



EDCTP Stakeholder Meeting on Malaria

Online Consultation Feedback

1 Introduction

EDCTP set up an online consultation to gather views from stakeholders ahead and directly following the meeting. The comments and recommendations informed discussions at the respective meeting, provided input for the final meeting report and where appropriate shall contribute to EDCTP strategy in this field. The open consultative process involved a broad range of stakeholders from academia, industry, foundations, non-governmental organisations, civil society, governments and other interested parties working in the field of Malaria.

The feedback from the online consultation is presented in this document as they have been submitted.

2 Online Consultation Feedback

Prof. Salim Abdulla

Ifakara Health Institute, Tanzania

Current status of the field

Progress has been made in many parts of Africa, remain challenges is having new tools for elimination of the disease. in other areas increasing access to control tools in a big challenge (ITN ACTs etc) so either better and simpler to deploy tools are developed or approaches to scale up in ares with limited health infrastructure are developed

Future Directions

Malaria vaccines: the deployment of the potential first generation (RTSS) and new ones (whole sporozoite vaccines). Development of cheaper vector control strategies that can easily be managed by communities themselves

The role of EDCTP

Funding the R&D of the intervention mention

Convener of investigator groups on the specific topics by encouraging and funding consortia for the different intervention as was done for the development of RTSS

**Dr Pietro Alano**

Istituto Superiore di Sanità, Italy

Current status of the field

One challenge to ensure long term success to current efforts is to face in due time the possible spread of parasite reduced sensitivity, if not direct resistance, to artemisinin derivatives, which would bear dramatic consequences in the African settings. Another key issue is to improve our understanding of aspects of human-mosquito transmission dynamics (e.g. gametocyte reservoirs in asymptomatic carriers; persistence of gametocytes between transmission seasons; gametocyte development in the human host; epidemiological implications of the differences in gametocyte physiology and maturation time between *P. vivax* and *P. falciparum*)

Future Directions

Novel drugs are required to prepare artemisinin replacement in order to aggressively treat *P. falciparum*, ideally targeting also the comparatively more elusive ring stages, as well as to target *P. vivax* hypnozoites and *P. falciparum* gametocytes with safer drugs than primaquine. As five to ten years is a short time to introduce such tools in the field, significant advances are foreseen only if current efforts in establishing novel/better screening assays on the such parasite stages are adequately supported

The role of EDCTP

Besides the traditional support to clinical trials, EDCTP could strengthen the North-South networking activities towards the formation of a new generations of DC researchers engaged in fundamental research. This activity, properly integrated with clinical and field work, could ultimately create a self-sustainable critical mass of fundamental research in DC whose unique proximity to the field could identify the most relevant scientific questions and the most appropriate experimental approaches. Malaria research network such as EVIMalaR (Europe), which is planning to continue its activities beyond 2014, or the Italian Malaria Network could be partners in such networking and capacity building activities

Prof. Per Ashorn

University of Tampere, Finland

Current status of the field

Provision of reliable and inexpensive diagnostic tools and affordable and effective drugs and vaccines - and of course improvement of the health systems in malaria endemic areas.

Future Directions

Rapid tests can be improved (in terms of performance, ease of use and price). New drugs could be developed for malaria in pregnancy. Some vaccine candidates might come a long way.

The role of EDCTP

EDCTP is a funding agency that has a mandate to fund controlled trials. I would suggest it stay that way - whilst liaising with other funding agencies.



Prof. Karen I Barnes

University of Cape Town / WWARN

Current status of the field

Limited focus on high risk target populations, and role of antimalarials for reducing transmission

Future Directions

Optimal dosing in key target populations, and improved use of drugs to reduce gametocyte carriage

The role of EDCTP

Capacity building for PKPD studies

Better use of available data by supporting harmonisation efforts for data collection, and sample assays and pooled individual patient data analyses

Dr Isabella Beretta

State Secretariat for Education, Research and Innovation SERI, Switzerland

Current status of the field

limitations are the lesser economic interest in poverty related diseases, political instability important are research, capacity building, training, sustainable health systems

Future Directions

Comments from government perspective

foster solid basic research into new products and CT collaborations

The role of EDCTP

EDCTP has delivered fundamental outcomes as first initiative fostering NN and NS collaborations

collaboration with industry has to be improved

Dr Pedro Berzosa

Instituto de Salud Carlos III (ISCIII) National Center of Tropical Medicine, Spain

Current status of the field

I think we need greater involvement of local governments, and of course support from developed countries in the development of new antimalarial cheap and effective. Support disease control, and try to avoid the emergence of resistance.

Future Directions

Future work should be aimed at creating an effective vaccine against malaria, but meanwhile it is necessary for there to support appropriate treatment, makes extensive use of the TPI, distribution of bed nets. Trying to control the production of antimalarials drugs to avoid that are in poor condition and control of stocks and free access to the antimalarial drugs.

The role of EDCTP

I think it is necessary collaboration between laboratories working on different aspects of malaria, and try to get projects to fund activities in endemic countries aimed at improving the situation. I think the TVET can be a good mediator to facilitate international relations and facilitate contacts laboratories.

**Dr François Bompert**

EFPIA/Sanofi, France

Current status of the field

Key issues are not specific to malaria but are related with the overall poor status of healthcare systems in most sub-Saharan countries (lack of political priority, infrastructures, trained staff, sustainable financing mechanisms, etc.).

Future Directions

Better integration of malaria control programs by MoH in overall healthcare management at country level.

The role of EDCTP

EDCTP has a fundamental role to play in building capacity, fostering partnerships and funding landmark clinical trials to develop the drugs and vaccines that will be needed to overcome current and future challenges.

Dr Steffen Borrmann

Magdeburg University School of Medicine, Germany

Current status of the field

Besides the challenges posed by weak health infrastructures/economic issues, the well known key biological challenges are of evolutionary nature: drug resistance and immune evasion that underpin therapeutic and prophylactic obstacles.

Future Directions

Perhaps our best hope is to press on with whole organism-based vaccine approaches. Sporozoite infection/treatment is the current benchmark for an experimental malaria vaccine and encouraging and rapid progress is made in this area. As far as therapeutic choices are concerned, I believe that we will have to continue to develop the "next" drug/combination as resistance will emerge to any new drug/combination eventually and as long as malaria is around. In general, the emphasis should be shifted to encourage long-term research agendas. Even though I wish we could, we may not beat malaria within the next five years - even though the budgetary constraints imposed by cyclical donor needs suggests otherwise?

The role of EDCTP

By exactly continuing to foster long-term thinking and investment.

Prof. Christian Burri

Swiss TPH, Switzerland

Current status of the field

- Lack of vaccine – crucial to move towards elimination /eradication
- Unknown status of resistance against artemisinin derivatives – potential threat for complete drug class
- Understanding haemolytic anaemia potentially caused by i.v. artesunate
- Treatment of *P. vivax* – true impact only recently realized - crucial to move towards elimination / eradication

Future Directions

- Proof of concept testing of a variety of malaria vaccines (preventive and transmission blocking), conduct of confirmatory trials in variable settings and populations, full development of one to two most promising candidates
- Development of compounds belonging to new drug classes with mode of action different



from artemisinin derivatives

- Study haemolytic anaemia potentially caused by i.v. artesunate, develop solutions or alternatives
- Understanding optimal matching of partner compounds for combination treatment
- Treatment for *P. vivax*, ideally also active against *P. falciparum*.

The role of EDCTP

- Funding of several competing early phase projects in parallel (vaccines and drugs), contribution to funding in pivotal trials after careful analysis of potential of respective candidate
- Fund research on Study haemolytic anaemia potentially caused by i.v. artesunate and follow up projects
- Drugs: All companies, organizations with a product in development > Phase IIa (see global malaria portfolio) – direct exchange, plus support to ancillary trials

Dr Badara Cisse

Malaria Capacity Development Consortium, Senegal

Current status of the field

Key issues: New drugs needed and role of primaquine, resistance to bed nets, Challenges: accurate mapping of the malaria burden. Limitations: financial resources expertise and political will to tackle malaria

Future Directions

Large scale implementation of effective interventions should be conducted (SMC, MDA, MSAT etc..) Interventions should also target foci of residual transmission.

The role of EDCTP

Work more closely with the MoHs [ministries] & the NMCPs Improve expertise on malaria morbidity mapping.

Dr Michel Cot

IRD, France

Current status of the field

- Resistance to antimalarials and insecticides
- Lack of building up capacities
- Lack of clinical trial sites with adequate GCP and GLP
- Lack of information and awareness of target populations
- Adequate funding beyond malaria eradication goals
- Technical and financial barriers to the development of a vaccine
- Political barriers in Sub-saharan countries
- Sub-optimal diagnostic tests
- Insufficient lab equipment

Future Directions

- Research on new antimalarial drugs and insecticides
- Research on efficacious and affordable vaccines
- Research on better field diagnostic methods
- Studies on local practices and care seeking
- Cost-effectiveness analyses



The role of EDCTP

- Improve capacity building in African countries
- Develop North-South networks (student exchanges, training in GCLP)
- Provide adequate equipment for local clinical trial sites
- Promote the creation and development of local research teams
- Encourage multidisciplinary research (biology, epidemiology, pharmacology and social sciences)
- Administrative and financial management training
- Support the creation and functioning of ethics committees and IRBs
- Involvement in vector control trials

Dr Janice Culpepper

BMGF, USA

Current status of the field

Limited set of imperfect tools available to prevent and treat malaria and developing new tools is expensive and time consuming.

Future Directions

Single does cure for malaria treatment, new vaccines, new vector control products, ne more sensitive point of care diagnostics, and new ways of using interventions such as screen and treat.

The role of EDCTP

EDCTP can contribute to funding trials for new drugs and vaccines as well as for pharmacovigilance studies of new drugs and vaccines.

Prof Umberto D'Alessandro

ITM Belgium & MRC Gambia, The Gambia/Belgium

Current status of the field

In settings where malaria transmission has decreased substantially, the main challenge is to understand the dynamics of malaria transmission and the importance of the human reservoir of infection (sub-patent infections) in maintaining it. Could asymptomatic carriers be identified with adequate diagnostic tools and treated to stop transmission or should not we treat the whole population to reach such result? The potential role of gametocytocidal drugs for interrupting transmission should be explored. In settings where malaria transmission is still substantial, the challenge is to reach a good coverage with existing interventions. As coverage is often patchy and lower in the higher risk groups, there is the need of adapting existing interventions for attaining a high coverage in these groups. In all settings, the threat of antimalarial and insecticide resistance represents a major challenge.

Future Directions

The use of gametocytocidal drugs should be explored. Mass drug administration or systematic screening and treatment, the former with sensitive diagnostic tests should be tested. The role malaria vaccines (including RTS,S) may have in malaria elimination should be explored.

The role of EDCTP

The EDCTP should be able to fund both large community-based intervention trials exploring the impact of combined interventions on the malaria burden and also phase 3 trials on new interventions. It should also support the development of African scientists by offering "long-term" training, i.e. PhD followed by postdoc. Support to African research institutions by providing the means of carrying out high quality trials is essential. Key players are European and African research institutions and major international funders.

**Dr Philippe Deloron**

IRD, France

Current status of the field

- Key issues challenges and limitations include:
Efficacy and safety of IPT for the infant/child and the pregnant woman, especially in the context of increasing SP resistance
- Vaccine development. Numerous candidates are identified, and the lead (RTSS) is much less effective than claimed
- Prevention and treatment of severe malaria in the context of the identification of a new endothelial receptor for cytoadherence (although this has to be confirmed), and of peculiar PfEMP1 variants associated with severe/cerebral disease.

Future Directions

As said above, there is great potential for significant advances in the domain of disease-targeted vaccines (severe malaria, pregnancy-associated malaria). Also, better definition of IPT may be promising.

The role of EDCTP

EDCTP should originate calls related to topics with expected important benefits (see above) in relation with all stakeholders. EDCTP should keep assessing whether the expected work is correctly done in line with the expectations.

Dr Alioune Dieye

Institut Pasteur Dakar, Senegal

Current status of the field

Malaria changing epidemiology raises new questions and innovative solutions/strategies toward elimination/eradication for MDGs achievements in Africa.

Future Directions

- Re-characterisation of malaria in the context of different level at which countries are (control, elimination) using several skills like entomology, modelling etc
- Evaluation of malaria prevention and control e.g. Vaccine development in pregnancy associated malaria
- Training and capacity building for competencies.

The role of EDCTP

Partner with others funding agencies (Gates Foundation, WHO, etc) and African and European States Initiatives (DG development, African Union, etc)

Prof. Abdoulaye Djimde

University of Science, Techniques and Technologies of Bamako, Mali

Current status of the field

Drug resistance, Insecticide resistance, lack of an efficacious vaccine, sustained funding for implementation of current tools

Future Directions

New non-artemisinin derived antimalarial drugs, whole organism vaccines, Rationally designed vaccines, better understanding of malaria biology and epidemiology, increased research capacity in malaria endemic countries

**The role of EDCTP**

Public-Private-Partnership product development program, capacity development in research in developing countries, including basic and pre-clinical research, strengthening regulatory and Ethical landscape, Networking. Key players, Academia, Pharmaceutical companies, Governments. NGOs

Dr Stephan Duparc

MMV, Switzerland

Current status of the field

Drug access for the population needing malaria treatment
Need for new drugs with a very good safety profile to replace the ACTs

Future Directions

To be successful in the development, registration and launch of new drugs, affordable, efficacious against drug resistant parasites and very well tolerated

The role of EDCTP

EDCTP can help to the development of these new drugs and can also help for the safety and pharmacovigilance of these drugs after registration.

Dr Thomas Egwang

Med Biotech Laboratories, Uganda

Current status of the field

Lack of infant-optimized vaccine formulations
Overcoming the barriers to successful immunization in infants
Limited knowledge about neonatal and infant immunology
Top-down vector control; communities are onlookers rather than drivers.

Future Directions

Development of animal models or artificial/in vitro systems for testing and optimizing vaccines especially for infants
Development of infant-centric adjuvants
Identification of early markers of vaccine efficacy in infants

The role of EDCTP

By supporting training fellowships in neonatal/infant immunology
By supporting clinical trials for optimizing vaccine/adjuvant formulations in infants
By supporting a non-human primate baby challenge model

Ms Sally Ethelston

PATH Malaria Vaccine Initiative, USA

Current status of the field

Challenges facing efforts to make progress in the prevention, control, and treatment of malaria in sub-Saharan Africa include insufficient funding overall (i.e, global and local levels), weak health systems in many countries, and political instability/civil strife in some countries affected by malaria. Other challenges are more specific to malaria, including especially emerging resistance to pesticides and the potential threat posed by drug resistance that is emerging in other regions (specifically, Asia). Related to these challenges is the question of whether there is adequate information on the epidemiology of the disease in the region and, as new interventions are introduced, sufficiently strong systems to ensure effective pharmacovigilance.

Future Directions



Research and development continues to advance on all fronts, including diagnostics, drugs, vaccines, and vector control tools. In the vaccine field, final results from the Phase III trial of the RTS,S malaria vaccine candidate are expected in 2014; the World Health Organization has indicated that it could issue a policy recommendation as early as 2015.

The role of EDCTP

EDCTP has tremendous opportunities to not only help shape future research, but to contribute to the effective implementation of new interventions by fully utilizing its strengths as a catalyst, convenor, capacity builder, and co-funder. One specific opportunity lies in the area of pharmacovigilance, where various regional and global organizations are already active (WHO, INDEPTH, others), but where EDCTP could make a significant contribution.

Dr Heiner Gruninger

Novartis Pharma AG, Switzerland

Current status of the field

Access to medicines, stock outs. Correct diagnosis and compliance with taking medicines correctly. Transmission blocking.

Future Directions

Test and Treat. Integrated management of childhood fever. Interventions that block transmissions.

The role of EDCTP

Enabler of clinical studies. Broaden in-country capacity to perform quality clinical studies.

Prof Adrian Hill

Jenner Institute, Oxford University, UK

Current status of the field

Our major limitation is the lack of a highly effective vaccine.

Future Directions

EDCTP has supported the development of vectored vaccines through the Malaria Vectored Vaccine Consortium. This consortium has recently undertaken a trial with vectored vaccines in Kenya showing the highest known efficacy of any malaria vaccine in a field setting. There is a strong case for EDCTP supporting the further development of this very promising approach.

The role of EDCTP

EDCTP needs to build on current strengths in malaria field evaluation of vaccines. But in addition EDCTP must support technology transfer to allow pre-clinical candidate vaccines designed in Africa to progress to clinical development. No EDCTP funds have been allocated to this technology transfer activity so far and this deficit should be corrected.

Ms Jenny Hill

Liverpool School of Tropical Medicine, UK

Current status of the field

The global refocus on malaria elimination and eradication has meant that key funding agencies such as the Bill and Melinda Gates Foundation have reorganised their strategies around elimination and have prioritised transmission reduction research. There is a danger that malaria control in vulnerable populations, such as pregnant women, is neglected and yet much of sub-Saharan Africa remains in the control phase and few have reached the consolidation phase.



For pregnant women, key issues are: increasing resistance to SP for IPTp and lack of safe and effective alternative drugs to replace SP or standardized methods to monitor the impact on effectiveness of IPT; alternative drugs for IPTp or strategies such as intermittent screening and treatment are more complex to deliver will require detailed studies on acceptability and feasibility; limited knowledge of women's exposure to and risks of inadvertent exposure to ACTs in the first trimester of pregnancy and poorly developed PV systems for tracking this; poor coverage of existing interventions delivered through antenatal clinic (IPTp and ITNs) to pregnant women in sub-Saharan Africa; poorly resourced health systems through which malaria control interventions are delivered.

Future Directions

Data from several multicentre clinical trials of new drugs for treatment and prevention of malaria in pregnancy will become available, with potential to guide policy on the treatment and prevention of malaria in pregnancy. A key challenge will be to ensure sufficient attention is paid to operational research to explore the feasibility of delivery of these more complex interventions (e.g. multiple dose drug regimens for IPTp, intermittent screening and treatment) in poorly resourced countries. Success probably lies in greater integration of malaria in pregnancy interventions with reproductive health programmes, but research is needed to guide how this can be done most effectively.

The role of EDCTP

EDCTP's earlier proposal to support phase IV studies in its Phase II will be critical for malaria control in Africa in the medium to long term.

Dr Egeruan Imoukhuede

Oxford University, UK

Current status of the field

The key issues include the ability to direct available funding for malaria research (especially vaccine trials) to the relevant areas, significant participation of African governments in malaria research, correlates of protection, sincere collaboration by partners working in the field, efficient use of available resources including distribution of and accessibility to proven malaria control tools (drugs, bednets), inadequate data for computation of specific country needs.

Future Directions

For malaria vaccines, extensive and relevant work have been done and results from the RTS,S malaria vaccine trials have been promising. In addition work in the development of malaria vaccines at the Jenner Institute, University of Oxford have been very exciting in recent times. Then vaccine portfolio evaluating the ChAd63-MVA vaccination strategy currently undergoing efficacy testing in paediatric populations in West Africa is promising. However, the ultimate aim is a combination vaccine that should include all the promising antigens which have shown efficacy in field trials.

The role of EDCTP

For malaria vaccines, I can definitely say as former Project coordinator of MVVC and MVVC2 that the integrated strategy which involved project management, capacity building and networking in the conduct of clinical trials of malaria vaccines is a model to be continued into the future. Minor adjustments may be required but the model works! Future key players for malaria vaccine development include University of Oxford, GSK, American Navy, Sanaria, Okairo, University of Lausanne, Statens Serum Institute, Denmark

**Mag. Christa Janko**

Medical University of Vienna, Austria

Current status of the field

Well-designed research projects based on clinical, pharmaceutical and epidemiological evidence and carried out by well trained researchers. Combined with well-shaped alliances between the private, academic and public sectors to allow fast access to as well as cost-effective manufacturing and distribution of high-quality and efficacious medicines and vaccines.

Future Directions

Whatever priorities EDCTP will set in their future funding priorities, proposals must continue to be evaluated according to the feasibility of medicines and vaccines truly becoming accessible to the affected people in the endemic regions. This must be based on demonstrated research evidence related to safety, efficacy, and effectiveness in the endemic regions, affordability and long-term sustainability. These criteria should be included in the future call texts.

The role of EDCTP

In order to assure long-term accessibility to high-quality and safe medicines and vaccines, there is no way around building strong alliances with the private sector. Strategies for quality manufacturing, distribution and funding of required malaria medicines and vaccines should be required in any future proposal - including in early phase trials.

Dr Simon Kariuki

Kenya Medical Research Institute, Kenya

Current status of the field

- Poor health infrastructure
- Drug stock-outs
- Sustainability of interventions
- Vector resistance to insecticides
- Threat of parasite resistance to ACTs
- Decline in funding for malaria control

Future Directions

Improvement in health infrastructure, investment in scaling up proven interventions and development of additional control tools such as; efficacious malaria vaccine, new formulations of insecticides and single dose ACTs

The role of EDCTP

Supporting development of newer, longer lasting and potent insecticides, single dose and long half-life ACTs, efficacious malaria vaccines and transmission reduction strategies.

**Prof Peter Kazembe**

Baylor College of Medicine Children's Foundation Malawi, Malawi

Current status of the field

Development of an effective malaria vaccine; better mapping of artemisinin derivatives parasite resistance; better competitiveness in international funding for malaria activities.

Future Directions

Vaccines, particular attention to the transmission blocking vaccines. Better modelling for artemisinin resistance in the Africa region.

The role of EDCTP

EDCTP is a key funding source outside the US and needs to reposition itself through supporting south-north and also south-south research collaboration. Apart from Universities, Ministries of health are key partners though their NMCPs.

Dr Jean-Rene Kiechel

DNDi, Switzerland

Current status of the field

Appropriate use of the available medications

Future Directions

Multi line treatments

The role of EDCTP

The malaria programs and their clinical and scientific counterparts in the countries

Prof Sanjeev Krishna

St. George's, University of London, UK

Current status of the field

1. Identification and clinical development of new classes of antimalarials that can work in a one day treatment course
2. Diagnosis of infection with appropriate sensitivity to aid the elimination agenda, as well as recognition of drug resistance at point of care
3. Safe and effective alternatives to artesunate for managing severe malaria
4. Validation of molecular markers of drug resistance and a consensus as to what artemisinin resistance might mean.

Future Directions

1. A portable, affordable point of care diagnostic platform for malaria and drug resistance detection to optimise existing therapies using nanotechnology. A working model will become available within a year
2. New drug classes and new combinations (partners, MMV) should be trialled in the next 2-3 years in phase II - III studies
3. Development of parenteral formulations, and rectal formulations of antimalarials that are suitable for severe malaria - 3-5 years
4. Validation of drug resistance markers is a continuous process that is iterative and needs large clinical datasets also. Key antimalarials will be reliably assessed in the 3-5 years.

The role of EDCTP

Academic and thought leaders - through processes such as this one and by hosting conferences not only to showcase funded studies but also to answer difficult questions. SMEs as well as big pharma - here growth can be accelerated if selection is carried out



carefully.

MMV - and other PPPs involved in malaria at all levels (vaccine to drug)

Dr Martha Lemnge

National Institute for Medical Research, Tanzania

Current status of the field

Current Challenges and Limitations in malaria prevention, control and treatment in SSA are: Inadequate funding, few drugs for treatment of malaria in pregnant women, barriers in uptake of useful interventions like ITNs, Delays in seeking medical care for children may lead to deaths, potential for emergence of resistance to Artemisinin combination therapy (ACT), insecticide resistance, few new antimalarials. Lack of knowledge on how best to eliminate malaria.

Future Directions

Prospects for making significant advances in malaria prevention, control and treatment in future will be: to increase awareness on uptake of useful interventions like ITNs and IPTp, continue with research on new antimalarials; including combination of old and new antimalarials, consider scaling up use of village helpers in the provision of early diagnosis and treatment of malaria at the community level, conduct studies for proof of concept in the elimination of malaria.

The role of EDCTP

EDCTP can best contribute to this research by: supporting Networks and Consortia for capacity building and actual execution of multi-centre clinical trials, supporting clinical trial sites in the maintenance of GCP/GCLP laboratories across SSA. Key players are: WHO, BMGF, EC, World Bank, UNICEF, WT, DANIDA, NIH, GC Canada.

Prof Odile Leroy

EVI, Germany

Current status of the field

From the perspective of the low efficacy of the leading candidate, and the dramatic decrease of funding during the last 3 years, it is critical to re-stimulate the field as a lot of unknown are not yet address. The malaria vaccine technology roadmap priorities should be taken seriously with allocated funding

Future Directions

Investments should be made on

1. Biomarkers
2. Analysis of all existing data to understand the low efficacy in infants
3. New antigens
4. Have a consensus on PPCs
5. Invest in phase IIb in Africa
6. Address vivax
7. Further develop PAM
8. Harmonisation immuno assays, biomarkers, and safety.

The role of EDCTP

key players:

Malaria vaccine funders group; EVI; MVI and pharma

**Dr Eusebio Macete**

Manhiça Foundation, Mozambique

Current status of the field

In the Sub-Saharan Africa region, for any future progress the quality of data still a change. Any effort that could be done regarding malaria control or elimination the Health Information System has to be reinforced.

Future Directions

The countries have to prepare then self to get the accurate information, introducing new tools for data collection, such as mobile phone etc.

The role of EDCTP

EDCTP, have to reinforce the collaboration with the research institutions and putting the data and information collected under research activities to the national programs

Dr Francesco Marinucci

PARTEC Essential Healthcare, Germany

Current status of the field

Clear identification and classification for proper treatment and management of fever cases. WHO guidelines for parasitic confirmation of malaria cases has not yet been widely implemented. Need for training and re-training on correct use of malaria RDTs. Need for External Quality Assessment schemes for malaria testing centres regardless of the diagnostic product in use.

Future Directions

Partec CyScope is portable, battery-operated LED fluorescent microscope for immediate identification of malaria parasites provided with ready-to-use slides with dried reagent. Multiplex instrument able to identify several pathogens for differentiation of fever cases Single instrument to perform malaria parasite, Hb, Hct, and platelets counts. Fast and easy identification of drug-resistant malaria parasite strains.

The role of EDCTP

EDCTP should closely support partnership between academia and industry with the goal of sharing different expertise in the field to accelerate research, development, and production of new malaria diagnostics.

Prof. Jurgen May

Bernhard Nocht Institute, Germany

Current status of the field

Appropriate diagnostics, new treatment, vaccination, guidelines for co-infections.

Future Directions

Improvement of reliable diagnostics, development and evaluation of guidelines for rational treatment of malaria co-infections.

The role of EDCTP

Funding of improved diagnostic facilities as prerequisite of clinical trials and better therapeutic interventions.



Prof. Wilfred Mbacham

The Biotechnology Centre University of Yaounde, Cameroon

Current status of the field

Lack of funding, redundancy in research projects, limited number of lead compounds. Limited number of clinical test sites.

Future Directions

New approaches to drug and vaccine discovery need to be initiated. Implementation/operational research needs to be encouraged to find out why interventions are not reaching the target group

The role of EDCTP

To promote and sustain clinical trial test sites that performs Phase 1 and II trials as well as Phase III. To foster operational/implementation research that ensures effective delivery of products(drugs and vaccines)

Prof. Frank Mockenhaupt

Institute of Tropical Medicine and International Health, Germany

Current status of the field

With respect to drug-based interventions, the possible emergence of artemisinin resistance in Africa is a major threat, and efforts need to be made to be prepared to detect, monitor and possibly halt such a development. So far, the methodological set-up is insufficient in this regard, and strategies to cope with this threat need to be developed. Drug resistance, particularly to SP, threatens the current approach of intermittent preventive treatment, and alternative and tolerable drugs for this purpose are limited. New drugs and approaches of intermittent preventive intervention are thus needed. For population-wide malaria control, health facility based treatment has several advantages but also limitations. Deficiencies with respect to staff availability and performance, integration of malaria control activities into routine services and other disease-specific activities, diagnostic tools, and quality of care partially prevent full effect of health facilities and to be addressed. Community-based malaria detection and treatment may be useful in some settings but their characteristics, effectiveness and limitations have yet to be established across areas of differing endemicity. At lower endemicity, the detection of transmission hotspots and their subsequent control or elimination are essential but a consistent approach in addressing this issue is lacking. The actual usefulness (and safety) of large-scale intervention with gametocytical drugs to lower or terminate transmission is not well established. ITNs/LLINs have greatly contributed to the decline of malaria in some areas. Continuing replacement of these devices and emerging insecticide resistance are problems in maintaining this success. The magnitude and impact of insecticide resistance is not fully comprehended, and alternative substances are scarce. Similar limitations apply to insecticide residual spraying which additionally requires logistical efforts not possible everywhere. Changes in the behaviour or composition of mosquito populations are further issues. A vaccine would be a great addition to the available amentarium but currently tested vaccines provide only imperfect protection. The successes of the last decade in controlling malaria are not observed everywhere in Africa, particularly in high-endemicity regions. This may indicate that there is no linear correlation between control activities and malaria control, are the actual reasons are not clear. Lastly, weak health systems, multiple and parallel disease-control activities and insufficient integration of activities appear to impede full effect in malaria control.

Future Directions

For effective malaria control, significant advances and maintenance of what has been achieved in the last decade may result from:



- Setting up methodology and structures to detect, monitor, and possibly halt artemisinin resistance in Africa
- Evaluation of new/alternative drugs and approaches for intermittent preventive treatment/intervention
- Strengthening health systems incl. staff availability and performance, diagnostic abilities, and integrative health care
- Use of community-based intervention, e.g., community health worker based diagnosis and treatment, where applicable
- Maintaining ITN/LLIN supply at a high level
- detection and monitoring of insecticide resistance, and change to yet to be identified alternative insecticides when needed
- Improvement of current vaccine efficacy- identification why current control interventions are unsuccessful in some regions of high endemicity

The role of EDCTP

The impact of EDCTP may improve by widening its approach from funding the traditional development of device or product based interventions towards procedure related interventions. Such may involve systems of detection and addressing drug resistance in the field, improvement of procedures in health facilities and communities, or the use of the available amentarium beyond its traditional purpose (one example, IPT or intermittent screening and treatment). The innovations produced by the BMGF, trying to bridge the gap between traditional pharma development and community reality, are one notable example. In this regard, EDCTP could place itself as a flexible intermediate between BMGF and GFAMT.

Dr Victor Mwapasa

University of Malawi, College of Medicine, Malawi

Current status of the field

Finding a safe and efficacious antimalarial drug to use in pregnant women and finding effective strategies to increase access to antimalarial prevention and treatment interventions to poor vulnerable women in hard-to-reach areas.

Future Directions

Prospects are moderate, in view of the few drug candidates under development and the increase in mosquito resistance to insecticides.

The role of EDCTP

Support private-partnerships in developing and testing novel antimalarial drugs and insecticide and funding the WHO to build capacities on national malaria control authorities to implement proven malaria control strategies.

Prof. Francine Ntoumi

Congolese Foundation for Medical Research, Congo

Current status of the field

The universal coverage and its evaluation; funding for sustaining control; and development of new interventions.

Future Directions

Detection of G6PD deficiency in the field; development of more sensitive and easy-to-use diagnostic tools.

The role of EDCTP

Support testing of these new tools in the field

**Dr Benrhards Ogutu**

KEMRI, Kenya

Current status of the field

1. Investment from the African governments. African inspired, owned and driven agenda for malaria
2. Sustainable resource commitment.

Future Directions

1. Using the current tools and new tools available in innovative ways to shrink the malaria map
2. Capacity enhance from within the region.

The role of EDCTP

1. A catalyst in bringing the key players together and providing seed funding to leverage long term internal support
2. The key players are the African scientists, political leaders, African economic blocks and African philanthropists.

Mrs Inmaculada Peñas Jiménez

European Commission, Belgium

Current status of the field

In recent years, progress has been made in malaria control as a result of effective treatment and insecticide-treated bed nets. But the development of resistance to medicines and mosquito-resistances as well as the poor quality of the health systems in many affected countries pose threats to these achievements.

Future Directions

The priority should be put in ameliorating the health systems addressed against wrong practises that lead to antimicrobial resistance.

The role of EDCTP

The size of the EDCTP network, knowledge, experience, training capacity and the current momentum, make out of the EDCTP the perfect player to check, confirm and disseminate the best practises to avoid drug resistance and to promote better health systems.

Prof Stephane Picot

University Lyon, France

Current status of the field

Accurate diagnosis is an issue to be address to avoid unnecessary treatments and false drug resistance. Challenge is to combine RDTs and data gathering at local and regional level Evaluation of long term effects of intermittent preventive treatment is urgently needed.

Future Directions

Drug easy to administer to children suffering severe malaria, one dose, to avoid premature deaths. Training of local staff for clinical management of severe cases and development of real Intensive care units.

The role of EDCTP

There is no one single solution against malaria. EDTCP should support different approaches that can be combined later in the field. Every good idea need to be tested, since the parasite is highly adaptable and we need different weapons to win that war. Key players are innovative PI.

**Dr Michael Ramharter**

Medical University of Vienna, Austria

Current status of the field

Adequate treatment of children (paediatric drug formulations) and pregnant women; evaluation of alternative IPTp regimens in case of further development of SP resistance.

Future Directions

Development of child friendly drug formulations. Development of alternative regimens for IPTp with the potential for multi-disease prevention (e.g. malaria plus schistosomiasis, or malaria plus STI). Targeted prevention programs for high risk groups (oviparous women, adolescent pregnant women)

The role of EDCTP

Funding of innovative clinical development programs for improved prevention strategies in pregnant women. Development of tailored treatment and prevention strategies for high risk groups. Collaboration of research teams representative for all African regions (West, Central, East and Southern Africa) to build consortia to tackle these issues.

Prof Christophe Rogier

Institut Pasteur de Madagascar, Madagascar

Current status of the field

Capacity to ensure sufficient effectiveness of present control interventions, resistances of humans (behaviour), parasites and vectors to the interventions.

Future Directions

New vector control approaches. Better evaluation of the actual effectiveness of present interventions. Better targeting of the interventions to those who need them.

The role of EDCTP

Develop clinical trials of vector control interventions that are NOT based on insecticide. Evaluate the effectiveness (not only the efficacy) of present malaria control interventions.

Prof Robert Sauerwein

Radboud University Nijmegen Medical Centre, the Netherlands

Current status of the field

Key issues: Small toolbox for malaria control and eradication because of emerging resistance against drugs and pyrethroids; no vaccines available. Malaria has been dropped in upcoming EU programs as key topic. Successful investments and malaria FP programs and NOE (e.g. EViMalar) desintergrate. This will threaten success of future EDCTP program.

Future Directions

New tools and tests for malaria transmission, essential for eradication. Malaria vaccines entering the clinical pipeline. Application of new diagnostics and monitoring of drug resistance.

The role of EDCTP

EDCTP should more link with EU research groups and facilitate/support translation of new tools and findings to the endemic settings. Not only limit to execution of clinical trials. Strengthen north south collaboration with collaborative PhD programs and post-doc projects.

**Dr Sodiomon Sirima**

CNFRP, Burkina Faso

Current status of the field

Access to effective and affordable treatment for some vulnerable population. Availability of effective and affordable vaccine.

Future Directions

- vaccine development including vaccine for Malaria during pregnancy,
- new none ACT drug
- safe drug for SMC and IPT

Dr Valerie Snewin

Wellcome Trust, UK

Current status of the field

Transmission blocking interventions:

- Improved insecticides
- Transmission blocking vaccines
- More focus on *P. vivax*
- Artemisinin resistance and lack of data on drug resistance.

Dr Ambrose Talisuna

University of Oxford, UK

Current status of the field

Weak health systems, including community systems and referral systems, Inadequate human resources for health,
Price/affordability of life saving medicines: especially in the private sector, Procurement supply chain management challenges especially in the public sector, Weak organisational, supervisory and management capacity,
Inadequate monitoring and evaluation systems,
Inadequate capacity for communication of knowledge to the public, Sub-optimal quality in the management of severe , malaria- a neglected population, Continued use of artemisinin monotherapy, Un-regulated informal private sector use
Inadequate coverage of curative and laboratory services,
Inadequate integration of different sectors and programmes, threats such as drug and insecticide resistance

Future Directions

New drugs that are non artemisinin based and development of a vaccine.

The role of EDCTP

EDCTP could support phase II and III clinical trials for new drugs.

Dr Anja Terlouw

Liverpool School of Tropical Medicine, UK

Current status of the field

A key challenge - insecticide resistance, and the urgent need for safe, new products for vector control. Timely, local data on disease burden and intervention coverage that can guide targeted control efforts and allocation of resources will be key. Accurate risk stratification at sub-national level could help focus limited resources. Optimisation of the use and lifespan of new antimalarials, both during the development stage, and subsequent delivery in programmatic settings. Drug safety data is needed to inform evidence based dosing, and guide post-registration dose optimisation where needed. Further strengthening of the current drug development process may need to include phase 3B dose optimisation and assessment of



programmatically applications (e.g. age-based dose regimens for case-management and MDA). Strengthening local capacity to conduct phase 3a, 3B, and IV will be crucial to support talented scientists and academic institutes and needs to be a core component of any global malaria control efforts. The set-up required for clinical trials will help strengthen core systems within southern universities. Apart from strengthening universities and research centres, strengthening research and control programme networks that can support cross-border initiatives will be crucial once national malaria control programmes are successful.

Future Directions

Our ability to make significant advances may be just as dependent on the delivery systems as the inherent qualities of new interventions and products.

The role of EDCTP

Some initial thoughts include: EDCTP's expansion to phase IV studies is an important development that fits well within its remit to strengthen trial capacity and encourage partnership between European and African Institutes. Due to its presence in a large number of African countries EDCTP holds a key position to encourage cross-border or regional initiatives.

In terms of the identified need for better safety data to guide dose optimization of drugs EDCTP could play an important leadership role by encouraging standardization and compilation of safety data collected in trials that are available for meta-analyses. As EDCTP supports a large number of trials they are in a strong position to push such a development and work with other stakeholders. In terms of capacity building in research, EDCTP may contribute by supporting the establishment of research programmes that bring together a critical mass of scientists and support staff and ensure the development of stable programmes that are resilient to changes in team composition. Easier said than done, but large funders like EDCTP, alone or in collaboration with other funders, could drive this process. Vibrant research centres need a critical mass that may require more investment than can be reasonably justified by individual research projects. As soon as one pushes the continue button one will likely discover a key forgotten point.

Prof. Thor Theander

Copenhagen University, Denmark

Current status of the field

There is a need to develop better tools for malaria prevention and control. The development of such tools requires considerable investments, and the current funding research funding mechanisms are not appropriate for such endeavours.

Future Directions

There are promising developments and new concepts to be tested within malaria vaccine development.

The role of EDCTP

By continuing its effort to fund clinical trials and research capacity in Africa.



Dr Michael Theisen

SSI, Denmark

Current status of the field

Re vaccines: First of all a surrogate marker for protection against clinical disease is lacking. Secondly we need more knowledge regarding vaccines which provide community benefits i.e Transmission Blocking Vaccines.

Future Directions

Clinical development of combination vaccines which provide both personal protection and block the transmission of Plasmodia from mosquito to man.

The role of EDCTP

1. Motivate research in surrogate markers for protection against clinical disease. 2. enter into proof-of-concept clinical trials of new Transmission Blocking Vaccine candidates, including production and preclinical toxicology testing.

Prof. Jean-Pierre van Geertruyden

Unit of International Health, University of Antwerp, Belgium

Current status of the field

Diagnosis:

- Although RDTs were a breakthrough in the malaria diagnosis, there is still need for a very sensitive and specific diagnostic tool which does not need a permanent supply chain and can be used by staff with limited training.
- Diagnosis of malaria in pregnancy including 1st trimester.
- 1st trimester malaria prevention
- A cost-effective alternative to SP-IPTp
- Early diagnosis and treatment of severe malaria (or similar life threatening disease) in rural area
- Vivax malaria research, especially treatment of live stages
- (asymptomatic) malaria in schoolchildren is a neglected field and has probably high, though not clear impact on child development in all its aspects.

Future Directions

- We're at present involved in developing a malaria diagnostic tool based of spectrophotometry (already licenced).
- We finished a trial using CTX prophylaxis as an alternative to SP in not HIV-infected pregnant women

The role of EDCTP

Continue financing diagnostic and interventional trials. Best is to let several research groups in different settings conduct similar studies as policies are seldom based on one unique Proof of Concept study.

EDCTP may also focus on countries, regions with limited research output so far as clinical trials develop individual and institutional capacity.

EDCT could also in a public-private partnership finance clinical validation.

**Dr Michael B. van Hensbroek**

Emma Children's Hospital / University of Amsterdam Academic Medical Centre, the Netherlands

Current status of the field

In relation to malaria in children: * Better understanding of the relative contribution (by region) of malaria as contributor to (severe) morbidity and mortality in children. * Better integration of malaria preventive programme's into existing health interventions. * Translation of findings of RCT's into practise (and evaluation of their effect when implemented). * Better programme's to evaluate the impact of reduced malaria transmission on disease morbidity (by age). EG do you see a shift in morbidity rather than a reduction in morbidity when malaria transmission decreases in a holo-endemic area?

Future Directions

In relation to malaria in children: * 'Package approach interventions (with area specific packages) with respect to health interventions in children. * Better understanding of the relationship between development of malaria immunity, age and clinical disease presentation and outcome.

The role of EDCTP

*Funding streams that allow to study malaria in the context of other diseases and child health in general. * Long term funding streams that allow studying clinical as well as immunological parameters in (paediatric) populations in malaria endemic areas.* Key players: Local (University based) research institutes preferably run by local researchers (thereby EDCTP will contribute to local research capacity building and local research ownership).

Prof. Mats Wahlgren

Karolinska Institute, Sweden

Current status of the field

- Lack of interest of politicians & funding bodies
- Failure of ACT-combinations
- Mosquito resistance to insecticides
- Lack of adjunct drugs for severe malaria
- Lack of vaccines
- Lack of rapid diagnosis of virulent parasites.
- Lack of diagnostics for hypnozoites.

Future Directions

New drugs to replace ACT-combinations may become available. We might understand and be able to manipulate mosquito resistance to insecticides. Development of new insecticides. Development of adjunct drugs for severe malaria. First vaccines will be available. New diagnostics of virulent parasites and for hypnozoites.

The role of EDCTP

Funding of drug- and vaccine trials. Following research and suggest activities also outside of areas of primary responsibility. Key players include research support and agendas of governments, WHO, MVI, MMV, Global Fund etc. Meetings and co-ordination of activities is of importance.

**Miss Kate Whitfield**

Malaria Eradication Scientific Alliance (MESA), Spain

Current status of the field

As we look to drive malaria transmission right down and support countries to embark on elimination programmes, we need strengthen the knowledge base and promote quality research which answers questions critical to advancing the science of malaria elimination.

MESA background- The Malaria Eradication Scientific Alliance (MESA) works with the community to advance the science of malaria eradication. MESA takes the follow-up actions and builds upon the Malaria Eradication Research Agenda (malERA), a research agenda to underpin malaria eradication. Through agile grant making, MESA supports projects on research questions critical to malaria eradication. And as a platform for knowledge sharing, MESA reviews evidence and disseminates new knowledge.

In its first year (2012), MESA awarded six grants on research tackling key questions for malaria elimination and eradication: how to measure very low levels of transmission; and how to diagnose when a health system is ready to move into the elimination phase?

MESA's grant making is guided by core principals of: scientific excellence; innovativeness; inclusiveness; agility and transparency. The aim of MESA's 2013 call for research proposals will be to tackle areas which are yet under-invested in today's research landscape, with a focus on operational research and health systems.

MESA governance - Ten global institutions are represented in the MESA Steering Committee, which is chaired by Pedro Alonso at the Barcelona Institute of Global Health (ISGlobal). The MESA Strategic Advisory Council provides overall guidance. The MESA Secretariat is hosted by ISGlobal.

Future Directions

Science for cross-cutting issues, operational and health systems research is needed.

The role of EDCTP

EDCTP and MESA align on central issues and principals with regard to enabling research which advances the state-of-the-art in malaria, promoting endemic country capacity building and building partnerships. We present these comments for consideration as part of EDCTP's stakeholders' consultations, particularly in response to the meeting objective on new partnerships.

Dr Michael Wolzt

Medical University of Vienna, Austria

Current status of the field

Education & training related to human medicines, interventions, and information of clinical trials of all stakeholders

Future Directions

Structured networks of specialists (hub and spoke concept), easy access to info

The role of EDCTP

Creation of centres of excellence with seed financing, early self-sustainability of key competences, liaison with partner organisations.