



## On the Trail of a Cure: Reality and Rhetoric on Treating Malaria

By Roger Bate

*New treatments for malaria were developed in response to a resurgence of the disease in the 1990s. Since then, funding for these treatments has increased significantly through bilateral and multilateral aid, corporate and private assistance, and national government programs in malarial countries. Yet problems in the drug purchase and delivery processes and threats to future treatments persist. These problems are relatively easy to solve, but the international community seems reluctant to tackle them, which means the funding is not being used as effectively as it should.*

In the mid-1960s, U.S. troops confined the peripatetic Vietcong (and many Vietnamese civilians) to the Ho Chi Minh Trail. This corridor was a great breeding ground for malaria-carrying mosquitoes, and one in ten travelers succumbed to the disease. Malaria was so prevalent that it killed more soldiers than combat did. In desperation, the North Vietnamese leadership appealed to their Chinese allies to assist with developing a malaria treatment. A covert Vietnamese military group convened in 1967 to search for a malaria cure identified a drug developed from the sweet wormwood plant (*Artemisia annua*), an herbal remedy that had existed for over two thousand years.<sup>1</sup> Although this medicinal discovery came too late for most of those walking the Ho Chi Minh Trail, its efficacy against malaria was astonishing.

Soon Thailand, where treatment-resistant malaria was a growing problem, began studies on combinations of mefloquine with the artemisinin derivatives, artesunate or artemether.<sup>2</sup> Each of the combinations proved highly effective in reducing the incidence of malaria. Vietnam saw the evidence of this breakthrough firsthand when extensive artemisinin derivative deployment in 1991

led to significant reductions in malaria rates.<sup>3</sup> These favorable results launched a global initiative to evaluate artemisinin-based combination therapies (ACTs) in Africa and South America.<sup>4</sup>

### The Spread of ACTs

*Artemisia annua* cultivation expanded to the West in the 1980s,<sup>5</sup> when China's economy opened up and skepticism about traditional Chinese medicine in general—and artemether in particular—diminished. Evidence was then mounting globally of rising parasitic resistance to “monotherapies” like chloroquine and—increasingly—to its replacement, sulfadoxine-pyrimethamine, which succumbed to resistance within five years of extensive use.<sup>6</sup> New remedies were required—and soon.

In association with the Swiss company Novartis, the Academy of Military Medicine in China combined a long-standing but low-resistance anti-malarial drug, lumefantrine, with artemisinin to make the first ACT, called Coartem. The drug worked faster than any previously available drug, and to date has had no documented clinical failures. Coartem, however, involved a three-day treatment regimen and was substantially more expensive than existing drugs—over two dollars

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FIGURE 1  
AFRICAN COUNTRIES ADOPTING COMBINATION THERAPIES

ACT					<b>South Africa</b>	Zambia	<b>Burundi</b> Comoros Gabon	<b>Cameroon</b> Ghana <b>Kenya</b>
AQ+SP <sup>a</sup>					Rwanda		Senegal	
CQ+SP <sup>a,b</sup>			Ethiopia	Uganda Zimbabwe		Eritrea		
SP or AQ <sup>a,b</sup>	Malawi <b>South Africa</b>	Botswana <b>Kenya</b>	Tanzania		<b>Burundi</b> Democratic Republic of the Congo	<b>Cameroon</b>	Côte d'Ivoire	
	1993	1998	1999	2000	2001	2002	2003	2004

SOURCE: Adapted from Roll Back Malaria (RBM), "Facts on ACTs: An Update on Recent Progress in Policy and Access in Treatment," fact sheet (Geneva: World Health Organization, 2004), available at [www.who.int/malaria/cmc\\_upload/0/000/015/364/RBMInfosheet\\_9.htm](http://www.who.int/malaria/cmc_upload/0/000/015/364/RBMInfosheet_9.htm) (accessed March 1, 2007).  
NOTES: a) AQ=amodiaquine, SP=sulfadoxine/pyrimethamine, CQ=chloroquine; b) none of these therapies are recommended by WHO.

per adult treatment compared with less than one cent for chloroquine.

Costs notwithstanding, South Africa became the first African country to use Coartem extensively in KwaZulu-Natal province in February 2001.<sup>7</sup> Along with DDT use, compliance with the three-day ACT regimen helped overcome an epidemic in the area. In subsequent years, several other African countries followed South Africa's lead in moving from monotherapies to ACTs (see figure 1).

In 2001, the World Health Organization (WHO) recommended that all countries experiencing resistance to conventional monotherapies, such as chloroquine against *P. falciparum* malaria, switch to combination therapies, preferably with artemisinin derivatives.<sup>8</sup> WHO commends

[t]he potential value of drug combinations, notably those containing an artemisinin derivative, to improve efficacy, delay development and selection of drug-resistant parasites and thus prolong the therapeutic life of existing antimalarial drugs. Combinations that do not contain an artemisinin derivative could be a preferred option for reasons of cost and accessibility in some countries.<sup>9</sup>

Countries that could afford to change treatment policy adopted the new drug quickly. For poorer countries,

Novartis agreed to subsidize Coartem production and distribution.<sup>10</sup> Given the costs of the new drugs, supply-chain management, and training for doctors and nurses, donor-dependent nations claimed to be unable to afford the transition, and donors were equally reluctant to foot the bill in a timely fashion.

When the Global Fund to Fight AIDS, Tuberculosis and Malaria was launched in 2003, many people believed it would solve the problems of inadequate funding and weak donor commitment to malaria treatment. The Fund would act as a clearinghouse for additional funding to help countries switch to ACTs. To make it responsive to developing country requirements, the Fund was designed to support country-formulated proposals and not explicitly make recommendations, so it continued to finance chloroquine and other less-effective drugs in areas where resistance rates were unacceptably high.<sup>11</sup> But pressure from the growing malaria advocacy community eventually compelled the Fund to change its policy and move toward meeting the huge new demand for ACTs.

To its credit, the Global Fund was the first major aid agency to authorize the purchase of ACTs as first- and second-line treatments for malaria. In the latest round of grant allocations, funds for fighting malaria were substantial (\$202 million in nineteen countries)<sup>12</sup> and deserve commendation. The Fund has committed

\$30 million over the full five-year life of Fund board-approved proposals from African countries for the purchase of ACTs in three proposal rounds.<sup>13</sup> According to the Fund's 2005 annual report, 5.6 million people have been treated with antimalarial therapies, including ACTs for drug-resistant malaria.<sup>14</sup>

After a somewhat slow start, the Global Fund has become the largest financier of ACTs (see table 1), accounting for over 70 percent of the total purchased in 2006. But certain significant challenges remain.

### Global Fund Procurement: Hassles and Inefficiencies

The Global Fund's procurement process is lengthy and tedious. It is plagued by bureaucratic holdups, bloated forecasting, supply chain mismanagement, and graft. A June 2005 report by the U.S. Government Accountability Office (GAO) dubbed the entire process "cumbersome."<sup>19</sup>

In order to submit grant applications to the Global Fund, representatives from all interests—donor countries, nonprofit and nongovernmental organizations (NGOs), academics, and disease-burdened countries—assess the needs and interests of their own constituencies. These representatives constitute the Global Fund's country coordinating mechanisms (CCMs), which involve aid-recipient countries in the decision-making process. Following the Global Fund's approval of the grant, the CCM process allows the nomination of one organization, the principal recipient, to receive the bulk of the funding in order to track the implementation of the aid. For the most part, this supervisory role is given to the recipient country's finance ministry. The ministry then transfers the funds to internal recipients responsible for placing orders with the drug procurement agent, such as WHO and the United Nations Children's Fund (UNICEF). The procurement agent contacts the pharmaceutical company with the country's drug request. The next steps involve the collection of the drug order by the procurement agent and its shipment to the country for widespread distribution. The procurement process culminates in the remuneration of the participating pharmaceutical company.<sup>20</sup>

Because of the length and haphazard pattern of the procurement process, funds can sometimes be held up by government bureaucracies, even further delaying the

TABLE 1

FUNDING FOR MALARIA TREATMENTS IN MILLIONS OF DOLLARS

Aid Organization	2005–06	2006–07	Total
Global Fund <sup>15</sup>	230 <sup>a</sup>	–	230
UNICEF	10.5 <sup>16</sup>	12 <sup>17</sup>	22.5
USAID <sup>18</sup>	2.4	19	21.4

SOURCE: WHO, United Nations Children Fund (UNICEF), and U.S. Agency for International Development (USAID). NOTE: a) amount donated over two years.

procurement process. In Ghana, according to the Global Fund secretariat, the government's slow, bureaucratic procurement processes caused delays that contributed to the grant's poor performance in helping people with HIV/AIDS and opportunistic infections.<sup>21</sup>

Further anecdotal and off-the-record reports show that malaria-specific financing is often stuck in ministries of finance for months without any treatments being procured for the sick. This has allegedly happened recently in Tanzania, Chad, the Democratic Republic of the Congo, and Nigeria, among other places.<sup>22</sup>

The Fund can choose to bypass finance ministries, which are usually the nominated principal recipients, and which give the money directly to drug manufacturers for delivery to another government ministry or NGO in the field. This happened in Zambia, where the Global Fund appointed an NGO and a faith-based body as principal recipients in 2004.<sup>23</sup> And as a consequence of corruption in Uganda,<sup>24</sup> the Global Fund procured directly through WHO, bypassing corrupt Ugandan officials altogether; drugs have since been procured more effectively. But such action is the exception, not the rule. This is partly because the Fund was established to be responsive to the needs of developing countries, and it requires delicate diplomacy to explain to a health minister that his cabinet colleagues in finance are either incompetent or corrupt. Therefore, corrupt politicians in the field usually continue to reap personal benefits from funds designated to save the lives of the sick.

To exacerbate matters, many of the drugs purchased are ineffective. An article in *The Lancet* noted that in East Africa, surveillance and clinical trial data show treatment failure rates of up to 64 percent in patients given chloroquine and 45 percent given sulfadoxine-pyrimethamine—and those figures are climbing.<sup>25</sup> At least 16 percent of drugs purchased by the Global Fund in the recent past were of indeterminate quality (this

figure includes drugs for combating tuberculosis and HIV, since the Global Fund does not break it down by disease).<sup>26</sup> And while the Global Fund is more transparent than any other multilateral agency, there is still much room for improvement.

To address some transparency and reporting shortcomings, Senator Tom Coburn (R-Okla.), a physician, introduced an amendment in Congress in February 2007 to require the Global Fund “to post on a publicly available website all internally and externally commissioned audits, program reviews, evaluations, and inspector general reports and findings.”<sup>27</sup> Like his successful inquest into U.S. Agency for International Development (USAID) disease-control funding,<sup>28</sup> Coburn now aims to expose the Global Fund to much-needed sunlight. But Congress has less oversight over the Global Fund or any of the United Nations (UN) operations based in Geneva than it does over USAID. One need look only to the 2005 oil-for-food debacle as an object lesson in how the UN’s expense accounts operate. The GAO, however, has some oversight over the UN, and it has been granted access to Global Fund data. The raw data that the GAO gets to see, however, is not available to anyone else—only the reports it issues can be made public. Without those data it is impossible to do external evaluations. Since it took Senator Coburn to expose failings at USAID, something the GAO largely failed to do, one should not expect the GAO to adequately address any failings of the Global Fund.

Of grave concern to Coburn is the fact that there are no consequences for waste, fraud, or abuse, primarily because the Fund is allowed to hide them. Even when the Global Fund’s inspector general (IG) issues a report, it is not available to Congress. According to an article in the *Boston Globe*,<sup>29</sup> the IG has attacked the spending of outgoing executive director Richard Feachem on items such as limousines, yachts, and entertainment. These expenses may have been legitimate, but one has to be skeptical: the Global Fund’s secretariat established a bank account with Credit Suisse to bypass its normal expense reimbursement processes. Congress has been denied access to the IG report on these expenditures, even though the United States has given almost \$2 billion to the Global Fund and will increase that sum to

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over \$2.7 billion by the end of 2007. The IG report on the Credit Suisse account was prompted only after a report by Deloitte declared that the account might be inappropriate. Oddly, the IG charged with coordinating this interrogation has now resigned, citing “health concerns.” Feachem claims the allegations are false. He informed me that the *Boston Globe* article contains “serious mistakes, inaccuracies, and false allegations—some of which are incorrectly attributed to the report of the internal auditor.”<sup>30</sup> Coburn’s amendment was blocked when Senate majority leader Harry Reid (D-Nev.) blocked all amendments in the new Congress, but informed sources indicate that there is “bipartisan interest in ensuring that similar language [to Coburn’s amendment] will be adopted into the spending bill that funds the Global Fund in 2008.”<sup>31</sup>

### Faux Forecasts

Forecasting by UNICEF and WHO is based on need, which is qualitatively different than what economists call “effective demand,” the amount that is actually going to be purchased. There is an international community-driven moral imperative for the manufacturers to be able to deliver what is needed at any given time. This means that production estimates—driven as they are by unrealistic expectations—may be higher than effective demand. In 2004, WHO projected that the global need for ACTs in 2005 would be over 130 million.<sup>32</sup> Most of this projected demand, however, never materialized; in 2005, maximum demand was only about 25 million treatments.<sup>33</sup> WHO and UNICEF are of course health cheerleaders, aiming for higher spending but bearing no cost for wildly unrealistic projections.

The long production cycle of ACTs—the key ingredient, *Artemisia annua*, needs a growth cycle of six months or more to mature—coupled with its short shelf life of only twenty-four months, make accurate demand forecasts essential.<sup>34</sup> Overestimation of demand means that excessive risk is taken on by manufacturers (and potentially farmers), but not really by anyone else in the supply chain. Given the contracts manufacturers have with farmers, the former usually bears all the risk. Better demand forecasting is even more important when one considers the fact that pharmaceutical companies are trying to provide the drugs at close to zero profit. Coartem demand forecasts have

been notoriously unreliable, resulting in shortages in 2004 followed by excess inventory in 2005 and 2006.<sup>35</sup>

As a result, major suppliers such as Novartis and Sanofi-Aventis have either destroyed product or declared a substantial loss in the past few years.<sup>36</sup> In December 2006, when funds were supposed to be flowing to treatment, Novartis shut down its production facility in Suffern, New York, to prevent too much medicine with a short shelf life from being produced. Therefore, unrealistically high estimates of the quantities of drugs needed by a particular country present several problems for drug manufacturers.

To shed light on the perils of poor demand forecasting and to sketch out potential solutions to this critical issue, the Center for Global Development convened a Global Health Forecasting Working Group in early 2006. Key recommendations from its report, published in February 2007, reveal that demand forecasting can be enhanced by “improving the capacity to develop credible forecasts; mobilizing and sharing information in a coordinated way; and sharing risks through contractual arrangements that are relatively new to global health but have been used successfully in other fields.”<sup>37</sup> The authors of the report believe that these recommendations “would result in a major enhancement in the relationship among funders, suppliers, intermediaries and users of health products, and go a significant distance toward achieving the sort of alignment across participants in the global health value chain that is essential for long-term improvements in access to quality products.”<sup>38</sup> The authors highlight the fact that in the procurement of ACTs, suppliers bear nearly all of the supply-side risks (inventory, storage, and drug safety), as well as the demand-side risks (grant approval timing and pricing), with national governments bearing only the risk that donor supplies may not be sustainable. The donors (Global Fund, USAID, etc.) bear almost no cost for the wildly unrealistic forecasts made by UN agencies such as WHO and UNICEF.<sup>39</sup>

One simple method for donors to ensure supply is to actually put their taxpayers’ money where their mouths are and purchase the products themselves, thereby taking on some of the risk borne by the manufacturers. In 2004, for instance, when WHO predicted that demand would surpass 100 million doses in 2005, few donors bought ACTs. In September 2004, I challenged USAID and other donors to actually buy ACTs, but it was not until 2006 that USAID and most others did so in any meaningful quantity.<sup>40</sup>

## Shortchanging Innovators

It appears that innovator companies—those companies which undertake research and development into new innovative products—are losing their market share of the drug purchases made with Global Fund financing.<sup>41</sup> The Global Fund and charitable foundations such as the William J. Clinton Foundation and UNITAID—an international drug purchasing and delivery NGO established by, among others, British chancellor of the exchequer Gordon Brown<sup>42</sup>—apparently in an effort to encourage market competition, have begun making advanced purchase deals with generic drug producers from India for upfront supply. Field sources suggest that Pakistan, Nigeria, Kenya,<sup>43</sup> Mozambique, and Ghana are buying very cheap antimalarials of uncertain quality.<sup>44</sup> Uganda is allegedly about to do the same.<sup>45</sup>

On the one hand, the arrival of new producers can stimulate supply. On the other hand, it has the negative effect of depriving innovator companies of revenue to offset substantial upfront costs. Declining market share for the innovators could mean they might have to quietly leave the business of providing antimalarial drugs at no profit. UNITAID is delaying delivery, possibly because Novartis, the market leader—and not a small competitor firm—won the tender. As the lowest bidder, Novartis was presumed to have won the contract, but UK government sources report that UNITAID is likely to share allocation in order to ensure that some of the tender amount of 15 million treatments goes to encourage smaller copy producers like India’s Cipla and Ajanta Pharma.

## More Important Problems: The Global Fund’s Compliance List

The Global Fund’s compliance list includes antimalarial drugs classified according to the Fund’s quality assurance policy. The list puts antimalarials into three distinct categories: products acceptable under the WHO Prequalification Program (A products), products authorized for use by a stringent regulatory authority (B products), and a final category of drugs classified as Ci or Cii products. Ci therapies are those submitted for prequalification, while Cii therapies have not yet been submitted. Although both C types of drugs are manufactured in production facilities WHO has approved for production of at least one drug (rarely an antimalarial), a C antimalarial has not passed bioequivalence testing.<sup>46</sup> Out of the thirty-three malaria

drug treatments listed, only four are designated “acceptable under the WHO Prequalification Program” or as “products authorized for use by a stringent regulatory authority.”<sup>47</sup> Moreover, Coartem is the only drug in categories A and B; the vast majority of the drugs listed have no bioequivalence data at all. Yet increasing numbers of these non-WHO approved drugs are being purchased.<sup>48</sup>

The Global Fund’s listing of therapies—particularly monotherapies—not approved by WHO has raised many concerns. Given the vital importance of artesunate, WHO policy is that it should never be used as a monotherapy, which reduces the odds of resistance development. Yet the Global Fund has listed artesunate monotherapy as an acceptable alternative to more expensive ACTs. To further complicate the issue, amodiaquine (AQ), listed as a partner drug to artesunate on the Global Fund’s list, has been shown to lead to recurrent infections of the disease. Among Kenyan children treated with the monotherapy in 2005, scientists found a “high prevalence of AQ-resistant parasites.”<sup>49</sup> Resistance to AQ in other parts of Africa has been inadequately tested. Therefore, ACTs with artesunate+AQ will be equivalent to monotherapy artesunate in some settings.<sup>50</sup> Since the choice of the partner drug is vital for any ACT to remain effective over time, these developments present serious concerns. The head of the WHO malaria program, Arata Kochi, has for this reason criticized the Global Fund for instigating the rise of drug resistance. Of particular concern to Kochi is the fear that some drug companies may seek to exploit the gap created by the Global Fund’s compliance list and boost their own monotherapy sales, a situation which will detrimentally affect the earnings of innovator companies.<sup>51</sup> Recently, the decision of China’s Kunming Pharmaceutical to continue with the sale of its monotherapy pill, despite concerns about the drug’s emerging resistance to the disease, shows that Kochi’s qualms are not without merit.<sup>52</sup>

Furthermore, as ever more competitors enter the market, innovator companies such as Sanofi-Aventis and Novartis face the risks of overproduction, given the contracts they have with farmers to purchase *Artemisia annua*. Such product loss and higher costs make it less likely that both companies will maintain a local presence that enables them to monitor potential failures of

their drugs (known as pharmacovigilance), and to react to prevent any treatment failure. None of the companies producing copies of ACTs or monotherapies undertake such activity.

In spite of these concerns, innovator companies are pressing on with various initiatives to bring new and existing treatments into the field. Novartis is working with Medicines for Malaria Venture to develop a pediatric version of Coartem.<sup>53</sup> Sanofi-Aventis, a firm with a long history in antimalarial drug research and development in quinine, chloroquine and amodiaquine,<sup>54</sup> is working with the Global Alliance for Vaccines and Immunization on a vaccine. In April 2005, Sanofi-Aventis also signed a collaborative agreement with the Drugs for Neglected Diseases Initiative to develop a new medicine against malaria.<sup>55</sup> This fixed-dose combination of artesunate and amodiaquine will be easier to use and cheaper than any other combination currently available (although it will contain amodiaquine, which may exhibit resistance problems in some settings). The drug, launched on March 9, 2007, is expected to be available to patients in sub-Saharan Africa later in the year.<sup>56</sup>

Novartis is taking its commitment even further, having recently established a new facility in Singapore to conduct research on malaria (as well as tuberculosis and Dengue fever).<sup>57</sup> This multimillion-dollar project is run by Alex Matter, who has screened the entire Novartis drug library (over 2 million compounds) for substances that may be effective vaccines and antimalarials.<sup>58</sup> So far, Matter and his team have identified 17,000 compounds active against malaria.

As admirable and promising as these efforts are, one has to question the sense of a for-profit company pursuing a perpetually nonprofit venture. Another consideration is the long-run impact of shareholder pressure on companies that continue to lose money on operations for which they get little credit or goodwill recognition in the other column of the balance sheet. While many U.S. companies’ share prices have fallen over the past five years, Sanofi-Aventis and Novartis remain anomalies, with both outperforming the market. But this performance may not be everlasting. Novartis donates about 2.2 percent of its revenue (in-kind and financial) every year to help combat diseases such as malaria.<sup>59</sup> Compare this with the UN member nations’ pledge of government aid

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Corrupt politicians in  
the field usually  
continue to reap  
personal benefits from  
funds designated to  
save the lives of  
the sick.

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of 0.7 percent of GDP per year, honored more in the breach than the observance. But if Novartis fails to perform so well in the future, perhaps this 2.2 percent of revenue will need to be reclaimed.

## The Way Forward

The Global Fund's funding for malaria treatment is commendable. The time is long overdue, however, for the Global Fund to improve its transparency, establish the quality of the drugs it will allow to be purchased with its funds, and establish where the drugs it purchases actually end up. It must also streamline its procurement system, bypassing lazy, incompetent, and corrupt bureaucracies. Countries that currently do not have the capacity to procure drugs on their own would be helped by the establishment of a centralized procurement center to coordinate with countries to calculate the quantity of drugs that can actually be used, while working with other agencies to expand capacity to enable countries to receive more in the future.

Wealthy funding agencies need to join innovator companies in producing useful demand forecasts in recipient countries. The agencies have to underwrite some of the risk involved in this process as well, thus improving the quality of forecasting. Improved country data collected by WHO or some other agency would be valuable in forecasting demand.

Like other donors, UNITAID should establish grants for multiple years. Countries need sustainable support, not media attention—grabbing, one-time donations. Transparent competitive bidding for supply contracts is important, without arbitrary changes of rules if the “wrong” supplier wins. And if the cheapest tender is of uncertain quality, it should be rejected. It appears that while USAID is trying to adhere to these approaches, UNITAID is politically biased toward copy manufacturers. This may prove counterproductive and short-sighted.

Sanofi-Aventis and Novartis are the only two companies doing research into new malaria drugs and new formulations of existing drugs, and while board-level support for loss-making charitable projects is still strong, support could be undermined if the procurement processes of UNITAID, the Global Fund, and other donors are perceived to be passive, nontransparent, and overly biased in favor of drug copiers.

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AEI research assistant Kathryn Boateng and editorial assistant Evan Sparks worked with Mr. Bate to edit and produce this Health Policy Outlook.

## Notes

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15. WHO, Global Malarial Programme, "Facts on ACTs: January 2006 Update," January 2006, available at [www.searo.who.int/LinkFiles/Drug\\_Policy\\_RBMInfosheet\\_9.pdf](http://www.searo.who.int/LinkFiles/Drug_Policy_RBMInfosheet_9.pdf) (accessed March 9, 2007).

16. Of the \$10.5 million worth of antimalarials procured by UNICEF's supply division in 2005, ACTs accounted for \$8.5 million of the amount providing over 9 million ACT treatments. For further details, see United Nations Children's Fund, "Supply Division Annual Report 2005," available at [www.unicef.org/supply/files/SD\\_AnnualReport\\_2005.pdf](http://www.unicef.org/supply/files/SD_AnnualReport_2005.pdf) (accessed March 9, 2007).

17. Melanie C. Renshaw (UNICEF senior malaria advisor), telephone conversation with author's staff, March 1, 2007.

18. In coalition with the President's Malaria Initiative (PMI), USAID in fiscal year (FY) 2006 allocated almost \$2.4 million for the procurement of ACTs and antimalarial drugs (out of the total PMI budget of \$30 million) in the first three focus countries: Uganda, Tanzania, and Angola. In FY 2007, PMI is allocating nearly \$19 million for ACTs and antimalarial drugs in seven focus countries, expanding to Malawi, Mozambique, Rwanda, and Senegal. For further details, see U.S. Agency for International Development, "Artemisinin-Based Combination Therapies Effective in Treating Drug-Resistant Malaria," program description, available at [www.usaid.gov/fightingmalaria/news/voices/acts\\_mozambique.html](http://www.usaid.gov/fightingmalaria/news/voices/acts_mozambique.html) (accessed March 12, 2007).

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21. GAO, *Global Health*, 26 n. 20.

22. Without alleging any corruption, Sanofi-Aventis spokesman René Cazetien said that his company produced 917,000 treatments of ART-AM for May 2006 delivery in the Democratic Republic of the Congo, but as of December 2006 they remained undelivered pending confirmation of the order.

23. Ruairí Brugha et al., "Global Fund Tracking Study: A Cross-Country Comparative Analysis" (draft study, GFATM, Geneva, August 2, 2005), available at [www.theglobalfund.org/en/files/links\\_resources/library/studies/IE13\\_full.pdf](http://www.theglobalfund.org/en/files/links_resources/library/studies/IE13_full.pdf) (accessed March 1, 2007).

24. Uganda had a Global Fund grant suspended for mass corruption. For further details on this story, see Felix Osike, "Uganda Loses \$16M Global Fund Aid," *New Vision* (Kampala), March 11, 2007.

25. Amir Attaran et al., "The World Bank."

26. The exact number was 635 out of 3,935 treatments. For further details, see GFATM, "Implementation of the Quality Assurance Policy" (records, Sixth Portfolio Committee Meeting, Geneva, February 22–23, 2007).

27. *Revised Continuing Appropriations Resolution of 2007*, HJRes 20, 110th Cong., 1st sess., SA 252, *Congressional Record* 153 (February 12, 2007): S 1870.

28. Senator Coburn hosted several key hearings exploring the efficacy of USAID's malaria programs in 2004 and 2005. He once likened the new criticisms to bursts of sunlight shining on the malaria program. The Senate subcommittee hearing in May 2005, coupled with persistently unfavorable coverage in the academic and popular press, marked a turning point for USAID's Bureau for Global Health. For further details, see Roger Bate, "Blind Hydra: USAID Policy Fails to Control Malaria," testimony before the Senate Committee on Homeland Security and Government Affairs, Subcommittee on Federal Financial Management, Government Information and International Security, *Examining USAID's Anti-Malaria Policies*, 109th Cong., 1st sess., May 12, 2005, available at [www.aei.org/publication22508/](http://www.aei.org/publication22508/).

29. John Donnelly, "Disease-Fighting Fund's Expenses Hit," *Boston Globe*, February 5, 2007.

30. Richard Feachem (GFATM executive director), personal communication with the author, February 13, 2007.

31. Senior Senate staffer, personal communication with the author, February 12, 2007.

32. WHO, Global Malarial Programme, "Meeting on the Production of Artemisinin and Artemisinin-Based Combination Therapies."

33. Lee Wells (Novartis) and René Cazetien (Sanofi-Aventis), personal communication with the author, February 25, 2007. Novartis supplied 9 million treatments of Coartem in 2005, which at the time was the most widely used ACT.

34. Dana G. Dalrymple, "Artemisia, Agriculture and Malaria in Africa: The Interplay of Tradition, Science and Public Policy" (working paper 1, International Center for Underutilised Crops, Colombo, Sri Lanka, July 1, 2006), available at [www.icuc-iwmi.org/files/Publications/Artemisia%20Agriculture%20and%20Malaria%20in%20Africa%20Consolidated-WHO%20.pdf](http://www.icuc-iwmi.org/files/Publications/Artemisia%20Agriculture%20and%20Malaria%20in%20Africa%20Consolidated-WHO%20.pdf) (accessed February 28, 2007).

35. Center for Global Development, *Consultation Report of the Global Health Forecasting Working Group* (February 2007),

available at [http://blogs.cgdev.org/globalhealth/archive/demand\\_forecasting/](http://blogs.cgdev.org/globalhealth/archive/demand_forecasting/) (accessed March 1, 2007).

36. Jessica Pickett, "Novartis Reduces the Price of Anti-Malarials below Costs," Global Health Policy blog, October 31, 2006, available at [http://blogs.cgdev.org/globalhealth/2006/10/novartis\\_reduce.php](http://blogs.cgdev.org/globalhealth/2006/10/novartis_reduce.php) (accessed March 1, 2007).

37. Center for Global Development, *Consultation Report of the Global Health Forecasting Working Group*, 55.

38. Ibid.

39. Ibid., 22.

40. Roger Bate, "Malaria in Africa," testimony before the House Committee on International Relations, Subcommittee on Africa, *Malaria and Tuberculosis in Africa*, 108th Cong., 2nd sess., September 14, 2004, available at [www.aei.org/publication21202/](http://www.aei.org/publication21202/).

41. GFATM, "Implementation of the Quality Assurance Policy."

42. Roger Bate, "Misguidance," *New York Sun*, December 13, 2006, available at [www.aei.org/publication25280/](http://www.aei.org/publication25280/).

43. At a seminar at the Safari Park Hotel in Nairobi, Kenya, on March 1, 2007, Willis Akhwale, the malaria program coordinator for the Kenyan government, said that his government would be buying Cipla's ACT later in 2007. When challenged that this drug was not proven to be bioequivalent to the drug it was copying (Coartem), he immediately backed down and said the order had not yet gone through.

44. It is important to note that Indian copycat drugs are often not tested for bioequivalence, which means they may not work properly. Patients may die or relapse. Survivors may become resistant to the drugs, undermining the only class of malaria treatments currently available for which resistance is not exhibited.

45. For further discussion of drugs of questionable quality, see Donald G. McNeil Jr., "In the World of Life-Saving Drugs, a Growing Epidemic of Deadly Fakes," *New York Times*, February 21, 2007.

46. For more information on the categories of approved products, see GFATM, "Global Fund Compliance List for Single and Limited Source Pharmaceutical Products," March 2, 2007, available at [www.theglobalfund.org/pdf/guidelines/Compliance\\_list\\_MALARIA.pdf](http://www.theglobalfund.org/pdf/guidelines/Compliance_list_MALARIA.pdf) (accessed March 9, 2007). According to the U.S. Food and Drug Administration (FDA), bioequivalence is "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered

at the same molar dose under similar conditions in an appropriately designed study." See FDA, Center for Drug Evaluation and Research, "The FDA Process for Approving Generic Drugs: Definition of Bioequivalence," slide presentation, October 29, 2002, available at [www.fda.gov/cder/ogd/02-10\\_BCBS\\_gjb/sld028.htm](http://www.fda.gov/cder/ogd/02-10_BCBS_gjb/sld028.htm) (accessed March 13, 2007).

47. Ibid.

48. GFATM, "Implementation of the Quality Assurance Policy."

49. Gabrielle Holmgren, José P. Gil, Pedro M. Ferreira, Maria I. Veiga, Charles O. Obonyo, and Anders Björkman, "Amodiaquine Resistant *Plasmodium falciparum* Malaria In Vivo Is Associated with Selection of *pfprt* 76T and *pfmdr1* 86Y," *Infection, Genetics and Evolution* 6, no. 4 (July 2006): 309–14.

50. Coartem contains lumefantrine, which was never used as a monotherapy and hence has no resistance problems. Amodiaquine was used as a monotherapy, which is why resistance is a problem.

51. Andrew Jack, "WHO Warns Global Fund on Malaria Policy," *Financial Times*, May 14, 2006.

52. Betsy McKay and Nicholas Zamiska, "Global Health, China's Pride on Line in Malaria Clash," *Wall Street Journal*, March 6, 2007.

53. Ann M. Thayer, "Fighting Malaria," *Chemical & Engineering News*, October 24, 2005, available at <http://pubs.acs.org/cen/coverstory/83/8343malaria.html> (accessed February 28, 2007).

54. Ibid.

55. Sanofi-Aventis and Drugs for Neglected Diseases Initiative, "New, Once-a-Day Drug Fixed Dose Combination against Malaria Now Available," news release, March 1, 2007, available at [http://en.sanofi-aventis.com/Images/070301\\_DNDI\\_en\\_tcm24-16018.pdf](http://en.sanofi-aventis.com/Images/070301_DNDI_en_tcm24-16018.pdf) (accessed March 1, 2007).

56. René Cazetien, personal communication with the author, January 15, 2007.

57. The Novartis Institute for Tropical Diseases was cofounded by Novartis with the Wellcome Trust, the Bill & Melinda Gates Foundation, the Swiss Tropical Institute and Singapore's Economic Development Board.

58. Matter's team is studying helicases, cyclohydrolases, hexose transporters, novel peroxides, and plasmodial kinases, among other approaches. They have eleven staff members working in Singapore on malaria, collaborating with many around the world. See Alex Matter, personal communication with the author, January 24, 2007.

59. Paul Herrling (Novartis), personal communication with the author, January 24, 2007.