.

from a country's national ADR surveillance authority and indicated that the country had no AEFI reports to forward to the UMC. This respondent further explained that the drug authority had been in contact with the manager of the immunization programme in the country and had been told that there were no reports requiring the attention of the drugs authority.

Countries not forwarding AEFI reports to the UMC cited the following reasons: (i) do not know about the UMC; (ii) do not have any AEFI reports to forward; (iii) not required to report AEFIs; (iv) no responsible authority for reporting AEFIs; and (v) AEFI data not compatible with the UMC's reporting format.

Factors hindering or limiting AEFI reporting to the UMC include: (i) insufficient or absent funding; (ii) internet and telecommunications too expensive; (iii) shortage of staff and competing demands on staff; (iv) time required to format reports; and (v) reports not forwarded by the vaccine authority to the NPC.

Respondents suggested that specific AEFI reporting instructions should be created and should include specific guidelines on how to handle programmatic errors, coincidental events, injection reactions and vaccine batch problems.

Methods of Forwarding Reports to the UMC

Factors impeding regular reporting of AEFIs to the UMC include (i) a shortage of staff; (ii) competing demands; (iii) an absence of reports to send; (iv) just starting to report; (v) currently setting up a new reporting schedule following a database change; and (vi) insufficient financial resources to purchase VigiFlow.

Two respondents who felt that the workload associated with AEFI reporting to the UMC is unmanageable cited as their primary concerns a lack of time and staff to address AEFIs. One of these countries indicated that their AEFI surveillance is separate from their ADR surveillance (the other did not indicate if it was separate or not). Both respondents indicated that AEFI reporting within their country is not mandatory and that reporting to the UMC does

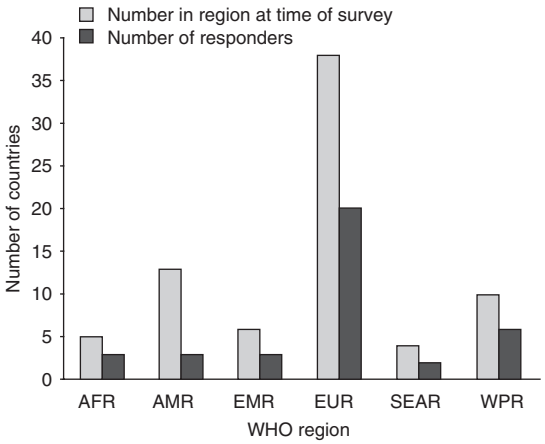

Fig. 1. Number of Programme for International Drug Monitoring (PIDM) countries responding to the survey by WHO Region: African Region (AFR), Americas Region (AMR), Eastern Mediterranean Region (EMR), European Region (EUR), South-East Asian Region (SEAR), Western Pacific Region (WPR).

not occur regularly. Both respondents indicated, however, that they do forward AEFI reports to the UMC, albeit in an irregular manner.

Respondents who had indicated that the workload is manageable also noted that there is a shortage of staff, reporting is time consuming, reporting is manageable so long as it is in the same format as ADRs and reporting AEFIs is no less manageable than for ADRs.

Types of AEFI Reports Forwarded to the UMC

Healthcare professionals are the primary reporters of AEFIs (figure 2). All 36 countries accept AEFI reports from physicians. Most countries accept reports from at least one other source as well. Sixteen of 36 countries (44%) indicated that they accept consumer reports.

Seven of 36 countries (19%) indicated that one or more population subgroups are systematically excluded from their country's AEFI surveillance system. Five of the seven countries exclude reports concerning recipients of travellers' vaccines, three exclude recipients of vaccines administered by private physicians outside the national immunization programme and supply scheme and five exclude reports from the military sector. One of the seven countries did not indicate which groups are excluded.

Among the 30 countries that forward AEFI reports to the UMC, 26 (87%) submit all AEFI reports. One country submits only serious and unexpected reports. One country indicated that it does not submit all AEFI reports, but did not specify which reports it does submit. Two countries did not indicate what type of reports they submit.

Respondents indicated that some AEFI reports are not submitted to the UMC because (i) they are considered 'non-cases', are unlikely associations or are not deemed 'certain', 'probable' or 'possible' following causality assessment; (ii) they are duplicate reports; (iii) they are not well investigated or less than the minimum amount of information on the case is available; or (iv) they were not forwarded by the immunization programme.

Terminologies Used to Code AEFI Reports

Twenty-seven of 36 countries (75%) are using WHO-ART to code adverse events in AEFI reports; seven countries (19%) are using MedDRA; and one country is using COSTART. One other country indicated that it is using a method other than WHO-ART

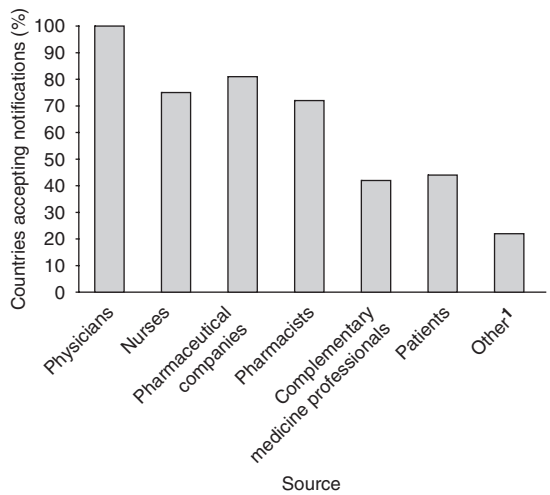

Fig. 2. Sources of adverse events following immunization (AEFI) notification within countries. **1** Questionnaire respondents indicated that 'Other' may include state or territory health departments, local government clinics, anti-vaccination lobby groups, dentists, coroners, regional hygiene inspectors, epidemiologists or 'anyone'.

or MedDRA but did not specify which terminology it is using.

Seventeen respondents indicated that they had not heard of the Brighton Collaboration. These respondents were referred to the Brighton Collaboration website and two of them indicated that they would be applying the Brighton Collaboration's definitions. Five countries indicated that they would not be applying the Brighton Collaboration's AEFI definitions for the following reasons: (i) need to consider further the implications and feasibility of adopting the definitions; (ii) do not want to treat the monitoring and reporting of ADRs and AEFIs separately; and (iii) have not yet decided whether to apply the definitions or not.

Utility of Communication Services Provided by the UMC

Reasons why countries are not satisfied or only partially satisfied with Vigimed include (i) a lack of responses to their queries; (ii) a lack of detail in responses; and (iii) misuse of Vigimed when Vigisearch should be used instead. Respondents suggested: (i) creating an archiving system by topic and consolidating associated responses (n = 4); (ii) updating email addresses; (iii) restricting enquiries to questions that cannot be answered through Vigisearch; and (iv) using Vigimed to exchange information on signals detected.

Respondents who indicated that they are dissatisfied with Vigisearch cited the following reasons: (i) it can be slow and difficult to use; (ii) it is difficult to search by ATC classification; and (iii) the frequency of connection breaks or the system being down for maintenance. Suggested improvements included (i) organizing a training programme on how to use Vigisearch; (ii) faster search capability; (iii) indicating how many reports were received for a particular substance; (iv) easier access to the total number of reports by AEFI; (v) more search parameters (e.g. seriousness, reporter qualification); (vi) easier searching by ATC classification; (vii) ability to identify the number of programmatic errors; (viii) permitting analyses for medication-error events; (ix) batch-related searching; (x) access to more than 30 case reports; and (xi) printable tables.

Overall Impressions of the PIDM and WHO Database

Narrative comments were invited on respondents' overall impressions of the PIDM and WHO database with respect to AEFI surveillance and vaccine safety. Twenty-six of 36 respondents provided comments in response to this question. Respondents' overall impressions were generally positive. Most respondents indicated that the programme and database were 'sufficient', 'useful' or 'excellent'. Some respondents made criticisms of the database, such as the AEFI data are of poor quality and the AEFI portion of the database is too small. Others indicated that they have made very little use of the database for AEFIs and therefore could not comment further about the programme or database.

Discussion

The majority of countries participating in the PIDM who responded to the survey combine ADR and AEFI surveillance under one authority. Separate surveillance systems can make communication and collaboration between ADR and AEFI surveillance authorities more difficult. If communication between authorities is hindered, AEFI reports may not be forwarded to the UMC. When a single authority is responsible for ADR and AEFI surveillance, vaccines may be grouped with drugs and specific vaccine considerations may not be addressed (e.g. AEFIs may not be adequately described because drug-specific terminology is used). A first important step is to recognise the differences between drugs and vaccines. Where ADR and AEFI surveillance are managed by different authorities, communication between the groups is essential, yet as highlighted in the results section, at times this communication is missing, which then hinders the exchange of information at the global level.

There are a number of ways to enhance the relationship between drug and vaccine authorities. One way would be to establish formal communication mechanisms, as part of a legislative process.

Another possibility is to create a new pharmacovigilance process for drugs, vaccines and herbs as part of a single government agency, an agency for patient safety or a non-governmental agency. It may not be possible to improve the communication between the ADR and AEFI vigilance centres, and it may be necessary for UMC to accept two NPCs.

Several survey respondents indicated that some AEFI reports may be screened, ruled-out and not submitted to the UMC. While it would not be appropriate to send duplicate reports to the UMC, it is inappropriate to withhold reports because they have not been investigated beyond the UMC's minimal data requirements. Reports of AEFIs received by the national surveillance system should be submitted to the UMC regardless of any causality assessment prior to submission. As there is no standardized method for assessing causality on individual reports and because each reporting country can perform its own causality assessments, it is likely that the standard categories for the likelihood of causal associations (such as 'probable' or 'possible') are applied differently by different countries. Rather, surveillance authorities should investigate cases quickly and forward complete reports to the UMC in a timely manner. Further, reporting bias will be introduced if AEFI reports are not all submitted to the UMC. Complete and timely AEFI reporting is needed in order to detect vaccine signals of possible international concern quickly. The signalling process will be compromised if reports are not forwarded or are delayed.

Theoretically, VigiFlow should facilitate more timely and regular reporting of adverse events to the UMC. For the system to be effective, countries must have the means to purchase the system and the computer technology to operate it. Further, national surveillance authorities must make their healthcare professionals and other reporters aware of the system and how to use it. Also, national surveillance programmes must employ an adequate number of trained staff to process incoming reports quickly. In spite of the presumed benefits of using VigiFlow and other internet applications, the operating costs may prevent some countries from participating fully in the PIDM, even when the initial costs can be overcome. The impact of VigiFlow on the timeliness of reporting and, in turn, the efficiency of signal detection has not been evaluated formally.

WHO-ART and MedDRA, the two most common adverse event terminologies used by PIDM-participating countries to code AEFI reports, were not designed with the specific needs of AEFI surveillance in mind. Consequently, describing AEFIs adequately can be difficult. Respondents to our survey reported that there are terms that cause problems for describing AEFIs and that there are AEFI terms missing from these terminologies (e.g. hypotonic-hyporesponsive episode, cerebellar ataxia, weakness in leg). This problem could be remedied by a review of the adverse event terminologies for the inclusion of AEFI-specific symptoms.

Half of the countries responding to our survey had heard of the Brighton Collaboration and most of these countries apply the definitions to their national AEFI surveillance system. While it is clear that the Brighton Collaboration's definitions are generally accepted, further promotion of the definitions is needed to encourage more countries to adopt them. As AEFI definitions and vaccine safety terminology are standardized and more countries use the standardized vocabularies, AEFI surveillance data will become more comparable between countries and will facilitate international surveillance.

Open questions provide the opportunity for respondents who feel strongly about an issue to voice their concerns. The thoughts and concerns raised by respondents who answered these questions may not represent the opinions of all AEFI surveillance authorities questioned. The responses are useful, however, because they provide interesting insights and potential focus areas for future research.

The results of this survey are limited by the small number of surveys returned. While the response rate to this survey was consistent with earlier surveys of NPCs, results may not be representative of all countries currently participating in the PIDM. Furthermore, in some cases, the questionnaire was completed and returned by someone other than the country's AEFI surveillance authority.

Conclusion

Generally, survey respondents have found the PIDM and WHO database to be useful. However, lack of regular reporting and incomplete reporting of AEFIs to the UMC limit the usefulness of the programme and its signalling ability for vaccines. The survey identified critical elements that should be quickly addressed to improve global vaccine safety monitoring. There is a definite need for activities to strengthen vaccine safety data, such as through the standardization of AEFI definitions and vaccine safety terminology, and communication on ongoing related initiatives such as the Brighton Collaboration should be enhanced. Communication between drug and vaccine surveillance authorities within countries is an issue of concern that should be promptly addressed within each country. Particular attention should be paid within the PIDM to address some of the vaccine specificities.

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