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A Competitive Analysis of Malaria Markets

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Abstract

This paper uses competition analysis to examine the malaria market and strategies that large buyers such as the Global Fund can use to increase access to anti-malarial medicine. We reach two principal conclusions. First, even small increases in competition can have a dramatic impact on global health goals. Thus, further efforts to increase competition are likely warranted and will likely save thousands of lives. Second, when considering different strategies to increase competition, we believe that efforts to increase competition among existing competitors may be more effective than efforts to increase the number of competitors, with the former strategy involving changing the bidding and procurement process by which large purchasers contract with QAACT suppliers.

Keywords: Market structure, competition, global health, malaria, developing countries

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I. Introduction

Competition is not necessarily the first thing one would think of when trying to increase access to essential medicines in low and middle income countries. Yet competition has become a focal point for important government and supranational organizations addressing global health. The virtues of competition in industry in general have given rise to agencies developed to ensure its existence (e.g., U.S. Department of Justice's Antitrust Division and the Federal Trade Commission in the U.S.). However, those charged with oversight of competition recognize that competition is a means, not an end; that is, competition is not encouraged or promoted for its own sake, but only encouraged to the extent that it increases welfare.

Determining welfare is difficult and often requires balancing different objectives such as the benefits of increased competition today versus the benefits of increased future competition. In other cases, tradeoffs may arise because limited demand for certain medicines may, absent intervention, result in a limited number of competing suppliers. And while it may be possible to intervene in the market to increase the number of competing suppliers and thus lower market prices, those interventions have their own costs. Thus, simple pronouncements that competition should be increased are not always correct.

There is also the question of how to view individual governments and multilateral organizations such as the Global Fund to Fight Aids, Tuberculosis and Malaria (GF) and GAVI that seek to provide low-cost medicines and aid to individuals in Africa and other countries. GAVI and the GF are comprised of governments (as well as other significant players) who are used to exercising authority in competition matters within their own borders. But while those government bodies have no similar authority over competition that occurs outside their own borders, those entities can nevertheless promote policies that affect competition.

Government bodies, however, can also usefully be viewed as major purchasers of essential medicine for use in other countries. As such, those entities have incentives to stimulate competition among existing suppliers, or increase competition by attracting new suppliers, if that will reduce procurement costs. In this way, individual countries and multilateral aid organizations have similar incentives as other private purchasers such as large auto manufacturers seeking to lower their costs via mechanisms such as ensuring multiple suppliers. Thus, for many strategies, the analysis is the same whether we are thinking of this as policy or as the appropriate procurement strategy for a large buyer and in those cases, we will often use the language of a competition authority. In other cases, it will be clear we are looking at this from a large buyer's perspective.

We consider these issues of how and when competition can be used and increased to improve welfare and lower procurement costs in the context of a specific, but very important, disease area: malaria. Although malaria can be easily and cheaply treated, malaria kills more than 400,000 individuals each year, mainly in Africa and Southeast Asia. Most of those deaths are of children under the age of five. Individuals remain untreated because, as with any buyer, budget constraints limit the purchase of anti-malaria (AM) medicines.[1] Increased competition that lowers the price of those AM medicines is an important means by which to relax that budget constraint and thus allow increased purchases of medicine without an increase in overall expenditures.

This paper discusses the extent to which increased competition with respect to anti-malarial medicines can increase welfare, and the different strategies by which to achieve that increased competition. We focus on three malaria-related markets: the market in which quality-assured artemisinin combination therapy (QAACT) medicines are sold by manufacturers to large buyers such as the GF or individual countries; the upstream input market in which artemisinin, a key input to QAACT medicines, is sold; and the downstream retail market in which AM medicines are sold to individuals.

1 There are a number of other strategies for addressing malaria including insecticide treated bed nets, spraying and chemoprevention. Although this paper focuses on the effect of competition on the price of antimalarials because of the importance place on that by global health organizations, a more global perspective requires decisions on how budgets and effort should be allocated across across these different malaria treatments (as well as how to allocate budgets across the treatment of different illnesses).

Although there may only be limited scope for increasing the number of competing QAACT manufacturers, even very small price decreases can potentially save tens of thousands of lives. Thus, even small increases in competition are worth pursuing. Moreover, even though it may be difficult to increase the number of competing QAACT manufacturers, there is significant scope for increasing competition among existing QAACT manufacturers by changing the manner in which QAACT medicine is procured. In particular, competition can likely be significantly increased, and with little cost, if purchasers become more selective with respect to the suppliers with which they contract.

We also observe that competition in the upstream artemisinin market is important, and that further work is warranted to better understand how the introduction of lab-produced semi-synthetic artemisinin (SS-ART) will affect the supply of agricultural artemisinin (AG-ART), and whether SS-ART is a potential threat to future AG-ART supply. And finally, while not our focus, we touch on several market failures in the downstream retail market that may reduce the effectiveness and even the desirability of increasing competition in that market.

II. Malaria and anti-malarial medicines

Malaria is a disease of low- and middle-income countries. While common in North America, Europe and other high-income countries as late as World War II, it is now largely limited to sub-Saharan Africa and lower-income regions of Asia and Eastern Europe.

The World Health Organization (WHO) estimates that there were approximately 214 million cases of malaria, and approximately 438,000 malaria deaths, in 2014. Approximately 70–80% of deaths in sub-Saharan Africa were of children under the age of 5, making malaria one of the leading causes of childhood death in that region.[2] This death count, however, understates the true cost of malaria: malaria also affects millions more who, while they recover from the disease, are temporarily disabled. In fact, the WHO estimates that a malaria-stricken family loses a quarter of its income due to lost earnings and associated costs of the disease.[3]

Malaria is a parasitic disease carried and transmitted by the Anopheles species of mosquito. Because weather affects mosquito populations, there can be significant and unanticipated variation in year-to-year demand for treatment. Although there are several different AM medicines, malaria is becoming increasingly resistant to many of those malarial medicines.[4] Chloroquine, heavily relied upon after World War II, and sulphadoxine-pyrimethamine (SP), are now largely ineffective against malaria in most parts of Africa and Southeast Asia. The most effective medicines in most parts of the malaria-prone world, and the only ones currently endorsed by

2 WHO Malaria Fact Sheet No. 94, October 2015, available at http://www.who.int/mediacentre/factsheets/fs094/en; and Unitaid Malaria Medicines Landscape, March 2015.

3 WHO African Malaria Day Fact Sheet, available at www.rbm.who.int/docs/AMD/factsheet.

4 We generally refer to a "medicine" as a particular molecule or, in the case of combination therapies, a combination of molecules. A particular medicine can come in different strengths (e.g., 100 mg vs. 250 mg), different formulations (e.g., tablet v. liquid), and different packaging (e.g., 12 tablets vs. 20 tablets).

the WHO for general treatment, are artemisinin combination therapies (ACT), a combination of an artemisinin-based drug and a second drug.[5] Simple malaria can typically be cured by following a 3-day ACT treatment protocol for which the wholesale cost of the medicine can be less than $1.[6]

Although there are many ACT manufacturers, there are a limited number of manufacturers that are designated by the WHO as Quality Assured ACT (QAACT) manufacturers. Those QAACT manufacturers must go through a costly regulatory approval process to ensure quality of output. The international donor agencies such as the GF and the U.S. President's Malaria Initiative (PMI) limit funding to manufacturers meeting the WHO's quality assurance criteria.[7]

III. Saving lives by relaxing budget constraints

In an ideal world, malaria deaths could be reduced by simply purchasing and distributing more anti-malarial medicine. Unfortunately, in a world of constrained budgets, that approach to reducing malaria deaths requires increased expenditures and is likely infeasible.[8] Thus, rather than try to reduce malaria deaths by calling for increased expenditures on AM medicines, purchasers need to work more efficiently with existing funding so that they can purchase more medicine with the same budget. Reducing AM prices through increased competition is one way of doing this—in effect, relaxing a binding budget constraint by lowering price rather than increasing expenditures.

Estimating the number of lives that can be saved by relaxing the budget constraint through increased competition, as well as the benefits to those who otherwise would fall ill but ultimately recover, is critically important for entities such as the GF and PMI. Purchasers of AM medicines need to choose how to allocate limited resources between different projects such as alternative malaria strategies (e.g., insecticide treated nets, spraying and chemoprevention) as well as treatment and prevention of other diseases (e.g., tuberculosis and HIV/AIDS). Ultimately, these entities need to know the payoff from efforts to increase competition among AM suppliers relative to other potential uses of those resources. Measuring the payoff in terms of the number of saved lives is one useful measure of that payoff.[9]

Estimating the number of lives that would likely be saved from increasing competition among AM suppliers is a difficult proposition. To determine more precisely how many lives would be saved from increased competition, we would need better information regarding several factors:

- The effect of a strategy on the price of the product;

5 There are currently 6 QAACTs currently approved by the WHO. The most commonly used ACT is artemether-lumefantrine (AL), accounting for approximately 73% of all QAACT treatments. The next most commonly used QAACT is artesunate-amodiaquine (AS-AQ), used for approximately 26% of QAACT treatments. The remaining 4 QAACT treatments collectively constitute just 1% of treatments, and consist of artesunate-mefloquine (AS-MQ), artesunate-sulfadoxine-pyrimethamine (AS-SP), dihydroartemisinin-piperaquine (DHA-PQP), and artesunate-pyronaradine-tetraphosphate (AS-PY). (WHO 2014 World Malaria Report) Artemisinin mono therapy (AmT) medicines – an artemisinin-based drug without a second drug - are also available. While the effectiveness of AmTs are comparable to ACTs, AmTs do not help to slow drug resistance to artemisinin.

6 Novartis recently reported a public-sector price of just $0.80 for its Coartem product. (See Novartis, "A committed partner in the fight against malaria," available at https://www.novartis.no/downloads/pdf/spc/Malaria_Initia-tives.pdf.) Costs for pediatric dosages are lower. (See, for example, Okell et al, "Contrasting Benefits of Different ART combination therapies as first-line malaria treatments using model-based cost-effectiveness analysis," *Nature Communications,* Nov. 26, 2014.) The costs of treating severe malaria can be much higher: patients with severe are typically hospitalized, thus requiring more intensive and costly medical care.

7 The PMI is limited to purchasing from manufacturers approved by the U.S. Food and Drug Administration (FDA) unless there is no FDA-approved supplier. In that case, or if product from the FDA-approved supplier(s) is unavailable, the PMI can purchase drugs that are WHO pre-qualified.

8 Alternatively, as discussed below, it would require diverting funding from other important areas, such as funding the provision of insecticide-treated nets to reduce malaria incidence, or treating other diseases such as tuberculosis.

9 Alternatively, one could try to estimate payoff in terms of the number of disability-adjusted life years (DALYs), thus taking into account not just impact on mortality rates but also illness in which the individual recovers.

- The effect of a price change on the quantity that can be purchased with a given budget;
- The percentage of treatments administered that actually save lives.

The first two factors above can be estimated using available techniques from the competition literature. The third factor is more difficult. To our knowledge, while we have estimates of number of lives lost to malaria, there is no estimate of what percentage of AM treatments save lives.[10]

Although we do not seek to precisely estimate the number of lives that can be saved through increased competition, our estimates show that even very modest increases in competition have the potential to save thousands of lives. Thus, the payoff to efforts to increase competition appear to be substantial. We estimate this payoff as follows.

We first approximate the potential number of lives that can be saved for each 1% reduction in QAACT prices. Assume a 1% competition-related price reduction for QAACT medicines. If the supply of ACT is relatively elastic (i.e. more output can be supplied without firms' realizing a significant increase in marginal cost), and assuming non-acquisition costs (e.g., transportation costs) account for approximately 30% of QAACTs' total costs,[11] then a 1% ACT price reduction would allow an 0.8% increase[12] in the volume of medicine purchases without any increase in expenditures. And as long as the marginal efficacy of ACT treatment is largely unchanged,[13] those additional medicines will in turn increase the number of saved lives by 0.8%.

Estimating the absolute number of saved lives from increasing treatment rates by 0.8% requires additional information. The challenge is that, as mentioned earlier, we have no definitive way of knowing the number of lives saved as a result of malaria treatment. Most treatments do not save lives because less than half of all treatments are given to patients that actually have malaria, the patient would have recuperated without treatment, or the patients effectively waste the treatment because they fail to follow proper treatment protocols.[14] Yet, even if as few as 1% of incremental treatments were to save a life, then an 0.8% increase in the 2014 total

10 As discussed further below, many AM treatments are given to individuals that are not actually ill with malaria. In addition, many treatments are given to ill patients (particularly adults) that would have recovered without treatment.

11 Estimate based on conversations with procurement officials in Kenya and Rwanda.

12 Equal to (1.3 – 1.29) / 1.3 = 0.77%.

13 The extent to which this assumption holds may differ across countries depending on the specifics of their supply-chain. In countries that frequently experience ACT stock-outs due to lack of medicine and in which additional supply would likely flow to those stock-out areas, the assumption is more likely to hold. In contrast, in countries where additional ACT supply would likely end up largely unused, perhaps due to supply chain problems that prevent medicine from being directed to areas of need, the marginal efficacy of additional ACT medicines may be low.

14 WHO 2015 World Malaria Report; Meek and Nankabirwa (2014) discuss a 2012 study finding that roughly one-third of all AM medicines being sold were falsified or sub-standard (Meek, S. and Nankabirwa, J., "Access to Quality Medicines and Other Technologies Task Force," March 2014). See also Bate, R., et. al, "Antimalarial Drug Quality in the Most Severely Malarial Parts of Africa: A Six-Country Study," Plos@ ONE 3, no. 5 (May 7, 2008), available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2324203/; Alphs, S., and Yadav, P., "Malaria in the Asia-Pacific: Challenges and opportunities for access to quality malaria medicines and other technologies," William Davidson Institute at the University of Michigan, October 2012, available at http://wdi.umich.edu/wp-content/uploads/Malaria-2012-Issues-paper-No-3-2.pdf; Dupas, P., "Getting Essential Health Products to their end users: Subsidize, but how much?" Science, September 12, 2014; and Arrow (2004).

public sector purchases of approximately 337 million ACT treatments[15] could save more than 25 thousand lives a year.[16, 17] Thus, lowering ACT procurement prices through increased competition has the potential to save thousands of lives each year.[18]

IV. Evaluating Competition in markets affecting QAACT medicines

Although AM medicines encompass many types of medicine, we focus on QAACT medicines. This focus reflects our belief that any benefits to increased competition are likely to stem from actions taken by entities such as the GF that largely limits its purchase of AM medicines to QAACTs.

As discussed below, there are several distinct markets that affect QAACT prices and output. And within each market, different factors affect how competition occurs and how competition can potentially be increased in ways that will lower price and increase output.

A. Key markets

Three markets affect QAACT prices and output: the manufacturing market in which manufacturers compete to sell QAACT medicine; the downstream retail market in which retailers compete to sell medicine to individuals; and the upstream API market in which firms compete to sell inputs such as artemisinin to QAACT manufacturers.

1. The manufacturing market for QAACT medicines

The GF restricts its financing of ACT medicines to medicine from manufacturers that meet WHO's quality assurance (QA) criteria.[19] **Table 1** identifies the 14 suppliers of QAACT medicines and the specific molecules that each firm offers.[20] As shown, not all firms provide all molecules.[21]

15 2015 WHO World Malaria Report.

16 We calculate this as 0.8% *x* 1% *x* 337 million = 26,960 additional saved lives.

17 The number of saved lives can alternatively be estimated based on the WHO's estimate that ACT medicines averted approximately 140 million cases (not deaths) (2015 WHO World Malaria Report). Although there appears to be no consensus on the average mortality rates from untreated malaria (see , for example, Lubell, Y., et. al, "Likely Health Outcomes for Untreated Acute Febrile Illness in the Tropics in Decision and Economic Models; A Delphi Survey", PLoS One, 2011, available at http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0017439), and how those rates differ by patient age and local malaria transmission rates, an average mortality rate of 2% associated with each of those cases would mean that lowering ACT prices by 1%, and thus increasing the amount of ACT treatments purchased by 0.8%, would save approximately 22,000 lives per year (= 140 million averted cases/year x 0.8% increase in ACT treatments x 2% deaths/case).

18 While there is a large margin of error associated with the parameters used to estimate of saved lives, any reasonable assumptions regarding these parameters leaves the basic conclusion unchanged: even small price reductions from increased competition are likely to save tens of thousands of lives every year.

19 A drug can be qualified under any of three different programs: qualification by a stringent regulatory authority (SRA), qualification under the WHO's prequalification (PQ) program, or authorization by a recipient country's National Drug Regulatory Authority (NDRA).

20 Based on GF PQR data, website searches, and WHO List of Prequalified Medicinal Products for Malaria (Active producers of Combination Therapies) at http://apps.who.int/prequal/query/ProductRegistry.aspx and the Global Fund List of Malaria Pharmaceutical Products at http://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web &cd=1&ved=0ahUKEwiN6tLjvv3LAhWHPxoKHfJxATQQFggcMAA&url=http%3A%2F%2Fwww.theglobalfund.org%2Fdocuments%2Fpsm%2FPSM_ProductsMALARIA_List_en%2F&usg=AFQjCNFcoYTDzN4DlkFjXdPPL_Eb12HcxQ&bvm=bv.118817766,d.ZWU.

21 Throughout the paper, we use the terms "manufacturers," "suppliers," "firms," and "competitors" interchangeably.

TABLE 1
Suppliers of QAACT Medicines

	QAACT Suppliers					
	Artemether-Lumefantrine (AL)	Artesunate-Amodiaquine (AS-AQ)	Artesunate-Mefloquine (AS-MQ)	Artesunate-Sulfadoxine-Pyrimethamine (AS-SP)	Dihyro-Artemisinin-Piperaquine (DHA-PQP)	Artesunate-Pyronaridine Tetraphosphate (AS-PY)
Ajanta	X	X				
Cipla	X	X	X			
Guilin		X		X		
IPCA	X	X				
MacLeods	X					
Novartis	X					
Quality Chemical Industries, Lmt. (QCIL)	X					
Sanofi Aventis		X				
Sigma Tau					X	
Strides Arcolab	X	X				
Mylan	X					
Mepha/Acino			X			
Holley-Cotec					X	
Shin Poong						X
Number of Suppliers	*8*	*6*	*2*	*1*	*2*	*1*

There are two principal categories of QAACT buyers: private-sector and public sector. Public sector purchasers are government entities that provide medicine to individuals through public-sector hospitals and clinics where patients incur little or no costs. Virtually all public-sector purchases financed through international agencies such as the GF are for the QAACT medications that the WHO endorses.[22] Approximately 60% of purchases by donor agencies of QAACT were financed through the Global Fund,[23] although some funding is also provided by other international donor agencies such as the U.S. President's Malaria Initiative (PMI) and the UK's Department for International Development (DFID). Other public-sector purchasers include governments that directly purchase QAACT such as Rwanda and Kenya.[24]

The remainder of malaria medications are purchased by private sector entities for sale to individual patients at local for-profit pharmacies and other retail outlets. Historically, private sector purchases of malaria medicine were almost exclusively non-ACT medicine. In part because of the reduced efficacy of non-ACT medicines, but more likely because of QAACT subsidies to private sector entities provided through the Affordable Medicines Facility for malaria (AMFm—now rolled into the GF's Private Sector Co-payment Mechanism), the private sector is increasingly distributing QAACT medicines.[25] Yet, even when available, unless subsidized through the

22 Public-sector purchasers often buy non-QAACT medicines when financing those medicines from their own budget. India and China, for example, often purchase non-qualified ACT medicines through their internal government tenders.

23 Meek and Nankabirwa (2014), *op cit*. Wafula, et. al report that the GF contributes nearly half of all international financing for malaria; that statistic includes funding for products and services other than medicine.

24 In addition to this market for QAACT medicine, there is a distinct market for non-QA ACT medicines. That market is characterized by very different buyers and sellers, with most of the non-QA medicine ultimately sold by private sector retailers or purchased by countries that do not purchase through the GF and that are willing to trade off quality assurance for the lower price associated with non-QA medicines.

25 Virtually all ACT medicine was distributed through the public sector through 2010. The share of QAACT provided through the private sector increased significantly in 2011 as AMFm began to subsidize QAACT medicines in that sector, with approximately one-third of total ACT deliveries in 2013. (See, for example, Gill, C. and Hamer, D., "Underpricing the Competition in the Other Drug War: A Novel Strategy for Combatting the Inappropriate Use of Artemisinin Monotherapies," Pathogens and Global Health, April 2013; and Schwarte, S., "Delivery Trends of Artemisinin-base Combination Therapies," 2014 Artemisinin Conference (Guangzhao, China), available at http://www.a2s2.org/upload/5.ArtemisininConferences/4.2014China/Day1/4.WHOACTSalesSCHWARTE.pdf.) More recently, however, the GF has begun requiring individual countries to allocate their GF financing between public-sector purchases versus private-sector subsidies. With most countries choosing to allocate that financing predominantly towards their own public-sector, private-sector purchases of QAACT fell significantly.

Private Sector Co-payment Mechanism, QAACT prices in the private sector are generally 5–10 times the price of non-QAACT medicines, with the result that there remains considerable private sector demand for non-QAACT medicine.

2. The downstream retail market

For-profit retailers (e.g., pharmacies, shops, and kiosks) often sell a mix of AMs: QAACTs, AmTs, and non-artemisinin-based medicine such as chloroquine and sulfadoxine-pyramethamine (SP).[26] Although the cost of those medicines are cheap by western standards (approx. $1–$2 for QAACT medicines and as little as $0.10 for some non-ACT medicines), the cost is quite high given very low incomes: ACT medicine can cost the equivalent of several days' wages for afflicted individuals.[27]

Retailers compete not only with other local retailers, they also compete to attract customers that can obtain their medicine at little or no cost from public-sector providers. Despite their higher price relative to public-sector providers, 40–60% of AM medication is provided through the private sector in many countries in Africa.[28] The substantial size of the private-sector relative to the public sector reflects the fact that, despite higher prices relative to public-sector providers, private sector suppliers are typically much more convenient: rather than queue to be seen at a public clinic or travel to a distant public health clinic or hospital (and, worse, run the risk that it will be out of stock), patients can quickly purchase AM medicines at a nearby retailer.[29] Individuals may also opt to purchase medicine at private sector retailers because stock-out situations at local health centers mean the "free" product is, in fact, prohibitively costly.[30]

3. The upstream input market

Artemisinin, an active pharmaceutical ingredient (API), is an essential input in the manufacture of ACT (and AmT) medicines. As such, the buyers of this product consist of all ACT (and AmT) manufacturers.[31] ART costs account for approximately 25% of total QAACT manufacturing costs.[32]

ART suppliers are distinguished by their production technology. The traditional, and still predominant, production technology is agricultural, with most agricultural artemisinin (A-ART) coming from farms in China.[33] A-ART from hundreds of small farmers is then processed by at least a dozen firms that then compete to sell their A-ART to ACT (and AmT) manufacturers. Although farmers' ability to plant more or less ART creates significant

26 Private sector retailers may also sell low-quality and counterfeit AMs. See, for example, Tren, R., et al, "Malaria Treatment in Africa," Africa Fighting Malaria Policy Paper, May 2008.

27 Cost in terms of wages differs considerably across countries but in the surveyed African countries, with a high of almost two weeks' wages in Ethiopia. See "Availability, Price, and Affordability of Artemisinin-Based Combination Therapies and Other Antimalarial Drugs in Oromia Regional State of Ethiopia," President's Malaria Initiative/Ethiopia, June 2014. Some countries elect to allocate part of their Global Fund financing to subsidize private sector purchases of QAACT medicine as a means of displacing non-ACT treatments with QAACT treatments, thereby slowing the course of drug resistance to artemisinin-based medicines and increasing treatment efficacy relative to the use of non-artemisinin-based medicines.

28 Yadav, P. et. al, "Trends in availability and prices of subsidized ACT over the first year of the AMFm: evidence from remote regions of Tanzania," *Malaria Journal*, August 28, 2012; and Sabot, O., et. al, "Piloting the Global Subsidy: The impact of subsidized artemisinin-based combination therapies distributed through private drug shops in rural Tanzania," PLos ONE, 2009. The significance of the private sector varies by country and region. While non-ACT medicines are much less effective than ACT medicines, they are typically available at a much lower price and their reduced (or absent) efficacy may not be known by patients or made known by the retailers selling the product.

29 Unlike public-sector providers, individuals are seldom tested for malaria at retail outlets. As a result, individuals often self-medicate even when they do not actually have malaria.

30 See, for example, Alphs, S. and Yadav, P., "Malaria in the Asia-Pacific: Challenges and Opportunities for Access to Quality Malaria Medicines and Other Technologies," William Davidson Institute, October 2012.

31 Buyers include non-QA ACT manufacturers.

32 Active Pharmaceutical Ingredient (API) Market Dynamics Information Services (MDIS), WDI/Howard University, Annual Technical Report for Unitaid, November 2014.

33 A-ART is also grown in India and parts of Africa.

medium- and long-run supply elasticity for A-ART, there are long lead-times between planting and delivery of processed A-ART: approximately 18 months. This, combined with the fact that A-ART's short shelf-life limits opportunities to carry A-ART inventories, results in a very inelastic short-run supply for A-ART. That inelastic supply, coupled with weather-related supply-side shocks and inelastic demand, has caused significant ART price fluctuations over time.[34]

A new production technology for ART was recently introduced in which ART is synthesized in a manufacturing plant. This semi-synthetic artemisinin (SS-ART) product, first offered by Sanofi in 2010, has a significantly shorter lead time than A-ART (approximately 6 months), and has a cost that appears to be generally competitive with A-ART (approximately $350–$400 ton).[35] Huvepharma purchased the SS-ART technology from Sanofi in 2016 and is currently the only manufacturer[36] with capacity of approximately 50–60 tons/years[37]—approximately 30% of market demand.[38] While Sanofi had offered to sell SS-ART to its QAACT competitors when it owned the technology, to date the only purchaser of SS-ART has been Sanofi.[39]

4. Relationship between markets

Figure 1 illustrates the relationship between markets, with each rectangle in **Figure 1** representing a market in which firms compete to sell their product to buyers.[40] As shown, in some cases, the same firms may compete to sell their products to different buyers: for example, QAACT manufacturers compete to sell to both public and private sector buyers. And since those two types of buyers have different substitution options (public sector buyers purchase only QAACTs, while private sector buyers also purchase non-QAACT products), the QAACT manufacturers compete in two distinct markets. **Figure 1** also shows that all ACT medications (principally AL and ASAQ), as well as artemisinin mono therapy (AmT) drugs rely on artemisinin as an input, but that buyers can substitute between the synthetic and agriculturally-based form of ART.[41]

34 For example, ART prices have varied between $250/kg and $900/kg in recent years. See AP MDIS Annual Technical Report (*op cit*).

35 Shretta, R. and Yadav, P., "Stabilizing supply of artemisinin and artemisinin-based combination therapy in an era of wide-spread scale-up," Malaria Journal, Dec. 2, 2012, available at http://www.ncbi.nlm.nih.gov/pubmed/23198961.

36 Sanofi, working with Amyris, was the original developer of SS-ART. Huvepharma purchased Sanofi's SS-ART technology in February, 2016. (Peplow, M., "Synthetic Biology's First Malaria Drug Meets Market Resistance," *Nature*, February 23, 2016)

37 Shretta, R. and Yadav, P., "Stabilizing supply of artemisinin and artemisinin-based combination therapy in an era of wide-spread scale-up," Malaria Journal, Dec. 2, 2012, available at http://www.ncbi.nlm.nih.gov/pubmed/23198961; and "Artemisinin & Synthetic Biology: A case study," etc group, May 2014, available at http://www.etcgroup.org/content/case-study-artemisinin.

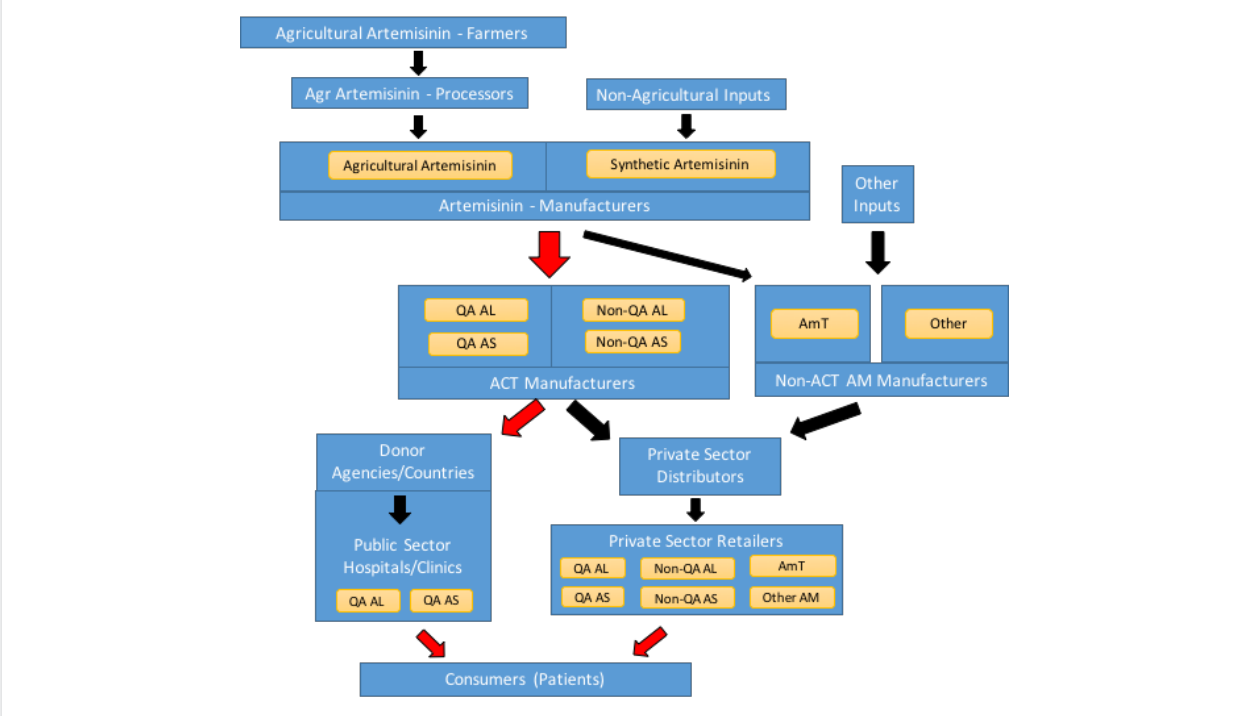
38 "Demand Forecast for Artemisinin-based Combination Therapies (ACTs) in 2013-2014," Unitaid, Q4-2013 Update, available at http://www.unitaid.eu/en/actforecasting.

39 There are reports that even Sanofi has been purchasing AA-ART rather than the SS-ART produced in what was, until recently, its own SS-ART plant (Nature (2016)).

40 **Figure 1** focuses on certain aspects of the supply chain while ignoring others such as markets relating to energy or labor inputs. The three key markets discussed above are identified by red arrows.

41 For illustrative simplicity, the only ACT medicines referenced in **Figure 1** are AL and AS—the two QAACTs that make up constitute the vast majority of QAACTs. More generally, however, **Figure 1** could also include other QAACTs.

FIGURE 1
Relationships among Malaria Markets



Finally, we note that there are also potentially important vertical relationships between firms that can affect competition. With respect to SS-ART, Sanofi was until recently both the sole manufacturer and the principle customer. In addition, many manufacturers of A-ART are vertically integrated into the production of ACT, both consuming the A-ART they produce and selling A-ART into the merchant market.

B. Market definition

Markets are typically defined by the identity or characteristics of the purchaser, what the buyer views as acceptable substitutes (the "product market") and where a firm can be located and still be considered an attractive supplier to the buyer (the "geographic market)."[42]

When assessing competition, the product dimension of a market identifies all products that a buyer views as acceptable substitutes. These are said to "compete" with each other. Thus, if buyers are willing to switch between a 24-count package of pills and as 12-count package (for small price differences), those two packages are viewed as competing in the same product market. In contrast, if buyers are unwilling to substitute between dispersible tablets and non-dispersible tablets (unless there are significant price differences), those two products are not considered competitors in the same market.[43]

For QAACT medicines, the behavior of the GF, a major buyer, suggests there is limited substitution between different QAACT molecules (e.g., AL vs. AS-AQ). Accordingly, each QAACT molecule likely falls into a different product market. More narrowly defined markets seem improbable, both because purchasers are likely willing to substitute (in part, even if not completely) between different package sizes, medicine strengths, and

42 In specialized contexts such as antitrust economics, terms such as product market have very precise definitions. Throughout this paper, we use those terms more loosely to characterize general competitive concepts and dynamics.

43 The product market can differ between buyers or buyer types. In Latin American countries where there is still only limited resistance to non-ACT medication, chloroquine and ACTs might be substitutes (i.e., in the same product market), while in African countries where chloroquine is largely ineffective, those medicines are unlikely to be good substitutes.

formulations, and because supply-side substitutability means that a manufacturer of one form of the molecule could likely begin offering other variants of the same molecule. And while different QAACT molecules are potential substitutes for many patients given their general medical equivalence,[44] the GF and many other purchasers do not choose between different molecules based on relative prices, but instead on their familiarity with the different medicines, on medical differences, or other factors.[45] Thus, unless the GF alters its procurement process to take price into greater account when allocating demand across different ACT molecules, different molecules are likely best viewed as competing in distinct markets.

The geographic dimension of a market identifies the area in which competing firms can be located and still be considered an attractive supplier to the buyer. With respect to QAACT medicines, buyers such as the GF are unlikely to care where the manufacturer is located, making the geographic market a worldwide market. In contrast, the geographic market in which private-sector retailers compete to sell AM medications to individuals will be local if individuals' limited access to transportation leave them largely unable to purchase from retailer in other towns.

C. Measuring concentration and competition

Traditional measures for the level of competition and concentration (e.g., a count of competitors, the 4-firm concentration level, and the Herfindahl-Hirschman Index (HHI)[46]) depend critically on what firms are identified as "competing" in the market. Identifying which firms compete in a market, however, can be very sensitive to how those markets are defined.[47] As discussed above, we believe the appropriate product market from the perspective of the GF and many other purchasers is likely the individual QAACT molecule (e.g., AL or AS-AQ). In that case, **Table 2** shows competitor counts, market shares and HHIs based on QAACT sales through the GF.[48]

44 This is not to say that there is total equivalence between the different molecules. But as long as purchasers are willing to substitute between medicines for *some* patients, even if not *all* patients, those medicines are viewed as competing, thus merit inclusion in the same product market.

45 Limited substitution between QAACT and either non-QA ACT or AmT medicines means that those medicines do not likely compete in the same product market. And while there may be increased future use of DHA-PPQ because of certain technical/medical benefits (e.g., a longer half-life), that substitution is unlikely to be attributable to relative price differences, and thus not a basis for viewing DHA-PPQ as "competing" with other QAACTs.

46 The four-firm concentration level is the sum of market shares of the four largest firms in the market. The HHI is equal to the sum of each firm's squared market share. Thus, in a market with four firms with shares of 40%, 30%, 20% and 10%, the HHI = $40^2 + 30^2 + 20^2 + 10^2 = 3{,}000$. Higher HHIs correspond to more concentrated (less competitive) markets.

47 The product market can differ between buyers or buyer types. Latin American countries where there is still only limited resistance to non-ACT medication such as chloroquine might view ACTs and chloroquine in the same product market, while African countries where chloroquine is now largely ineffective will not treat chloroquine as competing in the same product market as ACTs.

48 GF PQR data for 2015. Market shares based on total reported payments through the GF. For Kenya, reported payments reflect freight. Several of the manufacturers shown in **Table 2** made no sales through the GF in 2015 because they have only recently become qualified: Shin Poong, the only QA supplier of AS-PY, was not qualified until October 2015; Mylan was not qualified in AL until May 2014; and Ajanta was not qualified in AS-AQ until July 2013. Conversely, Guilin and Strides Arcolab are believed to be exiting the AS-AQ market. Guilin is believed to be shifting to obtaining pre-qualification for DHA-PPQ (where there are currently only two suppliers).

TABLE 2
2015 PQR Sales by Manufacturer

	AL	*AS-AQ*	*AS-SP*	*AS-MQ*	*DHA-PQP*	*AS-PY*
Ajanta Pharma	13%	0%				
Cipla Ltd	16%	22%		100%		
Guilin Pharmaceutical Co. Ltd		0%	100%			
IPCA Laboratories Ltd	16%	1%				
MacLeods Pharmaceuticals Ltd	11%					
Novartis Pharma	14%					
Quality Chemical Industries Ltd.	12%					
Sanofi Aventis		77%				
Sigma Tau					100%	
Strides Arcolab Limited	18%	0%				
Mylan	0%					
Mepha/Acino				0%		
Holley-Cotec					0%%	
Shin Poong						-
TOTAL	100%	100%	100%	100%	100%	
Share of 2015 QAACT Sales thru GF	**81%**	**17%**	**1%**	**0%**	**1%**	**0%**
Count of All QA Suppliers	***8***	***6***	***1***	***2***	***2***	***1***
HHI (2015 GF revenue)	**1,467**	**6,451**	**10,000**	**10,000**	**10,000**	**-**

By most measures, the AL market—accounting for approximately 81% of QAACT sales through the GF—is competitive: there are 8 competing suppliers, with a 2015 HHI of 1467.[49] In the U.S., that market would likely be sufficiently competitive that, even if a merger were to eliminate one of the smaller competitors, competition authorities would be unlikely to object.[50]

The second important ACT market, AS-AQ, also appears to be relatively competitive. Although almost all sales through the GF were made by just two firms, resulting in a GF-based 2015 HHI of 6,451, there appear to be four significant pre-qualified AS-AQ suppliers. Moreover, it is believed that both Guilin and Strides ArcoLab are exiting because competition had left margins too low to remain in the market. Such exit indicates that prices are at or even below competitive levels.

The remaining QAACT markets are much more concentrated, with only one or two suppliers in each of those markets. Those other QAACT markets, however, are quite small and collectively account for only 1–2% of total QAACT sales. Thus, while more concentrated, the economic significance of those markets is currently quite limited.[51]

49 QCI is owned in part by rival supplier Cipla. That cross-ownership reduces competition relative to what HHIs and simple competitor counts would suggest.

50 Although the increase in the HHI that would result from such a merger would likely mean the merger was "presumptively anticompetitive" under the 2010 USDOJ/FTC Horizontal Merger Guidelines, in practice the U.S. antitrust authorities often do not challenge such mergers.

51 We understand, however, that the DHA-PPQ segment is likely to increase significantly in the future and, but for existing capacity constraints limiting sales by Sigma Tau, would be much larger even today. Thus, the high concentration in that particular market is likely to result in high prices that increased competition would likely bring down. Those high prices, however, are likely to attract additional entry and may explain Holley-Cotec's decision to enter that market.

In addition to their sensitivity to market definition, traditional measures of competition can fail to properly account for differentiation between competing firms that affects the competition.[52] Moving away from those traditional measures, the competitiveness of a market depends on the strength of individual firms' incentives to offer lower prices, higher quality, and better service in an effort to attract buyers and increase sales. The intensity of this competition will depend on how buyers choose between firms, how differentiation among firms affects buyers' willingness to substitute and thus firms' incentives to offer lower prices, and how different procurement strategies can affect competition.[53]

D.The competitive game in the manufacturing market for QAACTs

Competition benefits consumers in several ways. First, in settings where firms set prices and most consumers are too small to influence those prices, competition prevents firms from charging excessive prices. Second, competition absolves consumers of the need to learn about firms' costs: consumers simply need to focus on firms' prices, knowing that competition ensures that those prices reflect firms' costs.

Unlike small buyers that have little or no direct influence of firms' prices, large buyers (such as those in QAACT manufacturing markets) can try to negotiate prices. At the extreme, a large buyer rather than the seller can specify the price they are willing to pay, with firms then deciding whether they want to supply at that price. In such cases, the buyer rather than seller is the price-setter.

In cases where a large buyer sets price, there could be monopsony concerns. Yet, as long as the buyer has increased access as an objective (as is likely the case with the GF), it might be more appropriate to view the buyer as a type of regulator.[54] If a large buyer cum regulator knows firms' costs, it can simply set price equal to the competitive price: in that case, regulation replaces competition but achieves the same outcome—at least in the short-run.[55] In the U.S., large buyers such as Medicare (accounting for as much as half of many health care providers' revenues) and the Department of Defense (accounting for the bulk of many defense-related firms' revenues) are sufficiently large that they can effectively dictate prices, subject to the need to ensure that those prices are sufficiently high to cover suppliers' costs. The GF, through which more than a third of all QAACT purchases flow,[56] similarly likely has the ability to dictate prices to QAACT manufacturers rather than rely on competition to determine price.

Typically, however, large buyers are neither price takers nor price setters and a large buyer's real choice is not between relying on either competition or "regulation" to determine price. Rather, large buyers typically determine price through negotiations with sellers. These negotiations can take the form of one-on-one negotiations or a variety of procurement auctions (e.g., sealed bids, multi-round bids, etc.). In these settings, a buyer can generally negotiate a better price when it can signal to a seller that it is more likely to walk away (or at least significantly reduce its volume of purchases) or when the cost to the supplier of losing a contract are greater.[57] Competition can help buyers obtain lower prices in these settings by increasing supply options, thus making it

52 For example, a low-cost firm may be a more vigorous competitor than a high-cost firm, a local firm that can offer low-cost shipping may be a more attractive competitor than a distant firm, a firm with reliability problems may be less attractive than others with a strong track record, and for some buyers a firm offering artemether-lumefantrine (AL) based ACTs may be more desirable than a firm offering artesunate-amodiaquine (AS-AQ) based ACTs.

53 In some cases, the threat of entry can also increase competition. Here, the most likely entrants are likely the non-QA ACT manufacturers (of which there are many). We understand, however, that the (primarily regulatory) costs of such entry, as well as the long lead time, minimize that entry threat.

54 There are two (relatively unimportant) distinctions relative to the classic case of regulation. First, regulators typically set prices on behalf of other parties. Second, in classic regulation, a supplier may be compelled (at least in the short-run) to supply at the regulated prices, whereas suppliers can always opt not to sell to large buyers if the specified price is too low.

55 Long-run effects, especially with respect to innovation, would be more difficult for the regulator to imitate.

56 As cited by Shretta, R. and Yadav, P. (2012), *op cit*.

57 The economic literature shows that the manner in which a buyer runs a procurement auction can have dramatic effect on price. As discussed in Section VII, there is limited public information on the details of the GF's procurement process.

easier for the buyer to walk away from a deal with any particular supplier. Information about firms' costs can also help a buyer negotiate optimal prices by educating the buyer about how costly it would be for a supplier to lose a contract: all else equal, firms with lower costs will be more willing to drop price.

V. Increasing competition by Lowering firms' costs

We briefly turn to potential strategies to lower suppliers' costs. As discussed in the following sections, competition can be increased by either of two routes: increasing the number of competitors in a market or by increasing competition among existing competitors. Lowering firms' costs helps to increase competition through both of those routes. First, lower costs can make entry more profitable, thus increasing the number of firms competing in a market. Second, lower costs increase incumbents' profit margins, thus creating incentives for those firms to compete more aggressively for increased sales.

We identify several possible strategies to lower firms' costs.

- *Reducing supply-side risks*. Fluctuations in upstream input (principally artemisinin) costs, downstream prices, and overall demand create significant uncertainty for QAACT manufacturers. With high fixed manufacturing costs for QAACT medicines, the resultant fluctuation in sales creates significant variation in year-to-year operating margins.[58] The Global Fund, however, may be less risk averse than generic ACT manufacturers and thus better positioned to absorb those risks. The Global Fund can help absorb the risk of those supply and demand shocks through strategies such as pre-committing to fixed volume purchases for ACT medicines regardless of ultimate market demand, reducing year-to-year variation in ACT prices based on changes in ACT demand, and contracting on behalf of ACT manufacturers for artemisinin or other inputs to ensure in a way that puts the Global Fund, rather than ACT manufacturers, at risk for input price variation.[59]

- *Lowering quality criteria and related regulatory costs*. Manufacturers incur substantial costs to obtain the QA certification they need to sell through the Global Fund. Reducing quality standards and associated regulatory costs would increase firms' profits, thus allow for increased entry, increased competition, and lower prices. Of course, the tradeoff of obtaining those lower prices is lower quality and lower safety. Historically, this has been an unacceptable tradeoff, although we are unaware of evidence on the relationship between quality and number of lives saved and how to balance the competing facts that, while lower quality can cost lives, lower costs can also increase treatment rates and save lives.

- *Reducing contracting costs*. Continued efforts by the GF and other large buyers to reduce transaction costs will increase the attractiveness of entry.

VI. Increasing the number of QAACT competitors

In this section, we discuss how increasing the number of competitors in the manufacturing market for QAACTs increases competition, while in the next section we discuss how to increase competition without increasing the number of competing firms.

The benefits from increasing competition can be assessed in the same way that competition authorities assess the competitive effects of mergers in which the number of competitors in an industry is reduced. Using that framework for analyzing competition, we show why increasing the number of competitors in the manufacturing market for QAACTs may yield only limited benefits. As discussed, however, even limited competitive benefits can translate into thousands of saved lives. Thus, given the importance of achieving even modest increases in competition, we discuss possible strategies for increasing the number of competitors.

58 For example, IPCA's AL sales to the Global Fund fell from approximately $32 million in 2013 to just $2.6 million in 2014, increasing to $4.0 million in 2015 (2015 represent partial year PQR sales).

59 The Global Fund is already working towards implementing several of these strategies.

In discussing the competitive effect of increasing the number of competitors, we distinguish between entry with "me-too" products (i.e., products such as generic drugs that are largely undifferentiated from existing products) and entry with more innovative products. We show that although entry with innovative products may have little or no impact on price, such entry can yield substantial consumer benefits, particularly in light of potentially reduced effectiveness of existing ACT medicines over time as drug resistance increases. Moreover, because innovative firms may be able to capture most or all market sales, such entry may be profitable, and thus more likely, than additional "me-too" entry.

A. Entry by additional QAACT manufacturers may be unlikely

Unless expected to be profitable, firms generally will not enter a market regardless of the benefits that such entry might confer to consumers.[60]

The evidence suggests that further entry into the two largest QAACT markets is unlikely. In fact, in the AS-AQ market, we see *exit* rather than entry, suggesting that overall demand is insufficient to support all six pre-qualified suppliers in that market. In AL, the largest QAACT market, we have seen entry as recent as May 2014 by Mylan. Further entry, however, is unlikely given the number of firms (8) currently competing in that market and what appears to be stable, and possibly even falling, demand over time.[61] And looking forward, total treatments, thus perceived market demand that an entrant can anticipate, may be falling for several reasons. First, success in reducing both malaria deaths and malaria cases may reduce total demand for QAACTs.[62] Second, an increased emphasis on testing to reduce unnecessary ACT treatment may further reduce demand for QAACT treatments, thus reducing the attractiveness and likelihood of entry.[63]

B.The benefits of additional QAACT entry may be limited

Some have argued that an increase in the number of competing suppliers reduced QAACT prices.[64] Such a causal relationship requires controlling for other factors that also affect price. However, even if we accept this premise, the benefits from further increases in the number of competitors may be limited. Based on the number of QAACT manufacturers already in the market, and evidence of how additional competitors can be expected to increase price, the evidence suggests that increasing the number of competing QAACT manufacturers may yield only limited price reductions even if it does occur.

1. Historical price/concentration relationship for pharmaceuticals

Economic studies of U.S. drug industry suggest that the benefits of increasing the number of competitors decrease rapidly as the number of competitors increases. For example, **Figure 2** shows the price/concentration relationship in the US generic drug industry, and suggests that while going from one to two generic competitors

60 The principal caveat to this is entry by not-for-profit firms or entities within for-profit firms. Such entry (e.g., by Novartis and Sanofi) has played an important role in the markets for AM medicine. Although entry by not-for-profits may not depend on whether expected profits are high or low, that entry nevertheless likely depends on whether such entry would be unprofitable or not.

61 Over the last several years, the number of QAACT treatments flowing through the GF has been relatively stable. (2015 WHO World Malaria Report at p. 33)

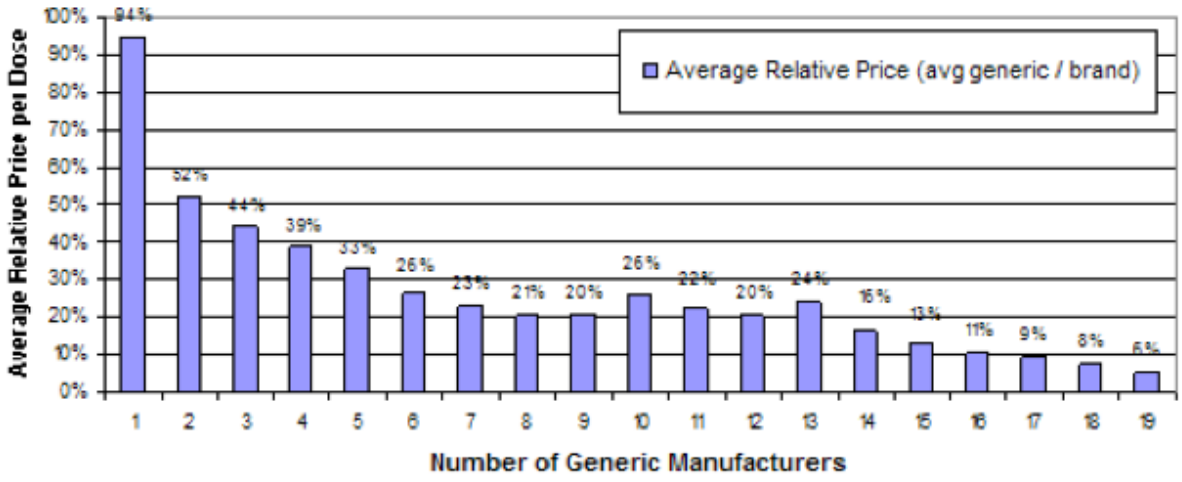
62 From 2010 to 2015, the number of worldwide malaria deaths fell by approximately 12%, and the number of malaria cases fell by approximately 21%, without any significant increase the number of QAACT treatments. (2015 WHO Worldwide Malaria Report at p. 9)

63 Entry may be more likely in the smaller QAACT markets where there are fewer competitors. In fact, it appears that Guilin may be seeking pre-qualification of its DHA-PPQ medicine where there is currently just one other supplier (Sigma Tau). Given the tiny size of those markets, however, entry is unlikely to have a significant effect.

64 See, for example, Yadav who states that "between 2004 and 2011, the prices of ACTs decreased due to economies of scale for existing manufacturers and the entry of several new manufacturers, which increased competition. (Yadav, P., "Malaria in the Asia-Pacific: Challenges and opportunities for access to quality malaria medicines and other technologies," WDI working paper, October 2012 at p. 11).

may lead to a substantial price reduction (approximately 45%), subsequent increases in the number of competitors has a smaller impact on price, with only limited price effects once there are 6 competing generics in the market.[65]

FIGURE 2
Generic Competition and Drug Prices



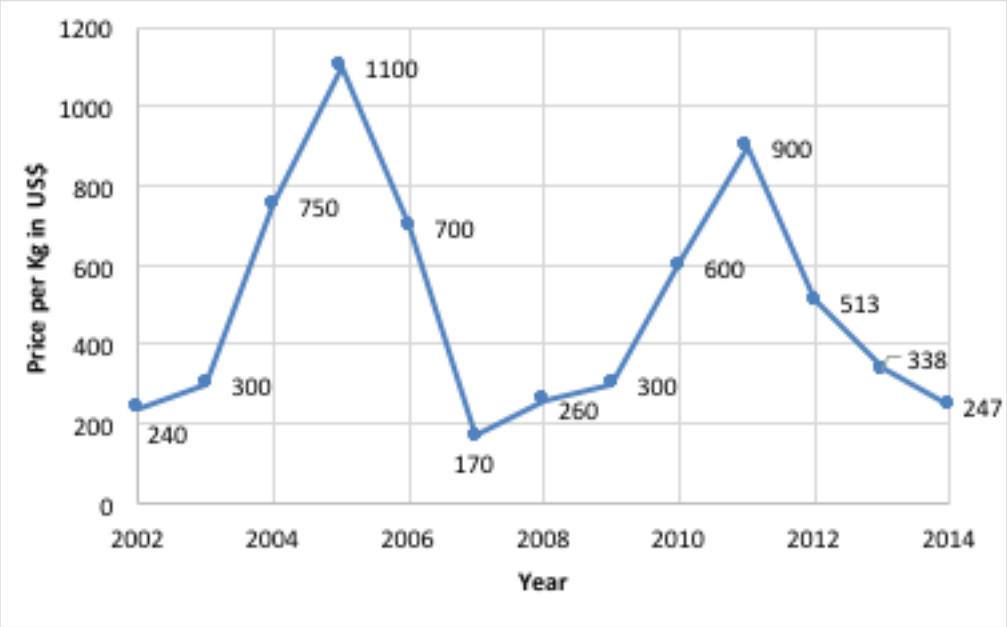
Source: FDA analysis of retail sales data from IMS Health, IMS National Sales Perspective (TM), 1999-2004, extracted February 2005

Although the relationship between the number of QAACT competitors and prices would be more instructive than looking at the relationship associated with other drugs and other countries, we are aware of no existing studies, no doubt in part because of the difficulty of reliably estimating that relationship: although there have been changes in the number of competing firms over time, there have also been significant confounding significant supply and demand shocks. For example, during the same time period that the number of ACT manufacturers has been increasing, **Figure 3** shows that the price of ART, a key input into the production of ACT drugs, has experienced substantial price fluctuations.[66]

65 Chart reproduced from U.S. Federal Drug and Administration (FDA) website, available at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.

66 WDI API Market Dynamics Information Services Report at p. 23.

FIGURE 3
A-ART prices over time



Similarly, overall demand for ACT drugs has been increasing dramatically over time, with ACT deliveries increasing from 11 million ACT treatment courses in 2005 to 392 million in 2013.[67] Thus, simply observing the relationship between ACT price and the number of competitors over time may say little about the actual causal relationship.

2. There are already several competing QAACT suppliers

Given the market sizes and likely competition across narrowly defined markets, the benefits from increasing the number of competing firms may be limited even if entry does occur. For AL, the molecule representing over 80% of GF ACT sales, there are already 8 competitors. With so many competitors already, **Figure 2** suggests that the incremental value of additional competitors may be minimal. The incremental value of additional competitors in AS-AQ is also likely limited: with six firms already qualified, there are unlikely to be significant benefits from encouraging more entry. Moreover, with two of those firms (Guilin and Strides) believed to be exiting the AS-AQ market, it may be that the market can only support four firms. In that case, encouraging additional entry might simply displace an incumbent, leaving the total number of competitors unchanged at four.

The likelihood, and benefits of, entry into the smaller ACT molecules is less clear. The limited number of competitors in those markets (just one supplier in AS-SP and AS-PY and two suppliers in DHA-PPQ and AS-MQ) suggests that an increase in the number of competitors in those very concentrated markets might result in significant price reductions. Yet, the very small market size for those molecules means the payoff from trying to increase the number of competitors in those markets is likely minimal.

3. Entry may have less impact on QAACT prices than on U.S. prices

The price/concentration relationship with respect to the US generics market shown in **Figure 2** may overstate the effect of entry on price in QAACT markets because of significant price and margin differences between US drugs and QAACTs. Margins for innovator (branded) manufacturers in the U.S. are often very high prior to generic entry. Those high margins allow for significant price reductions while nevertheless leaving entry profitable.

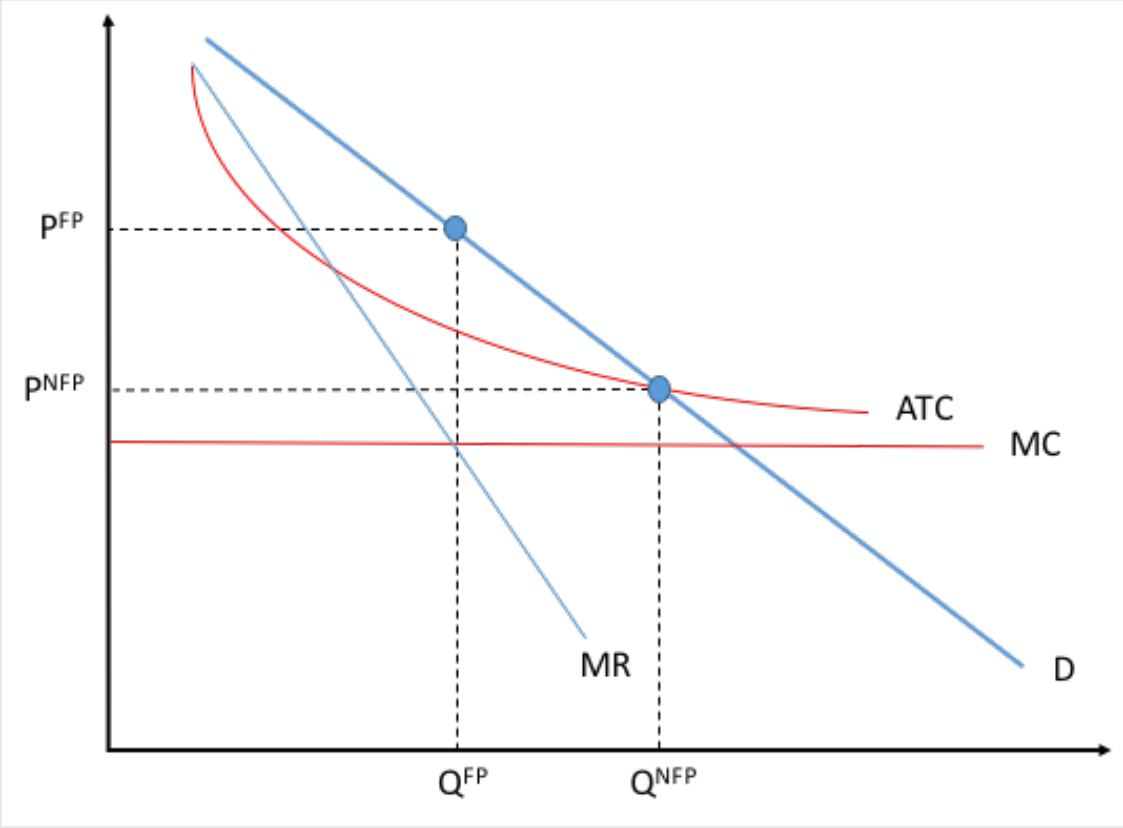
67 2014 WHO World Malaria Report at p. 25.

Manufacturers of QAACTs for sale into Africa and Asia do not enjoy the same high margins as drugs sold in the U.S. Those lower margins mean there is less opportunity for entrants to offer price reductions that remain profitable. Thus, the price/concentration relationship for QAACTs is likely much flatter than the one shown in **Figure 2**.

4. Not-for-profits may reduce the incremental impact of additional competitors

The two branded ACT drug manufacturers, Novartis and Sanofi, both operate as not-for-profit (NFP) with respect to their sales of QAACTs.[68] Instead of maximizing profits, NFPs may choose to maximize sales subject to a break-even profit constraint. In that case, and as illustrated in **Figure 4**, an NFP will choose a lower price and higher output $\{P^{NFP}, Q^{NFP}\}$ where price just covers average total cost (ATC), than its for-profit counterpart with the same costs would choose $\{P^{FP}, Q^{FP}\}$. The lower prices that NFPs tend to charge result in lower margins for all firms, thus less opportunity for entrants to drop price while still remaining profitable.

FIGURE 4
NFP Price to Output



It follows that markets in which NFPs are the innovators (the first firm in the market) are likely to have lower initial market prices than when for-profit firms are the innovators.

With respect to the price/concentration relationship shown in **Figure 4**, an NFP may be able to drive market prices down much more quickly than would occur in a market with all for-profit firms: a market in which an NFP is the innovator firm may have prices that otherwise would not be observed until there were several competing

68 See Novartis Malaria Initiative, available at http://www.malaria.novartis.com/downloads/malaria-initiative/Malaria-Initiative-Factsheet-May-2015-Malaria-Initiative.pdf and https://globenewswire.com/news-release/2014/04/25/629826/10078345/en/SANOFI-Sanofi-Reaches-New-Milestone-in-Fight-Against-Malaria-300-million-ASAQ-Treatments-Delivered-in-Africa.html. Novartis sells Coartem (an AL medicine) while Sanofi sells Winthrop (an AS-AQ medicine).

firms in the market. In effect, the impact of a second firm might not be to move along the price curve from one to two competitors in **Figure 2**, but if the innovator NFP had already pushed price down to levels that would otherwise require (e.g.) 4 firms, the impact of the second firm would be to move along the price curve from four to five firms, a much smaller incremental price effect. Similarly, if prices in a market with 5 firms, one of which is an NFP, are similar to what would otherwise emerge with (e.g.) 8 for-profit firms, then **Figure 2** suggests that entry by a sixth firm would have very little effect on price, i.e., the effect of going from 8 to 9 firms.

With NFPs already operating in the two largest ACT markets (AL and AS-AQ), this discussion again suggests that there will be limited price effects from increasing the number competing firms.[69]

C. Strategies for increasing the number of competitors

There are several ways in which large buyers such as the GF could encourage entry.

1. Sponsoring entry by increasing demand

Increasing demand for QAACT medicines creates opportunities for profitable entry into QAACT markets. Encouraging entry by increasing demand, however, may have unanticipated consequences: while entry will increase competition and thus create pressures to lower price, increasing demand tends to increase price. Thus, increasing competition by increasing demand could actually result in higher, not lower, prices.[70] The most direct means of increasing demand is to simply increase expenditures on QAACT medicines. This strategy, however, is likely infeasible given limited budgets.

2. Sponsoring entry by lowering costs

Lowering suppliers' costs makes entry more profitable, thus more likely. And unlike the previously discussed strategy of increasing demand, lowering suppliers' costs can result in both lower market prices and increased output, while not necessarily increasing overall expenditures.

A large buyer such as the Global Fund can lower suppliers' costs through a variety of strategies. As discussed below, however, the most effective means of lowering costs is not through a subsidy that essentially just transfers costs from suppliers to the subsidizing entity, but instead by taking steps to lower firms' actual costs.

a. Supply-side subsidies

Although subsidies lower firms' costs, they increase the cost of the party providing the subsidy: in effect, subsidies transfer costs from one party to another rather than reduce actual costs. Subsidies can target fixed costs or variable costs. Both with increase the likelihood of entry, but subsidizing fixed costs is the most direct way of reducing the barrier to entry. Subsidies are an expensive means of encouraging entry and not necessarily preferable to instead encouraging entry by increasing expenditures and thus overall demand.[71]

69 Although NFPs might reduce the incremental price effect of additional competitors, it is important not to conclude that NFPs are detrimental to competition. To the contrary, a single NFP can have the competitive effect of multiple for-profit competitors because the NFP prices so "aggressively." The only reason why additional for-profit competitors may have a limited impact on price is because the NFP has already pushed price so close to competitive prices. In fact, as discussed below, absent cost differences between NFPs and for-profit firms, a single NFP firm is sufficient to ensure competitive prices. Put differently, in certain respects, the presence of NFPs obviates the need for competition.

70 This emphasizes our earlier caveat: increased competition is not itself a goal, but simply a potential means of achieving another goal (e.g., lower prices or increased output). And in some cases, increasing competition may not achieve all of those goals.

71 The alternative of increasing expenditures and stimulating demand could be achieved through demand-side subsidies. One example of such subsidies are the AMFm's efforts to stimulate demand in the private sector through heavy subsidization of QAACTs purchased by private retailers. For a discussion on the relative merits of supply-side versus demand-side subsidies, see Taylor, T. and Yadav, P., "Subsidizing the Distribution Channel: Donor Funding to Improve the Availability of Products with Positive Externalities," working paper, 2011 and Taylor, T. and Xiao, W., "Subsidizing the Distribution Channel: Donor Funding to Improve the Availability of Malaria Drugs," Management Science, 2014.

A subsidy targeted towards entrants will be more effective at encouraging entry than a non-discriminatory subsidy made available to both entrants and incumbents since non-discriminatory subsidies make it more difficult for entrants to capture market share from incumbents.[72]

A subsidy targeted to just entrants, however, would face several challenges. First, benefitting one set of firms (entrants) at the expense of others (incumbents) raises equity and potentially political considerations. Second, a subsidy strategy targeted at just entrants may end up simply displacing non-subsidized incumbents with subsidized entrants. In that case, there will be no net change in the number of competitors, yet the subsidizing entity ends up incurring higher costs.[73] Third, and potentially most damaging, subsidies targeted towards entrants can create long-term incentive problems. An expectation that future entrants will be rewarded with subsidies will make firms reluctant to enter today: not only does delay mean that firm may get a subsidy itself, but it protects itself from the "unfair" competition that might otherwise emerge if rivals get subsidies but the incumbent does not. Such subsidies might also affect other markets, delaying entry in those markets where the potential entrants anticipate a subsidy might be forthcoming if they wait long enough and that they will forgo the subsidy if they enter too soon. Many of these problems can be avoided by offering the subsidy to both entrants and incumbents; the tradeoff is the entrant's inability to realize a cost advantage over incumbents may make it difficult for the entrant to achieve sufficient market share, thus discouraging entry.

b. Reducing suppliers' actual costs

Section 5 identified some costs that, if lowered, will increase the probability of entry.

There is one additional cost that is worth mentioning in the context of entry that is specific to entry: *reducing the suppliers' risk of entering new markets.* Entrants into QAACT markets are forced to incur significant fixed (and sunk) costs. If unable to capture enough market share, the entrant may be unable to recover those costs. Large buyers can reduce those risks by pre-committing to buy product from the entrant, thus "sponsoring entry."

D. Entry with an innovative new product

The preceding discussion focused on the case where entrants offer medicines that are undifferentiated from medicines already offered by incumbent manufacturers. This undifferentiated entry characterizes the situation where entrants offer generic equivalents to existing medicines. Yet differentiated entry in which firms enter with innovative new medicines can also occur.[74] Although differentiated entry may have less impact on market price than undifferentiated entry, entry with an innovative new product may provide the greatest consumer benefits. Entry with an innovative new product may also be more profitable than undifferentiated entry given the potential for an innovative new product to capture substantial sales *if* that entrant enjoys sufficient protection for its intellectual property.

1. The value of new anti-malarial medicines

While QAACT medicines are currently recognized as the most cost-effective, medically efficacious product to treat most forms of malaria, resistance to artemisinin is increasing. Resistance in parts of the Southeast Asia, particularly along the Cambodia/Thailand border, was reported as early as 2009,[75] with resistance now increas-

72 This is not to suggest that non-discriminatory subsidies might not still induce entry. If a non-discriminatory subsidy leaves entrants unable to capture sufficient market share from incumbents to cover their fixed costs, however, entry will not occur. In contrast, a targeted subsidy increases the likelihood that the entrant can capture sufficient market share from incumbents to cover its costs. This discussion highlights that subsidizing entrants' fixed costs may be a more attractive subsidy policy when firms' have high fixed costs.

73 In essence, the subsidizing entity pays to displace efficient firms with less efficient firms.

74 Innovations can be big or small. At one extreme, innovation may take the form of a unique new medicine—much as artemisinin-based therapies were in the 1990s. But innovation can also encompass new ACT molecules, or variants on existing ACT molecules that offer a longer shelf-life, a shorter treatment course, or some other benefit.

75 WHO Global Technical Strategy for Malaria: 2016–2030. See also Alphs and Yadav (2012); and Meek and Nankabirwa (2014), *op cit*.

ingly reported in parts of Africa. Such resistance threatens to render QAACTs increasingly ineffective over time, forcing a reliance on either more costly, or less effective, medicines. To avoid this outcome, new medicines to replace QAACTs (just as ACTs replaced chloroquine) are needed.

Although entry with innovative new products is an important form of competition, that competition does not necessarily result in lower price. In fact, the price of innovative new medicines can be higher than existing medicine.[76] The introduction of a "superior" innovative new medicine may, however, force incumbents to lower price on their existing products in an effort to maintain sales.

2. The profitability of introducing innovative AM medicines

Successful entry with an innovative new AM medicine is potentially quite profitable: while entrants with an undifferentiated product will share the market with existing suppliers, an entrant with an innovative new product can potentially capture the entire market. This represents a potential market size of more than $100 million.[77]

But while the potential payoff to entering with an innovative product can be high, so can the costs and risk: innovation can require significant research and development expenditures with no guarantee of success.[78] In contrast, while entry with an undifferentiated product promises less reward, it involves both lower costs and lower risks: a manufacturer that already offers a non-QA product only needs to incur the costs of upgrading its manufacturing process and associated regulatory costs in order to enter with an undifferentiated QA product. Not only are those costs likely to be much lower than the R&D costs associated with innovation, but undifferentiated entrants also have a lower risk of ending up with a marketable product.

3. Encouraging innovation

Positive externalities, together with weak intellectual property protection, provides an economic justification for interventions directed at increasing innovation.[79] The most effective way of supporting innovation is likely through direct subsidies of innovative effort.[80] Providing R&D subsidies rather than paying price premiums to innovators to reward innovation is an important means of preventing distortions in any post-innovation competition that emerges.[81]

To date, it appears that firms view the potential rewards from innovation as sufficiently attractive to warrant R&D efforts, with firms reportedly working to develop innovative new antimalarial products including:[82]

76 This was the case when artemisinin-based medicines were introduced: ACT medicines are generally 10–20 times more expensive than the non-ACT medicines they largely replaced.

77 Based on 2013 QAACT treatments financed through GF PQR and AMFm (as reported in Unitaid Malaria Medicines Landscape, March 2015). Total potential market for an innovative new product is even greater given the potential to make sales to additional purchasers. Unitaid reports that approximately 31% of the $2 billion/year total spend on malaria control and treatment is for anti-malaria medicine, suggesting a total potential market size of more than $600 million/year.

78 The profitability of innovative entry will also depend on what intellectual property protection an entrant enjoys. Absent patent protection, innovators can expect to rapidly face competition from generic manufacturers, thus diminishing margins and making it difficult to recoup the costs of R&D.

79 The appropriate *magnitude* of those subsidies, however, and whether current subsidies are sufficient, is less clear.

80 Unitaid reports current global funding for all malaria R&D as $610 million. (Unitaid Malaria Medicines Landscape, March 2015)

81 There is mixed evidence on whether the GF appears to be trying to support innovation by paying innovators higher prices than it pays generics. For example, 2015 PQR data shows that the Global Fund paid Novartis an average of $49.20 for one AL product, while it paid generic manufacturers just $28.75, a difference of more than 70%. (The product at issue is AL-FDC, 20mg + 120mg/24 tablet blister-720 packs (30*24), not including freight costs.) The same pattern, however, is not true for Sanofi where the GF paid Sanofi less ($18.95 vs. $20.25) for AS-AQ (100 mg + 270 mg – 6 tablet) in 2015, even though Sanofi was paid more in 2013 and 2014.

82 See also Unitaid Malaria Medicines Landscape, March 2015 at p. 12 for a list of pipeline products. Of interest, there is no indication that only NFPs are willing to pursue innovation in this area. See also http://www.malaria.novartis.com/downloads/malaria-initiative/Malaria-Initiative-Factsheet-May-2015-Malaria-Initiative.pdf; and Active Pharmaceutical Ingredient (API) Market Dynamics Information Services (MDIS), Market Summary Report, William Davidson Institute, November 2014. It should also be noted that there are also innovation efforts directed at developing an effective malaria vaccine. Such efforts are being made by several firms, including Sanaria and GlaxoSmithKline.

- In the last five years, Novartis scientists and collaborators have discovered three new classes of anti-malaria compounds.
- Guilin is reported to be working on a pediatric (dispersible) AQ-SP product.
- Sanofi is reported to be developing a synthetic peroxide product that could provide an alternative to artemisinin derivatives.
- Novartis is said to be developing a synthetic AM molecule that will likely be an alternative to artemisinin derivatives.
- Ranbaxy has gained approval to sell its non-artemisinin-based product Synriam in India, although it is unclear how extensively the product will be marketed.

VII. Increasing competition among existing QAACT suppliers

A firm faces increased competition if it experiences greater incentives to reduce price. As discussed in the previous section, one way to increase incentives to reduce price is to increase the number of competitors. But as discussed in this section, incentives to lower price can also be increased by lowering a firm's costs, increasing the buyer's willingness to substitute between products, or changing the manner in which buyers procure products.[83]

A. Reduce incumbents' costs

Lowering a firm's variable costs increases the unit profitability of sales, thus increasing the firm's incentive to make additional sales. One of the easiest ways for firms to increase sales is by lowering price. Thus, lower variable costs create incentives to lower price. As discussed in Section V, there are a variety of ways in which a large buyer can try to reduce firms' costs, including lowering firms' contracting costs and reducing supply-side risk.

Lowering a firm's *fixed* costs, however, does not increase the firm's incentive to lower its price. Thus, a lump-sum subsidy will increase a firm's profit but do nothing to increase competition among incumbent firms. The exception is with NFPs: if NFPs maximize output subject to a zero-profit constraint, then as can be seen from **Figure 4**, a fixed-cost subsidy that lowers a firm's average total cost (ATC) will lead to lower prices. In fact, if marginal costs are relatively flat, then by setting the fixed cost subsidy equal to an NFP's fixed costs, a buyer can achieve the competitive outcome in which price equals marginal cost with a single NFP firm in the market.

B. Increase purchasers' willingness to substitute between medicines

Increasing a buyer's willingness to substitute to lower-priced products increases a firm's incentive to offer lower prices. Buyers such as the GF can potentially increase substitution at several different levels: between branded and generic products; between different formulations of the same molecule; and between molecules.

Substitution does not need to be absolute in order to create competition: threatening to shift even a *fraction* of demand away from a supplier's product can create strong incentives to lower price. Thus, even if substitution between particular products is not appropriate for all patients, competition can exist as long as substitution is appropriate for *some* patients. The magnitude of that competition will then depend on the magnitude of substitution: the higher the fraction of the buyer's demand that can be shifted, the greater the competition.

Encouraging substitution when appropriate is an important strategy employed by pharmacy benefit managers (PBMs) in the U.S. to stimulate competition and control pharmaceutical prices. PBMs not only actively

83 These strategies are not mutually exclusive. The incremental value of any particular strategy, however, will depend on the overall level of competitiveness, thus the extent to which other strategies have affected competition.

encourage substitution between branded and generic products, they encourage substitution between different molecules when there are significant price differences between those molecules and when such substitution is medically appropriate.

C. Modify the procurement process

This section discusses insights from the economic literature on contracting and how those insights can be used to stimulate competition and lower prices.

1. Provide increased clarity on how the GF awards bids

There is limited public information about how the Global Fund determines which ACT suppliers get contracts and how the GF will then allocate demand across those selected suppliers. We understand that the process to occur as follows.[84] In the GF's last round of QAACT procurements (2014), the GF solicited bids from all QAACT manufacturers. Following that initial bid, the GF entered into discussions in which it solicited information about the manufacturers' costs. Based on those discussions, the manufacturers submitted a second-round bid at which point the GF selected suppliers and allocated demand across those suppliers, with each supplier receiving its second-round bid price. The GF then entered into two year contracts with all suppliers despite significant heterogeneity across some of those suppliers' bid prices.

There appears to be little information, however, about the following aspects of the bid process.[85]

- How the GF's total ACT demand will be divided across different ACT molecules (e.g., AL vs. AS-AQ) or across different formulations within a molecule (e.g., tablets vs. dispersible tablets; 50 mg. vs. 100 mg strength; or 12 tablet packs vs 24 tablet pack).
- How much information the GF provides on which firms are bidding, and for which products they are bidding, and the competitiveness of those bids.
- How a manufacturer's costs enter into the GF's allocation (or selection) decisions and the GF's willingness to drop firms that set too high a price.[86]
- What type of information the GF provides to the firm before the round 2 bids. Does the GF indicate any type of maximum allowable price such that, if the firm charges above that price, the GF is unlikely to contract? Does the GF share information about competitors' bids?
- To what extent does the GF inquire about bidders' capacities and to what extent does the GF seek to match expected demand to aggregate capacity across the winning bidders?
- Is the GF more "tolerant" of high bid prices from innovators or higher-cost firms? If so, what kind of tolerance exists?

84 See, for example, "The Global Fund Approach to Sourcing ACT, Lin Li, Global Fund Sourcing, The Global Fund, available at http://www.rollbackmalaria.org/files/files/partnership/wg/wg_procurementsupply/docs/6_LLIGlobal FundACTtenderandoutcome.pdf.

85 Of course, if the manufacturers bidding on these contracts know all these details, then increasing public awareness of the auction structure will have little or no impact on competition.

86 In the economic literature on contracting with monopolists, estimates of the monopolist's cost typically has a significant impact on how the optimal price, and output, is determined. See, for example, Baron, D. & Myerson, R. (1982), "Regulating a Monopolist with Unknown Costs," *Econometrica* (50), July; Baron, D. and Besanko, D (1984), "Regulation, Asymmetric Information, and Auditing," *Rand Journal of Economics* (15), Winter. At the other extreme, a firm's reported cost plays no role in the price a buyer should pay in competitive markets.

Absent information about how contracts and orders depend on bid prices, firms may either bid higher or lower than they would bid in a full-information world. More generally, however, uncertainty about how the bidding process works is likely to cause firms to build in a "risk premium" that will raise price. Thus, providing increased clarity about how the GF will award contracts may increase competition.

2. Reduce the number of winning bidders

We understand that in the GF's 2014 round of QAACT procurements, the GF contracted with all bidders despite significant heterogeneity in those bidders' prices.[87] Moreover, as illustrated in **Table 3**, the GF did not always reward low-priced bidders with higher volumes than high-priced bidders.[88] For example, the GF's purchases from Novartis were much greater than its purchases from either IPCA or Ajanta, despite Novartis having the highest price of all bidders. Similarly, while QCIL's price was 15% higher than Macleod's price, the GF's purchases from QCIL were 21% higher than its purchases from Macleod. In fact, as shown in **Table 3**, 85% of all GF purchases were from firms priced above Macleods, with 10% of total purchases from a firm charging an 89% pricing premium relative to Macleods.

TABLE 3
2015 PQR Sales: AL (20 mg + 120 mg 30x24 tablet blister packs)

	2015 Sales ($000)	Price	Price Premium relative to Lowest Price	Share of Sales ($)	Cumulative Sales to Firms with Pricing Premium
Novartis Pharma	1,098	49.2	89%	10%	10%
Quality Chemical Industries Ltd. (QCIL)	1,970	30.0	15%	18%	28%
IPCA Laboratories Ltd	193	30.0	15%	2%	30%
Ajanta Pharma	513	29.9	15%	5%	35%
Strides Acrolab Ltd.	2,763	28.8	10%	25%	60%
Cipla Ltd.	2,747	27.3	5%	25%	85%
Macleods Pharma	1,629	26.1	0%	15%	

More generally, as illustrated in **Figure 5**, there is simply not a strong relationship between bid price and sales volume. That could be due to capacity constraints but we have no information suggesting that is the case. And absent a strong relationship between price and volume when there is no capacity constraint, firms have little incentive to compete for sales by offering low price.

87 See http://www.rollbackmalaria.org/files/files/partnership/wg/wg_procurementsupply/docs/6_LLIGlobalFund ACTtenderandoutcome.pdf confirming that all QAACT bidders in the 2014 round were selected to supply. **Table 2** shows that, while qualified, several firms did not make QAACT sales in 2015 through the GF. We understand that those firms were either exiting the market, thus may not have submitted bids (Strides and Guilin) or became qualified too late in the process to be awarded a bid (Mylan was qualified in May 2014 and Ajanta in July 2013). We note, however, that even if some bidders were not selected by the GF, our basic arguments about the importance of reducing the number of bidders remain relevant.

88 **Figure 5** and **Table 3** show prices and sales for 20 mg + 120 mg 30x24 tablet blister packs (for products in which freight is reported separately) for AL, one of the highest volume QAACT products. Similar relationships exist for other products.

FIGURE 5
2015 PQR Sales: AL (20 mg + 120 mg 30x24 tablet blister packs)

By awarding contracts to all bidders, the GF seemingly failed to use the threat of walking away from a supply contract to create completion among suppliers and thus elicit lower prices.[89] Similarly, the GF seemingly did not use its information on firms' costs to determine which firms had such low costs that they would likely offer lower prices before walking away from a contract.[90] Instead, it appears the GF may have been acting more as a regulator than a buyer in a competitive market.[91] Rather than take advantage of firms' incentives to offer a lower price in return for higher volume, the GF seems to have collected information about firms' costs in an attempt to determine a "fair" price for each firm. In the period between when firms submitted their first- and second-round bids, the GF may have suggested to firms what that "fair" price should be, with the GF concluding that higher-cost firms (e.g., the innovator firm Novartis) may have deserved a higher price than lower-cost generic firms. Trying to determine "fair" prices, rather than creating incentives for firms to offer the best price they are willing to accept, creates more of a regulatory environment than a competitive environment and largely negates the benefits of increasing the number of suppliers in the market.

The implications of the GF's failure to create a stronger relationship between bid price and sales volume, and its apparent willingness to contract with all suppliers regardless of price, are significant. By failing to concentrate purchases from those firms offering the lowest prices, and cut off purchases from high-priced firms, the GF

89 The GF recognizes, however, the importance of reducing the number of winning bidders, flagging that a key objective in the GF's new procurement strategy is to enter into contracts "with a limited number of selected suppliers." The GF indicated, however, that the the maximum volume of (non-dispersible) AL or AS-AQ products supplied by any one firm would be capped at 40% of total demand. Presentation by Dr. M. Jallow, Head of Direct Procurement, "ACT Acquisition Strategy," ACT Supplier Conference, Geneva, March 2014, available at http://webcache.googleusercontent.com/search?q=cache:f54Wc7OPbfkJ:www.theglobalfund.org/documents/p4i/events/P4I_2014-03-14-ACT-Supplier-Conference_Presentation_en/+&cd=2&hl=en&ct=clnk&gl=us&client=safari.)

90 As long as the GF is involved in multi-period negotiations with several firms, greater information about each firm's actual costs allows the GF to better ascertain a firm's true walk-away threat points, thus better determine whether a firm's claim that it needs a certain minimum price is credible. This increased cost information can help the GF negotiate better prices.

91 See Unitaid Malaria Medicines Landscape, March 2015 for a discussion of how AMFm set maximum prices but did not appear to rely on competition to obtain lower prices.

largely eliminated firms' incentives to compete and offer lower prices in return for increased sales. Under those circumstances, the preceding section's discussion of increasing competition by increasing the number of competitors becomes largely moot—unless buyers take advantage of the competitive process and let competition work, it is largely irrelevant how many firms are in the market.

In order to take advantage of the competition among existing suppliers, the GF would need to increase the perceived elasticity of demand facing bidders by making purchase volumes much more sensitive to price. Thus, rather than award contracts to all bidders, the GF could rank firms in terms of their price, and working their way down that list from lowest-price to highest-price firm, determine the minimal set of suppliers that could satisfy GF demand.[92]

Awarding contracts based on bid-prices would not imply that the branded innovators in a market (Novartis in AL, and Sanofi in AW-AQ) will end up without a contract. In particular, while those innovators' fixed (and thus average) costs may be higher than their generic competitors' costs, it is not clear that innovator's marginal production costs will be higher. And as long as innovator's marginal costs are comparable to generic manufacturers', innovators would face no competitive disadvantage. Higher average costs, however, may mean that innovators have a difficult time recouping R&D costs in competitive markets. And absent an ability to recoup R&D costs, firms may be unwilling to innovate in the future. However, as mentioned earlier large buyers such as the GF can directly subsidize firms' R&D costs rather than indirectly subsidize R&D costs by allowing innovators to charge higher prices.[93]

Although reducing the number of suppliers with which the GF contracts will increase short-run competition, there is a risk that it could reduce long-run competition: given the GF's importance in purchasing QAACT medicine, firms that fail to win an award from the GF may exit the market, and thus become unavailable to compete the next time the GF seeks to award a contract. In that scenario, the GF's remaining suppliers would enjoy more market power in the subsequent round of bidding since GF would need to contract with each of the remaining suppliers in order to meet demand.[94] This suggests that, when awarding contracts, the GF may want to award contracts to additional suppliers as long as those suppliers' prices are not significantly higher.[95]

The extent to which the GF should contract with more than a minimal set of suppliers in order to protect long-run competition depends on several factors.

- **The likelihood that losing firms will exit the market**.
    - *The size of the GF relative to other QAACT buyers.* The GF accounts for approximately 60% of QAACT purchases by donor agencies.[96] Yet, because the GF splits its purchases among so winners, even those manufacturers that win a bid are often left serving less than 10% of GF demand, which amounts to less than 5% of worldwide QAACT demand. Thus, winning a bid may not be that beneficial. Moreover, a supplier that fails to win a GF contract can still compete to make sales to customers representing more than 40%

92 Consideration should also be given to ensuring supply in the event of supply-chain disruptions. Kenya, for example, is reported to have experienced widespread supply disruptions in 2008 when it relied on a single supplier (Ajanta) for AL that was ultimately unable to deliver product. See Tren, R., et. al, "Drug Procurement, the Global Fund and misguided competition policies," *Malaria Journal*, 2009.)

93 Direct lump-sum subsidization of R&D costs will likely reduce short-term distortions relative to the alternative of paying higher unit-prices. Few subsidies are without some distortion, however. A lump-sum subsidization could create its own distortions by encouraging excessive, or ineffective, R&D efforts in the anticipation that the cost of those efforts will be compensated.

94 This is a problem that often arises with major defense industry contracts in which there are a limited number of potential suppliers. The solutions, however, that are often discussed in that industry (e.g., teaming arrangements between winning and losing firms) are not necessarily apt in market for AM medicines.

95 Awarding additional contracts will also reduce the risk associated with supply interruptions from any individual supplier.

96 Supra note [22]. The GF's share of overall QAACT purchases will be less than 60% since not all QAACT purchases are made through donor agencies.

of worldwide QAACT demand—a market that can be several times larger than the sales the firm might have otherwise made through the GF. Thus, it is unclear that a firm that fails to win a GF contract will necessarily lose so many sales that they firm cannot afford to remain in the market

- *The duration of the GF's contracts.* The shorter the duration of the GF's contracts, the shorter the period a firm is unable to sell to the GF before it has another chance to obtain a contract. GF's current contracts are two years in length. This is not an inordinately long period of time that losing firms must abstain from selling through the GF, especially if the firm can continue making sales to those non-GF customers that collectively account for 40% or more of QAACT demand.
- *The likelihood that a losing firm will win a contract in the future.* A firm only has an incentive to remain in the market so that it can bid again in the next contract period if that firms believes it has a good chance of winning a contract in the next round. Low-cost firms that submitted an excessive price in the hopes of 'getting lucky' are more likely to stay in the market so that they can bid in the next round of contracts. High-cost firms that anticipate they will continue being beat out by lower-cost firms are more likely to exit. High-cost firms, however, do little to increase competition, and thus their exit from the market is of little competitive consequence.
- *The expected incremental profitability of future contracts.* In deciding whether to exit the market, a firm will compare its expected future margins (i.e., price in excess of variable cost) to the fixed costs that it could recover if it exited the market.[97] For many QAACT producers, a large share of their fixed costs may be stem from the regulatory cost of meeting QA requirements, and that cost may be non-recoverable. Producers' recoverable fixed costs may be small. Moreover, a producer's expected margin from future sales may be high if medicine prices tend to reflect (high) average costs rather than (low) variable costs. Under those conditions, exit may not be profitable: a producer may prefer to invest in remaining in the market in the hopes of realizing profitable sales in the future.
- *The ability of QAACT firms to make short-term sales in other markets.* Firms may be able to put idle QAACT capacity to other temporary uses in way that allow them to profitably remain in the QAACT market. QAACT firms may, for example, be able to sell into the non-QA ACT market. Although those QAACT firms' fixed (and sunk) costs may exceed their non-QA rivals' costs, they may nevertheless find this a profitable way of recouping at least some of their costs while waiting for the next round of contracts.

- **Degree of pricing separation between winners and losers**. The cost of increasing the set of winning bidders stems from the higher price that the buyer has to pay to those losers. If that price difference is substantial, the buyer incurs a substantial cost to maintain long-run competition. The smaller the price difference, the smaller the cost. This suggests that, unless there is little or no fear of market exit by losers, the buyer should award a contract to at least some higher-price bidders as long as their price does not significantly exceed the price of the winning bidder who had the highest price among the winners. We expect, however, that the optimal degree of allowable pricing separation is less than what the GF allowed in its last round of bidding.

Based on these factors, we do not anticipate a significant risk that reducing the number of firms with which the GF contracts would induce market exit and thus significantly reduce long-run competition.

3. Increase the relationship between price and sales

Firms' prices should not just affect whether they are awarded a contract with the GF: price should also affect their sales under that contract. Although PQR data suggests that there is some relationship between price

97 Economists refer to those "recoverable" fixed costs as costs that are not "sunk."

and sales, as shown in **Figure 5**, that relationship is often quite weak. Strengthening that relationship would increase the effective demand elasticity, thus create incentives for firms to offer lower prices in pursuit of increased sales.[98]

4. Delegate contracting authority to individual countries

For most countries purchasing QAACTs, the GF serves as their contracting agent by negotiating prices with suppliers. There are two rationales for the GF serving as a contracting agent. First, by consolidating demand across individual countries, the GF may realize superior volume discounts relative to what an individual country could realize. Second, the GF may have greater contracting expertise than many individual countries.[99]

In some situations, however, countries might do better by negotiating on their own: not only might countries have the procurement expertise necessary to engage in their own contracting,[100] they may be able to obtain more attractive contract prices *despite* negotiating for much lower volumes than does the GF.

An individual country's potential ability to negotiate better prices than the GF stems in significant part from the GF's past reluctance to reward low-priced bidders with high volume and punish high-priced bidders by denying them a contract.[101] In essence, regardless of the volume that the GF offers, an individual firm has no incentive to offer volume discounts unless the GF rewards that firm with increased volume. An individual country, by offering to steer volume to low-priced bidders, can take advantage of the competition that the GF has been less able to enjoy.

The volume that individual countries can offer suppliers can be significant: a sole-source contract with a single country can result in more sales than sharing a much larger contract with a purchaser such as the GF. For example, as shown in **Table 4**, a sole source contract to serve all of Uganda's QAACT needs would amount to approximately $7 million. That single contract exceeds Cipla's total QAACT sales ($5.3 million) through the GF.[102] Thus, a supplier's incentive to win a sole-source contract with a single country can actually be greater than it's incentive to win a contract with the GF.[103] Incentives to offer a low price will be further intensified if bidders know that price is a critical determinant of whether they will be awarded that contract.[104] Thus, individual countries—particularly those purchasing large volumes of QAACT medicines—can potentially create substantial competition among suppliers and thus expect very competitive prices.[105]

98 Of course, buyers must also ensure that suppliers are aware that selection and allocation of demand will become more sensitive to bid price: increasing buyer price sensitivity without informing suppliers of that change will not lead to lower prices – only very surprised bidders.

99 See, for example, Arney, L., et. al, "Strategic Contracting Practices to Improve Procurement of Health Commodities," *Global Health: Science and Practice*, 2014. The GF also plays an important role by helping forecast overall demand for medicines, thus reducing demand-size risk for suppliers. This function, however, is likely separable from the GF's role as countries' contracting agent.

100 For a discussion of individual countries' expertise in this area, see, for example, Yadav, P, "Kenya Medical Supplies Authority (KEMSA): A case Study of the Ongoing Transition from an ungainly bureaucracy to a competitive and customer focused medical logistics organization," Study for the World Bank, William Davidson Institute, April 2014, available at http://documents.worldbank.org/curated/en/2012/04/20330086/kenya-medical-supplies-authority-kemsa-case-study-ongoing-transition-ungainly-bureaucracy-competitive-customer-focused-medical-logistics-organization.

101 This may reflect a principal-agent problem in which the agent (the GF) is less affected by high medicine prices than is the principal (the individual country). Additionally, the GF may have somewhat different objectives than an individual country: political considerations may make it more difficult for the GF than an individual country to deny a contract to particular QAACT suppliers.

102 These revenues represent PQR data, partial year 2015. **Table 4** is limited (confirm) to sales in which freight costs are reported separately, and thus excludes purchases from Kenya, Rwanda and certain other countries.

103 This result could be reversed if a supplier's contracting costs are significantly greater when contracting with individual countries relative to the GF.

104 See, however, Tren, R. et al, "Drug Procurement, the Global Fund and misguided competition policies," *Malaria Journal*, December 2009 for potential dangers of focusing too much on price, and not enough on reliability, when awarding contracts.

105 Individual countries are also less likely to be concerned about the need to contract with multiple suppliers for fear that losing firms will exit the market.

TABLE 4
PQR sales: All QAACTs

	2015 Sales ($)			2015 Sales ($)
Nigeria	8,002,573		Cipla Ltd	5,342,494
Uganda	7,068,500		Strides Arcolab Limited	4,711,397
Mozambique	4,943,020		Sanofi Aventis	4,172,165
Congo (Democratic Republic)	1,662,547		IPCA Laboratories Ltd	3,650,030
Côte d'Ivoire	1,555,285		Quality Chemical Industries Ltd.	3,194,035
Malawi	1,521,579		Ajanta Pharma	2,901,687
Burkina Faso	1,186,036		MacLeods Pharmaceuticals Ltd	2,817,338
Zambia	1,076,176		Novartis Pharma	2,076,703
South Sudan	531,799		Guilin Pharmaceutical Co. Ltd	340,712
Central African Republic	372,494		Sigma Tau	234,020
Cameroon	340,712			
Cambodia	240,425			
Zimbabwe	232,595			
Chad	192,857			
Benin	152,928			
Solomon Islands	127,092			
Multicountry East Asia and Pac	92,664			
Guinea-Bissau	73,704			
Bangladesh	33,869			
Philippines	23,481			
Iran (Islamic Republic)	4,256			
Sao Tome and Principe	3,350			
Myanmar	2,639			

Whether individual countries can actually negotiate lower prices than the GF is an empirically testable question. While limited, the evidence suggests that individual countries can and do negotiate substantially lower prices than the GF. KEMSA, Kenya's office for procuring medical supplies including QAACT medications, negotiates directly with ACT manufacturers rather than relying on the contract prices negotiated by the GF. And while KEMSA's purchases of QAACTs are less than 5% of total QAACT purchases through the GF, KEMSA believes that the prices it negotiated are significantly lower than the prices available through the GF.

The apparent success of KEMSA in obtaining more favorable rates than the GF likely lies in its willingness to sole source those medicines. Unlike the GF that spreads its purchases across all manufacturers, thus reducing individual manufacturers' incentive to offer a low price, KEMSA offers all-or-nothing contracts for particular medicines to the lowest price firm: all AL dispersible tablets were sourced from Novartis, while all non-dispersible tablets were sourced from Strides (in 2014) or IPCA (in 2013). Similarly, Rwanda—another country that purchases its QAACT medication directly from manufacturers, reports purchasing all of its AL dispersible tablets in 2014 from Ajanta, and all its non-dispersible AL tablets from IPCA in 2013 and 2014. That sole sourcing strategy creates significantly more competition among suppliers, and may result in lower prices, than the prices that result from the GF's strategy.[106]

106 Of course, this suggests that, rather than delegate contracting authority to individual countries, the GF could instead modify its own contracting strategy to more closely mimic the sole-sourcing approach that KEMSA has found to be so effective. This approach might also be useful in cases where the GF is better situated from an institutional perspective to negotiate those contracts. Although KEMSA and other countries appear to have very professional staff that can take on that responsibility, that might not be the case in all countries.

The benefits of delegating contracting authority to individual countries might be further increased if individual countries, particularly countries with very small demand, join group purchasing organizations (GPOs). These GPOs could aggregate demand across several countries, and thus potentially realize even greater volume discounts than can any individual country. GPOs might also provide contracting expertise that some individual countries lack.[107]

In essence, GPOs may be able to provide many of the benefits that the GF is currently believed to offer but without the same drawbacks. In particular, GPOs might have greater ability than the GF to enter into exclusive contracts with a limited number bidders, both because individual GPOs may not face the same type of political constraints that the GF faces with respect to their ability to pick winners and losers, and because there is less worry that a supplier will exit the market if it fails to win a GPO contract than if it fails to win a GF contract. In addition, individual GPOs may have incentives to compete for member countries on the basis of providing superior contracting services than are available through the GF. Those superior services might include both superior contracting rates, but also better member service.

VIII. The upstream artemisinin market

The preceding discussion focused on competition in a market in which QAACT manufacturers sell to large buyers such as the GF or individual countries. The next two sections briefly discuss two other important markets: the upstream artemisinin market involving a key ACT input, and the downstream market involving the sale of AM medicine to individuals.

The upstream ART market merits discussion for several reasons. First, ART is a key input to QAACT medicine: ART is estimated to account from 17% to over 50% of QAACT costs.[108] Second, ART supply is likely very inelastic in the short-run. This inelastic supply, combined with frequent supply and demand shocks, means that, as shown in **Figure 3**, ART prices fluctuate dramatically over time absent strategies to more effectively match supply and demand. Lastly, the introduction of semi-synthetically produced ART (SS-ART) has the potential to create significant technological changes in the ART marketplace and with it, a reduced competition from AG-ART producers.

A. The supply of agricultural artemisinin

AG-ART is grown by hundreds of farmers in China, as well as Africa and India. AG-ART takes approximately 11–14 months from the time of planting seeds to when an artemisinin-based QAACT product can be delivered.[109] And because AG-ART has a limited shelf-live (approximately 24 months),[110] the supply of AG-ART is largely fixed at any point in time. This means that demand shocks, as well as weather-related supply shocks, can have a dramatic effect on AG-ART prices.

Inelastic supply of AG-ART also limits any benefits from increasing competition among QAACT suppliers: even if competition lowered the margins that QAACT manufacturer realized, QAACT prices would remain high because

107 GPOs are commonly used by hospitals in the United States as a means of realizing volume discounts on medical drugs, devices and medical equipment that they could not realize on their own. GPOs also reduce contracting costs by delegating numerous hospitals' price negotiations to a single GPO negotiator. Notably, however, many GPO member hospitals find it more cost-effective to purchase outside of the GPO, despite the GPO's greater volume. This provides additional evidence that principal-agent problems may render agents such as GPOs and GF less effective at negotiating prices relative to the case where the principal (hospitals or individual countries) negotiates directly with suppliers.

108 Active Pharmaceutical Ingredient (API) Market Dynamics Information Services (MDIS), WDI/Howard University, Annual Technical Report for Unitaid, November 2014. See also "Microbially Derived Artemisinin: A Biotechnology Solution to the Global Problem of Access to Affordable Antimalarial Drugs," Hale, V. et al, December 2007, available at http://www.ncbi.nlm.nih.gov/books/NBK1717/.

109 Malaria Treatment in Africa, Tren et. al (2008); and Affordable Medicines Facility-malaria (AMFm): Assessment of the effects of the AMFm on market dynamics of API and ACTs at the global level, Final Report, January 28, 2012, William Davidson Institute.

110 Tren et. al (2008), *op cit*.

the constrained supply of AG-ART would lead to higher AG-ART prices, and thus high prices for QAACT. In essence, limited availability of the AG-ART input creates a capacity constraint on QAACT output, with the market price then determined by where that capacity constraint crosses the market demand curve. This means that, even with increased competition among QAACT manufacturers driving down QAACT manufacturers' margins, there is no increase in QAACT output: increased QAACT competition simply ends up benefitting AG-ART producers in the form of higher margins.

Inelastic AG-ART supply in the short-term similarly limits the ability to achieve lower QAACT prices through increased competition among QAACT manufacturers. Recall that a firm's incentive to offer lower prices stems from the firm's desire to expand its sales of profitable product. But with a limited AG-ART supply in the short-run, the marginal cost of additional output becomes very high, thus reducing the profitability of increased sales. That reduced profitability, in turn, reduces incentives to compete for additional sales.

The supply of AG-ART is likely to be much more elastic in the long-run. Individual farmers are likely to respond to higher AG-ART prices by increasing their planting of AG-ART if those farmers can be reasonably assured that the higher expected prices will, in fact, materialize. This emphasizes the importance of trying to increase the accuracy of demand forecasting. It also suggests that the risk associated with demand shocks (and even supply shocks) should be transferred from the farmer to the QAACT manufacturers, with manufacturers committing upfront to the price and volume they will pay farmers.

B. Competition between AG-ART and SS-ART

Sanofi, partnering with Amyris in California, introduced a new technology by which ART can be manufactured in a lab rather than grown in an agricultural setting.[111] This semi-synthetic version of artemisinin (SS-ART) is identical to AG-ART, but has a much shorter production time: rather than an 11–14 month lag between planting seeds to the production of QAACT medicines, SS-ART has just a 3 month lag from lab to QAACT production.[112] This can significantly increase short-term supply elasticity, thus potentially dampen the historical price fluctuations caused by supply- and demand-shocks. To date, there is a single producer of SS-ART, with estimated production capacity of approximately 50–60 tons/year and costs of approximately $350–$400/kg. This capacity can satisfy approximately one-third of worldwide ART demand. Moreover, as can be seen from **Figure 3**, the cost of SS-ART is comparable to AG-ART.[113]

There has been considerable concern expressed that SS-ART will displace AG-ART and that this displacement would reduce welfare.[114] Much of this debate appears to center on the largely non-economic question of whether the displacement of small farmers in China by a manufacturing plant in Italy is desirable. But there are also several important economic questions. Is such displacement likely to occur? How will that displacement affect ART prices and supply? To what extent should this new technology be encouraged and potentially subsidized (and if so, how)? Are there legitimate concerns that a single firm with rights to the SS-ART technology might be able to engage in anticompetitive foreclosure of the AG-ART industry?

111 Sanofi recently sold its technology to HuvePharma, a for-profit pharmaceutical firm headquartered in Bulgaria. HuvePharma has not made public its plans regarding SS-ART (*Nature* (2016)).

112 "Semi-synthetic Artemisinin Project", Sanofi presentation at the RBM/Unitaid/WHO Artemisinin Conference, January 2013, available at http://www.rollbackmalaria.org/files/files/partnership/wg/wg_procurementsupply/docs/12_WLAUXSA Update.pdf. See also Unitaid Malaria Medicines Landscape, March 2015.

113 Supra notes [30], [31] and "Stabilizing the antimalarial drug supply," PATH, July 2014, available at https://www.path.org/publications/files/DRG_ssart_fs.pdf. Although never specified, we understand that these represent average total costs, not marginal or variable costs.

114 See, for example, "Malaria drug made in yeast causes market ferment," *Nature*, February 14, 2013 at pp. 160-61; "Synthetic anti-malarial compound is bad news for artemisia farmers," *The Guardian*, April 12, 2013, available at http://www.theguardian.com/global-development/poverty-matters/2013/apr/12/synthetic-malaria-compound-artemisia-farmers; and "Why Synthetic Artemisinin is Still a Bad Idea – A Response to Rob Carlson," June 2013, available at http://www.etcgroup.org/content/why-synthetic-artemisinin-still-bad-idea-response-rob-carlson.

A thorough discussion of these questions on how competition between AG-ART and SS-ART will materialize is beyond the scope of this paper. We note, however, a few important industry facts that will be relevant to that analysis.

- We understand that, although Sanofi has offered to sell SS-ART to its QAACT competitors, to date Sanofi is the only QAACT manufacturer to use SS-ART.
- In recent years, even Sanofi has chosen to rely exclusively on AG-ART.[115] This suggests that the marginal cost of SS-ART may be high relative to the cost of AG-ART.
- Although Sanofi historically committed to making its SS-ART available at cost, the firm that recently purchased that technology from Sanofi has not made any such commitment.
- We understand that the technology associated with SS-ART is proprietary and under the control of a single firm (formerly Sanofi, and now HuvePharma). There are reports, however, that other firms (Guilin and Cipla) are working on their own SS-ART technology.[116]
- We understand that there are few barriers to entry, or substantial sunk costs, associated with the farming of AG-ART,[117] although there are likely some costs incurred by AG-ART processors that turn the agricultural product into the API purchased by ACT manufacturers. All else equal, those limited costs and lack of entry barriers would make it difficult for a SS-ART manufacturer to foreclose competition from AG-ART manufacturers: any post-foreclosure strategy in which prices increase would be expected to induce farmers to re-enter the AG-ART market.
- HuvePharma (and formerly Sanofi) might nevertheless be able to successfully foreclose competition from AG-ART farmers. AG-ART farmers' decisions to plant are based on the expected price that will be realized when the crop is harvested. The expected price will be the result of a range of potential prices that result from demand and supply fluctuations. The ability of the SS-ART producer to decide how much to produce after the AG-ART producers' crops are planted may allow the SS-ART producer to credibly commit to a production level that will eliminate the possibility of the higher prices, thereby lowering the *ex ante* price expected by the AG-ART producers. If that lower expected price isn't sufficient for AG-ART producers, they may choose not to produce at all. Note that this can occur even though the AG-ART producers know it is happening because the AG-ART producers always know that the SS-ART producer will decide after AG-ART producers have already committed (planted their crops).

IX. Downstream Retail markets for anti-malaria medicine

A complete analysis of the downstream markets is not a goal of this paper. However, there are a few points worth noting because competition in the downstream market differs in several important regards from the upstream market.[118] First, information asymmetries are likely much greater in the downstream market. While

115 Peplow reports that Sanofi produced no SS-ART in 2015. (Peplow, M., "Synthetic Biology's First Malaria Drug Meets Market Resistance," *Nature*, February 23, 2016, available at http://www.nature.com/news/synthetic-biology-s-first-malaria-drug-meets-market-resistance-1.19426.)

116 *Nature* (2016).

117 See, for example, "The Global Fund Approach to Sourcing ACT," The Global Fund, available at http://www.rollbackmalaria.org/files/files/partnership/wg/wg_procurementsupply/docs/6_LLIGlobalFundACTtenderandoutcome.pdf.

118 This section provides only a brief overview of some of the issues relevant to retail markets for anti-malaria medicine. A more thorough discussion can be found in Patouillard, E., et. al, "Determinants of price-setting decisions on anti-malarial drugs at retail shops in Cambodia," *Malaria Journal* (2015); Goodman, C., et. al, "Concentration and Drug Prices in the Retail Market for Malaria Treatment in Rural Tanzania," *Health Policy and Planning*, 2015; Rusk, A., et. al, "Expanding Access to Malaria Diagnosis through Retail Shops in Western Kenya: What do Shop Keepers Think?" Malaria Research and Treatment (2013); and Alba, S., et. al, "Improvements in access to Malaria Treatment in Tanzania after switch to ACT and the Introduction of Accredited Drug Dispensing Outlets – a provider perspective," *Malaria Journal*, 2010.

buyers in the upstream market have good information about the relative efficacy of different drugs and the quality of different suppliers, individuals in the downstream market likely have very limited information about the alternative medicines that may be available to them. Thus, individuals frequently purchase anti-malarial medicines even in areas where resistance to that medicine is so great that the medicine is likely ineffective.[119] Individuals are also less likely to know the quality of the different suppliers, thus opening the door for counterfeit or poor quality suppliers.[120] Individuals' limited information also creates significant principal-agent issues in which pharmacists and others have significant influence over choice, thus leading to steering of patients to the most profitable products rather than the most appropriate products.[121]

Downstream competition may also be quite limited in certain regions.[122] Given high transportation costs between towns, individuals in many geographic markets may enjoy a limited number of competing providers for AM medicines.[123] Competition between towns may be further reduced if information asymmetries mean that individuals have greater trust in their local provider. Thus, even though individuals in certain regions may be able to choose from multiple suppliers' AM medicine at a particular retail outlet, that private sector outlet may face *de minimus* competition from other outlets, thus allowing substantial markups on that medicine.

The geographic market for individual patients may be quite narrow due to limited access to transportation, thus significantly reducing the number of competing providers. Competition may be further limited by stock-outs, especially of ACT by the public sector providers that offer the product at no cost. In areas where QAACTS are readily available for free at public sector clinics, however, there will be significant competition.

The product market defining the set of products and services that individuals consider substitutes is less clear. There is significant evidence of a willingness to substitute between different types of medicine on the basis of price.[124] In particular, a significant share of private retailers' AM sales typically include non-ACT medicines such as chloroquine and sulphadoxine-pyrimethamine.

There is less evidence on consumers' willingness to substitute between private and public sector providers. In principle, consumers choose between private and public sector providers based on their relative prices, their

119 See, for example, Laxminarayan, R. et. al, "A Global Subsidy: Key to Affordable Drugs for Malaria?" *Health Affairs*, 2009; and "Distribution of Artemisinin-Based Combination Therapies through Private-Sector Channels: Lessons from Four Country Case Studies," Resources for the Future, Jan, 2009. Estimates are that less than 60% of children under the age of 5 treated for malaria are treated with ACT medicines (Tougher, S., "Effect of the Affordable Medicines Facility-malaria (AMFm) on the availability, price, and market share of quality-assured artemisinin-based combination therapies in seven countries: a before-and-after analysis of outlet survey data," *The Lancet*, December 1, 2012.

120 Meek and Nankabirwa (2014), op cit, discuss a 2012 study finding that roughly one-third of all AM medicines being sold were falsified or sub-standard. See also Bate, R., et. al, "Antimalarial Drug Quality in the Most Severely Malarial Parts of Africa: A Six-Country Study," Plos@ ONE 3, no. 5 (May 7, 2008), available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2324203/; or Alphs, S., and Yadav, P., "Malaria in the Asia-Pacific: Challenges and opportunities for access to quality malaria medicines and other technologies," William Davidson Institute at the University of Michigan, October 2012, available at http://wdi.umich.edu/wp-content/uploads/Malaria-2012-Issues-paper-No-3-2.pdf.

121 These principal agent problems can also significantly affect the efficiency of malaria testing: absent appropriate pricing and other incentives, private sector retailers may discourage testing (or downplay the reliability of that testing) in order to continue making profitable sales of medicine. There is also evidence that individuals frequently disregard malaria test results, with a significant share of patients that test negative for malaria still purchasing AM medication (Cohen et. al (2015)).

122 Cohen et. al (2015) assume at market with radius of 4-km when assessing patients' choice of retail providers and find that individuals in Kenya travel, on average, approximately 1.7 km in order to use vouchers to purchase QAACT medicines. Sabot (2009) similarly assumes localized markets with radius of just 1 km around each retailer.

123 Transportation costs include both financial costs (e.g., the cost of a bus) and non-financial (lost time from travelling between towns).

124 Much of this evidence relates to the Affordable Medicines Facilities – Malaria (AMFm) program in which private sector sales of ACT medicines in certain countries were subsidized on the order of 90%. This resulted in dramatic private sector price reductions for ACT medicine, with a significant concurrent shift in patient demand from non-ACT to ACT medicine. The magnitude of substitution caused by smaller relative price changes, however, is less clear. See, for example, Cohen et. al (2015); Ye, Y. et. al, "The Affordable Medicines Facility-malaria (AMFm): are remote areas benefitting from the intervention?" *Malaria Journal*, Oct. 9, 2015; and Sabot (2009) ; and Morris, A., et. al, "Price subsidies increase the use of private sector ACTs: evidence from a systematic review," *Health Policy Plan*, March 14, 2014, available at http://www.ncbi.nlm.nih.gov/pubmed/24633915.

relative convenience (including expectations that either type of provider will have the desired medicine available), and their relative quality and service (are the providers likely to recommend the correct treatment). Thus, the availability of public sector providers should provide some price discipline on private sector providers even if there are few alternative private sector retailers available to a consumer. Information asymmetries, however, mean that the public sector likely provides less discipline with respect to quality and service: individuals may not know if they are being provided inferior or inappropriate medicine or treatment.

Despite the general acknowledgement that competition benefits consumers, policymakers and large buyers such as the GF should be cautious in seeking to encourage increased retail level competition among AM providers. In addition to the usual caveats that interventions can sometimes create unwanted and unanticipated distortions,[125] increasing competition in markets with significant information asymmetries can actually result in consumer harm. Private sector providers might compete, for example, by pushing less effective medicines, or distorting claims about the efficacy of the medicine they offer in order to maintain sales. And perhaps paradoxically, lower prices stemming may not benefit consumers: lower prices might induce excessive self-medication even in cases where treatment is unnecessary,[126] changes in relative prices of medicines might encourage consumers to select cheaper medicines while encouraging retailers to recommend more expensive medicines, with both of those decisions being largely uninformed by relative efficacy of the medicines.[127] Further, by stimulating increased use even when medically unnecessary, lower medicine prices can increase drug resistance. Thus, unless the form in which competition occurs can be carefully controlled,[128] increased retail-level competition is not necessarily desirable and increasing that competition is likely not the best use of policymakers or large purchasers' efforts.

X. Conclusion

This paper focuses on an analysis of the malaria market and strategies that large buyers such as the Global Fund can use to increase competition to obtain lower prices, thus allowing for increased purchases of anti-malarial medicine. Although specifics of the market matter in devising strategies to increase competition and in assessing the likely impact of increased competition, much of our malaria-focused discussion likely applies to the other markets in which the Global Fund fund participates—tuberculosis and HIV/AIDS—as well as the vaccine markets in which GAVI plays a similar role. Thus, the analytic framework introduced in this paper should provide a useful first step in analyzing not just malaria markets, but also those other important markets.

We reach two principal conclusions with respect to markets for anti-malaria medicine (particularly QAACT medicines). First, even small increases in competition can have a dramatic impact on global health goals. Thus, further efforts to increase competition are likely warranted and will likely save thousands of lives. Second, when considering different strategies to increase competition, we believe that efforts to increase the number of competitors may be less effective than efforts to increase competition among existing competitors, with the latter strategy involving changing the bidding and procurement process by which large purchasers contract with QAACT suppliers.

We have also highlighted several issues that, while beyond the scope of this paper, warrant additional attention. First, there is a need to assess the relative costs and benefits associated with efforts to increase competition in malaria markets with efforts to reduce malaria incidence through other strategies (e.g., increased use of bed

125 Increasing competition by subsidizing entry, for example, can inappropriately encourage firms to enter regions where there is too little demand.

126 Cohen et. al (2015) find that increased QAACT subsidy levels in Kenya increase the frequency with which medication is provided to individuals that test negative for malaria.

127 See, for example Yadav, P. (Malaria in the Asia-Pacific at p. 14).

128 We understand that Ghana controls retail-level competition through restrictions on geographic proximity between retail pharmacies and licensed medicine shops (see http://www.pharmacycouncilghana.org/registration_Application.html). The minimum physical separation between retailers (400 meters), however, may do little to control that competition.

nets) as well as strategies to save lives currently lost to other illnesses (e.g., tuberculosis). Second, we raise the question of whether a large synthetic supplier of a key ingredient in a market currently dominated by agricultural suppliers can foreclose competition from agricultural suppliers to the ultimate detriment of consumers. Finally, we note the importance of assessing the impact of additional retail-level competition in the provision of anti-malarial drugs and the potential downsides of such competition, especially vis-à-vis the provision of QAACT medicine versus less effective forms of anti-malaria medicines.

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