

Ref. No.

WHO - Roll Back Malaria

## Report

Mapping of malaria focused pharmacovigilance capacities and activities in countries served by the AMFm

Department of Medicines Research  
Swiss Tropical and Public Health Institute

Verena Renggli  
Christian Burri  
Paul Lalvani  
Alexander Dodoo  
Sten Olsson

28 January 2011

## Contacts

---



Swiss Tropical and Public Health Institute  
Schweizerisches Tropen- und Public Health-Institut  
Institut Tropical et de Santé Publique Suisse

### **Department of Medicines Research**

Swiss Tropical and Public Health Institute  
Socinstrasse 57  
P.O.Box  
4002 Basel  
Switzerland  
Internet: [www.swisstph.ch](http://www.swisstph.ch)

#### **Christian Burri**

Tel.: +41 61 225 26 61  
Email: [christian.burri@unibas.ch](mailto:christian.burri@unibas.ch)

#### **Verena Renggli**

Tel.: +41 61 284 81 66  
Email: [verena.renggli@unibas.ch](mailto:verena.renggli@unibas.ch)

#### **Paul Lalvani**

Tel.: +91 99 71 27 61 11  
Email: [paul.lalvani@rapidpharmacovigilance.org](mailto:paul.lalvani@rapidpharmacovigilance.org)

#### **Alexander Dodoo**

Tel.: +233-302-668219  
Email: [anododoo@ug.edu.gh](mailto:anododoo@ug.edu.gh), [alex.dodoo@who-umc.org](mailto:alex.dodoo@who-umc.org)

#### **Sten Olsson**

Tel: +46 (0)18656060,  
Email: [sten.olsson@who-umc.org](mailto:sten.olsson@who-umc.org)

## Disclaimer

---

The views and ideas expressed herein are those of the author(s) and do not necessarily imply or reflect the opinion of the institutes or of the different stakeholders presented in this report.

## Abbreviations

---

ACT	Artemisinin Combination Therapies
AMFm	Affordable Medicine Facility for malaria
CEM	Cohort Event Monitoring
GFATM	Global Fund to fight AIDS, Tuberculosis and Malaria
MoH	Ministry of Health
MSH	Management Sciences for Health
NDRA	National Drug Regulatory Authority
PMI	US President's Malaria Initiative
PV	Pharmacovigilance
RBM	Roll Back Malaria
Swiss TPH	Swiss Tropical and Public Health Institute
UMC	Uppsala Monitoring Centre

---

## Table of Contents

1	Executive Summary.....	5
2	Background .....	7
3	Aim and Objectives.....	8
4	Methodology .....	8
5	Results.....	9
5.1	Overall capacity of the national PV system in the country .....	9
5.2	The operations of the PV system .....	11
5.2.1	Data collection for anti-malarial drugs .....	11
5.2.2	Results from data collection .....	13
5.2.3	Advocacy for the PV system.....	14
5.2.4	Data analysis and use .....	15
5.3	Challenges in implementation and additional needs.....	16
6	Discussion .....	17
7	Conclusions and Recommendations.....	19
8	References .....	21
	Annex.....	22

---

## 1 Executive Summary

**Background:** The need to improve safety monitoring in developing countries becomes more important as access to essential medicines is increasing, and many of these medicines would be used in populations and patient groups where they might not have been studied and usage may not always be under the supervision of trained medical practitioners. One initiative recently launched which aims at increasing access to artemisinin based combination therapy (ACT) for the treatment of malaria is the Affordable Medicine Facility for malaria (AMFm). The Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) hosting this initiative made the inclusion of pharmacovigilance (PV) activities conditional when they invited countries to submit a proposal for their participation in the AMFm pilot phase 1 in 2009.

**Objective:** The current assessment was conducted with the aim to get an update on the PV capacities in low-resource settings, focusing on the countries participating in the AMFm pilot phase 1, and particularly focusing on advances in the field of PV activities done in the last few years; on assessing potential key limiting factors for implementing PV activities; on assessing the consistency of PV activities across grants and countries; and on analyzing which PV activities are included in the AMFm proposal, and which are targeting specifically the private sector.

**Methodology:** Used methodologies for this assessment included the tracking of information provided in the AMFm proposals, data collection through a structured questionnaire sent to the PV centre of the corresponding countries, and follow-up phone interviews.

**Results:** The proposals of all ten countries, namely Cambodia, Ghana, Kenya, Madagascar, Niger, Nigeria, Rwanda, Tanzania, Zanzibar and Uganda, which got their AMFm proposal approved by GFATM were available on the corresponding GFATM website and nine of the countries responded to the structured questionnaire. Four countries agreed on a short follow-up phone interview.

While all countries stated to have a PV system in place, which has been set-up between 1993 and 2008, one country is still in the planning phase and the other one has just started to implement its PV activities such as the collection of Adverse Drug Reaction (ADR) reports. Recent progress is reflected by the fact that two of the ten countries have become a member of the WHO programme for International Drug Monitoring in the last two years; four countries have already been member for more than two years. Six of the nine countries reported to have an advisory committee for PV which is defined by the WHO and partners as minimum criteria for a functional PV system. The countries have between 2 and 20 staff members working in the field of PV, but not all are specifically trained in PV; part of the staff receives only on the job training. In all countries trainings on PV for health care professionals are offered and through the implementation of the AMFm these training activities are expanded in all countries to also include staff working in the private health care sector, not only targeting private hospitals but also accredited retailers. Seven of the nine countries reported on specific activities already being implemented or in planning to stimulate specifically the reporting of ADRs in the private health care sector. Other activities which seem to be promoted through the AMFm are the set-up of a pregnancy register in four countries, the set-up or scale up of a cohort event monitoring (CEM) system in four countries, the set-up of regional PV centres in two countries, and the inclusion of PV in professional curricula in two countries.

The number of submitted ADR reports which is one of the key indicators of the PV system has not steadily increased in all countries over the last few years. Three countries reported a lower number of submitted ADR reports in 2009 compared with 2007, among others due to the missing of repeated training and awareness raising activities. Causality assessments, another important PV activity, are inexistent in three of the countries, due to a lack of human capacity and/or the availability of reference literature. Mentioned key challenges for the implementation of PV activities included lack of trained, experienced and dedicated staff, lack of “core” funding for PV systems, lack of a legal framework for PV, and slow and limited internet connection.

**Conclusion:** The participation in the AMFm pilot phase creates a good opportunity for these countries to scale up their PV system and/or to accelerate their development. However, the extent to which AMFm contributes to the strengthening of the PV system in each country has to be assessed at a later stage. The further implementation of PV activities should focus on regular training and awareness raising activities on PV, include PV as a topic in pre-service curricula, increase capacity to do causality assessments, allocate core funding to the PV system, create access to stable and fast internet connection, and provide a legal framework for PV activities.

---

## 2 Background

Pharmacovigilance (PV), defined by the World Health Organisation (WHO) as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problem, is a complex and difficult discipline, even in countries with well-developed health care systems. With increasing access to essential medicines in developing countries comes the need to monitor and promote the safety and effectiveness of these medicines especially those that are deployed on a wide scale for treating diseases of public health importance. The need to improve safety monitoring becomes more important as many of these medicines would be used in populations and patient groups where they might not have been studied and usage may not always be under the supervision of trained medical practitioners. Finally, even for products with years of experience in use in rich countries, it is obvious that safety data cannot just be transferred from high-resource settings because patients may present different susceptibility profiles for adverse events due to genetic, nutritional, co-morbidity, and other differences [1].

A systematic assessment of PV activities in 55 low and middle income countries was done by the WHO Programme for International Drug Monitoring in 2008. Only three of these 55 countries reported not to have any PV system in place. However, the assessment also revealed that many systems still lack the ability for proper implementation of PV. The article highlights lack of training and funding as major challenges to PV in many countries [2].

In 2008, the Roll Back Malaria (RBM) partnership issued guidelines for the inclusion of PV activities in the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) and other related proposals [1]. In the light of this recommendation, PV plans in the 26 GFATM Malaria Round 8 proposals and 15 U.S. President's Malaria Initiative (PMI) proposals were assessed. Three countries had proposals in both groups. Although only 27% of the PMI proposals and 46% of the GFATM proposals mentioned to have a PV system, only 47% of the PMI and 27% of the GFATM proposals included a request for funding of PV activities in the proposal. If activities were planned, the main focus was on spontaneous reporting systems only and only one country stated to have a pregnancy register. The analysis report concluded that emphasis on PV systems in recipient countries was lacking and that these findings should promote more active direction to strengthen active surveillance and spontaneous adverse event reporting systems [2]. The results of this situation analysis also reflected that despite having the opportunity to get funding for activities, few countries were implementing PV systems for malaria even when specifically requested and indicated.

In 2010, the GFATM issued an information note in which they recommended applicants to implement mechanisms to monitor adverse drug reactions according to existing international guidelines. Specific emphasis on the opportunity to build up and/or enhance national PV system has therefore been included in the GFATM Round 10 proposal form and guidelines [3].

The inclusion of PV activities was already a condition issued by the GFATM for countries submitting a proposal for their participation in the Affordable Medicine Facility for malaria (AMFm) Phase 1 in 2009. AMFm was developed in accordance with objectives and principles agreed upon by the Roll Back Malaria (RBM) Board [4]. AMFm aims to enable

countries to increase the provision of affordable artemisinin combination therapies (ACTs) through the public, private for-profit and not-for-profit sectors by reducing the net cost of ACTs to patients by over 95% through the use of subsidies to manufacturers and wholesalers. This will save lives and reduce the use of less-effective treatments to which malaria parasites are becoming increasingly resistant. It aims also at reducing the use of artemisinin as a single treatment or monotherapy, thereby delaying the onset of resistance to that drug and preserving its effectiveness [5]. In 2009, 12 countries (Tanzania and Zanzibar are calculated in this assessment as separate countries, despite Zanzibar being only semi-autonomous) already running GFATM grants were invited to submit a proposal for their participation in the AMFm pilot Phase 1. Different “supporting interventions” to be implemented were required by GFATM for the participation in the AMFm Phase 1, such as public awareness campaigns, training and supportive supervision for ACT providers, policy and regulatory measures, PV planning, and programs to improve access to ACTs among the poor and children [5]. At the time of AMFm proposal submission with the deadline of 1 July 2009, the status of the PV system in these countries ranged from non-functional; in early development; to well-established with potential for expansion; or advanced with many years of experience [6]. In order to support countries in the planning process, WHO and Medicine for Malaria Venture (MMV) issued guidelines for the inclusion of PV activities in AMFm proposals [6].

Ten of the 12 proposals for the AMFm pilot phase were approved by the GFATM Board in autumn 2009. The countries are Cambodia, Ghana, Kenya, Madagascar, Niger, Nigeria, Rwanda, Tanzania, Zanzibar and Uganda [7, 8].

---

### 3 Aim and Objectives

The aim of the current assessment was to get an update on the PV capacities in low-resource settings, focusing on the countries participating in the AMFm pilot phase 1. The specific objectives were:

- To analyze the advances in the field of PV activities in the last few years
- To assess potential key limiting factors for implementing PV activities
- To assess the consistency of PV activities across grants and countries
- To analyze which PV activities were included in the AMFm proposal, and which were targeting specifically the private sector

---

### 4 Methodology

For the assessment of the PV capacities and activities of the AMFm pilot countries the following methodologies were used:

- Basic data such as contact details of the PV centres and planned activities in the AMFm Phase 1 were retrieved from the AMFm proposals which are publicly available on the GFATM webpage [9].
- More detailed information was collected through a structured questionnaire which was sent to all PV centres of the AMFm pilot countries. The questionnaire was based on two questionnaires which had been used in earlier assessments, namely the questionnaire used by RaPID for the assessment of PV capacity in public health programmes, specific for malaria [10] and the questionnaire used by the WHO

Programme for International Drug Monitoring for the assessment in the 55 low- and middle income countries [6]. Questions specifically related to the AMFm pilot phase were added, targeting the private sector. The questionnaire contained 33 questions in total and covered the following areas: overall capacity of the PV system in the country, and the operations of the PV system, divided into data collection, results, advocacy and data analysis and use.

- Two reminders were sent out by email to PV centres which did not meet a given deadline to respond.
- Additional follow-ups by phone interview with PV focal persons were conducted.

Use of the same or very similar questions allowed the comparison with the results from the previous assessments and hence, analysis of the development of PV activities in the included countries over time. Results from the previous assessments were made available by the organisations which had conducted them, namely by RaPID and by the Uppsala Monitoring Centre (UMC).

---

## 5 Results

The implementation of the AMFm pilot phase started in all countries in July/August 2010, except for Rwanda where implementation has not yet started. Nine of the 10 contacted PV centres filled out the questionnaire and sent it back (response rate: 90%). Niger did not answer at all. Four centres also agreed to have a follow-up phone call for further clarification of some of the questions.

### 5.1 Overall capacity of the national PV system in the country

The PV systems of most countries were founded in the last six years, except for the systems in Tanzania and Ghana, which were founded in 1993 and in 1999 respectively. The PV systems in Cambodia and Rwanda were only founded in 2008; while Cambodia is still in the planning phase, Rwanda has just started to implement activities such as the collection of Adverse Drug Reaction (ADR) reports in October 2010. According to information provided in the AMFm proposal, the PV system in Niger was founded in 2006, but it is still lacking implementation. Under the AMFm pilot phase, Niger is planning to recruit one PV focal person.

Table 1 below shows the status of some key characteristics for a functional PV system in the country.

Six of the ten countries are Full members of the WHO programme for International Drug Monitoring, and three are Associate members (marked in Table 1 as in planning). Associate members are those countries who have expressed a willingness to join the WHO Programme but have not yet demonstrated the needed technical competencies to submit ADR reports to the WHO database, a key requirement of membership. Niger is not a member

In eight countries the PV centre functions under the responsibility of the National Drug Regulatory Authority (NDRA) while in Rwanda a Pharmacy Task Force under the Ministry of Health (MoH) heads the PV centre.

Of the nine responding countries, six stated to have an advisory committee for PV consisting of between 7 and 23 members, and meeting about twice to four times a year or more if needed.

Government budget for PV is inexistent in Cambodia, Madagascar and Zanzibar, rather limited in Rwanda, Tanzania and Uganda where it ranges between \$ 40'000 and \$ 70'000 per year, whilst there is a budget of between \$ 100'000 and \$ 180'000 in Ghana, Kenya and Nigeria.

All countries reported to get additional funds from WHO, GFATM, Management Sciences for Health (MSH) and/or other sources; these funds are, however, often linked to specific projects.

Kenya stated that financial support rarely came directly to the PV centre and was not committed in advance, but had to be requested in pieces for all different activities. Therefore, planning is difficult and implementation of activities can be delayed.

Table 1: Status of some key characteristics for a national PV system

Country	Existence of national PV centre, year of foundation	Government budget for PV	National PV advisory committee, meeting 2-4 times a year	Full member of WHO programme for International Drug monitoring
Cambodia	2008			
Ghana	1999			Since 2001
Kenya	2009			Since 2010
Madagascar	2006			Since 2009
Nigeria	2004			Since 2004
Rwanda	2008			
Tanzania	1993			Since 1993
Zanzibar	2004			
Uganda	2004			Since 2007

	existing		in planning		not existing
---	----------	---	-------------	---	--------------

All responding countries with PV activities collect data from the whole country with most of them having in addition to a national centre also regional PV centres and/or sentinel sites. Only Cambodia, Madagascar and Zanzibar reported to have a national centre only.

All PV centres have access to phone, email, internet, and in some cases facsimile; access to reference information on drug safety by internet and/or a library is available in all cases, except for Madagascar. In several countries internet connection is slow and limited. Cambodia and Madagascar stated not to have their own office space for PV.

The number of health professionals working in the PV systems, including regional centres ranges between 2 and 20 per country, with a number of them working only part-time for PV activities. Details are given in Table 2. While the number of staff compared with data collected in 2008 is the same for Ghana, Nigeria and Zanzibar, the number of health professionals working in the PV system increased in all other countries.

Only Rwanda and Tanzania reported that all staff members had been trained specifically in PV, all other countries stated that only some staff members received training. The trainings

had a duration of one to two weeks. In Uganda, 25 regional centre coordinators received a one-week training on the use of VigiFlow™ in 2009. Cambodia had not yet the possibility to train its staff.

Table 2: Number of health professionals working in the PV system

Country	No of staff working full time	No of staff working part time	No of staff with formal training in PV	No of supporting staff (administration)
Cambodia	3			
Ghana	5	3	3	1
Kenya	3		1	
Madagascar	4		3	
Nigeria	8		3	3
Rwanda	3	6	9	1
Tanzania	3	6	9	1
Zanzibar	1	1	1	2
Uganda	8	12	5	1

Except for the new PV centres in Cambodia and Rwanda, all countries reported on some staff members having worked in PV for several years, at least at the national level. Tanzania and Uganda reported on a high staff turn-over especially at regional level where staff often works only part-time in PV and is also busy with other activities.

From the countries implementing PV activities, Kenya, Madagascar and Cambodia stated not to have any administrative staff, the other countries have at least a part time administrative staff member.

## 5.2 The operations of the PV system

### 5.2.1 Data collection for anti-malarial drugs

All countries have a spontaneous reporting system with a nationally approved ADR reporting form, except for Cambodia where such a system is still in planning. The form is the same for all diseases. Ghana, Nigeria and Tanzania stated to also have a cohort event monitoring (CEM) programme for antimalarials in place. Nigeria plans to scale up the CEM system for ACTs during the implementation of the AMFm pilot phase and Rwanda plans the introduction of such a system. Pregnancy register do not exist in the countries yet, however, Ghana, Tanzania, Cambodia, and Rwanda stated that the implementation was planned. While in all countries doctors and nurses and in most countries also pharmacists and private retailers fill out the ADR forms, only Kenya stated that consumers were also involved in the reporting of ADRs.

Table 3 offers an overview of the status of the different data collection systems in the countries.

Table 3: Data collection systems used for anti-malarial drugs

Country	Spontaneous reporting system	Cohort event monitoring system	Pregnancy register
Cambodia			
Ghana			
Kenya			
Madagascar			
Nigeria			
Rwanda			
Tanzania			
Zanzibar			
Uganda			

	existing	in planning	not existing
--	----------	-------------	--------------

Table 4 offers an overview of the status of activities which were outlined in the WHO/MMV guidance document for countries participating in the AMFm pilot phase [6] to specifically stimulate the reporting of ADRs in the private sector were reported to be implemented or in planning.

Table 4: Overview of status of activities stimulating reporting of ADRs in the private sector

Country	Malaria patient register, kept by accredited retailers	Patient-held card with information about given medicine	Patient referral form for private accredited retailers	Simplified ADR form especially for private sector	Active follow-up of a random subset of patients
Cambodia					
Ghana					
Kenya					
Madagascar					
Nigeria					
Rwanda					
Tanzania					
Zanzibar					
Uganda					

	existing	in planning	not existing
--	----------	-------------	--------------

Madagascar and Zanzibar do not plan to implement any of the specific activities mentioned in table 3 for stimulating the reporting of ADRs in the private sector. Ghana and Nigeria plan to collect data from the private sector through a CEM system.

ADR forms are made available mostly through health care facilities and pharmacies, or they are provided on demand and during training sessions. Five countries have a webpage with information about PV, four of them offer an ADR form to download and to fill in, and three of them also provide guidelines on the webpage on how to report. Kenya and Tanzania reported that the ADR form was also made available through professional bulletins/newsletters/drug formularies, and Ghana stated that the form would be provided in

the drug safety newsletter being published soon by the PV centre. Rwanda will make the ADR form available on the MoH website.

In most cases, the ADR form can be returned by internet or email. In many countries the filled out forms are also collected by a transportation system which is used for other purposes as well. A toll-free phone number is only available in Rwanda and Zanzibar, but is planned in Tanzania, and needed for real time reporting in Ghana, as stated; prepaid postage is available in Ghana and Tanzania. Other systems which are used in some countries include the postal system, facsimile, and regular phone. In Nigeria the forms are also collected through the state offices of the NDRA.

### 5.2.2 Results from data collection

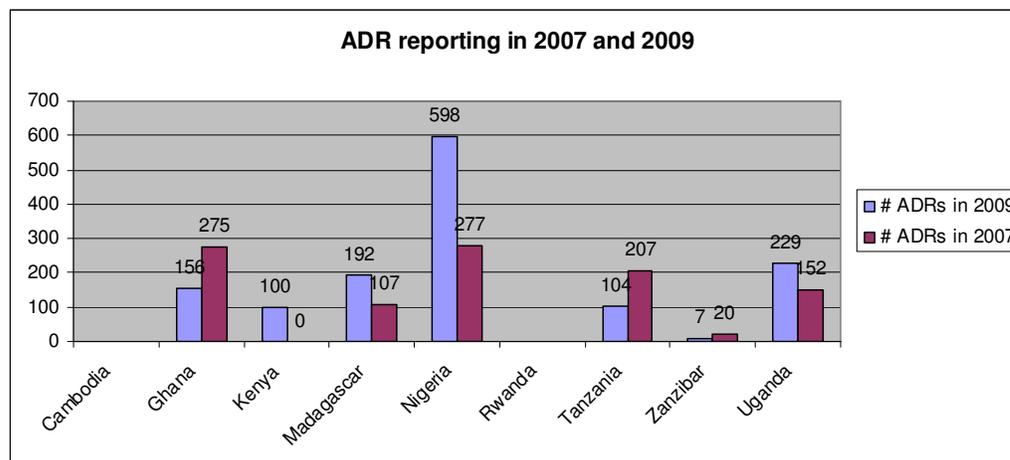
Table 5 shows the number of ADR reports which have been collected per country up to November/December 2010 since the introduction of the PV systems in the countries.

Table 5: Number of ADR reports collected

Country	# collected ADR forms cumulative	Introduction of ADR forms
Cambodia	0	In planning
Ghana	697	1999
Kenya	1050	2009 (national launch)
Madagascar	831	2006
Nigeria	5576	2006
Rwanda	0	October 2010
Tanzania	990	1993
Zanzibar	129	2004
Uganda	550	2005

The following graph (Graph 1) shows the number of collected ADR forms per country in 2007 and 2009. It can be recognized that in some countries such as Kenya, Madagascar, Nigeria and Uganda this number has increased while in other countries such as Ghana, Tanzania and Zanzibar the number has decreased.

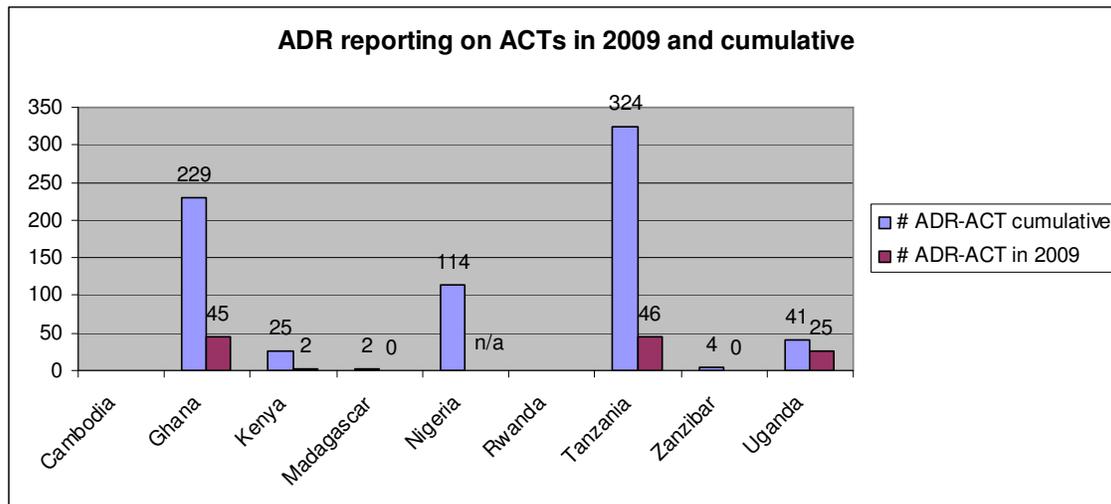
Graph 1: ADR reporting in 2007 and 2009



Sensitization and training activities seem to have an influence on reporting frequency. Tanzania for example stated during the phone interview that several sensitization activities had been implemented in 2006 but were not repeated thereafter. Ghana stated that less training activities were conducted in 2008/2009 compared with 2005-2007. This is reflected in the lower number of reports in 2009 compared with 2007. Kenya stated that they observed a steep increase in the number of received reports after the sensitization campaign in October 2009.

Graph 2 illustrates the number of ADR reports for ACTs in 2009 and the cumulative number since start of the data collection up to November 2010. Ghana, Nigeria and Tanzania, having a PV system in place for many years, had the highest number of reports.

Graph 2: ADR reporting on ACTs in 2009 and cumulative



### 5.2.3 Advocacy for the PV system

Training and sensitization activities for healthcare professionals working in the public sector are already conducted in all the countries except for Cambodia, although to a different extent. Activities particularly focusing on staff in the private sector are already implemented in three countries while it is in planning with the implementation of the AMFm programme in all other countries included in this assessment. In Kenya only a limited number of the staff working in private hospitals were included in these training activities up to now, however, further expansion to also include private accredited retailers in the training sessions is planned for next year. In Nigeria, only trainers of trainers have been trained so far, but for 2011 the offer of trainings directly targeting accredited retailers in the private sector is planned. Table 6 offers an overview of activities promoting the reporting of ADR which are already implemented or in the planning phase.

Table 6: Activities to promote ADR reporting

Country	Training and sensitization for healthcare professionals	Training and sensitization for accredited retailers / private sector	Advertisement in print media	Inclusion of PV in professional curricula
Cambodia				
Ghana				
Kenya				
Madagascar				
Nigeria				
Rwanda				
Tanzania				
Zanzibar				
Uganda				

	existing	in planning	not existing
--	----------	-------------	--------------

The implementation of the AMFm is not only boosting training and sensitization activities in the private sector, but also supporting the expansion of PV awareness through advertisement in the print media. PV as a topic in pre-service education is already integrated in the curriculum of clinical officers in Kenya and of pharmacy students in Uganda; both countries plan to include the topic also in the curricula of other health care professionals. In Nigeria and Ghana, the inclusion of PV training in the curricula of health care professionals is in the planning process.

#### 5.2.4 Data analysis and use

All countries reported to enter the collected ADR reports into the VigiBase™ database of the WHO which is a requirement for the members of the WHO programme for International Drug Monitoring. Ghana, Kenya, Madagascar, Nigeria, Tanzania und Uganda also have national databases using the data management software VigiFlow™ for data entry. Limiting factors for data entry into the VigiBase™ database include incomplete reports with missing data and a limited number of staff to manage data entry. In Kenya for example only 145 out of the collected 1050 reports could be entered up to now. In addition, the submission of information to VigiBase™ using VigiFlow™ requires internet connection at reasonable speed (0.5-1Mb/s) which is not always available. Ghana, Kenya and Madagascar also reported to enter the collected data into an Excel® spreadsheet for in-house use. Zanzibar reported on entering data into an electronic database (according to the assessment done in 2008 they use EpiInfo). Tanzania and Ghana stated that the set-up of a national database was in planning.

All countries already collecting ADR forms stated that the reporter of an ADR was contacted if further clarification was needed and all reports were acknowledged, either by phone, email or official letter.

Three of the nine responding countries stated not to do any causality assessment of the reported ADRs.

Collected information is used mainly for drug regulatory activities, and in the case of collected reports of antimalarial drugs, shared with managers of the malaria programme.

Only Tanzania reports on information exchange with pharmaceutical manufacturers. Few countries stated to use the collected information for the development of the essential drug list or of standard treatment guidelines. Some countries such as Nigeria, Rwanda, Tanzania and Uganda use the collected information for giving advice to consumer groups or the general public. Table 6 shows how the collected information is distributed in the different countries.

Table 7: Channels to distribute information on findings of ADRs

Country	Newsletter/ bulletin	Conferences/ workshop	Publi- cations	Website/ internet	Mass media	Targeted messages to consumers
Cambodia						
Ghana						
Kenya						
Madagascar						
Nigeria						
Rwanda						
Tanzania						
Zanzibar						
Uganda						

<span style="display: inline-block; width: 15px; height: 10px; background-color: #00FF00; border: 1px solid black;"></span> existing	<span style="display: inline-block; width: 15px; height: 10px; background-color: #00FFFF; border: 1px solid black;"></span> in planning	<span style="display: inline-block; width: 15px; height: 10px; background-color: #FFFF00; border: 1px solid black;"></span> not existing
--	---	--

Although Tanzania used to produce a newsletter, the country now stated that the drug information bulletin had not been produced for a while due to structural changes in the organizational set-up of the department. A new PV newsletter, however, is in planning. Also Ghana is planning the first edition of a drug safety newsletter. In Kenya and Nigeria the newsletter is only available as soft copy on the website and distributed as such per email. Printed versions to be distributed are in planning in both countries. Limiting factors are not only the lack of a budget for the printing, but also the length of the procurement process for this activity which can delay the printing process and reduce availability of a printed version to only twice instead of four times a year.

### 5.3 Challenges in implementation and additional needs

Different challenges are limiting the implementation of PV activities in the AMFm pilot countries. Most pronounced seemed to be human resource issues such as lack of trained and experienced or dedicated staff which is associated with underreporting and insufficient quality of submitted reports since staff are not able to have time to promote PV and also to train reporters on how to report. It further influences data management such as analysis of the findings.

Other important points influencing the implementation of PV activities are the need for “core”, sustained funding specifically dedicated to the PV system and not just allocated for specific PV activities on request, a legal framework for PV and the need for a stable and fast internet connection.

For further implementation of PV activities different needs have to be covered, depending on the status of the PV system in the country. There is an ongoing need to expand training activities countrywide in all countries, including the private sector and to increase awareness of the PV system in the professional and in the public sector. More staff working in PV is

needed in several countries, for example for data entry into VigiFlow™, and to allow staff at the regional PV centres to work full-time for PV. Meetings with public health staff, PV stakeholders, MoH and donors for information exchange and sensitization on PV issues as well as regular supervision visits to regional centres should be promoted. Nigeria, Madagascar and Rwanda particularly highlighted the need for a legal framework to strengthen PV activities in the country. Some countries emphasized the need to expand the PV system to regional centres, others the need to print ADR forms and reporting guidelines, to get access to a stable and fast internet connection, to include PV in training curricula of health care professionals, to receive an adequate annual budget, to get a car for transportation, and to do operational research on PV activities.

---

## 6 Discussion

Substantial effort has been made in the last few years to support the building up and implementation of PV systems in low resource settings. International donors, such as GFATM, have put the setting up of PV systems and increase in PV activities in the focus of recent proposal submissions and have made it a requirement for the AMFm proposals.

Recent progress is reflected by the fact that two of the ten assessed countries have recently become a member of the WHO programme for International Drug Monitoring, namely Madagascar in 2009 and Kenya in 2010. Kenya launched its PV system nationwide in 2009 and has created a comprehensive national PV system since then. The PV systems in Cambodia and in Rwanda both were set-up in 2008 and while Rwanda started to implement PV activities in October 2010, Cambodia is still in the planning process, though it will also start its activities soon. The PV system in Niger will start its implementation due to the participation in the AMFm pilot phase which offers the possibility to hire dedicated staff for PV activities.

The current assessment of PV capacities included all countries participating in the AMFm pilot phase which includes not only the public but also the private health care sector. The results of this assessment reflect the great opportunity given by the AMFm to plan and implement different activities for the further development of the PV system in the country. All countries reported to integrate the staff of the private health care sector into awareness raising and/or training activities on PV. About half of the countries have taken up the specific recommendations issued by WHO in collaboration with Medicines for Malaria Venture (MMV) for defining and implementing PV activities targeting the private sector. Ghana, Tanzania, Rwanda, and Cambodia stated to plan the introduction of a pregnancy register. Nigeria, Ghana, Rwanda, and Tanzania plan to implement and/or to scale up a CEM system for PV of ACTs. Nigeria and Tanzania reported to set-up and equip regional PV centres, and Ghana and Nigeria plan to include PV in professional curricula. Although all these activities put additional work on the system, it also creates an important opportunity to expand the PV system and to further increase the awareness of PV and the collection of ADR reports.

Despite increased effort to support the building up and implementation of PV systems in the last years, there has not been universally a steady increase in the number of submitted ADR reports, one of many key indicators for a functional PV system in the country. Tanzania, Zanzibar, and Ghana collected less ADR reports in 2009 compared with 2007. According to information from Tanzania and Ghana this could have been caused by decreased awareness

due to missing awareness campaigns and less training opportunities for health care professionals in the countries in the last three years. There seems to be a need for regular awareness campaigns and trainings as half-life of the distributed messages seems to be of short duration.

All countries still have a high degree of underreporting, despite some good advances in the last years. A well functioning PV system in the WHO programme would submit 200 ADR reports per million inhabitants per year, and all the assessed countries are still far below this target.

Another important PV activity is the causality assessment. Such assessments require access to reference literature, either online, or in libraries, in addition to availability of trained personnel to undertake this exercise. While all countries except for Madagascar state to have access to online or print reference literature, not only Madagascar, but also Rwanda and Zanzibar stated not to do any causality assessments. It is important to point out that whilst some national centres do not routinely carry out individual case causality assessments, the reasons for not undertaking this activity was not clearly stated by the countries surveyed.

Although all countries included in this assessment basically have a PV system in place, only a part of them fulfill the five minimum requirements for a PV system as defined by the WHO and partners [11]. These five requirements include (1) the existence of a national PV centre with designated staff, stable basic funding, clear mandates, well defined structures and roles, and collaborating with the WHO Programme for International Drug Monitoring; (2) the existence of a national spontaneous reporting system with an ADR reporting form; (3) a national database or system for collating and managing ADR reports; (4) a national PV advisory committee; (5) a clear communication strategy. Based on the information received in this assessment, only five countries fulfill all five requirements, namely Ghana, Kenya, Nigeria, Tanzania and Uganda. Zanzibar, Rwanda and Madagascar do not have a national PV advisory committee, and Cambodia is not (yet) a member of the WHO programme.

A key challenge for the implementation of PV activities highlighted by all countries in one or another way is related to human resources. There is a lack of trained staff, because training opportunities are limited. Only part of the staff is trained, and the training often took place years ago. The need is high to expand training opportunities, and also to include PV in pre-service curricula, as it is already done in Kenya for clinical officers and in Uganda for pharmacy students. However, even if PV is included in the curricula, there is often still a lack of trainers with adequate knowledge and experience to conduct the trainings. In addition, refresher trainings are needed on a regular base, to keep staff up-to-date, and to maintain awareness of PV. Networks and conferences also contribute to update and exchange of knowledge, such as the PV meeting focusing on the perspective of developing countries which took place in August 2010 in Nairobi entitled "National Pharmacovigilance Systems: Ensuring the Safe Use of Medicines".

A well functioning PV system needs dedicated and motivated staff. Staff motivation can be influenced by offering training opportunities, but also by good working conditions. Especially at regional level there seems to be an issue with staff being dedicated to PV activities because they are only working part-time for PV, and are distracted by many other responsibilities. In addition, staff turnover at regional level is rather high which makes the building up of a system and continuity difficult. There is a need to create full-time positions for PV activities not only at national but also at regional level.

In order to stimulate ADR reporting in the country there is also a need for regular general awareness raising and sensitization. This is reflected for example by the high number of ADR reports received in Kenya after awareness raising campaigns and by the reduction of ADR reports received in Tanzania between 2007 and 2009 when no additional awareness raising has been conducted.

The successful introduction of PV requires firm institutional base and solid political and financial support. While the availability of funding was raised by several countries to be a challenge, Kenya and Uganda emphasized more the need for “core” funding for the PV system; currently not the availability of funding seems to be the limiting factor but how this funding is made available. Funding is allocated in small pieces to specific PV activities on request, which makes the systematic planning and implementation of PV activities rather difficult and unpredictable. The issue of solid political support can be strengthened if a legal framework is available; countries such as Nigeria, Rwanda and Madagascar, which do not have a legal framework for PV in the country, raised this point as a challenge for implementation.

The current assessment also identified a range of smaller challenges which could be rather easily addressed by focused interventions. One such challenge which is of high importance is the limited or unreliable internet access. Internet connection at a speed of 0.5-1Mb/s is needed to for an optimal use of VigiFlow™/VigiBase™ which is in many countries the national PV database. In addition, there should be also a focus on the size of files to download from webpages. Kenya for example has an online ADR form with a size of 1.53 MB and guidelines on how to report ADRs with a size of 3.85MB. This can be a limiting factor in using these documents as download will be too time-consuming.

In order to do causality assessments of reported ADRs, each PV centre needs access to reference documents, and it would be recommended to have a library with some printed standard reference documents besides access to reference documents on the internet. However, the constant availability of the latest version of these printed standard reference documents needs to be assured. Furthermore, as causality assessment is not always straight forward, PV staff needs to be trained, and at least one experienced employee should be in the team.

Another challenge is related to PV newsletters which are a good tool to distribute information about PV and to increase awareness. Some countries stated to issue a newsletter every quarter, but these newsletters are rarely printed. However, printing the PV newsletter would allow much wider distribution as computer access is often not available in the whole country. The limiting factor for the printing is not only the availability of funding, but apparently also the speed of the procurement process for conducting the printing. This has been raised as a possible factor for delaying the printing process in Kenya.

---

## **7 Conclusions and Recommendations**

The current assessment of PV capacities of countries participating in the AMFm pilot phase shows that there is increased awareness of the importance of PV and that the development of the PV systems in the countries is progressing. New countries joined the WHO programme for International Drug Monitoring in the last two years. Kenya which joined the WHO Programme as full members in 2010 could expand its PV system nationwide with a

substantial increase in its already relatively high ADR reporting rates. Rwanda has just started its PV activities and Cambodia is on the way to start soon. The participation in the AMFm pilot phase creates a good opportunity for these countries to scale up their PV system or to accelerate their development. There are many PV activities in planning. However, the extent to which AMFm contributes to the strengthening of the PV system in each country has to be assessed at a later stage, namely at the end of the two-year pilot phase where a direct evaluation of the activities undertaken using funding from AMFm could be made. In addition, the data from this survey can be used as baseline to compare progress in subsequent years. The need for key universally agreed Pharmacovigilance Indicators would help in this process.

The assessment of PV activities in low- and middle income countries conducted in 2008 identified a range of challenges such as for example training of staff, adoption of laws and regulations, low level of reporting, lack of funding and limited skills for causality assessment. These challenges are still all present and need to be further addressed.

Based on the current assessments, the following recommendations are raised.

a) Recommendations to the National PV system:

- Regular training and refresher training for health care professionals should be offered at all levels to keep staff up to date on recent developments and to maintain the awareness of PV to stimulate reporting on ADRs
- Regular PV sensitization campaigns should be conducted to increase awareness of PV and its importance and to stimulate reporting on ADRs
- The capacity to do proper causality assessment for all received ADR reports should be increased by training of the responsible staff, and by assuring availability of up-to-date reference literature
- Access to a stable and fast internet connection should be assured in order to ensure unlimited access to VigiFlow™

Recommendations to Global Agencies such as WHO, RBM and GFATM

- Funding for PV activities should be dedicated to the PV system as “core” funding and not dedicated to specific activities on request

Recommendations to Policy Makers:

- PV as a topic should be included in all relevant pre-service curricula; countries already offering PV in pre-service curricula for health care professionals could share their expertise and experience and offer support
- All countries should introduce a legal framework for PV

---

## 8 References

- [1] Stergachis A et al. A situation analysis of pharmacovigilance plans in the Global Fund Malaria and U.S. President's Malaria Initiative proposals. *Malaria Journal* 2010; 9: 148
- [2] Olsson S et al. Pharmacovigilance activities in 55 low- and middle-income countries – a questionnaire-based analysis. *Drug Saf* 2010; 33: 689-703
- [3] Pharmaceutical Systems Strengthening and Pharmacovigilance – information note. The Global Fund, 2010, accessible at:  
[http://www.theglobalfund.org/documents/rounds/10/R10\\_InfoNote\\_Pharma\\_en.pdf](http://www.theglobalfund.org/documents/rounds/10/R10_InfoNote_Pharma_en.pdf) (1 Sept 2010)
- [4] Affordable Medicine Faculty-malaria (AMFm) – technical design – November 2007, accessible at: <http://rbm.who.int/partnership/tf/globalsubsidy/AMFmTechProposal.pdf> (1 Sept 2010)
- [5] About AMFm - The Global Fund Website, accessible at  
<http://www.theglobalfund.org/en/amfm/about/?lang=en> (1 Sept 2010)
- [6] WHO and MMV. Pharmacovigilance guidance for countries participating in AMFm Phase 1, 2009, accessible at  
[http://www.who.int/malaria/publications/atoz/pv\\_for\\_amfm\\_phase1.pdf](http://www.who.int/malaria/publications/atoz/pv_for_amfm_phase1.pdf) (1 Sept 2010)
- [7] Global Fund Observer, Issue 111, 2009. <http://www.aidspace.org/documents/gfo/GFO-Issue-111.pdf>, accessed 1 December 2010
- [8] Global Fund Observer, Issue 134, 2010. <http://www.aidspace.org/documents/gfo/GFO-Issue-134.pdf>, accessed 1 December 2010
- [9] The Global Fund. <http://www.theglobalfund.org/en/>, accessed 4 August 2010
- [10] RaPID questionnaire for PV capacity in malaria programmes.  
[http://www.rapidpharmacovigilance.org/update\\_file/RaPID%20Questionnaire%20for%20PV%20Capacity%20in%20Malaria%20Programs.pdf](http://www.rapidpharmacovigilance.org/update_file/RaPID%20Questionnaire%20for%20PV%20Capacity%20in%20Malaria%20Programs.pdf), accessed 29 September 2010
- [11] WHO and partners. Minimum requirements for a functional pharmacovigilance system. Accessed at:  
[http://www.who.int/medicines/areas/quality\\_safety/safety\\_efficacy/PV\\_Minimum\\_Requirements\\_2010\\_2.pdf](http://www.who.int/medicines/areas/quality_safety/safety_efficacy/PV_Minimum_Requirements_2010_2.pdf) (24 November 2010)

## Annex

### AMFm pilot countries - Assessment of the Pharmacovigilance Capacity

The following questionnaire aims at assessing the current pharmacovigilance capacity in the AMFm pilot countries; it is structured into 3 main parts with part 3 having 4 sections.

- *Part 1: Background information*
- *Part 2: Overall capacity of the pharmacovigilance system in the country*
- *Part 3: The operations of the pharmacovigilance system*
  - a) *Data collection*
  - b) *Results*
  - c) *Advocacy*
  - d) *Data analysis and use*

Overall it contains 33 questions with most of the questions being closed question where you only have to click the corresponding answer(s) which are reflecting your situation. For the open questions, there is always a grey text field in which you can type the answer.

Overall, it takes you about 20 minutes to go through the questionnaire.

**Many thanks for filling it in and returning it up to 30 November 2010 latest!**

Country:

Date:

#### Part 1 – Background information respondent

Name of respondent	
Designation of respondent	
Department, Ministry etc	
Address	
Email	
Phone (landline; mobile)	

#### Part 2 – Overall capacity of the national pharmacovigilance system in the country

##### 2.1. History

When was the national pharmacovigilance system in your country founded? Please indicate the year:

##### 2.2. Governance:

a) What organization or agency oversees or is responsible for the pharmacovigilance system?

b) Is there an established pharmacovigilance advisory committee in your country?

yes; if yes, how many persons are in the committee?

if yes, how often does the committee meet per year?

no

### 2.3. Coverage:

a) How is your national pharmacovigilance system organized?

National centre only

Network with national and regional centres

Network with national centre and sentinel sites\*

Network with national and regional centres and sentinel sites\*

(\*Sentinel sites are usually clinics or hospitals where a pilot programme takes place)

b) What is the geographical coverage of the pharmacovigilance system?

Information collected from the whole country

Information collected for some region(s) only

### 2.4. Infrastructure:

a) Does the national pharmacovigilance centre has its own office space?  Yes  No

b) Does your pharmacovigilance centre have access to the following facilities?

Telephone  Facsimile

Computer facilities (without internet)  Email

Internet; communication speed, if available:

Library with reference books on drug safety

Reference information on drug safety available by the internet

### 2.5. Human Resources:

How many staff are working within the pharmacovigilance system in the national programme, including the regional centres if available?

a) Number of health professionals with expertise (doctors, pharmacists, etc.):

Out of them, how many are working full-time , working part-time:

b) How many of these health professionals have received some formal training in pharmacovigilance?

Please indicate the year and the number of days of the training for each staff member:

c) For how many years are these health professionals already working in the pharmacovigilance system? Please indicate it separately for each staff member:

d) Number of supporting staff e.g. for administration working in the pharmacovigilance system:

Out of them, how many are working full-time , working part-time:

**2.6. Budget:**

a) Is there a budget designated to pharmacovigilance provided by a governmental authority?

Yes; size of annual budget:  No

b) Does the national pharmacovigilance system receive funding from any other source? If yes which one(s)?

**2.7. Are there any specific comments or additional information?****Part 3 – The operations of the pharmacovigilance system****Section 3a – Activities for data collection with special focus on antimalaria medicines****3.1. What system of pharmacovigilance is used for anti-malaria drugs?**

	Previously available	Available since AMFm started	In Planning with AMFm; to be developed
Spontaneous reporting system;	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cohort event monitoring system	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pregnancy register	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
other; please specify:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**3.2. Is there a nationally approved adverse drug reaction (ADR) reporting form?**

yes; if available only since start of AMFm, please tick here:

in planning with AMFm; to be developed

no

**3.3. Who fills out the ADR forms?**

Physician, Clinical Officer, Medical Assistant  Nurse

Accredited retailers (private sector)  Pharmacist

Others (including patients); please specify:

**3.4. Is this ADR form the same one for all different diseases or is there a special form for malaria?**

yes, the same form for all diseases

no, special form for malaria

**3.5. To stimulate reporting, with a special focus on the involvement of the private sector, does the pharmacovigilance system in your country include one of the following approaches?**

*(This question has been adapted from the AMFm guidance document for countries participating in AMFm Phase 1 by WHO and MMV)*

	Previously available	Available since AMFm started	In Planning with AMFm; to be developed
Malaria patient register, kept by private accredited retailers	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Patient-held card with information about given medicine, dosage, and supplier of medicine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Patient referral form for private accredited retailers	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Simplified ADR form, especially for the private sector	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Active follow-up of a random subset of patients	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Please add comments and explanations if needed:

**3.7. How are the ADR forms made available to the health care professionals and to the accredited retailers? (please tick all possibilities)**

- direct mailing to individual health care practitioners / accredited retailers
- through health care facilities
- through pharmacies
- from an internet site; please specify site:
- in professional bulletins / newsletters / drug formularies
- provided on demand
- distributed during training session
- other; please specify:

please describe here if anything is in the planning process:

**3.8. What mechanisms are used to return the completed forms to the pharmacovigilance centre? (please tick all possibilities)**

- postal, not prepaid postage
- postal with prepaid postage
- telephone – regular
- telephone – toll-free number
- facsimile
- submission by internet, email
- transportation system which is also used for other purposes
- specific transportation system or pick-up system for the forms
- other; please specify

please describe here if anything is in the planning process:

## Section 3b – Results from data collection

### 3.9. How many individual ADR forms were filled out and received at the national pharmacovigilance centre?

Number of forms since the introduction of ADR forms:           ; introduction of ADR forms in which year?

Number of forms filled out in 2009:

### 3.10. How many of these ADR reports were related to ACTs?

Number of forms related to ACTs since introduction of ADR forms:

Number of forms related to ACTs in 2009:

## Section 3c – Advocacy for the pharmacovigilance system

### 3.11. Which activities are carried out to promote the reporting of ADRs?

*(please tick all possibilities)*

	Previously available	Available since AMFm started	In Planning with AMFm; to be developed
training and sensitization for healthcare professionals	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
training and sensitization for accredited retailers / private sector	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
payment / incentive for reporting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
advertisement / articles in general media	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
advertisement / articles in professional media (journals, newsletters, etc)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Regular reminders / email messages to potential reporters	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
inclusion of pharmacovigilance in professional curricula			
other; please specify:			

## Section 3d – Data analysis and use

### 3.12. Which system/approach is used for recording the information from the completed ADR forms?

- forms are filed without processing
- information is entered into a spreadsheet, such as Excel® for example
- information is entered into an electronic database
- information is entered into VigiFlow from the UMC
- other; please specify:

please describe here if anything is in the planning process:

**3.13. Is the pharmacovigilance centre expected to contact the reporter of the ADR in order to validate the information if it is not clear or to get further details?**

- yes; if yes, how often does this happen ?  
 no

**3.14. Does the pharmacovigilance centre provide any individual acknowledgement or feedback to the reporters of the ADR?**

- yes; please specify how (by telephone, email, letter, incentive, etc):  
 no

**3.15. Does the pharmacovigilance centre classify reports received according to some causality grading?**

- yes to all cases  
 yes, but only some cases; please specify which cases:  
 no  
 other; please specify:

**3.16. How is the information (findings from the ADR forms) from the pharmacovigilance activities utilized? (please tick all possibilities)**

- shared with managers of the malaria programme  
 shared with pharmaceutical manufacturers  
 used for drug regulatory activities  
 actively disseminated to health professionals/ drug and therapeutic committee  
 advice to consumer groups or general public  
 background for the development of national essential drug list  
 background for the development of the national treatment guidelines  
 other; please specify:

**3.17. How is the information distributed? (please tick all possibilities)**

- newsletter / bulletin; please specify how many times per year:  
 conferences / workshops  
 articles in professional journals  
 through the mass media  
 targeted messages for consumers  
 internet website  
 other; please specify:  
 information is not disseminated

**3.18 What are the challenges in the implementation of the pharmacovigilance system in the country? State all which apply**

**3.19. What activities are in planning for the further development of the pharmacovigilance system in the country? Please specify if these activities are related to the AMFm pilot phase or not.**

**3.20. What is your need for being able to further develop the pharmacovigilance system in your country.**

---

Many thanks for filling out the questionnaire. Please save the filled out form on your computer and then send it back per email as an attachment to the following email address: [Verena.renggli@unibas.ch](mailto:Verena.renggli@unibas.ch); **Deadline: 30 November 2010**

Please do not hesitate to send an email in case of any question.