WHO-EM/MAL/355/E

Report on the

Workshop on the use of serological techniques in malaria epidemiology and management for HANMAT countries

Alexandria, Egypt
2–4 June 2009

World Health Organization
Regional Office for the Eastern Mediterranean

WHO-EM/MAL/355/E

Report on the

Workshop on the use of serological techniques in malaria epidemiology and management for HANMAT countries

Alexandria, Egypt
2–4 June 2009

World Health Organization
Regional Office for the Eastern Mediterranean

Document WHO-EM/MAL/355/E/02.10/70

CONTENTS

1. INTRODUCTION

A workshop on the use of serological techniques in malaria epidemiology and management for HANMAT countries was organized by the World Health Organization (WHO) Regional Office for the Eastern Mediterranean in Alexandria, Egypt, from 2 to 4 June 2009. The workshop was attended by representatives from NAMRU-3, the Foundation for Innovative New Diagnostics (FIND), the World Wide Antimalarial Resistance Network (WWARN) and the London School of Hygiene and Tropical Medicine (LSHTM). The objectives of the workshop were to:

- update countries on the use of serological techniques for conducting malaria surveys;
- brief countries on new developments related to the use of rapid diagnostic tests (RDT) for malaria diagnosis;
- review results of drug efficacy studies and plan for studies to be conducted in 2010–2011;
- provide updates for resistance to ACTs and containment strategies;
- update objectives of HANMAT and discuss inclusion of monitoring and evaluation and surveillance activities;
- train laboratory technicians on the use of ELISA techniques for malaria.

Dr Hoda Atta, Regional Adviser for Roll Back Malaria, delivered the opening remarks of Dr Hussein A. Gezairy, WHO Regional Director for the Eastern Mediterranean. Dr Gezairy reminded participants that the emergence of artemisinin-tolerant malaria parasites had been reported from the Thailand–Cambodia border. This highlighted the need to maintain and strengthen surveillance activities for monitoring parasitic response to artemisinin. The introduction of ACTs and other prevention strategies had decreased transmission intensity in many countries, and had resulted in reducing and localizing the risk to defined geographical areas. Due to the reduction of the *P.falciparum* burden, it was necessary to highlight the importance of a correct estimation of the vivax problem and to ensure that *P.vivax* was still responsive to chloroquine.

Dr Gezairy noted that immunodiagnosis was the key tool for donor blood screening but had no role in confirmation of malaria in endemic areas. Outside endemic areas, it had clinical utility in ruling out malaria in microscopically-negative feverish patients returning from endemic areas. However, in epidemiological studies, serology provided species-specific information on past exposure to the infecting agent and could be applied to define and measure the intensity of malaria transmission, particularly in areas with low, sporadic transmission and to confirm the absence or presence of malaria in cities, high altitude areas, and in areas declared to be malaria-free. Serological markers appeared to be a promising tool in detecting spatial variation in malaria exposure and in evaluating malaria control efforts in areas with low transmission. At very low levels of transmission, parasite prevalence by microscopy was not a sensitive tool to evaluate interventions. Serology could be used as an alternative to parasite prevalence to assess transmission intensity, evaluate interventions and inform control programmes. During 2008–2009, this tool had been used in some Member States of the Region, namely: Afghanistan, Djibouti and Somalia.

The Chair was shared on a rotating basis. The programme and list of participants were included as Annexes 1 and 2, respectively. Annex 3 contains country plans for current/planned drug efficacy monitoring 2009 to 2010.

2. MALARIA CONTROL IN HIGH-BURDEN COUNTRIES: PROGRESS, CHALLENGES AND LESSONS LEARNT

2.1 Djibouti

Mrs Hawa Hassan Guessod

Fifty percent (50%) of the Djiboutian population are living in areas with risk of malaria transmission. In 2008, the total number of reported malaria cases was 3569, of which only 119 were confirmed. From February to March 2008 large scale distribution of LLINs was started with children under-5 years of age and pregnant women, with the objective of reaching 70% coverage of the at-risk population. In 2008 more than 90 000 LLINs were distributed. Implementation of the new antimalarial drug policy started from February 2008. The malaria programme received US$ 650 000 from different sources, including the World Bank, WHO and national funds.

Strengthening supervision and monitoring and evaluation of malaria case management, decentralization and improving vector control interventions, strengthening epidemiological and entomological surveillance and development and implementation of the communication strategy are the main priorities for the malaria programme over the next coming year, in addition to improving the malaria database.

2.2 Eritrea

Mr Afeworki Araya Ghebremariam

Studies in 2006 have shown that only 50% and 96% of Pf cases are responsive to CQ+SP and AS+SP, respectively. The 2007 study was to compare coartem and AS+AQ. While 100% of cases were sensitive to coartem, 94% of pf cases were adequately responsive to AS+AQ.

In 2008, malaria treatment and diagnosis guideline revised and ACTs and RDTs were distributed to selected malaria agents at community level. RDTs are used for parasitological diagnosis at health stations where there is no laboratory service. RDTs are also being gradually distributed at community level in order to treat confirmed cases through eligible health workers.

2.3 Saudi Arabia

Dr Mohamad Alzahrani

Saudi Arabia is at risk of many vector-borne diseases like most tropical and subtropical countries. Since 1948, anti-malaria activities started around the oil fields in the Eastern province by the ARAMCO (Arabian American Oil Company). In 1963, the government of

Saudi Arabia and WHO signed the first joint plan of a pre-eradication programme in line with the global malaria eradication programme at that time. Malaria in Saudi Arabia is mainly transmitted by *An. arabiensis*. Malaria foci are concentrated in the south and south-western part of the Kingdom (Jazan, Aseer, Qunfoda Regions).

The achievements in 2008 included updating the national policy of malaria case management, developing the integrated vector management strategy, intensifying human resource development activities, strengthening the surveillance and information system, developing epidemic preparedness and response national plan, strengthening collaboration and cooperation with Yemen, as well as promoting advocacy, health education and community participation plans and activities.

Challenges and future plans include:

1. the huge influx of imported cases from neighbouring countries and Horn of African countries (high vulnerability);
2. strengthening surveillance and case detection, both PCD and ACD, mobile teams to trace the immigrants for investigation and treatment;
3. monitoring the efficacy of AMDs jointly with Yemen at border areas;
4. working together with the national malaria control programme in Yemen to pursue the Malaria Free Arabian peninsula initiative;
5. an efficient malaria vector (*An. arabiensis*) and climatic changes favourable of malaria transmission (high receptivity) at the south-western regions;
6. Integrated vector management;
7. Monitoring the bionomics of the vectors, including the susceptibility of the vector to insecticides in sentinel sites;
8. intersectoral collaboration;
9. health education and community participation;
10. shortage in highly qualified and experienced professionals in some key areas of malariology, e.g. vector control, entomology and malaria case management;
11. development of the national training and research centre in Jazan to be a WHO collaborating centre for the Region and Horn of African countries.

2.4 Somalia

Dr Jamal Amran

The groups most severely affected are young children, pregnant women and nomadic populations. *P. falciparum* is the predominant parasite species. In 2008, the total reported number of cases and deaths were 24 136 and 21, respectively. The range of reported malaria parasite prevalence in different areas of Somalia in 2007–2008 was between 0% to more than 19%.

The main implemented activities in 2008 were: training on malaria microscopy and its quality control in referral and peripheral laboratories, supporting training of four entomology technicians in an MSc course in Sudan and two fellows in a planning course in the Islamic Republic of Iran, establishing four referral laboratories providing continuous supplies to 60

peripheral laboratories, supporting operational research in three zones and conducting quarterly supervisions.

Malaria control in Somalia is facing many challenges, including the lack of a strong central government resulting in instability in security, the increasing number of internally displaced persons, weak health management information systems/management information systems, frequent trained staff turnovers and lack of national staff motivation, doubt about the sustainability of the supply of ACT and RDTs for Somalia and inadequate human capacity in malaria microscopy and entomology and vector control and the lack of a central reference laboratory for quality control.

2.5 Sudan (north)

Dr Tarig Abdulghader

High skills in management of round 2 malaria grant from GFATM concerning resulted in high performance A+ (117.1%) in achieving programme-specific indicators. With this achievement the malaria programme became eligible for additional funds through the RCC (Rolling Continuation Channel) from the GFATM. The main achievements are as follows: high coverage of health facilities (90.8%) by ACTs in a very short time beside that home management of malaria was implemented in 150 villages with a population of 450 000, coverage by LLINs vis-à-vis to the targeted group approaching 97% for 2008 target while it represented 444% from the overall target set for 2012. Malaria programme has distributed 850 000 LLINs from January to May 2009 and expected to receive and distribute 4.5 to reach 70% coverage by the end of 2009.

Malaria morbidity has been reduced by 60% and this is due to a package of interventions that have been applied through the programme, including the treatment of 3.07 million malaria episodes using effective antimalarial drugs and large implementation of a large malaria project, that includes 97 hospitals, mainly in the areas with the highest burden which has contributed to decreasing the severe malaria cases.

Sudan has four sites for monitoring efficacy of antimalarial drugs. In 2008, drug efficacy studies were carried out in Kassala, Gezira, Blue Nile and White Nile States. Also, Sudan has conducted artemisinin + piperaquine (granules and tablets) with 96.2% and 100% as ACPR, respectively. Post-marketing surveillance was focusing on AS+SP in four sentinel sites (KRT, Atbara, Gedaref, Obied). The results showed that all brands were complying with standards.

The main challenges facing that malaria control programme are: weak monitoring and evaluation system, sustainability of free health service delivery both prevention and case management and continuation of high performance of GFATM grants. To address these challenges malaria programme is planning to invest more in human resources development particularly at the peripheral level, improve and expand microscopic diagnosis, scaling up of the available effective preventive and treatment tools (ACTs and LLINs), and selective operational research.

2.6 Sudan (south)

Dr Jeylani Mohamoud

The yearly report on disease morbidity, including malaria, has been produced by UNICEF since 2003. These data were collected from outpatient dispensaries supported by nongovernmental organizations receiving regular essential drug kits from UNICEF. The number of reported malaria cases has been decreased from 620 000 in 2003 to 148 343 in 2008 which is mainly due to lack of reports from substantial number of health facilities.

Based on the data from the Sudan Household Health Survey, 2006, 18.1% of households have at least one insecticide treated bednet and 27.8% of children are sleeping under a bednet. By the end of 2008, approximately 9 million people were covered by bednets. It is expected that the coverage of LLINs is very close to targets; this should be confirmed by the planned household survey in 2009.

Main challenges of malaria control programme for scaling up malaria control measure are: very weak health system, limited trained human resource within the programme, weak coordination of partners at different levels, country-wide shortage of commodities—ACT and RDTs, inadequate monitoring and evaluation capacity at all levels, weak drug procurement and supply management system, weak laboratory network system, quality control and quality assurance.

2.7 Yemen

Dr Adel Aljassari

The greatest burden of malaria in the Arabian Peninsula occurs in Yemen. In an effort to reduce the burden of malaria in the country the national malaria control programme has implemented an integrated malaria control strategy of case management, integrated vector control, including long-lasting insecticide bednets, indoor residual spraying (IRS) and larviciding and community health education. 725 285 LLINs have been distributed since 2006 which means at least 1.5 million people are protected with this effective vector control tool.

In 2008, pilot implementation of home management of malaria with support from Kuwait started in two districts with functioning BDN projects. Activities included conducting entomological and parasitological surveys to establish baselines, LLINs were distributed to reach universal coverage with one net for every two individuals, an adequate number of ACTs and RDTs were provided. Male and female volunteers were trained on diagnosis and treatment, IRS and larviciding. There is a plan to pilot community implementation of IRS and larviciding with technical guidance from the national malaria control programme.

Yemen hosted the first regional training on RDTs (training of master trainers). There is no reliable data about the magnitude of RDTs use in the country; however, the private sector and some main public hospitals and nongovernmental organizations are using RDTs. RDT is being used in the household survey for diagnosis and treatment of positive cases and also outbreak investigations. There is a plan to scale-up RDTs through the R7 GFATM grant.

For strengthening malaria monitoring and evaluation and surveillance the malaria monitoring and evaluation plan updated to accommodate the Global Fund and Gulf Cooperation Council (GCC) plans, a fully-fledged monitoring and evaluation unit is being established, and building monitoring and evaluation capacities at the subnational level is considered as a priority. To have a better understanding of the malaria burden and converge of main interventions Implementation of household survey in two phases started in 2009.

A technical panel from the MoPHP and the academia approved the final draft of national malaria treatment guidelines and the new policy was officially announced during the celebration of the World Malaria Day. Training and orientation of 2680 of medical staff all over the country during and procurement of 18 000 doses of ACTs and implementation of a supervised plan for the distribution of 130 000 doses of ACT in the whole county and recruitment of a supply management officer through GFATM funds are the main activities for scaling up of effective malaria treatment.

Providing proper case management in private sector, establishment of mechanisms for the distribution and utilization of the ACT, weak health information system, inadequate monitoring and supervision mechanisms and weak community participation for malaria control are the main challenges.

Support Socotra pre-elimination phase, updating the national programme's strategic plan 2010–2020, improvement of the quality and expanding the microscopy services and strengthening the quality assurance and quality control systems, strengthening monitoring and evaluation and surveillance systems, and conduction of a national risk-mapping exercise are the nest steps.

3. UPADTE ON TECHNICAL ISSUES

3.1 Updates for antimalarial drug monitoring, status of resistance to ACTs and its containment strategies

Dr Pascal Ringwald

Antimalarial drug resistance is a major public health problem, which hinders the control of malaria. Faced with this growing burden, the establishment of a surveillance system for monitoring is urgently needed to allow better containment.

In 1996, WHO developed a new protocol for assessing antimalarial drug resistance for high-transmission areas. This protocol has recently been updated and the protocol for low to moderate transmission areas has been validated. The fundamental design of these protocols for surveillance is intended to provide essential information for monitoring the therapeutic efficacy of a range of antimalarial drugs against uncomplicated falciparum malaria and to ensure a minimal evidence base from which ministries of health can develop informed treatment policies and guidelines. The use of a standardized protocol will allow the comparison of the results in country and among countries in the same region.

The recent version of the efficacy test protocol was adopted in 2001, later adjustments made to incorporate the changes recommended by the Technical Expert Group on Malaria Chemotherapy, which met in 2005. In 2008, the most recent changes, which are incorporated into this document, are:

- applications of the same definitions of treatment responses at all levels of malaria transmission, with slight adjustment of patient inclusion criteria;
- administration of rescue treatment to patients with parasitological treatment failure at all levels of malaria transmission;
- requirement for 28 or 42 days of follow-up as a standard, depending on the medicine tested; and
- requirement for genotyping by polymerase chain reaction (PCR) to distinguish between recrudescence and reinfection.

The introduction of artemisinin-based combination therapy and other control strategies has decreased transmission intensity in many countries, reducing and localizing the risk to defined geographical areas. Several suggestions have been made to overcome this problem.

- Reduce the minimum parasitaemia limit
- Include a wider age range
- Use others tools, such as molecular markers
- Include all patients (of all ages and parasitaemia levels) when countries are in an elimination phase.

Through their routine monitoring system, Thailand and Cambodia have been able to observe over the last five years a gradual decline in the efficacy of artemisinin-based combination therapies (ACTs)-i.e. artesunate-mefloquine and artemether-lumefantrine-at their sentinel sites in particular at the Thailand-Cambodian border. It was initially believed that this was due to resistance to the amino-alcohol partner drugs, i.e. mefloquine and lumefantrine. However, parasite clearance times (PCT) were also increasing, raising concerns of artemisinin resistance.

Results of additional research studies coordinated by WHO, confirmed prolonged PCTs following treatment with ACTs and artesunate monotherapy. There is no clear evidence that artesunate resistance has emerged. Higher doses of artesunate (6 and 8 mg/kg) did not overcome resistance. Vigorous control efforts are under way to contain the artesunate resistant parasite in this area which includes:

- eliminating artemisinin tolerant parasites by detecting all malaria cases in target areas and ensuring effective treatment and gametocyte clearance
- decreasing drug pressure for selection of artemisinin resistant malaria parasites (including monotherapy ban)
- preventing transmission of artemisinin tolerant malaria parasites by mosquito control and personal protection
- limiting the spread of artemisinin tolerant malaria parasites by mobile/migrant populations

- conducting basic and operational research to fill knowledge gaps and ensure that strategies applied are evidence-based.

3.2 To brief countries on new development related to the use of RDT for malaria diagnosis

Dr David Bell

Parasite-based diagnosis is essential to guide appropriate use of anti-malaria drugs, for monitoring of malaria incidence and response to interventions, and to guide early management of non-malarial febrile illness. While light microscopy remains essential and requires increased support, the widespread use of rapid diagnostic tests is necessary for most endemic country programmes if all populations at risk are to have access to appropriate case management.

The number of RDTs available has increased rapidly over the past few years, driven partly by recognition of the need and availability of increased funding. However, published trials have shown a wide variation in sensitivity and stability of these tests, resulting in uncertainty regarding their effectiveness in remote tropical and sub-tropical areas. To ensure safe case management and to provide health personnel with the confidence necessary to rely on RDTs when making decisions on treatment, RDTs must be of high and consistent quality at the site of their use, and demonstrated to be so. While introduction and effective use of RDTs in malaria programmes requires detailed planning, from logistics and training to community education to management capacity for non-malarial febrile illness, the programmes' success relies first on the tests providing a correct result to guide treatment decisions. This requires good manufacture, safe transport and storage, and correct test preparation and interpretation.

Manufacturers have been hampered in addressing consistency and quality by a lack of standards and materials for quality control and lot-release testing, while programmes have had limited information on product performance on which to base procurement decisions and limited capacity to monitor test quality after procurement. The recent round of product testing at US Centers for Disease Control (CDC), conducted by WHO and FIND, has provided a snapshot of performance of a large number of commercially-available RDTs. The results show a wide variation in performance, and also show that current manufacturers are capable of producing high-quality and potentially reliable tests. The availability of lot-testing under the same programme currently allows countries to ensure RDTs are of acceptable quality for most case management on receipt, and developments over the next few years will provide much more accessible and sustainable methods for ensuring quality and consistency from the place of manufacturer to the patient in the remote village. Countries should now be using RDTs as a basis for case management on a wide scale, but using available information and capacity to assure the quality of these tests.

While RDTs are appropriate for case management, more sensitive platforms are needed for parasite detection in population screening surveys to assess progress towards malaria elimination. At present, DNA detection by conventional PCR methods is the only method available, but it is expensive and limited to large laboratories. Lower cost, high-throughput

methods of DNA detection such as LAMP (Loop-mediated isothermal amplification) offer potential solutions to this, but still remain to be proven in the field.

3.3 Malaria risk mapping: Somalia

Dr Abdisalam M. Noor

The Malaria Atlas Project (www.map.ox.ac.uk) has just released a global malaria risk map. The map was created by first defining the limits of transmission of *Plasmodium falciparum* infection. This was done using a combination of medical intelligence data, annual parasite incidence, temperature and aridity. The limits were defined as: no risk, unstable and stable risks. These maps were produced from *P. falciparum* parasite prevalence using Bayesian geo-statistical techniques. For the Eastern Mediterranean Region, data were mainly available for most of Somalia, western part of Yemen, eastern part of Iraq, Afghanistan, and southern Sudan. All other countries had minimal or no data. Majority of the population lived in areas of no risk or unstable risk. Most of those populations in the stable risk areas were in Somalia, southern Sudan and western Yemen. Additional data are required especially for Saudi Arabia, northern Sudan, central and eastern Yemen, Islamic Republic of Iran, Egypt and Iraq. Somalia was presented as an example of detailed analysis possible for countries where rich data exist. An example of prospective parasitological surveys was presented using Djibouti. The results of the Djibouti malaria indicator survey for the period 2008–2009 show a national parasite prevalence of 0.6%; an overall household insecticide-treated net (ITN) coverage of 12 people per net; and 13% of individuals sleeping under a net before the survey.

3.4 Briefing on WWARN perspective and progress

Dr Philippe Guerin

About 40% of the world's population is at risk of malaria, mostly those living in the poorest countries. Of these 2.5 billion people at risk, more than 500 million become severely ill with malaria every year and more than 1 million die from the effects of the disease. Currently, there is no vaccine to prevent malaria, so treatment relies only on antimalarial drugs. As a consequence of this reliance on drug treatment, the parasites that cause malaria have evolved resistance to most of the antimalarials used in the past.

The Worldwide Antimalarial Drug Resistance Network (WWARN) has been recently established. The initiative comes at a crucial time of renewed focus on the eradication of malaria. The successful use of drugs for treatment and prevention required to achieve this long term goal depends critically on a steady supply of solid intelligence on the efficacy of antimalarial drugs. Resistance to current therapies may have already evolved in Southeast Asia, highlighting the need for comprehensive surveillance data to provide evidence to justify and guide the huge effort to contain emerging resistance.

WWARN will impact four areas that are critical to the control and elimination of malaria:

- Reliable, current, and site-specific information on efficacy must underpin the drug choices made. WWARN will provide the evidence required for policy-makers at national, regional, and international levels to optimize antimalarial use.

- There is a need to identify new foci of drug resistance rapidly, even at low levels. WWARN will link clinical outcomes and validated surrogate molecular and in vitro markers of resistance to ensure that resistance will be identified and confirmed as it emerges, and permit, for the first time, vigorous containment and control actions to eliminate resistant parasites before they spread.

- By linking pharmacological data with clinical, in vitro, and molecular measures of resistance, it will be possible to optimize drug combination, dosing and delivery strategies to improve efficacy and deter resistance.

- Finally, the comprehensive data sets and global coverage will permit mapping and modelling of temporal and geographical trends in antimalarial resistance. This predictive capacity is crucial to ensure that alternative malaria control, elimination, and eventually eradication strategies, are reviewed objectively and operational decisions optimized.

WWARN relates to all stakeholders involved in antimalarial drug treatment and prevention activities, including WHO, ministries of health, policy-makers, health-care providers, funding bodies and research groups, to maximize the breadth, quality, timeliness, and utility of efficacy data. WHO has prepared a model for support to country-based collection of treatment efficacy data to complement WWARN's system for data collation, analysis and quality assurance.

WWARN will create a central database of information from all malaria-endemic areas, in order to collate and analyse: clinical drug efficacy, critical pharmacological information as it relates to efficacy and safety, in vitro susceptibility of parasites to antimalarial drugs, and molecular markers of drug resistance. This database will have appropriate tools to allow comparison of data sets so that the geographic and temporal trends in drug efficacy can be monitored effectively and provide evidence in a timely manner to policy-makers.

WWARN will not conduct primary data collection, but rather build capacity within malaria-endemic countries and encourage researchers to contribute high-quality data to the WWARN database. Crucially, WWARN will provide technical support for data collection teams to build capacity in malaria-endemic countries. These teams will, in turn, be the most effective voices engaging with policy-makers locally to use and act upon the evidence generated.

WWARN is extremely keen to develop a strong collaboration with HANMAT, under the umbrella of WHO Regional Office and headquarters and hope the tools that are being developed will serve the interest of the Ministry of Health, and in particular, national malaria control programmes in the Region.

3.5 Update countries on use of serological techniques for conduction of malaria surveys: value, limitations, sampling design and data collection, analysis and interpretation

Dr Christopher Drakeley

Antibodies are made as part of the immune response to malaria infection and therefore represent a marker of exposure. Antibodies can be detected by a variety of measures, the most commonly used current methods are the immunofluorescence microscopy (IFAT) and the enzyme-linked immunosorbent assay (ELISA). In broad terms the IFAT is sensitive but subjective assay requiring specific microscopy expertise and the ELISA is specific and objective. Results are recorded as either antibody negative/positive (ie sero-prevalence) or the magnitude of antibody response: for IFAT a titre and for ELISA an optical density (OD) measurement.

In epidemiological terms the major advantage of serological analysis is that antibodies persist for a considerable time after an infection and can be detected at very low levels. This means that serology can be used in areas where conventional malariometric measures, EIR and parasite rate, become less viable and reliable. This adds considerably to the utility of MIS in this such that:

- when antibody data are combined with age they can provide information transmission intensity (and changes in this);
- when used alongside other indicators (travel, occupation, net use) that can indicate potential risk factors;
- when combined with geographical data (GPS or other) they can indicate potential foci of transmission.

In the 1960s and 1970s much use was made of sero-epidemiology in the context malaria control elimination, including two classic studies by Bruce-Chwatt and colleagues, which were used to confirm malaria elimination in Mauritius and Turkey. However, widespread use was limited by a lack of comparability between assays.

Key developments to adapt this to low transmission settings in the current control and elimination are for standardized ELISA-based assays for both Pf and Pv together with a series of technical tools that allow easy data manipulation and analysis. These should be available as part of a standard training package to country members. Detailed statistical, mathematical and spatial modellings are provided by LSHTM and these will be refined as data are collated. The rationale for using sero-epidemiology will depend on the country and region though several broad uses can be envisaged:

- Situational analysis – to provide preliminary serological data to compare with that on parasite rates etc. in initial MIS surveys;

- Monitoring and surveillance – to assess the affect of control measures over time with reductions in sero-prelavence and antibody titres as sensitive survey endpoints;

- Surveys for malaria free status – to show no indigenous or local transmission in a specific target population (e.g. children under 5 years of age).

3.6 Validity of Blood Spot, Filter Paper Storage and ELISA

Drs Hanan El-Mohamady and Isabelle Nakhla

Dried blood spot specimens are clinical specimens collected by carefully applying a few drops of blood, freshly drawn by finger stick from adults and children, or by heel stick from infants, onto specially manufactured absorbent specimen collection (filter) paper. Avalid dried blood spot (DBS) should be dried properly and stored appropriately. DBS should be inspected for spot quality since blood drop is considered a volumetric measure.

Several advantages of DBS are: 1) easy to collect, store, and transport; 2) stable and adaptable for a variety of techniques; and 3) relies on whole blood as the matrix and it is safer to handle than liquid. Some of the disadvantages of DBS are 1) a skin puncture is required; 2) only small sample volumes can be collected ;and 3) samples must be diluted for analysis.

The most applicable fields for DBS are antibody testing and DNA/RNA amplifications. A DBS is considered invalid if the quantity of specimen is not enough to allow for testing, the specimen appears scratched or abraded, the specimen has been stored prior to complete drying, the spot is supersaturated with specimen, a serum ring appears around the spots, and/or the specimen appears clotted or layered.

4. PRESENTATION OF THE LATEST RESULTS OF DRUG EFFICACY STUDIES AND DEVELOPMENT OF PLAN OF ACTION FOR 2008–2009

Based on the recommendations of technical discussions, country representatives developed plans of action for conducting drug efficacy studies during 2010–2011 (see Annex 3).

5. CONCLUSIONS

It was agreed to assign a coordinator and administrative assistant to manage the activities of the Horn of Africa Network for Monitoring Antimalarial Treatment (HANMAT). The national malaria manager from Sudan was selected as coordinator for HANMAT for one year and WHO was requested to recruit an administrative assistant. The coordinator, in collaboration with the previous chairman of HANMAT, will update the objectives of HANMAT and define terms of reference for the coordinator and administrative assistant and share them with countries of HANMAT for comments.

Countries decided to expand the mandate of HANMAT beyond drug efficacy monitoring to include serological diagnostic assays, molecular biology techniques and quality assurance of microscopy/rapid diagnostic tests (RDTs).

Countries appreciated the current collaboration between WHO and the U.S. Naval Medical Research Unit No. 3 (NAMRU-3) and strongly supported expansion of this collaboration to include the London School of Hygiene and Tropical Medicine and the Worldwide Antimalarial Resistance Network (WWARN).

All countries agreed to cooperate and share raw data related to drug efficacy studies with WWARN through WHO.

Saudi Arabia expressed interest in supporting HANMAT countries in various areas related to vector-borne diseases through the national training and research centre in Jazan. HANMAT countries welcomed the initiative and requested Saudi Arabia to support assessment of the capacity for, and feasibility of, antigen production for serological studies in national research/academic institute(s).

The London School of Hygiene and Tropical Medicine agreed to develop guidelines for sampling, designing, conduct and statistical analysis of seroprevalence studies and NAMRU-3 agreed to provide standard operating procedures for collection, storage, shipment and analysis of samples within the next three months.

6. RECOMMENDATIONS

To HANMAT countries

1. Assess the needs for strengthening national capacity in the areas of drug efficacy monitoring, serological assays, molecular biology techniques and quality assurance of microscopy and RDTs and share them with the HANMAT coordinator and WHO Regional Office within the next three months.

2. Include sufficient funding for activities in the above-mentioned areas, as well as for national capacity-building in proposals submitted to donors, particularly the Global Fund to fight AIDS, Tuberculosis and Malaria.

3. Continue drug efficacy studies of the first- and second-line medicines and new antimalarial medicines for faciparum malaria using the updated WHO protocol (2009). Studies on drug efficacy in relation to *P. vivax* should be considered in areas where there is local vivax transmission. Molecular marker studies should be conducted simultaneously with in vivo studies, if the molecular markers are known and have been validated (i.e. mefloquine, sulfadoxine–pyrimethamine and chloroquine).

4. Conduct a multiple-centre study or joint study in border areas with neighbouring countries for areas that do not have enough cases for drug efficacy studies. Other tools of the early warning system should also be used, such as molecular marker studies and in vitro studies.

5. Take all action necessary to address the serious issue of counterfeit antimalarial medicines, including reviewing legislative measures regarding importation of

antimalarial medicines and monitoring the quality of medicines introduced into countries through the post-marketing surveillance system.

6. Consider the results of the recent evaluation of RDTs conducted by WHO and other partners in decision-making for procurement of RDTs in light of the many poor performing RDTs available on the market.

To WHO and partners

7. Recruit an administrative assistant to support coordination and information-sharing among HANMAT countries, and continue to support the annual meeting/workshop for HANMAT countries.

8. Conduct the regional training of trainers course on RDTs annually in Yemen.

9. Organize a training course on the polymerase chain reaction (PCR) technique in conjunction with the next HANMAT meeting in 2010, in coordination with NAMRU-3 and other partners.

10. Provide technical support for assessment of the technical capacity of academic or research institutes in Saudi Arabia with regard to production of the antigen needed for serological studies.

Annex 1

PROGRAMME

Tuesday, 2 June 2009

08:00–08:30	Registration	
08:30–09:00	Opening session • Opening remarks from WHO/EMRO • Opening speech by NAMRU-3	 *Dr H. Atta* *Dr M. Mansour*
09:00–09:30	Updates for antimalarial drug monitoring, status of resistance to ACTs and its containment strategies	*Dr P. Ringwald*
09:30–10:00	Discussion	
10:00–10:15	Report on 2008-2009 activities by acting Chairman	*Dr T. Abdelgadir*
10:30–16:00	Country presentations on activities conducted in 2008, with emphasis on drug efficacy, ACT and RDT implementation • Djibouti • Eritrea • Ethiopia • Saudi Arabia • Somalia • Sudan (north) • Sudan (south) • Yemen	*Country Representatives*
16:00–16:15	Discussion	
16:15–16:45	To brief countries on new development related to use of RDT for malaria diagnosis	*Dr D. Bell*
16:45–17:00	Discussions	

Wednesday, 3 June 2009

08:30–09:00	Briefing on WWARN perspective and progress	*Dr P. Guerin*
09:00–09:30	Discussions	

09:30–10:00	Update countries on use of serological techniques for conduction of malaria surveys: value, limitations, sampling design and data collection, analysis and interpretation	*Dr C. Drakeley*
10:30–11:00	Validity of blood blot, filter paper storage, ELISA interpretation Feedback on the training conducted 31 May–1 June 2009 on serological techniques	*Dr H. El Mohammady* *Dr I. Nakhla*
11:00–11:30	Discussion	
11:30–12:30	Partnership between WHO, LSHTM, NAMRU-3	
13:30–14:00	Report on Djibouti malaria survey	*Dr A. Noor*
14:00–14:30	Update on MAP	*Dr A. Noor*
14:30–15:00	Discussions	
15:30–17:00	Future of HANMAT: discussion on Chairmanship, administrative issues, fund for HANMAT from GF grants, developing regional proposal for HANMAT to GFATM – Round 10 and plan for future drug monitoring	*Dr A. Adeel* *Dr H. Atta* *Dr P. Ringwald*

Thursday, 4 June 2009

08:30–09:15	Update on surveillance guidelines; *World malaria report* and next biennium planning	*Dr G. Zamani*
09:15–11:00	Group work: Planning for next biennium	
11:00–12: 30	Group presentation and discussion	
11:00–12:30	Future for HANMAT: Discussion on Chairmanship, administrative issues, fund for HANMAT from Global Fund grants, developing regional proposal to GFATM – R10	
13:30–14:30	Conclusions, recommendations	
14:30	Closing session	

Annex 2

LIST OF PARTICIPANTS

DJIBOUTI
Mrs Hawa Hassan Guessod
National Malaria Coordinator
National Malaria Control Programme
Ministry of Health
Djibouti

Mr Maoulid Mohamed Barkad
Head of National Laboratory
National Public Health Laboratory
Ministry of Health
Djibouti

EGYPT
Dr Ahmed El Taher Khater
ELISA Focal Point
General Administration for Malaria and
Filariasis
Ministry of Health
Cairo

ERITREA
Mr Afeworki Araya Ghebremariam
Zonal Malaria Coordinator
Malaria Unit
Ministry of Health
Gash Barka-Barentu

MOROCCO
Mrs Noura El Maimouni
Principal State Engineer
Department of Parasitology
National Health Institute
Ministry of Health
Rabat

SAUDI ARABIA
Dr Mohamed Al Zahrani
Director of Malaria Department
Ministry of Health
Riyadh

Dr Adel Ali Al-sheikh
Director of the National Centre for Training and Research (TD)
Ministry of Health
Jazan

SUDAN
Dr Tarig Abdelgadir Mohamed
National Malaria Control Programme Coordinator
Federal Ministry of Health
Khartoum

Dr Abdalla Ahmed Ibrahim
Monitoring and Evaluation Focal Person
Federal Ministry of Health
Khartoum

Mr Mahmoud Ali Mudather Mohamed
Quality Assurance for Diagnosis Officer
National Malaria Control Programme
Federal Ministry of Health
Khartoum

Mr Abe Gordon Abias
Deputy Director
Public Health Laboratory
Ministry of Health/Government of southern
Juba

YEMEN
Dr Adel Nasser Al Jasari
National Malaria Control Programme Manager
Ministry of Public Health and Population
Sana'a

Dr Abdul Rahman Saleh Abdulmalik Al Aleemi
Director General
National Malaria Control Programme
Ministry of Public Health and Population
Sana'a

OTHER ORGANIZATIONS

EGYPT
Dr Moustafa M. Mansour
Director of Research Sciences
US Naval Medical Research
Unit #3 (NAMRU-3)
Cairo

Dr Hanan El Mohammady Ismail
Head, Immunology Section
Clinical Trials Research Programme
US Naval Medical Research
Unit #3 (NAMRU-3)
Cairo

Dr Isabelle Antoun Nakhla
Clinician and Clinical Research
Clinical Trials Research Programme
US Naval Medical Research
Unit #3 (NAMRU-3)
Cairo

UNITED KINGDOM
Dr Philippe Guerin
Executive Director
WorldWide Antimalaria Resistance
Network (WWARN)
Oxford

KENYA
Dr Abdisalam M. Noor
Post-Doctoral Research Scientist
Malaria Public Health and Epidemiology Group
Centre for Geographic Medicine
KEMRI-University of Oxford-Wellcome Trust
Collaborative Programme
Nairobi

WHO SECRETARIAT

Dr Hoda Atta, Regional Adviser, Roll Back Malaria, WHO/EMRO
Dr Pascal Ringwald, Medical Officer, Global Malaria Programme, WHO/HQ
Dr Ghasem Zamani, Medical Officer, Roll Back Malaria, WHO/EMRO
Dr Mohamed Ali Khalifa, Medical Officer, WHO Office, Saudi Arabia
Dr Jamal Ghilan Hefzullah Amran, Medical Officer, WHO Office, Kenya
Mr Kamal Salih Mustafa, RBM Technical Officer, WR Office, Yemen
Mr Mohamoud Wais, RBM Technical Coordinator, WR Office, Sudan
Dr Jeylani Abdullahi Mohamoud, RBM Technical Officer, WHO Office, south Sudan
Professor Ahmed Adeel, WHO Temporary Adviser, Saudi Arabia
Dr Abdisalam M. Noor, WHO Temporary Adviser, Kenya
Dr Christopher Drakeley, WHO Temporary Adviser, United Kingdom
Ms Nahla Ibrahim, Secretary, Division of Communicable Disease Control, WHO/EMRO
Mrs Fatma Abdel Meguid, Help Desk Assistant, WHO/EMRO

Annex 3

CURRENT/PLANNED DRUG EFFICACY MONITORING, 2009–2010

Table 1. Current/planned drug efficacy monitoring, 2009–2010

Country	Sentinel sites	Antimalarial medicines needed	Starting date	Source/ funding available	Molecular laboratory/ laboratory to be used	Other needs	Comments
Saudi Arabia	Villages at the border area inside Yemen	ASU+SP	Fourth quarter of 2009	WHO US$ 30 000	NAMRU 3	WHO Consultant	The details will be decided jointly with Yemen
	Villages at the border area inside Yemen	ART+LUM	Fourth quarter of 2009	WHO US$ 20 000	NAMRU 3	WHO Consultant	The details will be decided jointly with Yemen
Somalia	Jammame	ASU+SP	Oct/Dec 2009	GFR6	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (September 2008)
	Janale	ASU+SP	Oct/Dec 2009	GFR6	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (September 2008)
	Jowhar	ASU+SP	Oct/Dec 2009	GFR6	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (September 2008)
	NWZ and NEZ	ASU+SP	Whenever there are enough malaria cases	GFR6	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (September 2008)
	Jammame	ART+LUM?	Sep/Nov 2010	GFR6?	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (August 2009)

	Janale	ART+LUM?	Sep/Nov 2010	GFR6?	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (August 2009)
	Jowhar	ART+LUM?	Sep/Nov 2010	GFR6?	NAMRU3	Technical assistance Slide recheck (ext. slide ex)	Planning and training will start one month earlier (August 2009)
Sudan (north)	Obeid	AS+SP	Sep/Nov	7000/ GF R7	NAMRU3	Technical assistance Drugs: Laboratory requirements: Filter papers Reagents Slide recheck	
	Damazin(BN)	ART+LUM	Aug/Nov	7000/ GFR7	NAMRU3		
	Kassala	AS+SP	Aug/Nov	7000/ GFR7	NAMRU3		
	Gezira	ART+LUM	Aug/Nov	7000 / GFR7	NAMRU3		
Sudan (south)	Juba Teaching Hospital	AS+AQ	Sep 2009	GFATM round 7	KEMRI	Training, Laboratory Supplies and equipment, communication, internal and external quality control	NAMRU 3, as an alternative option for PCR Drugs in test and filter papers for PCR as well as external QC have to be sent by WHO. For all sentinel sites. Consultant for basic training to the study teams in all sentinel sites.
	Malakal Teaching Hospital	ART+LUM	Oct 2009	GFATM round 7	KEMRI	Training, Laboratory Supplies and equipment, communication, internal and external quality control	
	Wau Teaching Hospital	AS+AQ	Oct 2009	GFATM round 7	KEMRI	Training, Laboratory Supplies and equipment, communication, internal and external quality control	

Yemen	Al-Malahedh (Hajjah governorate)	ART+LUM	Oct 2009	Yes	NAMRU 3	Drugs, slides, reagents, transportation costs, stationeries, photocopying	
	Bajil (Hodidah governorate)	ART+LUM	Oct 2009	Yes	NAMRU 3	Drugs, slides, reagents, transportation costs, stationery, photocopying.	
	Al-Mesemeer (Lahj governorate)	ASU+SP	Oct 2009	Yes	NAMRU 3	Drugs, slides, reagents, transportation costs, stationery, photocopying.	
	Jabel Al-Sharq (Dhamar governorate)	ASU+SP	Mar 2010	Yes	NAMRU 3	Drugs, slides, reagents, transportation costs, stationery, photocopying.	
	Al-Odein (Ibb governorate)	ASU+SP	Mar 2010	Yes	NAMRU 3	Drugs, slides, reagents, transportation costs, stationery, photocopying.	
	Al-To Bani Qais	ASU+SP	July 2010	Yes	NAMRU 3	Drugs, slides, reagents, transportation costs, stationery, photocopying.	