TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Pathway to Patients
Charting the Dynamics of the Global TB Drug Market

Study Methodology

1. Introduction

In 2006, the Global Alliance for TB Drug Development (TB Alliance) commissioned *Pathway to Patients: Charting the Dynamics of the Global TB Drug Market.* The study is the first comprehensive analysis of how today's TB drugs reach patients on a global scale. It includes an assessment of ten strategically selected countries — Brazil, China, France, India, Indonesia, Japan, the Philippines, South Africa, the UK and the US — as well as an appraisal of today's worldwide TB drug market value.

The research for *Pathway to Patients* was conducted in partnership with IMS Health, Inc., a global strategic consulting group focused on the pharmaceutical and healthcare industries. The project was financed by a grant from the Netherlands Ministry of Foreign Affairs' Department of Development Cooperation (DGIS) and with the support of the Bill & Melinda Gates Foundation.

This report describes the research methodology used to gather and analyze information in *Pathway to Patients*. A compendium of findings, as well as an abridged study overview, are available online at www.tballiance.org.

1.1 Background

More than a century after the discovery of Mycobacterium tuberculosis (M.tb), the bacillus that causes tuberculosis (TB), and a half-century after the discovery of antibiotics to treat the disease, TB is second only to HIV as the leading infectious killer of adults worldwide.

TB kills someone every 20 seconds — about 4,400 people every day, or approximately 1.6 million in 2005 alone, according to the latest estimates from the World Health Organization (WHO.)[1] It accounts for more deaths among women than all other causes of maternal mortality combined and is the leading infectious cause of death among people with HIV/AIDS.[2]

The WHO estimates that one third of the world's population is infected with M.tb, which causes TB, with the greatest burden relative to population concentrated in the developing world, with high incidence of infection in sub-Saharan Africa, Asia and South America. Furthermore, today's TB epidemic is fuelled by a surge in HIV-M.tb co-infection and compounded by the growing emergence of drug resistant strains.

Apart from its devastating health consequences, the economic impact of the disease is staggering, making TB a significant contributor to world poverty. TB is estimated to absorb US$12 billion from the incomes of the world's poorest communities. In some countries, loss of productivity attributable to TB is in the order of four to seven percent of gross domestic product.[3]

The current TB drug regimen, a product of the best scientific advances of the 1960s, works for active, drug-susceptible TB — as long as patients complete the six- to nine-month treatment. However, today's four-drug combination, taken ideally under direct observation by a healthcare worker or community member, is burdensome for patients and care providers alike and despite the enormous advances in provision of services over the past few years, many patients do not or cannot complete treatment.

The poor adherence and improper administration of existing antibiotics have led to the emergence of multi- and extensively drug resistant TB strains, known as MDR-TB and XDR-TB, respectively. Further, the global HIV/AIDS pandemic is fuelling an increase in TB, resulting in a

[1] *Global tuberculosis control: surveillance, planning, financing. WHO report 2007.* Geneva, World Health Organization.
[2] *Frequently Asked Questions About TB and HIV*. World Health Organization. http://www.who.int/tb/hiv/faq/en/. Accessed 2/27/07
[3] *HIV/AIDS, Tuberculosis and Malaria: The Status and Impact of the Three Diseases.* The Global Fund to Fight AIDS, Tuberculosis and Malaria, 2005.

dramatic rise in the number of co-infected individuals. An estimated one-third of the 40 million people living with HIV/AIDS worldwide are co-infected with TB. People with HIV are up to 50 times more likely to develop TB in a given year than HIV-negative people, and TB is one of the leading causes of death in HIV-infected people, particularly in low income countries.[4] In sub-Saharan Africa, up to 80 percent of tuberculosis patients are also HIV infected.[5] Unfortunately, the current TB drug regimen is not compatible with certain common antiretroviral therapies used to treat HIV/AIDS.

Critical to fighting this ancient disease is the development — and subsequent adoption — of affordable, new, faster and simpler drug regimens. After almost half a century of virtual inactivity, TB drug development has resurged. Bolstered by new scientific information on the bacillus, transforming international funding from philanthropic sectors and government donors, and the appearance of innovative business models designed to breach the drug development gap, the current global TB drug pipeline is the largest in history.

Experience has demonstrated that attrition rates are very high in drug development and it is expected that TB drugs will be no exception. However, the strength of the portfolio underscores the fact that even more new TB drug candidates and novel drug regimens are likely to be forthcoming within the next five to ten years.

Experience has also demonstrated that the uptake of innovation is a process that requires understanding of market forces, distribution channels, purchasing power and myriad other considerations. The promising new TB cures will be ineffective and the resurgent movement for TB drug development will have failed if the new treatments do not reach patients.

1.2 Study Description

Of the ten countries studied, six were chosen from among the 22 identified by the WHO as high burden countries (HBCs): Brazil, China, India, Indonesia, the Philippines, and South Africa. Together, these countries carry approximately 50 percent of the world's TB burden.[6] The project also encompassed four high income countries, France, Japan, the UK and US. Although the latter have a low burden of disease, they represent a significant value of the TB market because of higher cost of treatment. These countries are of particular interest to drug manufacturers because they account for a 61 percent of the total global market for all pharmaceuticals.[7] Moreover, they were chosen because they reflect different geographies, different pricing and different health systems structures.

For the study, research on Indonesia and Japan was limited to determining market value and did not examine procurement and distribution.

In order to achieve the project objectives, research was segmented into three overlapping phases, which corresponded to key project deliverables.

1.2.1 Phase 1: Global Procurement Service Agencies

The first phase consisted of a quantitative and qualitative analysis of the trends and dynamics of the global TB marketplace, with global marketplace defined as purchase and procurement from global procurement service agencies (PSAs). Given the significant roles of the Global Drug Facility (GDF) and the Green Light Committee (GLC) in procurement and distribution of TB

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[4] *Frequently Asked Questions About TB and HIV*. World Health Organization. http://www.who.int/tb/hiv/faq/en/. Accessed 2/27/07

[5] Reid A, Scano F, Getahun H, et. al. Towards universal access to HIV prevention, treatment, care, and support: the role of tuberculosis/HIV collaboration. *Lancet 2006;* **6:** 483-495

[6] *Global tuberculosis control: surveillance, planning, financing. WHO report 2007.* Geneva, World Health Organization.

[7] IMS Knowledgelink. http://www.imsknowledgelink.com

medicines on a global scale, these service agents were the primary focus for analysis of global procurement. Other procurement agents dealing with TB drugs were also reviewed, including Royal Crown Agents, the Pan American Health Organization (PAHO) and the United Nations Children's Fund (UNICEF).

The main focus areas examined for the global segment included the major sources of funding for TB medications; the role of global procurement mechanisms; the flow of drugs from supplier to customer; and the value and volume of drugs distributed through these systems.

1.2.2 Phase 2: High-income Countries Overview

In the second phase, case studies were conducted in several countries that represent the largest pharmaceutical markets today, including France, Japan, the United Kingdom and the United States.[8]

The following are among the key questions addressed in the second phase:

- What is the value and volume of TB medications today?
- Are the distribution mechanisms for TB drugs different from those utilized for the bulk of the pharmaceutical marketplace? If so, why?
- Who are the key payers for TB medications? What roles are played by the public sector (including single-system government payers in the European Union and Medicaid in the United States) and the private sector (cash-paying patients and private insurance)?
- Are TB drugs priced differently than other pharmaceutical products? If so, why?

1.2.3 Phase 3: In-depth Case Studies in High-burden Countries

Phase 3 consisted of in-depth case studies of several high-burden countries, including Brazil, China, India, Indonesia[9], the Philippines and South Africa.

The following are among the key questions addressed in each of these countries:

- What role do global groups have in procuring and distributing drugs in the country's market? Are there other public or private procurement mechanisms in place?
- How are TB drugs procured and distributed, to what settings (e.g., regional programs, hospitals and clinics), and via what channels?
- What role does the government have in determining suppliers and pricing of TB medicines?
- How are TB medications reimbursed, at what level, and by whom?
- Who are the primary payers of TB medications (e.g., government public health programs, government insurance programs, private insurance or national- or regional-level TB programs)? Do payment issues differ in terms of first- and second-line TB medications, and if so, how?
- What is the value and volume of TB medications today?

[8] Japan is included for the market-sizing exercise only.
[9] Indonesia is included for the market-sizing exercise only.

2. Overview of Methodology and Data Sources

The objective of the study was to characterize the global and country-specific TB markets from a qualitative and quantitative perspective.

2.1 Qualitative Analysis

Qualitative characterization of the TB market included mapping the flow of TB medicines from the supplier to the end user, the selection process for suppliers, and the role of public and private payers for first- and second-line TB medicines.

Qualitative characterization involved a triangulation of several secondary and primary data sources:

1. Secondary data were collected from a number of publicly available sources accessed through search engines and directly from the WHO website
2. Primary research was conducted through face-to-face interviews with global and country stakeholders by telephone and in person
3. Additional data and reports were collected from individual stakeholders after face-to-face or telephone interviews

2.2 Quantitative Analysis

Quantitative characterization of the TB market focused on measuring the actual value (defined as market value) and volume (defined as patient volume) in the public and private sectors. Data were collected from several secondary sources:

1. IMS Health databases provided data on value and units sold in the private market in all countries where a private TB market exists (India, Philippines, U.S., China and Japan), and public market in some countries (France, U.K., South Africa, and U.S.)
2. Global organizations including the Stop TB Partnership's Global Drug Facility (GDF) and the Green Light Committee (GLC) provided data on costs and supply of products on a global level and by country through their respective procurement mechanisms
3. Suppliers provided data on costs and sales of TB products sold
4. Country TB programs provided data on the number of patients treated in the public sector, level of funding allocated to drug procurement and costs per product and regimen in the public sector

For the public first-line market, and second-line market where applicable, both value and volume are included and were corroborated through interviews and secondary data. For the private first- and second-line markets, IMS Health databases, where available (e.g., India and the Philippines), were used to estimate value. Value estimates are based on the actual value of drugs sold in the private marketplace. Volume estimates, however, were deemed unreliable, especially for the second-line marketplace, where there are significant variances in treatment regimens and patient adherence rates; therefore, first- and second-line volume estimated in the private sector are not available in the TB compendium report.

3. Detail on Methodology for Each Phase

3.1 Phase 1: Global Analysis

3.1.1 Qualitative analysis

Secondary Research

Initial searches were conducted in the second half of February 2006 using several search engines, including

- PubMed (www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed), a service of the U.S. National Library of Medicine that includes over 16 million citations from MEDLINE and other life science journals for biomedical articles,
- LexisNexis (www.lexis.com/research),
- PubList Search (www.publist.org),
- ScienceDirect (www.sciencedirect.com), and
- High Wire Press (http://highwire.stanford.edu/).

In addition, online databases of several academic journals were accessed, including the *Journal of the American Medical Association* and the *American Journal of Public Health*.[10]

Next, targeted searches were conducted between March and April 2006 using several sources including WHO websites, technical assistance organizations, international aid agencies, and information from key informants.

International aid agencies and funder websites that were scanned include the Canadian International Development Agency (CIDA), the Japan International Cooperation Agency (JICA), the U.K. Department for International Development (DFID) and the U.S. Agency for International Development (USAID). Press releases and articles were extracted with descriptions of TB programs that are funded by each organization. The information sought included the level of financing and activities funded, country proposals for projects, current project descriptions, and evaluations of completed TB projects. Searches on the website of the Global Fund to Fight AIDS, TB and Malaria (GFATM) focused on resources describing the application process and criteria for recipients as well as country applications for funding from the countries studied.

Next, more targeted searches were conducted on the WHO and Stop TB Partnership websites. In particular, the WHO's 2005 and 2006 reports on Global TB Control were accessed for epidemiological data on TB burden, national TB control program funding, and treatment outcomes in each of the top 22 high-burden countries.[11]

The GDF website provided extensive information on the first-line TB marketplace. It also contains background and objectives of the organization, the criteria for country approval for direct purchase of drugs or in-kind grants, and explains the GDF's process for selecting procurement agents for distribution, and for selecting suppliers. GDF's complete catalogue provided additional detail on TB products available through GDF and outlined costs by manufacturer.

Significant information on the second-line TB global marketplace was found on the GLC website. This site provided details on the background and objectives of the organization, the criteria and process for approval for second-line drugs through GLC,[12] and the flow of drugs from manufacturers to the approved treatment programs for multi-drug resistant TB (MDR-TB). Programs to treat MDR-TB are known as DOTS-Plus projects.

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[10] Refer to Appendix VII for a complete list of references and citations.
[11] "Global Tuberculosis Control: Surveillance, Planning, Financing." 2006. WHO Report 2006. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.362).
[12] "Instructions for Applying to the Green Light Committee for Access to Second-Line Drugs.

Primary Research

After initial data were collected from secondary resources, the TB Alliance developed a list of target participants for interviews. Individuals were contacted and asked to participate in one-on-one discussion; the interviews began in mid-March and continued through mid-April.

During each discussion, interviewees were questioned according to a structured interview guide (for sample, see Appendix VII). In addition, they were asked to name additional people to interview based on the objectives of the project at both global and national levels. Potential additional interviewees were identified as key opinion leaders and staff at NGOs, technical assistance agencies and manufacturers.

For the work on global procurement systems and market size, some 20 interviews were conducted with a range of informants, including staff from multilateral organizations, funders, procurement service agents, technical assistance providers and NGOs.[13] These interviewees also provided valuable written materials used in both the qualitative and quantitative analysis.

3.1.2 Quantitative analysis

The 2005 and 2006 versions of the WHO report "Global Tuberculosis Control: Surveillance, Planning, Financing"[14] provided data on DOTS coverage; epidemiology of TB control, including incidence and prevalence of TB and MDR-TB; and financing in each country. GDF staff provided data on the value and volume of GDF drugs supplied to each country from the years 2003–2005.[15]

GLC provided data on the number of patients approved for each program in each country. It also supplied information on costs per unit and per pack by manufacturer, for each drug on the GLC-approved list[16].

3.2. Phase 2: High-income Countries

3.2.1 Qualitative analysis

Secondary Research

Background

Information on each healthcare system was collected from IMS Market Prognosis Reports.[17]

Additional statistics on TB and information on diagnostic and treatment guidelines were sourced from publicly available documents on government websites, including the Ministry of Health in France (www.sante.gov.fr), the U.K. Office of National Statistics (www.statistics.gov.uk) and the Health Protection Agency in the United Kingdom. (www.hpa.org).

Primary Research

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[13] Refer to Appendix I for full list of individuals interviewed.

[14] "Global Tuberculosis Control: Surveillance, Planning, Financing." 2006. WHO Report 2006. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.362).

[15] Provided directly by GDF.

[16] Provided directly by GLC.

[17] IMS reports, which are revised on an annual basis, provide insight into the healthcare and pharmaceutical environment across the world's major pharmaceutical markets. For each country in every region, primary research is conducted with industry experts and combined with IMS Health sales information to develop five-year forecasts.

In the developed countries, 15 interviews in total were conducted with stakeholders including government payers in Japan, hospital administrators and pharmacists in all countries, prescribers in all countries, and staff from the U.S. CDC and Japan's National TB Program.

3.2.2 Quantitative analysis

In the high-income countries, several key assumptions were made to help guide quantitative analysis. They include the following:

- IMS Health databases (which deliver projections on the total market size in each country) are assumed to capture 100 percent of the first- and second-line TB markets in the high-income countries studied;
- in France and the United Kingdom, it is assumed that there are no sales in the private hospital sector for TB;
- for the first-line calculation, use of rifampicin, isoniazid, pyrazinamide and ethambutol and all fixed-dose combinations of those medications, are assumed to be used exclusively for first-line TB; and
- for second-line calculations, treatments are assumed to be used mostly in indications other than TB. Therefore, all data were factored by indication and estimates incorporate TB use only.

IMS Health databases were used to estimate the value and volume of the first- and second-line markets in the high-income countries.[18] No additional data (e.g., government or supplier-provided data) were used.[19]

In France and the United Kingdom, estimates of the value of the first- and second-line markets in each country were derived from IMS Health's MIDAS database. Data on a value and volume (unit) basis were collected by product. All prescriptions dispensed by pharmacies in public hospitals and retail pharmacies are captured in the data. Public hospital data include prescriptions dispensed by both hospital inpatient and outpatient pharmacies. Therefore, IMS Health data are assumed to capture 100 percent of the TB market in these two countries.

In order to determine the final volume for the TB products, all drugs falling under the TB ICD-10[20] codes were pulled by product and all pharmaceuticals not associated with TB treatment were removed from the total volume and value.

In the United States, the total size of the public and private markets on a value and volume basis was derived from three different databases: IMS National Sales Perspectives (NSP), IMS National Prescription Audit (NPA) and IMS National Disease and Therapeutic Index (NDTI). Sales figures were collected from the IMS NSP database. The volume of each product was adjusted based on percent use for TB versus other indications using estimates derived from IMS National Disease and Therapeutic Index and IMS National Prescription Audit, and value was calculated based on these estimates.

In each market, top-line calculations of the aggregate market value of first- and second-line drugs were cross-checked through a patient-based market valuation approach. In this approach,

[18] Refer to Appendix III for detailed descriptions of the following databases: IMS MIDAS, IMS NSP, IMS NPA Plus, and IMS NDTI.
[19] Refer to Appendix IV for details on methodology used for each country.
[20] International Classification of Diseases.

incidence figures were collected from government sources[21] for each patient category (active, latent, retreated and resistant patients). The size of each patient population was multiplied by the average cost per regimen for each regimen and figures were added together to derive the total value of the first- and second-line markets. The cost of each regimen was derived by using costs per unit based on the recommended treatment guidelines in each country and assumes a patient receives a full course of therapy at the recommended doses.

3.3 Phase 3: High-burden Countries

3.3.1 Qualitative analysis

Secondary Research

Background

Information from the initial literature search was analyzed country by country. In addition to resources collected from the WHO website, international aid agency websites, NGO websites and other sources, relevant resources were collected from country ministry of health websites.[22]

Epidemiology and statistics

Within the high-burden markets, the WHO TB Database[23] and the 2006 WHO surveillance report[24] were used to collect data on epidemiology including incidence and case notification and treatment outcomes.

Primary Research

A primary focus of Phase 3 was discussions conducted in each country with key stakeholders. An initial target list of individuals was developed based on recommendations from the global phase, prior knowledge of the countries, and secondary research.

In each country, the manager of the NTP and the WHO regional office were contacted and requested to participate and provide additional suggestions.

Subsequently, the target list was expanded based on initial recommendations. The research team, including staff from IMS Consulting and the TB Alliance visited each country and conducted a total of 106 interviews with stakeholders; including TB program administrators (national, regional and local), NGOs and international organizations, prescribers, manufacturers, pharmacists and pharmacy chains.

After discussions, additional secondary sources such as annual reports were collected directly from interviewees. These sources provided information on number of patients treated in the public sector, financing figures for drugs, manufacturers and supply levels, and costs per regimen.

3.3.2 Quantitative analysis

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[21] For the European markets, figures on prevalence and case notification, resistance rates, and treatment outcomes, were sourced from the Health Protection Agency (www.hpa.org) and Euro TB (www.eurotb.org). For the United States, data on prevalence and case notification, resistance rates and treatment outcomes were sourced from the U.S. Department of Health and Human Services 2004 report, "Reported Tuberculosis in the United States," 2004.

[22] Refer to Appendix VII for full list of references and citations.

[23] World Health Organization: Global Health Atlas. 2005. www.who.int/globalatlas/dataQuery/default.asp

[24] "Global Tuberculosis Control: Surveillance, Planning, Financing." 2006. WHO Report 2006. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.362).

In the high-burden countries, estimates of value and volume were derived from information obtained through primary interviews with national TB program managers and IMS Health databases.[25]

NTPs provided estimates of the value of the market in the public sector and the number of patients in each treatment category. Additionally, TB program managers provided estimates on the cost per regimen and per product.

In some countries the IMS Multinational Integrated Data Analysis System (MIDAS) provided data on TB drugs procured by the public sector where they are purchased and distributed through traditional distribution and dispensing channels (e.g., distributed through third party wholesalers and dispensed at a hospital pharmacy or retail pharmacy) (see Appendix 3 for further information about MIDAS). For example, in the Philippines, where data are collected at the distributor level, IMS captures data on TB medicines procured through local government units from local and international suppliers and distributed directly to public health units; however, drugs procured from GDF are not included in the IMS Health data. In China, IMS MIDAS database capture drugs distributed within traditional commercial channels in provinces where patients pay for medicines and are reimbursed by the province. In South Africa, IMS MIDAS database capture information from provincial medical stores, which distribute all TB medications in the public sector.

For the private sector, in countries where the private sector engages in TB drug distribution, value and unit volume for each drug sold on an annual basis was available through IMS Health databases. Among the countries studied, this includes India, Indonesia, the Philippines and to a lesser extent, China and South Africa. In India, Indonesia, and South Africa, sales value and units sold were factored by indication for each product. In the Philippines, where data are only available by product and not by indication, estimates on percent use for TB versus other diseases were used based on a national index[26] conducted annually by IMS Health, which captures use by indication, and applied to the aggregate figures for each product. In China, where sales data are also only available by product, value and unit volume data were pulled for product. Percentages on use for TB versus other diseases were estimated based on qualitative inputs from physician interviews.

[25] Refer to Appendix III for more details on data sources by country; Appendix IV for methodology by country; and Appendix V for tables with global estimates and estimates for each group.

[26] Estimates derived from The Philippine Medical Data Index (PMDI) collects data every six months from 565 MDs in the Philippines (75-80% fixed panel and 20-25% moving panel) by ICD10 Diagnosis.

4. Methodology for Developing First-Line Market Estimates

To derive the global estimates, the world was segmented into three groups based on available information of burden of disease, economic trends, and anticipated cost per patient:[27] high-income countries, high-burden countries, and "rest of world".

- High-income countries include 20 countries Western Europe as well as Australia, Canada, Japan, New Zealand and the United States.
- High-burden countries are defined based on the WHO definition of the top 22 countries in terms of absolute TB burden.
- "Rest of world" includes all countries and territories listed in the WHO 2006 Global TB Control Report that were not counted in either the high-burden or high-income country segments.[28]

The countries in the first two groups were included in the research. Therefore, calculations from this analysis on market size [29] were built for each group and then extrapolated to the remaining countries. Extrapolations were conducted using three possible price points (a low, medium and high price) for each segment and WHO data on incidence and case notification (except for the high-income countries, where only case notification was used). Prices within the high-income segment and high-burden segment differ significantly and thus different points were used. However, within each segment, the same price ranges were used for all countries.

As "rest of world" is meant to denote countries outside of those researched in this study, figures are based on extrapolations from the high-burden country research.

4.1 High-income Countries

In the high-income countries, estimates on the market size for the four researched countries—France, Japan, the United Kingdom and the United States—were derived in Phase 2 of this study. In total, the high-income countries represent about 2 percent of worldwide incidence of TB, with the four researched countries representing about half of that incidence.

Two key assumptions around volume and price per regimen were made to estimate the value of the other countries in the high-income segment:

- WHO case notification figures are assumed to represent the actual number of patients treated for TB in each country and were used to derive patient volume, and
- price per regimen varies based upon the country, payer, and regimen used. The range of US$250 to US$450 per patient is assumed to represent the relative price range in this country segment

To extrapolate the size of the entire high-income country segment, for those countries not covered in the in-depth research, case notification figures were collected from the WHO TB database.[30] Case notification figures were used because it is assumed that figures are accurately reported and recorded and thus are the best estimate for actual patients treated.

Next, three price points were used: US$250, US$350 and US$450 per patient. These prices were determined based on the price per regimen for a 70 kg patient with active TB in the countries researched. Prices are based on average prices, with France on the low end and the United Kingdom at the high end. The U.S. prices were deemed as outliers and thus excluded. In each

[27] Appendix II contains a detailed list of countries included in each group.
[28] This includes 168 countries and territories.
[29] Appendix IV contains detailed explanation of methodology for calculating the market size in each researched country included in Phases 2 and 3 of the study.
[30] World Health Organization: Global Health Atlas. 2005. www.who.int/globalatlas/dataQuery/default.asp

un-researched country in the high-income group, these three price points were multiplied by the case notification to develop an estimated market range.

Finally, this extrapolated total derived from the remaining high-income countries was added to the total derived from the researched markets to come up with a final range for the high-income countries.

4.2 High-burden Countries

Within the high-burden countries (HBCs), a similar approach was used whereby primary research inputs were aggregated with extrapolated estimates for the non-researched high-burden countries. The countries researched represent 66 percent of the total HBC TB burden. Since HBCs are estimated to represent 80 percent of the worldwide TB burden, this equates to approximately 54 percent of the worldwide burden.

A couple of key assumptions around volume and price per regimen were made to estimate the value of the other countries in the high-burden segment:

- it is assumed that TB cases reported from DOTS services may underestimate the actual number of patients treated, This assumption stems from the belief that most if not all HBCs are not able to record and report all cases, particularly if some are treated in the private sector;

- it is assumed that incidence would represent the highest possible number of patients treated, or the market potential from a patient volume perspective;

- it is assumed that price per regimen varies by and within country, by payer (public or private), and by regimen used; and

- given these variances, it is assumed that in most HBCs, price for a full course of treatment range from US$20 to US$40 per patient (see below).[31]

For the patient estimates, TB cases from DOTS services in 2004 as listed in the WHO TB database were used to derive a low-end estimate. This is considered a low-end or conservative estimate because it includes only those patients treated public sector DOTS programs. Estimated incidence from the same source was used to derive the high-end estimate in each country. The high-end estimate assumes that every incident TB case receives a full course of treatment for TB. Therefore, the high-end estimate is more a measure of market potential than of the actual market.

For the cost per patient, three different price points were used: US$20, US$30, and US$40 per year. Prices were derived from GDF prices at the low end and public market prices in the researched countries at the high end. These prices represent the cost per patient for new TB cases using a 70 kg as the average weighting (in countries where doses are titrated by patients' weight).

In these countries, there are no known sources of data for the private sector on market value or patient volume. However, it is assumed that the high end of the range would account for private markets, as they include estimates for all incident cases of the disease (not just those being treated by DOTS programs).

[31] In discussions with Kathryn Floyd of WHO, this assumption was confirmed with the exception of Russia, which may have considerably higher prices.

Several countries in the "non-researched group" of the high-burden countries source TB medicines from GDF. They include Afghanistan, Bangladesh, the Democratic Republic of Congo, Ethiopia,[32] Kenya, Mozambique, Myanmar, Nigeria, Pakistan, Tanzania and Uganda.

For the above countries that received TB medicines from GDF in the form of direct procurement or grants, extrapolated figures were checked versus GDF reported values for 2005. In any instance where the GDF value exceeded the low end of the extrapolated range (under US$20 and US$30 pricing scenarios), GDF values were used to represent the total market for that country. This occurred in two instances (Mozambique and Nigeria) Figures therefore were adjusted upwards to reflect GDF reported values.

The market calculations for the researched countries were then added to the extrapolated market range for the non-researched countries (including adjustments for the GDF value). This yielded the estimated size of the first-line TB market on a value basis within the top 22 high-burden countries.

4.3 Rest of World

Within the "rest of world" segment, the market value for the entire group of countries was extrapolated based on assumptions on annual cost per patient and numbers of patients treated. The same assumptions that were used in the high-burden country segment were used for the "rest of world" segment. It is assumed that the same price points, based on GDF prices and prices in the public market in researched HBCs, apply for the "rest of world": US$20, US$30, and US$40 a year. Notably, many of these countries are supplied, at least partially, by GDF.

As with the HBCs, the WHO TB Database listing TB cases reported from DOTS services, was used for the low-end estimate and incidence was used as the high-end estimate.

In each country, each of the three price points was multiplied by the case notification rate and the incidence. These figures were added together to generate a total estimate for the "rest of world" countries.

For these "rest of world" countries, no data exist on the value or patient volume of the private market. However, as per above, the researchers assumed that the high end of the range would account for both the public and private sectors combined.

Similar to the high-burden country segment, GDF-supplied data for each country receiving TB medicines in the form of direct procurement of grants was compared to ranges calculated from the price and patient data. If the GDF value was greater than the lower end of the range, the GDF values were used instead. In accordance with this methodology, GDF values were used for Albania, Azerbaijan, Benin, Bosnia-Herzegovina, Burkina Faso, Cameroon, Cape Verde, Central African Republic, Cote D'Ivoire, Iraq, province of the United Nations Mission of Kosovo, Micronesia, Nepal, São Tomé and Principe, Sierra Leone, Sri Lanka, Tajikistan and Turkmenistan.

As this segment is based on extrapolations, there is less confidence around the market value attributed to it. For example, it is possible that some country prices may diverge from the range of $US20–US$40. Two caveats include those middle-income countries in this segment whose public healthcare system may pay more [33] or private-sector prices in those countries with a private sector. This would raise the value of this segment. However, the impact on the overall size of the overall TB market would not be significant given that "rest of world" represents about 22 percent of worldwide incidence and between 7 and 19 percent of the total value of the TB market.

[32] GDF provides isoniazid only to Ethiopia.
[33] Interview with Diana Weil and Kathryn Floyd, WHO.

5. Methodology for Developing Second-Line Market Estimates

In order to evaluate the potential range of the size of the second-line TB market, figures on the estimated incidence and prevalence of MDR-TB were sourced from "Global Incidence of Multidrug-Resistant Tuberculosis," an article published in the *Journal of Infectious Diseases* in July 2006.[34] Because the actual treated patient population globally is uncertain but is estimated to be relatively low given the hurdles in diagnosing and maintaining patients on the full course of treatment, the following ranges were used: 5 percent, 10 percent, 15 percent, 20 percent, and 25 percent of total MDR-TB patient population.

Next, a range of prices were used. The low end was derived using GLC-negotiated prices to develop estimated cost per patient, for patients resistant to isoniazid + rifampicin (HR), isoniazid + rifampicin + pyrazinamide + ethambutol (HRZE), and isoniazid + rifampicin + pyrazinamide + streptomycin + ethambutol + kanamycin HRZSEK (US$500, US$1,300, and US$2,600, respectively). To estimate the high end of the range, higher cost per range was derived based on unit costs in researched countries (US$5,000, US$6,000 and US$7,000)[35].

The prices were multiplied by the assumed treated patient population to derive estimates on the second-line market range under the above scenarios.

The global second-line TB market is difficult to estimate with high confidence because of the limited number of patients treated in the public sector and the uncertainty and variability in regimens and costs in the private sector. Most countries do not report case detection or treatment of second-line patients, particularly if they are not treated in the public sector. Compliance in the private sector is unknown. Many second-line options are available to private patients; therefore, drugs included in regimens and length of regimen may vary significantly. Cost of medicines may also vary significantly and thus there is no real "average cost" of a second-line patient. All these factors are reasons why the second-line market is extremely difficult to measure accurately without conducting extensive primary research in each country. The range developed and reported in the compendium is for illustrative purposes only..

[34] "Matteo Zignol, Mehran S. Hosseini, Abigail Wright, Catharina Lambregts van Weezenbeek, Paul Nunn, Catherine J. Watt, Brian G. Williams, and Christopher Dye. "Global Incidence of Multidrug Resistant Tuberculosis." *Journal of Infectious Diseases*. 12 July 2006; 194:479–85. www.journals.uchicago.edu/JID/journal/contents/v194n4.html

[35] Treatment prices could be higher depending on treatment regimen used.

6. Appendices

Appendix 1: Stakeholder Lists

NA = not available

Global Stakeholders

Individual	Organization	Position
Espinal, Marcos	Stop TB Partnership Secretariat	Executive Secretary
Evans, Peter	Consultant	Independent consultant to GDF
Floyd, Kathryn	WHO	Acting Head of TB Monitoring and Evaluation, WHO
Foley, Christina	CIDA	TB Advisor
Jaramillo, Ernesto	WHO/GLC	MDR-TB Working Group Secretariat
Jouberton, Fabienne	GDF/GLC	Procurement Officer (second-line)
Kempton, Kathryn	PIH	Director of Drug Procurement
Korsten, Marieke	IDA	Area Manager
Matiru, Robert	GDF/GLC	Manager of Operations, Procurement
Molari, Elisabetta	GFATM	Procurement, Supply Policy & Management Team Leader
Muller, Poul	UNDP-IAPSO	Account Manager, Procurement Services Health Commodities
Perez, Sue	Results International	Donor Country Project Manager, Global TB Campaign
Rack, Ralph	John Snow Inc (JSI)	Pharmaceutical and Logistics Advisor
Rankin, Jim	Management Sciences for Health	Director, Centre for Pharmaceutical Management
Raviglione, Mario	Stop TB Department, WHO	Director, Stop TB Department
Rouse, Doris	RTI International	Director, Global Health
van Gorkom, Jereon	KNCV	Senior Consultant, KNCV
Vaughan, Hilary	Royal Crown Agents	Senior Health Advisor
Vrakking, Hugo	GDF/GLC	Procurement Advisor
Weil, Diana	Stop TB Department, WHO	Senior Public Health Specialist, Stop TB Department

Brazil:

Individual	Organization	Position
Alburquerque, Paulo	Policlinica Amaral Peixoto	Physician
Batista Oliveira, Joao	Farmanguinhos	MOH consultant to Farmanguinhos
Cavalacante, Solange	Rio de Janeiro Municipal TB Program	
dos Santos, Joseney	National TB Program	National TB Program Manager
Durovsky, Betaina	Rio de Janeiro Municipal TB Program	Municipal TB Program Manager

Edilson, Dr.	Minas Gerais State TB Program	State TB Program Manager
Filho, German	Fundação Ataulfo de Paiva-R.J.	Director and former PNCT Program Manager
Fiuzza, Fernando	Instituto Clemente Ferreira TB Reference Center, São Paulo TB Reference Center	Physician
Freitas, Lisia	Rio de Janeiro State TB Program	State TB Program Manager
Galesi, Vera	Sao Paulo State TB Program	State TB Program Manager
Gustavo Bastos, Luis		MSH/practicing physician
Hijjar, Miguel	National Reference Lab (Helio Fraga)	Director of National Reference Lab
Keravec, Joel	MSH (TB MR Program)	MSH / former Anvisa
Komatsu, Naomi	Sao Paulo Municipal TB Program	Municipal TB Program Manager
Kritski, Afranio	Universidade Federal do Rio de Janeiro	Director of Academic TB Program
Regina, Ana	Centro Municipal de Saúde Píndaro de Carvalho Rodrigues (DOTS)	Physician
Rocha, Jorge		MSH/practicing physician
Rosangela, Dr.	Bahia State TB Program	State TB Program Manager
Silva, Waldir	National TB Program	MOH
Sousa de Ataide, Andrea	MOH/ National TB Program	Pharmacy services
Thome, Marcio	BEMFAM (NGO)	Director of Logistics and Supply
Vinhas, Marilene		Pharmacist at warehouse

China:

Individual	Organization	Position
Chenguang, Sun	Shanghai CDC	Director of Shanghai Changning District CDC
Chin, Daniel	WHO	Medical Officer, STB
Dias, Vimal	Management Sciences for Health	MSH Project-RPM Plus
Fan, Xiao	Guangzhou Thoracic Hospital	Physician & Director of Internal Medicine
Fen, Lin	Hainan CDC	Hainan CDC Director
Hennig, Cornelia M	WHO	Medical Officer, STB
Hongdi, Li	Shanghai Changning CDC	Doctor in Charge, Manager of TB Prevention Section
Jian, Mei	Shanghai CDC	Director of TB Prevention Department
Jianjun, Liu	NCTB, China CDC	Director of NCTB, China CDC

Li, Dr.	Hainan Dong Chuang County CDC	Physician at Hainan CDC
Lin, Wang	NCTB, China CDC	Associate Researcher, Director, Dept. for Health Promotion, Director, Dept. of Drug and Facility Resources
Mei, Shen	Shanghai CDC	Associate Director of TB Prevention Department
NA	First-Line Supplier	Vice General Manager
NA	Second-Line Supplier	Sales and Marketing Director
NA	National Distributor	Vice General Manager
Ni, Wang	NCTB, China CDC	Department of Drug and Facility Resources
Qiang, Zhang	Guangzhou Thoracic Hospital	Surgeon and Deputy Director
Tao, Tao	Guangzhou Thoracic Hospital	Director of Pharmacy
Xi, Zhang	Beijing Thoracic Tumor and TB Hospital	Manager of Pharmacy
Xiaomei, Wang	GFATM China TB Program	Program Officer
Yanbing, Chen	Guangdong CDC	Assistant of Guangdong CDC Director
Ying, Xu	Guangdong Panyu County Chronic Diseases Hospital	Director of Pharmacy
Yu Wen, Zhang	Hainan Dong Chuang County CDC	Physician at Hainan CDC
Yu, Dr. Fu	Beijing Thoracic Tumor and TB Hospital	Director, TB Clinical Center, President of Beijing Thoracic Tumor and TB Hospital
Zhang, Shuo	World Bank	Health Operations Officer, Human Development Sector
Zhao, Wang	China CDC	Former Director of China CDC

France:

Individual	Organization	Position
Pharmacist	Hospital	Chief Pharmacist
Specialist	Hospital	Pulmonologist

India:

Individual	Organization	Position
2 Directors	RK Mission Clinic and GTB Chest Clinic	NA
3 PPM Providers	NA	NA
Alex, Rajiv	Sandoz	General Manager, Global TB Business and Exports
Chaudury, Dr.	State TB Division	State TB Officer for Maharashtra
Chauhan, LS	Central TB Division	Deputy Director General (TB)

Deo, Mandar	Sandoz	Marketing Manager, Global TB
Dhiman, Dr.	WHO-RNTCP Department	PPM Coordinator, Delhi
Gupta, Ritu	RITES	Additional General Manager
Kabu, Rajesh	Macleods	Vice President, Sales and Marketing
Khushu, Ritu	Central TB Division-Strategic Alliance	Project Leader
Malik, Alok	Macleods	Sr. General Manager, Marketing
Patel, Jayanti	Maheshwar Distributors Private Ltd.	Chairman, Managing Director
Pradham, RK	Drug Controller Office	Representative
Sahu, Suvanand	WHO-RNTCP Department	National Professional Officer, TB
Salhotra, VS	Central TB Division	Chief Medical Officer
Sapte, Vinay	Maneesh Pharma-Svizera	Managing Director
Saxena, Pradeep	Central TB Division	Chief Medical Officer
Shah, Tariq	Central TB Division	Medical Officer
Toraskar, Preetish	Lupin	General Manager, Sales and Marketing
Vashist, RP	State TB Division	State TB Officer for Delhi
Wares, D. Fraser	WHO-RNTCP Department	Medical Officer

Indonesia:

Individual	Organization	Position
Barraclough, Andy	Management Sciences for Health	Principal Program Associate
Heitkamp, Petra	Stop TB Partnership	
Voskens, Jan	KNCV	Senior Consultant

Japan:

Individual	Organization	Position
Inoue, Hajime	Ministry of Health, Labor and Welfare - International Affairs Division	Director
Pharmacist	Hospital	

Philippines:

Individual	Organization	Position
Anden, Asuncion	DOH Center for Health Development, Metro Manila	Director
Arabit, Michael	Makati Medical Center	Pharmacist
Banzon, Eduardo	PhilHealth	Vice President, Health Finance Policy & Services Sector and OIC, Benefits Development Office

Basa-Dalay, Victoria	DeLaSalle University (Private DOTS Program)	Chairman TB Research Unit
Benedicto, Jubert	PhilCAT	Chairman
Costello, Marilou	PhilTIPS	Health Systems Advisor
Escarda, Ruben	Visaya Community Medical Center (Private Hospital)	Physician and Department Chairman of Internal Medicine
Javier, Nereza S.	Provincial TB Program, Cavite	Provincial Coordinator for TB Program
Loquias, Dory C.	Provincial TB Program, Cebu	Provincial Coordinator for TB Program
Medina, Amelia	DOH Regional Office, Metro Manila	Regional Coordinator for TB Program, National Capital Region (Metro Manila)
Morfe, Jose Hesron D.	PhilTIPS; University of St Thomas Hospital (Private DOTS Program)	Physician and DOTS Program Manager
NA	University of St Thomas Hospital (Private DOTS Program)	DOTS Nurse Coordinator
NA	DOTS-Plus Committee of Stop TB	
NA	Philippines General Hospital	Pharmacy Manager
NA	National Pharmacy Chain (PDI)	Pharmacist; Purchasing Manager
NA	Supplier	Marketing Coordinator; General Manager
Noval-Gorra, Marilyn	PhilTIPS	Policy and Finance Advisor
Pascual, Erlinda	Drugstores Association of the Philippines	President
Perez, Earl Stanley	Watsons Personal Care Stores	Comptroller - Merchandizing Division
Ricero, Fulgencia	DOH, Batangas City	RHP
Rivera, Leticia	Provincial TB Program, Batangas City	Provincial Coordinator for TB Program
Tiu, Marilyn	Med Express	Purchasing Manager
Tupasi, Thelma[28]	Tropical Disease Foundation (TDF), Makati Medical Center	President of TDF, Chairman of DOTS-Plus Committee
Vianzon, Rosalind	DOH, Office of Infectious Diseases	National TB Program Manager
Villahermosa, Sergio	Provincial TB Program, Cebu	Supply Officer
Villanueva, Andre Daniel	PhilTIPS	Pharmacy DOTS Initiative- Program Manager
Wong, John	PhilTIPS; Asian Development Bank Health Sector Development Program	Specialist for Drug Management and Finance

Yu, Charles Y.	PhilTIPS	Senior Advisor

South Africa:

Individual	Organization	Position
Banoo, Shabir	MSH	Senior Program Associate
Beattie, Alan	Aspen Pharmacare	National Sales Manager (Public Sector)
Churchyard , Gavin	Aurum Institute	CEO
Cross, Elaine	Sandoz	Head of TB Supplies
de Azeveda, Virginia	Sub-district TB Control Program (Kylitscha)	Sub-district NTP Director (Kylitscha)
Du Plessis, Deon	Netcare	Medical Director
Fourie, Bernard	Medical Research Council (MRC)	Research Associate/Clinical Trials Advisor to the MRC; Chief Scientific Officer/Director, South African Operations of MEND
Grant, Ria	TB Care Association	Director
Heinrich, John	SANTA	CEO
Helle, Mandisa	Pharmacy Planning and Policy	Dir of Pharmacy Services
Kruger, James	District TB Control Program (Boland Overberg)	District NTP Director (Boland, Overberg)
Liezel Channing	Provincial TB Control Program, West Cape	Pharmacist ARV Program
Makhetha, M.	WHO	TB Program Coordinator / NPO – TB
Makoena, Ethel	SANTA	Chairman
Mawela, Reuben	Sanofi-aventis	District Sales Manager, TB
Mkalipe, Penny	ESKOM	Medical Officer
Molongoana, Tumi	MSH	Senior Program Associate
Mthathi, Sipho	Treatment Action Campaign (TAC)	CEO
Mvusi, Lindiwe	National TB Control Program	NTP Director
Preller, Ann	Provincial TB Control Program, North West	Provincial NTP Coordinator
Sallet, Jean-Pierre	MSH	Regional Technical Advisor
Swartz, Mandisa	Provincial TB Control Program, West Cape	Provincial NTP Coordinator, Assistant Director, TB Control

UK:

Individual	Organization	Position
Pharmacist	Hospital	Chief Pharmacist
Pharmacist	Retail	Owner of a small chain of retail pharmacies

Specialist	Hospital	Consultant in Respiratory Diseases

US:

Individual	Organization	Position
Anwar, Muhammad	St. Joseph's Hospital	Pulmonologist
Castro, Kenneth	Division of Tuberculosis Elimination, U.S. CDC	Medical Director
Ehren, Mike	Florida State Health Dept., Broward County Tuberculosis Control Clinic	Pharmacist
Munsiff, Sonal S.	Bureau of Tuberculosis Control, U.S. CDC, The City of New York	Medical Officer
O'Brien, MaryAnn	Quincy Medical Center	Pharmacist
Reichman, Lee	New Jersey Medical School, National Tuberculosis Center	Executive Director
Spieldenner, Susan	TB Control Branch - California Department of Health Services	Public Health Advisor
Wallace, Charles	TB Control Branch - Texas Department of State Health Services	Program Manager

Appendix 2: Country List Within Each Grouping (High-income, High-burden, and "Rest of World")

High-income Countries

Australia
Canada
Denmark
Finland
France[1]
Germany
Greece
Ireland
Italy
Japan[1]
Luxembourg
New Zealand
Netherlands (including Netherlands Antilles)
Norway
Portugal
Spain
Sweden
Switzerland
United Kingdom[1]
United States[1] (including U.S. Virgin Islands)

1: These countries were included in in-depth case studies; market estimates were based on research.

High-burden Countries

	Average Value of GDF-Supplied Drugs, 2003–2005[36] (all figures US$)		
	Grants	Direct procurement	Total
Afghanistan	$162,212	$184,319	$346,531
Bangladesh[2]	$592,449	$383,611	$976,060
Brazil[1]	NA	NA	NA
Cambodia	NA	NA	NA
China[1]	NA	NA	NA
Congo, The Democratic Republic of [2]	$1,347,842	NA	$1,347,842
Ethiopia[2]	NA	NA	$2,632
India[1]			
Indonesia[1]	NA	NA	$3,421,586
Kenya[2]	$1,637,391	$20,401	$1,657,792
Mozambique[2]	$780,136	NA	$780,136
Myanmar[3]	$1,468,504	NA	$1,468,504
Nigeria[3]	$1,076,480	$326,556	$1,403,036
Pakistan[2]	$235,099	NA	$235,099
Philippines[1]	NA	NA	$5,555,873
Russia	NA	NA	NA
South Africa[1]	NA	NA	NA
Tanzania	$544,175	NA	$544,175
Thailand	NA	NA	NA
Uganda[2]	$690,829	NA	$690,829
Vietnam	NA	NA	NA
Zimbabwe	NA	NA	NA

1: These countries were Included in in-depth case studies and therefore market estimates were derived from primary and secondary data sources and analyses.

2: These countries were not included in in-depth case studies but are GDF countries. GDF data were compared to ranges developed according to the extrapolation methodology. GDF data were below extrapolated estimates and thus extrapolated estimates were used.

3: Nigeria and Myanmar were not included in in-depth case studies but are GDF countries. GDF data were compared to ranges developed based on extrapolation methodology. GDF data were above the lower end of the extrapolated estimates (at the lowest price point of $20 using the case notification rate). Therefore, GDF values were used in place of the lower end of the estimates for these countries.

[36] Data provided by GDF.

Rest of World

Albania[3]
Algeria
American Samoa
Andorra
Angola[3]
Anguilla
Antigua & Barbuda
Argentina
Armenia[2]
Austria
Azerbaijan[3]
Bahamas
Bahrain
Barbados
Belarus
Belgium
Belize
Benin[3]
Bermuda
Bhutan
Bolivia
Bosnia-Herzegovina[3]
Botswana
British Virgin Islands
Brunei Darussalam
Bulgaria
Burkina Faso[3]
Burundi[2]
Cameroon[3]
Cape Verde[3]
Central African Republic[3]
Chad[2]
Chile
China, Hong Kong SAR
China, Macao SAR
Colombia
Comoros
Congo[2]
Cook Islands
Costa Rica
Cote d'Ivoire[3]
Croatia
Cuba
Cyprus
Czech Republic
Djibouti[2]
Dominica
Dominican Republic[2]
Ecuador
Egypt[2]
El Salvador
Equatorial Guinea[2]
Eritrea[2]
Estonia
Fiji
French Polynesia
Gabon
Gambia[2]
Georgia
Ghana
Grenada
Guam
Guatemala
Guinea
Guinea-Bissau
Guyana
Haiti[2]
Honduras
Hungary
Iceland
Iran
Iraq[3]
Israel
Jamaica
Jordan
Kazakhstan
Kiribati
Kosovo[1, 6]
Kuwait
Kyrgyzstan
Lao PDR
Latvia
Lebanon
Lesotho
Liberia[2]
Libyan Arab Jamahiriya
Lithuania
TFYR Macedonia[7]
Madagascar[2]
Malawi
Malaysia
Maldives[5]
Mali[2]
Malta
Marshall Islands
Mauritania[2]
Mauritius
Mexico
Micronesia
Micronesia[3]
Moldova[2]
Monaco
Montserrat
Morocco
Namibia[2]
Nauru
Nepal[3]
New Caledonia
Nicaragua
Niger[2]
Niue
North Korea[2]
Northern Mariana Is
Oman
Palau
Panama
Papua New Guinea[2]
Paraguay
Peru
Poland
Puerto Rico
Qatar
Rep. Korea
Republic of Moldova
Romania
Rwanda2
Saint Kitts & Nevis
Saint Lucia
Samoa
San Marino
São Tomé and Principe[3]
Saudi Arabia
Senegal
Serbia and Montenegro[2]
Seychelles
Sierra Leone[3]
Singapore
Slovakia
Slovenia
Solomon Islands
Somalia[2]
Sri Lanka[2]
St Vincent & Grenadines
Sudan[2]
Suriname
Swaziland
Syria[2]
Tajikistan[3]
Timor-Leste[2]
Togo[3]
Tokelau
Tonga
Trinidad & Tobago
Tunisia
Turkey
Turkmenistan[3]
Turks & Caicos Islands
Tuvalu
Ukraine
United Arab Emirates
Uruguay
Uzbekistan[2]
Vanuatu
Venezuela
Wallis & Futuna Is
West Bank and Gaza Strip
Yemen
Zambia[2]

1: The United Nations Mission of Kosovo

2: These countries were not included in in-depth case studies but are GDF countries. GDF data were compared to ranges developed based on extrapolation methodology. GDF data were below extrapolated estimates and thus extrapolated estimates were used.

3: These countries were not included in in-depth case studies but are GDF countries. GDF data were compared to ranges developed based on extrapolation methodology. GDF data were above the lower end of the extrapolated estimates (at the lowest price point of $20 using the case notification rate). Therefore, GDF values were used in place of the lower end of the estimates for these countries.

4: Cape Verde and the Central African Republic were not included in in-depth case studies but are GDF countries. GDF data were compared to ranges developed based on extrapolation methodology. GDF data were above the lower end of the extrapolated estimates at all three price points ($20, $30, $40) when using the case notification rate. Therefore, GDF values were used in place of the lower end of the estimates for these countries.

5: For the Maldives, which was also not included in in-depth case studies but is a GDF country, GDF data were compared to ranges developed based on extrapolation methodology. GDF data were above the lower end of the extrapolated estimates when using the case notification rate and incidence at lower price points ($20 and $30). Therefore, GDF values were used in place of the lower end of the estimates for these countries.

6: No case notification or incidence data available through the WHO Database so GDF data used instead.

7: No case notification or incidence data available through the WHO Database or GDF data – not included in estimates.

Appendix 3: Description of IMS Health Databases

MIDAS Database

IMS Health's pharmaceutical audits for individual countries served as the main source of comparative sales data on the pharmaceutical industry. The audits are continuous, periodic market surveys based on statistically representative samples, the data from which provide regional and national estimates. Estimates include data on total sales, prescriptions, units, and specialist percribing pattenrs. In the countries covered, the pharmaceutical audits incorporate transaction data from wholesalers resulting in a near-census of the total retail market.

Each country audit records the data according to local requirements. Therefore the way data are collected and held varies from country to country. In the European countries and in North America, Mexico and Central America, the majority of pharmaceuticals are dispensed or sold through retail pharmacies and drug stores. Thus sampling at the retail pharmacy level in such countries will represent a major proportion of the total market. Consequently, most of the IMS Health audits are sampled through retail pharmacies. IMS Health also has hospital audits in more than 45 countries.

With respect to countries researched in this study, hospital and retail data were available in Indonesia, France (public hospital data only), Japan, the Philippines, South Africa, the United Kingdom (public hospital data only) and the United States. In India and Brazil, data are only available in the retail sector, and in China data are only collected at the hospital level. In a few selected countries, such as the Japan and the United States, IMS Health audits other distribution channels as well, including mail order, food stores, long-term care and home health care.

In this study, the MIDAS database was used to estimate the value of the public-sector TB market in France, Japan, South Africa, the United Kingdom and the United States. The MIDAS database was also used for estimating the size of the private market in China, India, Indonesia, the Philippines and the United States.

The audits provide a comprehensive record of purchases of pharmaceuticals in each country. A number of retail pharmacies and wholesalers are chosen for sampling (sample size) and sales data are collected by IMS Health on a regular basis. These data are then projected to estimate sales for the total number of retail pharmacies in a country (this is referred to as the universe). With some variation in each country, the sales estimates shown represent direct and indirect purchases by retail pharmacies from pharmaceutical wholesalers and manufacturers.

All audits are conducted at the level where products are dispensed, i.e., the hospital pharmacy or retail pharmacy, and thus represent the ex-manufacturer price to that facility, or the value of drug sales when sold by the manufacturer (not the value of sales to the end user).

The principal types of information are as follows:

Pharmacy Sales	Reporting sales of local and international brands in both retail and hospital sectors.
	Tracking of new product progress and comparing success in each country of launch.
Chemical Information	Relating to the active ingredients marketed in each country.
	Using mass weight to forecast demand cycles over the year.
Medical Information	Monitoring patient consultations and prescribing practices in primary care in over 30 countries.
Promotional Information	Reporting on the ways in which the promotional mix has been used by companies to promote prescribable (i.e., ethical) brands.

In addition to this, the MIDAS database contains information on the launch dates of brands, their licensing status, the companies marketing the brands (or their generics) and reimbursement categories.

Appendix 4: Methodology for Country Case Study Market Estimates

France Methodology

For France, all sales data were obtained from the IMS MIDAS database. MIDAS data in France are collected for government-funded hospitals and retail pharmacies. Drugs dispensed by private hospitals were not included. All prescriptions dispensed by pharmacies in public and semi-private hospitals and retail pharmacies are captured in the data. Hospital data include prescriptions dispensed by both hospital inpatient and outpatient pharmacies. The value data used are collected at an ex-manufacturer price and so represents the value of drug sales when sold by the manufacturer (not the value of sales to the end user). The volume data used collect units sold. The figure given covers the number of individual units sold. In most cases a unit is a single tablet. For injectables it is a single pre-filled syringe.

Pharmaceutical Audit

The French Sell Out pharmaceutical audit includes sales figures from 11,000 pharmacies. The universe size is 22,823 pharmacies. Projection of the data is based on the following criteria: regions, socio-economic profile of towns and shop turnovers. The audit covers approximately 75 percent of total French pharmaceutical market sales.

Hospital Audit

The sample for the French hospital audit is 905 hospitals (132,333 beds). There are 12 projection factors, one for each hospital type. The universe is 611,139 beds with 1,976 hospital trusts.

Japan Methodology

For Japan, all sales data were collected from the IMS MIDAS database. IMS MIDAS provides data on the private- and public-sector drugs from both a retail and hospital audit. The audits are continuous, periodic market surveys based on statistically representative samples, the data from which provide regional and national estimates. A number of retail pharmacies and wholesalers are chosen for sampling (76 wholesalers) for retail sector and a number of hospitals are chosen for sampling (76 wholesalers) for the hospital sector. Sales data are collected by IMS Health on a quarterly and monthly basis. These data are

then projected to estimate sales for the total number of retail pharmacies or hospitals in a country to estimate the universe.

MIDAS data including the value and volume (standard units) were obtained for all drugs falling under the latest version of the international classification of diseases (ICD-10) codes associated with the treatment of TB. This includes all drugs to treat the inherent disease as well as those to treat co-morbidities associated with the disease. In an effort to adjust for the over-estimated value and volume, the data were segmented by products directly used for the treatment of TB and those products used to treat co-morbidities associated with the disease.

Through associated diagnosis codes this data source breaks down the percent use of the product diagnosed for TB versus the percent use of the product diagnosed for all other indications. By applying these percentages IMS Health was able to arrive at a utilization estimate of each product's total value and volume for the TB indication versus other indications.

By applying the total prescription percentages to the total sales and standard units, the final sales and units used for the treatment of tuberculosis for the years 2001–2005 was calculated. This was broken down into both first-line total value and second-line total value.

United Kingdom Methodology

For the United Kingdom, all sales data were derived from the IMS MIDAS database, which covers public hospitals and retail pharmacies. Drugs dispensed by private hospitals are not included, but private hospitals generally comprise a very small segment of the drug market in the country. All prescriptions dispensed by pharmacies in public hospitals and retail pharmacies are captured in the data. Public hospital data include prescriptions dispensed by both hospital inpatient and outpatient pharmacies. The volume data used collect units sold. The figure given covers the number of individual units sold. In most cases a unit is a single tablet. For injectables it is a single pre-filled syringe.

Pharmacy Audit

In the United Kingdom, the retail pharmacy audit includes sales figures for the Channel Islands, the Isle of Man, and Northern Ireland, Scotland and Wales), providing an analysis of purchases made by retail pharmacies and dispensing doctors. The universe used by IMS Health is approximately 12,500 retail pharmacists and all dispensing doctors. Data are provided by virtually all the pharmaceutical wholesalers operating in the United Kingdom, on all their distribution to retail pharmacies and dispensing doctors. Many manufacturers provide full details of their direct sales to retail pharmacies and dispensing doctors. This accounts for almost 95 percent of direct sales. The remaining segment of the market is estimated from the purchase data of approximately 800 chemist shops (pharmacies). Approximately 98 percent of all sales to retail pharmacies and dispensing doctors are received from wholesalers and manufacturers as census (i.e., unprojected) data. There is an active policy of recruitment of additional data suppliers in order to improve this census data coverage.

Sales of generics are provided by members of the British Association of Generic Manufacturers, which accounts for 80 percent of the generic manufacturers in the country. Additional sales of generics are supplied via wholesalers and the retail panel of chemists. Parallel import sales have improved since 1989, when wholesalers acquired a license for distribution of parallel imports. However, because it is not always possible to identify parallel import transactions or sources, the figures are usually approximately 80 percent of the true parallel import totals. The remainder is not lost but assigned to the brand.

Hospital Audit

The U.K. hospital audit provides a record of purchases of medicinal products by National Health Service hospitals. Data are included for the Channel Islands, the Isle of Man and Northern Ireland, Scotland and Wales).The hospital universe is approximately 3,200 national health hospitals, representing 262,422 beds. Data are provided by all major wholesaling groups, on all their distribution to hospital pharmacies. This market segment is approximately 20 percent of the total market for pharmaceutical sales.

United States Methodology

The value and volume determination utilized one approach for both the private and public sectors. Three data sources were used to derive estimates:

1. IMS National Prescription Audit (NPA)
2. IMS National Sales Perspective (NSP PLUS)
3. IMS National Disease and Therapeutic Index (NDTI)

The following section provides background on each of the databases.

IMS National Prescription Audit (NPA PLUS)

The NPA PLUS is designed to measure dispensing of prescriptions by retail pharmacies in the United States. To determine the population and components of this universe, IMS Health consults data from a number of sources, among which are: *Drug Store News*, *Drug Topics*, *Chain Store Directory*, and the *U.S. Census of Business*. The NPA PLUS universe is updated monthly.

The NPA PLUS measures the retail pharmacy universe using a two-panel sample. One panel (consisting of approximately 22,000 stores) is used for dispensed data projection and the other (from an automated sample design of approximately 3,000 pharmacies) is used for substitution activity.

NPA PLUS data come primarily from a panel of 22,000 computerized stores selected randomly from IMS Health's pharmacy database of more than 35,000 reporting stores, which account for more than half of all retail pharmacies in the United States. From the computerized pharmacies, IMS Health collects and records every new and refilled prescription for every day of the month.

IMS National Sales Perspective (NSP)

The IMS National Sales Perspective (NSP) Data provide data on the private- and public-sector drugs for retail and non-retail channels in the United States. The NSP measures sales volume of units and dollars of pharmaceutical products purchased by retail and non-retail channels. These products include prescription pharmaceuticals, over-the-counter pharmaceuticals, and self-administered diagnostic products.

The universe for the retail channel consists of: independent pharmacies, chain pharmacies, mass merchandisers, proprietary stores, food stores with pharmacies, and mail service (unprojected). The universe for the non-retail channel consists of, among others, non-federal hospitals, clinics, federal facilities, HMOs, long-term care and home health care.

National projections are calculated differently depending on whether sales are direct or indirect. Direct sales include manufacturers participating in the survey while indirect sales include all wholesalers, mail pharmacies and chain warehouses. Most of the data are projected on a regional basis, using the nine census regions, and is then compiled to arrive at a national figure.

When calculating the value, the unit and dollar purchase price is the actual cost to the outlets; prompt-payment discounts and bottom-line invoice discounts are not reflected. With indirect sales, dollar information is obtained by multiplying the product units by price (prices provided by the warehouse). Often times an average price is used. With direct data, prices are extracted from direct participating manufacturers' records. Finally, for indirect mail service and hospitals the prices are adjusted to reflect price paid by the pharmacy or hospital, respectively.

IMS National Disease and Therapeutic Index (NDTI)

The National Disease and Therapeutic Index (NDTI) is a continuous compilation of statistical information about the patterns and treatment of disease encountered by office-based physicians in the continental United States. NDTI estimates from 2006 are based on a universe of 483,681 office-based physicians in private practice. A total of 1,381 physicians report per month, and 4,143 physicians report per quarter.

The sampling methodology employed is a two-stage stratified cluster, randomly drawn. In the first stage, physicians are sampled. Two workdays per month are sub-sampled from each doctor in the second stage. The sample is selected by primary specialties and the nine census divisions.

Each physician reports on all patient contacts during two consecutive workdays in each calendar quarter. Data are collected on at least 2,762 workdays each month and 8,286 workdays each quarter. Reporting days are randomly assigned to ensure that all workdays in a report period are covered. Saturdays, Sundays and holidays are assigned as reporting days to physicians who practice on those days. The sample that was used was based on confidence levels of 95 percent.

Methodology

In calculating the size of the U.S. market, the NSP data provided a total value for both first- and second-line products in retail and non-retail sectors. The NPA data provided total volume for retail sectors only. The NDTI data were then used to account for the use of each product outside of the TB indication in order to arrive at a more exact and accurate total value and volume.

To determine the final value for the U.S., TB products, all drugs falling under the TB ICD-10 codes were pulled by product and all pharmaceuticals not associated with TB treatment were removed from the total value.

IMS Health's NPA PLUS database was used to calculate the aggregate volume of each first- and second-line product. The data collected through NPA PLUS are based on total prescriptions in extended units. This provided the total number of units in pills and vials of each product. To determine the final volume directly for the TB products, all drugs falling under the TB ICD-10 codes were pulled by product and all pharmaceuticals not associated with TB treatment were removed from the total volume.

IMS NDTI data were used to reconcile product use outside of TB indication. This data provides details regarding physician use of each product for TB (percent) vs. other diagnoses (percent). This enables the application of these percentages to each product's value, determined by the National Sales Perspective, and volume, determined by the National Prescription Audit, to arrive at a more accurate estimate of the value and volume of products directly used for treating TB.

For the first-line calculations, several assumptions were made, including:

- for years, where no percentage was provided, the previous year's data were used for calculations;
- Rifater (rifampin, isoniazid and pyrazinamide) and Rifamate (rifampin and isoniazid) were assumed to have similar percentage usage in TB; and
- Myambutol (ethambutol) was assumed to have 5 percent use in TB

For the second-line calculations, cycloserine (Seromycin) was included in the estimates. However since it was not included in the NDTI database, cycloserine was unable to be factored down for use in TB versus other indications. Additionally, PAS was not found in the NSP database and no estimates were available for inclusion in the estimates of the total second-line market.

These calculations resulted in final sales and units used for the treatment of tuberculosis for the years 2001–2005. This was broken down into both first-line total value[37] and volume and second-line total value.[38]

[37] National Sales Perspective data is based on the average acquisition cost for each channel and therefore would incorporate any mark-ups from the distributor to the appropriate channel. In an effort to account for this, final value estimates were reduced by 10% to make up for the mark-up in price.

[38] Second-line volume could not be recorded as there were no U.S. audits capturing the non-retail market in terms of standard or extended units. These products were mainly injectables and hospital/office-based products and therefore the total units would have been grossly underestimated as these channels are not included in the estimates.

High-burden Countries

Brazil Methodology

In Brazil, public-sector estimates on the value and volume of the first- and second-line TB marketplace were collected from the Brazilian Ministry of Health.

IMS Health collects data at the retail pharmacy level in Brazil. However, TB drugs in Brazil do not flow through the traditional distribution channels and are not sold in retail pharmacies. All TB drugs are procured by the central government and provided for free at the hospital level, and thus no private market exists. Therefore, data are not reflected in the IMS Health databases.

The Brazilian Ministry of Health provided data for each of the following categories of patients:

Scheme 1: New TB Cases (Basic scheme)
Scheme 1R: Previously treated (Basic + ethambutol)
Schema 2: TB Meningitis
Scheme 3: MDR-TB
Scheme 4: TB MR (rifampicin + isoniazid + one other drug)

The following data were provided for each patient category:

- annual cost of regimen (Scheme 1-4);
- number of patients treated in 2004 (Scheme 1-4); and
- total market value (Scheme 1-4).

Additionally, the following data were provided for each first- and second-line drug for each product:

- projected level of 2006 supply (planned and buffer stock);
- cost per unit; and
- suppliers for each product.

Public market estimates were based on Ministry of Health data, where the cost per regimen was multiplied by the number of patients treated. Patient numbers for Scheme 1, 1R and 2 patients were multiplied by cost per regimen in order to calculate the total value of the first-line regimens. Patient numbers for Scheme 3 and 4 patients were multiplied by cost per regimen to calculate the total value of the second-line market.

China Methodology

In China, two key data sources were used:

- IMS Health MIDAS data (public and private market), and
- data supplied by the National TB Control Program (NCTB), public market only.

The China CDC-NCTB provided data on the number of units purchased and cost per unit for each product from 2001 to 2005. First-line data were provided for the following products: HRZE, HR, HRE, streptomycin, injection water, syringes, and needles.

For each product, the number of units sold and cost per unit was provided by the following funding sources: the central government, the Japan International Cooperation Agency (JICA) and the World Bank. Since the cost per unit differs by financing source, the number of units purchased and price per unit were multiplied for each source and then aggregated to generate a total public first-line estimate.

This was corroborated by the CDC-NCTB, which provided a high level estimate of the total budget allocated to TB control and drug procurement. Some inconsistencies exist as the total value figure provided by the China CDC was approximately 1.5 million higher than the estimate. This is likely due to the fact that the estimate represents a budget allocation for each year rather than an actual expense.

Provincial funds for procurement of drugs in the public sector are not included in the estimate. Some of this (e.g., in Shanghai) is captured through the IMS Health data—such as when drugs are distributed through traditional distribution channels and patients purchase at the hospital pharmacy and are reimbursed by insurance. Each province differs, so further research would be required to estimate the value by province, and thus information is not captured in the first-line drug estimates.

IMS MIDAS provides data captured at the hospital pharmacy level. The data were collected for first- and second-line drugs from hospital audit. Break-out between private and public is unavailable, though private is assumed to be very small. Definition of "locally procured drugs" refers to the procurement and distribution channels. Drugs are purchased locally by the province or the hospital. Drugs are both publicly financed (through insurance or the province) and privately financed (through private insurance or out-of-pocket). For the private sector, estimates include value of TB sales from patients seeking treatment at specialized pulmonary hospitals and paying out of pocket or getting reimbursed by private insurance. (For the public sector, estimates include value of TB sales from patients seeking treatment at hospitals and getting reimbursed through government insurance. This may occur in some provinces and autonomous regions that procure their own medicines and distribute through commercial channels or reimburse patients after treatment, as noted in Shanghai.)

Since the CDC-NCTB does not cover second-line drug procurement, no data on second-line drug value and volume were collected from the central government.

The China Hospital Pharmaceutical Audit is based on pharmaceutical purchase data from a representative panel of hospitals in China. The panel is stratified into six regions. Data are collected using a sample size of 527 general hospitals (209,007 beds) and 201 specialist hospitals (20,750 beds) giving a total of 728 hospitals (269,937 beds) each with over 100 beds each. Projection factors used are based on hospital size, bed size, and specialty. The market audit is estimated to account for 80 percent of the total market in China. IMS Health gives a hospital universe of 7,529 (1,849,855 beds).

In China, data are available only at the product level, not by indication. Therefore the panel survey did not provide estimates of percentage use of a drug for TB versus other indications. Based on information from providers and NTP interviews, 100 percent of use of first-line products was assumed to be for TB. Data were collected at the hospital level and thus included both private paying patients as well as patients who pay and are later reimbursed by the provincial authorities for drugs. The latter only happens in exceptional cases and only in provinces or autonomous regions that are responsible for funding drug procurement, for example, in Shanghai. In this instance, rather than procuring at the provincial level and distributing for free to designated healthcare centers, patients go directly to the designated center and receive treatment as they would for any other disease, and are then reimbursed afterwards.

Since second-line products are used for many indications, it is assumed that aggregate second-line numbers are highly overestimated. Instead, findings from qualitative interviews, in which physicians were asked to estimate use of each product for TB versus other diseases, were used to estimate the value and volume of second-line products specifically for TB. Since the estimates of TB use are based on limited qualitative inputs, results represent a range only and are less accurate.

India Methodology

The market sizing for India was generated via two distinct approaches: one for the public sector and one for the private sector.

Sizing of the public sector included only first-line drugs, as the public sector does not currently have a formal program in place for the second-line treatment of TB. Drugs used in the public sector in India come from one of two main procurement mechanisms: a national tender and GDF. Because India's NTP is entering a new phase of funding and implementation in 2005-2006, expenditure on drugs through both procurement mechanisms is expected to increase significantly and reports from past financial reports cannot be considered a reasonable proxy for current and future expenditures. Thus, figures were derived from discussions with stakeholders in the NTP of India, specifically from discussions with RITES and Strategic Alliance (two key agencies in India's national tender mechanism) and the Central TB Division.

These discussions first yielded value estimates for the national tender arm of public-sector procurement based on the latest tender issued by RITES on behalf of the NTP. Figures for the GDF arm of public-sector procurement were based on the amount of funding that DFID has committed to the NTP over five years to serve approximately 500M of the population (all of which will be sourced from GDF). The total value of drugs flowing through GDF was extrapolated using the population to drug funding ratio multiplied by the portion of the population estimated to be "covered" by GDF. Based on this calculation, the annual value of drugs flowing through GDF to India was added to the national tender estimates to derive a total public-sector value.

Value estimates for the private sector were relatively more complex than those of the public sector, the reason being that the private sector includes second-line drugs, which may or may not be used for TB.

To conduct the top-line value sizing of the private sector, figures were sourced from IMS Health databases, more specifically the ORG-IMS Secondary Stockist Audit. The first database is an audit of the stockist sales of approximately 13,000 of the 18,000 total secondary stockists throughout India. These are then extrapolated upwards to estimate the total market of any given drug. All drugs falling under the classification "tuberculostatics" were pulled from the database and additional drugs, such as the fluoroquinolones, were pulled on a product-by-product basis. Products were then segmented into first- and second-line drugs so that each market could be sized accordingly. Figures were then adjusted in order to eliminate the 8 percent stockist mark-up included in the original figures and to reflect ex-manufacturing sales, which are more appropriate figures for comparison to public-sector sales. In order to account for second-line drugs' frequent use in non-TB indications, prescription data (i.e., the percentage of prescriptions for any given product that were written for TB) were adjusted to give the second-line sales figures.

Philippines Methodology

The Philippines market sizing was conducted for both the public and private sectors. The public sector in the Philippines consists only of first-line drugs procured from two sources: GDF and local manufacturers. The national TB program is responsible for purchasing drugs for Category 1 and 2 patients. As the national TB control program purchases all drugs through GDF, that facility's figures represent 100 percent of the market procured through the NTP itself. Value and patient volume figures were provided by the NTP per patient category.

Local government units in the Philippines may procure additional TB medicines from local manufacturers for Category 3 patients. However, since they are procured and distributed through commercial channels to the local health unit, these drugs are included in the private market estimates captured by the IMS Health data described below. Therefore, the IMS Health data include procurement by local government units as well as by patients in the private market.

Private-sector calculations followed a similar approach to other countries. Data were provided by the IMS MIDAS database. Since MIDAS does not include data on diagnosis by ICD code, first-line sales figures were left unadjusted. Second-line figures were based on an annual panel survey conducted by IMS Health of physicians in the Philippines. The Philippines Medical Data Index (PMDI) collects data every six months from 565 doctors in the Philippines (75-80 percent fixed panel and 20-25 percent moving panel) by ICD-10 Diagnosis. This survey provided rough estimates on percentage use of drugs for TB vs. non-TB indications.

The exact value and volume breakdown between local government units and patients is unknown in the first-line market. Since the IMS Health data are captured at a manufacturer level, only the value and volume by manufacturer is known. Additionally, the NTP provides guidance on the amount local governments should procure, but does not record the actual value and volume procured on an annual basis.

Indonesia Methodology

The study analyzed both the public- and private-sector markets in Indonesia. The public sector in Indonesia consists only of first-line drugs. They are procured from two sources: GDF and local manufacturers. Unlike the sizing calculations for other countries, value figures in Indonesia were based on a bottom-up approach which multiplied units by price. Volume figures (in units, by product) for 2003–

2006 were provided by Management Sciences for Health (MSH) while prices for most products were sourced from stakeholder discussions and supplemented by the latest prices in the product catalog listed on the GDF website. Figures were confirmed through stakeholder discussions. Initial calculations yielded 2005–2006 results that were inconsistent with stakeholder discussions. The cause of the inconsistency was that a certain volume of drugs were ordered in 2005 but received in 2006 (and initially allocated to 2005). This volume of drugs was later reallocated to 2006.

Private-sector data were sourced from the IMS MIDAS database. First-line sales figures were left unadjusted whereas second-line figures were adjusted according to prescription data that indicated the percentage of prescriptions written for TB vs. non-TB indications.

South Africa Methodology

South Africa's market sizing focused primarily on the public sector, which is the primary distributor of TB drugs and distributes both first- and second-line drugs. Stakeholder discussions included the two key suppliers of first-line drugs for the South African national tender that provided sales figures for this sector. Sales figures for the 2005 calendar year were available from Sandoz. However, due to differences in record-keeping, the most recent sales figures obtainable for Sanofi Aventis were for August 2004–2005, which was used as a proxy for the 2005 calendar year. In addition to providing top-line sales figures for sales to the public sector, both suppliers were also able to provide sales figures for each province in South Africa as well as volume figures (in standard units) for each of the products supplied to the national tender. These figures were corroborated by discussions with other TB drug suppliers and discussions with national government officials.

The second-line market for the public sector in South Africa includes a wider variety of suppliers, and supplier sales figures were not available at the time of this study. IMS MIDAS database includes a component that covers drugs flowing through the provincial depots on behalf of the public sector. These top-line figures were extracted from the database and adjusted upwards to account for the coverage gap that this database typically demonstrates, i.e., reported figures were assumed to be 85 percent of the total market. IMS Health prescription data, which are collected in South Africa, were used to screen out use in non-TB indications.

Value estimates for the entire private sector were very similar to those for the second-line public-sector market. The IMS MIDAS database covers the private sector and includes sales to pharmacies, dispensing physicians, private hospitals and clinics, buying groups, mail order/courier medicine distributors and other private outlets. The coverage of this particular component is 95 percent, and sales figures were adjusted upwards accordingly. The second-line drug sales were adjusted with IMS Health prescription data to screen out non-TB indication use.

Appendix 5: Tables from Global First-Line Market Estimates

Table 1: Estimates for High-burden countries (based on price for the full course of treatment of US$20, US$30, and US$40 per patient and using case notification as the low end and incidence as the high end of the range). All figures in US$.

Market at $20		Market at $30		Market at $40	
Low: Case notification	High: Incidence	Low: Case notification	High: Incidence	Low: Case notification	High: Incidence
$192.6 million	$223.5 million	$203.7 million	$250.8 million	$15.3 million	$278 M

Table 2: Estimates for "rest of World" (based on price of US$20, US$30, and US$40 per patient and using case notification as the low end and incidence as the high end of the range). All figures in US$.

Market at $20		Market at $30		Market at $40	
Low: Case notification	High: Incidence	Low: Case notification	High: Incidence	Low: Case notification	High: Incidence
$9.9 million	$20.1 million	$13.9 million	$30.1 million	$18.4 million	$40.1 million

Table 3: Estimates for High-income countries (based on prices of US$250, US$350, US$450). All figures in US$.

	Based on case notification
Low ($250 per patient)	**$41.8 million**
Moderate ($350 per patient)	**$49 million**
High ($450 per patient)	**$56.4 million**

Table 4: Aggregate Estimates Using Low-End Approach (patient numbers based on case notification in HBCs and "rest of world" [ROW]). All figures in US$.

Price ranges	**HBCs**	**ROW**	**High-income**	**Total**
Low	$192.6 million	$ 9.9 million	$43.7 million	**$246.1 million**
Medium	$203.7 million	$13.9 million	$47.2 million	**$264.8 million**
High	$215.3 million	$18. 4	$50.7 million	**$284.4 million**

Table 5: Aggregate Estimates Using High-End Approach (Patient numbers based on incidence in HBCs and "rest of world" [ROW]). All figures in US$.

	Market			
	HBCs	**ROW**	**High-income**	**Total**
Low	$223.5 million	$20.1 million	$43.7 million	**$287.3 million**
Medium	$250.8 million	$30.1 million	$47.2 million	**$328 million**
High	$ 278 million	$40.1 million	$50.7 million	**$368. 8 million**

Appendix 6: List of Acronyms

APHA American Public Health Association

ARV	antiretrovirals
BEMFAM	BEM-ESTAR Familiar No Brasil
CDC	U.S. Centers for Disease Control and Prevention
CIDA	Canadian International Development Agency
DFID	U.K. Department for International Development
DGIS	Directorate-General for International Cooperation
DOH	Department of Health
DOTS	directly observed therapy, short course
EMB	ethambutol
EU	European Union
FDC	fixed-dose combination
GDF	Global Drug Facility
GFATM	Global Fund to Fight AIDS, TB and Malaria
GLC	Green Light Committee
CHR	isoniazid, Rifampin
HRE	isoniazid, Rifampin, ethambutol
HRZE	isoniazid, Rifampin, pyrazinamide, ethambutol
IAPSO	Inter-Agency Procurement Services Organization
IBEF	India Brand Equity Foundation
IDA	International Dispensary Association
INH	isoniazid
JICA	Japan International Cooperation Agency
JSI	John Snow Inc.
KNCV	Royal Netherlands Chemical Society
MIDAS	Multinational Integrated Data Analysis System
MDR-TB	multi-drug resistant tuberculosis
MOH	Ministry of Health
MRC	Medical Research Council
MSH	Management Sciences for Health
NA	not available
NCTB	National TB Control Program (China)
NDTI	National Disease and Therapeutic Index
NGO	non-governmental organization
NPA	IMS's National Prescription Audit
NSP	IMS's National Sales Perspective
NTP	national TB control program
OPPI	Organisation of Pharmaceutical Producers of India
PAHO	Pan American Health Organization
PDI	Pharmacy DOTS Initiative
PhilCAT	Philippines Coalition Against Tuberculosis
PhilTIPS	Philippines TB Initiatives in the Private Sector
PIH	Partners in Health
PMDI	Philippines Medical Data Index
PPM	public-private mix program
PSA	Procurement Service Agency
PZA	pyrazinamide
RIF	rifampicin
RNTCP	Revised National TB Control Program (India)
ROW	rest of world
RTI	Research Triangle International
TAC	Treatment Action Campaign
TB	tuberculosis
ICD-10	International Classification of Diseases
UNICEF	United Nations Children's Fund
UNDP	United Nations Development Program
USAID	U.S. Agency for International Development
WHO	World Health Organization

Appendix 7: Resources and References

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