Being a member of the WHO Programme for International Drug Monitoring

the UPPSALA MONITORING CENTRE

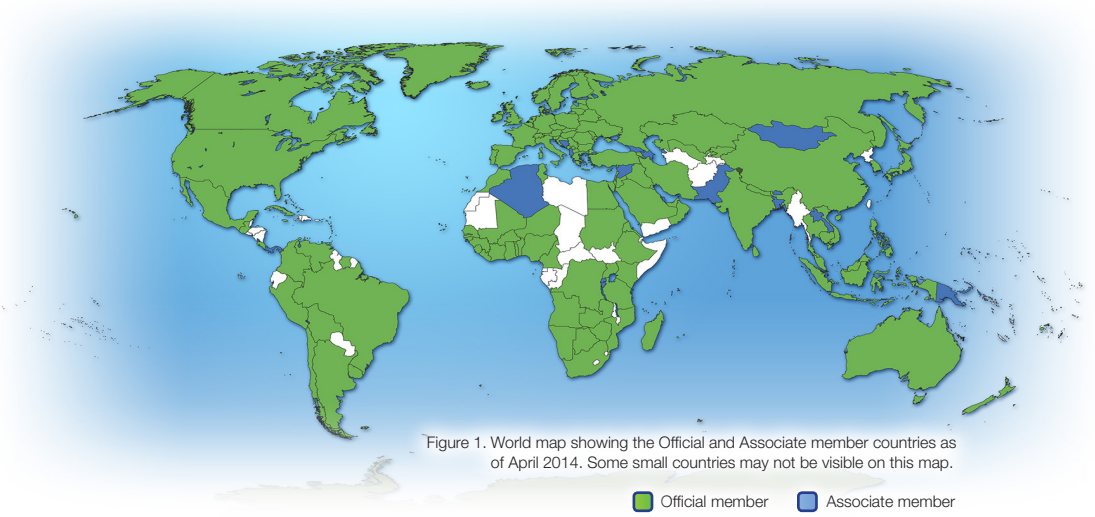

Figure 1. World map showing the Official and Associate member countries as of April 2014. Some small countries may not be visible on this map.

Background

When a country becomes a member of the WHO Programme for International Drug Monitoring, it is essential for National Centre staff to be aware of the benefits and obligations of membership. This document gives an overview of the services provided by WHO and UMC as well as the requirements National Centres are expected to meet.

The WHO Programme for International Drug Monitoring was set up in 1968 as a direct consequence of the thalidomide tragedy. In the 1960s it was discovered that this medicine could cause limb deformities in babies if taken by pregnant women. This was the modern starting point of pharmacovigilance, the science focusing on patient problems caused by the use of medicines. The intention of the WHO Programme was to ensure that early signs of previously unknown medicine-related safety problems would be identified and information about them shared and acted upon throughout the world. The WHO Programme for International Drug Monitoring has grown to become a global network of pharmacovigilance centres in over 140 countries.

In each participating country the Ministry of Health, or equivalent, has appointed a National Centre for pharmacovigilance responsible for maintaining contacts with WHO on issues related to medicine safety. The network of National Centres is co-ordinated by the WHO Collaborating Centre for International Drug Monitoring in Uppsala, Sweden, known as the Uppsala Monitoring Centre (UMC). This is a foundation created by the Swedish government on the basis of an agreement with WHO. A provision of this agreement is that WHO is responsible for all policy issues related to the WHO Programme.

UMC manages a database of Individual Case Safety Reports (ICSRs) received from National Centres in the WHO Programme network. The database, named VigiBase®, currently contains 9 million descriptions of individual cases in which medicines, including vaccines, biologicals and traditional medicines, have been suspected of contributing to an adverse reaction in the exposed patient.

Membership benefits – what you get from us

- Access to VigiBase®
  – containing worldwide medicine safety data
- Early information about potential safety hazards
  – based on analyses of worldwide data and communications from member countries
- Terminologies and software
  – tools for reporting, storing, structuring, searching, and analysing ICSRs
- Support, training, guidelines and resources
  – on pharmacovigilance practice and tool
- Access to the international network
  – knowledge and expertise of member countries

Access to VigiBase: using the VigiLyze™ tool

VigiBase is the name of the WHO global ICSR database containing close to 9 million case reports of suspected adverse drug reactions submitted by the increasing number of member countries since 1968. The case information in VigiBase is shared with member countries of the WHO Programme, however member countries may have different approaches to confidentiality of case information and provision of data to third parties. The present WHO position on confidentiality is that case information from VigiBase may be provided to any inquirer with a health professional education, provided the rules of a Caveat statement are accepted. This statement explains the limitations of the data in VigiBase and the implications for interpretation. ICSRS in VigiBase do not contain information which might identify patient or reporter.

VigiBase is a valuable reference source for medicine safety information on global and national experiences. An easy-to-use web-based tool, VigiLyze™, enables member countries to search, filter and analyse data in the global database more efficiently. This includes clickable graphic objects and summary data using several standard presentation formats. The integrated access to ICSRs allows more in-depth analysis of drug safety issues through an interactive, streamlined and intuitive interface. VigiLyze brings VigiBase data set within reach of member countries and will contribute further to improving patient safety.

VigiLyze is provided to member countries and if facilities in VigiLyze are not sufficient for users, customized searches of VigiBase can be performed on request by UMC staff. Non-members of the WHO Programme will be charged for this service.

Information about potential safety hazards: SIGNAL document

The case information submitted to VigiBase is screened on a regular basis for signs of any medicine-induced problems that have yet to be identified.

Since 1998, routine data mining of VigiBase has been performed on a quarterly basis, using statistical methods. A triage (filter) procedure is used to find drug-ADR pairs of interest and expert clinical review is undertaken by UMC and an international panel of experts. The results of these intensive analyses are available to national centres as a restricted memorandum called **SIGNAL** and in the **WHO Pharmaceuticals Newsletter**.

Terminologies and software: WHO Drug Dictionaries, WHO-ART™ and VigiFlow®

The **WHO Drug Dictionaries** (WHO DDs) and **WHO Adverse Reaction Terminology** (WHO-ART) are maintained by UMC. These terminologies are used for coding and analysis of medicinal product information and adverse reactions. The WHO DDs are accessible via VigiLyze, **VigiFlow®** (see information below) and **WHO Drug Dictionary Browser**. WHO-ART is available via VigiLyze and VigiFlow or as a file distributed to member countries on request.

National Centres are requested to transfer national ICSRs to UMC in the international standardized format (ICH-E2B). For member countries lacking an ICH-E2B compatible database for ICSR management, UMC has developed VigiFlow that is designed to function as a complete case management system and national ICSR database. No local installation is needed and the only requirement is an internet connection (minimum speed of 1 Mbit/s) and a web browser.

VigiFlow is currently available in English, French, Spanish and Russian can be used both at a central and regional level, with an unlimited number of users, which facilitates the work flow and saves resources. VigiFlow is easy to handle with built-in help texts and error messages. Search and statistics can be performed on the case reports entered, which are also easily forwarded to UMC to be included in VigiBase.

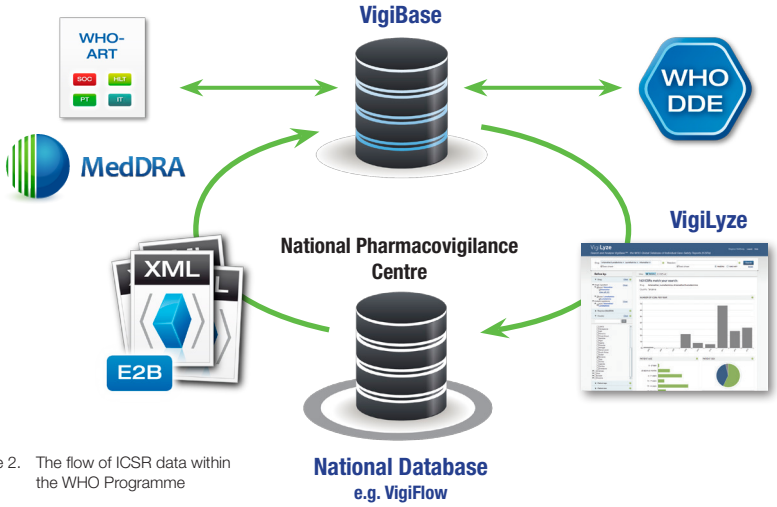

Figure 2. The flow of ICSR data within the WHO Programme

To facilitate direct patient reporting, eReporting is an optional module for VigiFlow users.

In addition to WHO DDs and WHO-ART, VigiFlow also provides access to the International Classification of Diseases (ICD-10) and MedDRA (Medical Dictionary for Regulatory Activities). Since UMC is maintaining and constantly developing VigiFlow, an annual licence fee is charged for access to the complete version of the system. However, a limited version is available free of charge, intended for countries not interested in the full case report management functionality but needing a system for submitting ICSRs to the WHO Programme.

Support and resources: guidelines, publications and websites

UMC offers guidance and support for the establishment and running of a pharmacovigilance centre and a national programme. Several guidelines and publications for good pharmacovigilance practice have been developed by WHO/UMC and are available in several languages.

The UMC and WHO also produce their respective newsletters: **Uppsala Reports** and WHO Pharmaceuticals Newsletter, available to a wide audience. Uppsala Reports, issued four times a year, contains information about developments in pharmacovigilance in general, at UMC and at National Centres in particular. The WHO Pharmaceuticals Newsletter, issued six times a year, provides a record of regulatory decisions, warnings and labeling changes made by countries on grounds of safety. Through an agreement with the publisher, member countries are also offered a discounted subscription to the secondary literature review journal Reactions Weekly, the main journal for scanning the medical literature on adverse drug reactions.

The WHO and UMC websites have a lot of useful information about the WHO Programme, current activities, definitions and concepts in pharmacovigilance, meetings and courses around the world, and an FAQ section. Most of the publications mentioned are also available as pdf-files for download from the websites. Please make frequent visits to: www.who.int/medicines and www.who-umc.org.

Access to the international network: Vigimed, meetings and courses

Since worldwide collaboration and information-sharing is crucial in pharmacovigilance for promotion of patient safety, member countries are encouraged to communicate frequently with each other. One forum for such communication is **Vigimed**, a web platform set up by UMC to stimulate discussions and facilitate rapid exchange of information between National Centres. Vigimed is a closed site so that members feel confident sharing preliminary findings, suspicions and opinions with other pharmacovigilance professionals, knowing that such information will not be seen by or given to other parties, the public or to media without consent of the originator.

Member countries are invited by WHO to the **Annual National Centres Meeting** usually held at some time between October and December. These meetings provide good opportunities for learning, networking and discussions regarding topical pharmacovigilance issues both in relation to methodological developments and individual medicines. It is highly recommended for National Centres to be represented at these meetings, although funding and some knowledge of English are required.

UMC also runs a **Pharmacovigilance training course** in Uppsala in May each year. The course is intended for healthcare professionals who have recently become engaged in the operation of spontaneous adverse reaction reporting programmes in a hospital, regulatory or industry setting. Theoretical and practical aspects of adverse drug reactions and pharmacovigilance are covered.

WHO supports or organizes pharmacovigilance training courses in regions of the world on an ad hoc basis, depending on local needs and the availability of funds. These training courses are sometimes focused on pharmacovigilance in Public Health Programmes (PHPs), e.g. for programme managers in malaria, tuberculosis or HIV/AIDS.

WHO also organizes **Technical Briefing Seminars** annually in Geneva with the objective of advancing collaboration between WHO and other stakeholders from governmental and non-governmental organizations engaged in promoting the quality and safety of medicines in the global community.

Membership obligations – what we expect from you

To ensure the most effective global safety monitoring by keeping VigiBase up to date with international patient safety data, member countries are expected to submit ICSRs to UMC at least every quarter and preferably more frequently than once a month. If a member country, for any reason, temporarily cannot comply with this obligation, UMC must be informed. Failure to communicate with UMC could lead to loss of some membership privileges.

Reporting format compatibility and quality of ICSRs

ICSRs should be transferred to UMC in the global **ICH-E2B** format, a defined structure for automatic transmission of information between database systems. The format includes all relevant data fields, which allows for a comprehensive medical analysis of the data.

For new member countries and current members who want to convert to an ICH-E2B compatible national database, there are three main options; to build a new national database, to adjust their current national database system or to use a third party software (for example the ICSR management system, VigiFlow).

To ensure the availability of high quality data in VigiBase, member countries are requested to submit as complete case reports as possible to UMC. With the exception of confidential patient and reporter details, no information available on the original report should be left out when transmitting an ICSR; the more information on a case, the simpler and more accurate the assessment. UMC complies with EU data protection directives and adheres to the guidance in ICH-E2B for protecting patient and reporter confidentiality.

Member countries are expected to submit **all post-marketing ICSRs** to VigiBase, irrespective of their origin, source or reporter type, causality, or seriousness. ICSRs on all types of drug-related problems should be submitted, also those associated with biological medicines (including vaccines), traditional medicines, counterfeit/substandard medicines as well as medication errors. VigiBase does not include ICSRs on veterinary medicines, cosmetic/hygiene products or medical devices.

Drug references

To be able to find ICSRs by searching a medicinal drug name in VigiBase, the names and basic details of the medicinal drug must be included in WHO DDs. To perform this task, UMC staff need reliable reference sources for local medicinal drug information. Therefore, member countries are requested to send a printed or electronic version of their **National Drug Formulary** or equivalent (e.g. reference to a website approved by the national drug authority) to UMC.

Regulatory information

Production of local and national **ADR newsletters and bulletins** is recommended as a good way of sharing important information within a country. Member countries are requested to provide UMC with information about their medicine safety newsletters if available. If available, UMC wish to receive the website address of the National Centre to publish as a link on the UMC website.

Active participation

Member countries are expected to **actively participate** in the WHO Programme; this can be achieved in various ways. National Centres should maintain **good communication** with UMC and provide updates on re-organizations, changes of staff and other relevant information. National Centres are encouraged to be active participants in **Vigimed** (page 5) and contribute to discussions and information exchange. If possible, member countries should also send at least one delegate to the Annual **National Centres Meeting** (page 5) where topics of current interest are addressed and important relationships are formed. Established National Centres are encouraged to assist in training professionals from newly established centres to promote pharmacovigilance.

Please do not hesitate to contact us if you:

- need support on ICSR reporting issues and/or VigiFlow
- need a VigiLyze user account to access VigiBase
- need a WHO-DD Browser user account to access WHO DDs
- need any WHO/UMC publications, or Reactions Weekly
- need a user account to access the Vigimed web portal
- want to attend our meetings and/or courses

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