KINGDOM OF CAMBODIA
NATION RELIGION KING

MINISTRY OF HEALTH

DEPARTMENT OF DRUGS AND FOOD

ESSENTIAL DRUGS BUREAU

STANDARD OPERATING PROCEDURES OF CAMBODIAN PHARMACOVIGILANCE CENTER

Prepared by CAMBODIAN PHARMACOVIGILANCE CENTER

With the Technical Assistance of WORLD HEALTH ORGANIZATION

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Preface

Cambodian Pharmacovigilance Center(CPVC) was established in 2008 for drug safety monitoring which benefit to human health in Cambodia. Due to the needs of CPVC, we created the national pharmacovigilance system, a program for adverse drug reactions reporting and it is mandatory for registration holders of all products registered by Department of Drugs and Food to submit reports of all ADRs encountered to CPVC in accordance with MOH announcement (PRAKAS) number 0973 dated on 23rd of November 2011.

All of the activities in CPVC as ADR report collecting, monitoring or evaluating are based on Standard Operating Procedures (SOP). This SOP was drafted with the technical assistance of World Health Organization by applying the ideas from the consultative workshop on reviewing the SOP and other documents of CPVC which was held at MOH on 30th and 31st October 2014.

CPVC is collaborating with WHO on reviewing SOP in order to gain ideas and edit this document.

We expect this SOP is designed as general orientation and practical reference for the practice in CPVC and as a reference for PV performance.

We would like to acknowledge the financial and technical support received from the Global Fund and WHO for producing this guideline.

Dr. MAM BUNHENG
MINISTER OF HEALTH

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- Pharm. D. YANG DARAVUTH, Deputy Director of Department of Drugs and Food
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- Pharm. D. CHUON VIBOL, PV technical staff
- All officers of the Department of Drugs and Food, namely Deputy Director Chiefs and Deputy Chiefs of each bureau for their kind recommendations and cooperation to develop and enhance this SOP to be an appropriate and practical one for CPVC.
- Ms. **Sufu Comfort Kanak,** World Health Organization (WHO) Consultant
- Ms. **Vanchinsuren Lkhagvadorj,** World Health Organization (WHO) Consultant for the technical assistance.

Contents

CAMBODIAN PHARMACOVIGILANCE CENTER

FUNCTIONS AND RESPONSIBILITIES OF THE PHARMACOVIGILANCE CENTER

Under the guidance of the Pharmacovigilance Advisory Committee, the Center is, on the overall, responsible for monitoring the safety of medicines through:

1. Promoting the reporting of adverse reactions through education and training efforts to multiple stakeholders such as health facilities managers, public health program managers and staff, medical doctors, pharmacists, nurses, and patients/consumers.
2. Collecting case reports of adverse reactions through a simple, user-friendly, confidential system with provisions for feedback to reporters.
3. Collating, analyzing and evaluating patterns of adverse reactions through an identified agency or national expert committee.
4. Reporting incidents of lack of efficacy and suspected quality defects to relevant agencies and institutions for appropriate evaluation tests and advising relevant actions to take.
5. Disseminating the information on substandard and counterfeit medicines and how to prevent occurrence.
6. Working with the MOH to take regulatory action in response to findings.
7. Alerting prescribers and manufacturers to risks of adverse reactions for both old and new drugs.
8. Educating and informing patients of adverse reactions caused by specific medicines and actions that can be taken through a variety of advocacy channels.
9. Submitting reports to the WHO international ADR database (Vigibase) and contributing to the international drug safety efforts of more than 100 countries
10. Promoting rational and safe use of medicines through communication and education of ADRs and the prevention of medication errors and drug toxicities.
11. Building a library of literature and human resources (speakers' bureau or trainers) to maintain the growth and expansion of PV activities and to include PV topics into undergraduate health professional curriculum.

STANDARD OPERATING PROCEDURE FOR DETECTING AND REPORTING ADVERSE DRUG REACTIONS USING THE ADR REPORTING FORM

SOP Name	SOP for Detecting and Reporting Adverse Drug Reactions using the Cambodian ADR reporting Form
SOP Number	
Version No and Date	01 - 07 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

The purpose of this SOP is to provide a systematic process to be used by healthcare providers to detect and report ADRs. It also describes the step-by-step procedure to be followed in completing the Cambodian ADR reporting form and for submitting an individual case safety report to the CPC under the spontaneous reporting system.

Scope

These procedures described in this SOP apply to healthcare providers including doctors, nurses and pharmacists that interact with patients and may be able to detect suspected ADRs. It also covers the process of filling an ADR reporting form and sending it to the CPC.

Definitions/Acronyms

Individual Case Safety Report (ICSR): – A report that contains 'information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient...'

A valid report is one that contains the following minimum information; an identifiable patient, a suspected adverse event, a suspected medicine and a source of report (identifiable reporter).

Severity of ADR - The term 'severe' is not synonymous with serious. In the English language, 'severe' is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache).

Serious ADR - A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- ☐ Results in death
- ☐ Requires inpatient hospitalization or prolongation of existing hospitalization
- ☐ Results in persistent or significant disability/incapacity
- ☐ Is life-threatening

Responsibilities

This SOP is written specifically for healthcare providers (doctors, nurses, pharmacists) that interact with patients and therefore are in the position to detect and report ADRs on behalf of the patient.

1. It is the responsibility of the healthcare provider to detect ADRs in their patients.

2. It is the responsibility of the healthcare provider to fill and ADR reporting form and report suspected ADRs to the CPC on behalf of the patient
3. It is the responsibility of the healthcare provider to ensure that sufficient information to ensure a valid report is obtained from the patient while the patient is still available
4. It is the responsibility of the healthcare provider to ensure that the information provided in the ICSR is clear, legible, relevant and meaningful
5. It is the responsibility of HCP to ensure timely submission of all ICSRs (filled ADR reporting forms) to the CPC.
6. It is the responsibility of the PV focal person to retrieve all filled ADR reports from HCPc and forward to the CPC
7. It is the responsibility of the PV focal person to ensure that ADR forms are available at all times to HCPs in consulting rooms, hospital wards, pharmacies and other places where HCPs interact with patients
8. It is the responsibility of staff of the CPC to ensure that ADR reporting forms are available to the PV focal person in the institution

General considerations/instructions

The sending of an ADR report is by no means admission of wrong doing by the healthcare provider. It does not in any way mean that the healthcare provider is responsible for the occurrence of ADR either by negligence or improper practice. HCPs should therefore not hesitate to detect and report ADRs in their patients.

All reports sent by HCPs to the CPC will be held in absolute confidentiality and will not be used for any legal processes whatsoever.

ADR reports are collected for knowledge enhancement purposes only i.e. to enhance understanding about drugs so as to improve rational use and patient healthcare delivery outcomes. Use of any information originating from ADR reports will involve anonymizing such information.

The information that must be provided when filling an ADR form has been highlighted (bold) under the section on ‘Filling an ADR form’. It is imperative that HCPs provide this information while filling an ADR from.

Procedures

1. Detecting ADRs

When a patient complains about ill health to the healthcare provider, take the following steps to try to determine if an ADR should be suspected

1.1. Ask the patient about the use of any medicine prior to commencement of the problem

1.2. If yes, consider the possibility of a drug related problem and investigate further especially if a new medicine is involved
1.3. Clinically examine the patient for classical signs of ADR e.g. skin eruptions
1.4. Order laboratory investigations (if possible)
1.5. Check if laboratory findings support a case for ADR i.e. are indicative of ADR
1.6. If yes, manage the patient for ADR as appropriate
1.7. Fill an ADR reporting form with all relevant details about the case

2. Filling an ADR reporting form

2.1. Take out and ADR reporting and fill while the patient is still with you

2.2. Provide information concerning the patient in the section titled 'patient information'. The information to be provided include

- **Patient name or initials**
- **Age or date of birth,**
- **Sex**
- Weight (if known),
- Pregnancy status including how many weeks of pregnancy (if known) and
- Patient telephone number

2.3. Provide information on the suspected medicines in the section titled 'suspected drugs'. The information to be provided include

- **Generic and or brand name of the medicine** including batch number and expiry date especially when it is a suspected case of lack of efficacy
- **Route** of administration
- **Dosage**
- **Reason for use** (indication)
- **Date started**
- Date stopped

2.4. Provide information on concomitant medicines used including herbal medicines in the section titled 'Other medicines in use'. Include all information listed on 2.3. above

2.5. Provide information about the suspected adverse drug reaction in the section titled 'Adverse drug reactions'. The information to be provided include

- **Description of the reaction**
- **Date the reaction started** (onset date)
- Date the reaction stopped (if applicable)
- Severity of the reaction (refer to definitions section above for definition of severity)
- **Seriousness of the reaction** (refer to definitions section above to see what makes an ADR serious)
- **Outcome of the reaction**
- Treatment(s) used for the reaction (if any)

2.6. Provide any other comment you may have on the reaction

2.7. Provide information on the reporter in the section titled 'Reporter Information'. The information to be provided include

- **Name of reporter**
- Indicate the profession of the reporter
- **Contact detail** (telephone number or email address) of the reporter
- **Date the report was filled**
- **Signature** of the reporter

2.8. Review all information to ensure that the report is valid and the information is correct and relevant

2.9. Cross check that the report is signed and dated

2.9. I don't know if you require HCPS to do preliminary causality assessment, if so indicate it here if not delete this point

2.9. Forward the completed report to the Pharmacovigilance focal person in the institution for onward sending to the CPC

3. Sending of completed ICSR to CPC by PV focal person

3.1. Cross check that the report is signed and dated

3.3. Cross check that all information for a valid ICSR are provided on the form

3.4. Send the report to the CPC using any of the identified means of reporting

Documentation:

A copy of the ADR report should be retained in the patient's hospital record.

Quality Control & Quality Assurance:

All ICSRs must be checked and cross-checked by the focal person for completeness and quality of information

References

WHO-UMC. Glossary of terms used in Pharmacovigilance

STANDARD OPERATING PROCEDURE FOR PROCESSING INDIVIDUAL CASE SAFETY REPORTS (ICSRS)

SOP Name	SOP for Receiving & Processing Individual Case Safety Reports (ICSRs)
SOP Number	.CPC/DDF/2013/06/01
Version No and Date	1-06 June -2013
Implementation Date	06-June-13
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	.
Authorized by	Director of Department of Drugs and Food
Signature and Date	.
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

The purpose of this SOP is to establish a uniform procedure for processing of Individual Case Safety Reports (ICSRs) received by the Cambodian PV Centre from the spontaneous reporting system.

Scope

These procedures apply to all Cambodian PV Centre staff that receive, process, evaluate, file, enter data and send feedback on ADR reports. It covers ICSRs received from healthcare providers in the public and private sector, Public Health Programmes (PHPs) as well as those received from Marketing Authorization Holders in Cambodia.

Definitions/Acronyms

Individual Case Safety Report (ICSR): – A report that contains 'information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient...'

Responsibilities

This SOP is written specifically for CPC staff that receives, process and assess ICSRs. All personnel who perform activities with this SOP must have understanding of the PV system including the need for confidentiality.

1. It is the responsibility of the technical associate to receive and process all incoming ICSRs.
2. It is the responsibility of the technical associate to cross check and ensure that all received ICSRs are complete and of good quality with all the information necessary for assessing the reports.
3. It is the responsibility of the technical associate to ensure proper recording and filing of all received and processed ICSRs.
4. It is the responsibility of the ….. (immediate supervisor) to review all reports prior to assessment.

General considerations/instructions (applies primarily to technical SOPs)

Staff should handle all reports with great care ensuring that patient confidentiality is maintained at all times. Copying of ADR reports containing patient information should be kept at the minimum to prevent potential loss of confidential patient information. No one outside the PV Centre should be allowed to handle ADR reports. All Reports must be constantly kept under lock and key.

Procedures

1. Receiving reports

1.1. **Reports received by post**

- Open the envelope and remove the report
- Check that the report has the name of the hospital sending the report
- If not, get the hospital name from the envelope and fill the information on the report

1.2. **Reports received by fax**

- Check that the report has the name of the hospital sending the report
- If not, call the reporter to obtain the information and fill the information on the form.

1.3. **Reports downloaded from email.**

- Print out the report
- Check that the report has the name of the hospital sending the report
- If not, call the reporter to obtain the information and fill the information on the form

1.4. **Reports received by phone.**

- Fill all information on the form by asking the reporter.
- Ask the reporter to send the report again by one of the official ways (post, fax, email or online software)
- Keep the filled report out of processing until receive the official report

2. Checking reports for duplication, completeness and quality

- Using the name or initial of the patient, date of birth or age, name of suspected medicine and ADR reaction details including date of onset of reaction check for potential duplication of report
- If it is a duplicate from the same hospital, check to ensure that all reported information are captured then remove the duplicate report
- If it is a duplicate report on the same patient from different hospitals, check to ensure that all reported information are captured and remove the duplicate report then make a note in the thank you letter to the second hospital that another hospital has sent the report already
- If it is not a duplicate report, check to ensure that all information necessary for a valid report have been provided, are potentially ‘correct’ and logical
- If all information necessary for a valid report have not been provided, contact the reporter to obtain the missing information and any other useful information
- If the report is established to be a valid ICSR, proceed with further administrative processing of the report

3. Processing reports

- Generate a report code
- Make a photocopy of the report
- File the original copy of the report (indicate location for filing)
- Send the photocopy of the report for further technical processing

4. Sending acknowledgment letter/confirmation of receipt of ADR report to all reporters

- Extract relevant information from the report such as name of reporter, date the Centre received the report, date of filling the report and suspected medicine(s)
- Check if the reporter used the old reporting form (if so, inform the reporter to use the new form in the future in the letter of thanks with information on where to obtain the new form)
- Fill the details in the relevant sections of the letter of thanks/confirmation. See template for acknowledgement letter.
- Send the acknowledgement letter to …(indicate responsible person) for review and signature
- Send the signed acknowledgement letter to the reporter and file a copy

Documentation:

If there is SOP for filing of reports, then cross reference it here
Indicate where reports should be filed for future reference
Refer to template for acknowledgement letter
Refer to current version of ADR form in use

EQUIPMENT (Generally applicable to technical SOPs)

- Stamping pad
- Photocopier
- Scanner
- Telephone
- Fax

Quality Control & Quality Assurance:

All ICSRs must be checked for completeness and quality of information
Checks must be done to pick out all duplicate ICSRs
All acknowledgement letters must be reviewed and signed before they are sent to the reporters

References

None available

STANDARD OPERATING PROCEDURE FOR MANAGING INDIVIDUAL CASE SAFETY REPORTS (ICSR) DATA WITH VIGIFLOW SOFTWARE

SOP Name	SOP for Managing ICSR Data with VigiFlow Software
SOP Number	CPC/DDF/2013/06/08
Version No and Date	01 - 07 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

The purpose of this SOP is to establish a uniform procedure for managing Individual Case Safety Reports (ICSRs) received by the Cambodian PV Centre from the spontaneous reporting system with the VigiFlow software.

Vigiflow is a web-based Individual Case Safety Report (ICSR) management system that is specially designed for use by national centres in the WHO Programme for International Drug Monitoring. Data analysis can also be done with the software.

Scope

ICSR data managed in VigiFlow can be shared to stakeholders such as MAHs, Healthcare providers, PHPs, WHO or other regulatory agencies either as PDF files (hardcopy or electronic) or in E2B formatted XML files. The submission manager in VigiFlow helps to keep track of which ICSRs should be sent to an external contact and which have already been sent.

ICSRs will automatically be flagged for being copied to VigiBase, the WHO Global ICSR database when they are committed; however, national centres can easily remove this and thereby keep a specific report private.

This SOP gives an overview of how to use the VigiFlow software. Users of the software a re advised to read the user's guide contained in the software for detailed guidance and help on how to use the software. The procedures described here apply to all Cambodian PV Centre staff that enter, commit to VigiBase, retrieve and analyse ICSR data with the VigiFlow software. It covers ICSRs received from healthcare providers in the public and private sector, Public Health Programmes (PHPs) as well as those received from Marketing Authorization Holders in Cambodia.

Definitions/Acronyms

E2B is the standard format for electronic submission of individual case safety reports. The format includes provisions for transmitting all the relevant data elements useful to assess an individual adverse drug reaction or adverse event report. The data elements are sufficiently comprehensive to cover complex reports from most sources, different data sets, and transmission situations or requirements; therefore, not every data element will be available for every transmission.

E2B formatted XML (Extensible Markup Language) files – XML is a computer language designed to describe data.

MAH – A company/or individual or PHP that has been granted authorization in Cambodia to market any medicinal product.

PHPs – Public Health Programmes such as malaria, HIV/AIDS, TB, Vaccines, etc

Responsibilities

This SOP is written for CPC staff that manage ICSR data with VigFlow. All personnel who perform activities with this SOP must be computer literate and have basic understanding of the PV system as well as the VigiFlow software. Staff with these responsibilities must be able to navigate the software, analyse data and conduct relevant searches in the data.

1. It is the responsibility of …CPC staff.. (indicate the relevant staff) to correctly enter ICSR data into VigiFlow.
2. It is the responsibility of …..CPC staff that entre data into VigiFlow to review and clean entered data and ensure integrity of all data in VigiFlow
3. It is the responsibility of …..CPC staff to commit ICSR data entered into VigiFlow to VigiBase
4. It is the responsibility of …..CPC staff to periodically analyse data entered into VigiFlow and generate periodic reports/statistics related to the data
5. It is the responsibility of …..CPC staff to share such reports with other staff so as to improve management of ICSR data
6. It is the responsibility of …..CPC staff to liaise with the UMC on issues relating to the maintenance, management and use of the software.
7. It is the responsibility of …..CPC staff to share with all staff reports relating to the use of the software emanating from UMC especially reports relating to completeness of committed ICSRs
8. The head of the PV Centre is responsible for determining who within the Cambodian PV system e.g. staff of the PV Centre, PV focal persons, MAHs, etc, should be granted access to VigiFlow

General considerations/instructions

A web browser, preferably Mozilla Firefox or Internet Explorer, and an Internet connection are required in order to access VigiFlow. Adobe Acrobat Reader and Microsoft Office Excel are also required to view and access the output files. The Internet access is encrypted and any information stored in VigiFlow is only accessible by users within the same country/organisation identified by their individual user name and password.

All persons with access must keep their login credentials safe and must not grant access to unauthorized persons. They must maintain confidentiality of information in the software at all times.

Persons who are not familiar with the structure and functions of the VigiFlow software should first of all read the user guide provided in the upper left corner when you login to the software for detailed guidance on how to use the software before attempting to enter or retrieve data.

It is advisable to always code entries (where possible) especially information relating to medical conditions, suspected adverse drug reactions/events and drug names. Coding of ADRs should be done using the lower level term in WHO-ART that is closest in meaning to the description given by the reporter. Disease conditions and medicines are coded according to ICH-10 and WHO-DD respectively (embedded in the software).

Supplementary information on an ICSR that has already been entered into VigiFlow should be added when it becomes available. This can be done by retrieving the report using either the CPC report number of the worldwide unique number generated by VigiFlow.

Procedures

1. Entering data into VigiFlow

1.1. Using a Mozilla Firefox or Internet Explorer browser open the VigiFlow site on the internet webpage https://adr.who-umc.org
1.2. Enter your username and password to login and access the database
1.3. To enter a new ICSR, go to the top menu and select the option **report handling**, then select **new report**, then **standard report**.
1.4. If it is a standard report (not parent –child) go to the **Report information section** and fill all the information
1.5. Enter all information provided in the ICSR into the section on **information on sender** (see User guide for more details).
1.6. Enter all information provided in the ICSR into the section on **information on primary source(s)** (see User guide for more details). Note that the sender and the primary source is the same if the report was sent directly from the HCP to the CPC.
1.7. Go to the **Patient page** and enter all information on **patient characteristics** provided on the form (initials, date of birth/age at onset/age group, sex, etc). It is possible to expand the section to provide more information by clicking on **additional patient info**
1.8. Go to the **Test and procedures page** and enter all information on the results of any laboratory tests and procedures on the form. This information can be entered as free text or as structured information by clicking on ***add test*** and filling the information
1.9. Go to the **Relevant medical history page** and provide information on any relevant medical history of the patient provided in the form. The information can be entered as free test, structured text by clicking on ***add relevant medical history***
1.10. Go to the **Relevant past drug therapy page** and provide information on any relevant medicines the patient took in the past. This information is provided in a structured format. Information on more medicines can be provided by clicking on ***add past drug therapy***.

1.11. Go to the **Reaction page** and provide information on the suspected ADR. Information on suspected ADR is provided as structured text. Click on ***add new event*** to provide information on the patient's reaction. Each reaction on the report must be provided a reaction term by filling the 'reaction term' section. Information on the reaction as provided by the reporter is also entered in the section on 'Reaction/event as reported by the primary source' is also completed. See user guide for more details on providing information on suspected ADRs.

1.12. Go to the **Drugs page** and provide information on the suspected and concomitant (if available) drugs. Click in ***add new drug*** to provide information on any drug. See user manual for more information on how to edit, delete or switch a drug from suspected to concomitant or vice versa.

1.13. Go to the **Causality assessment page,** which is found either on the **reactions or drugs page** under the heading **'relatedness of drug to reaction'** and do an assessment on the relatedness of drug(s) to reaction(s). See user guide for more details on this.

1.14. Go to the **Overview page** on the left hand menu to see an overview of all information provided. All mandatory information not provided will be highlighted in red. Review all entered data to ensure that they were captured correctly as reported in the form.

1.15. Crosscheck to make sure that all medicines including their indication for use have been coded correctly and that information on dosing, administration and dates of use have been entered correctly

1.16. Go to the left hand menu and **Save report**. Reports can be saved at any time during the data entry process and come back to it.

1.17. Reports that have been saved can be made available to others by checking it in from the **list of reports** under assessment by clicking on ***check in*** icon next to the report on the list. See user guide for more information.

2. Reviewing and committing of reports to VigiBase

2.1. Enter your username and password to login and access the database

2.2. Using the **'list report'** (Reports under central assessment) function access all reports that have been submitted and pending review. See VigiFlow user guide for more information.

2.3. Review all pending reports by checking completeness and validity of entered information

2.4. Reports that have been reviewed can be made available to others by checking it in from the **list of reports** under assessment by clicking on ***check in*** icon next to the report on the list. However, reports will be automatically checked in when you commit them. See user guide for more information.

2.5. Commit all reviewed reports by clicking on **send report** then **commit report** to the search and statistics database or by clicking on the commit icon.

2.5. When the result of verification page appears, click on **send the report to the Uppsala Monitoring Centre when committed** to forward the report to VigiBase.

3. Retrieving and or analyzing data from VigiFlow

Committed reports can be found in the **list of committed reports**. Committed reports can be viewed, printed in pdf format or exported in E2B format. Committed reports can also be opened for editing as follow-up or amendment. See user guide for more details.

The full function in the search and statistics module is only available to users that have purchased the full version of VigiFlow. Users with the limited access version of VigiFlow can only see a listing of committed reports. See the User guide for more information on this and how to conduct search and statistics depending on the version available to your Centre.

4. Retrieving and or analyzing data from VigiBase

VigiLyze is a tool that can be used by national pharmacovgilance centres to analyse data committed to VigiBase.

Documentation:

A copy of all ICSRs entered into VigiFlow should be filed and retained in the Centre. Supplementary information received on an ICSR should be mapped to the original report and filed.

All reports generated from a query should be saved either electronically or as printed hard copies.

Quality Control & Quality Assurance:

All ICSRs must be checked for completeness and quality of information

Checks must be done to ensure that medical conditions, suspected adverse reactions/events and medicines are coded appropriately.

All entered reports must be reviewed by a supervisory prior to committing the report to VigiBase.

References

UMC VigiFlow user guide

STANDARD OPERATING PROCEDURE FOR ASSESSING INDIVIDUAL CASE SAFETY REPORTS (ICSRs)

SOP Name	SOP for Assessing Individual Case Safety Reports (ICSRs)
SOP Number	CPC/DDF/2013/06/03
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Implementation Date	06 June 2013
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

The purpose of this SOP is to establish a uniform procedure for conducting causality assessment on Individual Case Safety Reports (ICSRs) received by the Cambodian PV Centre.

Scope

These procedures are for all those who conduct causality assessment on ICSRs received by the Cambodian PV Centre. It covers ICSRs received from healthcare providers in the public and private sector, Public Health Programmes (PHPs) as well as those received from Marketing Authorization Holders in Cambodia.

Definitions/Acronyms

Individual Case Safety Report (ICSR): – A report that contains 'information describing a suspected adverse drug reaction related to the administration of one or more medicinal products to an individual patient...'

Serious adverse reaction - A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose:

- ☐ results in death,
- ☐ is life-threatening,
- ☐ requires inpatient hospitalization of prolongation of existing hospitalisation,
- ☐ is a congenital anomaly/birth defect,
- ☐ is medically important

Unexpected adverse reaction - An adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization, or expected from characteristics of the drug.

Dechallenge - The withdrawal of a drug from a patient; the point at which the continuity, reduction or disappearance of adverse effects may be observed.

Rechallenge - The point at which a drug is again given to a patient after its previous withdrawal

Marketing authorization holder (MAHs)

A valid report – a valid report is an ADR report that has all of the following information: An identifiable patient (name or initials, age/date of birth and sex); a suspected medicine (brand and/or generic name, date taken, indication for use, dose and route of administration); a suspected adverse reaction (with description of the reaction and onset date); and an identifiable reporter (name and contact details).

Responsibilities

This SOP is written specifically for CPC staff that receive, process and assess ICSRs. All personnel who perform activities with this SOP must have understanding of the PV system including the need for confidentiality.

9. It is the responsibility of the Technical Associate to ensure that all ICSRs received by the Centre have sufficient information for causality assessment
10. It is the responsibility of the Sub-coordinator and Technical Associate to conduct preliminary assessment on all ICSRs
11. It is the responsibility of the CPC coordinator to review all causality assessment done by the Sub-coordinator and the Technical Associate
12. It is the responsibility of members of the Expert Committee to review and conduct further causality assessment on all serious and unexpected ADR reports

General considerations/instructions (applies primarily to technical SOPs)

Healthcare providers (including MAHs) in Cambodia are required to report serious or unexpected suspected ADRs. However, the Centre also receives reports on non-serious ADRs. ADR reports will be classified into serious and non-serious reports for the purpose of conducting causality assessment.

Causality assessment should be carried out within 3 days of receipt for reports that have been classified as serious.

Staff should handle all reports with great care ensuring that patient confidentiality is maintained at all times. Copying of ADR reports containing patient information should be kept at the minimum to prevent potential loss of confidential patient information. No one outside the PV Centre should be allowed to handle ADR reports. All Reports must be constantly kept under lock and key.

Procedures

1. Classification of ADR reports

- Check the report to ensure that it is a valid report and has all information necessary causality assessment i.e.
- If not, make effort to get the information from the reporter
- If it is a valid report relating to suspected adverse reaction classify the report into serious or non-serious reaction based on the outcome of the reaction (see section on definitions for definition of serious reaction).
- If the report is on suspected lack of efficacy or quality issue, classify it in accordance with the categories below
- If the report is on medication error, classify it in accordance with the categories below

- Mark the report with the appropriate letter for its category as shown below;

'S' – Serious
'NS' – Non serious
'Q' - Quality issue/lack of efficacy

2. Conducting causality assessment on reports marked as non-serious reactions

- Check if there is a temporal relationship between the suspected medicine and the ADR (i.e. if the suspected medicine was taken prior to onset of the reaction) and note your finding.
- If the reaction occurred before the medicine was taken, cross check the information and consider other explanations for the event.
- If the medicine was taken before the reaction, note the time to onset of reaction i.e. the time from use of the medicine to when the adverse reaction started or occurred
- Check and note the duration of the reaction i.e. how long did the patient have the reaction
- Check literature sources to find out if the reaction can be explained by the pharmacological properties of the medicine
- Check if there was a rechallenge and or dechallenge and note the outcome of that
- Check if there was any change in dose and note the outcome of the change in dose (if any)
- Check literature sources for any known association between the suspected medicine and the reaction
- Check if the patient is taking any other medicine(s) that may be responsible for the reaction and note your findings
- Check if patient has any other disease condition that may explain the observed suspected reaction and note your findings
- Based on the answers to the above questions, assign a causality assessment grade using the WHO causality assessment criteria
- Record your assessment along with the reasons for the assessment and forward to the coordinator for review

3. Conducting causality assessment on reports marked as serious reactions

- Carry out causality assessment as soon as a serious reaction category has been established on a report
- Check if there is a temporal relationship between the suspected medicine and the ADR (i.e. if the suspected medicine was taken prior to onset of the reaction) and note your finding.
- If the reaction occurred before the medicine was taken, cross check the information and consider other explanations for the event.
- If the medicine was taken before the reaction, note the time to onset of reaction i.e. the time from use of the medicine to when the adverse reaction started or occurred
- Check and note the duration of the reaction i.e. how long did the patient have the reaction

- Check literature sources to find out if the reaction has been previously documented i.e. is a known reaction to the medicine.
- Record if it is a known reaction to the medicine or not, record findings
- Check literature sources to find out if the reaction can be explained by the pharmacological properties of the medicine
- Check if there was a rechallenge and or dechallenge and note the outcome of that
- Check if there was any change in dose or mode of administration and note the outcome of the change in dose (if any)
- Check if the patient is taking any other medicine(s) that may be responsible for the reaction and note your findings
- Check if patient has any other disease condition that may explain the observed suspected reaction and note your findings
- Based on the answers to the above questions, assign a causality assessment grade using the WHO causality assessment criteria
- Record your assessment along with the reasons for the assessment and forward to the coordinator for further review

3.1. Reviewing serious unexpected ADR reports

- If the reaction is previously unknown, in addition to the causality assessment and review by the Supervisor, forward the report to the Expert Committee for further assessment and review
- Send reports along with results of preliminary review to members of the Expert Committee for further assessment
- Obtain results of assessment from members of the Committee

3.2. Providing feedback on serious ADR reports

- Check national database and other ADR databases e.g. VigiBase for similar reports
- Conduct literature search on how to manage such reactions
- Check how the patient was managed for the ADR
- Provide feedback to healthcare giving information on the number of similar reports in local and or global database and information on suggested management of the reaction

4. Processing reports with quality/lack of efficacy issues

- Mark all reports with suspected lack of efficacy as ‘Q’
- Contact reporter for more information especially information on the product especially brand name, batch number, date of manufacture and expiry, name of manufacturer.
- Make effort to obtain the product (if possible the same one used by the patient) or a similar batch
- Send the product to the quality laboratory for analysis (if possible)
- Obtain report from the laboratory and review findings
- Provide feedback to reporter (if possible) based on findings

Documentation:
Cross reference WHO causality assessment criteria
Develop template for providing feedback to reporters

EQUIPMENT (Generally applicable to technical SOPs)

- Stamping pad
- Photocopier
- Scanner
- Telephone
- Fax

Quality Control & Quality Assurance:
Preliminary causality assessment should be done by individuals with sufficient PV on clinical assessment
Review of causality assessment on serious unexpected reactions should be done by persons with extensive clinical knowledge and experience

References
WHO-UMC. Glossary of terms used in Pharmacovigilance

A Guide on Signal detection/generation and analysis in PV

The primary purpose of spontaneous adverse drug reaction (ADR) reporting is to provide early warnings (signals) of hazards, which were not recognized prior to marketing of a drug due to the limitations of clinical trials. The process of searching spontaneous ADR data to identify hazards is known as signal generation. Once a signal has been generated, other sources of data are investigated and, if sufficient evidence of a public health issue is found, steps are taken by regulatory authorities to minimize the risks and inform users (1). Spontaneous reporting is therefore primarily a system for signal (hypothesis) generation after which further study using the most appropriate method (s) is required to test the hypothesis (2) in order to inform regulatory and policy decisions.

A signal is defined by WHO as "Reported information on a **possible causal relationship** between an adverse event and a drug, the relationship being **unknown or incompletely documented** previously." Usually more than one report is required to generate a signal, depending on the seriousness of the event and the quality of the information.
It is an **evaluated** association between a drug and an adverse drug reaction, which is considered **important to investigate further**, and may refer to **new information on an already known** association which further qualifies a simple association of a drug product with an ADR, for example, information on the range of severity of reaction, its outcome; postulating a mechanism; indicating an "at risk" group; a dose range which might be more suspect; or suggesting a pharmaceutical group effect or indeed a lack of such an effect by a particular drug (3,4,2). **A signal does not establish that a drug and event combination is causally related but suggests that further investigation is needed to clarify the observed association** (5). A signal is therefore a hypothesis together with data and arguments in favour and against the hypothesis. It is not only uncertain but also preliminary in nature as the situation may change substantially over time one way or another with availability of more data. A signal may also be more documentation

Sources of signals
Signals in pv are usually derived from observations in individual patients or in populations or from experimental studies and have qualitative and quantitative dimensions. Table 1 presents possible sources of signals (2,6).

Table 1. Possible Sources of signals (copied from ref 2 with slight modifications)

Type of signal	**Source**
Observations in patients (Qualitative signals)	Spontaneous reporting systems
	Anecdotal literature reporting
	Intensive hospital monitoring
	Prescription event monitoring (PEM)
	Follow-up studies
	Monitored release programmes
Observations in populations (Quantitative signals)	Large databases on morbidity, prescriptions and outcomes, drug use and pregnancy registries including record linkages
	Case control studies, case control surveillance
	Follow-up studies
	PEM
	Intensive hospital monitoring
	Large spontanoeus reporting systems eg WHO, USFDA, Adverse Drug Reaction Online Information Tracking (ADROIT) database of UK
Experimental findings	Clinical trials
	In vitro experiments
	Animal toxicology

Signal detection/generation process

Discovering an ADR from collated data is a step-wise process consisting of (i) hypothesis generation ii) hypothesis strengthening and preliminary assessment of available data and iii) signal testing, evaluation and explanation. The process of signal detection in PV refers primarily to the first 2 steps – generation and preliminary assessment of hypothesis (7).

The simplest method for detecting signals (hypothesis generation) involves periodic review of crude frequency data generated from spontaneously reported data to identify potential drug-ADR combinations of interest. Careful, informed, systematic and standardized clinical assessment of reports at point of collection facilitates the earliest possible generation of hypotheses (8).
National centres that have a small number of reports in their databases (perhaps less than 50,000 reports) can use this method. Regular and systematic review/screening of what is new in the database in the context of what was there previously should be undertaken. Usually this is done by reviewing all data for individual drugs (within-drug and between-drug crude numerical comparisons of reporting frequency or time trends) or products to find potentially interesting reactions. Another way is to get all data related to a particular reaction and review the suspected drugs (5,6). For example, to detect a signal previously, the UMC would periodically (usually

every 3 months) review all new ICSR reports received during a given time period to generate a list of all drug-ADR combinations. This combination data was then sent to a panel of experts for review and selection/detection of possible signals. The summaries of the signals detected by the experts were sent to National Centres (3).

Limitations to the application of this method in signal generation include the inherent limitations of spontaneous reporting systems viz underreporting, lack of exposure data, incomplete data, biases, etc (5). As the volume of generated data increases, it becomes difficult if not impossible; to effectively review such data on a case-by-case basis at the point of entry, as was the case in the UMC, necessitating clinical review of case series. Furthermore, lack of automation and follow-up within the system also negated continued use of the manual system of signal generation by the UMC (3). As many national centres around the world collected ICSRs of suspected ADRs by the tens of thousands, the traditional case-by-case assessment of reports was no longer feasible. The need for automated screening programs with the ability to identify signals of possible importance in large electronic databases becomes evident and inevitable

Automated and quantitative signal detection/generation

This is the use of automated screening programs to quantitatively compare combinations of drug-ADR against a background of all reports in the database and use statistical parameters to select the first signal. (2). In most cases, automated signal detection has been applied to post approval safety databases that are global in extent and contain hundreds of thousands to millions of adverse event reports. As at 2003, the smallest database to which automated signal detection was studied is The Netherlands Pharmacovigilance Foundation, which contained 39, 790 adverse event reports involving 17, 330 different drug-adverse event combinations (5).

Several statistical methods, which can be grouped into denominator- dependent methods and numerator-based methods have been suggested for quantitative calculations in surveillance activities including postmarketing safety surveillance. The denominator based methods use some form of exposure estimates and are mostly designed to detect temporal changes in reporting rates or frequencies by constructing a probability model and corresponding test statistic to assess the probability that observed temporal changes reflect random sampling variability. Examples are cumulative sum (cusum) techniques, time scans and Poisson methods. Most of these methods have had limited testing with spontaneous reports. On the other hand, numerator-based methods though based on similar principles are ‘self contained’ in that they do not require access to external data sets for exposure estimates. The proportional reporting ratios (PRRs) used by the UK, Bayesian Confidence Propagation Neural Network (BCPNN) used by the UMC and Empirical Bayes screening (EBS) used by the USFDA represent some of the most widely used numerator based quantitative methods (5).

The details of the underlying statistical model for these methods are outside the scope of this presentation and not discussed here. However, although the underlying models for these quantitative methods vary considerably, a common feature is an assessment of how much the observed reporting frequency of a given drug-event combination differs from that expected, given statistical independence between drug and event (5). With these methods, the computer selects the drug-ADR pairs that statistically stand out against the background of the database, according to prefixed statistical criteria (2,9). These are called associations. Once the computer has identified the associations that meet the preset quantitative criterion, individual assesors then select those associations that they consider deserve futher attention (2).

Since the number of associations generated by automated methods can be considerable and very often include false positives (10), many Centres employ triage strategies that use additional filtering criteria to prioritize associations and identify those that are more likely to be relevant signals. In addition to prioritizing associations, triaging also helps to reduce the volume of potential signals sent to experts (MDs, Pharmacists, specialists) for evaluation (1,5,11). Given that the number of associations generated by these methods for any given time period can be considerable, institutions planning on automated signal generation are advised to consider the resources required to evaluate the detected associations.
Some of the cirteria often employed in the triage process include; whether or not the association has been previously recognized (labelled in the product information on described in literature); how expected or unexpected the connection is from pharmacological point of view; the clinical characterisitics of the ADR (ie. Is it characteristic or non-specific, objective or subjective, rare or common, typical drug reaction or recognized infectious or endogenous disorder); relevance of the association (seriousness, severity); system organ cass (SOC) of interest e.g. foetal, neonates, neoplasms; potential preventability; herbal/ essential medicined (2,5,12).
In the case of UMC, identified priority associations are sent to relevant experts for clinical assessment to identify those they consider pertinent. Once the reviewer has identified pertinent signals that are worth notifying the collaborating centres, s/he writes a short report on the signal. After careful review within the UMC, the report may be included in the Signal document for distribution to national centres for signal strenghtening and testing. The report is also sent to the drug manufacturer for comment.

Automated quantitative signal detection methods have a number of advantages which include transforming of very large unmanageble amounts of data into portions of limited size that are easier to handle; detecting associations with the potential of being signals; objective and transparent data selection process that is not influenced by prior knowledge or bias of the investigator; and reproducibility of results. The fact that the selection process is purely quantitative and does not take into account medical and pharmacological considerations and could miss true connections that are not statisitically prominent are some of the limitations (2). It is crucial to remember that automated signal detection methods do not replace clinical case

review and interpretation by drug safety experts with experience in pharmacoepidemiology and clinical medicine.

How many reports of an individual drug/ADR combination are needed in a database before a drug related problem can be investigated?

There is no minimum on the number of reports required before a drug related problem can be investigated e.g: 5 reports in Australia on lumiracoxib and serious hepatic disorders triggered an investigation & alerted other countries (8).

A signal usually consists of a series of case reports of similar suspected ADRs to a particular drug of varying quality and likelihood. A single case is usually not sufficient for a signal. Often there is a minority of well documented 'index cases' supported by a large number of reports of lower quality (feasible cases) (6,13). When the ADR is a rare disease in the general population eg. aplastic anaemia, TEN, a small number of cases with the same drug is unlikely to be a chance finding, even when the drug has been widely used. In such a case, 3 cases may be considered a signal and 5 cases a strong signal. On the other hand, if the event is common in the general population then a large number of cases will be needed to detect a signal (6). See box 1 for explanation of index and substantial cases.

Box 1. Case information items and criteria for index cases copied from Ref 14.

Essential information: case-report "unassessable" if any item missing
Identification of source of case (e.g. reporting doctor)
Identification of case
Description of reaction
Name of drug
Treatment dates
Reaction dates

"Feasible" cases (Doc grade 1): all of the above items
Sex
Age
All drugs (product name specified) with the doses and date
Indication for treatment/underlying diagnosis
Outcome

"Substantial" (Doc grade 2) cases all of the above
Positive rechallenge = "presumptive" → "index case"
Negative rechallenge or no rechallenge and no confounding variables → "index case" (Doc grade 3)

Each information heading should be compered with negative statement where it does not apply rather than leaving plank. The decision to make a "substantial" case an "index case" should be fully documented with reasons e.g. no confounding variables relevant and pharmacological support for the hypothesis.

Explanatory note: "Case-reports containing information on all eleven major items were designated "substantial" and, and in the absence of any available confounding variables constitute an "index case", warning of a possible problem with the medication. (Rarely, substantial cases will include a positive rechallenge, which is generally accepted as strong evidence for causality; such cases could be regarded as "presumptive".) Cases with less documentation are labelled either "feasible" or, if the missing informations does not permit a judgment, "unassessable"." "The level of documentation needed for publication is suggested as three index cases; two index cases plus two substantial or four (4) feasible cases; or one index case plus four substantial or eight feasible or any other combination making equivalents of three index cases." (14). This could provide some guidance on the question of how many reports are needed to initiate signal investigation.

How to know when events are not recognised reactions?

The following resources need to be checked to determine if an identified potential signal is labeled or not - the *Martindale extra pharmacopeia, DrugDex, Physicians Desk Reference* (PDR). All available on website of Micromedex Healthcare Series http://www.micromedexsolutions.com. Other sources include published case reports, product information leaflet, drug safety bulletin, etc (8,9).

Signal strengthening

Once a signal has been recognised and assessed, there is need to follow up the signal to see how it evolves over time in the database. The absolute number of cases, statistical parameters, exposure to the drug (utilization), persistence of the characteristics and consistency of reporting, causality assessment at individual case level are all elements to be looked for in the database. Often further analysis of the database can provide preliminary assessment of the strength of the signal. Making a variety of comparisons using the database e.g. comparing different drugs, different drug groups or drug combinations, can help produce a better picture of the connection in the drug-ADR combinations. Beyond the database other data sources such as looking at reporting patterns in different countries (possibly with similar population) is also very helpful as a signal with reports from multiple countries may be stronger than reports from just one country, VigiBase, experimental observations, drug safety bulletins, etc may provide useful information that will support or explain the signal (2,15).

The strength of the signal is therefore determined by a combination of assessment of individual reports on a case-by-case basis, assessment of the aggregated data and information from other sources (2,8).

Detected signals should be reported to the advisory committee &/or regulatory authority, local health practitioners, the Uppsala Monitoring Centre, local ADR bulletin and medical journals.

Box 1. A summarized practical 8-step procedure to provide guidance to national centres on how to manage signals. Copied from Ref 7.

Step 1. Select the relevant data (case reports) and delineate the signal hypothesis

Step 2. Conduct literature search

Step 3. Survey available data to identify missing data and unanswered question

Step 4. Gather missing data (follow-up of cases, structured enquiry)

Step 5. Consult with the UMC

Setp 6. Contact the pharmaceutical company. Study the data in the registration file

Step 7. Assess or reassess all available data including complete case reports using quantitative criteria that determine the strength of the association such as number of cases in relation to exposure to the drug, statistical disproportionality and significance. Qualitative criteria should also be applied such as consistency of data (presence of characteristic feature or pattern and absence or rarity of converse findings), exposure-response relationship (site, timing, dose response, reversibility), biological plausibility of the hypothesis (pharmacological and pathological mechanisms), experimental findings (rechallenge, diagnostic markers, abnormal metabolites), nature and quality of data (accuracy and validity of documentation, case causality assessment)

Step 8. Write a report containing (i) a summary of the signal, (ii) a presentation of the original data, (ii) a presentation of additional information (iv) discussion with reference to positive and negative arguments, (v) a conclusion even if preliminary and (vi) suggestions for further study.

Signal testing

In view of the limitations of the spontaneous reporting systems, signals generated from these systems are considered as hypothesis and therefore are uncertain in nature. Before any action can be taken based on this hypothesis, it becomes critical that further studies using the most appropriate method(s) have to be undertaken to test the hypothesis and resolve outstanding issues.

Comprehensive pharmacoepidemiological studies may aid signal testing and add to the scientific basis of post-approval decision-making. However, since pharmacoepidemiological studies take time and require funding, and serious safety issues require immediate action, immediately available sources of retrospective information such as epidemiological databases may be used to provide rapid answers to important questions and facilitate risk management decisions (2,6).

Signal detection: points to remember

1. A **statistical** association is **not** a signal, but it needs clinical review (8).

2. Just reaching above a treshold is not a signal.

3. Signal detection depends on;
   - Seriousness of the ADR, e.g macular rash vs SJS
   - Risk-benefit profile for that drug, e.g. painkiller vs chemotherapy agent
   - Temporal relationship between drug & ADR
   - Causality assessment (i.e. certain, probable, possible, unlikely)
   - If it is an expected or unexpected reaction?
   - Quality of the reports (value-added information provided e.g. Date of onset, concommitant drug, etc)

   Other considerations
   - Occurrence of ADR during the first years post launch
   - Drug with a high media attention
   - Risk perception by general population
   - Report from multiple countries
   - Clustering of events

4. Signal triaging/prioritization is a necessary step - points to consider:
   - New unexpected reactions
   - Medically significant
   - Important public health impact (e.g wide usage, significant off-label use,direct to consumer programmes)
   - Presence in vulnerable population
   - Rapidly increasing disproportionality
   - Presented as potential risk in risk management
   - Potential preventability

5. Analysis of reported case series should consider
   - confounding by disease or co-medication
   - known mechanism
   - consistency between cases
   - time to onset
   - dechallenge/rechallenge

- reporting geographics

Box 2. Signal detection/generation process flow in a nutshell.

- Systematic review of database (Qualitatively or quantitatively) to detect 'interesting' Drug-ADR combinations
- Triage/Prioritise to find 'most relevant' associations
- Obtain further information to review and analyse 'most relevant' associations to identify potential signals
- Strengthen signal with more information from various information sources
- Notify Partners
- Test signals

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STANDARD OPERATING PROCEDURE FOR PROVIDING DRUG INFORMATION TO HEALTHCARE PROVIDERS AND RELEVANT STAKEHOLDERS

SOP Name	SOP for Providing Drug Information to Healthcare Providers and Relevant Stakeholders
SOP Number	CPC/DDF/2013/06/03
Version No and Date	Draft 1.0 - 04 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

The purpose of this SOP is to establish a uniform procedure for processing requests on and providing drug information to healthcare providers and relevant stakeholders in Cambodia.

Drug information is a vital aspect of Pharmacovigilance. It avails healthcare providers with up-to-date and objective information on medicines to enhance rational use of medicines and patient safety.

Scope

These procedures apply to all Cambodian PV Centre staff that receive, process, obtain and share drug information with stakeholders. It covers requests for drug information received from healthcare providers in the public and private sector, Public Health Programmes (PHPs), Marketing Authorization Holders, public and private hospitals and the general public in Cambodia.

Definitions/Acronyms

Responsibilities

This SOP is written specifically for CPC staff that receive, process and provide drug information to relevant stakeholders.

1. It is the responsibility of any staff of the Centre to receive requests for drug information.
2. It is the responsibility of the Technical Associate to search literature sources for and obtain information relevant to the request.
3. It is the responsibility of the Technical Associate to compile the information in a logical and easy to understand manner for the recipient.
4. It is the responsibility of the Coordinator to review the information and ensure its accuracy, currency and relevance to the request and to provide approval for responding to the request based on the gathered information.
5. It is the responsibility of the Administrative staff to send the response to the requester.

General considerations/instructions (applies primarily to technical SOPs)

Staff should ensure that information that is being provided on medicines is up-to-date, accurate, relevant and objective. Hence, thorough research on the issue must be done prior to providing information as the information provided may have a bearing on the use of such products. The need to ensure patient safety must be at the forefront of all medicine related information.

It is important to keep record of all information requests and the responses provided to such requests for reference purposes. Such records could be kept, maintained and managed in either hard or electronic format or both.

Procedures

1. Receiving medicine requests

1.1. **Requests received by email**

- Check the Centre's email account on a daily basis and print out all mails requesting for medicine information
- Forward the email to relevant members of the Centre for information and necessary faction
- Check that the following information about the person or organization requesting the information including the drug information request are provided in the email;
  - Name of the requester
  - Name of organization
  - Profession
  - Job position
  - Contact details (phone number, email address, etc)
  - Date of enquiry
  - Urgency of request
  - Date on which response/feedback is needed
  - Preferred means of receiving response/ feedback
  - Drug information request
- If not, contact the requester to get the necessary information
- Document the details of the information request in the system used for managing drug information requests.
- Forward the request with all necessary information about the requester to the responsible staff for further action

1.2. **Requests received by phone call or one-on-one interactions.**

- Obtain the following information about the person or organization requesting the information;
  - Name of the requester
  - Name of organization
  - Profession
  - Job position
  - Contact details (phone number, email address, etc)
  - Date of enquiry
  - Urgency of request

  - Date on which response/feedback is needed
  - Preferred means of receiving response/ feedback
  - Drug information request
- Carefully write out the question(s) being asked by the requester on a sheet of paper or notebook and if possible read it back to the person to make sure that the question was clearly understood
- Indicate the name of the staff that received the request as well as time and mode of reception
- Document the details of the information request in the system used for managing drug information requests.
- Forward the request with all necessary information about the requester to the responsible staff for further action

2. Obtaining information and responding to drug information requests

- Consult various literature sources for information that will assist in responding to the request including:
  - Micromedex
  - Drug Information Handbook
  - Martindale
  - Pubmed
  - MedicinesComplete
- Drug use in pregnancy and lactation
- Website of other drug regulatory agencies in the world
- Draft a response to the request based on information obtained from the literature sources
- Crosscheck information in draft response to ensure that it is accurate, current and relevant to the drug information request.
- Send draft response to the Coordinator to review and approve before it is sent to the requester
- Send the reviewed and approved response to the person(s) or organization that requested the information within the requested time, using the preferred means of receiving feedback indicated by the requester
- If you are unable to send the response within the agreed timeframe, contact the requester and explain the reason for the delay and agree on a new date to send the response
- Document the response sent to the requester
- Follow up with the requester after sending the response to confirm receipt, adequacy of response and satisfaction with provided information
- Note result of follow-up (if applicable)

Documentation:
Specify where requests should be filed/ documented for future reference

EQUIPMENT (Generally applicable to technical SOPs)

- Stamping pad
- Photocopier
- Scanner
- Telephone
- Fax
- Reference materials such as: Evidence-based portals (Micromedex, MedicinesComplete, etc); official books (Martindale, Drug benefits &Risks, BNF, National formularies, etc); ADR journals and other publications (WHO Newsletter, Reactions Weekly, Signal, Drug Safety); websites of well established PV Centres (FDA, EMA, New Zealand PV Center, TGA, France, etc); databases (Cambodian national ADR database, VigiBase); information from countries with similar population, etc.

Quality Control & Quality Assurance:
All out going information on medicines must be checked by the Coordinator to ensure that it is current, adequate and relevant to the information requested.
It is advised that the Coordinator endorses all responses by signing them before they are sent to requesters.

References
None available

STANDARD OPERATING PROCEDURE FOR MAINTAINING THE WEBSITE OF THE CAMBODIAN PHARMACOVIGILANCE CENTRE

SOP Name	SOP for Maintaining the Website of the Cambodian Pharmacovigilance Centre
SOP Number	CPC/DDF/2013/06/07
Version No and Date	01 - 06 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

A Pharmacovigilance website is a vital and additional tool used by PV Centres to fulfill the functions of:

i) providing latest and up-to-date information about the Centre's activities
ii) giving drug information and providing access to some relevant Pharmacovigilance (PV) databases
iii) educating healthcare providers on drug safety issues through interactive question and answer/ discussion / chat forums
iv) providing online access to clinical and therapeutic bulletins of the Centre and other websites
v) providing access to the Centre's ADR reporting form, receiving ADR reports and providing information on ADR related issues
vi) encouraging cooperation and collaboration with partners through information sharing.

This SOP describes the procedures for maintaining the PV website to ensure that visitors to the site always get the latest information about the activities of the PV system in Cambodia as well as accurate and up-to-date information about drug and patient safety issues.

Scope

These procedures apply to those who maintain the website of the Cambodian PV Centre staff. It covers issues related to receiving, reviewing, updating, and uploading of information on the website.

Definitions/Acronyms

Define any relevant acronyms

Responsibilities

- The staff of the Centre are responsible for furnishing the Information technology and communication staff with the materials/documents that will form the content of the website
- The staff of the Centre are responsible for ensuring correctness of all materials/documents provided to the Information technology (IT) personnel for uploading on the website
- The Information technology (IT) personnel is responsible for technical administration of the website
- The IT personnel is responsible for ensuring that the website is running smoothly and meets all the functions for which it was set up
- The IT personnel is responsible for ensuring timeliness of currency of content provided on the website

- The IT personnel is responsible for ensuring that all news items/articles posted on the website meet all legal requirements and do not infringe local, regional or global publication laws relating to use of the Internet.
- The IT personnel is responsible for determining and obtaining relevant local authorizations needed to maintain a website to ensure compliance with extant laws and regulations
- The head of PV Centre is responsible for reviewing all documents to be uploaded on the website and giving final approval for posting/publishing such documents/news articles on the website

General considerations/instructions (applies primarily to technical SOPs)
If none applies, remove this section

Procedures

1. For technical administration of website:

1.1. Constantly check to ensure that the website is running smoothly and can be accessed from any where at all times

1.2. Constantly ensure that there is sufficient system storage space on the website to handle programme database and traffic to the site

1.3. Ensure that all uploaded files are in the right format and size to ensure ease of access by readers. If uploaded files are large, compress them to create more memory space.

1.4. Always check for technical errors that may impede the functioning of the website and make sure that all identified errors are promptly fixed

1.5. Periodically defragment and compact the database for more efficient operation

1.6. Upgrade software and associated applications, as necessary

1.7. Perform routine virus checks on incoming and outgoing files

1.8. Manage all accounts (add, alter and delete users, roles and privileges) on the website:

1.8.1. Maintain an approved list of valid users
1.8.2. Create or add new accounts/users
1.8.3. Delete accounts/users
1.8.4. Grant, alter or deny permission to access the website

1.8.5. Define and control roles and privileges (grant special permission to access; write, read and modify contents of website
1.8.6. Ensure that all activated accounts are live and have the right permission.
1.8.7. Constantly check the access and usage of all valid accounts to ensure security of data system and prevent misuse of website.

2. For content administration of website

2.1. Ensure that the website is constantly updated with accurate, current and relevant information with date of the last update clearly stated
2.2. Remove news items and other information that have become obsolete and no longer relevant
2.3. Keep readers informed about upcoming events being planned and organized by the Centre such as conferences, meetings, training courses, etc
2.4. Ensure that news about events that have taken place such as conferences, meetings, training courses, etc is published as soon as possible but not later than one day after the event has taken place
2.5. Ensure that the Pharmacovigilance bulletin/newsletter (if in hard copy) is published online no later than 10 days after publication of the hard copy
2.6. Check to ensure that each information/news item on the website is placed in the right section for such information on the website
2.7. Ensure that the following information is provided for each information/news item on the website:

- Title
- Full content with illustration/images (where available)
- Sources of information/news and images
- Authors of information/news items
- Name of images
- Keywords
- Date information was published on the website
- Download link

2.8 . Ensure that links and attachments to information/news items are correct and live
2.9 Ensure approval is obtained from the head of the PV Centre before posting/publishing all information/ news items on the website
2.10 Ensure that all contents of the website comply with extant laws and regulations of the country regarding such online publication

Documentation:
Indicate if any documentation requirements exist otherwise delete this section

Quality Control & Quality Assurance:
All information must be reviewed and approved by the head of PV Centre before being published on the website. Strict access control to the content of the website will be maintained with only few people granted access to add, edit or delete website contents.

References
None available

STANDARD OPERATING PROCEDURE FOR ORGANIZING TRAININGS AND WORKSHOPS

SOP Name	SOP for Organizing Trainings and Workshops
SOP Number	CPC/DDF/2013/06/06
Version No and Date	01 – 5 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose
The purpose of this SOP is to establish a uniform procedure for organizing in-service trainings for healthcare providers, workshops, meetings and or conferences with relevant stakeholders in PV. The SOP provides step-by-step- guidance and activities to be undertaken in organizing these events to ensure that such outings are efficiently and successfully organized and participants participate effectively.

Scope
The SOP covers the activities that need to be undertaken before, during and after the event. It also identifies those responsible for each activity throughout the process

Definitions/Acronyms
Define all relevant acronyms if available

Responsibilities
This SOP is written specifically for CPC staff involved in organizing trainings, workshops and or conferences on behalf of the Centre.

- It is the responsibility of staff of the Centre to ensure that all necessary arrangements such as identifying and securing the venue of the meeting, sending out invitations and confirming participation, booking hotel accommodation and flight tickets, photocopying and packaging of meeting materials, etc are made prior to the evet
- It is the responsibility of the Head of the PV to set the date for the meeting, establish the agenda and set budget for the event.
- The Head of the PV Centre is also to ensure that resource persons are given adequate information about their participation at the event i.e. if they are expected to make presentations or provide expert guidance on particular issues
- During and after the event, staff members are responsible for registering participants and giving them the meeting materials, recording proceedings at the event, covering the event electronically with camera and video coverage if possible, developing reports of such outings, reconciling actual expenditure with the budget and ensuring proper documentation of all expenses.

General considerations/instructions
None relevant to this procedure

Procedures

Planning for the Event

1.1. Develop an event plan with the following details
- Date of event (proposed)
- Objective/agenda for event

- Category of participants with tentative list of participants
- Estimated Budget

1.2. Identify relevant and potential resource persons and or key stakeholders and assign topics for presentation or roles for the event

1.3. Notify identified resource persons (if any) of the date, location, objective of the event and their expected role and or topic(s) for presentation to confirm their availability for the proposed day of the event

1.4. Identify and secure the venue of the event by preparing and signing a contract with the provider and ensuring availability of the following:
- Equipment: laptop, projector & screen, sound and light system, etc
- Tea break and lunch

1.5. When the date for the event has been agreed with the resource persons and or key stakeholders, and the venue has been secured, produce invitation letter for resource persons and participants with the following details clearly outlined

- Organizer
- Agenda
- Date & time
- Location
- Category of participants
- Perdiem for participants
- Contact person
- Deadline for confirming participation

1.6. Send out invitation letters to all resource persons and participants)

1.7. Confirm participation by calling or sending emails to get a list of confirmed participants

1.8. Book hotel accommodation and flight tickets for participants (if applicable)

1.9. Inform participants about their hotel and travel arrangement (if any) and send all information related to their participation

1.10. Remind resource persons to prepare their presentations and send the slides to the Centre not later than three days before the event and review sent presentations

1.11. Translate all presentations that need to be translated

1.12. Design the cover page of the training manual/event brochure and event banner for the venue and obtain approval for it before printing

1.13. Purchase bags, stationeries, name tags and other items to be used for the event (if applicable)

1.14. Print and photocopy all presentations, agenda and other documents for the event

1.15. Pack all documents and stationeries into the bags, get bags ready for conveyance to event venue

1.16. Prepare payment vouchers and other documents that will be signed by participants upon receipt of travel allowances

1.17. Calculate and package monies to be paid to each participant (if applicable)

2. Executing the Event

2.1. Welcome all participants and resource persons to the venue, register them by getting them to sign the attendance sheet and give out the meeting materials
2.2. Ensure that all presentations are downloaded on the laptop connected to the projector for use during the meeting
2.3. Pay travel and other allowances to participants (if applicable)
2.4. Take record of proceedings at event including writing minutes, photographic and video coverage (where possible) and perform other secretarial duties as may be necessary.

3. Post meeting activities

3.1. Develop a draft report of the event and present to the Head of PV Centre for review

3.2. Revise the report based on the input/comments from the Head of PV Centre to produce the final version

3.3. Send final report to Head of PV Centre for final approval

3.4. Share final report with all participants at the event

3.5. File the final report of the outing appropriately

3.6. Produce final financial report by collating and reconciling all payments and submitted supporting documents

3.7. File the financial reports appropriately.

Documentation:
Ensure proper documentation and filing of technical and financial reports of all such outings organized by the PV Centre.

Quality Control & Quality Assurance:
Reports of events should be reviewed by the head of PV Centre before it is finalized.
Where payment is to be made, care must be taken to ensure that proper financial checks and controls are followed.

References
None available

STANDARD OPERATING PROCEDURE FOR ORGANIZING EXPERT COMMITTEE MEETING

SOP Name	SOP for Organizing Expert Committee Meetings
SOP Number	CPC/DDF/2013/06/05
Version No and Date	01 – 5 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose
The purpose of this SOP is to establish a uniform procedure for organizing regular meetings of the Expert Committee for the Cambodian PV Centre. It describes the steps and activities to be undertaken in organizing meetings of the Expert Committee to ensure that such meetings are efficiently and successfully organized and executed.

Scope
The SOP covers the activities that need to be undertaken before, on and after the meeting day. It also identifies those responsible for each activity throughout the process

Definitions/Acronyms
Define all relevant acronyms if available

Responsibilities
This SOP is written specifically for CPC staff involved in organizing expert committee meetings.

- It is the responsibility of staff of the Centre to ensure that all necessary arrangements such as identifying and securing the venue of the meeting, sending out invitations and confirming participation, booking hotel accommodation and flight tickets, photocopying and packaging of meeting materials, etc are made prior to the meeting
- It is the responsibility of the Head of the PV to set the date for the meeting, establish the agenda and set budget for the meeting.
- The Head of the PV Centre is also to ensure that Committee members are given adequate information about their participation at the meeting i.e. if they are expected to make presentations or provide expert guidance on particular issues
- During and after the meeting, staff members are responsible for registering participants and giving them the meeting materials, recording proceedings at the meeting, covering the meeting electronically with camera and video coverage if possible, developing and sharing minutes of the meetings, reconciling actual expenditure with the budget and ensuring proper documentation of all expenses.

General considerations/instructions
None relevant to this procedure

Procedures

1.Planning for the meeting

1.1.Develop a meeting plan with the following details

- Date of meeting (proposed)
- Objective/agenda for meeting
- Estimated Budget

1.2.Contact all Expert Committee members to confirm their availability for the proposed date and fix date for the meeting based on availability of majority of Committee members

1.3.Identify resource persons that will make presentations at the meeting (if necessary) including external experts (where their particular expertise may be required for the issues to be discussed)

1.4.Notify resource persons (if any) of the date, location, objective of the meeting and their expected topic(s) for presentation/discussion

1.5.Identify and secure the venue of the meeting and ensure availability of the following;

- Equipment: laptop, projector & screen, sound and light system
- Refreshment

1.6.Produce invitation letter for all Expert Committee members clearly stating the date, time and venue of meeting

1.7.Send out invitation letters with meeting agenda, minutes of the previous meeting, all relevant reference materials for discussion (if any)

1.8. Confirm attendance by calling or sending emails to get if necessary and develop list of confirmed participants

1.9.Book hotel accommodation and flight tickets for participants (if applicable) and inform participants about their hotel and travel arrangement prior to the meeting date

1.10. Print and photocopy all presentations, agenda, minutes of previous meeting and other documents for the meeting

1.11. Prepare and pack all documents ready for meeting

1.12. Prepare payment vouchers and other documents that will be signed by participants upon receipt of travel allowances

1.13. Calculate and package amount to be paid to each participant (ifapplicable)

2. Executing the meeting

2.1. Welcome Committee members to the venue, register them by getting them to sign the attendance sheet and give out the meeting materials

2.2. Ensure that all presentations and minutes of the previous meeting are downloaded on the laptop connected to the projector for review at the meeting

2.3. Pay travel and other allowances to participants (if applicable)

2.4. Take record of proceedings at meeting including writing minutes

3. Post meeting activities

3.1. Develop the draft minutes of the meeting and present to the Head of PV Centre for review

3.2. Send a copy of the reviewed draft minutes of the meeting to Committee members who were present at the meeting for their review and input

3.3. Revise the minutes based on the input/comments from Committee members and send the revised minutes to the Head of PV Centre for final review

3.4. Approve final minutes for circulation to members

3.5 Circulate final copy of minutes of the meeting to all members including those that did not attend the meeting

3.6. File the minutes of the meeting appropriately

3.7. Produce final financial report by collating and reconciling all payments and submitted supporting documents

3.8. File the financial reports appropriately

Documentation:
Document and file all the minutes and financial reports for each meeting

Quality Control & Quality Assurance:
Minutes of the Committee meetings should be reviewed by all Committee members and head of PV Centre before it is finalized.
Where payment is to be made, care must be taken to ensure proper financial checks and controls are followed.

References
None available

STANDARD OPERATING PROCEDURE FOR DEVELOPING AND PUBLISHING PHARMACOVIGILANCE BULLETIN/NEWSLETTER

SOP Name	SOP for Developing and Publishing Pharmacovigilance Bulletin/Newsletter
SOP Number	CPC/DDF/2013/06/04
Version No and Date	Draft 1.0 - 04 November 2014
Implementation Date	
Prepared by	
Signature and Date	
Reviewed and Approved by	Head of Pharmacovigilance Center
Signature and Date	
Authorized by	Director of Department of Drugs and Food
Signature and Date	
Unit	Cambodian Pharmacovigilance Centre
Department	Department of Drugs and Food (DDF)
Ministry	Ministry of Health

Purpose

This SOP outlines a step-by-step procedure to be followed for developing and publishing a Pharmacovigilance bulletin/newsletter.

A PV bulletin/newsletter is a veritable means through which a PV Centre can communicate with healthcare providers by either providing general information on use of medicines, specific medicine safety related issues or giving specific feedback on safety issues arising from information on ADRs collected by the PV Centre. It also provides stakeholders an avenue to contribute to the discussion on and participate more actively in drug and patient safety monitoring. Doctors, pharmacists and nurses are the primary audience for the PV bulletin/newsletter. Other health providers such community health workers and the general public may also access the bulletin. It is necessary therefore to provide practical, reliable and up-to-date information about medicines so as to promote rational and informed use of medicines.

Scope

The SOP covers procedures related to how to select topics for publication, responsibilities of various persons, setting up editorial teams, reviewing articles and publishing the finished bulletin/newsletter.

The procedures described apply to all Cambodian PV Centre staff that are involved in developing and publishing PV bulletin/newsletter.

Definitions/Acronyms

Provide all relevant acronyms in final SOP

Responsibilities

It is advisable that an editorial team made up of dedicated individuals from different fields should be set up for handling the bulletin. An editorial team can range from one or two people to around 25 people. This does not include technical staff, external reviewers or advisers. The members of the editorial team ideally should:

- have relevant training in therapeutics and/or public health
- be capable of critical analysis and synthesis of data
- have reasonably good knowledge of English, as many scientific articles are available only in English
- include health practitioners e.g. doctors, pharmacists and or nurses
- include patients and lay people in addition to the above if the bulletin is aimed at the public and patients.

It is useful to build and have a database of critical reviewers who could become new members of the editorial team over time. It may also be strategic to institute an advisory board and ask

influential persons such as the dean of a medical faculty, the president of a professional association of doctors or pharmacists or an official of the Ministry of Health, to become advisers or board members.

The editorial team is responsible for selecting and defining the outline of topics for articles, producing articles, editorial planning, ensuring the necessary documentation, organizing the work of authors and reviewers, quality control, and analysis of feedback from readers. The team will be responsible for ensuring that information provided in every issue of the bulletin/newsletter is always fresh, current, relevant to the local context and timely. Care should be taken to ensure that translation of articles that are originally in English does not lead to a change in the meaning.
In the absence of an editorial team, these responsibilities should be handled by trained staff of the CPC.

The Editor-in-chief has overall responsibility for the content bulletin.

General considerations/instructions (applies primarily to technical SOPs)
A decision should be made abinitio on the regularity for publication of the bulletin/newsletter i.e. whether new editions will be publish on a weekly, monthly, quarterly, semi annually or annual basis. Every effort should be made to ensure that the frequency of publication is adhered to.

If there is an editorial team, advisory group and or external reviewers, care should be taken to ensure that members do not have any conflict to interest for example, that they do not have financial ties to the pharmaceutical industry.

Procedures

1. Researching topics for use in each edition of the bulletin/newsletter
Each member of the editorial team (or CPC staff where editorial team does not exist) should

- Check ADR databases (local and global) and reference sources to find potential issues of current interest that may be published in the Bulletin/newsletter (see section on potential sources of materials for publication (internal and external sources)
- Check for potentially interesting safety issues from the following sources:
    + cluster of serious ADR reports on a particular product brand in the local ADR database
    + numerous reports of non serious adverse effects to a particular product brand within a short period of time
- Itemise the potential issues of interest and submit for review (by the whole team or by the Coordinator if no editorial team) and selection of suitable topics for publication.
- If no topic was found suitable for the next issue of the publication, further review of the reference sources should be done for other topics of interest.

- If any of the identified topics is deemed suitable for publishing, editorial team or Coordinator (whichever is applicable) should communicate the decision and solicit for articles.

2. Developing articles for publication

- Inform all editorial team members (or staff members) of the topic for the next edition of the bulletin
- Solicit for articles from members and other stakeholders especially, professionals who are experts on the topic or assign topics to staff to write
- Give all authors a timeframe for submitting written articles
- Send reminders to authors at various time intervals before the deadline for submission of completed articles.
- Collect completed articles at the expiration of the deadline for review

3. Reviewing articles

- Forward completed articles to different members of the review team, if available for review. Different reviewers may be used for different topics based on their specializations/areas of interest.
- If a review team has not been instituted, completed articles should be forwarded to members of the editorial team for review
- Give all Reviewers a timeline within which to return reviewed articles with their comments
- If minor reviews/modifications were made to the article, effect corrections and move on with the process.
- If major modifications were made, return the article with the review/comments to the author for revision giving a timeframe for the return of a revised article
- If no modification is needed, move on with the process as described below
- Submit all articles to the designer/printer to typeset and produce a dummy copy.
- The Designer/printer develops a maquette based on the submitted articles.
- The Designer sends maquette to Coordinator and members of the Editorial committee (email) for review
- If no modification is needed for the maquette, continue with publishing
- If modification is needed, return the maquette to the designer/printer for necessary modification and give timeline for submission.
- Send revised publication (in colors) to editorial team for final comments
- Send finalized revision to Editor-in-chief for sign off and authorization to publish

4. Printing/publishing of bulletin/newsletter

- Give go ahead to print the new issue of the bulletin/newsletter (if publication is by hard copy) or put it in a format that cannot be edited (if publication is by electronic means)
- Upload Bulletin/newsletter to the PV website
- Distribute copies (if printed)
- Share the link to the website with stakeholders via email
- File all documents related to the publication and index the Bulletin/newsletter

Documentation:

Index all issues of the bulletin/newsletter for future reference. Update the index immediately after publication of each issue. Properly document all documents and correspondence arising from each issue of the publication.

MATERIALS (Generally applicable to technical SOPs)

Useful sources of information include other bulletins, local or national drug formularies, standard treatment guidelines or protocols, selected medical and pharmaceutical journals and books. Develop links with universities, medical and pharmaceutical associations, research centres, libraries, consumer organizations, government departments and non-governmental organizations.

Some valuable reference materials include: Evidence-based portals (Micromedex, MedicinesComplete, etc); official books (Martindale, Drug benefits &Risks, BNF, National formularies, etc); ADR journals and other publications (WHO Newsletter, Reactions Weekly, Signal, Drug Safety); websites of well-established PV Centres (FDA, EMA, New Zealand PV Center, TGA, France, etc); databases (Cambodian national ADR database, VigiBase).

Quality Control & Quality Assurance:

Articles must be properly reviewed and revised if necessary to ensure correctness of information.

- Check that each time a reference is cited, the information in the article corresponds to the information in the reference (figures, dates, doses, quotations, claims, etc.)
- Check that the content of tables, figures and graphs corresponds to what is stated in the text
- Make sure that editing of complicated sentences has not changed their meaning or introduced errors. Care must be taken to ensure accuracy of translation of articles that were originally in English.
- Check each article's coherence and how well it hangs together as a whole
- Make a final check of the conclusion – check that it still reflects the content of the text.

The use of an editorial team and a team of independent critical reviewers will help to ensure that quality is inputted in the production of the bulletin/newsletter.

References

1. ISDB, WHO, EC 2005. Starting or strengthening a drug bulletin: A practical manual Available from http://apps.who.int/medicinedocs/pdf/s8111e/s8111e.pdf. Accessed December 19, 12

2. Joshi M. 2010. Report on Technical Assistance for Drug Information and Pharmacovigilance Activities of the DI & ADR Centre in Vietnam. Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health.

3. Pharmacovigilance Toolkit version 2.0 24th January 2001

List of Annexes

1. Potential useful local topics/issues for publication in bulletin
2. On-line sources for information on global health issues

Annex 1

POTENTIAL USEFUL LOCAL TOPICS/ISSUES FOR PUBLICATION IN BULLETIN Copied from Joshi M report on TA to Vietnam.

Sources from which relevant topics for the bulletin can be identified are listed below (Adopted from Report on Technical Assistance for Drug Information and Pharmacovigilance Activities of the DI & ADR Centre in Vietnam. Moshi J

1. Comparative presentation of different drugs used in treating a particular disease (efficacy, safety, cost, convenience).
2. Confusingly similar brand names (The look-alike and sound-alike products available in Cambodia).
3. Traditional or herbal practitioners prescribing modern medicines and sometimes secretly putting them in powder form in their traditional preparations.
4. Medication errors or real stories in prescribing, dispensing, administration errors that have occurred in hospitals in Cambodia. Make the stories anonymous.
5. Problems with fixed-dose combination (FDC) products (e.g., drugs for tuberculosis or malaria).
6. New drugs marketed in Cambodia.
7. Real case stories of drug Interactions, serious adverse drug reactions (ADRs), and treatment failures.

8. Antimicrobial resistance (AMR)/ drug resistance in Cambodia.
9. Summaries and implications of interesting/ useful drug use studies and other pharmaceuticals related studies in Cambodia, including master/PhD dissertations (thesis) in pharmacy, n drug use by the public. Problems of non-adherence (non-compliance) to medications and ways to improve adherence. ursing, medicine, and other health professionals' courses.
10. Drugs banned or recently withdrawn.
11. Recent regulatory decisions, or safety warnings/ issues in Cambodia, and also global-warnings/issues that have local relevance.
12. Reproduction (with permission and acknowledgement) of very useful drug information, medication error, or safety/pharmacovigilance related articles from other countries' bulletins along with some locally relevant editorial comments at the end.
13. Stories, issues around over-the-counter (OTC) products and self-medication/ irrational
14. National treatment recommendations by public health programs. Treatment regimen changes in public health programs (HIV/AIDS, TB, malaria, etc). National vaccination program (AEFI in Cambodia).
15. Comparative analysis of national medicines policies (NMPs) in Mekong countries.
16. How to stimulate ADR reporting in Cambodia. Publicity of the spontaneous ADR reporting form.
17. Interesting/ useful question-answer enquires received by the CPC.
18. Possible ways to minimize adverse events due to high risk medicines
19. Awareness and management of local epidemics in Cambodia
20. Interview with key experts in the pharmaceuticals field (DDF, MOH, doctors, pharmacist, researchers, specialists, super-specialists, etc).

Annex 2

On-line sources for information on global health issues. Culled from ISDB website

Sites for Journal articles

- Medline (PubMed) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed)

Sites for Systematic reviews

- The Cochrane Library. A Database of systematic reviews (http://www.cochrane.org)
- Clinical Evidence (http://www.clinicalevidence.com/ceweb/conditions/index.jsp)

Sites for National disease prevention and control, health promotion, etc,.

- Centers for Disease Control and Prevention (CDC), USA (http://www.cdc.gov/)
- Health Protection Agency, UK (http://www.hpa.org.uk/infections/default.htm)

- UK National Institute for Clinical Excellence (NICE) UK (http://www.nice.org.uk/page.aspx?o=20)
- Scottish Intercollegiate Guidelines Network (SIGN) (http://www.sign.ac.uk/)
- New Zealand Guidelines Group (http://www.nzgg.org.nz/index.cfm?screensize=1024&ScreenResSet=yes)
- Prodigy (http://www.prodigy.nhs.uk/ClinicalGuidance/ReleasedGuidance/GuidanceList.asp)

Sites for Formularies/Essential medicines

- British National Formulary (http://www.bnf.org
- WHO Medicines Library (http://Mednet3.who.int/EMLib)
- WHO Model Formulary (http://www.mednet3.who.int/EMLib/wmf.aspx)

Available in Arabic, English, Russian and Spanish. Also available on CD-ROM

- WHO Model List of Essential Medicines

(http://www.who.int/medicines/organization/par/edl/expertcomm.shtml)

- WHO Medicines Bookshelf 2004. CD-ROM of publications related to essential medicines

Sites for Clinical guidelines

- Guidelines International Network
- Regulatory authorities European Medicines Agency (EMEA)(http://www.emea.eu.int/home.htm)
- European portal of all European national agencies (http://www.heads.medagencies.org)
- U.S. Food and Drug Administration (http://www.fda.gov/)
- Japanese Pharmaceutical and Medical Device Agency (PMDA)

(http://www.info.pmda.go.jp/shinyaku/shinyaku_index.html)

Sites for information on Adverse effects

- Australian Adverse Drug Reactions Bulletin (http://www.tga.gov.au/adr/aadrb.htm)
- Current problems.Provides articles and alerts from the UK medicines regulatory agency. (http://www.medicines.mhra.gov.uk/ourwork/monitorsafequalmed/currentproblems/currentproblems.htmCSM)
- Canadian Adverse Drug Reaction Newsletter (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adrindex_e.html)
- U.S. Food and Drug Administration Medwatch Safety Information and Adverse Event Reporting Program (http://www.fda.gov/medwatch/)
- Institute for Safe Medication Practices, USA (http://www.ismp.org/)
- The Importance of Pharmacovigilance: safety monitoring of medicinal products, 2002, World Health Organization (http://www.who.int/medicines/library/qsm/ip_booklet.pdf)

- Safety of Medicines: a guide to detecting and reporting adverse drug reaction (http://www.who.int/medicines/library/qsm/who-edm-qsm-2002-2/esd_safety.pdf)
- WHO Collaborating Centre for International Drug Monitoring. Uppsala, Sweden (http://www.who-umc.org/index2.html)
- Vigimed (https://collaboration.who-umc.org)
  An online communication and conferencing facility for fast communication and discussion of topical pharmacovigilance issues, exclusive to member countries of the WHO Programme for International Drug Monitoring. Please contact info@who-umc.org for a personal user account.
- HealthInsite, Australia (http://www.healthinsite.gov.au/index.cfm)
- WHO publications on pharmacovigilance

Some Useful Journals

1. BMJ (British Medical Journal)
2. The New England Journal of Medicine
3. The Lancet
4. JAMA (Journal of the American Medical Association)
5. Drug Safety
6. Pharmacoepidemiology and Drug Safety
7. The International Journal of Risk & Safety in Medicine
8. Reactions Weekly
9. Prescrire
10. Drug Information Journal
11. ADR Newsletters from National Centres
12. Pharmacoepidemiology & Drug Safety
13. Uspharmacist.com

Internal sources:

Include any locally relevant journals such as the Pharmacy bullet

CAMBODIAN PHARMACOVIGILANCE CENTER (CPC)

DEPARTMENT OF DRUGS AND FOOD (DDF)
MINISTRY OF HEALTH
#80 Samdach Penn North Blvd, Sangkat Boeung Kok 2,
Toul Kok District, Phnom Penh
Email: pv.center@ezecom.com.kh
Phone/Fax: 023 9904 99

Date ……

ACKNOWLEDGMENT OF ADVERSE DRUG REACTION (ADR) REPORT

Dear Dr/Pharm/Mr/Mrs ……
We write to acknowledge receipt of the ADR report you sent to the Cambodian Pharmacovigilance Centre with the following details
Name of suspected medicine
……
Brief description of ADR
……..
Date of reaction (if available)
……
Date report was received at CPC
…….
The report has been assigned this number…….. and entered into the ADR database for analysis (please quote this number if you wish to provide the Centre with additional information on this report).
Your report will help in the effort to make medicines safer for patients. The Centre may contact you for more information or to provide specific feedback on your report (if necessary).
Thank you for sending an ADR report to the CPC and we look forward to receiving more reports from you.

Head, CPC