For schistosomiasis the paradigm has shifted from morbidity control to elimination as a public health problem. There is thus a global push for all endemic countries to increase control efforts and move towards elimination. The first conference of the Global Schistosomiasis Alliance (GSA) Research Working Group, held in mid-June 2016 in Shanghai, reviewed current progress in schistosomiasis control and elimination, identified pressing operational research gaps that need to be addressed and discussed new tools and strategies required to make elimination a reality.

I. Status Quo and Facts

- There is historic evidence that schistosomiasis elimination is feasible; key features where this has been achieved are strong political will, a paradigm shift from morbidity control to interruption of transmission, and an integrated, cross-sectoral approach that is tailored to social-ecological systems and transmission pattern, especially in high transmission hot spots.

- Geostatistical mapping is an innovative tool to help estimate infection risk across sub-Saharan Africa where there is a need to intensify efforts and to more accurately estimate the annual number of doses of praziquantel needed.

- With the increase of the praziquantel donation from Merck to up to 250 million tablets annually more countries than ever are implementing preventive chemotherapy.

- Additional treatment choices with new mechanisms of action are needed due to risk of drug resistance towards praziquantel. A revised formulation of oxamniquine (activity currently restricted to *Schistosoma mansoni*), for instance, could become a new effective drug also against *Schistosoma haematobium*, which in turn might also be combined with praziquantel.

- Innovative xeno-monitoring tools hold promise for schistosomiasis (and other neglected tropical diseases) as a tool to monitor transmission in elimination programmes.

- There is a need for new cut-offs/thresholds to be decided upon in regard to prevalence, as determined in low endemicity areas by the use of the point-of-care circulating cathodic antigen (POC-CCA) urine cassette test for *S. mansoni* diagnosis.

- In addition, a new diagnostic tool to support control programmes leading to and evaluating transmission interruption or even elimination of schistosomiasis could become available at large scale in the form of an up-converting phosphor (UCP)-lateral flow circulating anodic antigen (CAA) assay provided support for wide-scale implementation or commercialisation is coming forth.

- A paediatric formulation of praziquantel will be available by 2019 for a target population of approximately 28 million preschool-aged children (<6 years) in sub-Saharan Africa. Access and use of such formulation on a large scale needs to be determined and requires engagement of the global schistosomiasis community.

http://www.eliminateschisto.org/
II. Uncertainties and Unknowns

Unknowns / Uncertainties

- It is currently not clear what the official World Health Organization (WHO) treatment data reflect; school-aged children (SAC) and adults or SAC only. The Merck Praziquantel Donation Programme has a focus on treating SAC in sub-Saharan Africa.
- There is uncertainty regarding the current principal age target population. The WHO Road Map in 2012 set the target to reach with regular treatment by 2020 at least 75% of the SAC population at risk in endemic areas. WHO should define new goals and target populations such as preschool-aged children and adults beyond 2020 for achieving transmission control and elimination in consultation with the schistosomiasis community.
- It is not clear for certain areas where hot spots of schistosomiasis are concentrated.
- In some high transmission hotspots, control efforts alone cannot reduce prevalence and intensity of infection (especially in Lakes Victoria and Albert) - transmission control in such settings needs thorough investigation in order to move towards elimination.
- The role of reservoir hosts (e.g. dogs and rodents) in addition to bovines in the People’s Republic of China and the Philippines in areas where transmission control is challenging needs to be clarified.
- The dynamics of female genital schistosomiasis (FGS) need to be investigated - to prevent irreversible pathology associated with FGS it appears that treatment needs to be given early in life. The dynamics between FGS and HIV also infection require further research.
- Globalisation and climate change play an increasingly important role in spreading schistosomiasis to previously schistosomiasis-free countries and regions, such as recent reports from Corsica in Europe.

The Main Gaps Identified Are:

- Revised strategy according to recent results from the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) going beyond preventive chemotherapy.
- Drug availability (amount of medication, correct distribution, etc.).
- Coverage data / mapping, especially. at the more local level to understand, amongst others, local transmission sites.
- Insufficient surveillance work and risk assessment.
- Lack of real schistosomiasis-specific WASH activities (consider cost-effectiveness with regards to other preventable diseases/malnutrition etc.).
- Need of new molluscicides and transmission control in terms of snail control.
- Knowledge and skills of social scientists to introduce behaviour change to reduce water contact and contamination.
- Lack of methodologies to define interruption of transmission as well as updated protocols for drug-efficacy monitoring.
- Non-enrolled SAC are not reached or not reached regularly and may represent the most important reservoir of transmission.
III. Call to Action

A number of issues were raised by the group that require action by the schistosomiasis community at large, the research community and the GSA. These actions address different aspects of schistosomiasis, which are split below in the following topics: (i) research; (ii) advocacy; (iii) support; and (iv) general issues. No deadlines have been set by which to address these topics; however, it was the overall aim of delegates at the conference to jointly focus existing and new efforts in a timely manner.

Research

We need to:

- Increase data collection, mapping and intervention trials for high transmission hotspots to better understand transmission dynamics (requires improved morbidity measures and intensity measures based on newer improved diagnostics for transmission control towards elimination).
- Get better understanding of the biology of schistosomes in order to rationalize drug development, e.g. repositioning of kinase inhibitors such as Imatinib.
- New -omics and screening technologies have the potential to advance the schistosomiasis research field with respect to a better understanding of schistosomiasis biology, the discovery of new markers (potential use as diagnostics and vaccine development), drug targets and new drugs.
- Explore biological control and habitat modification as natural snail control options in the African setting.
- Add intermediate host snail distributions to improve schistosomiasis risk profiling and employ GNTD in the process.
- Vaccine development needs to be brought to the forefront again.

Advocacy

Concrete steps to be taken include:

- Taking the feedback and input etc. from this conference and working towards the WHO working group meeting.
- Ensuring international and especially national commitment to elimination programmes beyond reaching the 2020 road map target.
- Promoting the use of praziquantel during lactation and pregnancy as standard management in all maternal and child clinics in endemic areas according to WHO recommendations.
- Develop training programmes for doctors and other field researchers to make them aware of problems they may not know about (e.g. FGS).
- GSA to help promote WHO FGS Pocket Atlas.
- Raise awareness of schistosomiasis via e-learning tools/modules, which are increasingly used and available (e.g. combine schistosomiasis with other subjects, such as soil-transmitted helminthiasis and neglected tropical diseases more broadly).
  o Jutta Reinhard-Rupp (Merck) is already in contact with providers of such tools.
- Determining how to present schistosomiasis at the 5th anniversary of Uniting to Combat Scorecard.
- Updating the research milestones of the UTC scorecard with the help of this research group. GSA will support and enable this process just as with the reworking of the programme milestones.

Support from the GSA

- GSA is encouraged to initiate the development of a database where information, including field data such as screening results, can be shared, is regularly updated as well as used, and make this known and accessible to everyone.
  - As a next step, an app could be developed that allows the transfer of data by smartphone and the looking up of actual data as an alternative to Laptop/PC.
- GSA should provide treatment information, and the Patient Information Leaflet of praziquantel on its website for easy access.

General

Conference participants agreed on:

- The development of updated guidelines.
  - It is recommended that WHO policies be upgraded and geared to meet the challenges of elimination of schistosomiasis / have differentiated guidelines for morbidity control and elimination.
  - Measurable recommendations for WASH and behaviour change are needed.
  - Need for specific recommendations for snail control and the management of hotspots.
  - GSA to support committees to develop such draft guidelines, using the information and knowledge present at the conference / in the research field.
- Reinforcing the case for snail control, especially in hot spots, and in areas where the intermediate host is present even without transmission in view of permanent transmission control and elimination.
  - Requires: capacity building in countries for snail mapping and control.

Summary

The central outcome of this 2-day international meeting was an agreement on the need to better tailor preventive chemotherapy and to include other public health measures especially in high transmission areas if transmission control and elimination are to be achieved. The substantial increase of praziquantel supply based on the perceived need for adult treatment plus the potential lowering of thresholds for mass drug administration will be difficult to achieve before the first schistosomiasis deadline of 2020. An increased use of praziquantel may further raise selective pressure on the parasite, heightening the risk of drug resistance. This in turn demands for other public health approaches, including other drugs and combination therapy, examples of which are outlined above. A number of concrete action points were raised that now require timely attention by all partners of the schistosomiasis community.