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Selected National Pharmacovigilance Websites

An Analysis of Contents

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Abstract

Background: Pharmacovigilance involves the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs), nationally and internationally. Effective communication, which relies increasingly on the Internet, is a crucial aspect of pharmacovigilance activities.

Aim: The aim of this study was to perform an exploratory survey of national pharmacovigilance websites and compare their contents.

Methods: Of 99 international pharmacovigilance organizations known to us (listed in the *Side Effects of Drugs Annual 30*), 45 included website addresses and 35 provided some or all of the information in English. We reviewed 10 of these 35 websites in order to identify their contents. The 10 sites that we selected contained the most extensive information on pharmacovigilance of those that we were able to access. Reviewing these sites, we identified 32 items of information that we used to assess the scope of each website systematically, using a scoring system based on the presence or absence of those items.

Results: All the websites gave clear descriptions of national pharmacovigilance requirements and the reporting systems for ADRs, and all included devices. Beyond this, there was great variability in content from site to site. Few websites allowed access to raw pharmacovigilance data, such as individual case reports.

Conclusions: Online drug safety communication from the selected national websites we examined is highly variable from site to site, although a wider study is needed to confirm this. Agreement on the key components of pharmacovigilance websites would facilitate the development of a standardized format to improve online communication.

Pharmacovigilance Websites: A Brief Background

Pharmacovigilance, defined by the WHO as the ''science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems'',[1] relies increasingly on electronic communication. International pharmacovigilance is coordinated by the WHO Programme for International

Drug Monitoring at the Uppsala Monitoring Centre (UMC) in Sweden.[2] The development of the Internet has facilitated global flow of information and improved access to databases that store huge quantities of pharmacovigilance information. At a national level, websites hosted by regulatory authorities act as a key interface between patients, professionals, and pharmacovigilance experts, and include sections containing information relevant to pharmacovigilance. However, the information content of such websites has not been systematically scrutinized, and there is no standard format. We therefore decided to carry out an exploratory qualitative comparison of the drug safety sections of ten national websites, with outcomes that may facilitate the improvement of online communication and contribute to the formation of an up-to-date standardized website template. For the sake of brevity, we shall refer to these sections as 'national pharmacovigilance websites', although we appreciate that there are many functions in pharmacovigilance that they do not serve.

Effective communication is a crucial aspect of pharmacovigilance activities. National pharmacovigilance websites typically form subsections of the websites of drug regulatory authorities (DRAs)/competent authorities. These websites serve as widely accessible tools, which provide a portal for disseminating up-to-date pharmacovigilance information, educating practitioners, patients, and pharmaceutical companies, and collating information about adverse drug reactions (ADRs) nationally.

Analysing health-care websites in general, and the information they provide, is an area that has been considered by various groups.[3,4] In pharmacovigilance, the quality of the available website information is paramount: content, clarity, and accessibility are vital in facilitating the optimal transfer of information between national and international agencies, and also between patients, professionals, and pharmacovigilance experts. However, we are aware of only three studies that have focused on the pharmacovigilance content of national websites, two of which have been published in full[5-7] and one as an abstract.[8] A 2001 WHO analysis,[5] updated in 2009,[7] aimed to improve the quality and usefulness of these websites by identifying key criteria, assessing 51 websites against those criteria and using the results to develop a prototype 'WHO model website' for DRAs. Vitry et al.[6] focused on the transparency of DRAs and reviewed seven websites to assess the 'type and availability of information' provided. In contrast, in this analysis we have assessed websites from the perspective of product safety, since this constitutes such a critical factor in public health that it warrants further detailed investigation, in isolation from other unrelated areas that must factor into synoptic assessment of DRA websites. We have scrutinized the contents of selected websites in order to determine the type and quality of the information they contain and how well the contents are communicated.

Methods

Of 99 international pharmacovigilance organizations known to us (listed in the *Side Effects of Drugs Annual 30*[9]), 45 included website addresses and 35 provided some or all of the information in English, although some did that only via a translation tool. Reviewing these sites, we selected 10 national DRA websites available in English, which contained the most extensive amount of pharmacovigilance information of those that we were able to access, for this exploratory analysis and reviewed them in order to identify their contents. The URLs of the selected websites are given in table I.

Charlotte Barker surveyed the selected websites, recording the categories of pharmacovigilance information that they contained; this resulted in 11 categories of information (table II). She then identified 32 subcategories relevant to pharmacovigilance that were found in any of the sites, excluding items that were country-specific (table III). Charlotte Barker and Jeffrey Aronson then reviewed each website on separate occasions and determined whether they contained each item, creating a tabular comparison. This facilitated identification of common features of the websites, highlighting the available information and the areas in which information was lacking.

Table I. The URLs of the ten national pharmacovigilance websites surveyed (last checked 17 January 2011)

Country	Pharmacovigilance website
Australia	http://www.tga.gov.au/safety/information-medicines.htm
Canada	http://www.hc-sc.gc.ca/index-eng.php http://www.hc-sc.gc.ca/index-fra.php
Denmark	http://www.dkma.dk/1024/visUKLSArtikel.asp?artikelID=749 http://www.laegemiddelstyrelsen.dk/1024/visLSArtikel.asp?artikelID=608
Finland	http://www.fimea.fi/frontpage http://www.fimea.fi/etusivu http://www.fimea.fi/framsida
Ireland	http://www.imb.ie/ http://www.imb.ie/IE/Maidir-linn.aspx
Netherlands	http://www.cbg-meb.nl/cbg/en/ http://www.cbg-meb.nl/cbg/nl/
New Zealand	http://www.medsafe.govt.nz/
Switzerland	http://www.swissmedic.ch/index.html?lang=en http://www.swissmedic.ch/marktueberwachung/00091/00136/00137/index.html?lang=de http://www.swissmedic.ch/marktueberwachung/00091/00136/00137/index.html?lang=fr http://www.swissmedic.ch/marktueberwachung/00091/00136/00137/index.html?lang=it
UK	http://www.mhra.gov.uk/index.htm
USA	http://www.fda.gov/

This table was used to analyse the overall patterns of information availability and website quality, and to reveal potential areas for improvement.

Results

Table IV shows a tabular comparison of the national websites. If the information was present on the website and was clear, it was marked with a tick (✓). If it was not stated clearly or was difficult to find (for example, if it was not present in the sitemap or topic headings and required extensive searching), it was marked with a bullet (•). If it was absent, it was marked with a dash (–). Charlotte Barker kept a log with the URL of each data point, which is available on request.

As can be seen from table IV, all the websites gave a clear description of the national pharmacovigilance guidelines, provided a thorough description of the ADR reporting system used (with full instructions), gave information for pharmaceutical companies and information on medical devices, and provided an electronic search facility.

More than 70% of the websites also defined an ADR, had information on safety alerts, complementary medicines, and purchasing drugs online, provided information for patients and contact details for queries, and gave links to useful external websites.

However, several of the websites lacked a clear definition of pharmacovigilance, discussion of ADRs to non-medicinal products, and generic information on medicines in pregnancy, drug interactions, and the WHO monitoring programme. No other country had an equivalent to the UK's 'Black Triangle Scheme', which provides information on specific 'high alert' products.[10] There was also a widespread paucity of information regarding causality assessment, and there was significant variability in the availability of electronic access to original pharmacovigilance data and their format. This last result is consistent with the DRA website study findings of Anton et al.[8] in 2006, which were published only in abstract form.

Most of the sites were directly accessible using the Internet search engine Google to search for '[country] report adverse drug reaction[s]' or '[country] report drug side effect[s]'. This did not give direct website links for Finland, Ireland, or the Netherlands, but they were accessible indirectly via the links obtained. Regarding linguistic accessibility, more than half the websites were

Table II. Categories of pharmacovigilance information surveyed

	Category	Relevant items (table III)
1	Pharmacovigilance definitions	1–2
2	National requirements	3
3	Adverse drug reactions (ADRs) – definitions and causative products	4–7
4	ADR reporting system	8–12
5	Data interpretation and availability	13–15
6	Safety alerts and other useful information	16–23
7	Contact details for queries	24
8	Information specifically for consumers	25–26
9	Information for pharmaceutical companies	27
10	Links to useful URLs and the Uppsala Monitoring Centre	28–29
11	Accessibility	30–32

Table III. Subcategories for pharmacovigilance website assessment

1	WHO definition of pharmacovigilance
2	Other definition of pharmacovigilance
3	Description of national pharmacovigilance requirements and responsibilities
4	Full definition of adverse drug reaction (ADR)
5	Specific statements about products that can cause ADRs – medicines
6	Specific statements about products that can cause ADRs – vaccines
7	Specific statements about products that can cause ADRs – blood products
8	Description of the national ADR reporting system
9	Printable version of the ADR report form
10	Instructions on details required on the ADR report form
11	Instructions on where/how to submit the form
12	Information on what happens to the form/information submitted
13	Guide to causality assessment
14	Access to original data or individual case reports
15	Access to drug analysis prints or data summaries
16	Safety alerts from recent ADR news (advisories, warnings, recalls)
17	Information on newly released 'high alert' products
18	Generic information on drug-drug interactions
19	Generic information on the safety of medicines in pregnancy
20	Information about complementary medicines
21	Information about purchasing drugs online
22	Information about medical devices
23	Information about stem cells
24	Details of whom to contact with queries about pharmacovigilance or ADRs
25	Information specifically for consumers about ADRs and pharmacovigilance
26	Information for consumers wanting to report suspected ADRs
27	Information for pharmaceutical companies
28	Links (URLs) to external sources of pharmacovigilance information
29	Information about the Uppsala Monitoring Centre (UMC)
30	Electronic search facility available
31	Number of languages in which the website is available
32	Access to the website using Google [search terms: "[country] report adverse drug reaction" or "[country] report drug side effect"]

available in more than one language, according to the languages commonly spoken in that country. The websites of Australia, New Zealand, the UK, and the US were only fully available in English.

The overall results are summarized in table V.

Discussion

This analysis shows that there is significant heterogeneity across different national pharmacovigilance websites, as has been shown in previous studies of DRA websites.[5-8] While it is reassuring that most websites provide high-quality information on reporting of suspected ADRs, it is a concern that clear definitions are often lacking, creating the potential for confusion over terminology. We propose that full definitions of 'pharmacovigilance' and 'adverse drug reaction' should be a minimum requirement. Other definitions could be included,[11,12] as could the distinction between suspected adverse reactions and reactions that have been verified. Mechanisms of adverse drugs reactions and their classification could also be included.

The challenges involved in obtaining electronic access to raw pharmacovigilance data remain extensive, suggesting little improvement since previous analyses.[5-8] The Canadian website provides the best access to original data, and the Dutch website gives links to the website of the Dutch Pharmacovigilance Centre, Lareb, containing the relevant information. The US FDA website provides downloadable 'flat file databases', but these still require expertise and editing to interpret, as documented by Anton et al.[8] It is disappointing that original data remain elusive, despite being potentially available electronically. In the past, some have blamed these problems on the DRAs' lack of transparency.[5,6] However, there are also logistical problems in anonymizing data, uploading the correct information to the Internet, and updating it as necessary. Some pharmacovigilance agencies may hitherto have deemed this task too labour intensive in addition to providing regular safety alerts, which are, in most cases, already in place. On the basis of inquiries into a complaint, the European Ombudsman has made a draft recommendation to the European Medicines Agency as follows: "The Agency should carry out a full analysis, under Regulation 1049/2001, of the possibilities to grant access to the reports on suspected serious adverse reactions requested by

the complainant. The Agency's analysis should cover documents held by it in any form, such as paper form or electronic form. The Agency should also consider possibilities to provide public access to the requested reports in any form, including electronic form."[13] It is hoped that this recommendation will encourage improved access to pharmacovigilance data.

It is unclear if there is yet any evidence that providing access to original data will improve pharmacovigilance outcomes. However, such data could clearly be used for research by interested third parties. An excellent example of this is the study of Medawar and Herxheimer,[14] which revealed an unusual, previously little described ADR, based on an independent analysis of yellow

Table IV. A comparison of ten national pharmacovigilance websites (countries designated by the two-letter ISO 3166-1 α-2 codes) [for summary see table V]

	Information (contained on the website or found via links within)	AU	CA	CH	DK	FI	IE	NL	NZ	UK	US
1	WHO definition of pharmacovigilance	–	•	•	–	–	✓	–	–	–	•
2	Other definition of pharmacovigilance	–	–	–	–	–	–	✓	✓	✓	–
3	Description of national pharmacovigilance guidelines and responsibilities	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
4	Full definition of adverse drug reaction (ADR)	✓	✓	•	–	✓	✓	✓	–	–	•
5	Specific statements about products that can cause ADRs – medicines	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	Specific statements about products that can cause ADRs – vaccines	–	✓	•	–	✓	✓	✓	✓	✓	✓
7	Specific statements about products that can cause ADRs – blood products	–	✓	✓	–	–	✓	–	✓	✓	✓
8	Description of national ADR reporting system	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
9	Printable version of ADR report form	✓	✓	✓	e	✓	✓	✓	✓	✓	✓
10	Instructions on details required on ADR report form	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
11	Instructions on where/how to submit the form	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12	Information on what happens to the form/information submitted	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
13	Guide to causality assessment	–	✓	•	–	–	–	–	✓	✓	•
14	Access to original data or individual case reports	–	D	–	–	–	–	L	–	–	–
15	Access to drug analysis prints or data summaries	–	D	–	–	–	–	L	–	✓	D
16	Safety alerts from recent ADR news (advisories, warnings, recalls)	✓	✓	✓	✓	–	✓	✓	✓	✓	✓
17	Information on newly released 'high alert' products (e.g. black triangle drugs)	–	–	–	0	–	–	–	–	✓	–
18	Generic information on drug-drug interactions	–	–	–	✓	–	–	–	–	–	✓
19	Generic information on the use of medicines in pregnancy	✓	–	–	–	–	–	–	L	✓	✓
20	Information about complementary medicines	✓	✓	0	✓	✓	✓	✓	✓	✓	•
21	Information about purchasing drugs online	✓	✓	✓	✓	✓	•	–	•	✓	✓
22	Information about medical devices	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
23	Information about stem cells	✓	✓	L	•	–	✓	–	–	✓	✓
24	Details of whom to contact with queries about pharmacovigilance or ADRs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
25	Information specifically for consumers about ADRs and pharmacovigilance	✓	✓	–	✓	✓	•	✓	✓	✓	✓
26	Information for consumers wanting to report possible ADRs	✓	✓	–	✓	–	•	✓	✓	✓	✓
27	Information for pharmaceutical companies	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
28	Links (URLs) to external sources of pharmacovigilance information	–	✓	✓	✓	✓	✓	✓	✓	✓	–
29	Information about the Uppsala Monitoring Centre	•	–	✓	–	–	✓	–	✓	–	–
30	Electronic search facility available	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
31	Number of languages in which the website is available	1	2	4	2	3	2	2	1	1	1
32	Access to website using Google [Search "[country] report adverse drug reaction" or "[country] report drug side effect"]	✓	✓	✓	✓	•	•	•	✓	✓	✓

AU = Australia; **CA** = Canada; **CH** = Switzerland; **DK** = Denmark; **FI** = Finland; **IE** = Eire; **NL** = The Netherlands; **NZ** = New Zealand; **UK** = United Kingdom; **US** = United States of America; **D** = downloadable; **e** = electronic; **L** = link available; ✓ indicates present on the website, clear and easy to find; • indicates present but unclear or hard to find; – indicates not found in the search; **0** indicates not in English.

card reports.[15] In our view, it should be possible to access such data, and the national pharmacovigilance websites could act as portals. On the other hand, there is also a fear of jeopardizing patient confidentiality when case numbers are small, or of providing public access to information that might cause unnecessary or unfounded fears among patients; for example, when there has been a reported fatality putatively linked to an ADR. If these were thought to be important concerns, these data could be made available in restricted areas of the websites, accessible only to designated health-care professionals and researchers. Furthermore, even if such access resulted in the identification of signals, further actions beyond signal detection would be needed,[11] including confirmation of those signals, which is currently often not performed.[16]

There were also widespread differences between the other items of information provided. For example, all ten websites provided information about medical devices and complementary medicines, and seven gave clear advice regarding purchasing medications online, but only three had information on medicines in pregnancy and only two on drug-drug interactions. These differences highlight room for improvement in websites that lack important information and also reinforce our view that a standard template for websites could prove useful.

Only the UK website included information about a scheme for highlighting 'high alert' products, in which "a Black Triangle is assigned to a product if the drug is an active substance which has been newly licensed for use in the UK".[10] The use of such a scheme in other countries could enhance the available pharmacovigilance data, improving drug safety monitoring. That such schemes should be introduced has recently been recommended by the European Parliament.[17]

In addition to communicating drug safety information, pharmacovigilance websites play a role in conveying information about new and evolving medical technologies, such as stem cells. Although the WHO definition of pharmacovigilance does not include these new types of technology, monitoring their safety is increasingly coming under the remit of pharmacovigilance experts. Several of the websites refer to stem cells, but with variable details; for example, whether the different types of stem cell therapy (embryonic, fetal, adult, amniotic, pluripotent, etc.) are mentioned or not. Areas that deserve further clarification and agreement regarding what the public ought to know include biologics and biosimilars and their definitions, cell extracts, tissues, organs, xenografts, and radiopharmaceuticals (a category that includes drugs intentionally made radioactive for the purposes of diagnosis or therapy).[18]

Addressing the target audience appropriately is also important for tailoring the information to a suitable level. All the websites surveyed had sections dedicated to pharmaceutical companies, as would be expected of a DRA website. Most provided information specifically for patients (usually called consumers), but this was not always overtly signposted as such, which means that it may not always be clear to a patient which section is intended for them. To allow browsers to gain further information, the majority also gave links to useful sources of external information, a feature that has been identified as important in all websites and was specified as a WHO general criterion required of DRA websites.[5] An unexpected finding was that only three of the web-

Table V. A summary of the data shown in table IV

Accessibility of items	AU	CA	CH	DK	FI	IE	NL	NZ	UK	US
Clear and easy to find	20	25	19	20	17	20	21	23	26	22
Present but not easy to find	1	1	4	1	1	4	1	1	0	4
Absent	10	5	8	10	13	7	9	7	5	5

AU = Australia; **CA** = Canada; **CH** = Switzerland; **DK** = Denmark; **FI** = Finland; **IE** = Eire; **NL** = The Netherlands; **NZ** = New Zealand; **UK** = United Kingdom; **US** = United States of America.

sites surveyed provided information about the UMC, which coordinates pharmacovigilance on a worldwide scale, collating information from over 130 participating countries.[19]

In order to ensure website accessibility, it is important to confirm that the correct URLs are identifiable from a simple Internet search, for example using Google, as in this survey. We recognize that the accessibility of websites via Google, for example, is not under the control of DRAs; however, it is something that they could readily check and seek to improve if necessary. Websites should also be available in relevant languages, which may be multiple in some countries; for example, Switzerland. In countries with high levels of immigration the areas of the website that contain information for the public could be translated. Although accurate translations may be challenging to obtain, with international collaboration and motivation this should be a reasonable aim, and it would bring drug safety information to large sections of the public. We did not survey the extent to which the information purveyed in multilingual websites differs between languages. This is clearly important for the communication of information to a population whose primary language is not English. We consider it the responsibility of individual countries to ensure that the information given in different languages is equivalent.

Study Limitations

This study had limitations that require consideration when interpreting the results. First, the analysis was subjective, although it was checked by Charlotte Barker and Jeffrey Aronson independently. Charlotte Barker initially reviewed the pharmacovigilance websites in order to develop the reference items, which she then used in the survey as a standard against which to compare the websites; other items might have been included. Furthermore, only ten national pharmacovigilance websites were included, restricting the analysis to sites available in English; this number could be increased in future studies of larger scale, and the language problems could be overcome by recruiting reviewers of different nationalities or with wider language skills to survey websites. The survey was first carried out between October 2009 and March 2010, and checked and revised in January 2011. The results should become obsolete as websites are updated – we hope that they will.

Conclusions

From this survey of ten national pharmacovigilance websites, we conclude that the current state of drug safety communication by this means remains suboptimal and that there is much scope for improvement. The importance of clear definitions, in particular, cannot be overemphasized.[12] A wider study is needed to determine the extent of variability in other national websites.

The criteria that emerged from this study specifically for the pharmacovigilance section of DRA websites may prove a useful adjunct to future refinement of this section of the WHO model website for DRAs,[5] possibly in conjunction with the criteria developed by Vitry et al.[6] The WHO will remain pivotal in driving drug regulation to improve worldwide pharmacovigilance communication and outcomes.

While recognizing that the pharmacovigilance needs of different countries may vary, in particular when comparing developing and developed countries, we believe that the type of information highlighted in this analysis is internationally generic. Furthermore, since pharmacovigilance is an international activity, uniformity of information supplied is important.

Consensus on the critical components of a pharmacovigilance website will facilitate the development of an up-to-date standard, which could be used by the international pharmacovigilance community to improve online communication. This is something to which CIOMS could turn its attention. Optimizing the contents of websites will contribute to rapid and effective transfer of information. This will lead to enhanced awareness, understanding, and monitoring of ADRs, and increased rapidity of intervention and appropriate action when necessary. This will ultimately improve drug safety on a global scale, with great benefits to public health.

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