

Demand Forecasting For Essential Medical Technologies

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I. INTRODUCTION

Today's global health programs will attain their objectives only if products appropriate to the health problems in low- and middle-income countries are developed, manufactured and made available when and where they are needed. Achieving this requires mobilizing public and charitable money for more and better products to diagnose, prevent and treat HIV/AIDS, tuberculosis, malaria, reproductive health problems and childhood killers. But more money is only one part of the story. Weak links in the global health value chain—from research and development through service delivery—are constraining on-the-ground access to essential products. The consequences of those weak links are many: supply shortages, inefficient use of scarce funding, reluctance to invest in R&D for developing country needs and, most importantly, the loss of life among those who need essential products.

One of the weakest links is the forecasting of demand for critical medical technologies, including vaccines, medicines and diagnostic products. Demand forecasting, which may seem at first glance to be a small piece of the very large puzzle of access to medical products, is of central importance. Many of the shortcomings in funding and functioning of health systems impede accurate forecasting of demand—and without the ability to forecast demand with reasonable certainty and some assurance of a viable market, manufacturers cannot scale production capacity, make commitments to suppliers of raw materials or justify a business case for investing in costly clinical trials and other activities to develop future products. National governments and international funders rely on demand forecasts for budgeting, while health programs and implementing agencies depend on forecasts to plan their supply chain logistics. Thus, in the high-level policy debates about the volume, duration and use of donor funds to support R&D and purchase essential health products, one key fact has often been overlooked: if actions by the international community do not increase the ability to generate credible

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forecasts of demand—if, in fact, those actions contribute to a situation of greater uncertainty, with higher stakes—efforts to achieve greater access to life-saving and life-extending medicines will be undermined.

This article examines the ways in which better forecasting could contribute to improved short- and long-term access; outlines market-related risks and the ways in which the asymmetrical burden of risk across funders, regulatory and purchasing intermediaries and suppliers results in misaligned incentives with respect to producing optimal demand forecasts and broad access; and advances a set of specific recommendations for actions by donors and technical agencies that would help to reduce overall risk and correct those misalignments. The article summarizes the findings of the Center for Global Development's Global Health Forecasting Working Group.¹

II. THE CASE FOR BETTER DEMAND FORECASTS

Demand forecasting is defined as the ongoing process of projecting which products will be purchased, where, when, by whom, and in what quantities.² Demand forecasts measure effective demand in the market—that is, product needs that have or will have purchasing power behind them and will result in actual orders.³ Ultimately, effective demand can serve as a metric for assessing actual access to essential medical technologies at the patient level.⁴ This analysis focuses on global aggregate demand forecasts for “new products and new markets” — that is, products that are newly licensed or new entrants into use in developing countries, in contrast to currently available and widely distributed therapies.

While demand forecasting is hardly a new challenge, the need for better forecasting has become acute in the context of current efforts to increase access to essential medical technologies. Crucial decisions about which vaccines, medicines and diagnostics to produce and to buy hinge on realistic projections of the future market — not on what ideally would be required to meet the potential need. If forecasts are off, so are the outcomes: limited funds to purchase products do not stretch as far, and the chance of shortages is higher than would otherwise be the case. The most important consequences are to health: children fail to get malaria medicines and vaccines that will save their lives, pregnant mothers and their babies go unprotected from exposure to malaria and the transmission of HIV, and AIDS patients miss their medicine cycles, jeopardizing their lives and adding to the threat of drug resistance within their community.⁵

The negative economic effects are profound as well. Uncertainties about demand significantly weaken the business case for branded and generic manufacturers' involvement in developing countries and have both immediate and long-term impacts on access to life-saving products.⁶ In fact, when listing

¹ See Neelam Sekhri et al., *A RISKY BUSINESS: SAVING MONEY AND IMPROVING GLOBAL HEALTH THROUGH BETTER DEMAND FORECASTS* REPORT OF THE GLOBAL HEALTH FORECASTING WORKING GROUP (2007), www.cgdev.org/files/13784_file_RiskyBusinessFull.pdf.

² *Id.* at 1.

³ *Id.*

⁴ *Id.* at 3.

⁵ *Id.* at 2.

⁶ *Id.* at 3.

their biggest problems in serving the global health community, many pharmaceutical company executives cite poor demand forecasting as the most important one.⁷ In short, ensuring better demand forecasts is at the heart of the global health agenda and merits attention from all who are involved in funding, purchasing, setting specifications for, developing, supplying and distributing global health products.

Traditionally, demand forecasting for health products in developing country markets was seen as a relatively low-level function, left to firms with particular business interests, using some basic information about health conditions and health system coverage provided by technical agencies.⁸ In developing countries themselves, demand forecasting has been viewed as one of the many functions required of overburdened technical personnel within ministries of health or particular dedicated units, such as those that manage national immunization programs.⁹

More recently, with increased attention on getting new products into broad use to address highly visible public health priorities such as HIV/AIDS—and with significantly increased funding from governments and consumers in middle-income countries, plus new donor funding mechanisms for low-income countries – creating good demand forecasts that can be agreed to by multiple stakeholders has taken on a new and fundamentally different level of importance. In a piecemeal fashion, product-by-product, the global health community has responded. For example, the World Health Organization (WHO) has taken responsibility for developing forecasts for some products, and public-private partnerships have made impressive efforts for others.¹⁰ However, relatively little has been done to address the underlying weaknesses in data, methods and institutional incentives that are common to virtually all products and that severely constrain good decision making.¹¹

The forecasting challenges can only truly be understood by looking at the nature and distribution of underlying risks faced by the pharmaceutical industry, national buyers, regulatory and purchasing intermediaries, and funders. These risks are shaped by emerging features of the global health environment, including more money, new products and a more complex international market. Those risks, and their asymmetric distribution, generate distinct and misaligned incentives across important players in the global health market. Under current arrangements, those misaligned incentives conspire to impair demand forecasting and, more importantly, hamper broader access to critical medical technologies.¹²

⁷ NEELAM SEKHRI, FORECASTING FOR GLOBAL HEALTH: NEW MONEY, NEW PRODUCTS & NEW MARKETS, BACKGROUND PAPER FOR THE GLOBAL HEALTH FORECASTING WORKING GROUP 6 (2006), www.cgdev.org/doc/DemandForecasting/NewMoneyNewMarkets.pdf.

⁸ *Id.* at 17.

⁹ Neelam, *supra* note 1, at 6.

¹⁰ *Id.* at 2, 7.

¹¹ *See generally id.*

¹² PRASHANT YADAV ET AL., MAPPING & REALIGNING INCENTIVES IN THE GLOBAL HEALTH SUPPLY CHAIN, BACKGROUND PAPER FOR THE GLOBAL HEALTH FORECASTING WORKING GROUP (2006), www.cgdev.org/doc/DemandForecasting/RealigningIncentives.pdf.

III. THE NEW WORLD OF GLOBAL HEALTH

Understanding demand forecasting is key to future progress in global health, and requires a look at five recent changes: new amounts and sources of money, new and future products, new buyers, new suppliers and business models, and new intermediaries. While demand forecasting for many medical products is challenging, it is the “new products and new markets” for which the hurdles are highest and for which donor actions can have the greatest impact.

A. NEW AMOUNTS AND SOURCES OF MONEY

The three main sources of finance for health products in developing countries are private, out-of-pocket spending; national or subnational public sector payers, typically channeled through ministries of health; and international public and private donors.¹³ Although expenditures by all three sources have been increasing gradually in most countries, the expansion in international public sector donor funds is creating a discontinuity in the resources available, particularly in the lowest income countries.¹⁴ As this has happened, the policies and practices of both traditional and new donor agencies have become a driving force in the market.¹⁵

Donor funding for global health has increased substantially in the past five years, particularly for HIV/AIDS, tuberculosis, malaria and vaccines. The United States alone authorized up to \$15 billion for HIV/AIDS through the President’s Emergency Plan for AIDS Relief (PEPFAR) in 2003–08 and \$1.2 billion for malaria through the President’s Malaria Initiative in 2005–10.¹⁶ The US House of Representatives recently voted to reauthorize PEPFAR for \$50 billion over the next five years.¹⁷ Through December 2007, the Global Fund to Fight AIDS, Tuberculosis and Malaria had approved proposals totaling more than \$10.1 billion, and already disbursed \$5.0 billion in funds.¹⁸ Globally, annual funding for AIDS, tuberculosis and malaria has more than doubled from 2001 to 2005; by 2007, the annual funding target was \$15 billion for the three diseases.¹⁹

The situation for vaccines is similar. In 2004, UNICEF purchased 2.8 billion doses of vaccines worth a total of \$374 million, compared with only 969 million doses, worth \$55 million in 1990—an almost 600% increase in spending.²⁰ In addition to increases for polio eradication, much of this new money has come through the GAVI Fund (formerly the Vaccine Fund), which has received more than \$1.8 billion in donor commitments from its inception

¹³ See Christopher Lane & Amanda Glassman, *Bigger And Better? Scaling Up and Innovation In Health Aid*, 26 HEALTH AFF. 935 (2007).

¹⁴ *Id.* at 935–36, 939.

¹⁵ *Id.* at 935–36.

¹⁶ The President’s Malaria Initiative, www.fightingmalaria.gov; The President’s Emergency Plan for AIDS Relief, www.pepfar.gov.

¹⁷ David Brown, *House Votes to Continue and Expand President’s Global Effort Against AIDS*, WASHINGTON POST (April 3, 2008).

¹⁸ The Global Fund to Fight AIDS, Tuberculosis and Malaria, www.theglobalfund.org/en/funds_raised/commitments (last visited Feb. 29, 2008).

¹⁹ Neelam et al., *supra* note 1 at 12.

²⁰ UNICEF (UNITED NATIONS INTERNATIONAL CHILDREN’S EMERGENCY FUND), 2004 UNICEF SUPPLY DIVISION ANNUAL REPORT 4 (2004).

through the end of 2006.²¹ In 2007, the International Finance Facility for Immunization was launched with the expectation of generating an additional \$4 billion over the next 10 years to purchase vaccines through GAVI.²²

These new funds are being channeled through new mechanisms. Beyond the Global Fund and GAVI, which are now reasonably well established players in global health funding, newer approaches are being launched. In 2006 the UNITAID international drug purchasing facility was created and is expected to mobilize at least \$300 million a year from the French airline ticket levy and other donors to be dedicated specifically to health products.²³ Several donors, including Canada, Italy, Norway, Russia, the United Kingdom and the Bill & Melinda Gates Foundation, have joined forces to fund a pilot Advance Market Commitment, which has mobilized \$1.5 billion for the procurement of vaccine against pneumococcal disease for low-income countries if and when an appropriate product is deemed eligible for purchase.²⁴ A global subsidy program for artemisinin-based combination therapy (ACTs) for malaria is under development by the World Bank, which would establish a separate, product-specific funding stream.²⁵ Other proposals are in the offing.²⁶

The increase in funds and funders has had significant impacts on the overall supply chain that affects demand forecasting. Donor funding is notoriously unpredictable and tends to be more subject to rapid fluctuations than is the national public finance base in developing countries.²⁷ Commitments are not always reflected in disbursements, and funding can be cut off instantly when there are allegations of corrupt practices or other major governance concerns (as in the case of Uganda).²⁸ While several of the new funding instruments are designed to create a more predictable flow of funding, the risks associated with relying on donor funding are a major challenge for forecasting demand.

The increase in demand for products is a major step for global capacity, not an incremental one. The major increase in funding and subsequently in demand for products requires large investments by manufacturers to scale up production capacity to keep pace. Within countries it necessitates greatly expanded procurement, warehousing, storage and logistics capabilities. Both require accurate forecasts to plan and justify investments.

²¹ GAVI Alliance, Donors to the GAVI Alliance/Fund (2007), www.gavialliance.org/resources/donor_contributions_may2007.xls.

²² Press Release, GAVI Alliance, International Finance Facility for Immunisation Issues Inaugural Bonds (Nov. 7, 2006), www.gavialliance.org/Media_Center/Press_Releases/pr_ IFFImBondLaunch_7Nov2006.php.

²³ UNITAID, www.unitaid.eu/ (last visited Feb. 29, 2008).

²⁴ Press Release, AMC, Five Nations and the Bill & Melinda Gates Foundation Launch Advance Market Commitment for Vaccines to Combat Deadly Disease in Poor Nations (February 9, 2007), www.vaccineamc.org.

²⁵ Roll Back Malaria Affordable Medicines Facility for Malaria (AMF-m) Taskforce, www.rbm.who.int/globalsubsidytaskforce.html (last visited Feb. 29, 2008).

²⁶ Brookings Global Health Financing Initiative Snapshot Series, www.brookings.edu/projects/global-health/health-snapshot.aspx (last visited Feb. 29, 2008).

²⁷ Aelx Bulir & A. Javier Hamann, *Volatility of Development Aid: From the Frying Pan into the Fire?*, INTERNATIONAL MONETARY FUND 4 (June 26, 2006).

²⁸ Press Release, *The Global Fund to Fight AIDS, Tuberculosis and Malaria, The Global Fund Welcomes Ugandan Corruption Inquiry Report* (June 2, 2006), www.theglobalfund.org/en/media_center/press/pr_060602b.asp.

B. NEW AND FUTURE PRODUCTS

As a beneficial result of recent investments in global health, including both the large appetite of donors to purchase global health products and the growing support for global health R&D, many new products for developing country markets are available or in development. The array of new products has many payoffs for health. For example, new products that contain artemisinin are effective against malaria that is resistant to traditional chloroquine products.²⁹ Also, the dozens of antiretroviral medicines in use in developing countries are needed for the clinical management of AIDS patients.³⁰ However, the emergence of so many products creates challenges for funders, intermediaries and consumers, who are all accustomed to having only a few commodity-type products with quite well established supply and procurement relationships. Those challenges will be exacerbated as the late-stage products — new vaccines, antimalaria drugs and tuberculosis drugs, in particular — are licensed and brought to market.³¹

Over the next five years, 15–20 new vaccines with significant value to developing countries are expected to be prequalified by WHO.³² These products enter a supply chain that has struggled in recent years with two new antigens, *Haemophilus influenzae* type b and hepatitis B, following decades when immunization programs in developing countries were focused on delivering just six relatively low-cost vaccines.³³ Beyond vaccines, those who follow the pipeline of tuberculosis products expect to see 12 new diagnostic products and seven new therapeutics by 2013.³⁴ One of the public-private partnerships, the Medicines for Malaria Venture, has anticipated four new antimalaria drugs between 2007 and 2009 alone.³⁵ In short: excellent news about bringing new science into the service of global health, but major hurdles and questions as the fruits of recent investments come to market.

Beyond simple numbers of new entrants, the pharmaceuticals, biologicals and diagnostics now available and soon to come to the market differ from their older generation therapies. These differences highlight why the stakes for good demand forecasting are high, and particularly why manufacturers who are engaging in the global health market are keen to see major progress in forecasting accuracy.

First, many products are still on patent. As a result, their prices reflect manufacturers' business need to recoup R&D investments. Consequently, the unit prices are higher than for earlier generation products that are now off

²⁹ See N.J. White et al., *Averting a Malaria Disaster*, 353 LANCET 1965, 1965-67 (1999).

³⁰ See World Health Organization HIV/AIDS Programme, Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public Health Approach (2006), www.who.int/hiv/pub/guidelines/artadultguidelines.pdf.

³¹ Christopher Elias, *Can We Ensure Health is Within Reach for Everyone?*, 368 LANCET S40, S40-41 (2006).

³² World Health Organization, *The Evolving Vaccine Pipeline* (2007), www.who.int/immunization_delivery/new_vaccines/en/.

³³ UNICEF, World Health Organization, The World Bank, *State of the World's Vaccines and Immunization* (2002).

³⁴ *New Technologies for TB Control: A Framework for their Adoption, Introduction and Implementation* (2007), www.stoptb.org/retooling/assets/documents/New%20Technologies%20for%20TB%20Control%20Final%20version%20with%20design%2025May2007.pdf.

³⁵ Medicines for Malaria Ventures, *Partnerships Hold the Key: Africa Malaria Day* (2007), www.mmv.org/article.php?id_article=358.

patent. The technology behind many of these products is also very complex, which makes the possibility of low-cost generics less likely in the short term even leaving aside the question of patents. For example, conjugate vaccines require advanced technology and production know-how that are still out of the reach of most emerging manufacturers, and future products are likely to rely on even more complex recombinant processes.³⁶

Second, some products, such as artemisinin-based combination therapy (ACTs), have short shelf lives and long production cycles with active ingredients that depend on unreliable agricultural processes.³⁷ Production from raw materials to finished ACTs averages almost 14 months, and building and accrediting manufacturing facilities takes at least three years.³⁸

Third, for some key products, manufacturing shortages or retail stockouts at any point in the distribution chain have major negative public health consequences. For antiretroviral drugs, for example, an interruption in a patient's treatment can quickly lead to death for the patient or viral drug resistance in the community. For tuberculosis drugs, stockouts bring the possibility of developing multidrug resistance. Some 420,000 new cases of multidrug resistant tuberculosis are diagnosed around the world each year,³⁹ and 7% of them show resistance to three or more drugs.⁴⁰

Fourth, many of the new products—particularly those emerging as a result of specific global health research subsidies from foundations and other funders—have little or no market in the developed world. Thus, unlike for earlier generation products, manufacturers cannot expect to recoup costs from lucrative markets and effectively provide products at marginal prices to developing countries through tiered pricing. All costs will have to be recouped from sales in developing countries, implying that there may be a long delay before significant decreases in prices.

Finally, some products are provided by a limited number of quality suppliers, or produced only by generic manufacturers in emerging countries. These suppliers may find it prohibitive or impossible (for example, if the drug is still under patent) to apply for approval through a stringent regulatory authority. To respond to these issues, WHO has set up a new prequalification system for the approval of safe, high-quality drugs for developing countries.⁴¹ However, so far the approval process for a single drug has averaged two years,

³⁶ See Julie Milstien et al., *Access to Vaccine Technologies in Developing Countries: Brazil and India*, 25 VACCINE 7610 (2007).

³⁷ Dana G. Dalrymple, *Artemisia, Agriculture and Malaria in Africa: The Interplay of Tradition, Science and Public Policy*, 7-12 (U.S. Agency for Int'l Development (USAID), Draft Working Paper, 2007).

³⁸ PRASHANT YADAV ET AL., MAPPING AND REALIGNING INCENTIVES IN THE GLOBAL HEALTH SUPPLY CHAIN, BACKGROUND PAPER FOR THE GLOBAL HEALTH FORECASTING WORKING GROUP 11 (2006), www.cgdev.org/doc/DemandForecasting/RealigningIncentives.pdf.

³⁹ See M.A. Aziz et al., *Epidemiology of Antituberculosis Drug Resistance (the Global Project on Anti-Tuberculosis Drug Resistance Surveillance): An Updated Analysis*, 368 LANCET 2142 (2006).

⁴⁰ Centers for Disease Control and Prevention, *Emergence of Mycobacterium Tuberculosis with Extensive Resistance to Second-Line Drugs-Worldwide, 2000-2004*, 55 MORBIDITY & MORTALITY WEEKLY REP. 301 (2006).

⁴¹ McKinsey & Company, *Market Dynamics and the Global Fund: Background Research and Analysis* (Geneva 2006).

which has further limited the number of qualified suppliers on the market for a variety of products.⁴²

C. NEW BUYERS

With new funds have come new buyers, some with limited experience in international pharmaceutical procurement. This has consequences for forecasting the volume and timing of purchases. The most prominent example is in the grants provided by the Global Fund, which has decentralized purchasing power to more than 400 buyers in 132 countries, including public entities, nongovernmental organizations and faith-based organizations.⁴³ The original intent of the Global Fund's procurement design was to promote country ownership and improve local capacity in purchasing and supply chain management.⁴⁴ In practice, however, this approach has significantly burdened in-country supply chains by creating a market of small, disaggregated buyers with limited ability and experience to influence product quality, price, packaging, shelf life, availability or delivery times.⁴⁵

Many of these smaller new buyers have little capacity and experience in demand forecasting, negotiation, procurement and contract management. Their decision processes, price sensitivities, competing priorities and political realities are poorly understood by suppliers and others in the market. This makes it difficult to accurately predict their demand and costly to forge the partnerships required to generate trust among participants in the market, on both the supply and demand sides. Disaggregated purchasing also has consequences: the Global Fund's price reporting mechanism shows an almost eightfold difference across countries in the price paid for Nevirapine, a common first-line antiretroviral drug; in 2006, purchase prices in low-income African countries ranged from \$58 per patient per year to \$438.⁴⁶

In contrast to the Global Fund's approach, the GAVI Fund, which provides grants to countries for vaccines, injection supplies and immunization programs, has traditionally used UNICEF procurement arrangements.⁴⁷ Because the GAVI Fund has a longer funding horizon than the bilateral donors that have traditionally financed UNICEF vaccine purchases, it has been possible to engage in longer term procurement arrangements.⁴⁸ This has clear benefits but makes it essential to forecast medium- and long-term demand accurately.

⁴² *Id.*

⁴³ Based on the fact that the Global Fund has signed more than 400 grant agreements. See The Global Fund to Fight AIDS, Tuberculosis and Malaria, www.theglobalfund.org.

⁴⁴ The Global Fund to Fight AIDS, Tuberculosis and Malaria, Guide to the Global Fund's Policies on Procurement and Supply Management 2 (2006), www.theglobalfund.org/pdf/guidelines/pp_guidelines_procurement_supplymanagement_en.pdf.

⁴⁵ GLOBAL FUND WORKING GROUP, CHALLENGES AND OPPORTUNITIES FOR THE NEW EXECUTIVE DIRECTOR OF THE GLOBAL FUND: SEVEN ESSENTIAL TASKS 17 (2006), www.cgdev.org/doc/HIVAIDSMonitor/GlobalFund_sevenTasks.pdf.

⁴⁶ The Global Fund to Fight AIDS, Tuberculosis and Malaria, Price Reporting Mechanism, web.theglobalfund.org/prm/rc?requesttype=html&topmodel=%5BPRM_Reports_Pricing_fromLogin_Instruction%5D.

⁴⁷ GAVI Alliance, www.gavialliance.org.

⁴⁸ *Id.*

D. NEW SUPPLIERS AND BUSINESS MODELS

The number of suppliers continues to grow, in part because some multinational companies are showing a willingness to license production in developing countries to respond to urgent public health needs. However, this does not necessarily guarantee more access to quality products; bottlenecks are seen in the regulatory and post-regulatory steps established to ensure the safety and quality of medicines and vaccines. For example, Cosmos, a producer in Kenya, has received voluntary licenses from Roche and Boehringer Ingeheim to produce two AIDS drugs.⁴⁹ Because it has not completed the WHO prequalification process, however, Cosmos is unable to bid for government tenders to provide antiretroviral drugs through donor-funded programs.⁵⁰ Although more than four suppliers have been deemed qualified to provide the common first-line antiretroviral drugs, problems with prequalification and cumbersome national registration processes have led to a situation in which only one or two suppliers are registered in any given country.⁵¹ Countries are therefore more vulnerable to suppliers' production or delivery problems.

Even as the number of developing country suppliers expands, recent changes in developed country markets may actually decrease the security of supplies in developing countries. Several wealthy countries have introduced initiatives to reduce the rate of increase in drug costs and expand markets for generics; these actions increase the attractiveness of developed markets for generic manufacturers based in developing countries.⁵²

As with new buyers, new suppliers in developing countries often lack expertise in forecasting demand, negotiation and procurement. Their motivations, decision processes and internal realities are not well understood by buyers or international agencies, and partnerships based on trust are still being formed with these new suppliers. Yet the stakes are even higher for these suppliers than for traditional manufacturers because they lack the deep pockets to bear the financial risks of poor forecasting.

For traditional multinational manufacturers, the situation is complicated by the fact that prices in some low-income countries are set to recover costs rather than to generate profit.⁵³ Faced with vast public health needs and the threat of reputational damage, suppliers have been willing to accept low or even zero margins, but this greatly impedes their willingness and ability to invest in production capabilities without some assurance of demand and constrains their appetite for spending large sums to obtain market intelligence.⁵⁴ In some cases, the low returns compared with other markets mean that suppliers' sales objectives are to make the drug available but not necessarily to promote sales.⁵⁵ At the same time, the costs of doing business in

⁴⁹ Dagi Kimani, *Roche Gives Kenyan Firms Right for AIDS Drug*, EAST AFRICAN, Oct. 23, 2006, available at www.bioportfolio.com/november_06/25_10_2006/Roche_Gives_Kenyan_Firms.html.

⁵⁰ *Id.*

⁵¹ McKinsey & Company, *Market Dynamics and the Global Fund: Background Research and Analysis* (Geneva 2006).

⁵² SEKHRI, *supra* note 7, at 11.

⁵³ *Id.*

⁵⁴ *Id.*

⁵⁵ *Id.*

developing countries tend to be higher than in developed markets because of supply chain complexities, country-specific packaging in multiple languages and other registration requirements, and uncertainty of funding.⁵⁶

Further complicating the picture is competition in the market between quality pharmaceutical products and counterfeits. As the healthcare market in developing countries has grown, often without parallel strengthening of the regulatory framework and enforcement, low-quality and counterfeit products have taken a firm foothold in many countries. According to WHO, about a quarter of the medicines consumed in developing countries are counterfeit; in some countries nearly half are.⁵⁷ One study, for example, found that up to 40% of antimalarial products that were supposed to contain artesunate in fact contained no active ingredients at all.⁵⁸

E. NEW INTERMEDIARIES

In addition to more funders, buyers and suppliers, many new intermediary organizations have entered the global health products market, each to play a particular role—albeit not always in coordination with other players. Some of these organizations have novel structures involving relationships between the public and private sectors, and these institutions are characterized by evolving management and governance. For example, over the past few years several public-private partnerships have been created to encourage the development and introduction of specific new products for neglected diseases (most with significant funding from the Bill & Melinda Gates Foundation); these include, among others, the Foundation for Innovative Diagnostics, International Partnership for Microbicides, Aeras Global TB Vaccine Foundation, PneumoADIP, International AIDS Vaccine Initiative, Medicines for Malaria Venture, Institute for OneWorld Health, Rotavirus Vaccine Program and the Global Alliance for TB Drug Development.⁵⁹

In addition to managing or facilitating product development, several of these partnerships have taken responsibility for creating demand forecasts through the product development phase and for managing the introduction of new products into the market. Recently, the Clinton Foundation HIV/AIDS Initiative has become a central player in the antiretroviral drug supply chain by negotiating prices with suppliers and active pharmaceutical ingredient manufacturers, preparing demand forecasts and advising countries on procurement and supply management.⁶⁰ In 2007, its role expanded to include similar functions for ACTs for malaria.⁶¹

⁵⁶ *Id.*

⁵⁷ World Health Organization, Counterfeit Medicines, Fact Sheet 275 (Nov. 14, 2006), www.who.int/mediacentre/factsheets/fs275/en/ (last viewed Feb. 29, 2008).

⁵⁸ Paul Newton et al., *Fake Artesunate in Southeast Asia*, 357 LANCET 1948, 1949 (2001).

⁵⁹ MARY MORAN ET AL., THE NEW LANDSCAPE OF NEGLECTED DISEASE DRUG DEVELOPMENT 33-39 (2005).

⁶⁰ Omar Galárraga et al., *Forecast of Demand for Antiretroviral Drugs in Low and Middle-Income Countries: 2007-2008*, 21 AIDS S97, S99 (2007).

⁶¹ Cathel Kerr, *Clinton Foundation Launches New Malaria Test Scheme*, 7 LANCET INFECTIOUS DISEASES 574, 574 (2007).

As new entities have sprung up, agencies with longer histories have expanded or deepened their involvement in health product markets and supply chains as well. WHO is involved in prequalifying a wide range of products and procures specific drugs, in addition to its normative role of establishing treatment guidelines and proposing essential drugs lists.⁶² Public-private partnerships have been established under the WHO umbrella, such as Roll Back Malaria and the Stop TB Partnership, which are involved in drug policy, forecasting and procurement.⁶³ The Joint United Nations Programme on HIV/AIDS has also created an Accelerated Access Initiative with major antiretroviral drug manufacturers to increase availability of these products.⁶⁴

All of these changes make forecasting both more important and more difficult. For example, looking only at the new antimalarials, ACTs: While there are significant new sources of funding to purchase the drugs through the Global Fund and the US President's Malaria Initiative, great uncertainty exists about the uptake patterns. Since the manufacturing lead time is more than one year and the antimalarials have essentially one market – the donor-funded poor countries where the disease is endemic and chloroquine-based products are now ineffective – the manufacturer has to make key investment decisions based on forecasts of what donors will buy on behalf of developing countries. The information provided in the past about likely ACT demand was based on estimates of need, rather than on realistic estimates of funding availability and country choices. The result has been a major overestimate of aggregate demand, as described in a later section, and consequently major miscalculations in the expansion of manufacturing capacity and the production of ACTs.⁶⁵

IV. DEMAND FORECASTING WITHIN THE VALUE CHAIN

At virtually each step in the supply chain – from supplier to manufacturer to wholesaler to retailer to consumer – and the broader value chain (including R&D) for pharmaceutical products, decision makers depend on information about demand: how many units of a product will be purchased and used in the near, medium and long term?

Aggregate forecasting, as defined here, estimates the overall size of effective demand in the market, taking into consideration assumptions about price, funding availability, uptake rates and other key factors.⁶⁶ Although it is only one step in the long and often complicated value chain, this process represents a key input into decision making for both buyers and suppliers. For health products, demand forecasting starts when a product is first

⁶² See World Health Organization, WHO Prequalification of Medicines Programme Update for 2006 (2007), www.who.int/prequal/info_general/documents/Prequal_AnnualReport2006EN.pdf (describing the WHO's ongoing efforts to work in cooperation with national regulatory agencies and partner organizations to make quality priority medicines available in developing countries throughout the world through its Prequalification Programme).

⁶³ See CHERI GRACE, GLOBAL HEALTH PARTNERSHIP IMPACT ON COMMODITY PRICING AND SECURITY 2-10 (2004), www2.ohchr.org/english/issues/development/docs/WHO_3.pdf.

⁶⁴ *Id.* at 17.

⁶⁵ YADAV ET AL., *supra* note 12, at 11-16.

⁶⁶ SEKHRI ET AL., *supra* note 1, at 4.

conceived during the R&D phase and continues through the lifecycle of that product and through the value chain.⁶⁷ If not done in a way that optimally uses information and that is seen as credible by decision makers — particularly in newer markets, given their inherent uncertainties — the rest of the value chain cannot be efficiently mobilized to deliver.

Demand forecasting serves five critical functions in the market for global health products and the effective delivery of medicines and supplies, all of which result in lives saved:

- *Essential products are available because there is enough supply to meet demand.* Demand forecasting allows manufacturers to plan and invest in manufacturing capacity, ensuring sufficient supply to meet demand and taking advantage of production efficiencies.
- *New products are developed because there is a realistic picture of future markets.* Demand forecasting provides manufacturers with information about new market potential, permitting them to efficiently allocate resources to develop, produce and commercialize new products that respond to developing country opportunities and accelerating the pace of product availability.
- *Supply chain capacity is increased so products can get to people who need them.* Demand forecasting enables health systems in developing countries to expand their capacity to deliver products to more patients, matched to the scale and mix of products required.
- *Funders plan purchases and make the most of the money available.* Demand forecasting allows donors and national governments to efficiently allocate their resources by ensuring appropriate prices and adequate supplies of products.
- *The public health community sees bottlenecks and understands opportunities to expand use.* Demand forecasting highlights key demand- and supply-side constraints and can guide policy and advocacy efforts to reduce those constraints and achieve broader access. This can even include influencing the characteristics of future products to respond to potential demand.

The demand forecasting process starts early in the product lifecycle and forecasts are continually refined as the product gets closer to launch and then to widespread usage. When a candidate is still in the development pipeline, long-term strategic forecasts are produced, assuming various product specifications. These forecasts, which are based on a set of early assumptions about product characteristics and efficacy, are used to make an R&D investment case for suppliers and funders.

⁶⁷ *Id.* at 3.

BOX 1: FORECASTING DEMAND FOR A PREVENTIVE AIDS VACCINE

The International AIDS Vaccine Initiative recently developed a long-term strategic demand forecast to assist decision makers in national and international institutions with both immediate, as well as longer-term, strategic action to streamline regulatory systems, improve healthcare capacity and infrastructure, inform design of R&D incentive mechanisms, and increase political will and financial commitment.⁶⁸ They found that the global demand for a first-generation preventive HIV vaccine could range between 28-142 million courses annually over a 30-year period, depending on the specifications of the vaccine developed.⁶⁹ It is hoped that this model and forecasts will also help inform strategic investment decisions by private sector developers and financiers of AIDS and other early-stage vaccines.

Strategic forecasts present unique challenges because they are made in an environment of significant uncertainty, many years in advance of when a product may actually be available. At this stage demand forecasts can best be considered demand scenarios based on a set of assumptions about the likely product and its future uses. For products with particularly long product development cycles, such as vaccines or tuberculosis drugs, the uncertainty is even greater. Long-term strategic forecasts serve as the beginning of the forecasting process and are in a continual state of refinement as the product progresses through its lifecycle, with iterative feedback loops to other areas in the organization and the external environment, reflecting changes as they occur.

As a product becomes more clearly defined and is ready to reach the market—or in the case of existing products, when the product is entering new markets—forecasts evolve to provide greater and greater specificity to guide production investment decisions. Once a product has entered the market, demand forecasts are further refined and detailed to guide short-term production decisions and management of the supply chain.

Demand forecasts are essential for every level of the value chain and throughout the product lifecycle. They are used by local health facilities, ministries of health, procurement agents, international organizations and suppliers. The forecasting process and basic principles are the same for all of these forecasts, but their specificity and accuracy change over time and differ at each level.

This analysis focuses on forecasts that are combined across regions and countries to produce an overall indication of demand for products in the market. As a product gets closer to launch and becomes available to patients, these aggregate forecasts will rely more and more on good country level and local forecasting. In fact, short-term or supply chain forecasts depend heavily on the accuracy of country and local buyer forecasting processes. However, there is still a need to aggregate these forecasts for suppliers to help them scale up production capacity and smooth out fluctuations in demand between countries and regions.

⁶⁸ Gian Gandhi, *Forecasting the Global Demand for Preventive HIV Vaccines* 37 (Int'l AIDS Vaccine Initiative Policy Research Working Paper No. 15, 2007), available at www.iavi.org/global_demand.

⁶⁹ *Id.* at 2, 28.

Given the importance of forecasting at each stage and the number of stakeholders that would benefit from better forecasts, it is initially surprising that forecasting is such a problem in global health. Why hasn't this been fixed? Part of the explanation is the recent major changes in funding, products and other factors without yet a corresponding improvement in forecasting methods or institutional accountability. The rest lies in the fact that risks in the current market are unequally distributed across key actors whose decisions affect supply of and demand for products, and as a result not all stakeholders' incentives are aligned toward better forecasts and greater access to critical medical technologies.

V. RISK ALLOCATION IN THE GLOBAL HEALTH VALUE CHAIN

The two-way relationship between demand forecasting and risk is clear. First, because major risks are inherent in both the supply of and demand for health products, particularly in developing countries, accurate forecasting is difficult. Second, weaknesses in demand forecasts exacerbate risks for those who are selling and buying products and those who are preparing for future engagement in the market. Patients ultimately bear the consequences for poor management of market risks.⁷⁰

The nature of the market for medical products and the functioning, or failure to function, of the value chain from R&D to consumer can be understood in part by identifying a set of common risks. Each underlying risk affects the ability of main actors (including suppliers of raw and finished products, intermediaries, consumers and others) to make economically efficient decisions and to ensure that products are available in the quantity, quality, place and at the price that yields maximum health benefits. In particular, the risks affect the ability to accurately predict the size and features of the market.⁷¹

While not exhaustive, the list below illustrates one way to identify the core risks that affect product supply, demand and entry into the market related to regulatory factors and logistics of delivering products.

On the supply side, risks are associated with the development and manufacture of the product, including:

- *Uncertain outcomes in the scientific and technical pathway.*

The transition from the basic scientific discovery process to viable molecules or biological agents that merit clinical studies, and the survival of those products through multiple phases of clinical studies, is fraught with uncertainty. To some extent, public-private product development partnerships aim to reduce this risk through diversification: funding multiple scientific pathways to address a complex challenge, as in the search for vaccines, drugs, diagnostics and microbicides, for malaria, tuberculosis and AIDS. Without public or charitable subsidies, individual manufacturers bear this risk alone.

⁷⁰ OWEN BARDER ET AL., AN INTRODUCTION TO RISK & UNCERTAINTY, BACKGROUND PAPER FOR THE GLOBAL HEALTH FORECASTING WORKING GROUP (2006), www.cgdev.org/doc/DemandForecasting/RiskUncertainty.pdf.

⁷¹ *Id.*

- *Batch or production yield failure.* A firm may produce batches of products that fail tests for effectiveness, uniformity or safety because of failure in a process, component or system or because of human error, as in the case of the recall of Roche's antiretroviral Viracept.⁷² Products with relatively short production track records are particularly vulnerable to this type of risk, which is typically borne exclusively by the manufacturer.
- *Input shortfall and/or price shocks.* A firm may face an inelastic supply of inputs required for the finished product, such as raw materials or active pharmaceutical ingredients. This is a particularly acute concern for products like ACTs, whose production requires active ingredients from agricultural materials, which are subject to a host of weather, market and other risks.

The demand side also faces multiple risks, related to the likelihood that a product will be attractive to those who might place orders and the ability to translate a desire for the product into orders to suppliers. Major risks include:

- *Competition.* Some products benefit from a temporary period of exclusivity through intellectual property protection; others face little competition because of complex production or regulatory barriers. However, where alternative products yield health benefits, the price and availability of those substitutes can make a significant difference to demand for a company's product.
- *Obsolescence.* A long-term risk for some products is that they will be rendered obsolete. For example, a better alternative may be developed, or the need for a product may be eliminated or greatly reduced because of the entry of an entirely new class of products for the same condition or because underlying risk factors may change. For example, demand for treatment for diarrheal disease may be reduced by the introduction of an effective vaccine and/or major improvements in water and sanitation. This is a particular problem if manufacturing assets are specific to a product that becomes obsolete.

⁷² See Elisabeth Rosenthal, *Low-Key Recall of AIDS Drug Hits World's Poor*, N.Y. TIMES, July 23, 2007, available at www.nytimes.com/2007/07/23/health/23recall.html.

- *Unpredictable policies and preferences.* Adoption and post-regulatory approval of medical technologies frequently depend on a range of uncertainties, such as the availability of data about the burden of disease, public attitudes to the disease, an understanding of the range of interventions and stigma, and understanding about a particular product or intervention. Whether a country decides to adopt a new technology or therapy after regulatory approval as part of a national disease control program is a significant risk that can be further amplified by a lack of clarity at the country level on how such decisions are made and how long it would take to roll out a new technology, if adopted.
- *Uncertain budgets and purchasing power.* Volatility in donor budgets for global health leads to unpredictable demand. Furthermore, if developing countries pay for some or all of the costs (for example, through a co-financing mechanism), uncertainty about domestically financed health also affects demand. This risk category also includes the possibility that funding aimed at product purchase is diverted, through legal or illegal means.
- *Weak credit.* A borrower, supplier or customer might fail to honor its contractual obligations. This may be quite pronounced if the contractual obligations are weakly enforced—again, a characteristic of developing country pharmaceutical markets.
- *Price volatility.* Key decisions are made based on particular assumptions about near- and long-term prices, which may behave differently than expected. For example, because large purchasers are in a stronger negotiating position than anticipated, they can bargain down prices.

Regulatory and quality assurance factors also convey significant risks, especially in developing country environments, where regulatory agencies may have a poorly defined role, have a shorter track record than in advanced markets, and be less predictable.

- *Unpredictable regulatory and post-regulatory regimes.* Regulatory regimes change in unpredictable ways. This includes new requirements concerning manufacturing processes, changes in intellectual property regimes and new clinical trial requirements.
- *Weak regulatory enforcement.* Where enforcement of regulations is weak or changing quickly, there is the risk that poor quality and/or counterfeit products will enter the market and crowd out good quality and/or branded products.

Finally, a set of major risks is associated with logistics affect decision making, particularly in developing countries:

- *Untimely delivery.* These are risks associated with unforeseen weaknesses and bottlenecks throughout the supply chain, including transportation breakdowns, leading to stockouts.
- *Losses in distribution chain.* Waste due to leakage or lack of appropriate storage (for example, breakdown of cold chain), if not predicted in placing orders, pose a risk.
- *Shortfalls in complementary inputs.* Human resources, accompanying products (for example, testing kits needed prior to some treatments and injection supplies) or other inputs may not be available in the quantity or location needed to make use of a product. This may occur, for example, if scale-up of services occurs rapidly with inadequate ability to respond with newly trained or deployed personnel, vehicles or other complementary inputs. It may also occur if orders are placed without bundling complementary products, such as those for testing and treatment.

The consequences of these core risks are financial and human:

- *Shortages.* If the supplier underestimates demand, has difficulty obtaining inputs or suffers batch failures, supply can undershoot demand. If the price is not fixed, it will rise, and only purchasers who can pay the higher price will be served. If the price is fixed, the shortage will be felt across the board as drug stockouts. This has negative financial implications for the purchaser and, more importantly, serious health consequences such as unprotected populations and untreated individuals. This is of particular concern when interrupted treatment quickly worsens a disease process (as with antiretroviral drugs in the treatment of AIDS), or creates the risk of drug resistance (as with tuberculosis, malaria, AIDS and other viral and bacterial conditions). In addition, the supplier may suffer reputational damage from being unable to supply life-saving or life-extending medications.

- *Excess inventory.* If estimates of short-run effective demand are incorrect—for example, if expected orders do not materialize or national programs' uptake of new products is slower than hoped—the supplier is left with excess inventory. For example, in 2005, after a sudden change in global treatment recommendations, WHO forecasted demand for 55 million courses of Coartem, a fixed-dose ACT.⁷³ In response, Novartis invested in scaling up its production capacity accordingly and produced 30 million treatments.⁷⁴ But only 9 million treatments were sold that year, due to slower-than-anticipated uptake, and Novartis experienced even larger surpluses and excess inventory in 2006.⁷⁵ While Novartis has scaled-up its production capacity to produce 120 million treatments (based on the initial WHO forecast in 2004), the realized sales continue to be about 60 million as of 2007.⁷⁶
- *Long-term overcapacity.* If a supplier's estimates of long-run effective demand are incorrect—for example, if competing technologies are licensed earlier than anticipated and capture part of the demand—the supplier is left with excess manufacturing capacity and potentially costly supply agreements with the firms that provide key inputs. This has negative financial consequences for the supplier and affects prices and willingness to participate in the market. For example, GAVI initially estimated the amount of hepatitis B vaccine required based on available funding and epidemiological projections without accounting for country willingness to adopt the monovalent vaccine rather than waiting for their DTP-HepB combination vaccine. Several manufacturers, particularly in India, scaled up production, and many more entered the market to accommodate this anticipated demand. However, uptake of the vaccine was much slower than predicted, with initial supply exceeding actual demand; only 11% of the volume that was requested by UNICEF in 2001 was actually bought.⁷⁷ As a result, competition drove down the price by almost 80%, causing some developing country manufacturers to go out of business and making many others nervous about future investment.⁷⁸

⁷³ YADAV, *supra* note 12, at 10.

⁷⁴ *Id.*

⁷⁵ *Id.*

⁷⁶ *Id.*

⁷⁷ Global Alliance for Vaccines and Immunization, Immunization Focus, Tough Lessons – and Rapid Reform – for Vaccine Procurement System, www.gavialliance.org/resources/july2002.pdf.

⁷⁸ GRACE, *supra* note 63, at 14.

- *Inefficient use of financial resources.* Firms may manage risk by keeping prices higher than they would be otherwise, to buffer the consequences of being left with unsold inventory or of encountering other situations with negative financial implications. Although suppliers try to keep prices as low as possible for developing country markets, typically as part of a corporate social responsibility agenda, they are rarely able to operate in a money-losing position over the medium or long term. Thus, products may be supplied to developing country markets and supply chains at higher prices than would be the case if less risk were present, meaning that donor, national government and private funds do not go as far as they otherwise would. In fact, one of the primary ways that the Clinton Foundation HIV/AIDS Program has been able to negotiate dramatically lower prices for ARVs and diagnostics is by facilitating better demand forecasts and shifting towards longer-term purchasing agreements, ultimately reducing the risks faced by manufacturers.⁷⁹ In other cases, donor and government dollars are inefficiently spent on products that expire before they can be put to use, as in the recent case of Uganda, where \$700,000 worth of drugs had expired while sitting in the National Medical Stores and another \$1 million were well on their way to doing so.⁸⁰
- *Lack of investment in next generation products.* The functioning of the value chain and the rewards that market engagement confers on both suppliers and donors strongly influence their interest in R&D. For example, if pharmaceutical firms face extremely high transaction costs in supplying developing countries and uncertainties around effective demand result in absolute or relative financial losses, their appetite for developing new products for that market will be weak. Inefficiencies in the existing value chain that result in higher prices or reduced access to products jeopardize the ability to consistently mobilize more funds over the long term. Moreover, investment in the public-private partnerships that are now seen as important to development of products for developing countries can be sustained only if current and near-term products are effectively moved into the market through well-functioning distribution channels.

⁷⁹ Anil Soni & Ira Magaziner, Global Health Council, D.C., *Getting More for the Money: How Lower Prices Were Possible, Progress to Date & the Challenges Ahead*, www.globalhealth.org/reports/report.php3?id=224.

⁸⁰ Weekly TB/Malaria Report, Malaria, Other Drugs Set To Expire in Ugandan Storage Facility (Jul 12, 2007), www.globalhealthreporting.org/article.asp?DR_ID=46170.

- *Poor health.* The most serious public health consequence of poorly managed risks is men, women and children dying or becoming incapacitated because they cannot access life-saving products. Inefficient resource allocation, shortages and insufficient R&D each constrain access in the short and long term, measured in unnecessarily high levels of morbidity and mortality.

While some of the risks described above are unavoidable, many could be reduced by the actions of buyers, sellers or intermediaries. For example, policy and preference risks are reduced when regulatory and post-regulatory bodies are transparent about the criteria and timing of decisions that have implications for the market. Budget risks are reduced when funders commit to a particular funding stream, under transparent rules, over a multiyear period. Risks related to the entry of new products are reduced if awareness about the size and characteristics of the potential market drives decisions about the publicly subsidized product development pipeline. Risks associated with logistics and distribution are reduced when those who were responsible for operating and strengthening the supply chain make sufficient and well-organized investments in its smooth functioning.

In a well-functioning supply chain, where risks are shared across stakeholders, all parties have an incentive to keep an efficient flow of funds, information and products. In fact, the market has mechanisms (typically contracts) to distribute risks so that they have incentives to take actions that reduce overall risk and make it more likely for products to move efficiently to consumers. When risks are distributed so that each party is better off through collaboration, that collaboration is likely to occur. In contrast, the global health market does not have risks broadly distributed across actors. Therefore, individual funding agencies, regulatory authorities, firms and intermediaries are less likely to work together to improve access. More narrowly, the misalignment in incentives may interfere with the aim of obtaining aggregate demand forecasts that are as accurate and credible as possible.⁸¹

Few attempts have been made to systematically reduce risk, in large measure because those who experience and suffer the consequences of the risks are not in a position to reduce them. In terms of other stakeholders, under current arrangements, most of the consequences are felt by two parties: first, manufacturers, who face the possibility of short-term excess inventory and long-term overcapacity as well as the reputational damage from being seen as responsible for shortages; second, patients and communities in developing countries, who are insufficiently protected against products that are unavailable due to shortages or stockouts, unnecessarily high prices, substandard quality and other conditions that jeopardize their health. Consequences may also be felt decision makers, for example, within ministries of health. Consequences are felt only indirectly by funders and intermediaries, who could reduce the underlying budgetary, policy-related and logistics risks.

⁸¹ YADAV, *supra* note 12, at 24.

The situation is particularly pronounced because so many parties in a position to reduce risks are subject to a set of organizational imperatives that may conflict with taking actions to do so. These parties include bilateral and multilateral funders, public-private partnerships, specialized organizations that undertake procurement such as UNICEF, international authorities such as WHO, and national buyers. For example, decision makers in agencies that provide funding for the purchase of global health products may be responsive to the need to show success in negotiating low prices, and may disburse funds only to well-governed nations or may maintain year-to-year flexibility in setting priorities for the use of scarce resources. In organizations that support product development with research grants, success may be measured by the number of products in the pipeline rather than the viability of the resulting market for manufacturers that may supply products over the long term. Despite the potential health-related value of expanding the range of products and suppliers, procurement agents may face unwelcome costs associated with building relationships with multiple suppliers, creating information interfaces, evaluating numerous bids and administering multiple contracts. Agencies that have a role in product regulation and quality assurance may be extremely averse to implementing any acceleration or change in procedures that could increase the risk of a quality lapse, even very slightly, but have no countervailing pressures to speed up the approval processes. National buyers and health authorities may face uncompensated costs if they choose to introduce new products and thus may be inclined to rely upon older, less effective therapies.⁸²

While many of these challenges exist to some extent in developed country markets as well, historically higher levels of health spending have allowed manufacturers and buyers to develop and use responsive, higher capacity supply chains and excess inventory to buffer against market uncertainties.⁸³ Developed country markets are also characterized by relatively good information and market research, in part because more money has been invested for information gathering. Purchasers and suppliers have established relationships and balanced market power,⁸⁴ and both formal and informal risk-sharing is a common feature of market relationships in developed countries.

Developing country markets, on the other hand, are rapidly becoming much more complex. Data are limited and unreliable, few tools exist to gather good market research, and both money and human resources are in short supply. At the same time, disaggregated and small purchasers combined with multiple layers of international and national decision makers make the process more uncertain and expensive for manufacturers and buyers. In addition, health goods are delivered by multiple supply chains, including those in the public, nonprofit, nongovernmental organization, formal private

⁸² *Id.*

⁸³ However, the use of excess inventory has become more restricted even in developed markets as a result of the U.S. Sarbanes-Oxley legislation, which counters “dumping” in the market by preventing drug companies from producing inventory above forecasts. See Thomas Craig, *Sarbanes-Oxley and Supply Chain Management*, WEBPRONEWS, May 12, 2005, webpronews.com/topnews/2005/05/12/sarbanesoxley-and-supply-chain-management.

⁸⁴ Marshall L. Fisher, *What Is the Right Supply Chain for Your Product?*, 75 HARVARD BUS. REV. 105 (1997).

and informal sectors. Despite a trend toward greater and more sustained demand for products through new funding and funders, the current situation still makes it unrealistic to expect manufacturers and private intermediaries alone to make significant investments in the information and supply chain infrastructure that could help reduce and manage major sources of risk, and contribute to better demand forecasting.

In the ACT market, a recent study finds that suppliers bear the greatest burden of economic risks for excess inventory of ACTs because under current contracting arrangements they receive no purchase commitments but must have inventory available to fill orders as they are placed.⁸⁵ National buyers bear some risk (largely reputational, in the case of donor-funded products) for excess inventory if they order too much and products sit past their shelf life in warehouses; and funding agencies bear a lesser, indirect risk if their funds are ineffectively used when national buyers over-order, resulting in waste at the country level. National buyers also face acute risks from dependence on donors for sustainability of funding.⁸⁶

TABLE 1: ACT SUPPLY CHAIN RISK MAP

	Supply-side facilitators	Suppliers	Quality regulators	Global technical agencies	Aggregate demand forecasters	Funding agencies	Procurement agents	Logistics providers	National buyers
Supply-side risks									
Batch yield risk	No risk	Low risk	No risk	No risk	No risk	No risk	No risk	No risk	No risk
Excess inventory risk									
Economic	No risk	High risk	No risk	No risk	No risk	Low risk	No risk	No risk	Moderate risk
Reputational	No risk	No risk	No risk	No risk	Low risk	No risk	No risk	No risk	No risk
Long-term overcapacity risk									
Economic	No risk	High risk	No risk	No risk	No risk	No risk	No risk	No risk	No risk
Reputational	Low risk	No risk	No risk	No risk	Low risk	No risk	No risk	No risk	No risk
Shortage risk									
Economic	No risk	Moderate risk	No risk	No risk	No risk	No risk	No risk	No risk	No risk
Reputational	No risk	High risk	No risk	Low risk	Moderate risk	Low risk	No risk	No risk	Moderate risk
Demand-side risks									
Price increase	No risk	No risk	No risk	No risk	No risk	Moderate risk	No risk	No risk	Moderate risk
Price decrease	No risk	Moderate risk	No risk	No risk	No risk	No risk	No risk	No risk	Low risk
Budget and purchasing power risks									
Grant approval and disbursement timing	No risk	High risk	No risk	No risk	No risk	Moderate risk	No risk	No risk	High risk
Sustainability of funding	Low risk	Moderate risk	No risk	No risk	No risk	High risk	No risk	No risk	High risk
Obsolescence risk	Low risk	Moderate risk	No risk	No risk	No risk	No risk	No risk	No risk	Moderate risk
Regulatory and quality risks									
Lack of approved drugs	No risk	No risk	Low risk	No risk	No risk	No risk	No risk	No risk	No risk
Regulatory enforcement risks									
Counterfeit product	No risk	Moderate risk	No risk	No risk	No risk	No risk	No risk	No risk	Moderate risk
Safety of approved drugs	No risk	High risk	High risk	No risk	No risk	Low risk	No risk	No risk	Moderate risk
Logistical risks									
Nontimely delivery	No risk	Moderate risk	No risk	No risk	No risk	No risk	Moderate risk	Moderate risk	Moderate risk
Losses in the distribution chain	No risk	No risk	No risk	No risk	No risk	Low risk	No risk	Moderate risk	Moderate risk

The ACT supply chain shows significant scope for better risk sharing between stakeholders. If suppliers are expected to provide their products at low or zero margins, and guarantee access to products when and where they are needed, it is important that funding agencies and other stakeholders share some of the risks that suppliers are currently bearing. In the long run stakeholders who bear disproportionate risk but are not adequately compensated will either leave the market or engage in behavior that will

⁸⁵ Prashant Yadav, *Barriers to Access: An Assessment of Stakeholder Risks and Incentives in the Value Chain for Artemisinin Combination Therapy (ACT) Treatments* (Unpublished Working Paper, June 2007), available at ssrn.com/abstract=1008307.

⁸⁶ *Id.*

threaten the viability of the value chain. Although there are exceptions, in general, the intermediaries in the global health supply chain involved in procurement and distribution bear virtually none of the risks; they make neither purchase guarantees to manufacturers nor binding commitments to supply those who are further downstream. The consequences of these risks fall to patients and communities, who bear by far the largest burden—the health consequences of unbalanced risk sharing.⁸⁷

VI. MISALIGNED INCENTIVES

While the goal of the supply chain is to provide access to products, the extent of the risks borne by each party and their asymmetric distribution have led to misaligned incentives in several areas of forecasting. For example, suppliers incentives are balanced when it comes to forecasting long-term capacity: they have a disincentive to both overforecast and underforecast because they bear the costs of overcapacity, but must have sufficient inventory for orders. But the incentives faced by national buyers for long-term capacity forecasts are asymmetric: they have an incentive to overforecast so that they can guarantee capacity from the supplier but no incentive to underforecast, which would result in more accurate estimates of demand, because they bear no risk for overcapacity.⁸⁸

TABLE 2: ACT SUPPLY CHAIN INCENTIVES MAP

	Supply-side facilitators	Suppliers	Quality regulators	Global technical agencies	Aggregate demand forecasters	Funding agencies	Procurement agents	Logistics providers	National buyers
Supply side									
Develop innovative products	Incentive	Incentive	Indifferent	Indifferent	Indifferent	Indifferent	Indifferent	Indifferent	Indifferent
Increase size of the supply market	Incentive	Disincentive	Indifferent	Incentive	Indifferent	Incentive	Disincentive	Indifferent	Incentive
Decrease supply chain lead time	Incentive	Indifferent	Indifferent	Incentive	Indifferent	Indifferent	Incentive	Indifferent	Incentive
Overforecast in the short term	Indifferent	Disincentive	Indifferent	Indifferent	Incentive	Incentive	Incentive	Indifferent	Incentive
Underforecast in the short term	Indifferent	Indifferent	Indifferent	Indifferent	Disincentive	Disincentive	Disincentive	Indifferent	Disincentive
Overforecast in the long term (1-5 years)	Incentive	Disincentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Underforecast in the long term (1-5 years)	Disincentive	Disincentive	Indifferent	Disincentive	Indifferent	Disincentive	Indifferent	Indifferent	Disincentive
Sharing information on demand, inventory...	Incentive	Disincentive	Indifferent	Indifferent	Incentive	Indifferent	Indifferent	Indifferent	Indifferent
Demand side									
Decrease wholesale price of artemisinin-based combination therapy drugs	Incentive	Disincentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Decrease retail or end-customer price of artemisinin-based combination therapy drugs	Incentive	Incentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Indifferent
Expedite grant approval and disbursement	Indifferent	Incentive	Indifferent	Indifferent	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Rapid adoption of artemisinin-based combination therapy drugs	Incentive	Incentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Indifferent
Enhance the level and sustainability of funding	Incentive	Incentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Regulatory and quality									
Ensure regulatory compliance and safety	Incentive	Incentive	Incentive	Indifferent	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Expedite regulatory approval of new drugs	Incentive	Incentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Logistical and miscellaneous									
Improve efficiencies in distribution chain	Indifferent	Indifferent	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Incentive	Incentive
Ensure availability of complementary inputs	Indifferent	Disincentive	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Achieve long lasting success (eradication)	Incentive	Indifferent	Indifferent	Incentive	Indifferent	Incentive	Indifferent	Indifferent	Incentive
Have rigorous accountability in funds usage	Indifferent	Indifferent	Indifferent	Indifferent	Indifferent	Incentive	Indifferent	Indifferent	Incentive

There is a similar mismatch for short-term forecasting. In this case, manufacturers have an incentive to underforecast because they bear the costs of holding excess inventory, while others in the supply chain—funding

⁸⁷ *Id.*

⁸⁸ *Id.*

agencies, procurement agents and national buyers—have an incentive to overforecast because they have very limited risk for excess inventory but wish to guarantee sufficient availability of product. Experience in other industries shows that if forecasts are successively inflated, they will be ignored by suppliers, resulting in less supply rather than overproduction. To more accurately match supply and demand, stakeholders should have balanced incentives for under- and overforecasting. This would be achieved by more evenly sharing forecasting risk among key stakeholders.⁸⁹

Another critical misalignment that affects forecasting is sharing supply and demand information, which serves as inputs into forecasts (such as buyer intentions, inventory levels, etc.). On the demand side for funders, technical agencies, procurement agents, global health partnerships and in-country supply chain managers, where all these entities have critical data elements, there are few if any consequences for poor forecasting. Thus, there is no incentive to share information or to ensure its quality. On the supply side, manufacturers may directly bear a financial risk for inadequate forecasting, particularly for excess capacity, but they have a disincentive to share individually identified supply information that could make them vulnerable to competitors or to antitrust allegations. However, if the information is shared in aggregate and without attribution, the supplier's disincentive to share this information is removed. Sharing forecasting information to obtain more accurate long- and short-term forecasts requires these misalignments to be corrected.⁹⁰

Other areas in which incentives are misaligned show that national buyers lack clear incentives to rapidly adopt new therapies, such as ACTs, because they bear the costs of switching from older therapies, even though donors may provide the drugs free of charge. National buyers also do not necessarily benefit by reducing the retail price of ACTs (for example, by providing them free at the point of treatment) if they rely on cost recovery to fund the health system's delivery capacity. If widespread adoption of ACTs and other global health products at no or affordable costs to patients is a public policy objective, these misalignments need to be addressed.⁹¹

The situation is even more complicated for some stakeholders. For example, while the large R&D companies in the market may be able to absorb some of the financial risks, the fundamental maldistribution of risk makes it difficult for smaller suppliers, including many firms based in developing countries, to enter the market. The risk and analysis audit could be further expanded to include obsolescence risks for suppliers, such as the increasing use of other technologies such as bednets to reduce malaria incidence as well as the potential introduction of a malaria vaccine. This adds further uncertainty to future demand and makes it less attractive for new suppliers to enter the market.

⁸⁹ *Id.*

⁹⁰ *Id.*

⁹¹ *Id.*

VII. GLOBAL SOLUTIONS

Against this backdrop solutions must be found to the challenge of forecasting demand that facilitate better sharing of risk and aligning incentives among those who influence market dynamics. This can be achieved by three mutually reinforcing actions, described below.

A. IMPROVING TECHNICAL FORECASTING CAPACITY

First and foremost, demand forecasting must become imbedded in all global efforts to increase access to essential medicines and technologies. This requires a clear understanding of what is meant by “demand forecasting” and how it differs from estimating needs and from advocacy and demand creation activities (and the importance of political independence in maintaining that distinction), as well as investment in technical forecasting capacity and models specific to forecasting for developing country health products.

BOX 2: PRINCIPLES OF DEMAND FORECASTING

1. Identify the principal customers or decision makers of the forecast and clearly understand their needs.
2. Understand and clearly communicate the purpose of the forecast and the decisions that it will affect.
3. Create a forecasting process that is independent of planning and target setting.
4. Protect the forecasting process from political interference and ensure it is transparent.
5. Embed the forecast into the broader environment taking into account market conditions, public policy, competitive forces, regulatory changes, health program guidelines and the like.
6. Create a dynamic forecasting process that continually incorporates and reflects changes in the market, public policy and health program capabilities.
7. Choose the methodologies most appropriate to the data and market environment and obtain customers’ and decision makers’ agreement on the methodologies.
8. Keep the methodologies simple and appropriate to the situation, but include enough detail to address the level of investment risk and accuracy required.
9. Make forecast assumptions clear and explicit.
10. Understand data and their limitations, using creativity and intelligence in gathering and introducing data into forecasts.

In addition, agencies involved in forecasting demand at global, regional, national and sub-national levels should universally adopt ten basic principles for good forecasting to ensure that forecasts will meet the needs of customers and have the greatest impact on the decision they are intended to inform; to create a credible forecasting process and develop, present and understand the forecast in relation to the overall market and public policy environment; and

to select the right methods of the nature of the forecast being developed and effectively incorporate qualitative and quantitative information.⁹²

Together, these will increase market understanding and credibility, help the actors involved better understand and mitigate system-wide risk, and increase value for money.

B. CREATE A GLOBAL HEALTH INFOMEDIARY

Up-to-date, credible and comprehensive information is essential to good forecasting, but requires that key organizations and individuals collect and share high-quality data. Currently, funding agencies, procurement agents, technical agencies, product development and other global health partnerships and national buyers each have access to several important data elements but do not systematically share them with others in the value chain—or invest enough in the focused market research required to build the most accurate forecasts possible.

The resulting opacity of data increases both demand uncertainty and its associated risks. This suggests the need for an information intermediary, or infomediary, for global health to effectively gather and analyze data to forecast demand across a variety of diseases and products and to make information available to all stakeholders.⁹³ The key functions of the infomediary would be to:

- Serve as central repository of all relevant demand and supply data by collecting, synthesizing and disseminating information related to forecasting that individual organizations may not be willing or able to share independently.
- Ensure data integrity and perform the labor-intensive tasks of cleaning and analyzing data received from multiple sources.
- Establish a mechanism for ongoing, continual gathering and updating of core forecasting information.
- Generate transparent baseline aggregate forecasts by product category based on the information sets provided to serve as the common starting point for stakeholders to produce their own forecasts, and build aggregate and country-level models for generating demand forecasts that consider the unique developing country environment.
- Incorporate information from specific market research studies that are conducted by the infomediary or other market research firms and stakeholders to provide a more complete data repository and refine assumptions for forecasts.

⁹² Neelam Sekhri et al., *Principles for Forecasting Demand for Global Health Products* (Center for Global Health Products, Working Paper, 2006), available at www.cgdev.org/forecasting.

⁹³ The infomediary would place particular emphasis on the importance of gathering inputs from existing in-country programs. In turn, they will benefit from better information and technical assistance, which will help enhance country-level forecasting capacity. It is important that countries retain partial ownership in the infomediary through representation.

- Serve as a neutral party responsible only for collecting information and generating baseline forecasts and remain uninvolved in demand generation, advocacy, target setting or other functions that could compromise the integrity and independence of activities, while maintaining strong relationships with public and private supply chain partners and establishing credibility with stakeholders.

C. SHARE RISK AND ALIGN INCENTIVES THROUGH A BROADER MENU OF CONTRACTING OPTIONS

While not all of the misalignments in incentives across key players can be corrected in the short term—and some are a structural feature of donor funding that is divorced from accountability to beneficiary communities—an important and immediate opportunity exists to better align incentives and share risks by restructuring contractual arrangements. Effective contracting is also critical for ensuring that pooled purchasing mechanisms, which are being considered by many funders, achieve their objectives. However, global health funders in general have made only limited use of the wide range of risk-sharing arrangements.

BOX 3: EXAMPLES OF CONTRACTING ARRANGEMENTS⁹⁴

Minimum purchase commitments: Minimum purchase commitments require that a buyer agree to purchase a specified quantity of a product, either in a single transaction or over time. By accepting some of the supplier's risk of production, the buyer has an incentive to accurately forecast demand. Typically, suppliers offer incentives to buyers to take on this risk through reduced prices for the minimum purchase commitment. Suppliers are not committed to producing above the specified amounts, so this arrangement works best for the purchaser when long-term demand is stable, substitutes are available that prevent stockout risk or there are opportunities to off-load excess inventory.

Flexible-quantity contracts: When demand uncertainty is high, buyers may prefer committing to a lower level of demand while retaining the flexibility to purchase more product to guard against stockouts. Flexible quantity contracts allow the buyer to commit to a minimum amount at a certain price, while binding the supplier to make a specified additional quantity available at a premium price should demand be greater than expected. Suppliers may be interested in these contracts if the marginal cost of production is low but the base setup costs are high, if there are multiple suppliers, or if there is uncertainty about which supplier a purchaser will select. The contract may also allow suppliers to collaborate to buy and sell excess inventory, which limits each supplier's individual risk.

Buyback contracts: Buyback contracts are useful in situations where demand is unstable but the risk of stockouts is asymmetrically distributed among stakeholders and has significant public health consequences. Such contracts are often used when the production cycle is long and it is difficult to

⁹⁴ See YADAV, *supra* note 12.

scale up supply rapidly in cases of higher than expected demand or where the presence of supply can stimulate demand.⁹⁵

Revenue sharing: Like buyback contracts, revenue sharing is useful in situations where demand is uncertain but the presence of the product stimulates demand. This mechanism also encourages the sharing of demand and supply information between purchasers and suppliers. For example, the widespread and visible availability of bednets can stimulate their use. However, small local retailers may not have the cash flow to purchase a large number of bednets. In this case the supplier may make the bednets available to local retailers at a nominal price with the opportunity to share in the retailer's profits from bednet sales. Revenue sharing passes risk to the supplier but also aligns supplier and retailer incentives and encourages suppliers to produce sufficient levels of supply. When this system works well, suppliers get timely information about actual sales since they share in the profits generated by those sales and can adjust production capacity accordingly.

Real options: This contracting mechanism protects buyers against price uncertainty. An option gives the buyer the right (but not the obligation) to take some action at a future time for a predetermined price. Real options involve the actual sale and purchase of goods if and when the option is exercised. An option is defined by the option price (upfront price paid to acquire the option), exercise price (price at which the product can be purchased if the option is exercised) and an exercise date (typically a date range). An example of a real-options contract involves the buyer making a firm commitment to the manufacturer for future year purchases (years 1, 2, 3) for a certain amount of product and purchasing an option to buy additional units at predetermined prices in years 2 and 3. Based on observed demand in the first year, the buyer decides whether to exercise the option in the second and third years.

No single contracting option is optimal across all types of products and situations. Rather, a range of approaches could and should be considered to shift the current risk allocation in which funders, procurement agents and national buyers accept little or no risk, while suppliers gear their decisions about pricing and investments in capacity to a market in which they face significant, unshared risk.

VIII. CONCLUSION

The international community's ability to forecast demand has not caught up with its ambition to reach those in need with life-saving medical technologies, in large part because risks in the current market are unequally distributed across key actors whose decisions affect supply of and demand for products. As a result, not all stakeholders have incentives aligned toward better forecasts and greater access to critical medical technologies.

⁹⁵ Prashant Yadav & Charles P. Schmidt, Buy-back Contracts and Forecasting Incentives in a Supplier-Retailer Channel (Sept. 2005) (Unpublished Working Paper, Sept. 2005), available at ssrn.com/abstract=929713.

The inability to accurately predict demand has exacerbated risks for suppliers, resulted in higher costs, supply shortages and concerns about the long-term viability of investing in R&D for health products that benefit the world's poor. It has also limited the ability of donors and national governments to use their aid dollars effectively to improve public health and save lives.

Correcting the misaligned incentives that currently impede forecasting and access – by taking forecasting seriously, as a core element of the value chain for global health; taking action to share information more systematically; and reducing overall market risk and better sharing the remaining risks in the market through more effective contracting methods – would greatly enhance the relationships among funders, suppliers, intermediaries and users of health products, and induce alignment across participants in the global health value chain that is essential for long-term improvements in access to quality products. Far from being small technical patches, these recommendations would improve the efficient functioning of the global health market, making the new monies and new products realize their potential in better health outcomes in the developing world.

The recommendations are mutually reinforcing. Armed with better information from a credible infomediary and the adoption of key principles of forecasting, funders will be able to comfortably assume a greater portion of the risk currently borne by suppliers, which will allow for a greater return on their aid investment in the form of improved public health outcomes. Efficient contracting arrangements, in turn, will establish the incentives to improve the forecasting process itself, creating a virtuous cycle. Fully implemented, these recommendations can save lives by dramatically improving aggregate demand forecasts for critical medical technologies at the global level, and will lay the groundwork for a broader and longer-term agenda of strengthening health systems and building supply chain capacity in-country; increasing the market-orientation of product development; enhancing the regulatory regimes and enforcement for global health products; and improving the predictability of donor funding.