Containment of artemisinin resistance in Southeast Asia - how to ensure that progress towards malaria elimination does not falter

Abstract:# 3211

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ABSTRACT

Recent exceptional progress in controlling malaria is raising hopes globally that this major burden on a large proportion of the poorest people in the world really can be beaten. This has been achieved through serious investment of effort and funds in ensuring wide-scale access to effective interventions. The shift over the last few years away from failing drugs to the highly effective artemisinin-based combination therapies (ACTs) has been a breakthrough, and it was hoped that their design as combinations of two efficacious drugs with different modes of action would preserve them for many years of use. However, recent evidence from the Artemisinin Resistance Confirmation, Characterization and Containment (ARC3) programme and other studies indicates that artemisinin resistant *Plasmodium falciparum* (Pf) parasites are present on the Thai-Cambodian border. The spread of artemisinin resistance through Asia to Africa would be a catastrophic setback to global efforts to control malaria, as there are not yet any equally effective alternative drugs. It is therefore essential to act immediately to mount a vigorous response to stop further spread from areas where artemisinin resistance has been identified (Fig 1), whilst simultaneously undertaking further research to define the nature and geographical extent of the problem.

Asia has fought resistance to one drug after another from the 1970s. Research in recent years has confirmed an increased parasite clearance time on the Thai-Cambodian border. The biggest problem is knowing how far it has spread, but we cannot wait for more information without response, so a special containment programme is underway in the areas where there is evidence.

The goal is to contain artemisinin-resistant Pf parasites by removing selection pressure and reducing and ultimately eliminating falciparum malaria.

Key areas of focus:

- ***Mobile and migrant populations***, who have limited access to control services but potential to spread resistant parasites to new areas. The programme explores how to reach these people, including new economic migrants;
- ***Surveillance and information systems***, which need to be rapidly upgraded to detect hotspots in transmission, to capture areas with higher frequency of slow parasite clearance and to be complete and timely for rapid response;
- ***Suppression of monotherapies***
- ***Private sector strategies*** to ensure more rational drug use;
- ***Understanding patient behaviour*** to support changes which will limit risk of spread;
- ***Joint action by Thailand and Cambodia***

Conclusion. Extraordinary efforts are needed to control malaria even where it is less common, but there will be beneficial side-effects in improving surveillance and learning for elimination. A major question is whether we are missing the main target, as information on drug efficacy is patchy. We cannot be complacent and rely on current tools lasting for ever, but we shall continue to lose good tools prematurely if we do not strengthen health systems and regulation. The lessons learnt from this effort will be fully documented and highly relevant to the development of approaches to eliminate malaria.

OBJECTIVES OF THE CONTAINMENT PROJECT

1. To **eliminate artemisinin resistant parasites** by detecting all malaria cases in target areas and ensuring effective treatment and gametocyte clearance
2. To **prevent use of artemisinin-based monotherapy** (AMT), fake drugs and inappropriate treatment in the **private sector**
3. To **prevent transmission** of artemisinin resistant malaria parasites by mosquito control and personal protection
4. To limit the spread of artemisinin resistant malaria parasites by **mobile and migrant populations**
5. To support containment/elimination of artemisinin resistant parasites through comprehensive and **harmonized behavior change communication (BCC), community mobilization and advocacy**
6. To undertake basic and **operational research** to fill knowledge gaps and ensure that strategies applied are evidence-based
7. To provide **effective management system**, including surveillance, monitoring and evaluation, and coordination to enable rapid and high quality implementation of the strategy

Fig 1. Map of Containment Zones

PROGRESS TO DATE

- This initial two-year project, started on 1 January 2009 and will continue through 31 December 2010. It is anticipated that longer term funding will be secured to ensure that the momentum for this project is not lost.
- Key project staff in place (Fig 2)
  - Project management staff for CNM and BVBD have been recruited
  - WHO: Containment Project Manager and Technical Advisor
  - Malaria Consortium: Epidemiologist, data manager, communications specialist and field officer
  - Recruitment of village malaria workers (VMWs) and mobile malaria workers (MMWs) in Cambodia completed and trained
- National Task Force meetings held in Thailand and Cambodia; Joint International Task Forces meeting (Figs 3 and 4) and project launching held
- Large-scale procurement (mainly through WHO WPRO and SEARO) finalized
- Ban on artemisinin monotherapies issued on 23 March 2009 by the Cambodian Department of Drugs and Food (DDF) with support from the Minister of Health (Fig 5).
- Family-size LLINs and hammock nets procured and distributed in Zones 1 and 2 (following micro-planning)
- Cross-border technical workshops (organized by Malaria Consortium) on monitoring and evaluation, migrants, and BCC/IEC held in Thailand and Cambodia
- Monitoring and Evaluation system in place (household, outlet and health facility surveys planned for Thailand and Cambodia in November)
- Screening and treatment of populations near to origins of infection of day 3 positive cases initiated
- Surveillance systems being developed
- Project documentation (including film) initiated
- International advocacy (e.g., radio, print, video, new media) to highlight containment efforts and malaria drug resistance
- Situational analysis on migrants and other operational research initiated

Fig 2. Project Organogram

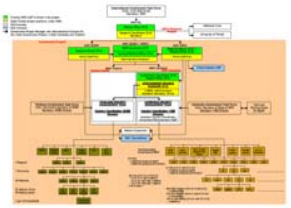


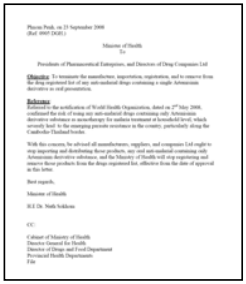
Fig 3. Project Structure

NEXT STEPS AND PRIORITIES

- Ongoing intensive project implementation
- Use results of mobile population surveys to intensify efforts to detect and treat their infections
- Engaging the private sector and piloting innovative approaches
- Surveillance, including mapping of Day 3 Pf positive cases
- Intensify cross-border cooperation
- Health system strengthening
- M&E: Indicator surveys (household, outlet, and health facility) planned for Q4 2009
- Focal screening and treatment
- 2nd International Task Force and project midterm meeting planned for Q1 2010

Fig 4. International Task Force Meeting in Phnom Penh

Fig 5. Ban on artemisinin monotherapies



SUMMARY AND CONCLUSIONS

- Operations (including procurement, full project staff and roll-out of each component) are fully underway and ready for continued intensified implementation.
- There is a need to ensure continued funding support from other donors and partners (including GFATM Round 9 applications).
- Development of the strategy was an inclusive process involving other potential supporters (USAID, in particular, has built on its existing support for controlling drug resistance to contribute to the strategy) and provincial staff on both sides of the border
- Careful and frequent monitoring is critical in this project. In addition to surveys, data will be collected from routine systems as much as possible and coordinated among multiple partners and the two countries.
- Lessons learned from this project will be fully documented and shared to further refine our strategies towards the goal of malaria elimination and to guide containment efforts elsewhere.
- A key challenge was to mobilise resources to mount a rapid response at the same time as confirming the existence of resistance. Given the relatively low incidence of malaria in the region, it was difficult to communicate the urgency for action.

Post-script. *Since the preparation of this abstract, evidence of artemisinin derivative resistance in Myanmar and China has emerged.*

Expansion of efforts to prevent further spread is now urgent.