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Swiss Centre for  
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## **Malaria update 2002**

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### Disclaimer

This paper was commissioned by the Swiss Agency for Development and Cooperation (SDC). The views and ideas expressed herein are those of the authors and do not necessarily imply or reflect the opinion of the Agency.

## 1. Executive summary

At the end of the 1990s, WHO has initiated the Roll Back Malaria campaign, which aims to launch substantial expansion in effective malaria prevention and treatment. The focus is on sub-Saharan Africa, where malaria is among the most important disease. Policy makers need relevant and accurate information on current trends in malaria research and interventions. Therefore, **this document aims to update the Swiss Agency for Development and Cooperation (SDC) and its collaborators with recent developments in the area of malaria prevention and control.** Four topics are reviewed: (\*) The economic impact of malaria, (\*) Anti-Malarial drug policies, (\*) Intermittent Preventive Treatment, and (\*) Insecticide treated mosquito nets.

With regard to **economic impact of malaria:**

- It has been estimated that **malaria lowers** the average per capita growth of the **GDP up to 1.3% per year in some of the most affected African countries.** Malaria causes various types of costs including costs at health system and household level. The disease negatively affects the current and future potential for development through eroding human resources and the social capital.
- Currently around **US\$ 100 million per year are spent globally** for malaria prevention and control. The Commission on Macroeconomics and Health (CMH) of WHO has been calculating that an additional US\$ 2.5 billion per year as of 2007, increasing to US\$ 4 billion per year as of 2015 will be necessary for effective malaria prevention and treatment. The newly established Global Fund is hoped to be able to provide partially new additional assistance, but will not be able to address the full range of interventions suggested by CMH. Priorities, such as further promotion of the use of insecticide treated nets or intermittent preventive treatment have thus to be made.
- **Cost-effective interventions against malaria are:** (\*) case management, (\*) the use of insecticide-treated bednets, (\*) indoor residual spraying, and (\*) environmental control measures such as filling and draining breeding sites.

With regard to **preventive intermittent treatment,** the systematic and preventive application of anti-malarial drugs among children and pregnant women, current knowledge indicates that:

- The **intervention is efficient and cost-effective for significantly lowering the malaria and anaemia burden** among pregnant women and has to be recommended for inclusion in national strategies in Africa and for systematically being offered at antenatal care level.
- The **intervention** is very promising for reducing malaria and anaemia rates at the level of children and **has to be considered for** being included in the national **Expanded Programmes on Immunization (EPI).** WHO, GAVI and UNICEF are thus thinking about recommending scaling-up EPI programmes.

With regard to **anti-malarial drug policies,**

- **The raising resistance level** resulted recently in a shift of various African countries to combination therapies usually based on Artemisinin derivatives.

- The **affordability, acceptance and compliance of people to combination therapy** as well as health systems capacities to manage and offer high quality malaria combination therapy needs **further to be observed** and inquired .

With regard to **insecticide treated mosquito nets (ITNs)**:

- Local and regional projects (such as KINET in Tanzania ) for the promotion and the use of ITNs have been very successful. Thus, **ITNs have become a key intervention for preventing malaria and are currently being promoted through national programmes.**
- While experiences indicates that **nets should not been distributed at large-scale for free** or very cheaply they may be subsidised by governments or donors to selected vulnerable groups. The selling of relatively cheap nets may effectively be done by the private - profit or non-profit making - sector. While waiting for long-lasting and wash-resistant nets, **governments may promote higher reimpregnation rates of nets through offering insecticides for free or at highly subsidies prices.**

## 2. Introduction

It is still estimated that annually around one million persons are dying worldwide due to malaria and that the number of clinical cases is situated between 90 and 500 million<sup>1</sup>. About 90% of all these cases are thought to occur in Africa. With these figures, malaria remains a leading disease in sub-saharan Africa and impinges heavily on the health and wealth of nations and individuals. Today the disease is seen as both a disease of poverty and a cause of poverty.

**In order to update the Swiss Agency for Development and Cooperation (SDC) and its collaborators with relevant information in the area of malaria prevention and control, this document reviews recent developments in malaria prevention and control.** The document is focusing on the situation in Africa as this continent is hardest hit and hosts the highest share of the global malaria burden.

The update on malaria includes sections on **the following topics:**

- Economic impact of malaria
- Anti-Malarial drug policies
- Intermittent Preventive Treatment
- Insecticide treated mosquito nets

## 3. Economic impact of malaria

Malaria-endemic countries are not only poorer than non-malarious countries, but they also have lower rates of economic growth<sup>2</sup>. **It has been estimated that the average per capita growth of the GDP between 1965 and 1990 was up to 1.3% lower per year in some African malaria endemic countries<sup>3</sup>.**

Malaria causes various types of costs and they can be categorised into different classes. Usually they are separated into provider (programme) and household costs. Provider cost, are those associated with developing and operating a health care programme or service as well as cost related to vector control, education or research. They include staff costs (e.g. medical assistants, nurses, etc.) as well as supplies and equipment (e.g. microscope, reagents, cars, etc.) needed for making diagnosis and providing treatment for malaria.

Personal or household costs are those that are borne by patients and their families. They include both direct and indirect costs. Direct cost contain medical costs, i.e. payments made to investigate and treat symptoms and cover expenditure for hospitalisation, consultation fee, drugs or expenditure for bednets. People suffering from malaria can also incur direct non-medical costs as a result of the illness or as part of treatment. Such

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<sup>1</sup> Currently there is discussion on definite numbers of malaria related morbidity and mortality and no definite numbers are known

<sup>2</sup> Sachs J, Malaney P (2002). The economic and social burden of malaria. Nature Vol 415(7): 680-865

<sup>3</sup> Roll Back Malaria. Economic costs of malaria. RBM Infosheet 10 of 11. March 2002 Available at <http://mosquito.who.int/cgi-bin/rbm/>, accessed 23. August 2002

costs may include transport to obtain care and modification of accommodation at home such as buying a bed or necessary facilities for treatment. In addition to direct costs related to health care, patients and their families often incur indirect costs. These costs include reduced levels of work output and loss of productivity that result from inability to work or a change of employment. For example, in Kenya it was found that primary school students miss 11% of school days per year because of malaria, and secondary school students miss 4.3% of school days. The cost of care provided by relatives and friends may be direct, if they are reimbursed or indirect, in the form of time spent by household members on care rather than other work.

It is estimated that **currently around US\$ 100 million per year are spent for malaria prevention and control**. The Commission on Macroeconomics and Health of WHO has been calculating that an **additional US\$ 2.5 billion per year as of 2007**, increasing to US\$ 4 billion per year as of 2015 will be necessary for effective malaria prevention and treatment<sup>4</sup>. These amounts would obviously correspond to a massive scaling-up. However, Roll Back Malaria, created by WHO in 1999, is still considerably underfunded relative to estimated needs and expected returns on such investments in poorer countries.

The newly established **Global Fund** which **aims to carry forward malaria prevention and treatment**, besides HIV/AIDS and malaria, is hoped to be able to provide additional assistance although the fund is still lacking crucially funds at this point (by 1 October 2002 about 2 billions have been pledged to the Fund). With current available resources it will not be able to address the full range of interventions suggested by the Commission on Macroeconomics and Health and priorities in malaria prevention and control need to be established. They may include the further promotion of the use of insecticide treated nets or intermittent preventive treatment have thus to be made.

A range of **cost-effective interventions is available to alleviate the burden of malaria**. The work of the commission of Macroeconomics and Health<sup>4</sup> and other studies<sup>5</sup> have shown that **they do include**: (\*) case management, (\*) the use of insecticide-treated bednets, (\*) indoor residual spraying, and (\*) environmental control measures such as filling and draining breeding sites. Each of these interventions appears to be of good value for the money spent. Effective malaria control programmes can be developed using a combination of these approaches adapted to local needs based on specific ecological, epidemiological, economic and social conditions.<sup>2</sup>

#### Outlook:

- Around US\$ 100 million per year are spent globally for malaria prevention and control. It has been calculated that several additional billion US\$ are necessary for effective malaria prevention and treatment, resources which are not likely to be all available. It will be necessary to set priorities at global, national and regional level

<sup>4</sup> WHO (World Health Organization) (2001). Macroeconomics and health: Investing in health for economic development. Report of the Commission on Macroeconomics and Health. World Health Organization: Geneva

<sup>5</sup> Goodmann CA, Coleman PG, Mills A (1999). Cost-effectiveness of malaria control in sub-Saharan Africa. Lancet 354: 378-385

and to promote cost-effective interventions for malaria which do include: (\*) case management, (\*) the use of insecticide-treated bednets, (\*) indoor residual spraying, and (\*) environmental control measures such as filling and draining breeding sites.

#### 4. Anti-malarial drug policies

The emergence of resistance of malaria parasites to drugs, first documented in the 1950s and 1960s is considered one of the major obstacles to successful control. Drug resistance is a concern as the cheapest and most widely available anti-malarial drugs are increasingly becoming ineffective. This is especially true for Chloroquine (brand name: Nivaquine®) which has been in many African countries the drug of first choice. For example, in eastern and southern Africa **Chloroquine resistance is very high and is rapidly spreading to other countries**<sup>6</sup>. If targets formulated during the Abuja summit in 2000<sup>7</sup> are to be achieved (e.g. reducing the number of young children who die of malaria by 400,000 per year by the year 2010), then, the raising levels of drug resistance is the key challenge.

In some African countries unfortunately resistance not only to Chloroquine is spreading, but also to alternative drugs such as sulfadoxine-pyrimethamine (SP) (brand name: Fansidar®), which were being used as first-line treatment.

**The World Health Organization (WHO) recommends countries to change their policies from single drug therapies to combination therapy**, a strategy that is thought to minimise resistance. Several African countries did so over the last year with no uniform national policies over countries<sup>8,9</sup>. Burundi for example decided to change the treatment policy to Amodiaquine plus Artesunate based on the results of efficacy studies conducted in country and on consideration of costs. More generally, combination therapies based on Artemisin, drugs derived from a Chinese herb *Artemisia annua*, are currently seen as having the highest potential for malaria therapy<sup>10</sup>.

**However, the shift to combination therapy implies various challenges.** Combination therapies require the regular availability of different drugs, an issue which is difficult to guarantee for many African health care delivery systems. The health personnel needs to be trained, in the public as well as in the private sector. The latter is known to provide especially in cities a high number of malaria treatments. Combination therapies are also

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<sup>6</sup> For more details see:

Bloland PB (2001). Drug resistance in malaria. WHO/CDS/CSR/DRS2001.4. Available at: [www.who.int/emc/amrpdfs/Drug\\_resistance\\_in\\_malaria.pdf](http://www.who.int/emc/amrpdfs/Drug_resistance_in_malaria.pdf), accessed 28. August 2002

<sup>7</sup> WHO (2000) The African summit on Roll Back on malaria. Available at: [www.rbm.who.int/docs/abuja\\_declaration.pdf](http://www.rbm.who.int/docs/abuja_declaration.pdf), accessed 29. August 2002

<sup>8</sup> For an overview on anti-malarial drug policies see: <http://mosquito.who.int/cgi-bin/rbm>

<sup>9</sup> Kindermann JM (2002). Changing national malaria treatment protocols: What is the cost and who will pay? Case studies: Burundi, Kenya, Rwanda, Tanzania and Uganda. Médecins sans Frontières

<sup>10</sup> WHO (2001). Antimalarial drug combination therapy. Report of a WHO technical consultation. WHO/CDS/RMB/2001.35, WHO, Geneva

more expensive than the historically used single drug therapies implying that new sources of financing for assisting malaria treatment have to be found or that household have to carry higher financial costs.

In October 2002, international research teams<sup>11</sup> announced that they have **completed genome sequences of the most lethal malaria-causing parasite, *Plasmodium Falciparum*, and a mosquito that transmits the parasite to humans, *Anopholes gambiae*.** Besides that this event makes possible a much fuller understanding of malaria and its transmission, in the long run, there is hope that this will speed efforts to investigate and develop control strategies in the area of vaccine and insecticide development. Ultimately, such a detailed understanding of host-parasite interactions could improve mosquito control efforts.

**There are not many options for tackling and overcoming the malaria drug resistance issue.** As long as vaccines remain a far away hope, medicines and their effective and efficient use are the most realistic option for curing malaria. However, there is urgency to discover new drugs at affordable prices for affected countries. A major obstacle to the discovery of new anti-malarials is the lack of investment in this area due to enormous costs and time needed and the disinterest of the pharmaceutical companies in making these investments in the area of malaria. Out of this reason the Malaria Medicine Venture (MMV) has been launched in 1999 as public-private partnership for addressing the development of new drugs in order to address those healthcare issues which neither the public nor the private sector can solve on their own.<sup>12</sup> MMV receives support from development agencies, foundations, industry, and health agencies and is among the first of these public-private partnerships established to tackle a major global disease. The initiative arose from discussions between the World Health Organization (WHO) and the representative body of the pharmaceutical industry, the International Federation of Pharmaceutical Manufacturers Associations (IFPMA). Early partners in these exploratory discussions were the Global forum for Health Research, the Rockefeller Foundation, the World Bank, the Swiss Agency for Development and Cooperation, the Association of the British Pharmaceutical Industry and the Wellcome Trust. MMV is currently focusing on the improvement of existing drugs such as the artemisinin derivatives and intends in the medium to longer term to bring forward new classes of drugs.

Outlook:

- Resistance to anti-malaria drugs, especially Chloroquine and Sulfadoxine-pyrimethamine, is quickly rising and various African countries have recently been shifting their treatment policies to combination therapies which often are based on Artemisin. While waiting in the mid-term for the discovery of new drugs and in the

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<sup>11</sup> The sequencing of *P. falciparum* resulted from an international collaboration established in 1996. Besides National Institute of Allergy and Infectious Diseases (NAID), consortium support came from the Wellcome Trust, the Burroughs Wellcome Fund and the U.S. Department of Defense, Sequencers worked at The Institute for Genomic Research (TIGR) in Rockville, MD, the Stanford Genome Center in Palo Alto, CA, and the Wellcome Trust Sanger Institute in the United Kingdom.

<sup>12</sup> For further information on the Malaria Medicine Venture see:  
[http://www.mmv.org/pages/page\\_main.htm](http://www.mmv.org/pages/page_main.htm)

longterm for a malaria vaccine, the improvement of existing drugs and combination therapies is the only feasible option in the area of malaria therapy. However, many things are still not known about the acceptance, the affordability and the compliance of people to combination therapies.

## 5. Intermittent Preventive Treatment

In malaria endemic countries in Africa, anaemia imposes a high burden of disease and mortality. It has been estimated that there are between one and six million cases of anaemia each year, killing several hundred thousand children below 5 years old and many pregnant women<sup>13</sup>. Iron deficiency, intestinal worm infections and HIV are important contributors to high anaemia frequencies. However, over the last years it also has become increasingly evident that **malaria is a major cause of anaemia and contributes in an important way to anaemia, particularly in countries with high malaria transmission intensities.**

Therefore, **prevention strategies based on antimalarial treatments are potentially an important intervention for anaemia prevention, specifically among women and children.** In Tanzania, a study has recently shown that a single dose of sulphadoxine-pyrimethamine, an antimalarial drug, applied at the same time as routine vaccination of the immunisation programmes (EPI) for healthy children (two, three, and nine months) can not only reduce malaria episodes in children below one year by 60% but also cut down anaemia rates by 50%<sup>14</sup>. Other antimalarial drugs are reported to have similar effects<sup>15</sup>.

These results are very promising as they indicate the feasibility of interventions against malaria and anaemia through existing channels of EPI. But before moving from research to action they need yet to be confirmed by other studies. Several issues remain to be clarified until preventive intermittent treatment can be launched at large scale among children. One issue that must be tackled is the question if the oral administration of antimalarial drugs is compatible with vaccine injections applied by EPI programmes and/or if anti-malarial drugs (especially sulphadoxine-pyrimethamine and artesunate) can be applied as a liquid formula. Another issue that must be resolved prior to large scale implementation of preventive intermittent treatment is the question of the absence of a negative influence of antimalarial drugs on the serological response of children to EPI vaccines. Finally, more knowledge is necessary on the relation between the epidemiological setting / the malaria transmission intensity and the effect of preventive intermittent treatment as it might be possible that the intervention reveals less effective in

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<sup>13</sup> Murphy SC, Breman JG. Gaps in the childhood malaria burden in Africa: cerebral malaria, neurological sequelae, anemia, respiratory distress, hypoglycaemia, and complications of pregnancy. *Am J Trop Med Hyg* (2001); 64 (1-2 suppl): 57-67

<sup>14</sup> Schellenberg D, Menendez C, Kahigwa E et al. Intermittent treatment for malaria and anaemia control at time of routine vaccinations in Tanzanian infants: a randomised, placebo-controlled trial. *Lancet* (2001); 357:1471-77

<sup>15</sup> WHO-UNICEF. Intermittent Preventive Treatment in Infants. A promising antimalarial intervention against anaemia. Available at <http://mosquito.who.int/cgi-bin/rbm/>, accessed 26. August 2002

areas of intense or seasonal transmission as the ones under study so far with a relatively low transmission rate. Various studies on the above mentioned topics have been initiated and results are expected to be available within the next year.

**The World Health Organization (WHO), the Global Alliance for Vaccination and Immunisation (GAVI) and the United Nations Children’s Fund (UNICEF) consider the current knowledge as a possible important new method for preventing malaria and anaemia through EPI.** UNICEF is considering to focus its priorities on ‘Immunization Plus’ by adding new interventions such as vitamin A supplementation and intermittent preventive treatment to the already existing EPI programmes<sup>16</sup>. First trials on scaling-up the EPI programmes might take place in 2003.

Beside children, pregnant women are one of the groups most at risk from malaria as their immunity level is reduced. It is estimated that in Africa malaria is responsible for up to 15% of maternal anaemia and for 35% of low birth-weight besides that it is also associated to higher rates of abortion and still birth. Intermittent preventive treatment appears to be a cost-effective intervention at ante-natal care level to address these problems.

Among pregnant women the intervention includes a full treatment with antimalarial drug at predefined intervals. The treatment should be initiated in the second trimester and should be applied in regular, monthly intervals. In areas with high resistance to chloroquine it is recommended that one treatment with sulfadoxine pyrimethamine during the second and third trimester is used.

Preventive intermittent treatment among pregnant women is an effective and cost-efficient intervention. So far, two African countries, Kenya and Malawi have integrated this treatment as an additional strategy in their national control programme. Others countries including Nigeria, Uganda, and Zambia are considering in doing so.

Outlook:

- Among children, there is currently not enough evidence for advocating preventive intermittent treatment at large scale, for example through EPI. However, first results are promising and indicate that the application of anti-malarial drugs has the potential of being a highly effective intervention against malaria and anaemia through and that this intervention has to be considered for inclusion in EPI programmes. Among pregnant women, preventive intermittent treatment is a relevant and cost-effective intervention against maternal anaemia and low birth-weight. Advocating and further promoting its inclusion in national strategies appears as important.

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<sup>16</sup> for further information see:

<http://www.unicef.org/programme/health/focus/community/malaria/overview.htm>

## 6. Insecticide treated bed nets

The promotion and increase in the use of insecticide-treated netting (ITN) is a key intervention for preventing malaria and as such an important component of malaria control strategies in many African countries. **Experiences during the last years have shown that ITNs significantly reduce malaria related morbidity and that regional projects such as the SDC supported Kilombero Valley treated net programme (KINET) in Tanzania<sup>17</sup> can be highly successful.**

Subsequently, the Abuja summit of African political leaders in 2000<sup>7</sup>, formulated the highly ambitious target for expanding ITN use to 60% of people at risk by 2005. Various African countries such as Tanzania and Uganda have started to scale-up their ITN activities from local and regional trials to national programmes.

KINET supported by **SDC and other projects promoting the use of ITN have allowed to learn many lessons.** These lessons do include that large-scale and untargeted distribution of free or very cheap nets is not sustainable and is likely to be counter-productive in the medium and long term. It has then been concluded that nets should not be given for free. Roll Back Malaria has recently pointed out that subsidies from governments or donors should strictly be targeted to vulnerable groups, and at a strengthened and expanded commercial market that provides ITNs at the lowest possible prices for the general population<sup>18,19</sup>. Others have pointed out that the aspiration by poor rural homesteads to protect themselves with ITNs is not compatible with their ability to pay<sup>20</sup>.

With regard to the role and function of the public and private sector it has appeared that **the promotion of ITNs should not only include the public sector, but also rely on the private sector and non-governmental organizations (NGOs).** This as the buying and selling of nets through the public sector has shown to be more costly. The exact role of these sectors depends on the African country under consideration, as health services and the private sector markets may differ heavily.

Another experience relates to the **reimpregnation of nets which constantly has been found to be very low** (usually 20% or less). One reason for this might be that insecticides are invisible and intangible and that most people are not familiar with them resulting in a low availability. Furthermore, many people perceive reimpregnation prices as too high. The prospects for nets are thus more obvious than for insecticides. Potentially governments may play an important role in subsidising reimpregnation (this is consis-

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<sup>17</sup> For further information see: <http://www.mimcom.org.uk/ifakara/KINET.htm>, or <http://www.medicusmundi.ch/bulletin/bulletin7807.htm>

<sup>18</sup> Roll Back Malaria. Scaling-up insecticide-treated netting programmes in Africa. A strategic framework for coordinated national action. Available at <http://mosquito.who.int/cgi-bin/rbm/>, accessed 23. August 2002

<sup>19</sup> SDC funded KINET in Tanzania made available discount vouchers through MCH clinics for pregnant women and those with young children. These vouchers could be used as part-payment for a treated net (approximately 15%).

<sup>20</sup> Guyatt HL, Ochola SA, Snow RW. 2002. Too poor to pay: charging for insecticide-treated bednets in highland Kenya. *Tropical Medicine & International Health* 7 (10): 846-850

tent with experience from Vietnam and China, the two countries with the longest experience in ITN promotion and where impregnation is provided for free). Another perspective relies in new technologies which are hoped to allow that the netting material becomes more long-lasting and wash-resistant, with the possibility that insecticide treatments will become as long lasting as nets (between four and five years).

Outlook:

- ITNs have become a key intervention for preventing malaria. Local and regional programmes, such as the highly successful SDC supported KINET project in Tanzania, are currently being scaled-up to national programmes. Large-scale and untargeted distribution of free or very cheap nets is not sustainable and subsidies from governments or donors should be targeted to vulnerable groups. Low and unsatisfactory reimpregnation rates of nets indicate that in the short- to mid-term governments should either subsidize insecticide use or offer them for free. In the mid- to long-term improved, long-lasting and wash-resistant impregnated nets may be a sustainable solution.

## Annexe 1. Key links

Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria:  
<http://www.globalfundatm.org/index.html>

Roll Back Malaria:  
<http://mosquito.who.int>

The African summit on Roll Back on malaria:  
[http://www.rbm.who.int/docs/abuja\\_declaration.pdf](http://www.rbm.who.int/docs/abuja_declaration.pdf)

Malaria Medicine Venture:  
[http://www.mmv.org/pages/page\\_main.htm](http://www.mmv.org/pages/page_main.htm)

Unicef and malaria:  
<http://www.unicef.org/programme/health/focus/community/malaria/overview.htm>

Kinet:  
<http://www.mimcom.org.uk/ifakara/KINET.htm>

## Annexe 2. Key references

### Economic impact of malaria

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### Anti-malarial drug policies

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Kindermann JM. 2002. *Changing national malaria treatment protocols: What is the cost and who will pay?* Case studies: Burundi, Kenya, Rwanda, Tanzania and Uganda. Médecins sans Frontières

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### Intermittent Preventive Treatment

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### **Annexe 3. Worldwide malaria risk 2002**

(adapted from SDC lunchtime presentation by C. Lengeler 2001)

