Disease control and surveillance

CONTRAST periodic activity report 1. October 2009 – 30. September 2010

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SIXTH FRAMEWORK PROGRAMME

DISEASE CONTROL AND SURVEILLANCE

CONTRAST Periodic Activity Report
1. October 2009 – 30. September 2010

SPECIFIC TARGETED RESEARCH AND INNOVATION PROJECT

Full title:	***A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa.***
Acronym:	***CONTRAST***
Contract No.:	***PL 032203***
Project duration:	**4 years – 1. October 2006 – 30. September 2010**
Date of Preparation of report:	**15th November 2010**

Project coordinator (partner 1)
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2.1 CONTRAST Periodic Activity Report

(1 October 2009 – 30 September, 2010)

CONTRAST

"A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa"

Contract no.: 032203

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Publishable executive summary

"A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa"

Acronym
CONTRAST

Project summary

CONTRAST is a multidisciplinary alliance bringing together key skills and expertise to generate new knowledge on biological, environmental and socio-economic factors relating to schistosomiasis in sub-Saharan Africa. The project complements ongoing chemotherapy campaigns based on the drug praziquantel and will deliver more effective strategies for long-term control of this debilitating disease.

What is schistosomiasis?
Schistosomiasis, or bilharzia, is a tropical disease caused by intestinal worms of the genus Schistosoma. The transmission cycle requires contamination of surface water by excreta, specific freshwater snails as intermediate hosts, and human water contact.
According to WHO 200 million people are infected worldwide and more than 650 million people live in endemic areas, a majority of these in Africa. As a result schistosomiasis leads to the loss of 1.53 million disability-adjusted life years (DALY), although these figures need revision.

Aim of project
CONTRAST focused on integrated long term solutions leading to improved and sustainable local control of schistosomiasis. To reach this goal, **CONTRAST**s five European partners (established research institutes and a representative from the commercial sector) have together with 9 African institutions established a strong research node network across sub-Saharan Africa.

The research nodes in Africa have been established and are focusing on:

- innovative molecular tools to characterize both snails and schistosomes.
- the importance of host-parasite dynamics across different ecological and epidemiological settings.
- developing new spatial models for disease risk maps and prediction.
- encouraging and assessing novel local control interventions using a social science approach.
- ensuring widespread dispersal of knowledge and access to information facilitating research into practice.

CONTRAST is committed to creating a new and much needed platform for integrated schistosomiasis control in Africa, which will be effective and sustainable at the local, national and regional level.

CONTRAST has created strong south/south collaboration, and will secure a more effective dissemination.

Contractor/Partner list

Partner no.	Partner	Country
1 (coordinator)	DBL - Institute for Health Research and Development	Denmark
2	Natural History Museum	UK
3	Swiss Tropical Institute	Switzerland
4	Imperial College London	UK
5	Makerere University	Uganda
6	University of Zambia	Zambia
7	National Museums of Kenya	Kenya
8	Institut Senegalais de Recherches Agricoles	Senegal
9	Programme National de la lutte contre la Bilharziose	Niger
10	Centre for Schistosomiasis and Parasitology	Cameroon
11	Ministry of Health- Helminth Control Laboratory	Tanzania (Zanzibar)
12	National Institute of Medical Research	Tanzania
13	Coris Bioconcept	Belgium
14	Ministry of Health-Vector Control Division	Uganda

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Work performed

The official starting date of the project was 1st October 2006, when a kick-off workshop for all partners was held in Entebbe, Uganda.

Having finalised the project period all 23 work packages have been implemented and finalised.

CONTRAST has established 5 new state-of-the-art research nodes that have formed the back bone of the CONTRAST project they are ready for future research work on neglected tropical diseases at partners and their associated institutes. The research nodes and their aims are:

1. A node for molecular biological studies creating innovative molecular tools to characterize both snails and schistosomes. This is placed at the Makerere University (MU) in Kampala, Uganda.
2. A node who defines the importance of host-parasite dynamics across different ecological and epidemiological settings. The research node is placed at Centre for Schistosomiasis and Parasitology (CSP) in Yaoundé, Cameroon
3. A GIS research node for developing new spatial models for disease risk maps and prediction. This is placed at the University of Zambia (UNZA), in Lusaka, Zambia.
4. Node 4 is working for encouraging and assessing novel local control interventions using a social science approach. This is placed National Institute of Medical Research (NIMR), in Mwanza, Tanzania and
5. The aim of research node 5 is twofold: 1) to ensure widespread dispersal of knowledge and access to information facilitating research into practice (this include a comprehensive Database called Fireflower), and 2) create reference collections for all parasites and snails. The reference collection is established at the National Museums of Kenya, (NMK) in Nairobi, Kenya.

Field activities took place in all the planned field sites in Senegal, Niger, Cameroon, Uganda, Kenya, Zambia, Tanzania and Zanzibar. Control treatments, snail samples and other material were collected in the field. This made it possible to initiate laboratory research. Georeferenced field data were used to develop predictive models in CONTRAST's third objective group.

Below the outcome of the work in CONTRAST is summarized for each of the 5 obejctive groups.

Objective 1

Within **objective group 1** the research node was established according to the schedule and at the involved partners all work packages has been engaged and exciting results have been obtained. Barcodes for schistosomes and intermediate host snails has been established to the extent it is possible, what seems to be a new snail species has been found and new tools has been developed. Insight in genetic diversity of schistosomes and snails has been revealed and genetic consequences of chemotherapy have been established. Findings from these studies are currently being implemented in the studies on host-parasite relationship in optimizing control of the disease.

The expected outcome of Objective group 1 was

(1)) An established molecular research node in Uganda and a biological reference research collection node in Kenya.

(2) An international standardized molecular nomenclature based upon DNA barcoding and selected micro-satellite loci for classification of genetic variation within schistosomes, and their associated snail hosts. (3) Real-Time PCR rapid diagnostic tests for detection of schistosome DNA in freshwater snails and establish patterns of schistosome infestation in aquatic environments through time.

The actual outcome has been:

(ad 1) – A fully functional well equipped molecular biology laboratory at an internationally acceptable standard has been established at Partner no 5.

(ad 2) - Species specific DNA sequence barcodes for the schistosomes has been established for *Schistosoma mansoni*, *S. haematobium* and *S. bovis.* The application of DNA barcodes for the differentiation of both the intermediate host snail genera *Biomphalaria* and *Bulinus* across Africa has been shown as a promising method.

(ad 3) - The use of the Dra1 repeat Real-Time PCR assay for the detection of schistosome infections in snails is now developed. The method has been used to detect parasites in naturally infected species of snails.

Objective 2

Within **objective group 2** a full functional host-parasite relationship research node was established and susceptibility experiments have been carried out. A parasitology training course for technicians in field collection and laboratory facilities and the latest techniques in packing, preservation, shipment and infection in laboratory has been performed. Extremely interesting results concerning co-infection and treatment aspects has been obtained. It has been shown how different parasites from different regions react to chemotherapy and how different some parasites are in productivity in different snails . These results will have significant influence on planning of future control regimes.

The expected outcome of objective group 2 was:

(1) Identification of key biological factors that shape the distribution of schistosomiasis by ascertaining exact compatibility spectra of key snail species, with particular attention paid to snail infection rate population dynamics such as seasonality and major ecological transformations.
(2) Key biological data concerning the distribution of *Bulinus* and *Biomphalaria* and their associated compatibility with schistosomes to annotate spatial databases and verify transmission predictions.
(3) An established snail-parasite research node in Cameroon.

The actual outcome has been:

(ad 1) A significant increase in knowledge os schistosomiasis prevelance in the investigated reas has been revealed, both in single and co-infections. This will have outstanding importance for future control initiatives.
(ad 2) - Knowledge of susceptibility of possible intermediate host snails and their distribution in place and time has been revealed.
(ad 3) – A fully functional research node has been established at Partner 10

Objective 3

A unique and very comprehensive open access database of historical and present information on schistosomiasis prevalence revealing disease distribution in sub-Saharan Africa has been produced in **objective group 3**. These data has been used and are being used in mapping disease distribution in Sub/Saharan Africa. This is useful in planning schistosomiasis control interventions. The research node is fully up and running. The node has implemented several course activities both for CONTRAST partners and other sub-Saharan participants. The open access database including disease distribution data is not to be confused with the other CONTRAST database, Fireflower, which include CONTRAST provided data only and has been established at research Node 5. In objective group 3 also risk mapping for the areas involved has been carried out. This will also contribute to a better and more optimized planning of control initiatives.

The expected outcome of objective group 3 was:

(1) Comprehensive GIS databases and schistosomiasis risk maps for selected eco-epidemiological settings across sub-Saharan Africa.
(2) Spatial refinement of control interventions for cost-effective allocation of scarce resources.
(3) Spatially-explicit databases of schistosome and snails annotated by molecular nomenclature maintained on a web-based interface.
(4) Integration of spatial databases with other neglected diseases.
(5) An established spatial epidemiology research node in Zambia.

The actual outcome has been:

(ad 1) Gis data base on climate and other environmental data has been established at the research Node and risk maps developed.
(ad 2) Optimised spatial refined risk mapping is under development.
(ad 3) CONTRAST database, Fireflower, created for all data collected in the project period on schistosomes and intermediate host snails.
(ad 4) An open access database for schistosomiasis (later extended to NTD) has been created with about 10 000 locations from Africa.
(ad 5) A fully functional GIS and remote sensing Research Node capable of investigate spatial epidemiology has been established at Partner no 6 in Zambia

Objective 4

Within **objective group 4** the research node has been established and the work packages implementing KAP (Knowledge, attitudes and practices) toward schistosomiasis control and PHAST (Participatory Hygiene and Sanitation Transformation) approach have been implemented. The results is very promising and PHAST has shown to have an impact on peoples performance and attitudes concerning their water contact behaviour. A manual for PHAST in schistosomiasis control has been developed.

The expected outcome of objective group 4 was:
(1) An established research node in Tanzania for integrated social and economic policy analyses.
(2) Evaluation of PHAST strategy .
(3) The performance of biological control of *S. haematobium* using refractory snail species and feasibility of using this method in coastal eastern Africa.

The actual outcome has been
(ad 1) A research node for integrated economic and social policy analysis has been established
(ad 2) The PHAST strategy has been implemented and evaluated successfully
(ad 3) Experiments are ongoing but final results not revealed.

Objective 5

Within **objective group 5** a website for the project was launched in January 2007: http://www.eu-contrast.eu. In this website two levels of access were created; one public 'popular' website, presenting news and stories relating to CONTRAST and other schistosomiasis related information, and one restricted to CONTRAST partners and the European Commission (as well as those bodies with local relevance and any others appointed by the EU.

The CONTRAST website has received over half a million hits during the three years it has been active. During the last 12 months there has been over 250.000 hits on the website. The project coordinator and the secretariat has agreed to continue supporting the website up to 2 years after the project ends.

CONTRAST has been proactive in dissemination of its results through publications in special issues of the well recognised International Journal Parasitology and an upcoming special issue exclusively for CONTRAST in Acta Tropica another well recognised international Journal. Also CONTRAST has reach out to national and international health care stakeholders by participating in meetings and arranging press conferences in correspondence to annual meetings. In this way CONTRAST has been made known through newspapers, radio and television. Like wise CONTRAST partners has played an important role at WHO expert and technical review meetings.

Open access database of schistosomiasis prevalence

CONTRAST have throught he work accomplished in WP13 established a unique georeferenced database on schistosomiasis prevalence throughout Africa. In September 2010, a scientific paper was submitted PLoS Neglected Tropical Diseases, describing the database, and the visions we have for it. The database can be found at www.globalntddatabase.org, where you can register for access to all data. The database currently features data on 10.000 individual schistosomiasis surveyed locations.

CONTRAST Final Report

Section 1
Project objectives and major achievements
(1 October 2009 – September 30, 2010)

CONTRAST

"A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa"

Contract no.: 032203

Partners/Contractor:

Partner 1. DBL, Denmark. Coordinator
Partner 2. NHM, United Kingdom
Partner 3. STI, Switzerland
Partner 4. ICL, United Kingdom
Partner 5. MU, Uganda
Partner 6. UNZA, Zambia
Partner 7. NMK, Kenya
Partner 8. ISRA, Senegal
Partner 9. PNLB, Niger
Partner 10. CSP, Cameroon
Partner 11. HCL, Zanzibar
Partner 12. NIMR, Tanzania
Partner 13.CB, Belgium
Partner 14.VCD, Uganda

Projects current relation to the State of the art and innovation of the project:

Schistosomiasis is a chronic, debilitating and poverty-related disease and in many areas within Sub-Saharan Africa it continues to drain the socio-economic development of already impoverished rural communities. The availability of low-cost praziquantel (PZQ) together with political leverage for initiation of national control programs has stimulated a shift in the global control strategy from transmission containment to morbidity control. Today control is a dual approach of morbidity reduction followed by consolidation of most appropriate measures in low transmission environments.

There are some real and potential limitations of strategies based upon the sole use of chemotherapy. While PZQ treatment can be straightforward, schistosomes remain present in aquatic environments such that re-infection can be rapid, eroding the longer lasting beneficial impact of treatment. Furthermore, the indefinite dependence on the drug itself can potentially reduce its effective life-span. Similarly although PZQ is cheap, costs associated with its delivery may not be. Cost-effectiveness has to be given careful consideration both from short and long-term perspectives, to minimize wastage and maximize the beneficial impact. If for example, mass-treatment continues in areas where treatments were not actually required (as initial geographic targeting was poor) or that levels of re-infection were subsequently low (owing to local dynamics of transmission), the economic rationale for repeated mass-treatment is altered.

To promote longer-term sustainability, control resources need to be targeted and streamlined to meet the local needs of both present and future drug delivery requirements. Detailed consideration of suitable methods to identify areas of high transmission and re-infection are therefore needed together with local solutions for reduction of environmental contamination and transmission of schistosomes. In so doing, this will help rationalise and maximise the beneficial impact of chemotherapy-based morbidity control during the maintenance phase. Such detailed information should be integrated with other control programmes and – where resources allow – safe-water initiatives, to build towards more streamlined delivery of essential drug packages and environmental modifications.

To identify areas associated with high transmission and re-infection risk, further information on the snail-schistosome relationship is required as the dynamics of snail-schistosome interactions (together with human water contact patterns) are major determinants of the local, often complex, geographic pattern of disease. From a control perspective, this biological complexity has sometimes been over-looked, leading to superficial understanding of major processes shaping the local pattern of disease and weakening the forecasting ability of spatial models.

It is well known that the distribution of schistosomiasis closely follows the distribution of susceptible snails and it is around these habitats that re-infection can also be highest. As not all aquatic snail species have the ability to transmit schistosomiasis it is important to identify susceptible hosts from those that are not. With morphological methods, however, reliable incrimination of intermediate host populations has been elusive such that molecular DNA approaches are required. Through phylogenetic analysis of DNA sequences, stable classification systems can be derived as well as development of rapid identification assays based upon polymerase chain reaction (PCR). Increasing interest has been placed upon classification of parasites and pathogens using DNA barcodes or multi-locus sequence tags. By taking advantage of mitochondrial DNA sequences information from both snails and schistosomes, a DNA barcode nomenclature could be developed to shed new light on the schistosome-snail cross-talk. In addition, variation within microsatellites may document the genetic changes influenced by selection pressures imposed by PZQ.

This will provide important information for annotation of geographic information system (GIS) databases, further validating initial schistosomiasis forecasting models, similar to that used for malaria. Once high transmission areas are identified further focusing of available control resources would be best applied for environmental improvement and initiation of local behavioural change. Assessing the most appropriate local method of environmental improvement and behavioural change can be problematic but a PHAST (Participatory Hygiene and Sanitation Transformation) strategy could be useful. It hopes to empower the local community to find their own most appropriate interventions.

Operating at a smaller scale a multidisciplinary approach has already had proof of principle in Zanzibar as part of the "*Piga vita Kichocho*" or "*Kick out Kichocho*" programme. **CONTRAST** will develop this approach and provide new molecular DNA assays for detection of schistosomes in the environment and establish a much needed biological nomenclature for classification of the schistosome-snail relationship. The information gathered from these new systems and tools will provide fresh insight into the spatial epidemiology of schistosomiasis and identify the factors that maintain the disease at high levels. Integration of new biological information with demographic, environmental and socio-economic factors will greatly improve understanding of disease management, and be an effective step towards sustainable control.

It was the overall aim of the CONTRAST project to achieve sustainable schistosomiasis control at the public health level in selected countries in sub-Saharan Africa through development of locally adapted and appropriate intervention strategies, complementary with ongoing morbidity control using the anthelmintic drug praziquantel (PZQ).

Background for the project

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CONTRAST Final Report

Section 2
Final status of Work packages
(as of 30 September 2010)

CONTRAST

"A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa"

Contract no.: 032203

Partners/Contractor:

Partner 1. DBL, Denmark. Coordinator
Partner 2. NHM, United Kingdom
Partner 3. STI, Switzerland
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Partner 6. UNZA, Zambia
Partner 7. NMK, Kenya
Partner 8. ISRA, Senegal
Partner 9. PNLB, Niger
Partner 10. CSP, Cameroon
Partner 11. HCL, Zanzibar
Partner 12. NIMR, Tanzania
Partner 13.CB, Belgium
Partner 14.VCD, Uganda

Summary of work performed and the main achievements during the project.

The CONTRAST activities were focussed on field work in partner countries (Senegal, Niger, Cameroon, Uganda, Kenya, Tanzania, Zanzibar and Zambia) coupled with establishment of the 5 research nodes carrying out the scientific analyses. The figure below shows the location and role of each of the five research nodes.

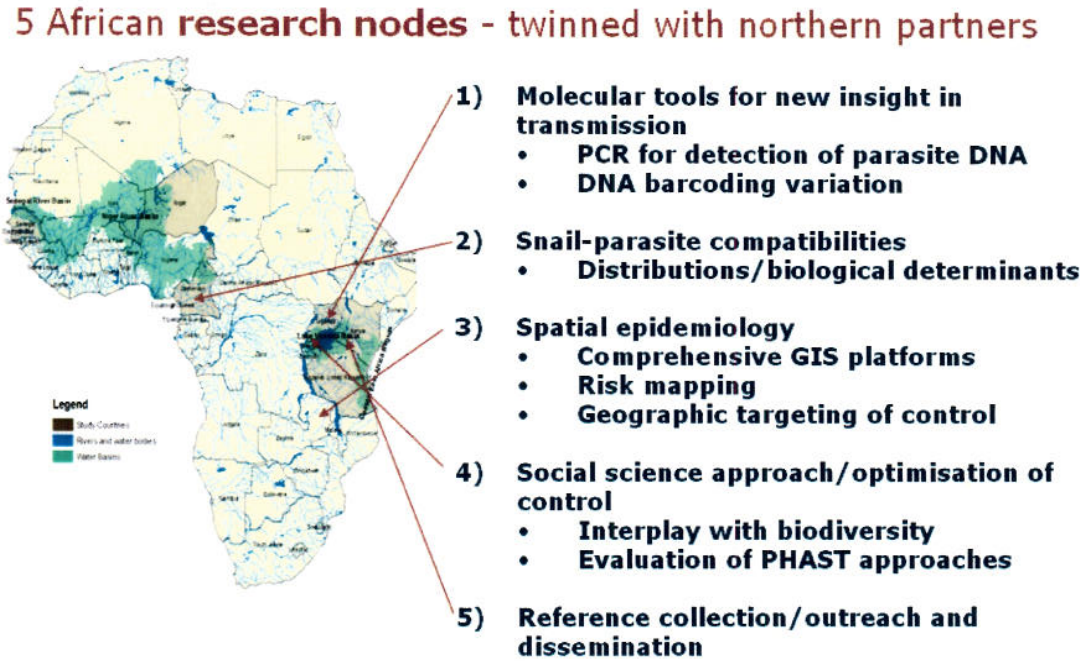


Figure 1. The location of the five research nodes in Africa, Partner countries and study areas.

Below is given a detailed report on the activities in the current active CONTRAST work packages. For a complete overview of the work in CONTRAST, please see the Final Report. each work package and it's deliverables will be reported upon. A full list of work package titles, deliverables and milestones can be found in Appendix XXX on p. XXX

Objective 1. Molecular tools for new insight into snail-schistosome transmission biology.

The objectives were to develop and implement novel molecular DNA assays based upon polymerase chain reaction (PCR) approaches upon collections of schistosomes and snails, from selected West- Central- and East African environments.

Work Package 1 ***"Establishment of a molecular research node in Africa"***

Finished. The implementation of this work package was achieved in collaboration between partner 1, 2, 4 and 5.

Work Package 2 ***"Establishment of a resource database and biological reference collection research node"*****.**

Finished. The implementation of this work package was achieved in collaboration between partner 1, 3 and 7.

Work Package 3 *"Development of DNA sequence barcoding nomenclature for characterization of schistosomes and snails".*

In this WP fieldwork was carried out between the 25th Jan to February 8th 2010 in the two Senegalese villages Bakerdji and Richard Toll. Involved in the field activities were partner 2 and 8.
Fieldwork objectives

- Livestock parasitological surveys (cows, sheep and goats). Identify schistosome infections and investigate inter species interactions involving, S. bovis, S. curassoni and S. haematobium.
- Human parasitological surveys to S. mansoni and S. haematobium foci and collect miracidia for DNA barcoding.
- To do a follow up survey in the mixed infection (S. mansoni and S. haematobium) foci in the village of Nder and collect miracidia for DNA barcoding.
- Carry out snail surveys to identify snails and their role in transmission

Prevalence of S. haematobium and S. mansoni infections were recorded. S. haematobium and S. mansoni miracidia were stored on FTA cards and in RNA later for DNA barcoding. Prevalence of S. bovis and S. curassoni recorded and many worms collected for molecular analysis.

Barcoding work

Schistosome COX1 barcoding

- S. mansoni populations barcoded from: Senegal, Uganda, Cameroon, Coastal Kenya, Tanzania, Niger, Zambia
- Detailed population sampling of S. mansoni from 25 localities around Lake Victoria, in Kenya, Tanzania and Uganda.
- S. haematobium populations barcoded from: Senegal, Cameroon, Zanzibar, Coastal Kenya, Tanzania, Zambia, Malawi, Niger. Individual barcodes from; Gambia, Guinea Bissau, Liberia, Mali, Nigeria, Egypt, Sudan, Tanzania, Mafia, Sloth Africa, Madagascar, Mauritius
- S. bovis barcoded from: Tanzania, Senegal, Kenya, Uganda, Ghana, Niger, Burkina Faso
- S. curassoni barcoded from: Senegal

Findings

- Very little genetic diversity found within and between populations of S. haematobium throughout mainland Africa. There is no geographical differentiation and there is 1 dominant successful genotype. The exception is the S. haematobium populations from Zanzibar, Coastal Kenya, Madagascar and Mauritius where there is high genetic diversity. These populations fit into 2 distinct clades: 1 that is unique to the Islands and the other that falls with the main land African populations. Diagnostic assays have been to developed to distinguish between these 2 clades.
- Very high genetic diversity is found within and between the S. mansoni populations. Good geographical isolation exists between the populations analysed. The development of PCR assays for geographical population identification of S. mansoni has now been considered impossible due to the amount of variation.
- In Lake Victoria there is extensive variation within worms examined, falling into 3 of 5 well-defined lineages of S. mansoni. There appears to be variation at both macro- (between country) as well as micro- (within country levels).
- Population genetics analyses of S. mansoni COI barcodes shows low levels of population structuring around Lake Victoria, perhaps due to high levels of human migration and ubiquitous compatible snails.

- S. haematobium / S. bovis hybrids have been found infecting children in Senegal and Niger.

Snail COX1 barcoding.

- In Lake Victoria there appears to be confusion over the taxonomy of populations traditionally identified as Biomphalaria choanomphala/sudanica. Preliminary barcoding results have shown the likely existence of 2-3 cryptic taxa within each group broadly partitioning into lacustrine and marsh ecophenotypes. As with S. mansoni, the diversity of the Biomphalaria COX1 region was very high, preventing the development of general assays for distinguishing between ecophenotypes or even species within the Great Lakes region.
- For Bulinus, the most significant finding to report is the existence of a new species, which has so far been found in 3 locations across East Africa. Sufficient biological material has not been collected to enable a formal species description, which will be done in due course upon presentation of other taxonomic characters.

Publications

STANDLEY, C.J., KABATEREINE, N.B., LANGE, C.N., LWAMBO, N.J.S. AND STOTHARD, J.R. (2010). Molecular epidemiology and phylogeography of Schistosoma mansoni around Lake Victoria. Parasitology 137 (13): 1937-1949. Published Online by Cambridge University Press 21 June 2010 doi: 10.1017/S0031182010000788

STOTHARD, J.R., WEBSTER, B.L., WEBER, T., NYAKAANA, S., J.P. WEBSTER, F. KAZIBWE, KABATEREINE, N.B. AND ROLLINSON, D. (2009). Molecular epidemiology of Schistosoma mansoni in Uganda: DNA barcoding reveals substantive genetic diversity within Lake Albert and Victoria populations. Parasitology. Published Online by Cambridge University Press 23 Jul 2009 doi:10.1017/S003118200999031X

DAVID ROLLINSON, JOANNE P. WEBSTER, BONNIE WEBSTER, SILVESTER NYAKAANA, J. RUSSELL STOTHARD (2009). Genetic diversity of schistosomes and snails: significance for control. Parasitology. Published Online by Cambridge University Press 27 Jul 2009 doi:10.1017/S0031182009990412

B.L. WEBSTER, D. ROLLINSON, J.R. STOTHARD AND T. HUYSE (2009). Rapid diagnostic multiplex PCR (RDPCR) to discriminate Schistosoma haematobium and S. bovis. Journal of Helminthology. Published online by Cambridge University Press 03 Aug 2009 doi:10.1017/S0022149X09990447

TINE HUYSE*, BONNIE, L. WEBSTER*, SARAH GELDOF, RUSSEL STOTHARD, OUMAR T. DIAW, KATJA POLMAN, DAVID ROLLINSON (2009) Snapshot on Evolution: Introgressive hybridization of schistosomes. Plos Pathogens 5(9): e1000571. (*Joint 1st Authorship)

BONNIE L WEBSTER (2009). Isolation and preservation of schistosome eggs and larvae in RNAlater® facilitates genetic profiling of individuals. Parasites and Vectors. 2:50 doi:10.1186/1756-3305-2-50

(a full list of CONTRAST publications can be found in the Final Report)

Work Package 4 *"Development of rapid SNaPshotTM DNA barcodes for multi loci sequence typing (MLST) for schistosome and snails.*

DNA barcoded information has been gathered for several Schistosome and snail populations. Primary analysis has been carried out to design primers for rapid SNaPshotTM.

Very high genetic diversity has been found within and between *S. mansoni* populations from several geographical areas. In contrast very low genetic diversity has been found within and between *S. haematobium* populations from several geographical areas on mainland Africa. But *S. haematobium* on Zanzibar also shows high genetic diversity.

On this background we have come to the result Snapshot packages have been developed for some schistsosomes:, *S.haematobium*, *S. bovis* and *S. curassoni*, but as it was discovered that there is no specific barcode per snail – so SNAPSHOT is not really appropriate. Moreover, molecular techniques moved on, and now no obvious future for snapshot – and could not really publish with snapshot analyses alone – so partly done, partly inappropriate now. D 7 satisfied.

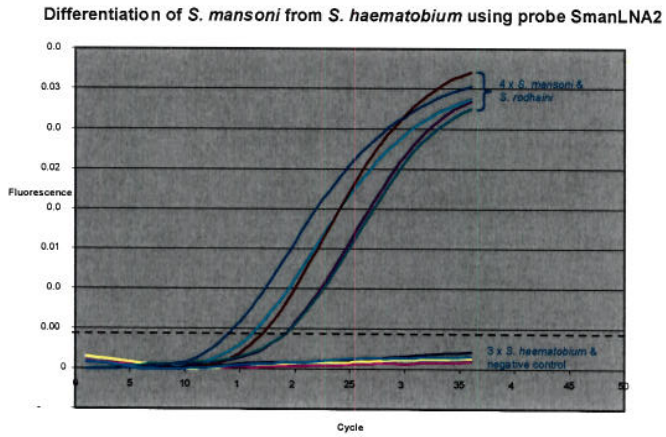
Work Package 5 *"Detection, identification and quantification of schistosome DNA in snails by Real-Time PCR assays.*

Development of an assay commercially available from partner 13 (Coris Bioconcept), linked with partner no. 2. Partner 13 (Coris BioConcept) has made oligochromatographic test strips based on the modification and development of RT-PCR work involving fluorescently labeled Locked Nucleic Acid probes carried out at the Natural History Museum in London.

Runthrough of the major findings

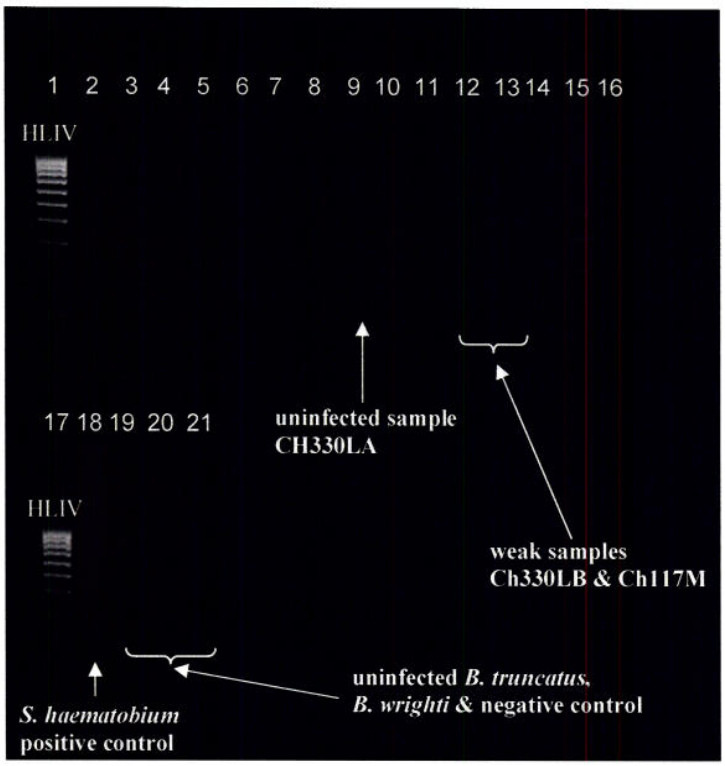
Two LNA probes have been developed for the RT-PCR detection, identification and quantification of parasite DNA within molluscan hosts (*Bulinus* and *Biomphalaria*) through the utilization of the ribosomal intergenic spacer region (rIGS). SmanLNA2 is a probe which will specifically identify *S. mansoni* group schistosomes and ShaemLNA5 will perform the same function for *S. haematobium* group parasites. The oligochromatographic versions of these probes are not the same having been modified for a different technology but the rIGS region upon which the probes are targeted remains common in both methods.

The PCR primers and probes were tested against a panel of schistosomes containing 12 geographical isolates and 6 species including the two main species groups. Below is an example of a RT-PCR trace showing the specificity of the SmanLNA2 probe.

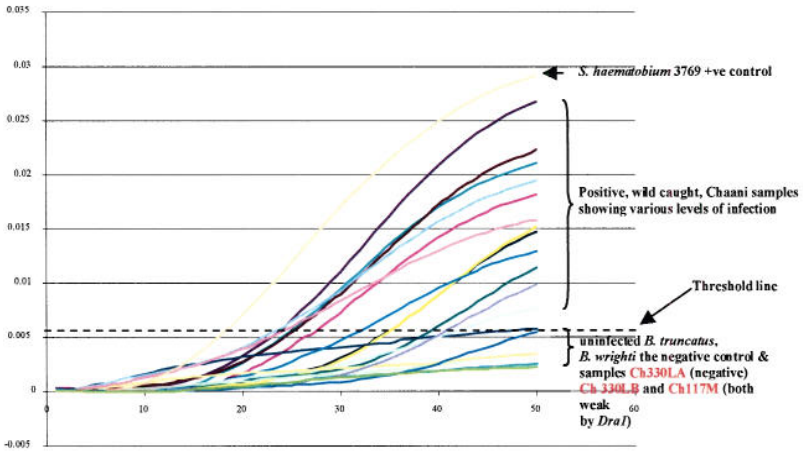


Both probes work well against adult schistosomes but required testing against wild caught populations of snails which might or might not be infected. The probes needed the ability to identify minute quantities of parasite DNA from amongst large amounts of host genomic DNA and other contaminants. There was also a necessity to validate the probes against existing molecular methods of parasite detection. This was achieved with *S. haematobium* through comparison with the *Dra1* repeat method of Hamburger *et al* (2001) and in the case of *S. mansoni* with a technique involving partial ribosomal 18S amplification developed by Hanelt *et al* (1997). Comparison with these conventional PCR techniques indicated that the probe methodology had similar levels of sensitivity but with the advantage of a more objective measure to levels of parasite infection/concentration.

The image below shows a population of *Bulinus globosus* snails from Chaani in Unguja which have been screened for *S. haematobium* infection using the *Dra1* repeat. Only one sample (9) appears to be free of infection.

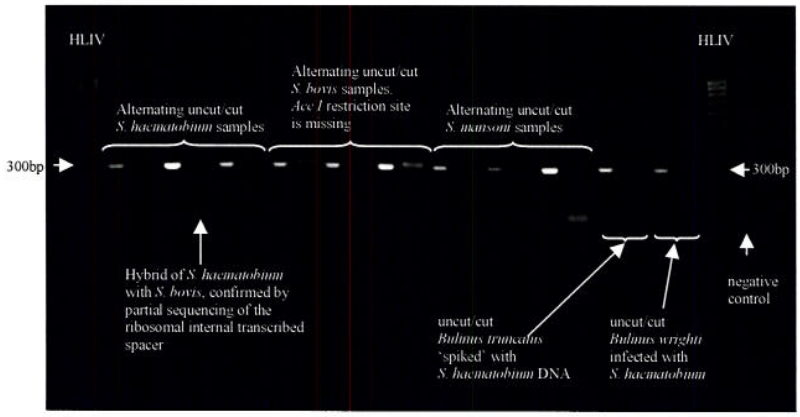


Shown below, the same wild caught snails from Chaani, Unguja screened for *S. haematobium* using the ShaemLNA5 probe. The graphical representation reveals the widely varying levels of infection amongst individual snails. Two weak positives identified by *Dra1* here show as negatives demonstrating that optimized PCR conditions appear to be crucial in selecting the most weakly infected snails. Overall, however, the levels of detection between the two methods are comparable and if standards are included with the RT-PCR then estimates of concentration can be obtained from a linear standard curve.



An additional benefit of rIGS amplicon is that the *S. haematobium* version has a restriction enzyme site, *Acc1* embedded in the center whereas in *S. bovis* this cut site does not exist. Consequently, a restriction digest of this fragment can determine which species is present. Additionally, the test can reveal whether or not the schistosome is a hybrid between *S. haematobium* and *S. bovis* which is an

important factor given the recent discovery of such hybrids infecting children in Senegal (see Huyse *et al*, 2009). The figure below illustrates this test:



Work Package 6 *"Use of oligochromatography: adaptation of Real-Time PCR assays to low technology laboratories.*

Samples from Kenya were obtained. These have been sequenced and genotyped and their population genetic parameters analysed alongside those obtained from Uganda localities.

Publications

Nalugwa, A., Kristensen, T.K,Jørgensen, A. and Nyakaana, S. (submitted). Microsatellite analysis of population structure and genetic variability in the tetraploid Bulinus truncatus freshwater snail of the Albertine Rift (submitted).

A. Nalugwa, Thomas Kristensen, Silvester Nyakaana and Aslak Jørgensen (2010). Mitochondrial DNA variations in sibling species of the Bulinus truncatus/tropicus complex in Lake Albert, Western Uganda. Zoological studies, 49(4): 515-522

A. Nalugwa, A. Jørgensen, S. Nyakaana and T. Kristensen (2010). Molecular Phylogeny of Bulinus (Gasxtropoda: Planorbidae) reveals the presence of three species complexes in the Albertine Rift fresh water bodies. International Journal of Genetics and Molecular Biology, 2(7): 130-139

Work Package 7 *"Characterisation of the (microsatellites) population structure of* Bulinus *over space and time.*

Samples from Kenya were obtained, sequenced and genotyped and their population genetic parameters analysed alongside those obtained from Uganda localities.

Fieldwork was carried out in November 2009 with partner 7, NMK, to obtain samples from the NMK collections and collect samples from water bodies and rice fields in and around Lake Victoria Basin - Kisumu area (Kenya). Also joined the fieldwork did staff from partner 14, VCD.

A second field trip was carried out in January 2010, where B. africanus where sampled from coastal Kenya *staff from NMK, VCD and MU.

The usual basic materials for lab work were procured (e.g. DNA extraction kits, oligonucleotides, PCR enzymes, quantitative real time PCR reagents) during the course of the year

One Manuscript has been submitted for consideration for publication

Nalugwa, A., Kristensen, T.K,Jørgensen, A. and Nyakaana, S. (submitted). Microsatellite analysis of population structure and genetic variability in the tetraploid Bulinus truncatus freshwater snail of the Albertine Rift

Two publications have been published during the course of the year, namely:
1. Allen Nalugwa, Thomas Kristensen, Silvester Nyakaana and Aslak Jørgensen (2010). Mitochondrial DNA variations in sibling species of the Bulinus truncatus/tropicus complex in Lake Albert, Western Uganda. Zoological studies, 49(4): 515-522
2. A. Nalugwa, A. Jørgensen, S. Nyakaana and T. Kristensen (2010). Molecular Phylogeny of Bulinus (Gasxtropoda: Planorbidae) reveals the presence of three species complexes in the Albertine Rift fresh water bodies. International Journal of Genetics and Molecular Biology, 2(7): 130-139

Work Package 8 *"Characterization of the (microsatellite) population structure of* S. mansoni *parasites over space and time in relation to habitat, chemotherapeutic pressure, and human infection and morbidity levels.*

Overall brief summary of activities in WP8

Novel microsatellite markers, Whole Genome Analyses (WGA) and multiplex analyses were developed and optimised for both Schistosoma mansoni and S. haematobium.

Field work to collect samples was performed by ICL partners in Niger, Uganda, Kenya, Tanzania and Cameroon (and non-CONTRAST country of Mali here). Additional field samples were supplied by CONTRAST partners for Niger (and Uganda).

Key findings revealed significant sub-structuring within S. mansoni and, for both Tanzania and Uganda within East Africa, a clear impact of PZQ on population genetic structure, with a significant bottleneck in genetic diversity post Mass drug administration (MDA). Such a bottleneck was not consistently apparent within S. mansoni from Kenya in East Africa nor Niger in West African.

Preliminary analyses of S. haematobium from Tanzania, Cameroon, Niger (and Mali) revealed very limited genetic sub-structuring, indicating few barriers to gene flow in these populations, and less impact of MDA on genetic diversity. Further analyses are ongoing.

In regions of sympatric S. mansoni and S. haematobium, there was evidence that coinfections within the indivual human host alter the genetic diversity of both parasite species, with genetic diversity indices and inbreeding being higher in coinfections relative to single infections. MDA with PZQ also had an impact on the genetic diversity of species populations, where, for instance, the impact of coinfections on S. haematobium diversity as observed at baseline appeared to be removed 12 months post MDA, potentially indicating a disruption of interspecific interactions by MDA.

Likewise, in regions of sympatric S. mansoni and S. haematobium, there was evidence that coinfections alter the moribidty profile observed within the human host, where, for example, S. haematobium-associated morbidity, was lower in the coinfected group relative to single S. haematobium infections, even when accounting for infection intensities. Thus an inter-specific interaction between the two species is suspected to affect the outcome of schistosomiasis-associated morbidity profiles.

Activities/Deliverables in period:

1) Continued sampling and collection of material from CONTRAST partners.
2) Development and optomisation of novel Whole Genome Amplication (WGA) methodology for *S. haematobium.*
3) Continued characterization of *S. mansoni* and *S. haematobium* microsatellite population population structure from Uganda, Tanzania, Niger, Cameroon and Kenya.
4) Elucidation of the impact of single versus mixed *S. mansoni* and *S. haematobium* coninfections on parasite population genetic structure and associated host morbidity in Taveta, Kenya.
5) Provision and incorporation of population genetic data for novel predictive mathematical models (wp12)
6) Preparation and submission of papers for publication.

Fieldwork
July 2010 – Kisorya and Bunda, Tanzania (ICL partners with Tanzanian partners)

A longtidinal sampling follow-up in Kisorya and Bunda, Tanzania was undertaken in July 2010 (all travel and field work costs funded by JPW's Royal Society Fellowship grant) .

A primary aim was to characterize current population genetic structure and to identify any potential differential in PZQ efficiency in this area following MDA. A secondary aim was to identify any potential costs of resistance associated in these *S. mansoni* populations using sibship analyses. Approximately 6 % of the tested miracidia were identified as less susceptible to PZQ treatment using a phenotypic assay, although neither genetic clustering nor differences in sibship sizes were detected between susceptible and less susceptible field isolates.

D12 Elucidation of the potential impact of mass chemotherapy on the population genetic structure of the parasite host populations

1. ***Tanzanian S. mansoni dataset analyses completed and paper published in ASTMH.*** (2010) 83:951-957

2. ***Ugandan S. mansoni longitudinal dataset analyses completed.***
Key findings: A similar bottleneck in genetic diversity was observed following MDA, to that observed for Tanzania, and this continued to decline with the number of Praziquantel (PZQ) treatments . Furthermore, distinct genetic sub-structuring was observed, with genotypes from those children with four or five PZQ treatments separating distinctly from those with nor or 1-3 PZQ treatments only.

Paper in preparation for submission. Lamberton et al.

3. Development, optomisation and application of novel Whole Genome Amplication (WGA) methodology for S. haematobium.

Key findings: This represents first time that the whole genome amplification technique (WGA) has been optimized and used for *S. haematobium*. This should be of great benefit for current and future research on schistosome genetics – in particular this technique provides a practical method of increasing the quantity of template DNA thereby allowing for repeat genotyping of individual samples across a range of molecular techniques and tools.

Paper, combining WGA of both *S. haematobium* and *S. mansoni* data, is in preparation. Gouvras et al.

4. Tanzanian S. haematobium longitudinal dataset analyses across all schools completed.

Key findings: Preliminary data indicate that there was only limited evidence of population subdivision between individual children or between schools or regions, or indeed over time, suggesting that there may be few barriers to gene flow exist in this *S. haematobium* population.

Data to be included in special edition Acta Tropica volume.

5. Cameroonian S. haematobium baseline dataset analyses across all schools completed. Longitudinal follow-up post PZQ data requested from Louis Albert Theume Tchente.

Key findings: Preliminary data indicate that there was only limited evidence of population subdivision between individual children or between schools or regions, suggesting that few barriers to gene flow exist in this *S. haematobium* population.

Data to be included in special edition Acta Tropica volume.

6. Niger S. mansoni single and S. haematobium single and dual co-infection longitudinal dataset analyses completed across all three regions (Kollo, Tilaberi, Dosso).

Key findings: Allelic richness was observed to be significantly higher in *S. mansoni* coinfections compared to single *S. mansoni* infections across two villages. There was also evidence of a non-significant trend of higher allelic richness in *S. haematobium* coinfections relative to single infections, potentially indicative of inter-species competitive interactions within their hosts. Furthermore, in coinfected villages, it was apparent that *S. haematobium* was rapidly being replaced by *S. mansoni* after praziquantel treatment, as no eggs hatched from samples collected post treatment whereas *S. haematobium* in single species villages persisted post treatment. However, in contrast to that recently observed for *S. mansoni* in East Africa, no generalized post praziquantel genetic bottleneck appeared to be occurring for either species here in West Africa, within single or coinfection villages, with the exception of Diambala in Tillaberi region, where small yet significant structuring was observed across treatment time points.

Paper in preparation for submission, Gouvras et al.

7. Kenyan S. mansoni single and S. haematobium single and dual co-infection longitudinal dataset analyses completed from the Taveta regions.

Key findings: Whole Genome analyses (WGA) developed as described above, together with our novel microsatellite markers , were used to test the hypothesis that interspecific interactions between *S. haematobium* and *S. mansoni*, and a subsequent differential impact of praziquantel (PZQ) treatment between species, are affecting the intraspecific genetic diversity of both species in this Kenyan East African setting. The results obtained support the hypothesis that coinfections do alter the genetic diversity of both parasite species, with genetic diversity indices and inbreeding being higher in coinfections relative to single infections, for both species at baseline. Mass drug administration (MDA) with PZQ also had an impact on the genetic diversity of species populations, reducing the genetic diversity of the *S. haematobium* population and conversely increasing the genetic diversity of the *S. mansoni* population in this Taveta setting, within single species infections. Moreover, the impact of coinfections on *S. haematobium* diversity, as observed at baseline, appeared to be removed 12 months post MDA, potentially indicating a disruption of interspecific interactions by MDA.

Paper in preparation for submission, Gouvras et al.

D13 Identification of parasite genotypes and/or parasite genotype combination with potential of causing severe morbidity for targeted control

1. *S. haematobium* genetic analyses combined with infection intensity datasets to test for potential associations between genotype/genotype combination to host morbidity assessed.

Key findings: Sixteen novel polymorphic microsatellite markers for *S. haematobium* were developed, optomised for muliplex analyses and first applied to complementary (non-CONTRAST country) data from Malian schoolchildren. There was no evidence of an overall association of the diversity of the infection with infection intensity (infection intensity as an indirect measure of morbidity here). However, older children and boys harboured more diverse infections, as measured by the number of unique adult genotypes present, although there was no difference in the average diversity of their larval populations. Individual parasite genotypes had variable reproductive success, and parasite fitness was reduced in older children. Rare alleles were more commonly found in the most heavily infected children.

Paper submitted for publication, Gower et al.

2. Kenyan (Taveta) *S. mansoni* single and *S. heamatobium* single and dual co-infection longitudinal population genetic dataset analyses combined with complementary morbidity datasets to test for potential associations between parasite species (and subsequently genotype/genotype combination) to host morbidity assessed.

Key findings

A study was undertaken in two neighbouring schools in Taveta, Kenya. Clinical examination of the liver and spleen was performed and urinary albumin levels were recorded at baseline. At 12 months post MDA these tests were repeated with the addition of ultrasonographic profiles of the liver, spleen and bladder for a more differential diagnosis of schistosome morbidity. It was found that *S. haematobium*-associated morbidity, was lower in the coinfected group relative to single *S. haematobium* infections even when accounting for infection intensities. Thus an inter-specific interaction between the two species is suspected to affect the outcome of urinary schistosomiasis in this focus. Little impact of coinfections on *S. mansoni*-specific
morbidity was detected , although there was an association of S. haematobium infections
with liver morbidity.

Paper on morbidity parameters prepared for Acta Tropica special volume, Gouvras et al.

Molecular analyses of associated genetic data are ongoing and a paper will be prepared, Gouvras et al.

Thesis completions.

October 2010. PhD Thesis. Anouk Gouvras. Title: Intestinal and urinary schistosomiasis dynamics in sub-Saharan Africa.

September 2010. MPH Thesis Florian Gehre. Title: Efficacy of Praziquantel against *Schistosoma mansoni* field isolates collected in Tanzania.

- Awarded prize for best MPH/MSc thesis 2010.

Publication relating to the work in WP8

Norton, A.J, Gower, C.M., Lamberton, P.H.L., Webster, B. Lwambo, N.J., Blair, L., Fenwick, A. & Webster, J.P. (2010). Genetic Consequences of Mass Human Chemotherapy for Schistosoma mansoni: population structure pre- and post- praziquantel treatment in Tanzania. American Journal of Tropical Medicine and Hygiene. 83:951-957

Garba, A., Barkiré, A., Djibo, A., Lamine, M.S., Sofo, B., Gouvras, A.N., Bosqué-Oliva, E., Webster, J.P., Stothard, J.R., Utzinger, J. and Fenwick, A. (2010). Revealing a neglected public health burden of schistosomiasis: infection of Schistosoma in infants and preschool aged children in a single Schistosoma haematobium and a mixed S. heamatobium: S. mansoni foci of Niger. Acta Tropica. 115: 212–219

Webster, J.P., Koukounari, A., Lamberton, P.H.L., Stothard, J.R. & Fenwick, A. (2009). Evaluation and Application of potential schistosome-associated morbidity markers within large-scale mass chemotherapy programmes. Parasitology. 136, 1789-1799.

Rollinson, D., Webster, J.P., Nyakanna, S. & Stothard, J.R. (2009). Genetic diversity of schistosomes and snails: significance for control. Parasitology. 136, 1801-1811.

Stothard, J.R., Webster, B.L., Weber, T., Nyakaana, S., Webster, J.P., Kazibwe, F., Kabatereine, N.B. & Rollinson, D. (2009). Molecular epidemiology of Schistosoma mansoni in Uganda: DNA barcoding reveals substantive genetic diversity within Lake Albert and Lake Victoria populations. Parasitology. 136

***Objective 2.* Characterisation of schistosome-snail relationships and transmission potential**

To investigate the schistosome-snail relationship in greater detail in various eco-epidemiological settings across West-, Central- and East Africa to assess and quantify disease transmission potential

Work Package 9 *"Establishment of a snail-parasite research node".*

The objective in WP 9 was to establish a research node for snail-parasite relationship by strengthening the laboratory capacity of partner 10 for culturing and compatibility testing of living parasites and snails and to develop a regional capacity to train researchers in experimental parasitological methods. Also it was the objective to develop snail parasite information and establish live biological specimen collection. This has been finalized and these facilities are in use used according to need in the Su-Saharan countries. Deliverable 14 is by this satisfied.

Work Package 10 *"Dynamics of transmission and interactions between schistosomes in sub-Saharan Africa.*

WP 10 is a very comprehensive work package involving nine partners 2, 4, 6-11 and 14. It is the objectives to assess the competitive dynamics of schistosome species in mixed infection foci of *S. mansoni* and *S. haematobium* from study areas in Cameroon, Niger, Senegal, Kenya, Tanzania, Uganda and Zambia, and to provide biological material for molecular studies. Referencing WP 3-8. Also re-infection patterns at mixed infection loci following PZQ administration referencing WP 12 will be determined.

Briefing on the activities in Senegal
ONGOING ACTIVITIES FROM OCTOBER 2009 TO SEPT 2010

- - Month 12 Survey in Guia : January 2010
- -Malacolgical surveys (Wp.11) in Guia Nder, and Temeye.
- -Characterization of Schistosomes in the Ferlo (area with temporary transmission) and impact of treatment in Nder
- -Trip in Niger (collaboration inter-team (ISRA-PNLB/Niger –NMH)
- -Analyse of data and exploitation of results
- - Publications

Activities at fieldsite 1 in Guia
SURVEY OF MONTH 6 + 2 TREATMENTS / SURVEY N° 4 (M 6 + 2 Treatments) (17 to 19 June 09)

After the 2 treatments separated by 3 weeks people were re-examined (from each child, collect and examine of1 stool sample and 1 urine sample on 3 consecutive days and preparation of 2 slides per sample).

Prevalence

% prevalence of *S. mansoni* : 0 % (0 /108 examined)
% prevalence of *S. haematobium* : 0 % (0 / 128 examined)

SURVEY OF MONTH 12 JANUARY 2010 / SECOND RE-INFECTION AFTER TREATMENT (Survey from 22 to 24 January 2010)

Prevalence

102 children were concerned
% prevalence of *S. mansoni* : 0 % (0 /77 examined)
% prevalence of *S. haematobium* : 84 % (86 / 102 examined)

This prevalence is very high as the level of the baseline (95%)

Eggs count
Maximum: 316 eggs / 10ml and 18 +/- 39 eggs

Treatment of the cohort: In relation with the health authority of the center and the teachers, all these 102 children were treated.

DYNAMICS OF INFECTIONS AND TRANSMISSION

- **-W0 / S1**: High prevalence of Sh and S.m but more in Nder than in Temeye

- **-W6 / S2**: After the 2 treatments the prevalence decreases in survey 2, but is high with *S.haematobium* (47 % at Nder and 20 % at Temeye). Efficacy of PZQ ? .

- **- Month 6 / S3**: Situation of re-infection after treatment:

Very high re-infection rate particularly with *S.mansoni* (97 % at Nder and 92% at Temeye) more than initial levels and increase of eggs count. So to follow the dynamics of re-infestation after 12 month, ethically we were obliged to treat people. All children were re-treated twice separately 3 weeks after (T3 & T4)

- **- Month 6 + W6 / S4:** Situation after 2 more treatments (T3 & T4) Decrease of infection after the treatments T3 &T4 particularly with S.h infection (infection cleaned to zero in the 3 villages) but for *S.mansoni* it is high (67% at Nder and 67% at Temeye).

- **- Month12 / S5**: Situation of re-infection after 4 treatments

High re-infection concerning *S.mansoni* (92% at Nder and 46% at Temeye)

For S.haematobium the level of the prevalence is lower than at the beginning in Nder and Temeye (37% / 96% and 8%/ 66%) but at Guia where S.h is alone the prevalence is higher (84%) than at W0 (95%)

SUMMARY

- High prevalence and dynamic transmission of S.h. and S.m. in Nder, Temeye and Guia.
- The pattern is the same in Nder and Temeye
- Rapid re-infection after treatment, particularly S.m (Survey 3 and Survey 5)
- Efficacy of PZQ on schistosomes:

-S.h: Low re-infection rates and low eggs count (S2 and S4).
High response to PZQ.

- S.m: High re-infection rates and increased eggs count (S3 and S5)

Work Package 11 *"Role of the different species of intermediate hosts in the transmission of schistosomiasis in sub-Saharan Africa."*

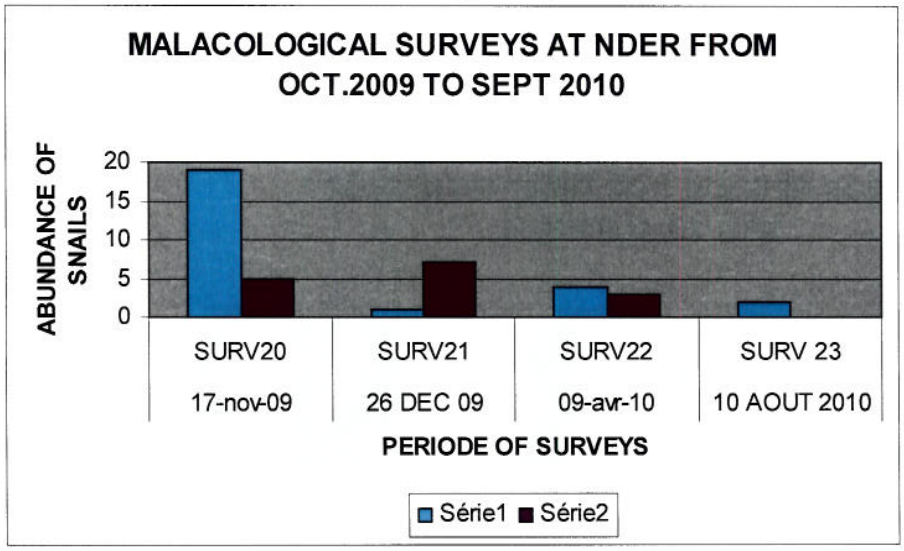
In WP 11 it is currently examined which role *Bulinus* and *Biomphalaria* species have in the transmission of schistosomiasis in project study areas referencing WP 10. Also this work package provided biological material for molecular studies, referencing WPs 3-8, and it is also the objective to determine factors that promote changes in schistosome-snail relationship referencing WP 14.

A total of ten partners are involved: 1, 2, 6-12 and 14.

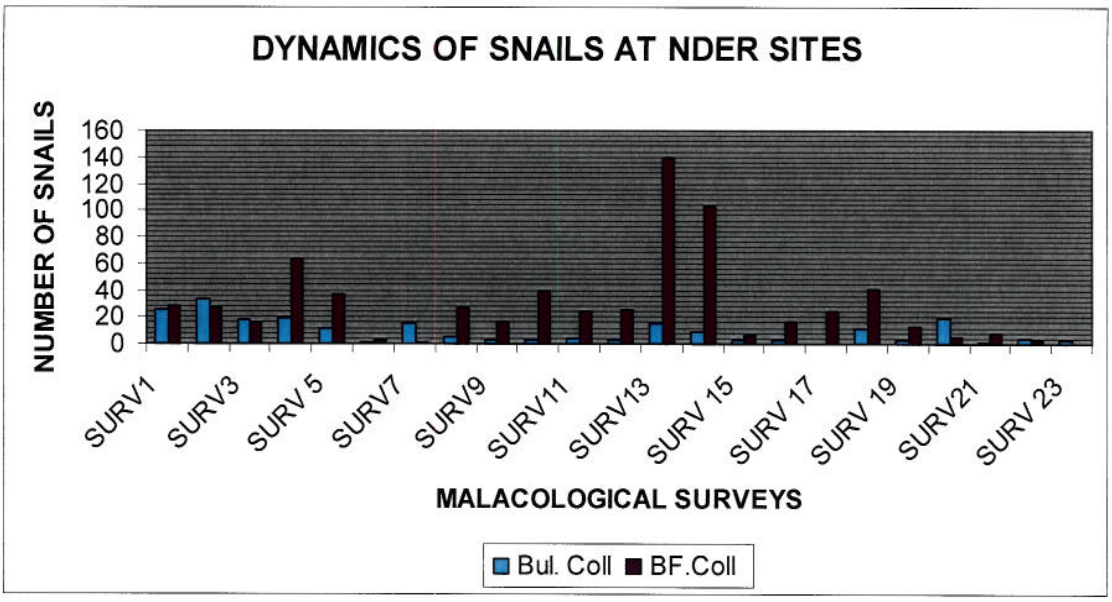
Senegal activities in WP11

MALACOLOGICAL SURVEYS IN NDER ,TEMEYE AND GUIA

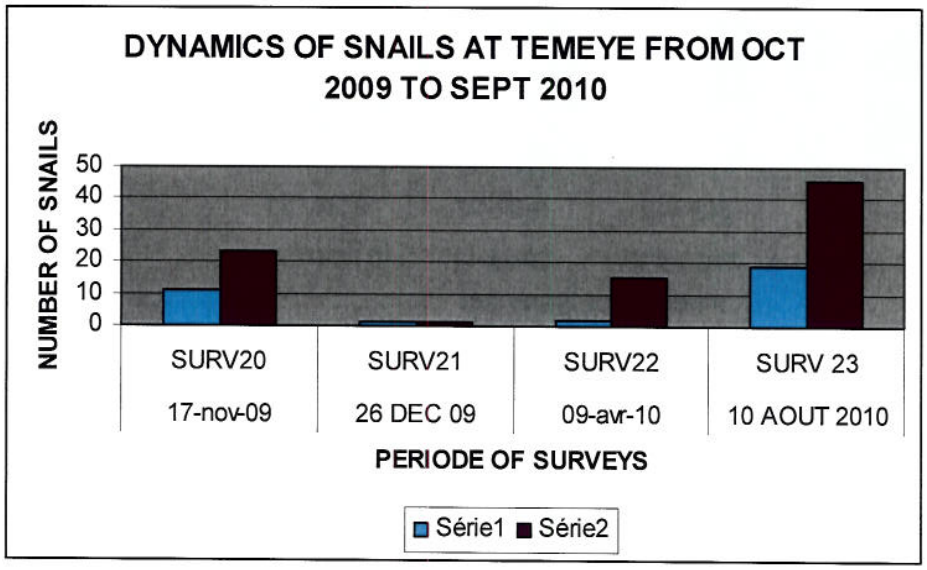
(Surveys at Nder from October 2009 to Sept 2010)



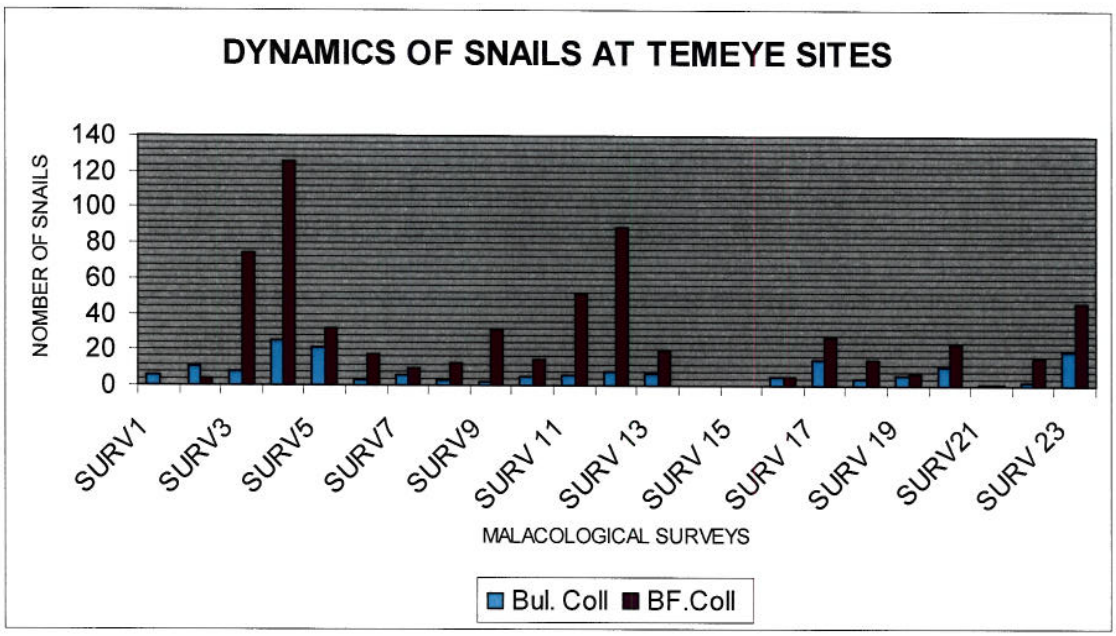
SUMARY OF ALL SURVEYS AT NDER



(Surveys from October 2009 to Sept 2010)



SUMARY OF ALL SURVEYS



- Summary of surveys

Two periods of reinfestation in Nder (3 sites):

- **From May 07 to Now 07 :279 snails collected**
  *173 Biomph : 4+/ 173 during May (survey 2)
  *106 Bulinus Sp: 3 +/ 106 during July (survey 4)

- **From Janu 08 to June 08 : 123 snails collected**
  *111 Biomph: 2+/111 during May 08 (survey 12)
  *12 Bulinus Sp : 0+/ 12

- Abundance of snails very low , more Biomph than Bulinus
- Very few transmitting snails (6 Biomph & 2 Bulinus)

Two periods of reinfestation in Temeye (4 sites):

- **From June 07 to Dec 07 :313 snails collected**
  *262 Biomp : 2+/ 262 (1+/ 74 survey 3 July and 1+ / 126 survey 4 August)
  *70 Bulinus Sp: 4+/ 70 (1+/ 8 survey 3 July and 3 + / 22 survey 4 August)

- **From Janu 08 to June 08 : 207 snails collected**
  *186 Biomph : 0+ / 186
  * 21 Bulinus : 0/ 21

- Abundance of snails very low , more Biomph than Bulinus

Very few transmitting snails (2 Biomph & 4 Bulinus)

Work Package 12 ***"To develop novel mathematical predictive models of schistosomiasis transmission under different selective pressures.***

Key responsible for this WP is partner 3. Contributors have been partner 2, 9 and 14.

Novel stochastic mathematical models which predict and describe the effects of parasite transmission on the genetic diversity of parasite populations, and to elucidate the optimum genetic sampling protocols, were developed and evaluated using field collected CONTRAST data from Tanzania for *Schistosoma mansoni* populations. The results indicate that in order to sample as effectively as possible, increasing the number of hosts sampled, rather than the number of miracidia per host, results in more robust estimates of population genetic diversity, results pertaining to this location and specific parasite population genetic structure. We hope that the results derived here will be useful to new research and control programmes, and help inform their M&E approaches.

Specific Objectives

Development of novel mathematical models which predict and describe the effects of parasite transmission on the genetic diversity of parasite populations. The models will be genetically explicit to take into account chemotherapy-induced selection (to investigate the transient dynamics of allele frequencies under selection during control programmes). Referencing **WP 8,10**.

The model/models will be useful for assessing the potential impact of chemotherapy intervention strategies and habitat on the levels and genotype combinations of human infection, which may have subsequent implications of predicting human morbidity. **WP 8,10**.

Deliverables:

D18 Provision of deterministic age-structured models which incorporate genetic structure.

D19 Validation of models against field collected data.

Specific objectives:

1. Using a stochastic modelling approach we aim to confirm the findings of reductions in population levels of genetic diversity in schistosomes following chemotherapy (e.g. see Norton et al, 2010), and provide confidence intervals for these reductions.

2. Given that collecting samples and carrying out molecular typing is time-consuming and relatively expensive, we aim to identify the most efficient approach in terms of numbers of hosts sampled, and numbers of miracidia per host sampled.
3. Treatment in these areas is school-based. We aim to use these models to identify whether the 7yr olds who enter the school system each year, and who are therefore presumably PZQ naïve, offer any insights into potential reductions in diversity in the wider untreated population.
4. Using a stochastic sampling approach, can we use these reductions in genetic diversity to estimate treatment coverage in the area and/or whether the observed reductions in diversity are random or more targeted?
5. Can we extrapolate these models for use of other locations and schistosome species?

Milestones in period:

- *Number and name:*

1. Collection of existing data from other work packages and literature review.
2. Development of initial model and preliminary evaluation using available data.
3. Formulation of fully stochastic models for the investigation of transient dynamics of allele frequencies under selective pressures.

Were the deadline met?:

Yes, in part, although final model developments are ongoing.

Activities:

- **Development of stochastic simulation models that capture the change in genetic structure of schistosome populations under chemotherapeutic pressure.**

Key findings: Using the molecular data from Tanzania (Norton et al., 2010), a stochastic sampling approach using the software R was developed. Our results demonstrated that significant reductions in measures of population genetic diversity (AR, H_O, H_E in this case) in the parasite population can be induced by one round of PZQ treatment of the human hosts, even without reaching universal coverage. Likewise, a reduction in genetic diversity observed in the PZQ-naïve 7yr olds entering the cohort each year was also demonstrated by the model, providing further support to the hypothesis that genetic diversity is indeed falling in the wider community. In this, the results here confirm using a stochastic sampling/resampling approach in order to provide confidence intervals for the findings of Norton et al., (2010) using the same dataset. Further simulations using genetic data from contrasting countries and regions, MDA regimes, and also for both *S. haematobium* as well as *S. mansoni* are required in order to test how widespread these findings are, and such simulations are in progress.

- **Development of simulation models to indentify the ideal sampling approaches required to capture the genetic structure of schistosome populations under chemotherapeutic pressure.**

Key findings: The collection of parasitological samples (miracidia in this case), and subsequent molecular typing of these samples is a relatively expensive and time-consuming process for Monitoring and Evaluation (M&E) and research programmes. Therefore identifying the most effective, and cost-effective, sampling approach that aids the identification of changes in the genetic structure of the population under chemotherapeutic pressure is highly desirable. Sampling methodological ideals are, however, one of the most under-represented areas in empirical studies of parasite populations. As a rule of thumb one study suggested 20 parasites per individual host, 5 hosts per site, and 10 sites. However, the specific recommendations will necessarily be dictated by the biological questions being addressed in each study.

Just as performing power and sample size calculation is now regarded as a standard step in epidemiological study design, we contend that estimating and justifying the sampling strategy should be in molecular ecology studies in order to most effectively utilize scarce time, and even scarcer resources. The aim of this initial study component was therefore to, using empiral data gathered from Tanzania (Norton et al., 2010), develop an optimum sampling framework (in terms of number of hosts, samples per host, and the definition of population) in order to identify the potential impact of MDA on parasite genetic diveristy.

An extension of the stochastic resampling approach was used and these indicated that there are significant implications for altering the definition of the parasite population, from that of infrapopulation (the schistosomes residing in one human host) to that of the component population (the pooled sample of all schistosomes residing in a population of humans) and vice versa. Using a component population approach highly significant differences in the measures of genetic structure following a single round of treatment were observed when sampling as few as 1 miracidia per host. Increases on the number of miracidia per host rapidly led to very low P-Values for the difference between years. Contrasted to this, the results generated when using an infrapopulation approach suggested only marginally significant results when sampling only 1 miracidia per host. In this case larger numbers of miracidia need be sampled before obtaining significant results for AR and H_O, but not H_E. When comparing the results obtained under the different population definitions, the results obtained for H_O were very similar, as may be expected. However, it was different for H_E ,where even small numbers of miracidia per host provide a reasonably stable estimate when using the component population approach, but take time to stabilise when using an infrapopulation approach, and do so at lower values, presumably due to the smaller sample sizes involved. With regard to altering the number of hosts sampled, rather than number of miracidia, we observe a smaller difference between the two population definitions. Here it takes a larger sample size (>10 hosts for all measures using a component population approach, and >15 for AR and H_O and > c.50 [projected] for H_E for an infrapopulation approach) to show statistical difference between the years.

Future plans:

- Validation of models and calculation of reductions in genetic diversity following multiple treatment rounds, using data already collected by the partner from Tanzania (*S. haematobium*), Uganda (*S. mansoni*) and Niger (*S. mansoni* and *S. heamatobium*), and comparison to initial Tanzanian model and results. These results will be written up for publication in the peer-reviewed literature and presented at International symposia.

Publications/associated publications:

French, MD, Churcher, TS, Gambhir, M, Fenwick, A, Webster, JP., Kabatereine, N. and Basáñez, M-G. Observed Reductions in *Schistosoma mansoni* Transmission from Large-scale Administration of Praziquantel in Uganda: a Mathematical Modelling Study" . PloS Neglected Tropical Diseases. In Press

French, MD, Churcher TS, Basáñez, M-G. and Webster, JP. Reductions in genetic diversity of *Schistosoma mansoni* populations under chemotherapeutic pressure: the impact of sampling approach. In Prep.

Objective 3. ***Spatial epidemiology for schistosomiasis risk mapping and prediction***

To identify key risk factors that govern the frequency and transmission dynamics of schistosomiasis and to quantify spatio-temporal disease patterns in selected eco-epidemiological settings across Africa.

Work Package 13 ***"To establish a GIS and spatial epidemiological research node."***
Finished. The implementation of this work package was achieved in collaboration between partner 1, 3 and 6.

Some development still has been achieved which will be briefed upon here.

Under this reporting period, an Assistant GIS Officer and Assistant Field GIS Officer operated well in providing technical input to the operations of the Node. An auxiliary officer who was employed under the project had worked for three years up to the end her contract of employment in line with the Year #4 Project Budget.

Computing equipment has been purchased and installed as follows:-

- Three Laptops
- Six desktops
- One A3 colour printer
- One A4 Scanner
- Three external hard drives for backing up data.
- One duplex printer –Non colour

One colour printer with A3 printing capability has been procured

Idrisi Kilimanjaro and other open source GIS software are being tried for processing remote sensed data.

The Project Motor vehicle has been maintained and coninued to fucntion well in supporting operations of the GIS Research Node through out the Reporting Year.

Internet Connectivity functional. Full connectivity functioning being refined by the national Internet Service Provider (ISP). Otherwise the Node is fully fucntional with goodenough connectivity for effective communication within Contrast Project Partnership and others.

Work Package 14 ***"Creation of comprehensive GIS databases for selected study areas."***

Finished. Summary of the year's achievements as below:

Historical schistosomiasis survey data extracted from published and unpublished sources have been compiled to an open access georeferenced database. The database includes surveys conducted in over 10 000 unique locations in Africa from 1900 onwards. To date, this is the only open access database of actual data on schistosomiasis. It is continuous being updated and extended to include other neglected tropical diseases with worldwide coverage. It is developed on MySQL language with a web-interface and can be accessed via www.globalntddatabase.org A manuscript by Hürlimann et al (2010) reporting on the results has been submitted for publication to PLoS NTD.

Data base of climate and environmental data has been established and is continuously being updated. Already 351 GB worth of land surface temperature and normalised difference vegetation (NDVI) has been archived. Land surface temperature data at 1KM has been downloaded for the whole Sub-Saharan Africa and has been archived at the GIS Research node, Normalised Difference Vegetation Index at km resolution will be has also been loaded in the data base.

A copy of this Ms Access database has been integrated into the GIS Node database. Beside its use in WP15, this database has also been used for supporting other Project Partner activities in mapping specific areas. It has also been sited on http://globalntddatabase.org. a real Open Source database for unlimited use by any researcher globally. This output by Contrast is first of a kind on helminthes data sharing. .

Accessing of climatic data in form of satallite images for Land Surface Temperature (LST) at 8km spatial resolution , Normalised Difference Vegetation Index (NDVI) at 1Km spatial resolution, Rainfal Estimates at 8km spatial resolution, has been done covering periods from 2000 to August 2010. The GIS Node at UNZA is now co-ordinating the collection and standardisation of environmental data from all involved Project Partners, a resource that grreatly benefits most sub-Saharan African Partner countries. .
Data summary:-
Aster elevation data for the whole Sub-Saharan Africa.
Land Surface Temperature (LST) at 8km spatial resolution running from 2000 to August 2010.covering the whole of Sub-Saharan Africa.
Normalised Difference Vegetation Index at 1km resolution running form 2000 to August 2010.Covering the whole of Sub-Saharan Africa.
Rainfall estimate at 8km resolution from NOAA Climate Prediction Center(CPC)
However, during the Period under Review, challenges were experienced in the transmission of data from partners, and further failure to download climate data directly from internet data portals because of poor internet connectivity.

During the work in this work packages it has been demonstrated how to utilize Google Earth in CONTRAST.

Work Package 15 ***"Development of Bayesian spatial models for risk factor analysis and mapping of high-risk areas."***

Bayesian geostatistical models have been developed to analyse *S. haematobium* and *S. Mansoni* survey data in (i) West Africa including Cameroon (Riedel et al 2010a) and (ii) East Africa (Riedel et al 2010b) in order to identify climatic and environmental factors related with the disease transmission and obtain spatially explicit estimates of risk and number of infected individuals of high geographical resolution. The above analyses involved development of data-driven statistical methodology to model very large geostatistical data (over 1000 locations). Methods have been also developed to standardise age-heterogeneous survey data across locations when spatial analyses are carried out on historical survey data. The writing up of this work is currently in progress by Riedel et al (2010c). A statistical issue in the spatial analysis of schistosomiasuis intensity data is the large number of not infected individuals resulting to excess zeros in the data, not accounted by the negative binomial distribution which is typically considered for egg intensity data. To address this problem, we developed Bayesian geostatistical zero-inflated models (ZIM) and analysed schistosomiasis egg count data in school-age children from Cote-d'Ivoire showing that ZIM produce more accurate maps of helminth infection intensity than their standard counterparts (Vounatsou et al, 2009).

Two papers have been published, several are in preparation. With this WP Deliverables 22-25 are fully satisfied.

Work Package 16 ***"Predicting infection risk in ecological zones similar to those of the study area"***

This work package is partly covered by WP 15.In WP 16 a large scale pattern analysis of schistosomiasis and its host snails across the CONTRAST study areas is prepared. In this study risk maps based on environmental, - climate -, human - and biotic data and their interactions has been developed.

Comprehensive diseases data in Africa covering all agro-ecological zones together with spatial statistical modelling and kriging enabled the production of regional maps in West and East Africa including Cameroon and Zambia.

Three publications have been published. Further results will be published in the special issue of Acta Tropica.

Deliverable 26 is by this satisfied.

Work Package 17 *"Construct integrated infection risk maps for schistosomiasis and other vector-borne diseases of socioeconomic importance in sub-Saharan Africa."*

Integrated risk mapping often relies on overlaying disease-specific maps. This approach leads to incorrect estimates of disease co-existence because it implies that the diseases are independent, an assumption which is not justified for diseases influenced by common climatic and environmental drivers. To enable reliable estimation of co-integrated disease risk, geostatistical shared component models have been developed to estimate the geographical distribution and burden of co-infection risk from independent single disease surveys allowing for between diseases correlation. The models have been validated on simulated data and applied on real data from Cote d'Ivoire to assess *S. mansoni* and hookworm co-infection. This work has been further extended to estimate co-integration risk between *S. mansoni*, hookworm and malaria in Cote d'Ivoire as part of an
Deliverbles 27 and 28 are by this satisfied

In this work package also studies from Uganda and Zambia is finalised. Manuscripts are to be prepared.

Three publications are in preparation. More will come.

Integrated risk mapping often relies on overlaying disease-specific maps. This approach leads to incorrect estimates of disease co-existence because it implies that the diseases are independent, an assumption which is not justified for diseases influenced by common climatic and environmental drivers. To enable reliable estimation of co-integrated disease risk, geostatistical shared component models have been developed to estimate the geographical
distribution and burden of co-infection risk from independent single disease surveys allowing for between diseases correlation. The models have been validated on simulated data and applied on real data from Cote d'Ivoire to assess *S. mansoni* and hookworm co-infection. The methodology and results are reported by Riedel et al (2011). This work has been further extended to estimate co-integration risk between *S. mansoni*, hookworm and malaria in Cote d'Ivoire as part of an MSc thesis which was successfully submitted by F. Chammartin at the Institute of Statistics of the University of Neuchâtel, in June 2010. The writing up of the related manuscript is in progress and it is planned to be submitted to the *Journal of Spatio and Spatio-temporal Epidemiology*.

Presentations

"Geostatistical model-based estimates of schistosomiasis risk in West Africa."by Riedel N, Hürlimann E, Garba A, Traore M, Ndir O, Ratard R, Tchuem Tchuente LA, Kristensen TK, Utzinger J, Vounatsou P. Presented in the American Society of Tropical Medicine and Hygiene, Atlanta, November 2010.

"Bayesian geostatistical modelling of co-infection risk from single disease survey data" by Riedel N, Gosoniu L, Raso G, Utzinger J and Vounatsou P. Presented in (i) Valencia International Meeting on Bayesian Statistics, Spain, June 2010 and (ii) Geospatial Health meeting, Vietri, September 2009

"Mapping the spatial distribution of schistosomiasis and building a parasitological database" by P. Vounatsou in European Congress on Tropical Medicine and Health, Verona, September 2009

"Contributions of spatial statistical modelling in geospatial health" by P. Vounatsou in Geospatial Health meeting in New Orleans, December 2008

Publications

Chammartin F (2010). Modelling the geopraphical distribution of Schistosoma mansoni, hookworm and Plasmodim falciparum co-infection risk in a rural area of western Cote d'Ivoire. Master thesis, Institute of Statistics. University of Neuchâtel.

Riedel N, Gosoniu L, Raso G, Utzinger J and Vounatsou P. (2011). Modelling the geographical distribution of co-infection risk from single-disease surveys. *Statistics in Medicine* (to appear)

Vounatsou P, Giovanna Raso, G, Tanner M, N'Goran EK, Utzinger J (2009). Bayesian geostatistical modelling for mapping schistosomiasis transmission. *Parasitology, Supplement*

Submitted manuscripts

Hürlimann E, Riedel N, Boutsika K, Stensgaard AS, Laizer N, Laserna de Himps M, Ziegelbauer K, Camenzind L, Simoonga C, Mushinge G, Saarnak CFL, Utzinger J, Kristensen TK, Vounatsou P. (2010). Toward an Open-Access, Real-Time Global Database for Mapping, Control, and Surveillance of Neglected Tropical Diseases. *PLoS NTD (submitted).*

Riedel N, Hürlimann E, Garba A, Traore M, Ndir O, Ratard R, Tchuem Tchuente LA, Kristensen TK, Utzinger J, Vounatsou P. (2010a). Geostatistical model-based estimates of schistosomiasis risk in West Africa. *PLoS NTD (submitted).*

Draft manuscripts/in progress

Riedel N, Hürlimann E, Chimfwemmbe K, Musingue G, Simoonga C, Kabatereine N, Kristensen TK, Utzinger J, Vounatsou P. (2010b). Bayesian modelling of schistosomiasis risk in East Africa *(in preparation for Acta Tropica)*

Riedel et al (2010c). Adjusting for age heterogeneity in spatial analysis of historical schistosomiasis survey data.

Vounatsou et al.(2010). Statistical methodological issues in mapping historical schistosomiasis survey data (in preparation for Acta Tropica)

Objective 4. ***Social sciences approaches to better understand and encourage local control interventions***

To assess and quantify the negative effect of schistosomiasis on the daily lives of people living in endemic areas, and to measure beneficial effects following local control interventions.

Work Package 18 ***"Establish a research node for integrated economic and social policy analyses."***

The research node has been established at partner 12, National Institute of Medical Research, Mwanza, Tanzania. The facilities were established in the first period and fieldwork & course activities have been carried out. By this Deliverable 29 was fulfilled.

Work Package 19 *"Knowledge, attitudes and practices towards schistosomiasis control, and dynamics of socio-economic status."*

A baseline KAP study (KAP stands for "Knowledge, attitudes and practices") was conducted and completed in the field study area. Data analysis has been performed and a publication is submitted.
Preliminary findings indicate that due to the PHAST intervention, there has been increase in people's knowledge of how schistosomiasis is transmitted which led to positive attitudes towards its control, hence adoption of preventive practices.

Furthermore the baseline study on observations of human-water contact activities was conducted and completed and also that will be included in the publications. Also baseline study on the dynamics of people's socio-economic status was conducted and completed and the study will be published. Deliverables 30 and 31 are satisfied.

Work Package 20 *"Evaluation of "Participatory Hygiene and Sanitation Transformation" (PHAST) approach."*

Five training workshops on PHAST strategy facilitated by 18 Community-Owned Resource People (CORPs) have so far been completed involving 750 members of the community. The initiative has now fully been implemented and a manusl has been prepared in Shahili and English

It can be concluded that respondents' knowledge about causes, transmission, symptoms and consequences of intestinal schistosomiasis improved significantly after PHAST intervention.

The traditional beliefs of attributing schistosomiasis-related symptoms to seeing a python and having a house gutted down by fire was significantly reduced during the follow-up;

Generally water contact behaviour of the study population changed. The following (good practices) were observed during the follow-up phase (12 Months after PHAST intervention) :

- Frequency of contacts was significantly reduced;
- Timing of contacts changed (mid-day times were avoided);
- Duration of activities were significantly reduced;
- Extent of body surface exposed in water was significantly reduced.

Thus evaluation suggest that PHAST intervention had positive impact on KAP of the study population . By this Deliverables D32 and D33 has been fulfilled.

Work Package 21 ***"Role of snail biodiversity in management of schistosomiasis and use of refractory snails to block schistosome transmission for biological control."***

Snail habitats along the Kenyan Coast were examined over a period and the snail diversity was revealed. It was shown that *B.globosus* was the dominating *Bulinus* species on the northern coast and *B. nasutus* was the dominat species on the Southern Coast. These results will be further investigated. This study satisfied Deliverable 34.

In order to do the necessary studies on refractory snails, snail breeding facilities were established in a snail laboratory facility at Fort Jesus in Mombasa. Collection and set-up of the first snail colonies were done in May, 2008 and currently species are breeding. Infection experiments has taken place until the end of September 2010 and the final results will be presented in publications.
A planned study examining the possibility for using refractory snail from Zanzibar on the Coast of Kenya and vice versa showed to be impossible to implement. Deliverable 35 still wait for the final analysis in Fort Jesus to see if it is fulfilled.

Objective 5. Outreach and dissemination facility established

To collate all information generated by the project and make available to partners and global audience.

Work Package 22 *"Outreach and dissemination of knowledge."*

The objectives of Work Package 22 was to 1) to promote outreach and dissemination of knowledge between participants, different level stakeholders and end-users using a combination of WWW, electronic and hard copy materials; 2) to promote publication of scientific results at the highest level and 3) to disseminate actively and promote results amongst health decision making structures.

The website inaugurated during the first project is still running successfully (http://www.eu-contrast.eu). The site is frequently used by both CONTRAST partners and external visitors. The site has received almost 50.000 hits during the project period. This gives CONTRAST partners access to information from all the activities of the project, gives the European Commission permanent update on state of progress, and provides access to information to the general public.

In CONTRAST we have deliberately worked on making the work and results known to decision makers in health Ministries, organisations etc. in the partner countries and at each annual meeting we utilized the activity to highlight our work through high profiled openings including Ministers and Permanent secretaries from relevant Ministries, and through television radio and news papers.

Besides the promotion of our work and results to stakeholders in the governmental organisers and planners the results have been disseminated through publication in highly international recognised peer reviewed scientific journals.

Also CONTRAST partners has been used by WHO as experts in committees and by that brought our extended information further on to decision makers.

Peer-reviewed CONTRAST publications between 2009 - 2010 (n=32)

1) French,M.D., T.S.Churcher, Gambhir, A.Fenwick, J.P.Webster, and M.-G.Basañez. Observed reductions in *Schistosoma mansoni* transmission from large-scale administration of praziquantel in Uganda: a mathematical modelling study. submitted to PLoS NTD 2010.

2) Garba,A., S.Touré, R.Dembelé, P.BOISIER, Z.TOHON, E.Bosqué-Oliva, A.KOUKOUNARI, and A.Fenwick. 2009. "Present and future schistosomiasis control activities with support from the Schistosomiasis Control Initiative in West Africa." *Parasitology*. 136:1731-1737.

3) Garba,A., N.Barkire, A.Djibo, M.S.Lamine, B.Sofo, A.N.Gouvras, E.Bosque-Oliva, J.P.Webster, J.R.Stothard, J.Utzinger, and A.Fenwick. 2010. "Schistosomiasis in infants and preschool-aged children: Infection in a single Schistosoma haematobium and a mixed S. haematobium-S. mansoni foci of Niger." *Acta Tropica*. 115:212-219.

4) Huyse,T., B.L.Webster, S.Geldof, J.R.Stothard, O.T.Diaw, K.Polman, and D.Rollinson. 2009. "Bidirectional introgressive hybridization between a cattle and human schistosome species." *PLoS Pathogens*. 5.

5) Kazibwe,F., B.Makanga, C.Rubaire-Akiiki, J.Ouma, C.Kariuki, N.B.Kabatereine, B.J.VENNERVALD, D.Rollinson, and J.R.Stothard. Transmission studies of intestinal schistosomiasis in Lake Albert, Uganda andexperimental compatibility of local Biomphalaria spp. Parasitology International 59, 49-53. 2010.

6) Nalugwa,A., T.K.Kristensen, S.Nyakaana, and A.Jørgensen. Mitochondrial DNA Variations in Sibling Species of the Bulinus truncatus/tropicus Complex in Lake Albert, Western Uganda. Zoological Studies 49[4], 515-522. 2010.

7) Nalugwa,A., A.Jørgensen, S.Nyakaana, and T.K.Kristensen. Molecular phylogeny of Bulinus (Gastropoda: Planorbidae) reveals the presence of three species complexes in the Albertine Rift freshwater bodies. International Journal of Genetics and Molecular Biology 2[7], 130-139. 2010.

8) Norton,A.J., C.M.Gower, P.H.L.Lamberton, B.L.Webster, N.J.S.Lwambo, L.Blair, A.Fenwick, and J.P.WEBSTER. Genetic Consequences of Mass Human Chemotherapy for Schistosoma mansoni: Population Structure Pre- and Post-Praziquantel Treatment in Tanzania. American Journal of Tropical Medicine and Hygiene 83[4], 951-957. 2010.

9) Riedel,N., L.Gosoniu, G.RASO, J.Utzinger, and P.Vounatsou. Modelling co-infection risk from single-disease surveys. Statistics in Medicine [Revised and resubmitted].

10) Rollinson,D., J.P.Webster, B.L.Webster, S.Nyakaana, A.Jørgensen, and J.R.Stothard. 2009. "Genetic diversity of schistosomes and snails: implications for control." *Parasitology*. 136:1801-1811.

11) Rollinson,D. A wake up call for urinary schistosomiasis: reconciling research effort with public health importance. Parasitology 136, 1593-1610. 2009. Cambridge Journals.

12) Rollinson,D., B.L.Webster, O.T.Diaw, N.B.Kabatereine, I.S.Khamis, and J.R.Stothard. A new molecular epidemiology of African schistosomiasis with focus upon schistosome diversity. Tropical Medicine and International Health 14[Issue Suppl. S2], 8. 2009.

13) Rollinson,D., J.P.Webster, B.Webster, S.Nyakaana, A.Jørgensen, and J.R.Stothard. 2009. "Genetic diversity of schistosomes and snails: implications for control." *Parasitology*. 136:1801-1811.

14) Sengupta,M.E., T.K.Kristensen, H.Madsen, and A.Jørgensen. 2009. "Molecular phylogenetic investigations of the Viviparidae (Gastropoda: Caenogastropoda) in the lakes of the Rift Valley area of Africa." *Molecular Phylogenetics.and Evolution*. 52:797-805.

15) Simoonga,C., J.Utzinger, S.BROOKER, P.Vounatsou, C.C.APPLETON, A.S.Stensgaard, A.OLSEN, and T.K.Kristensen. 2009. "Remote sensing, geographical information system and spatial analysis for schistosomiasis epidemiology and ecology in Africa." *Parasitology*. 136:1683-1693.

16) Standley,C., N.Lwambo, C.Lange, Kariuki, M.Adriko, and J.R.Stothard. Performance of circulating cathodic antigen (CCA) urine-dipsticks for rapid detection of intestinal schistosomiasis in schoolchildren from shoreline communities of Lake Victoria. Parasites & Vectors 3[7], 1-5. 2010.

17) Standley,C., M.Adriko, M.Alinaitwe, F.Kazibwe, N.B.Kabatereine, and J.R.Stothard. Intestinal schistosomiasis and soil-transmitted helminthiasis in Ugandan schoolchildren: a rapid mapping assessment. Geospatial Health 4[1], 39-53. 2009.

18) Standley,C., M.Adriko, M.Alinaitwe, A.Atuhaire, F.Kazibwe, A.Fenwick, N.B.Kabatereine, and J.R.Stothard. Epidemiology and control of intestinal schistosomiasis on the Sesse Islands, Uganda: integrating malacology and parasitology to tailor local treatment recommendations. Parasites & Vectors 3[64], 1-11. 2010.

19) Stensgaard,A.-S., C.F.Saarnak, J.Utzinger, P.Vounatsou, C.Simoonga, G.Mushinge, C.Rahbek, F.Møhlenberg, and T.K.Kristensen. Virtual globes and geospatial health: the potential of new tools in the management and control of vector-borne diseases. 2. Geospatial Health 3, 127-141. 2009.

20) Stothard,J.R. Improving control of African schistosomiasis: towards effective use of rapid diagnostic tests within an appropriate disease surveillance model. Transactions of the Royal Society of Tropical Medicine and Hygiene 103[4], 325-332. 2009.

21) Stothard,J.R., B.L.Webster, T.Weber, S.Nyakaana, J.P.Webster, F.Kazibwe, N.B.Kabatereine, and D.Rollinson. 2009. "Molecular epidemiology of *Schistosoma mansoni* in Uganda: DNA barcoding reveals substantial genetic diversity within Lake Albert and Lake Victoria populations." *Parasitology*. 136:1813-1824.

22) Stothard,J.R., L.CHITSULO, T.K.Kristensen, and J.Utzinger. 2009. "Control of schistosomiasis in sub-Saharan Africa: progress made, new opportunities and remaining challenges." *Parasitology*. 136:1665-1675.

23) Stothard,J.R., J.C.Sousa-Figueiredo, C.Standley, G.J.Van Dam, S.Knopp, J.Utzinger, H.Ameri, A.N.Khamis, I.S.Khamis, A.M .Deelder, K.A.Mohammed, and D.Rollinson. 2009. "An evaluation of urine-CCA strip test and fingerprick blood SEA-ELISA for detection of urinary schistosomiasis in schoolchildren in Zanzibar." *Acta Tropica*. 111:64-70.

24) Stothard,J.R., M.D.French, I.S.Khamis, M.-G.Basañez, and D.Rollinson. 2009. "The epidemiology and control of urinary schistosomiasis and soil-transmitted helminthiasis in schoolchildren on Unguja Island, Zanzibar." *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 103:1031-1044.

25) Tchuem Tchuente,L.A. and E.K.N'Goran. 2009. "Schistosomiasis and soil-transmitted helminthiasis control in Cameroon and Côte d'Ivoire: implementing control on a limited budget." *Parasitology*. 136:1739-1745.

26) Tchuem Tchuente,L.A., O.T.Diaw, A.Garba, B.L.Webster, J.R.Stothard, and D.Rollinson. Biological features of transmission and reinfection patterns of intestinal and urinary schistosomiasis after treatment. Tropical Medicine and International Health 14[Suppl. 2], 8. 2009.

27) Tchuem Tchuente,L.A. Control of soil-transmitted helminths in sub-Saharan Africa: Diagnosis, drug efficacy concerns and challenges. Acta Tropica [In Press]. 2010. Elsevier.

28) Utzinger,J., G.Raso, S.Brooker, D.De Savigny, M.Tanner, N.ÏRNBJERG, B.H.SINGER, and E.K.N'Goran. 2009. "Schistosomiasis and neglected tropical diseases: towards integrated and sustainable control and a word of caution." *Parasitology*. 136:1859-1874.

29) Vounatsou,P., G.Raso, M.Tanner, E.K.N'Goran, and J.Utzinger. 2009. "Bayesian geostatistical modelling for mapping schistosomiasis transmission." *Parasitology*. 136:1695-1705.

30) Webster,B.L., D.Rollinson, J.R.Stothard, and T.Huyse. 2009. "Rapid diagnostic multiplex PCR (RD-PCR) to discriminate Schistosoma haematobium and S. bovis." *Journal of Helminthology*. 84:107-114.

31) Webster,B. 2009. "Isolation and preservation of schistosome eggs and larvae in RNAlater(R) facilitates genetic profiling of individuals." *Parasites & Vectors*. 2:50.

32) Webster,J.P., A.Koukounari, P.H.L.Lamberton, J.R.Stothard, and A.Fenwick. 2009. "Evaluation and application of potential schistosome-associated morbidity markers within large-scale mass chemotherapy programmes." *Parasitology*. 136:1789-1799.

Management

Work Package 23 " *Alliance management and project review and assessment"*

CONTRAST there have been no major problems in relation to consortium management and all partners have fulfilled their part of the work as described in Annex 1 of the project.

The management is a nested hierarchy like described in Annex 1. Day to day business is run by the Management Secretariat at the Coordinator (DBL). This secretariat reports to the Management Committee (MC), who has 13 members. The MC has a South and a North representative from each of the 5 objectives and the Coordinator, Webmaster and the Financial Administrator of the coordinating institute. An Optional member can be invited for specific meetings e.g. technical advisor from SCI, WHO or governmental representatives when appropriate.

It is the overall objective for the MC to plan, coordinate and control the project implementation through half yearly meetings. One or more are held at the annual workshop, the other is held 6 moths after the workshop as an electronic conference.

The annual meeting, of which we have had five (including one kick off workshop), is held at different sub-Saharan partner each year. The Kick-Off Workshop was held at partner 5 (responsible for research node 1) in Entebbe, Uganda in October 2006, and The Second Annual Meeting was held at partner 9 (responsible for research node 2) in Yaoundé, Cameroon in October 2007. The third was held in Zambia at the GIS research node in October 2008. The fourth was held in Kenya in October 2009 and also the 5th and final was kept in Kilifi, Kenya.

In case of emergency decisions the coordinator, overall financial administrator from DBL, David Rollinson and Russell Stothard from NHM, form a Executive Committee (EC) acting on the behalf of the overall coordination with reference to the Management Committee.

CONTRAST has successfully followed the timetable as set out in the Gantt diagram in Annex 1. CONTRAST is working in association with and compliment the findings of the Bill & Melinda Gates Foundation supported Schistosomiasis Control Initiative (SCI).

Periodic Activity Report 4

Section 3
Consortium management
(1 October 2009 – 30 September 2010)

CONTRAST

"A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa"

Contract no.: 032203

Partners/Contractor:

Partner 1. DBL, Denmark. Coordinator
Partner 2. NHM, United Kingdom
Partner 3. STI, Switzerland
Partner 4. ICL, United Kingdom
Partner 5. MU, Uganda
Partner 6

Section 3 – Consortium management

Workpacakge 23: Alliance management and project review and assessment.

All partners involved

Overall responsible: Thomas K. Kristensen and Christian Gregart, DBL.

During the CONTRAST project there have been no major problems in relation to consortium management and all partners have fulfilled their part of the work as described in **Annex 1** of the project

The management is a nested hierarchy like described in **Annex 1** (project document). Day to day business is run by the Management Secretariat at the Coordinator (DBL). This secretariat reports to the Management Committee (MC), who have 13 members. The MC has a South and a North representative from each of the 5 objectives and the Coordinator, Webmaster and the Financial Administrator of the coordinating institute. An Optional member can be invited for specific meetings e.g. technical advisor from SCI, WHO or governmental representatives when appropriate.

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CONTRAST successfully followed the timetable as set out in the project document (see Gantt diagram in **Appendix III**).

CONTRAST has worked in association with and complimented the findings of the EU INCO-DEV-2 supported project MUSTSchistUKEMA also coordinated from DBL and also with the Bill & Melinda Gates Foundation supported Schistosomiasis Control Initiative (SCI).

Appendix I: Final plan for using and disseminating knowledge

The management secretariat has created a structure for dissemination of the project results **(WP 22)**, which involves establishing a project website, a project logo and various publications promoting the project. The project website has helped to keep the project partners informed on the development in the project, and has enabled data to be uploaded as well as downloaded (e.g. claim forms and administrative protocols/regulations, DNA sequence and spatial epidemiological data).

CONTRAST follows the original PUDK guidelines.

CONTRAST logo

Immediately after inauguration of the project, a working group was established to create a logo for CONTRAST. The logo should display CONTRAST's geographical focus, and at the same time indicating that we are working for improved schistosomiasis control.

The logo created can be seen in the figure to the right. The curved 'O' symbolizes the snail transmitting schistosomiasis, and the African countries involved in CONTRAST are highlighted on the map.

At the same time the CONTRAST Executive Committee decided to incorporate a tagline to be displayed on CONTRAST publications and on the internet. The tagline is *'Towards control of schistosomiasis'*.

Figure 2. The CONTRAST logo

Open access database of schistosomiasis prevalence

CONTRAST have throught he work accomplished in WP14 established a unique georeferenced database on schistosomiasis prevalence throughout Africa. In September 2010, a scientific paper was submitted PLoS Neglected Tropical Diseases, describing the database, and the visions we have for it. The database can be found at www.globalntddatabase.org, where you can register for access to all data. The database currently features data on 10.000 individual schistosomiasis surveyed locations.

Figure 3. The logo-banner on the http://www.globalntddatabase.org website.

CONTRAST website

The project website was launched on 2 January 2007. The website has two levels of access; one open access for the general public and one restricted to partners and the European Commission (as well as those bodies with local relevance and any others appointed by the EU) restricting the only authorized users to inspect data which has to have restricted access for ethical reasons or is for reference and not corruptible.

The secretariat has regularly requested research project output material from partners to keep the website up to date such as unpublished field- or laboratory reports.

On the website to the left an automatic newsfeed updates the viewer with the latest news on schistosomiasis and neglected tropical diseases from WHO and TropIKA.

The website features a news section so that all partners are kept informed on progress being made within each scientific objective, and as the project as a whole moves forward. The website enables each partners to access the information from all the activities of the project, the European Commission to obtain regular updates of the progress of the project, and provide information to any interested audience.

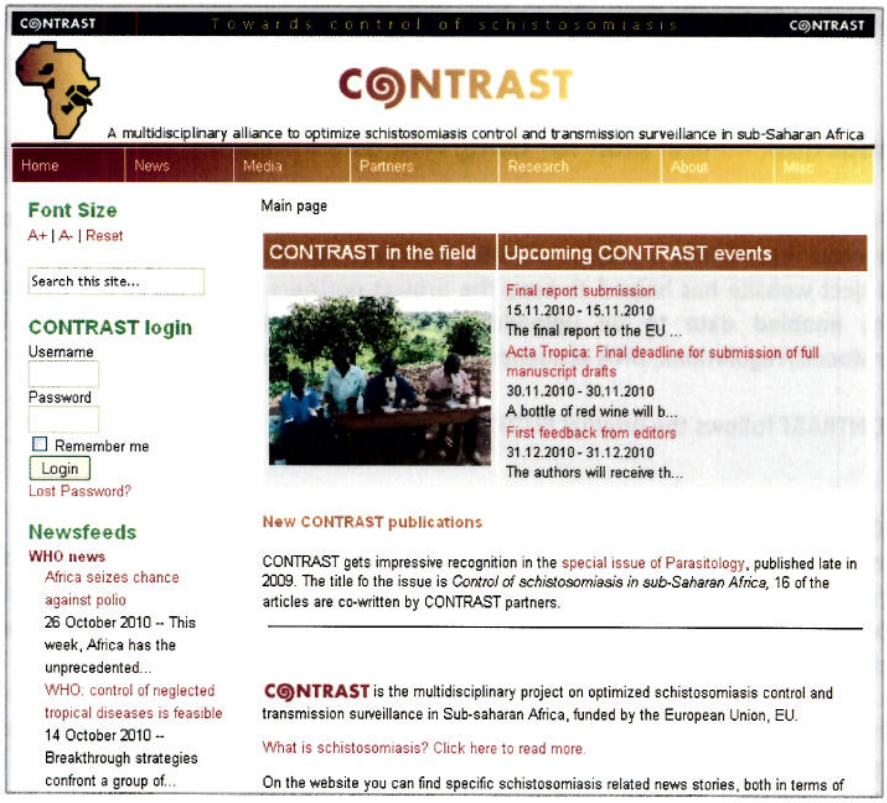


Figure 4. The fornt page of the CONTRAST website on 1 November 2010.

The website has educational materials such as images and video clips to enhance the public appeal **(WP 22)**.

The CONTRAST website has received over half a million hits during the three years it has been active. During the last 12 months there has been over 250.000 hits on the website. The project coordinator and the secretariat has agreed to continue supporting the website up to 2 years after the project ends.

Outreach

At the end of the project findings of this study will be fed back to members of the community in the district to facilitate discussions on the way forward in ensuring sustained schistosomiasis control. One dissemination workshop will be convened in the district to which members of the study community will be equally represented.

Community-owned Resource People, Staff from local health delivery facilities and other key district and regional officials are gong to be invited.

We will also hold one national stakeholders workshop to share our findings with officials from the Ministry of Health and Social Welfare (MOHSW), other relevant stakeholders such as members of CONTRAST

project, officials of the National Schistosomiasis and Soil-transmitted helminths Control Programme (NSSCP), officials of Schistosomiasis Control Initiative (SCI) and others to discuss ways of implementing study recommendations and come out with implementation strategies. Effective dissemination at both national and district levels will facilitate findings to be incorporated into NSSCP plans.

CONTRAST will organize a conference targeted at end-users and stakeholder in one of the African partner countries in 2011. Invited will be stakeholder and end-users in relation to schistosomiasis treatment and mass-drug administration. The findings in CONTRAST may very weel be able to lead to better local control solutions that are more sustainable. The strong research node network across sub-Saharan Africa are now able to establish innovative molecular tools to characterize both snails and schistosomes, define the importance of host-parasite dynamics across different ecological and epidemiological settings, develop new spatial models for disease risk maps and prediction, encourage and assess novel local control interventions using a social science approach and ensure widespread dispersal and access to information.

Appendix II: List of CONTRAST Work Packages, Deliverables and Milestones (and their deadlines)

WP1	**Establishment of a molecular research node in Africa**	**01/10/2006**	**30/09/2007**
D1	**Establishment of a well equipped laboratory facility capable of handling molecular analyses at internationally accepted standards**	**01/10/2006**	**01/10/2006**
wp1_m1	The enhanced physical facilities and initial information storage established in the laboratory	30/04/2007	30/04/2007
wp1_m2	A fully functional molecular research node	01/10/2007	30/09/2007
WP2	**Establishment of a resource database and biological reference collection research node**	**01/10/2006**	**30/09/2007**
D2	**Tangible facilities established for electronic and traditional database and collection at partner 7**	**01/10/2006**	**30/09/2007**
D3	**Database established and available on the WWW**	**01/10/2006**	**30/09/2007**
wp2_m1	The enhanced physical facilities to handle all present and future archival material requirements with except electronic accessibility	28/02/2007	28/02/2007
wp2_m2	A fully functional initial resource database and biological reference collection research node	01/10/2007	30/09/2007
WP3	**Development of DNA sequence barcoding nomenclature for characterization of schistosomes and snails**	**01/01/2007**	**30/09/2010**
D4	**Species specific DNA sequence barcodes for the schisto and intermediate host snails will be established 2 aid future molecular based id**	**01/01/2007**	**30/09/2010**
D5	**Dev of PCR assays for species id (RFLP and specific primers), less tech demanding to be implemented in laboratories with modest resources**	**01/01/2007**	**30/09/2010**
D6	**DNA and voucher specimen collections as a taxonomic resource for future reference will be established**	**01/01/2007**	**30/09/2010**
wp3_m1	Established preliminary classification system of DNA barcodes for Schistosoma, Biomphalaria and Bulinus	01/03/2008	29/02/2008
wp3_m2	Refinements of classification system for Biomphalaria and Bulinus as encountered from East and West Africa	30/09/2008	30/09/2008
wp3_m3	Establishment of comprehensive classification system for Schistosoma, development of lower technology assays and transfer to partner laboratories	01/03/2009	28/02/2009
wp3_m4	Establishment of comprehensive classification system for Biomphalaria and Bulinus, development of lower tech assays & transfer to partner labs	30/09/2010	30/09/2010
WP4	**Development of rapid SNaPshotTM DNA barcodes for multi loci sequence typing (MLST) for schistosome and snails**	**01/10/2007**	**30/09/2010**
D7	**A standardized SNaPshotTM protocol for rapid DNA barcoding of biological specimens and generation of electronic database in WP2**	**01/10/2007**	**29/09/2010**

wp4_m1	Development of initial assays for schistosomes and snails	01/03/2008	29/02/2008
wp4_m2	Application of standardized assays for Schistosoma spp	30/09/2008	30/09/2008
wp4_m3	Application of standardized assays for Bulinus spp. and Biomphalaria spp	01/03/2009	28/02/2009
wp4_m4	Finalization of SNaPshot database	30/09/2010	30/09/2010
WP5	**Detection, identification and quantification of schistosome DNA in snails by Real-Time PCR assays**	**01/10/2007**	**30/09/2010**
D8	**A standardized Real-Time PCR protocol for rapid detection of schisto DNA in aquatic snails leading to generation of info for electronic database**	**01/10/2007**	**30/03/2010**
wp5_m1	Validated Real-Time PCR assay using multiplexed TaqMan® probes for detection and identification of schisto DNA in biological spec in single tube format	30/04/2008	30/04/2008
wp5_m2	Generating data for WP 13,14,15,16 by identification of schistosome infected snail species	30/09/2008	30/09/2008
wp5_m3	Technology transfer to MU	30/09/2008	30/09/2008
wp5_m4	Generating of data for WP 20, 21 by assessing numbers of infected snails collected in study sites at both MU and NHM labs	30/09/2009	30/09/2009
wp5_m5	Completion of generation of data for WP 20, 21	30/09/2010	30/09/2010
WP6	**Use of oligochromatography: adaptation of Real-Time PCR assays to low technology laboratories**	**01/10/2008**	**30/09/2010**
D9	**Dev of oligochromatographic method for post-PCR detection of schisto DNA as an alternative, low tech format, to complement Real-Time PCR assays**	**01/10/2008**	**30/04/2010**
wp6_m1	Development of initial working protocol for oligochromatography of PCR amplified fragments	31/03/2009	31/03/2009
wp6_m2	Standardization of protocol for oligochromatography for detection of schistosome PCR amplified fragments	01/05/2010	30/04/2010
wp6_m3	Development of an assay commercially available from Coris Bioconcept	30/09/2010	30/09/2010
WP7	**Characterisation of the (microsatellites) population structure of Bulinus over space and time**	**01/01/2007**	**31/12/2009**
D10	**Development of suitable polymorphic microsatellite marker loci for Bulinus spp.**	**01/01/2007**	**31/12/2009**
D11	**Population genetic information for Bulinus across project working areas for WP14-17**	**01/01/2007**	**31/12/2009**
wp7_m1	Standardized protocol for amplification of DNA marker loci and initial assessment of population genetic variation	31/12/2007	31/12/2007
wp7_m2	Population genetic information for Bulinus from East Africa	31/12/2008	31/12/2008
wp7_m3	Analysis of population genetic parameters	31/12/2009	31/12/2009
WP8	**Charact of microsat. pop. struct. of S. mansoni paras. o. space & time in relat. to habitat, chemotherapeutic press., & human infect. & morb. lvl.**	**01/10/2006**	**30/09/2009**
D12	**Elucidation of the potential impact of mass chemotherapy on the population genetic structure of the parasite host**	**01/10/2006**	**30/09/2009**

	populations		
D13	**Identification of parasite genotypes and/or parasite genotype combination with potential of causing severe morbidity for targeted control**	**01/10/2006**	**30/09/2009**
wp8_m1	Standardized protocols for the collection of samples from the project areas (incl hatching, storage and multiplex PCR)	01/10/2006	31/03/2007
wp8_m2	Optimisation and processing of current Ugandan samples	01/12/2006	01/12/2006
wp8_m3	First CONTRAST sampling Uganda & any further training (tbc - Narcis)	31/01/2007	31/01/2007
wp8_m4	First CONTRAST sampling & field techniques training Niger (tbc - Amadou)	31/01/2007	31/01/2007
wp8_m5	Initial assessment of population of variation with S. mansoni	01/10/2007	30/09/2007
wp8_m6	Completion of first year field sampling	01/10/2007	30/09/2007
wp8_m7	Longitudinal sampling of schistosomes with regard to chemotherapy	31/12/2007	31/12/2007
wp8_m8	Longitudinal follow-up field samples (field teams & IC staff) and PCR analyses (IC)	01/10/2007	29/09/2008
wp8_m9	Completion of longitudinal sampling of schistosomes	30/09/2008	30/09/2008
wp8_m10	Completion of year-1 follow-up field sampling	30/09/2008	30/09/2008
wp8_m11	Analyses of data and peer reviews paper submission	30/09/2008	30/09/2009
wp8_m12	Completion of genetic analyses of schistosome material	30/09/2009	30/09/2009
wp8_m13	Completion (final revisions of publications)	30/09/2009	30/09/2009
WP9	**Establishment of a snail-parasite research node**	**01/10/2006**	**31/03/2008**
D14	**Fully functional host-parasite relationship research node established**	**01/10/2006**	**31/03/2008**
wp9_m1	The enhanced physical facilities to culture and maintain parasites and snails	01/10/2007	30/09/2007
wp9_m2	A fully functional initial resource database and biological reference collection research node	31/03/2008	31/03/2008
WP10	**Dynamics of transmission and interactions between schistosomes in sub-Saharan Africa**	**01/01/2007**	**31/12/2009**
D15	**Assembly of comprehensive core collection of biological specimens for selected project areas established**	**01/01/2007**	**31/12/2009**
D16	**Assimilation of comprehensive knowledge concerning natural population dynamics of schisto & snails in key transmission environments in E&W Africa**	**01/01/2007**	**31/12/2009**
wp10_m1	The initial collection of biological material from all study areas	01/07/2007	30/06/2007
wp10_m2	Commencement of longitudinal monitoring of dynamics of schistosomes	31/12/2007	31/12/2007
wp10_m3	Start of longitudinal following after chemotherapy	30/06/2008	30/06/2008
wp10_m4	Completion of first round of baseline longitudinal monitoring	01/03/2009	28/02/2009
wp10_m5	Final analysis of follow up data	31/12/2009	31/12/2009
WP11	**Role of the different species of intermediate hosts in the transmission of schistosomiasis in sub-Saharan Africa**	**01/01/2007**	**31/12/2009**
D17	**Deliver a precise understanding of the roles of intermediate**	**01/01/2007**	**31/12/2009**

	host spectrum of urinary and intestinal schistosomes in East and West Africa		
wp11_m1	Selection of key transmission environment for fieldwork	01/07/2007	30/06/2007
wp11_m2	Completion of initial baseline studies and reference collection assembled	01/10/2007	30/09/2007
wp11_m3	Initiation of longitudinal monitoring in selected site	31/12/2007	31/12/2007
wp11_m4	Completion of longitudinal monitoring at key sites	31/12/2009	31/12/2009
WP12	**To develop novel mathematical predictive models of schistosomiasis transmission under different selective pressures**	**01/10/2007**	**30/09/2010**
D18	**Provision of deterministic (and/or stochastic) mathematical models which incorporate genetic structure**	**01/10/2007**	**30/09/2010**
D19	**Validation of models against field collected data in Niger and Uganda**	**01/10/2007**	**30/09/2010**
wp12_m1	Collection of existing data from other WP8 (&10) and literature survey	31/12/2007	31/12/2007
wp12_m2	Development of initial (deterministic) model and preliminary evaluation	30/06/2008	30/06/2008
wp12_m3	Formulation of fully stochastic models for the investigation of transient dynamics of allele frequencies under selective pressures	31/03/2009	31/03/2009
wp12_m4	Evaluation of first year and longitudinal follow-up molecular data to the model	01/04/2009	31/03/2010
wp12_m5	Finalization of models	31/03/2010	31/03/2010
WP13	**To establish a GIS and spatial epidemiological research node**	**01/10/2006**	**30/09/2007**
D20	**Fully functional research node established at partner 6**	**01/10/2006**	**30/09/2007**
wp13_m1	Assessment and inventory of requirements necessary for schistosomiasis mapping needs finalized	01/01/2007	31/12/2006
wp13_m2	Procurement and installation of hard and software finalized	01/04/2007	31/03/2007
wp13_m3	Fully operational research node ready to receive data for risk mapping and prediction	01/10/2007	30/09/2007
WP14	**Creation of comprehensive GIS databases for selected study areas**	**01/03/2007**	**28/02/2009**
D21	**Comp. GIS databases, including demographic, environmental, malacological, parasitological and socio-economic data, for selected eco-zones of sub-S. Africa**	**01/03/2007**	**28/02/2009**
wp14_m1	Database of historical parasitological and snail survey data and gaps identified (i.e. non-sampled locations)	31/08/2007	31/08/2007
wp14_m2	Database of available demographic and socio-economic data and gaps identified (i.e. non-sampled locations)	29/02/2008	29/02/2008
wp14_m3	Database of climatic and environmental data	01/09/2008	31/08/2008
wp14_m4	Cross-sectional surveys completed and aforementioned data gaps filled	01/03/2009	28/02/2009
WP15	**Development of Bayesian spatial models for risk factor analysis and mapping of high-risk areas**	**01/03/2007**	**28/02/2009**

D22	**Epidemiologic risk factors for S. mansoni and/or S. haematobium infection**	**01/03/2007**	**28/02/2009**
D23	**Predictive risk maps of infection prevalence and intensity**	**01/03/2007**	**28/02/2009**
D24	**Validated spatial predictive models of schistosomiasis transmission in project study areas**	**01/03/2007**	**28/02/2009**
D25	**Innovative approaches developed for risk mapping and prediction of tropical parasitic diseases**	**01/03/2007**	**28/02/2009**
wp15_m1	Preliminary risk factors derived from non-spatial models for Lake Victoria basin	01/07/2007	30/06/2007
wp15_m2	Bayesian spatial predictive models for Lake Victoria basin	31/12/2007	31/12/2007
wp15_m3	Preliminary risk factors derived from non-spatial models for coastal East Africa zone	29/02/2008	29/02/2008
wp15_m4	Bayesian spatial predictive models for coastal East Africa zone	30/06/2008	30/06/2008
wp15_m5	Preliminary risk factors derived from non-spatial models for Cameroon, Niger and Senegal river basin	31/10/2008	31/10/2008
wp15_m6	Bayesian spatial predictive models for Cameroon, Niger and Senegal river basin	01/03/2009	28/02/2009
WP16	**Predicting infection risk in ecological zones similar to those of the study areas**	**01/06/2008**	**30/09/2010**
D26	**Climatic and statistical model based infection risk maps for schistosomiasis in different agro-ecological zones across sub-Saharan Africa**	**01/06/2008**	**30/09/2010**
wp16_m1	Preliminary risk factors derived from non-spatial models for agro zone corresponding to lake Victoria basin study area (zones A)	01/09/2008	31/08/2008
wp16_m2	Development of Bayesian spatial predictive models for zones A	02/03/2009	01/03/2009
wp16_m3	Smooth maps of zones A	01/06/2009	31/05/2009
wp16_m4	Preliminary risk factors derived from non-spatial models for agro zone corresponding to coastal East Africa study area (zones B)	31/07/2009	31/07/2009
wp16_m5	Bayesian spatial predictive models for zones B	01/11/2009	31/10/2009
wp16_m6	Smooth maps of zones B	31/12/2009	31/12/2009
wp16_m7	Preliminary risk factors derived from non-spatial models for agro zone corresponding to Cameroon, Niger and Senegal river basin study area (zones C)	01/03/2010	28/02/2010
wp16_m8	Bayesian spatial predictive models for zones C	01/08/2010	31/07/2010
wp16_m9	Smooth maps of zones C	30/09/2010	30/09/2010
WP17	**Construct integrated infection risk maps for schistosomiasis and other vector-borne diseases of socio-economic importance in sub-Saharan Africa**	**01/10/2008**	**30/09/2010**
D27	**Integrated risk maps on transmission of schistosomiasis and other relevant vector borne diseases developed**	**01/10/2008**	**30/09/2010**
D28	**Micro-geographic spatial variation within an existing demographic surveillance site (DSS)**	**01/10/2008**	**30/09/2010**
wp17_m1	Defined physical structure of an integrated database	31/03/2009	31/03/2009

wp17_m2	Functional integrated GIS database	30/09/2009	30/09/2009
wp17_m3	Developed integrated transmission risk maps	31/03/2010	31/03/2010
wp17_m4	Dissemination workshops held and hands-on orientations	31/05/2010	31/05/2010
wp17_m5	All risk maps available on the project web-site	30/09/2010	30/09/2010
WP18	**Establish a research node for integrated economic and social policy analyses**	**01/10/2006**	**30/09/2007**
D29	**Establishment of a fully functional research node for integrated economic and social policy analysis**	**01/10/2006**	**30/09/2007**
wp18_m1	Needs assessment	01/10/2006	31/12/2006
wp18_m2	Assessment of needs completed	01/01/2007	31/12/2006
wp18_m3	Purchase of material	01/01/2007	30/06/2007
wp18_m4	Training	28/02/2007	28/02/2007
wp18_m5	1-month economics training course	28/02/2007	28/02/2007
wp18_m6	1-week PHASE for core/TOTs	01/04/2007	31/03/2007
wp18_m7	The enhanced physical facilities established and training completed	01/07/2007	30/06/2007
wp18_m8	Refreshment of TOTs	01/10/2007	30/09/2007
wp18_m9	Establishment of functioning research node	01/10/2007	30/09/2007
WP19	**Knowledge, attitudes and practices towards schistosomiasis control, and dynamics of socio-economic status**	**01/10/2007**	**30/09/2010**
D30	**People's KAP towards schisto and local means of control at beginning of the project and two years after implementation of loc adapted schisto control intervention.**	**01/10/2007**	**30/09/2010**
D31	**Dynamics of people's soc-eco status over a 2-year period following schisto control intervention in two different eco-epidemiological settings**	**01/10/2007**	**30/09/2010**
wp19_m1	KAP 1 (People's Knowledge, Attitude and Practices)	01/10/2007	30/09/2007
wp19_m2	KAP 2	30/09/2008	30/09/2008
wp19_m3	KAP 3	30/09/2010	30/09/2010
wp19_m4	Socio-economy	01/10/2007	30/09/2010
wp19_m5	Water contact observations	01/10/2007	30/09/2010
wp19_m6	PHAST	01/01/2008	30/09/2008
wp19_m7	Process monitoring	01/01/2008	30/09/2008
wp19_m8	One study populations have been selected and data collection launched	30/09/2008	30/09/2008
wp19_m9	Baseline KAP carried out between months 9-12, first socio-economic and water contact patterns collected at month 12	01/12/2008	30/11/2008
wp19_m10	2nd KAP survey completed m 24. 2nd & 3rd soc-eco and water contact surveys completed m18 & 24. For detailed time see frame	30/09/2010	30/09/2010
WP20	**Evaluation of "Participatory Hygiene and Sanitation Transformation" (PHAST) approach**	**01/10/2007**	**30/09/2010**
D32	**Adapted and pre-tested PHAST manual readily available for deployment in selected study sites**	**01/10/2007**	**30/09/2010**

D33	**Efficacy and cost-effectiveness of PHAST approach examined in different eco-epidemiological settings**	**01/10/2007**	**30/09/2010**
wp20_m1	Adapted and pre-tested PHAST manual available.	31/12/2008	31/12/2008
wp20_m2	Trained personnel who will implement PHAST approach	31/03/2009	31/03/2009
wp20_m3	Community empowered to implement PHAST approach on a larger scale	30/06/2009	30/06/2009
wp20_m4	Efficacy and cost-effectiveness of PHAST assessed and cross-site comparison completed	30/09/2010	30/09/2010
WP21	**Role of snail biodiversity in management of schistosomiasis and use of refractory snails to block schistosome transmission for biological control**	**01/10/2007**	**30/09/2010**
D34	**Information on the distribution of intermediate and some non-intermediate host snails of human schistosomiasis at the selected study regions.**	**01/10/2007**	**30/09/2010**
D35	**Feasibility of use of refractory snails for biological control**	**01/10/2007**	**30/09/2010**
wp21_m1	Field study tools/equipment and personnel sourced	31/12/2007	31/12/2007
wp21_m2	Identification of study areas/sites established and aquaria	31/03/2008	31/03/2008
wp21_m3	Initial data on intermediate host snails interactions with targeted snails for biological control	31/03/2009	31/03/2009
wp21_m4	Initial data on feasibility of selected non-intermediate host snails as decoys of miracidia	01/06/2009	31/05/2009
wp21_m5	Study progress report, more malacological survey data, collection material & database including...	30/09/2010	30/09/2010
wp21_m6	...information on intermediate host snails interactions with targeted snails for biological control as well as decoy effect	30/09/2010	30/09/2010
WP22	**Outreach and dissemination of knowledge**	**01/10/2006**	**30/09/2010**
D36	**Establishment of the project website, including the project presentation and admittance to data for partners and EU**	**01/10/2006**	**30/09/2010**
D37	**Online MySQL database at partner 1, containing all sample data, and which should be accessible for all CONTRAST**	**01/10/2006**	**30/09/2010**
D38	**Media awareness events for the public and decision makers in each of the involved endemic countries**	**01/10/2006**	**30/09/2010**
D39	**Updates and electronic uploads of project results & key findings in appropriate format for potential end-users and decision-making bodies**	**01/10/2006**	**30/09/2010**
D40	**Publication of results in scientific peer-reviewed international literature and review articles in the general press**	**01/10/2006**	**30/09/2010**
wp22_m1	Project website online, including project presentation	01/04/2007	31/03/2007
wp22_m2	Detailed plan for use and dissemination of knowledge to use throughout the project	01/07/2007	30/06/2007
wp22_m3	Special sessions of dissemination for representative stakeholders, NGOs and general public within the annual meeting	01/10/2007	30/09/2007
wp22_m4	Special sessions of dissemination for representative stakeholders, NGOs and general public within the annual meeting	30/09/2008	30/09/2008

wp22_m5	Special sessions of dissemination for representative stakeholders, NGOs and general public within the annual meeting	30/09/2009	30/09/2009
wp22_m6	Conference presenting, results revealed and tools developed for all potential end-users including decision makers	30/09/2010	30/09/2010
WP23	**Alliance management and project review and assessment**	**01/10/2006**	**30/09/2010**
D41	**Effective coordination and control of day to day running of the project (Incl. workshop planning)**	**01/10/2006**	**30/09/2010**
D42	**Optimized communication (Exchange of information)**	**01/10/2006**	**30/09/2010**
D43	**Facilitation of EU progress reporting**	**01/10/2006**	**30/09/2010**
D44	**Facilitation of partner information**	**01/10/2006**	**30/09/2010**
D45	**Qualified general administration and accounting procedures**	**01/10/2006**	**30/09/2010**
D46	**Delivering of continuous financial management and administration during the project**	**01/10/2006**	**30/09/2010**
D47	**Delivering of final administration and audit report at the end of the project**	**01/10/2006**	**30/09/2010**
wp23_m1	Org of start up workshop for the alliance & detailed methodological protocols for all work packages and their compilation	31/10/2006	31/10/2006
wp23_m2	Project management committee meeting and progress report. Interim financial reporting	01/04/2007	31/03/2007
wp23_m3	General project meeting and annual report. EU reporting period 1 - Annual financial and audit report	01/10/2007	30/09/2007
wp23_m4	Project management meeting and progress report. Interim financial reporting	31/03/2008	31/03/2008
wp23_m5	General project meeting and annual report. EU reporting period 2 - Annual financial and audit report	30/09/2008	30/09/2008
wp23_m6	Project management meeting and progress report. Interim financial reporting	31/03/2009	31/03/2009
wp23_m7	General project meeting and annual report. EU reporting period 3 - Annual financial and audit report	30/09/2009	30/09/2009
wp23_m8	Project management meeting and progress report. Interim financial reporting	31/03/2010	31/03/2010
wp23_m9	Final general project meeting and final report. Annual financial and audit report	30/09/2010	30/09/2010

Appendix III: Work plan list, Gantt diagram of activities.

Obj.	Work package	Year 1				Year 2				Year 3				Year 4			
1	WP 1																
1	WP 2																
1	WP 3																
1	WP 4																
1	WP 5																
1	WP 6																
1	WP 7																
1	WP 8																
2	WP 9																
2	WP 10																
2	WP 11																
2	WP 12																
3	WP 13																
3	WP 14																
3	WP 15																
3	WP 16																
3	WP 17																
4	WP 18																
4	WP 19																
4	WP 20																
4	WP 21																
5	WP 22																
	WP 23																

Appendix IV: Field Reports

CONTRAST: A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa

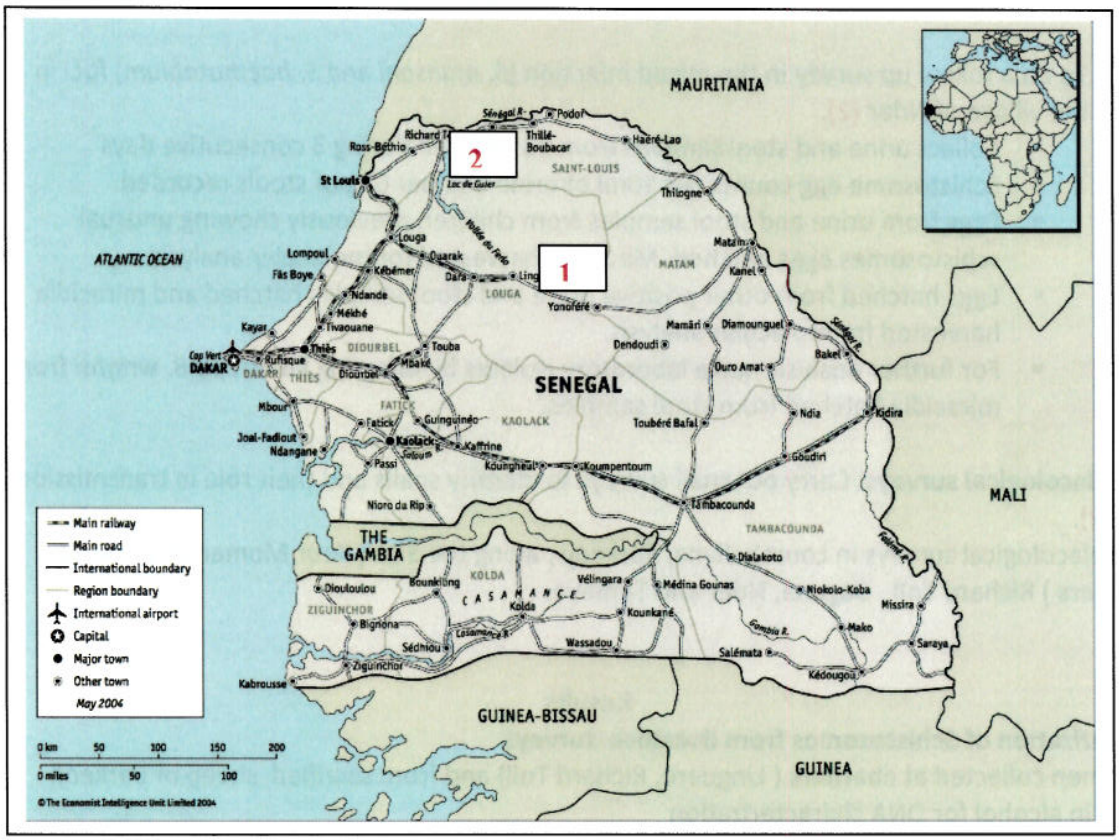
1) ISRA & NHM (Senegal Field Mission Jan 26th TO Feb 05th 2010)

- CHARACTERIZATION OF SCHISTOSOMES AND SNAILS IN A SAHELIAN AREA OF FERLO (Barkedj) AND SRB (Nder)

- BIOLOGICAL CONTROL OF SNAILS USING PRAWNS IN THE SRB

People involved

Dr Oumar Talla Diaw and Mr Mouhamadane Seye from ISRA.
Djibril Sarr Faye a PhD Student Senegal
Dr David Rollinson from NHM &Dr.Sanna Sokolw from University of Californie
Drivers: Ousseynou Diagne and Lamine Cisse from ISRA.



Places visited

1 : Sahalian Ferlo area : Linguere- Barkedji-Loumbellana

2 : SRB , Richard Toll , Dagana,Lac de Guiers, Nder

Objectives

Livestock parasitological surveys (cows, sheep and goats) (1)

- Visit abattoirs to identify schistosome infections and investigate inter species interactions involving, *S. bovis, S. curassoni* and *S. haematobium*.(Linguere, Barkedji, Richard Toll)
- Identification of schistosomes by morphology and DNA analysis.
- Observation of livers to detect eggs and by crushing to obtain miracidia (Linguere, Richard Toll)
- Sacrifice of 3 sheep suspected to be infected by S.curassoni (Barkedji)

Human parasitological surveys (1, 2)

- To identify children with potential *S. haematobium* infections and collect urine samples (1). Prevalence of infections recorded.(Barkedji 67 school children
  Use of Heamastix test, CCA test and urine filtration
  - Eggs from urine samples hatched and miracidia harvested for molecular analysis.
- To identify children with potential *S. haematobium* and or *S. mansoni* infections and collect urine and stool samples (2). Prevalence of infections recorded.
  - Eggs from urine samples hatched and miracidia harvested for molecular analysis.
  - Make laboratory isolates for further analysis by infecting lab breed *B. wrighti.*
  - Eggs from stool samples hatched and miracidia harvested for molecular analysis.

- To do a follow up survey in the mixed infection (*S. mansoni* and *S. haematobium*) foci in the village of Nder (2).
  - Collect urine and stool samples from 53 children during 3 consecutive days
  - Schistosome egg counts per 10ml of urine and per 01g of stools recorded.
  - Eggs from urine and stool samples from children previously showing unusual schistosomes eggs hatched. Miracidia harvested for molecular analysis.
  - Eggs hatched from other positive urine and stool samples hatched and miracidia harvested for molecular analysis.
  - For further analysis make laboratory isolates by infecting lab breed *B. wrighti* from miracidia hatched from stool samples.

Malacological surveys: Carry out snail surveys to identify snails and their role in transmission (1,2).

Malacological surveys in Loumbellana, Barkedji , along the SRB (Keur Momar Sarr, Lac de Guiers) Richard Toll , Dagana, Nder and Temeye.

Results

□ **Characterization of Schistosomes from livestock surveys**

The specimen collected at abattoirs (Linguere, Richard Toll) and from sacrified sheep of Barkedji were fixed in alcohol for DNA characterization

From collected eggs by crushing of livers of sheep, miracidia were fixed for further characterization .Studies underway at the NHM

□ **Human Parasitological surveys**

In the 2 schools visited in Barkedji the prevalences were:

- School of Bamol Sow : 46,7% Schistosoma haematobium
- School of Montagne : 83,7% Schistosoma haematobium

Tablets of PZQ were given to the school authorities and Health responsible in order to treat all the children investigated for diagnostic

Concerning the follow up in Nder the fixed miracidium are under investigation and the results from CCA test are analysed

□ **Malacological surveys**

During this period of survey there are few ponds and the abundance of snails was very low

INVESTIGATION ON BIOLOGICAL CONTROL OF SNAILS USING PRAWNS

By Sanna Sakolow

This mission on schistosomiasis was coupled by this investigation on the biological control of snails using prawns particularly Macrobrachium vollhonevenii . Dr Sanna Sokolow from University of California is studying the feasibility of this control.

The goal of this proposed research was to collect descriptive data on the current and historical abundance and spatial distribution of prawns in the SRB particularly in the estuarine ecosystem both upstream and downstream of the Diama Dam.

In 2007 a previous field mission had been done along the SRB by researchers of California University and a team of Senegalese Scientists to investigate the feasibility of a biological control of schistosomiasis using prawns. Specimen of Macrobrachim (04) were collected near Dagana .Three years after a second mission from University of California reinvestigates on this subject.

So some investigations on the existence of this prawn in the SRB (now and before the Diama Dam) were done among people of the SRB. The populations particularly fishermen were very interested and gave good informations about the localities and period of presence of this Macrobrachium. It is known in the delta particularly during the rainy season.

More informations were given by some structures of fishing and all these data collected will be analysed for further investigations: breeding prawns, testing their integration in natural pond and impact on snails population !!

Dr Sanna had used our expertise on transmission and particularly dynamics of snails (distribution, abundance, epidemiological role, etc) .The team will be involved if the project is accepted

TRIP IN NIGER FROM June 30th To July 14th COLLABORATION INTER TEAMS: ISRA –PNLB/NIGER AND NHM

People involved

VISITORS:

Dr Oumar Talla Diaw & Mr Mouhamadane Seye from ISRA.
Dr David Rollinson from NHM

PNLB/Niger, RISEAL:

Dr. Amadou Garba (Team leader of Niger CONTRAST, Coordinator of RISEAL)
Dr. Alfari Aichatou DJIBO (Coordinator of Schisto Control Niger)
Dr. Ali DJIBO (CHU University of Niamey)
Dr. Nouhou BARKIRE (University Abdou Mouminy of Niamey) Dr. Mariama Lamine (RISEAL), Mr. Rabiou LABBO (CERMES, RISEAL), Mrs. Yacouba HANNATOU (RISEAL), Mr. Adamou GARBA (RISEAL)

ISRA and PNLB/Niger are all involved in workpackages 10 and 11 and the principal objective of this mission was to exchange and compare the results of their activities and to have a better understanding of the dynamics of schistosomes and the re-infestation and impact of PZQ .
During a general meeting the agenda of the visit had been fixed after exchanges and discussions. It has been planed field visits, laboratory visits and meetings.

□ **–Results of CONTRAST: Workpackage 10 & 11**

The PNLB/Niger and ISRA presented their results of Workpackage 10 & 11 .It was the same protocol with more villages in Niger and in Senegal a second treatment has been done due to a high level of re-infestation after 6 months. But the pattern was the same and PZQ is more active on *S.haematobium* than on *S.mansoni*

□- **Livestock parasitological surveys (cows, sheep and goats). Interaction of schistosomes (S.bovis / S.curassoni / S.haematobium)**

(David Rollinson, Oumar Talla Diaw, Barkire Nouhou, Rabiou Labbo, Mohmoudane M.Seye, Adamou Garba)

In order to investigate on the relation of human and animal schistosomes, some surveys have been done on the abattoirs. Visit of abattoirs to identify schistosome infections and investigate inter species interactions involving, *S. bovis, S. curassoni* and *S. haematobium*

- Abattoirs of Kobague (situated at 55 Km from Niamey) :
23 cows observed: 4+ with Schistosoma sp
15 sheep and 6 goats observed: 0 + schistosoma sp
- Abattoirs of Niamey: here due to the high number of animal and the climate, animals are slaughtered from 11 PM to 06 AM
- 20 cows observed: 02 + with Schistosoma sp

-10 sheep observed: 01 + with schistosoma sp
- 05 camels observed: 0 + with schistosoma sp
Some fragments of liver from cows and sheep have been taken to try to get eggs of schistosomes (crushing method)
Some parasites are identified as S.bovis and are fixed on alcohol for DNA analyses (NHM)

□- **Malacological surveys:**
(David Rollinson, Oumar Talla Diaw, Barkire Nouhou, Rabiou Labbo, Mohmoudane M.Seye, Adamou Garba)
Some malacological surveys have been done to investigate dynamics of snails in CONTRAST sites (abundance, species and their infestation, etc).

- Sites in the Est. of Niamey :

Zama Kuara and Siberi (6 water contact sites)
Lebore : only sites n° 6, 8, 9 have been visited
Only Bulinus globosus, B. truncatus, B. forskalii, B.senegalensis have been collected

- Sites in the North of Niamey (04 localities visited):

Tilabery ,Diambala,Namari goungou and Bonfeba
Some snails were collected, identified and their infestation tested. (Bulinus globosus, B. truncatus, B. forskalii, B.senegalensis and Biomphalaria pfeifferi).

□- **Human parasitological surveys**
(David Rollinson, Oumar Talla Diaw, Barkire Nouhou, Rabiou Labbo, Mohmoudane M.Seye, Adamou Garba)
An experimental therapy with PZQ in syrup is running at Tilabery and Bonfeba with children from 0 to 5 years old. It has been observed that this portion of people were not involved during treatment due to difficulty of taking PZQ in tablets .It is the first test of PZQ in syrup and many children were involved . The first results are very interesting and ameliorate the control because more people particularly these children were involved and PZQ in syrup more practice

□- **Visite of LABCEL (Laboratoire Central Elevage du Niger)**
This visit has been done by ISRA team in order to have contact with this structure, to exchange and reinforce collaboration.

□ **CONCLUSION**
This visit was very benefit for all parties of the CONTRAST family. It was also a recess of our South – South collaboration. We have also discussed about the final meeting and what collaboration after CONTRAST (to share data and expertise on schistosomiasis, to organize training in Parasitology and malacology, etc)