

## **Informal Consultation on Expanding Schistosomiasis Control in Africa**



**Geneva, Switzerland, 26 January 2010**

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## **List of Acronyms**

API	Active Pharmaceutical Ingredient
ADG	Assistant to Director General of the World Health Organization
BMGF	Bill and Melinda Gates Foundation
CMSC	Coordination mechanism for schistosomiasis control
CPS	Contracting and Procurement Service
DfID	Department for International Development
EMRO	Eater Mediterranean Regional Office
IDA	International Dispensary Association
MDG	Millennium Development Goal
NTD	Neglected Tropical Diseases
QSM	Quality and Safety: Medicines
PZQ	Praziquantel
RTI	Research Triangle International
SCH	Schistosomiasis
SCI	Schistosomiasis Control Initiative
STAG	Strategic Technical Advisory Board
UN	United Nations
USAID	United States Agency for International Development
WHO	World Health Organization

## **1. Introduction**

The meeting was opened by Dr H. Nakatani, Assistant to the Director General (“ADG”), HIV/AIDS, TB, Malaria and Neglected Tropical Diseases.

Dr L. Savioli, Director of the World Health Organization Neglected Tropical Disease department (“WHO/NTD”) chaired the meeting. Dr Wendy Harrison (Schistosomiasis Control initiative (“SCI”), Imperial College) was rapporteur assisted by Dr Lester Chitsulo and Ms Munjoo Park (WHO/NTD).

## **2. Consultation objectives**

The aim of the informal consultation was to discuss the needs of schistosomiasis (“SCH”) control, especially, a coordinated effort to increase access to praziquantel (“PZQ”). Recognizing that SCH is a major public health problem particularly in Africa and Middle East and access to PZQ is the key issue for scaling up control of SCH, the objectives of the informal consultations are shared with participants as follow:

- to review the global status of schistosomiasis control and PZQ needs
- to analyse funding availability for PZQ procurement
- to address market failure of PZQ to identify a sustainable solution for PZQ supply
- to anticipate issues for quality assurance of PZQ
- to develop a purpose-specific coordination mechanism for the procurement and provision of PZQ for the expansion of preventive chemotherapy coverage which will optimize the use of available resources, and result in a significant reduction in SCH morbidity and transmission in the endemic countries

## **3. Definition and scope**

In 2001, WHO Member States *established*<sup>1</sup> the goal for the control of schistosomiasis (SCH) *of attaining a minimum target of regular administration of chemotherapy to at least 75% and up to 100% of all school-age children at risk of morbidity by 2010*”. They have also indicated that WHO approach to combating SCH should include *“advocating new partnerships with organizations of the United Nations system, bilateral agencies, nongovernmental organizations and the private sector, and by continuing to provide international direction and coordination”*. January 2010 estimates indicate that less than 10% of the population at risk of morbidity receives praziquantel (PZQ) preventive chemotherapy and that the coverage goal established in 2001 is far from being achieved.

There is insufficient knowledge as to how much PZQ is procured by endemic countries out-side of externally funded public health programmes. It may be that sporadic, uncoordinated and often

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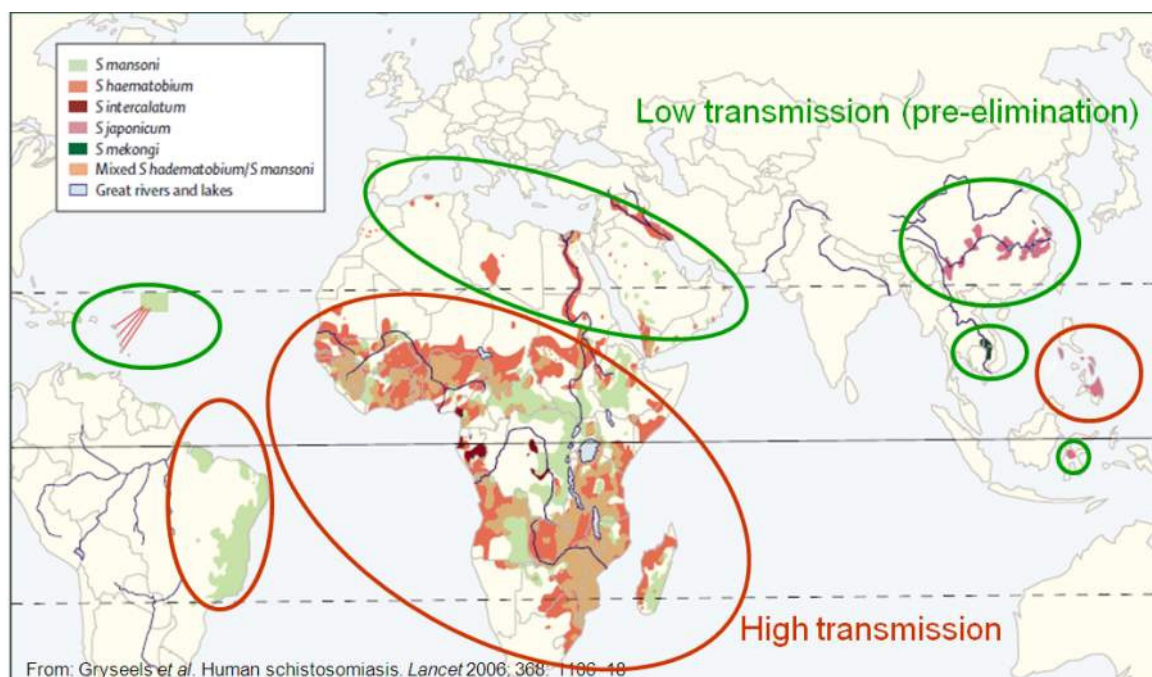
<sup>1</sup> Resolution WHA54.19, 22 May 2001

inconsistent strategies for the procurement of NTD medicines led to delays, medicines of questionable quality and high prices. This may have been the case of PZQ. Recently, the UK and US governments have decided to significantly increase their contribution to Neglected Tropical Diseases (NTD) elimination and control, including programmes based on preventive chemotherapy. This is expected to further increase the demand for PZQ, involving both the API and the finished drug product. Examination of market capacity to supply this demand and how resources can be most optimally allocated is therefore timely and essential to ensure the goal of significantly reducing SCH morbidity and transmission in the endemic countries is achieved.

#### **4. Discussion of strategic objectives of informal consultation**

##### **4.1 Global Status of SCH control and PZQ needs <sup>2</sup>**

Progress towards the sustainable control of schistosomiasis has been made in many endemic regions and most recently a major effort for schistosomiasis treatment is under way in Yemen. While more than 90% of people with schistosomiasis are in the WHO African region and there is a need for scaling up schistosomiasis control in this region, there is also need for scaling up control in the Philippines, Somalia, and Sudan (North and South).



**Figure 1:** Global distribution of schistosomiasis

Approximately 240 million people were estimated to be infected with schistosomiasis in 2008, according to data reported to the WHO only 17.5 million were treated<sup>3</sup>. Of those treated, 33% were in 8 countries outside of the African region, mostly in China, Egypt and Yemen. A total of 11.6 million people were

<sup>2</sup> Presentation given by Dr L. Chitsulo WHO/NTD

<sup>3</sup> A better and more understandable number of those eligible for preventive chemotherapy for schistosomiasis needs to be determined.

treated for schistosomiasis in 8 countries in the African region, accounting for 67% of all those treated globally. Except for Madagascar and Nigeria, all the reported schistosomiasis treatment campaigns in the African region had been initiated or associated with the Schistosomiasis Control Initiative (SCI). The 10 most endemic countries in sub-Saharan Africa account for 62% of the estimated global total of infected cases. Only 3 (Ghana, Madagascar, and Nigeria) of these had national treatment programmes. Data reported for schistosomiasis treatment in Africa by mid 2009 showed that there would be a significant increase in the number of people treated over the previous year. Some of this increase is due to the PZQ donation of Merck Serono through the WHO.

<b>Table 1 : Schistosomiasis estimated infected and populations treated in 2008 as reported to WHO/NTD</b>				
<b>Region</b>	<b>Estimated infected population</b>	<b>Estimated population at risk of infection</b>	<b>Population received treatment</b>	<b>Proportion of estimated infected population treated % *</b>
African	214,216,248	582,062,770	11,700,618	5.5
European	745	76,947	0	0
Eastern Mediterranean	14,038,111	106,638,907	2,665,029	19.0
Americas	7,138,100	51,066,739	65,335	1.0
South-East Asian	242	11,717	0	0
Western Pacific	1,332,264	20,797,325	3,069,475	>100
<b>Global</b>	<b>236,725,709</b>	<b>760,654,405</b>	<b>17,500,475</b>	<b>7.4</b>

\* Proportion of the number treated in the region compared to number estimated to be infected in the region

The major factor hindering schistosomiasis treatment continues to be the availability of in-kind PZQ donations from industry and finance with which to purchase. In the WHO/NTD business plan – Procurement of essential medicines for the expansion of preventive chemotherapy for neglected tropical disease, 2008 - it had been planned to scale up schistosomiasis treatment to 69 million (30% of those estimated to be infected) in 2009. This would have required 171 million PZQ tablets. Due to limited financing, only 50 million PZQ tablets were procured for the public sector in sub-Saharan Africa in 2009, through USAID/RTI funding and the Merck Serono donation. Thus for 2009, there was a gap of 121 million PZQ tablets. The NTD business plan projected PZQ need rising from 286 million in 2010 to 571 million tablets in 2013.

Even though scale up of schistosomiasis treatment will require increased donor funds with which to purchase PZQ, experience from countries that have successfully controlled schistosomiasis shows that the amount of PZQ required stabilizes after a few years of preventive chemotherapy, and gradually declines. Data from Egypt on schistosomiasis control show that with the use of mass treatment without individual diagnosis, the number of treatments for schistosomiasis was reduced from 9.9 million in 1997 to 1.8 million in 2007. In Burkina Faso, high treatment coverage of the target population with a single PZQ treatment resulted in an epidemiological impact where retreatment within two years would not be required for most of the country, except for high transmission foci. Thus while, the amount of PZQ required would be significant at the beginning of scale up, this demand for PZQ would not be open-ended, but would be reviewed in each endemic setting, after a few years of high coverage implementation. WHO East Mediterranean Regional Office (“EMRO”) intended to replicate the experiences and successes achieved in Egypt to Yemen, Sudan and Somalia.

## **4.2 Funding availability for PZQ<sup>4</sup>**

If there is to be investment in quality production of PZQ active pharmaceutical ingredient (“API”) and finished product, manufacturers need to be assured that there is an adequate market to support such investment. Therefore, in order to increase the probability of engaging manufacturers, UK Department of International Development (“DfID”), commissioned a study to make public a reliable estimate of likely demand, based on known donor financing<sup>5</sup> (see annex 3).

Analysis of the known donor financing for PZQ procurement and supply identified the United States Agency for International Development (“USAID”), DfID and Merck Serono as the major potential donors with some additional contributions from private donors and the World Bank (“WB”). Other than Egypt, Brazil and China, governments do not generally fund their own PZQ for public health use.

There was confirmation of USAID's increased interest on NTDs with USD\$ 65 million per year pledged for U.S. Fiscal year 2010 for NTD control. USAID support for NTD control is expected to continue from 2011 - 2014, however it should be noted that US funds are appropriated on an annual basis and subject to approval by the US Congress each year. Based on the current USAID NTD programme and assuming current global funding sources for drugs, it is estimated that the proportion of funding that will be allocated to ensuring an adequate drug supply will likely be 15% - 20% of the overall USAID's NTD Initiative. Based on the FY2010 budget level of \$65 million it is estimated that approximately \$9.75 - \$13 million will be allocated to drug supply. Praziquantel will likely comprise the majority of this expenditure. Assuming 85% of drug supply expenditures would go towards PZQ purchase, between \$8.29 and \$11 million USD annually would be available for PZQ purchase, equating to 104 and 138 million tablets annually. USAID's fiscal year 2010 funding of \$65 million will likely become available in October 2010. Therefore 2010 procurement levels – estimated below and marked with an asterisk - have been adjusted and represent only a slight increase on current procurement levels. USAID support is based on need, therefore the level of funding for PZQ will vary based on epidemiology and funding gaps.

For the same time period, 2010-2014, DfID, has also pledged USD\$3.2 million, which will allow purchase of 40 million PZQ tablets, per year. Historical data shows that other funding sources support purchases of an additional 10 million PZQ tablets per year. With the Merck Serono donation of 20 million PZQ tablets per year, the total pledged amount of PZQ is approximately 208 million tablets per year. See table 2 for summary.

This compares with an average annual donor financed PZQ procurement of 50 million tablets in recent years. The peak PZQ procurement was in 2007, when 80 million tablets were purchased by the Schistosomiasis Control Initiative alone, which dominated donor-funded PZQ procurement at the time.

Actual demand/uptake is a function, not only of donor financing, but also of capacity for implementation and country absorption. However with historical data indicating significant under-supply of PZQ, it is believed that donor financing will be the primary driver of demand until financing approaches a reasonable percentage of health need.

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<sup>4</sup> Presentation given by Dr C. Grace DfID Consultant

<sup>5</sup> Grace C. 2009. Projecting Praziquantel Demand Based on Donor Financing. DFID Health Resources Centre - Annex 3

<b>Table 2: Five-year summary of projected PZQ demand based on known donor financing and in-kind donations</b>					
<b>Donor agency</b>	<b>Number of PZQ Tablets donated per year (million)</b>				
	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>2013</b>	<b>2014</b>
USAID	60*	104 - 138	104 - 138	104 -138	104 -138
DFID	40	40	40	40	40
Other	10	10	10	10	10
<b>Total donor financed PZQ supply</b>	<b>110</b>	<b>154 -188</b>	<b>154 -188</b>	<b>154 -188</b>	<b>154 -188</b>
Merck Germany (in-kind donation)	20	20	20	20	20
<b>Total including Merck donation</b>	<b>130</b>	<b>174 - 208</b>	<b>174 - 208</b>	<b>174 - 208</b>	<b>174 - 208</b>

The projections of total tablets available per year, through the combination of expected donor financing and in-kind donations, are approaching half of the health need. With adequate implementation support, countries should be able to readily absorb this increased supply.

DFID's reflections on the theme of the meeting:

- Explore the market situation in more detail – what specific market failures are we attempting to correct? On what basis can we assume that the past problems with PZQ supply will repeat? Is supply and demand situation the same as historically?
- Explore a range of options for co-ordinating the procurement of praziquantel
- After understanding the market situation in more detail, understand and discuss the range of contracting and procurement options which can send strong signals to industry concerning sustained funding for PZQ procurement over the next few years.

#### **4.3 Market failure of PZQ and identification possible sustainable solution for PZQ supply through Private-Public Partnerships**

##### **4.3.1 Availability of quality PZQ API and requirements for expanded production <sup>6</sup>**

Currently a number of pharmaceutical companies manufacture PZQ for both the human and veterinary markets. Merck Serono is the only donor of PZQ currently; they provide in-kind donations of between 20 and 25 million PZQ tablets annually to endemic countries through the WHO using around 13-16 tonnes of API per year. Increasing supply to 100 million tablets at cost would require an additional 65 tonnes of API annually. Merck only works with suppliers who meet quality criteria, the defined regulatory and legal requirements, and have API that is compatible with formulation technology.

<sup>6</sup> Presentation given by Mr W. Eliot, Merck Serono and Mr W. J. Chang, Shin Poong Pharmaceutical Company

According to Merck's research, approximately 300 tonnes of pharmaceutical grade API (suitable for human and veterinary use) is available from 7 producers.<sup>7</sup> It is not known whether all this amount of API could be used to formulate tablets through the Merck process. This can only be determined by the results of a qualification process.

There appears to be a significant dichotomy in pricing of API dependent on geographical location of production, quality and capacity of the manufacturers, with prices varying from USD\$80/kg USD\$400/kg, assuming static market prices. These variations in cost would be reflected in the price of the manufactured tablet.

Merck is currently evaluating producers of API to identify an additional source. Once the appropriate API supplier was identified, it would take almost two years for Merck to formulate tablets, conduct stability tests, and to register the products with the appropriate authority. Shin Poong Pharmaceutical is another supplier of significant quantities of PZQ to endemic country SCH programmes. It produces its own API. It would not take that long for them to scale up production of API and additional tablets to meet an increased demand. However, they need to plan for such scaling up and would need a multi-year commitment to do so.

In Merck's view, it would be possible to scale up production of PZQ to meet the medium and long-term demand at reasonable prices provided there were firm commitments to purchase PZQ for a minimum of five years. In recent years, large scale purchases of PZQ have been sporadic and requiring immediate delivery for a limited time usually a year. Longer term multi-year donor commitments would allow pharmaceutical companies to:

- identify new sources of reliable API;
- give longer term commitments to API suppliers to guarantee reasonably priced API;
- build capacity, improve quality and registering of new API sources and
- provide a strong signal to industry and ensure a high number of suppliers remain in the market.

The following points summarize the discussion that followed these two presentations:

- 1) Concerning the importance of sending a strong signal to manufacturers two divergent views emerged:
  - a) the US and UK governments pledges are strong enough a signal for manufacturers to engage;
  - b) a written agreement covering the 5-year period between specific buyers and manufacturers is needed.

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<sup>7</sup> There may be additional capacity available from API sources not identified by Merck. During the meeting, IDA/RTI and Merck discussed the possibility of sharing information on the sources of available API supply, as it appears that at least one of IDA's known sources of API supply was not identified in Merck's research. Merck said it would have to check with its legal department regarding sharing such information.

2) There are possibilities for industry to meet the increased demand for PZQ. Other generic manufacturers of PZQ tablets may be coming on the market, although the quality of their API or final products is not known. Emphasis should be placed on developing appropriate quality assurance mechanisms for both API and finished product at the same time as expanding supply.

#### **4.3.2 Experience with procurement of PZQ<sup>8</sup>**

A number of implementation organizations have had extensive experience of procuring PZQ on a large scale. The SCI has procured about 224 million PZQ tablets from a number of sources since 2002 for use in control programmes in Africa. Much of the funding for these activities was from the Bill and Melinda Gates Foundation (“BMGF”), however there were other donors including USAID/RTI. In 2007 and 2008 SCI procured PZQ for Research Triangle International (“RTI”) who is contracted by USAID.

The USAID/RTI NTD control programme over the last 3 years has funded the purchase of 81.15 million tablets of PZQ for the treatment of school-age children and high-risk adults. The drugs are procured on a tender basis subject to USAID Federal Acquisition Regulations (FAR) and which include the need to purchase PZQ through a US registered company. RTI stated that the USAID waiver process substantiates the quality of the procured PZQ, and additional testing is conducted via a WHO prequalified laboratory. In addition, according to RTI’s market intelligence, there is enough capacity to meet USAID and UK projections, though RTI agrees that it would be good to co-ordinate USAID and UK procurements to smooth the demand curve and ensure there are not any temporal shortages.

DfID can only procure PZQ through a competitive bidding among prequalified companies.

International Dispensary Association (“IDA”) informed the meeting that all of the PZQ they supply is procured from three generic tablet manufacturers. The IDA Foundation claims to have in place an effective quality assurance and quality control process<sup>9</sup>. IDA has been selected by the Global Drug Facility as the exclusive procurement agent for second line tuberculosis medicines (2007–2010) and its designation and approval by the European Commission Humanitarian Aid Organization as a Humanitarian Procurement Centre. IDA also reported that they have had no problems with suppliers meeting IDA quality requirements and have had no problems to date with industry capacity to supply the quantities tendered within a suitable timeframe.

The WHO Contracting and Procurement service (WHO/CPS) is involved in the procurement, transport and logistics of a large variety of items including medicines, diagnostics and devices, for a total of \$150 million USD per year . Almost 61% of the workload and funds are in the procurement drugs and biologicals. WHO/CPS works with national ministries of health through WHO country and regional offices. The unit also works with the other UN agencies for economies of scale as well as to improve logistics. WHO/CPS procures and provides NTD drugs, as well as those for HIV and malaria. Drugs and supplies procured by WHO and the UN system do not attract customs taxes, duties, and clearance charges in recipient countries because of standing agreements.

#### **4.4 Anticipated issues for quality assurance of PZQ<sup>10</sup>**

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<sup>8</sup> Presentations given by Prof. A. Fenwick SCI, Dr C. Kim RTI, Dr M. Neve, IDA and Dr A Gould, WHO/QSM

<sup>9</sup> It would be useful for IDA to provide details of its quality assurance scheme.

<sup>10</sup> Presentation prepared by Dr. L Rago WHO/QSM and delivered by Dr A. Gould, WHO/QSM

With expanding demand and more widespread use of PZQ the need for well defined mechanisms to assure quality of product becomes acute.

WHO pre-qualifies drugs for public health use. Almost all the products that have been prequalified are essential medicines for HIV/AIDS, Malaria, TB, and reproductive health. The major reason for this is the guaranteed funding and demand provided by global funding agencies. A UN Prequalification Program of Quality Control Laboratories exists to facilitate the quality control of these prequalified products. All the essential medicines that have been pre-qualified are posted on the relevant website and available for transparent review. In addition the various dossiers under review are also posted.

Prequalification of finished medicines has taken up to 24 months and two thirds of this duration is due to time companies require to respond to issues raised by the assessment of submitted documentation and inspection of manufacturing sites or contract research organizations.

NTD medicines are currently not included in the WHO prequalification programme. A funding proposal for prequalification of NTD medicines was submitted to the Gates foundation and is being reviewed.

WHO does not as yet pre-qualify API for any drugs primarily due to lack of resources. API prequalification could entail a similar duration to finished medicines and a significant cost especially if currently no API is manufactured to a standard close to that required to meet compliance with established regulatory requirements. This therefore would not be possible without a guarantee of purchasing and a long term commitment of at least five years.

#### **4.5 Development of a purpose-specific coordination mechanism for the procurement and provision of PZQ for the expansion of preventive chemotherapy coverage**<sup>11</sup>

For many countries in the WHO African region, there is sufficient historical and health service epidemiological data on schistosomiasis to initiate control activities. Currently development partners select countries for support; however there is a need for transparency in this process and engagement of all stakeholders to ensure appropriate prioritization on the basis of agreed criteria including level of endemicity and existence of national plans.

With the increase in adoption of preventive chemotherapy in highly endemic countries with large infected and at risk populations such as the Democratic Republic of Congo, Ethiopia and Nigeria the demand for PZQ will be substantial ,especially in the initial stages of implementation. The estimates for PZQ can initially be based on national plans however incorporation of new mapping and monitoring data may significantly alter requirements over time.

Therefore there is a need for a coordination mechanism for schistosomiasis control (“CMSC”, see annex 4)) to enable all stakeholders to share information and as accurately as possible forecast demand to ensure procurement and regular supply of assured-quality PZQ, at the most convenient price, to WHO Member States upon request. The precise form of this co-ordination mechanism needs to be further explored and agreed amongst stakeholders.

WHO proposed one option for such co-ordination – a “CMSC” which could operate initially for 5 years. It is assumed that if high coverage is reached, the epidemiological situation will change dramatically.

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<sup>11</sup> Discussion led by Dr D Daumerie WHO/NTD

Although activities will have to continue, the context will also change and therefore a new assessment of the situation will be required, based on close epidemiological monitoring.

#### **4.5.1 Objectives of the CMSC proposed by WHO**

The specific objectives for the CMSC would be to:

- to coordinate large scale forecast of PZQ needs and optimize manufacture lead time;
- to act for ensuring a regular availability of assured-quality PZQ API and finished dosage forms;
- to ensure that resources devoted to procurement and provision of PZQ are used in the most cost-effective way by assuring quality, timely supply and smooth international transit, in the ultimate interest of at-risk populations;
- to provide advice and technical assistance to national programmes and other SCH control initiatives to ensure procurement and supply of assured-quality PZQ;
- to improve cost effectiveness of national SCH control programmes through promoting integrated delivery strategies;
- to implement a simple, reliable and transparent SCH information system to track progress, enable periodic evaluation of supported SCH control programmes as well as to provide a better basis for assessing future medicine needs and plan adequate supply;
- to continue to mobilize international public and private resources as well as operational and technical capacity to ensure that national control programmes have at their disposal sufficient quantities of assured-quality PZQ to attain established coverage targets.

#### **4.5.2 Partners**

The CMSC could be based on close collaboration of the following principal partners to leverage their respective complementary strengths:

1. Health authorities in the endemic countries, which have the primary responsibility for delivering preventive chemotherapy interventions in their jurisdictions;
2. Funding Partners: WHO Member States, European Commission, Regional Development Banks, Bill & Melinda Gates Foundation, GNNTDC, other NGOs;
3. Donating Partners: Research based and generic pharmaceutical companies and their associations;
4. UN System Partners: UNICEF, World Food Program, World Bank, UNITAID;
5. WHO: HQ, Regional Offices, WHO Country Offices and the network of WHO Collaborating Centres world-wide.

In addition, the CMSC could enter in contractual relationships with providers of specialized goods and services to support PZQ-related operations:

- i. WHO-pre-qualified manufacturers;
- ii. WHO-pre-qualified quality control laboratories to assist in the medicine quality assurance processes throughout the supply chain;
- iii. Major international freight forwarders to provide medicine delivery services at preferential prices.

WHO proposed to host the CMSC and to manage it in close cooperation with all participating partners, as it currently procures PZQ upon request from member states. In recent years it has been at the forefront in establishing public-private partnerships in the pharmaceutical field. WHO already has long

established partnerships with pharmaceutical companies and donors for the free supply of selected NTD medicines. Having regard to SCH, in 2007 WHO signed a Memorandum of Understanding with Merck KGaA to supply 200 million tablets of praziquantel as part of a 10- year donation which also includes funding for management of the donation and to cover air freight costs of delivery.

The CMSC would take advantage of WHO's expertise in the procurement of pharmaceuticals and extensive operational network in SCH endemic countries. WHO Country Offices interact directly with national health authorities at all levels and with managers of SCH control programmes in the countries, helping to design, plan and monitor control programmes. WHO technical experts in HQ and Regional Offices provide state of the art technical advice and help disseminate best practices. This will enable the CMSC to keep a simple and effective structure, without layers of committees and ad-hoc groups.

WHO acts as a procurement agent upon request from member states, and has achieved economies of scale in global procurement, brought down prices and developed supply mechanisms that could not have been implemented by smaller scale operations. This expertise can be made accessible to NTD implementing partners through the CMSC.

#### **4.5.3 Business model**

CMSC's business model is based on two basic premises:

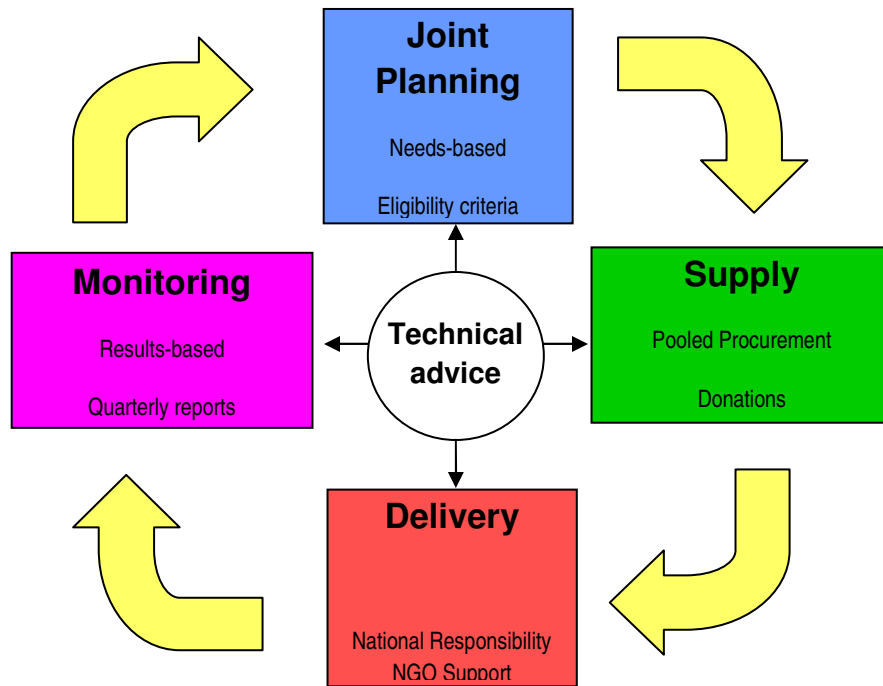
- (a) preventive chemotherapy interventions are a public health action conceptually similar to immunization and the public sector should play a leading role in most aspects of their implementation;
- (b) initially, preventive chemotherapy should be provided free to guarantee universal access and the required high coverage rates.

It is envisaged that in the first five years the CMSC will provide free PZQ to national control programmes in endemic countries. In low income countries it is unlikely that sufficient funds for PZQ will be available in the national health budgets in the near future. It is equally unlikely that communities surviving on less than US\$1 a day could afford, at least initially, to pay for PZQ<sup>12</sup>. Indeed, studies indicate convincingly that only providing medicines for free leads to high coverage, which is necessary to reduce diseases transmission, whereas introduction of even a small fee leads to a dramatic fall in the use of medicines.

Making PZQ (and, possibly, other NTD medicines) available to the target populations remains the most critical objective of the CMSC. Quality assurance, logistics, advocacy, fund raising, reporting and negotiations with potential donors of medicines are also of critical importance. The CMSC will be leveraging the respective strengths of participating partners to mobilize the necessary financial and technical resources as well as donations. Responsibilities, roles and commitment of the different CMSC participating partners will be defined in ad hoc written documents, such as Memoranda of Understanding. The CMSC will produce regular reports with up-to-date statistics and formally meet donors at least once a year to discuss progress, provide estimates of needs for the following year (based on country requests, an assessment of buffer stock requirements and longer term projections of needs). A suitable and easily accessible mechanism (e.g. web site) will be established to make information available to all partners.

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<sup>12</sup> It should be stressed that PZQ would in most cases be part of a multi-intervention approach requiring several drugs and/or vaccines to be used simultaneously. This entails much more than just drug cost issues.



**Figure 2** A schematic, simplified overview of CMSC approach to supporting SCH control programmes in an endemic country.

CMSC could be especially involved in three of the steps outlined above:

- Joint Planning:** country needs are the starting point. National authorities will lead this process assisted, if requested, by WHO and other CMSC experts advisers. The process will consider (and regularly re-assess) target population, patient load, new case detection in the previous year, actual PZQ consumption and current stocks. On this basis the CMSC will calculate the needs for the coming years. Other factors, such as a planned expansion of the programme, or the capacity of the programme to absorb extra medicines, will be taken in consideration in defining the final quantities of medicines to be shipped to the country concerned. The CMSC will organize country visits to provide technical advice and assistance to countries and to validate specific planning assumptions against the prevailing conditions. National SCH control plans will be available for review by all CMSC partners to come to a decision about supporting them.
- Supply** of PZQ for the approved national plans: the CMSC will ensure timely supply of the appropriate medicines (donated or procured) to agreed locations in the recipient countries. A simple and collaborative process will be used to avoid multi-layered supervisory and decision making committees to approve the applications for medicines. The CMSC will be in permanent contact with suppliers to manage unexpected situations (e.g. re-schedule shipments or provide early warning of likely extra demand), ensure that buffer stocks are at mutually agreed levels, and generally help to “troubleshoot” potential bottlenecks in the supply chain. Transparency, willingness to discuss problems and planning mistakes, and mutual

trust are the basis of effective cooperation. The exact mechanism for 'pooled procurement', can be summarized in four types:

- Information sharing platform
  - Pooled demand but separate purchase agreements by multiple buyers
  - One procurement agent on behalf of multiple buyers
  - Revolving fund in which one buyer buys for all buyers
- **Monitoring** of the national SCH control programmes: the CMSC will carry out results-based reviews, using independent experts in agreement with the concerned national authorities. The monitoring of medicine distribution in the field will be carried out by WHO, implementing partners and donor representatives, at sentinel sites as well as in randomly selected areas of the country. Official PZQ request forms signed by national authorities will include an ad hoc statement to allow CMSC monitors appropriate access to information and sites (e.g. “As part of regular monitoring and evaluation activities, and to meet contractual obligations with donors and other partners, the CMSC, through its appointed monitors, will be allowed to periodically inspect medicine stocks and related documentation at different levels.”)

Through the CMSC, WHO will continue to compile, make available and promote sharing of best practices and lessons learned during the reviews of SCH control programmes.

National SCH control programmes will be responsible for the delivery of PZQ provided by the CMSC to the target populations. The CMSC will require that national health authorities undertake to:

- prepare, jointly with WHO experts working on behalf of the CMSC, a multi-year plan to achieve agreed coverage and disease control targets;
- facilitate border control clearance, receive, and stock donated PZQ at national and regional level;
- distribute PZQ free of charge to the communities in need;
- provide annual detailed reports on SCH control performance;
- agree to independent monitoring of SCH control programmes.

NGOs and other implementing partners will provide the necessary operational assistance to national SCH control programmes.

The Business Model of the CMSC places the main emphasis on the following elements.

- **Measurable and verifiable Results:** rigorous, evidence-based, independent reviews will ensure that available funding and donated medicines are used in the most effective and efficient manner in the ultimate interest of the affected populations;
- **Process Transparency:** detailed reporting and adherence to Interagency Operational Principles for Good Pharmaceutical Procurement<sup>13</sup>;
- **Accountability:** the CMSC will be accountable to beneficiaries, donors and, where applicable, other partners in terms of results and costs. Detailed reports will be provided to all partners;
- **Flexibility and Responsiveness:** a simple organizational structure allows the CMSC to respond quickly to problems and take advantage of opportunities;
- **Sustainability:** during the first five years the CMSC will build a solid basis for long-term solutions while providing immediate improvements in the health conditions of SCH-affected populations in endemic countries.

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<sup>13</sup> <http://apps.who.int/medicinedocs/pdf/whozip49e/whozip49e.pdf>

The CMSC will use a pragmatic approach to establish close collaboration with counterparts in national programmes and WHO country offices. This adds to good governance and effective project implementation, especially when complemented by periodic independent evaluations of coverage and medicine utilization.

This simple business model and WHO's support will keep CMSC operational costs to a minimum.

#### **4.5.3 Expected benefits**

The most relevant benefits of CMSC are cost-effectiveness and improved efficiency that can be achieved through the coordinated action of all partners. The CMSC will reduce staff, procurement, shipment and logistics costs benefiting all participating partners by establishing one repository where all the relevant information for coordinated action will be available and accessible to all concerned parties. This includes for example:

- national plans and needs in terms of PZQ and other support;
- which countries are supported, by whom, to what extent, what are the unmet needs (if any);
- how does global demand match manufacturing capacity of reliable manufacturers;
- how much assured-quality PZQ can be available, at what price, where and when;
- how PZQ shipments can be reprogrammed if original plans cannot be met (e.g. a country's implementation capacity suddenly changes);
- Which countries are in greatest need of technical assistance to expand coverage and monitor impact.
- 

Improving cost-effectiveness and efficiency will permit to reach a greater number of people at risk and increase the credibility and technical skills of all CMSC participating partners.

#### **4.5.4 Budget 2010-2014**

The estimated PZQ cost alone amounts to about **US\$ 100 million** for this time period. (See Table 3) The additional funding is required as operating expenses for medicine procurement and supply. The following activities must be covered:

- Prequalification of API and finished dosage forms & manufacturing sites;
- Transport, insurance, logistics;
- Quality control of procured medicines;
- Advocacy, Fund Raising and Reporting;
- Technical advice and capacity building at national level;
- Coordination of logistics by a contracted specialist.

It is expected that coordinating SCH control programmes with other NTD programmes will permit to reduce certain logistics and technical advice costs.

It is assumed that all local costs for SCH control in countries will be covered by the relevant national/local budget and/or assisted by NGOs. Distribution costs are therefore not included in the budget estimates. On this basis, the budget for a five year time frame 2009-2013 for global PZQ procurement and provision to endemic countries is about **US\$ 116 million**.

<b>Table 3 Operating expenses for PZQ procurement and supply in USD</b>						
	<b>Year 1 (x000)</b>	<b>Year 2 (x000)</b>	<b>Year 3 (x000)</b>	<b>Year 4 (x000)</b>	<b>Year 5 (x000)</b>	<b>Total (x000)</b>
<b>Transport, insurance, quality control</b>	1,100	2,500	2,500	2,500	2,500	11,100
<b>Technical advice and capacity building</b>	450	450	250	250	250	1,650
<b>Pre-qualification of suppliers</b>	400	400	400	100	100	1,400
<b>Advocacy, fund raising, reporting</b>	150	150	150	150	150	750
<b>Coordination</b>	300	300	300	300	300	1,500
<b>Procured and donated PZQ</b>	20,000	20,000	20,000	20,000	20,000	100,000
<b>Total</b>	<b>22,400</b>	<b>23,800</b>	<b>23,600</b>	<b>23,300</b>	<b>23,300</b>	<b>116,400</b>

## **5. Conclusions, recommendations and timelines**

Participants agreed to form a task force with the following aims

- To better understand the capacity of quality API available to meet projected financed demand
- To develop a strategy to communicate to manufacturers a strong signal that funding will be reliably available for PZQ purchase for the next five years;
- To assess the feasibility and legal aspects of donor agencies participation in different approaches to pooled procurement;
- To assess mechanisms for joint planning (forecast system, information sharing, joint decision-making on which national plans to support and under which operational arrangements);
- Defining quality requirements to ensure sustained acceptability of preventive chemotherapy interventions as part of national NTD programmes

The proposed task force will include representatives of stakeholders: WHO (NTD and QSM), donor agencies (DFID and USAID), and selected implementing entities (SCI and RTI). Manufacturers of PZQ API and tablets will be excluded from the taskforce to avoid any potential conflict of interest.

The chairperson recommended the outcomes of the meeting to be shared by 5 Feb 2010. A tentative consolidated note addressing the above issues to be followed-up should be prepared by end February 2010. This process will be facilitated by WHO/NTD (focal point Dr V. Reggi).

The outcome of the task force for PZQ procurement is expected to be submitted to the Scientific Technical Advisory Group ("STAG") in April 2010 seeking their input and advice in order to move forward.

Dr Nakatani thanked all participants and declared the meeting closed.

**After the circulation of the draft report, a number of important comments were received. Some of these comments are related to but do not reflect the actual meeting discussions. However, they raise major issues that require further discussion. It may be these issues can be addressed in the proposed task force or another forum.**

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## Annex 2

**Informal Consultation on Expanding Schistosomiasis Control in Africa, Geneva, Switzerland, 26 January 2010 (Room X7)**

<b>PROVISIONAL AGENDA</b>		
<b>Tuesday 26 January 2010</b>	<b>Item</b>	<b>Name</b>
09:00 – 09:30hrs	Opening remarks	ADG/HTM
	Background and objectives of meeting	L. Savioli, WHO/NTD (Chair)
09:30 – 10:15hrs	The Global Status of Schistosomiasis Control and Praziquantel Needs (30' presentation, 15' discussion)	L. Chitsulo, WHO/NTD
10:15 – 10:30 hrs	<b>Coffee break</b>	
10:30 – 10:55hrs	PZQ demand projections based on donor financing (15' presentation, 10' discussion)	C. Grace, DFID Consultant
10:55 – 11:40hrs	Availability of Quality Praziquantel-API and Requirements for Expanded Production (30' presentation, 15' discussion)	Merck Serono S.A./Shin Poong Pharmaceutical Company
11:40 – 12:10hrs	Pre-qualification of API(20' presentation, 10' discussion)	L. Rago, WHO/PSM
12:10 - 12:30hrs	Discussion	Participants
12:30 – 14:00hrs	<b>Lunch</b>	
14:00 – 15.30hrs	Experiences with Procurement of Praziquantel (15' presentation, 15' discussion each)	RTI, SCI, WHO/CPS, IDA
15:30 – 15:45hrs	<b>Coffee break</b>	
15:45 – 17.30hrs	Discussion and drafting of a Proposal for Coordinated Procurement of Praziquantel	Participants
17:30 – 18:00hrs	<b>Concluding Remarks, Recommendations and Closure</b>	
		Dirk Engels, WHO/NTD

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**Projecting Praziquantel Demand**  
**Based on Donor Financing**  
**Final report**

Cheri Grace

15 February 2010

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The DFID Health Resource Centre (HRC) provides technical assistance and information to the British Government's Department for International Development (DFID) and its partners in support of pro-poor health policies, financing and services. The HRC is based at HLSP's London office and consists of an international consortium of three organisations: HLSP Ltd, UK; Ifakara Health Research and Development Centre, Tanzania (IHRDC) and ICDDR,B - Centre for Health and Population Research, Bangladesh.

This report was produced by the Health Resource Centre on behalf of the Department for International Development, and does not necessarily represent the views or the policy of DFID.

Title:           Projecting Praziquantel Demand Based on Donor Financing

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## **Background**

The Department for International Development is in the process of allocating its £50 million commitment on neglected tropical diseases (NTDs). Initial work (Crompton, Pearson 2008) suggested that a large portion of the commitment should be targeted towards financing the purchase of praziquantel (PZQ), a drug for controlling schistosomiasis (SCH), since health need for the drug far exceeds available PZQ supply.

DFID commissioned work (Grace 2009) to assess industry's capacity to respond to a surge in finance for praziquantel purchase, and the conclusion drawn was that industry had excess capacity with which it could immediately supply an additional 100 million tablets per year, a large increase on the average of 50 million tablets (approximate) per year purchased with aid finance. However, the report drew attention to the need to preserve the incentives for PZQ producers to remain in the market. Merck Germany began a donations programme in 2008 and new donor finance was not scaling up commensurate with the donation to offset the market "loss" for producers. Donor financing for praziquantel purchase has also otherwise been insecure with the recent change in administration in the United States, and changes in Gates NTD funding policies. Consequently, the risk - that producers might not have the incentives to maintain their capacity devoted to this product longer term, if more donor finance did not contribute to enlargening the market - was foreseen. "In the interest of maintaining secure and competitive supply, there is a need to signal to industry that there is robust demand based on predictable financing." (Grace 2009)

## **Purpose**

If there is to be investment in quality production of praziquantel active pharmaceutical ingredient and finished product, manufacturers need to be assured that there is an adequate market to support such investment. Therefore, in order to increase the probability of engaging manufacturers, DFID has commissioned this study to make public a reliable estimate of likely demand, based on known donor financing.

## **Scope of Work**

The demand forecast is based solely on known donor financing, in particular from USAID, DFID and Merck Germany. There is some additional contribution from private donors and from the World Bank, though precise figures were not available on the former at the time of writing this report. Further, the amounts coming from the World Bank and private donors are believed to be small in relation to the finance from the three main contributors over the period 2010-2014. Other than Egypt, Brazil and China, governments do not generally fund their own PZQ purchase.

While acknowledging that actual demand/uptake is a function, not only of donor financing, but also of capacity for implementation and country absorption, this report is limited to a demand forecast as a function of donor financing only. Information on country capacity for implementation cannot be obtained at this time, given that the major programme implementers are currently competing for the DFID tender to supply and implement SCH programmes. Previous reports have also documented significant under-supply of PZQ (because of limited donor financing) as a proportion of health need. Therefore, in theory, donor financing will be the

primary driver of demand until financing approaches a reasonable percentage of health need. Respondents interviewed during the course of this study confirmed the accuracy of this theory.

## Methodology

Interviews and document review were the basis for donor financing projections detailed below.

## Results

### USAID

USAID has just received news of their appropriation from US Congress for USD 65 million annually to be allocated to NTD control. USAID sources report that continued 65 million annual expenditure can be reliably predicted during the subsequent 5 years, and USAID projects that 20% of their entire NTD budget will be spent on NTD medicines purchase, following similar trends of the previous two years. Praziquantel comprises the majority of the NTD medicines expenditure. In the projections in the table below, it is assumed that 85% of the medicines expenditure would go towards PZQ purchase, which totals 11 million USD annually, equating to 138 million tablets annually. USAID's final year 2010 funding of \$65 million will likely arrive in July/Aug 2010 and would become available beginning of October 2010 for the purchase of PZQ. Therefore 2010 procurement levels – estimated in red highlight below - have been downward adjusted (compared to subsequent years) to represent only a slight increase on current procurement levels.

	2010	2011	2012	2013	2014
USAID total NTD finance (USD million)		65	65	65	65
Drug portion (USD million- 20% of total NTD finance) - m USD		13	13	13	13
Of which, assume 85% for PZQ - m USD		11	11	11	11
PZQ tablets (millions)*	60	138	138	138	138

\* Purchase dollars translated to tablets assuming cost of \$.08 per tablet

In addition to the USAID funds committed and noted above, there is advocacy activity currently underway to enable PEPFAR funds to be used for SCH as a form of HIV prevention. Reportedly, legislation has been changed to enable PEPFAR funds to be used for different modes of prevention, but the discussions have not yet progressed to the point where they can factor into credible finance projections.

DFID

DFID plans to allocate £25 million towards SCH control in the period 2010-2015, which will fund the purchase and programming to deliver approximately 75 million treatments for SCH and soil transmitted helminths (STH) in up to eight African countries. Up to half the funds provided will be for the procurement of drugs and the remainder will fund technical assistance in mapping and planning; training and health education; equipment; and monitoring and evaluation. Provision in the Aid Framework has been agreed and planned expenditure is expected to be programmed as detailed in the table below, although actual expenditure in each country will depend on the detailed planning at country level.

<b>Financial year</b>	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>2013</b>	<b>2014</b>
NTD finance allocated to PZQ (£ million)	2	2	2	2	2
(\$ million)	3.2	3.2	3.2	3.2	3.2
PZQ tablets (million)	40	40	40	40	40
PZQ treatments (million)*	16	16	16	16	16

\* Tablets translated to treatments assuming average consumption of 2.5 tablets per treatment course

Other (World Bank, private donors, foundations)

	<b>2009</b>	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>2013</b>	<b>2014</b>
PZQ tablets (million)	10, of which:	10	10	10	10	10
PZQ tablets (million)	6 million (World Bank financed supply to Yemen)					
PZQ tablets (million)	4 million (estimate) private donor supplied to Burundi and Rwanda					

For 2009, the World Bank financed the purchase of 6 million PZQ tablets, procured through WHO. An estimated 4 million PZQ tablets were financed by private donors towards SCH control in Burundi and Rwanda. Projections for 2010 – 2014 are based on the assumption that the World Bank and private donors will continue to fund some PZQ purchase.

The Bill and Melinda Gates Foundation (BMGF) does not fund PZQ purchase directly. BMGF funds the Global Network's fundraising and advocacy activities, and the Network may leverage this financing to secure other donors for PZQ. Currently, private donors are supplying PZQ to Rwanda and Burundi, via the Network.

Merck

Although technically not donor-financed demand, the PZQ supplied via the donation from Merck Germany is mentioned here for completeness. Merck Germany has donated 200 million tablets over 10 years and WHO can draw down on that amount in unequal annual portions, on a needs basis. WHO has channelled 25 m of the 100m tablets to endemic countries in 2009.

	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>2013</b>	<b>2014</b>
PZQ tablets (million)	20	20	20	20	20

## Totals

The table below provides a summary of the estimates of PZQ tablets (million) projected for financing, as detailed above:

	2010	2011	2012	2013	2014
USAID	60	138	138	138	138
DFID	40	40	40	40	40
Other	10	10	10	10	10
<b>Total donor financed PZQ demand</b>	<b>110</b>	<b>188</b>	<b>188</b>	<b>188</b>	<b>188</b>
Merck Germany (donation)	20	20	20	20	20
<b>Total including Merck donation</b>	<b>130</b>	<b>208</b>	<b>208</b>	<b>208</b>	<b>208</b>

This compares with an average annual donor financed PZQ procurement of 50 million tablets in recent years. The peak PZQ procurement was in 2007, when 80 million tablets were purchased by the Schistosomiasis Control Initiative alone, which dominated donor-funded PZQ procurement at the time. (Grace 2009).

## Health Need

According to experts<sup>14</sup>, the annual global health need for PZQ is approximately 600 million tablets. The WHO paper, “Procurement of essential medicines for the expansion of preventative chemotherapy for neglected tropical diseases, Business Plan” projects that a realistic scale-up to meet that need, could unfold as follows:

<i>Table 1</i>					
PZQ Forecasted Need (million tablets)					
	2009	2010	2011	2012	2013
WHO	171	286	428	486	571

<sup>14</sup> See: “Access: How do good health technologies get to poor people in poor countries?” Laura J. Frost & Michael R. Reich, January 2009 from Harvard Center for Population and Development Studies (Chapter on PZQ with contribution by Alan Fenwick) and WHO “Procurement of essential medicines for the expansion of preventative chemotherapy for neglected tropical diseases, Business Plan”

Therefore the projections of approximately 200 million tablets per year are approaching half of the health need, and with adequate implementation support, countries should be able to readily absorb this increased supply.

## **Literature**

Sources for this report include the following papers:

1. "Access: How do good health technologies get to poor people in poor countries? Laura J. Frost & Michael R. Reich, forthcoming January 2009 from Harvard Center for Population and Development Studies (Chapter on PZQ with contribution by Alan Fenwick)
2. WHO "Procurement of essential medicines for the expansion of preventative chemotherapy for neglected tropical diseases, Business Plan"
3. DFID Support to the Control of Neglected Tropical Diseases: Recommendations. David Crompton and Mark Pearson October 2008. DFID Health Resource Centre.
4. Options for DFID Support to Schistosomiasis Control Through Financing Praziquantel Purchase Confidential Report to DFID, March 23, 2009. Cheri Grace DFID Health Resource Centre.

## **Interviews**

Denis Daumerie, WHO

Charles Clift, DFID

Christy Hanson, USAID

Julie Jacobsen, The Bill and Melinda Gates Foundation

Patrick Lammie, US CDC (in his role with the Global Network)

## **Establishing a coordination mechanism for the procurement and provision of praziquantel for the expansion of preventive chemotherapy coverage**

A short background note for

**Informal Consultation on Expanding Schistosomiasis Control in Africa:**

**Coordinating the Procurement of Praziquantel**

**Geneva, Tuesday, 26 January 2010**

### **1. Background**

In 2001, WHO Member States have established<sup>15</sup> for the control of schistosomiasis (SCH) *"the goal of attaining a minimum target of regular administration of chemotherapy to at least 75% and up to 100% of all school-age children at risk of morbidity by 2010"*. They have also indicated that WHO approach to combating SCH should include *"advocating new partnerships with organizations of the United Nations system, bilateral agencies, nongovernmental organizations and the private sector, and by continuing to provide international direction and coordination"*.

January 2010 estimates indicate that less than 10% of the population at risk receives praziquantel (PZQ) preventive chemotherapy and that the coverage goal established in 2001 is far from being achieved.

Countries working towards control of SCH have been following strategies that take into account their specific socioeconomic conditions. However, many low income countries remain heavily if not totally dependent on international aid to support their efforts to reduce the burden of SCH infection in their populations.

More critically, it has been observed that sporadic, uncoordinated and often inconsistent procurement strategies have led to long procurement delays, medicines of questionable quality and high prices - especially for national procurement agencies in endemic countries, i.e. those in greater need and with most limited resources.

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<sup>15</sup> Resolution WHA54.19, 22 May 2001

Recently, the UK and US governments, have decided to significantly increase their contribution to Neglected Tropical Diseases (NTD) elimination and control, including programmes based on preventive chemotherapy. This is expected to further increase the demand for PZQ.

Experience shows that donor financing has been and is likely to continue to be for several years the primary driver of PZQ demand. Therefore, the decided increase in donor funding will result in a very significant increase in PZQ demand, involving both the API and the finished drug product. Rough estimates<sup>16</sup> indicate that demand could increase from the 50-80million tablets/year procured/donated during the last five years to over 230million tablets/year - assuming optimum country implementation capacity.

It is not sure that current manufacturers will be able to match this demand increase and this creates risks for the regular availability of supplies as well as for their quality (considering that less experienced and qualified manufacturers may be able to enter the supply chain).

Against this background, it is proposed to establish a time-limited and purpose-specific coordination mechanism which will optimize the use of available resources, meet the objectives outlined below, and result in a significant reduction in SCH morbidity and transmission in the endemic countries.

## **2. Purpose**

The main purpose of the proposed coordination mechanism for SCH control (CMSC) is to enable participating parties to share information and take all appropriate coordinated actions to ensure procurement and regular supply of assured-quality PZQ, at the most convenient price, to WHO Member States upon request.

The proposed CMSC will be operating initially for 5 years. It is assumed that if high coverage is reached, the epidemiological situation will change dramatically. Although activities will have to continue, the context will also change and therefore a new assessment of the situation will be required.

## **3. Objectives**

The following objectives are proposed for the CMSC:

- to coordinate large scale forecast of PZQ needs and optimize manufacture lead time;
- to ensure that resources devoted to procurement and provision of PZQ are used in the most cost-effective way by assuring quality, timely supply and smooth international transit, in the ultimate interest of at-risk populations;
- to act for ensuring a regular availability of assured-quality PZQ API and finished dosage forms;
- to provide advice and technical assistance to national programmes and other SCH control initiatives to ensure procurement and supply of assured-quality PZQ;

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<sup>16</sup> Summarized in a DFID note prepared by C. Grace.

- to improve cost effectiveness of national SCH control programmes through promoting integrated delivery strategies;
- to implement a simple, reliable and transparent SCH information system to track progress, enable periodic evaluation of supported SCH control programmes as well as to provide a better basis for assessing future medicine needs and plan adequate supply;
- to continue to mobilize international public and private resources as well as operational and technical capacity to ensure that national control programmes have at their disposal sufficient quantities of assured-quality PZQ to attain established coverage targets.

#### **4. Partners**

The CMSC will be based on close collaboration of the following principal partners to leverage their respective complementary strengths:

- Health authorities in the endemic countries, which have the primary responsibility for delivering preventive chemotherapy interventions in their jurisdictions;
- Funding Partners: WHO Member States, European Commission, Regional Development Banks, Bill & Melinda Gates Foundation, GNNTDC, other NGOs;
- Donating Partners: Research based and generic pharmaceutical companies and their associations;
- UN System Partners: UNICEF, World Food Program, World Bank, UNITAID;
- WHO: HQ, Regional Offices, WHO Country Offices and the network of WHO Collaborating Centres world-wide.

In addition, the CMSC will enter in contractual relationships with providers of specialized goods and services to support PZQ-related operations:

- WHO-pre-qualified manufacturers;
- WHO-pre-qualified quality control laboratories to assist in the medicine quality assurance processes throughout the supply chain;
- Major international freight forwarders to provide medicine delivery services at preferential prices.

WHO proposes to host the CMSC and to manage it in close cooperation with all participating partners. WHO has been playing a direct and proactive role in procuring PZQ, and in recent years WHO has been at the forefront in establishing public-private partnerships in the pharmaceutical field. WHO already has long established partnerships with pharmaceutical companies and donors for the free supply of selected NTD medicines. Having regard to SCH, WHO has signed a Memorandum of Understanding with Merck KGaA to supply 200 million tablets of praziquantel as part of a 10- year donation which also includes an element of funding for management of the donation and to cover air freight costs of delivery.

The CMSC will take advantage of WHO's extensive operational network in SCH endemic countries. WHO Country Offices interact directly with national health authorities at all levels and with managers of SCH control programmes in the countries, helping to design, plan and monitor control programmes. WHO technical experts in HQ and Regional Offices provide state of the art technical advice and help disseminate best practices. This will enable the CMSC to keep a simple and effective structure, without layers of committees and ad-hoc groups.

WHO, acting as the procurement agent on behalf of endemic countries, has achieved economies of scale in global procurement, brought down prices and developed supply mechanisms that could not have been implemented by smaller scale operations.

## **5. Business model**

CMSC's business model is based on two basic premises:

(a) preventive chemotherapy interventions are a public health action conceptually similar to immunization and the public sector should play a leading role in most aspects of their implementation;

(b) initially, preventive chemotherapy should be provided free to guarantee universal access and the required high coverage rates.

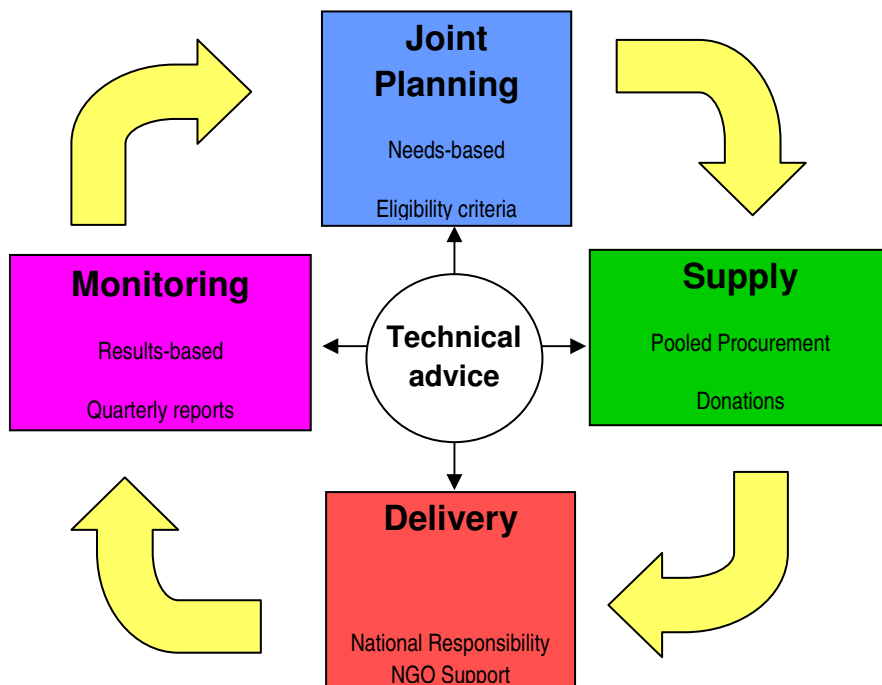
It is envisaged that in the first five years the CMSC will provide free PZQ to national control programmes in endemic countries. In low income countries it is unlikely that sufficient funds for PZQ will be available in the national health budgets in the near future. It is equally unlikely that communities surviving on less than US\$1 a day could afford, at least initially, to pay for PZQ<sup>17</sup>. Indeed, studies indicate convincingly that only providing medicines for free leads to high coverage, which is necessary to reduce diseases transmission, whereas introduction of even a small fee leads to a dramatic fall in the use of medicines.

Making PZQ (and, possibly, other NTD medicines) available to the target populations remains the most critical objective of the CMSC. Quality assurance, logistics, advocacy, fund raising, reporting and negotiations with potential donors of medicines are also of critical importance. The CMSC will be leveraging the respective strengths of participating partners to mobilize the necessary financial and technical resources as well as donations. Responsibilities, roles and commitment of the different CMSC participating partners will be defined in ad hoc written documents, such as Memoranda of Understanding. The CMSC will produce regular reports with up-to-date statistics and formally meet donors at least once a year to discuss progress, provide estimates of needs for the following year (based on country requests, an assessment of buffer stock requirements and longer term projections of needs). A suitable and easily accessible mechanism (e.g. web site) will be established to make information available to all partners.

A schematic, simplified overview of CMSC approach to supporting SCH control programmes in an endemic country is presented in the diagram below.

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<sup>17</sup> It should be stressed that PZQ would in most cases be part of a multi-intervention approach requiring several drugs and/or vaccines to be used simultaneously. This entails much more than just drug cost issues.



CMSC will be especially involved in three of the steps outlined above:

- Joint Planning:** country needs are the starting point. National authorities will lead this process assisted, if requested, by WHO and other CMSC experts advisers. The process will consider (and regularly re-assess) target population, patient load, new case detection in the previous year, actual PZQ consumption and current stocks. On this basis WHO will calculate the needs for the coming years. Other factors, such as a planned expansion of the programme, or the capacity of the programme to absorb extra medicines, will be taken in consideration in defining the final quantities of medicines to be shipped to the country concerned. The CMSC will organize country visits to provide technical advice and assistance to countries and to validate specific planning assumptions against the prevailing conditions. National SCH control plans will be available for review by all CMSC partners to come to a decision about supporting them.
- Supply** of PZQ for the approved national plans: the CMSC will ensure timely supply of the appropriate medicines (donated or procured) to agreed locations in the recipient countries. A simple and collaborative process will be used to avoid multi-layered supervisory and decision making committees to approve the applications for medicines. The CMSC will be in permanent contact with suppliers to manage unexpected situations (e.g. re-schedule shipments or provide early warning of likely extra demand), ensure that buffer stocks are at mutually agreed levels, and generally help to “troubleshoot” potential bottlenecks in the supply chain. Transparency, willingness to discuss problems and planning mistakes, and mutual trust are the basis of effective cooperation.

- **Monitoring** of the national SCH control programmes: the CMSC will carry out results-based reviews, using independent experts in agreement with the concerned national authorities. The monitoring of medicine distribution in the field will be carried out by WHO monitors and donor representatives, in randomly selected areas of the country. Official PZQ request forms signed by national authorities will include an ad hoc statement to allow CMSC monitors appropriate access to information and sites (e.g. “As part of regular monitoring and evaluation activities, and to meet contractual obligations with donors and other partners, the CMSC, through its appointed monitors, will be allowed to periodically inspect medicine stocks and related documentation at different distribution levels.”)

The CMSC will compile, make available and promote sharing of best practices and lessons learned during the reviews of SCH control programmes.

National SCH control programmes will be responsible for the delivery of PZQ provided by the CMSC to the target populations. The CMSC will require that national health authorities undertake to:

- prepare, jointly with WHO experts working on behalf of the CMSC, a multi-year plan to achieve agreed coverage and disease control targets;
- facilitate border control clearance, receive, and stock donated PZQ at national and regional level;
- distribute PZQ free of charge to the communities in need;
- provide annual detailed reports on SCH control performance;
- agree to independent monitoring of SCH control programmes.

NGOs will be encouraged to provide the necessary operational assistance to national SCH control programmes.

The Business Model of the CMSC places the main emphasis on the following elements.

- **Measurable and verifiable Results:** rigorous, evidence-based, independent reviews will ensure that available funding and donated medicines are used in the most effective and efficient manner in the ultimate interest of the affected populations;
- **Process Transparency:** detailed reporting and adherence to Interagency Operational Principles for Good Pharmaceutical Procurement<sup>18</sup>;
- **Accountability:** the CMSC will be accountable both to beneficiaries and donors in terms of results and costs. Detailed reports will be provided to all partners;
- **Flexibility and Responsiveness:** a simple organizational structure allows the CMSC to respond quickly to problems and take advantage of opportunities;
- **Sustainability:** during the first five years the CMSC will build a solid basis for long-term solutions while providing immediate improvements in the health conditions of SCH-affected populations in endemic countries.

The CMSC will use a pragmatic approach to establish close collaboration with counterparts in national programmes and WHO country offices. This adds to good governance and effective project implementation, especially when complemented by periodic independent evaluations of coverage and medicine utilization,.

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<sup>18</sup> <http://apps.who.int/medicinedocs/pdf/whozip49e/whozip49e.pdf>

This simple business model and WHO's support will keep CMSC operational costs to a minimum.

## **6. Expected benefits of CMSC**

The most relevant benefits of CMSC are cost-effectiveness and improved efficiency. The CMSC will reduce staff, procurement, shipment and logistics costs benefiting all participating partners by establishing one repository where all the relevant information for coordinated action will be available and accessible to all concerned parties. This includes for example:

- national plans and needs in terms of PZQ and other support;
- which countries are supported, by whom, to what extent, what are the unmet needs (if any);
- how does global demand match manufacturing capacity of reliable manufacturers;
- how much assured-quality PZQ can be available, at what price, where and when;
- how PZQ shipments can be reprogrammed if original plans cannot be met (e.g. a country's implementation capacity suddenly changes);
- which countries are in greatest need of technical assistance to expand coverage and monitor impact.

Improving cost-effectiveness and efficiency will permit to reach a greater number of people at risk and increase the credibility and technical skills of all CMSC participating partners.

## **7. Budget 2010-2014**

The estimated PZQ cost alone amounts to about **US\$ 100 million**. (See Table 1)

The additional funding is required as operating expenses for medicine procurement and supply.

The following activities must be covered:

- Prequalification of API and finished dosage forms & manufacturing sites;
- Transport, insurance, logistics;
- Quality control of procured medicines;
- Advocacy, Fund Raising and Reporting;
- Technical advice and capacity building at national level;
- Coordination of logistics by a contracted specialist.

It is expected that combining SCH control programmes with other NTD programmes will permit to reduce certain logistics and technical advice costs.

It is assumed that all local costs for SCH control in countries will be covered by the relevant national/local budget and/or assisted by NGOs. Distribution costs are therefore not included in the budget estimates. On this basis, the budget for a five year time frame 2009-2013 for global PZQ procurement and provision to endemic countries is about **US\$ 116 million**.

**Table 1 Operating expenses for PZQ procurement and supply**

	<b>Year 1</b>	<b>Year 2</b>	<b>Year 3</b>	<b>Year 4</b>	<b>Year 5</b>	<b>Total</b>
<b>Transport, insurance, quality control</b>	1,100,000	2,500,000	2,500,000	2,500,000	2,500,000	11,100,000
<b>Technical advice and capacity building</b>	450,000	450,000	250,000	250,000	250,000	1,650,000
<b>Pre-qualification of suppliers</b>	400,000	400,000	400,000	100,000	100,000	1,400,000
<b>Advocacy, fund raising, reporting</b>	150,000	150,000	150,000	150,000	150,000	750,000
<b>Coordination</b>	300,000	300,000	300,000	300,000	300,000	1,500,000
<b>Procured and donated PZQ</b>	20,000,000	20,000,000	20,000,000	20,000,000	20,000,000	100,000,000
<b>Total</b>	<b>22,400,000</b>	<b>23,800,000</b>	<b>23,600,000</b>	<b>23,300,000</b>	<b>23,300,000</b>	<b>116,400,000</b>