Pharmacovigilance Training at the Centre of Antipoison and Pharmacovigilance

Rabat, Morocco
November 3-14, 2008

Training Report

Dr. Latifa El Hadri,
Program Coordinator, Africa

U.S. Pharmacopeia Drug Quality and Information Program
12601 Twinbrook Parkway
Rockville, MD 20852 USA
Tel: (+1) 301-816-8160
Fax: (+1) 301-816-8374
Email: uspdqi@usp.org

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Author(s) Name: Latifa El Hadri
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About USP DQI

The United States Pharmacopeia Drug Quality and Information (USP DQI) Program, funded by the U.S. Agency for International Development (USAID) Cooperative Agreement HRN-A-00-00-00017-00), provides technical leadership to more than 30 developing countries to strengthen their drug quality assurance programs, ensure the quality of medicines and promote public health. USP DQI helps build local, national and regional capacity to improve the standards of drug manufacturing and distribution, reduce the impact of infectious diseases, mitigate the effects of the HIV/AIDS epidemic, and advance the appropriate use of medicines. This document does not necessarily represent the views or opinions of USAID. It may be reproduced if credit is given to USP DQI.

Abstract

USP DQI believes it is necessary to create an area of expertise in PV and drug information, and for this purpose, Dr. El Hadri attended this two-week training course in pharmacovigilance (PV) at the "Centre of Anti-poison and Pharmacovigilance" (CAPM) in Rabat, Morocco.

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Key Words

Pharmacovigilance, reporting, patient safety, drug events, adverse drug reactions, imputability, causality assessment, Vigiflow, Vigimed

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Dr. Latifa El Hadri would like to thank Dr. Rachida Soulaymani, Director of CAPM, for supervising my training in PV practices in the center. Special thanks to Dr. Rajae Benkirane and Dr. Souad Skali for working closely with me in planning my training.

I would like also to extend my gratitude to the rest of the staff of Centre of Antipoison and Pharmacovigilance in Morocco (CAPM) for providing me with all requested documents and information as well as for their hospitality and assistance.

My sincere appreciation to Dr. Patrick Lukulay, Director of USP DQI, and Mr. Anthony Boni and Ms. Veerle Coignez from USAID/HQ for supporting my training that will allow me to provide leadership in planning PV activities with the USP DQI team.

I would like also to extend my gratitude to the administrative and editorial staff of USP DQI for their valuable contributions in arranging logistics for the trip and editing this report.

ACRONYMS

ADR	Adverse Drug Reaction
AE	Adverse Event
CAPM	Centre of Antipoison and Pharmacovigilance in Morocco
EMEA	European Medicines Agency
FDA	Food and Drug Administration
ICSR	Individual Case Safety Report
PV	Pharmacovigilance
SOP	Standard Operating Procedure
SSA	Sub-Saharan African
UMC	Uppsala Monitoring Center
USAID	United States Agency for International Development
USP DQI	United States Pharmacopeia Drug Quality and Information
WHO	World Health Organization

Definition of pharmacovigilance

The etymological roots of phramcovigilance (PV) are: *pharmakon* (Greek), "drug;" and *vigilare* (Latin), "to keep awake or alert, to keep watch." PV is the science of collecting, monitoring, researching, assessing, and evaluating information from healthcare providers and patients on the adverse effects of biological products; herbal, traditional, and contemporary medicines; blood products; medical devices; and vaccines with a view to identifying new information about hazards associated with medicines and preventing harm to patients.

In particular, PV concerns adverse drug reactions (ADRs), which are officially described by the World Health Organization (WHO) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function." Because clinical trials involve several thousand patients, at most, less common side effects and ADRs are often unknown at the time a drug enters the market.

Overall, PV is the key to monitoring and evaluating ADRs. It identifies and quantitatively assesses the risks related to the use of medicines in an entire population or in specific population groups. PV activities are imperative to improve public health and patient safety.

Background

The WHO Programme for International Drug Monitoring has 108 member nations. Over 80 member nations have systems in place which encourage healthcare personnel to record and report ADRs in their patients. In July 2008, the program had 4 million ADR reports from countries contributing to the WHO Global Individual Case Safety Report (ICSR) database, Vigibase. These reports, sent via Vigiflow to Uppsala Monitoring Center (UMC) in Sweden, represent the concerns of health professionals around the world about possible harm caused to their patients by medicines.

In Africa, few countries are members of the WHO drug monitoring program, and many – mainly Sub-Saharan African (SSA) countries – have no ADR reporting mechanisms. To help remedy this situation, USP DQI assisted Madagascar and Senegal to implement PV activities. USP DQI is also assisting Uganda's PV center improve their ADR reporting system and is providing guidance on strengthening PV practices at regional and district levels.

Purpose of the training

This training will help Dr. El Hadri:

- better assist the USP DQI team plan and develop PV activities
- review the existing PV practices at the country level
- provide guidance on how to establish an ADR reporting system, organize a PV workshop, and create a training agenda that responds to a country's needs in improving reporting, data management, and communication.

Source of Funding

Funding was provided by the P.E.3.1.2 Malaria program.

Overview of Activities

November 3, 2008
Introduction to the CAPM staff and center visit
A round table meeting was organized by the director of CAPM to introduce Dr. El Hadri to the staff and to brief her on the main activities of the center. Following the meeting, a tour of each department was given by the unit heads. During the tour, Dr. Soulaymani pointed out that the center is constantly developing. She believes that the center always needs to meet international standards and the staff needs to be trained for any new activities related to their responsibilities.

November 4-5, 2008
Attend the CAPM monthly staff meeting
The majority of the staff attended the meeting and participated in the discussion. All planned activities, either for staff or for visitors, are discussed and coordinated at these meetings. Attending this 2-day meeting was highly beneficial as the discussions gave an idea about how the center functions and who is charge of which PV activity. Further, the meeting gave background on communication and coordination within each unit and how each unit reports activities to central and regional PV departments.

November 6-7 and 10-12, 2008
Meetings with the unit heads

Daily meetings were scheduled with the head of each unit with the purpose of understanding the role of the unit within the center and to have comprehensive training in their daily PV practice.

- ***Meeting with Dr. Rajae Benkirane, head of Pharmacovigilance Unit***

The PV unit, which was created in 1989, is a well-equipped and modern facility. It is used to perform PV activities and to hold trainings, seminars, and conferences. The PV unit is connected to UMC, allowing trainees a hands-on experience reporting and analyzing PV data. Trainees have direct online access to Vigiflow and to all current PV reference books and resources to facilitate the review of patient cases.

Most PV courses target countries with little or no PV experience, but training is also available for countries that have established PV programs but are facing some difficulties with reporting ADRs, training personnel, or strengthening their PV activities.

Dr. Benkirane supervises all PV training, reporting form collection from other regional PV centers, and the Standard Operating Procedures (SOPs) for each activity within her unit.

- ***Meeting with Dr. Ilham Semlali, head of Toxicovigilance Unit***

The Toxicovigilance unit was established in 1989 and is based on the in-depth medical assessments of acute or chronic intoxications on an individual basis. These require detailed information that unit doctors can rarely obtain via emergency telephone calls. Validation of this medical information is discussed with a team of doctors and clinicians of the center to help identify causal links between otherwise unexplained pathological conditions and documented toxic exposures. The most common intoxication reports received by the center are due to exposure to carbon monoxide, scorpion bites, and food poisoning. Therefore, the unit is divided

into 3 cells that handle each type of poisoning. The largest cell is the one dedicated for scorpion bites, due to the high number of reported cases – last year, more than 30,000 cases were reported.

It is noteworthy to mention that another cell is dedicated to managing a database of reported toxicovigilance cases and sharing results with concerned parties. All cases are reported and assessed according to international codes, and the coded data are computerized and updated after each received case. The database is used mainly for statistical purposes and for epidemiological studies. Regularly the information of the toxicovigilance revealed statements on:

- Identifying the epidemiological profile of poisoning in Morocco
- Detecting the evolution of morbidity and lethal toxicity due to various types of poisoning
- Assessing the therapies used by health professionals
- Defining the risk factors and circumstances related toxic substances

- ***Meeting with Dr. BenGhalem, head of Toxicological Information and Emergency Phone Calls***

All staff in this unit are trained in pharmacotoxicology and in emergency telephone answering. 24-hour assistance is maintained through rotation shifts of medical doctors and pharmacists.

The unit provides a range of services to national regulatory authorities, medicine procurement agencies, hospitals, practitioners, and patients. The unit ensures the decongestion of emergency services, reduces unnecessary travel expenses, educates the public, and helps prevent tragedies linked to toxic chemicals or aberrant behavior. Toxicology information covers all potentially toxic products (drugs, chemicals, plants, animals, food, etc.).

The doctors of toxicological information unit have the following responsibilities:

- Deliver information by phone 24 hours a day to the public, health professionals, and authorities and respond to requests for information received by mail
- Provide information on the diagnosis, prognosis, treatment, and prevention of poisoning
- Provide information on the cause of the encountered toxicity and its risk to health
- Compare the ingested dose to the toxic dose and lethal dose
- Assess the risk of exposure to various toxic substances based on their pharmacokinetics
- Provide information on the symptoms and predictable complications
- Advise decontamination, symptomatic treatment, care, and support
- Inform the public about first aid
- Make a follow-up clinic for the intoxicated patients
- Validate requests for toxicological analysis issued from emergency toxicological labs
- Participate in updating the center's database
- Record in a standardized form the necessary information to treat and diagnose poisoning
- Generate poisoning warnings/alerts in case of collective intoxication
- Develop a standard for coordinated responses

The database of this unit is used regularly for:

- Identifying new toxins in order to generate alerts
- Assessing the therapeutic uses in the management of poisoning in Morocco
- Providing a comprehensive overview of pathological toxicities in Morocco

- ***Meeting with Dr. Asmae Al-khattabi, head of Communication and Information Cell***

This cell was created in 1996 and promotes the scientific and technical results of the center. The cell works closely with data management of all units of the center and operates in two areas: public relations and publishing/dissemination.

Each topic or report designed for publication is the subject of a communication strategy. It defines the nature and content of the report, the objectives and means of the communication, and the targeted audiences. The content of each communication is coordinated between the cell's staff and the rest of center's units. All communications must be approved by the director of the center prior to dissemination.

Besides developing communication tools, this cell offers a reporting form on the CAPM website, encouraging health professional to report adverse drug events, including those suspected to have been caused by herbal, traditional, or alternative remedies. This program solicits reports of all reactions to any drugs which are suspected of significantly affecting a patient's management. All collected data is statistically analyzed and forwarded to the UMC.

Visit to the Laboratory of Toxicology and Clinical Pharmacology

This unit, functional since 1994, covers medical examinations and toxicological assays of drugs for therapeutic drug monitoring. This laboratory also analyzes performance enhancing substances used by athletes as well as controlled substances.

The toxicology clinic laboratory specializes in the identification of toxic substances in biological fluids. All available techniques are used to test for toxic substances that are most frequently encountered in Morocco, and the results are communicated to the inquiring doctors or hospitals.

Other meetings

Dr. El Hadri practiced with doctors of pharmacovigilance, teratovigilance, and vaccinovigilance on how to report AEs and how to perform imputability (drug causality assessment) of unexpected or toxic drug reactions.

Outcomes of the training

This training was helpful in understanding the set up of a well-established PV center, different practices within the center, personnel qualifications for each PV activity, and the national and international PV network. Further, this training explained how to create and use report forms, understand AEs, perform causality assessments, and report ADRs to UMC.

Next steps

- In coordination with CAPM, USP DQI will develop guidelines and appropriate PV training modules for how to set up a new PV center in developing countries. Details of this training will be included in those materials.
- USP DQI will coordinate a hands-on PV training for 2 PV staff (one from Senegal and one from Uganda). Dr. El Hadri will work closely with CAPM to plan the agenda
- USP DQI will evaluate Uganda's PV system

Annex 1

Pictures from the training in pharmacovigilance at the Centre of Antipoison and Pharmacovigilance in Morocco
November 3-14, 2008

Staff meeting at the Centre of Antipoison and Pharmacovigilance in Morocco

Meeting with Dr Rajae Benkirane and the Pharmacovigilance Unit

Visiting the Laboratory of Toxicology and Clinical Pharmacology

The Toxicology Unit receives blood samples for testing

Centre of Antipoison and Pharmacovigilance in Morocco

Annex 2

Staff of the Center of Antipoison and Pharmacovigilance in Morocco

Family Name	First Name	Title	Employment date	Designation Date	Department
ABADI	FATIMA	MEDECIN	14\05\2002	02/02/2006	RT
ACHOUR	SANAE	MEDECIN	01/02/2001	10/10/2002	R.T
AGHANDOUS	RACHIDA	INGENIEUR-D'ETAT	30/08/1995	01/01/2001	CCI
AIT MOUSSA	LATIFA	INGENIEUR -D'APPLIC	22/03/2002	22/03/2002	LAB
ALJ	LOUBNA	PHARMACIENNE	11/102002	21/10/2002	P V
BADRI	MOHAMED	TECHNICIEN	27/07/1987	27/07/1987	TV
BEKHAR	NABILA	TECHNICIENNE	01/11/2004	27/11/2006	LAB
BELKHYER	MOHAMMED	A TP	01/06/2001	01/06/2001	ADM
BENABDALLAH	GHITA	PHARMACIENNE	12/11/2003	07/05/2003	P V
BENJELLOUN	RAJAE	MEDECIN	26/12/1991	01/01/1992	P V
BENKIRANE	RAJAE	MEDECIN	22/10/1989	22/10/1989	P V
BENLARABI	SANAE	MEDECIN	02/01/1985	30/08/2001	TV
BENTAFRITE	MOUNA	IDE 2mè	03/11/2004	19/11/2004	LAB
BENZAHRA	MERYEM	AG.EXECUT	03/01/1994	03/01/1994	ADM
CHAFIQ	FOUAD	MEDECIN	13/12/1993	24/10/2002	R.T
CHAGRADEI	YOUNESS	IDE 2mè	02/07/2007	03/07/2007	CCI
EL MAATAOUI	ILHAM	ING D'APPLI	27/07/2000	20/03/2002	LAB
EL OUALTI	ABDELAZIZ	ING.APP1EG.	18/07/2002	29/07/2002	LAB
EL OUFIR	GHIZLANE	MEDECIN	23/06/2000	09/09/2002	TV
IDRISSI	MONCEF	MEDCIN	23/02/1998	20/03/2002	TV
JALAL	GHIZLANE	MEDCIN	25/09/1998	25/09/2002	R.T
JERHALEF	HIND	IDE 2mè	23/11/2004	02/12/2004	CCI
JOUAHRI	MOHAMED	ING DETAT P	10/07/1992	01/08/2001	ADM
KHATTABI	ASMAE	ASSIS-MED	AOUT/96	AOUT/96	CCI
LAASRI	ABDESLAM	AGENT DE PUBLIC	11/06/1905	11/06/1905	ADM
OUAI	AZIZ	ATP	02/04/1990	02/04/1990	ADM
OUAMMI	LAHCEN	ING-D'ETAT	04/10/1994	04/10/1994	LAB
OULEDRAKHIS	RACHIDA	PHARMACIENNE	10/06/2002	03/04/2007	PV
RHALEM	SAMIRA	TECHNICIEN 1ER GRADE	24/01/1997	24/01/1997	ADM
RHALEM	NAIMA	MEDECIN	24/12/1991	24/DEC/91	R.T
RHOLAMALLAH	ABDELKEBIR	TECHNICIEN 1ER GRADE	21/06/1991	21/06/1991	ADM
RIFI AGHAN	HAFIDA	ATP	01/08/1996	09/04/1984	LAB
SEFIANI	HOUDA	MEDECIN	28/07/2002	03/12/2007	PV
SEMLALI HASSANI	ILHAM	MEDECIN	30/03/1994	15/01/2003	TV
SKALI	SOUAD	ASSISTED-MEDECIN	01/08/1996	01/08/1996	P V
SMIRESS	NABIHA	MEDECIN	03/02/1993	07/03/1996	P V
SOLHI	OUAFAE	MEDECIN	26/01/2004	30/06/2008	IT
SOULAYMANI	RACHIDA	PROFESSEUR	01/07/1983	01/05/1987	ADM
TAHIRI-HASSANI	NADIA	MEDECIN	01/06/2000	01/01/2003	R.T
TALIBI	ISMAIL	PHARMACIENNE	27/01/2004	16/04/2007	PV
TEBAA	AMINA	MEDECIN	06/01/1993	06/01/1993	P V
TOUIL	MOHAMMED	ATP	14/06/1905	14/06/1905	ADM
WINDY	MARIA	MEDECIN	18/01/1999	03/01/2003	R.T
ZALAGH	FATIMA	ASSISTED-MEDECIN	19/05/2003	07/05/2003	LAB

Annex 3

Organigram for the Center of Antipoison and Pharmacovigilance in Morocco