ANNEX 1
Explanation of the GPSTB Cost Projections and TB Control Analysis

The *Global Plan to Stop TB* (GPSTB) estimates that TB-control activities over the next five years will cost $9.1 billion, covering all major TB-control activities:

- Expanding DOTS ($6.2 billion) in all TB high-burden countries and in all other low- and lower middle-income countries[1] (that is, countries with a GNP per capita of $3,000 per year or less[2]).
- Adapting and improving DOTS ($1.7 billion) to cope with TB-HIV co-infection and with multidrug-resistant TB.
- Research for new TB diagnostic tools, drugs, vaccines, and operational improvements ($1.1 billion).
- Partnership initiatives ($75 million)—including advocacy, communications, coordination, and resource development.

Expanding, adapting, and improving DOTS accounts for 87 percent of the GPSTB costs. This annex explains in brief how cost estimates for these components of the plan were analysed and evaluated. Complete detail of the methodology for cost estimates and the epidemiological projections is being published separately as *The Economic Annex to the Global Plan to Stop TB*.

The financial gap between five-year TB-control costs and the available resources is estimated at $3.8 billion, roughly 41 percent of total plan costs. The largest component of this gap is associated with DOTS expansion ($1.6 billion), and is estimated from national TB programme plans that are the basis for WHO's Global DOTS Expansion Plan (GDEP). The GDEP was first published in May 2001, and has been recently revised based on revisions to national TB-control plans (for example, in Indonesia, Pakistan, China, and India). Among these revisions are improved estimates of the general health-system capacity of high-burden countries to support DOTS expansion. The estimated financial gap in this GPSTB is consistent with these new GDEP estimates. The estimated financial gap between needed and available resources for DOTS expansion in other low- and lower-middle income countries is based on an extrapolation from what is known about the capacity in high-burden countries.

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[1] The total estimated plan costs shown in this table exceed the estimate of resources required for global TB control in a recent analysis conducted by WHO (see K. Floyd, L. Blanc, M. Raviglione and J.W. Lee, "Resources Required for Global Tuberculosis Control" Science 2002, in press). This is because the latter focuses on the costs for DOTS implementation, and does not include an assessment of resources needed for MDR-TB, TB/HIV, new diagnostics, drugs and vaccines, and partnership activities. Estimates for DOTS implementation in both publications are similar. In the analysis undertaken by WHO, it is estimated that $6 billion is required for DOTS implementation in the 22 HBC and in the low- and lower-middle income countries outside the 22 HBC during the period 2001-5 ($225 million less than is projected in this plan), and that the resource gap is about $1.5 billion (compared to $1.6 billion in this plan). The differences arise because the two studies were conducted independently and used slightly different methods to project cases to be treated, costs, and available resources. However, the fact that the two studies are broadly consistent strengthens the validity of both estimates. The main difference lies in the cost estimates for low- and lower-middle income countries outside the 22 HBC. This is to be expected given the limited data and the need for more assumptions in estimating costs for these countries. Both sets of estimates will be updated as more data become available.

[2] Appaix, Olivier. Tuberculosis Control: Financial Evaluation for the 2001-2005 Period (in Low- and Lower Middle-Income Countries). Economic Annex to the Global Plan to Stop TB Boston: Partners In Health, to be published in 2002.

The estimated financial gap for TB-HIV prophylactic strategies ($604 million) is projected based on current investment in TB-HIV pilot projects by donors and host governments, but not on any detailed national plans or budgets. Likewise, the gap projected for MDR-TB treatment ($834 million) is based on assumptions of likely national support for successful and cost-effective DOTS-Plus programmes. The projected gap for research and development efforts ($708 million) is based on known research and development commitments in 2001, and assuming that those commitments remain in place over five years. The estimated financial shortfall for the Stop TB Partnership ($65 million) is projected for five years, net of current partnership support, which is assumed to remain constant for the five-year period.

DOTS EXPANSION

Modelling DOTS Expansion in 114 Countries: To accurately capture the costs of TB control in high-burden and low- and lower-middle income countries, the authors of this study constructed a model that projects TB-control costs on a country-by-country basis over the 2001–2005 period. The model builds unit costs for specific TB-control elements in each country, deriving cost from national TB-control programmes plans for 13 high-burden countries, and from health-care cost studies and data from 17 additional low- and middle-income countries. This information was supplemented with questionnaires and personal communications with national programme coordinators from most of the 22 high-burden countries, and with WHO officials around the world. Where specific cost information was lacking, cost estimates for TB-control inputs in specific countries were derived by extrapolating from known costs in neighbouring countries, and/or from countries with analogous socio-economic and epidemiological profiles. Cost projections do not include any inflation adjustments. Costs are calculated in 2000 U.S. dollar equivalents.

Table 1: Cost Projections for DOTS Expansion[3] (in $ millions)

5-Year Costs	
In the 22 high-burden countries	
• TB Programmes	1,560
• General Health Services	3,000
Other low- and middle-income countries	
• TB Programmes	590
• General Health Services	850
DOTS Expansion Working Group	225
Total	**6,225**

[3] See footnote on the preceding page regarding the separate analysis of DOTS expansion costs, which estimated substantially similar costs using somewhat different methodologies.

The GPSTB estimates costs for all TB-control activities in the 114 countries it covers, including the following:

- All activities of national TB programmes—Training, operational research, diagnostic capacity (such as laboratories and equipment), public education awareness initiatives, and a reliable supply of quality drugs, including drugs supplied through the Global TB Drug Facility.
- Expenses for expanding existing DOTS programmes and establishing new programmes—providing capacity adequate to detect and treat the numbers of patients anticipated by the TB-control goals for 2005 and by WHO epidemiological projections.
- Costs for clinical management of routine TB as it is practiced in each country, including costs for the use of hospitals, clinics, dispensaries, and sanatoriums, regardless of whether they are under the control of the national TB-control programme.
- Administrative expense for the management and supervision of increasingly large and complex programmes.

DOTS expansion costs were estimated on a cash basis: how much will the country spend throughout the 2001–2005 period if it expands DOTS as required to meet the targets? The projections include, therefore, the full capital costs of new laboratories, for example, instead of amortizing depreciation costs over the useful life of these facilities.

Estimating the costs to general health-care systems of treating the expanded caseload is fraught with difficulty, not the least of which is uncertainty about the capacity constraints of existing systems. Being unable to predict whether or by how much general health services will have to expand facilities to treat increased numbers of TB patients, the model generated a range of possible costs. The low end of this cost range ($3.2 billion) assumed that, with the efficiencies introduced by expanding DOTS, there will be adequate capacity in health service facilities to handle increased patient populations. The high end of this range ($4.5 billion) assumed that facilities are now at capacity, and that increasing caseloads will require increased capacity. The cost of new capacity was then estimated by assuming that the incremental cost of expansion would be equal to the current average cost (per patient or unit of service) of existing facilities, times the increased number of patients in expanded programmes. In this case therefore, the cost projections include depreciation, and thereby approximate the capital costs of new facilities and equipment.

Within this range—$3.2 to $4.5 billion—we chose a midpoint of $3.85 billion as the estimated cost to general health-care systems of expanded TB control ($3.0 billion in high-burden countries and $850 million in other low- and lower middle-income countries). This represents over half the estimated cost of DOTS expansion. It is necessarily a tentative estimate, and will have to be carefully reconsidered as we learn more about health services capacity in individual countries and as DOTS expansion progresses.

The GPSTB cost projections substantially confirm parallel cost estimates made in the World Health Organization's *Global DOTS Expansion Plan* (GDEP), published last year (May, 2001), despite having used a slightly different methodology, and are consistent with updated GDEP cost estimates that will be published in 2002.

There are important limitations in our ability to project TB-control costs:

- Epidemiological uncertainty due to rapid change in factors affecting incidence of TB, MDR-TB, or TB-HIV co-infection. Estimates will change as we improve our ability to predict disease trends, when incidence falls as a result of TB-control investment, or with unexpectedly rapid progression of TB.
- Uncertainty of cost data. The quality of health-care cost information provided by countries varies considerably, and these costs are moving targets as countries reorganize health-care delivery and reallocate resources. Likewise, estimating the share of a nation's general health-care system devoted to TB control requires gross assumptions that provide indicative, but not fully accurate, cost estimates. This is due in part to evolving protocols and practices.

There are reasons to be cautious in estimating TB incidence, as the *WHO Global TB Control Report 2001* points out: "For high-burden countries, the difference between the lower and upper estimates of (TB) incidence is typically twofold."[4] The GPSTB used the WHO's epidemiological data for 1999 (the most recent available in September 2001). Assuming stable incidence rates, it projected the number of TB cases needed to be detected and treated in each country over the five-year period to achieve the WHO goals for detection of new cases (70 percent) and for successful treatment (85 percent). In 1999, there were an estimated 8.4 million new cases of TB, of which roughly 44 percent were infectious or sputum-smear positive (SS+). Assuming level progress towards the targets, the GPSTB estimates that there will be nearly 43 million new TB cases in the 114 countries covered over the 2000–2005 period, and that 44 percent of cases will be infectious, as shown in Table 2.

Table 2: TB-Control Projections for 2001–2005 in Low- and Lower-Middle Income Countries (cases in millions)

	Current Level of TB Control		Stop TB Goals	
	All Cases	SS+ Cases	All Cases	SS+ Cases
Number of New Cases (Incidence)	42.9	18.9	42.9	18.9
Cases Detected and Treated	19.1	7.7	26.0	11.3
• Covered by DOTS	8.7	4.7	21.5	10.0
• Covered by other protocols	10.4	3.0	4.5	1.3

As this table shows, the plan projects that TB cases detected and treated under DOTS will more than double, if proposed GPSTB investments are made. DOTS programmes will recruit 850,000 additional TB cases each year, of which at least 350,000 will be infectious

[4] World Health Organization. *Global TB Control: WHO Report 2001.* Geneva: World Health Organization, 2001, p.32.

(SS+ cases)[5]— that is, 5.3 million additional smear positive cases over five years. The projected growth in DOTS programme patients will be a function of two factors, reflecting the WHO goals—an increase in TB case detection (+ 6.9 million cases) and in increased DOTS treatment of TB patients whose cases are now being treated under non-DOTS protocols (+ 5.9 million cases).

DOTS is the recommended and generally accepted strategy for TB control throughout the world, but in many countries it is not the exclusive mechanism. Currently, only 46 percent of patients treated for TB worldwide are cared for under DOTS programmes. The remaining patients are treated by other means—often less efficiently and effectively—in national TB programmes, in private practices, or through general health services. In India, for example, only 6 percent of estimated smear-positive TB cases were notified and treated under DOTS (1999), but the DOTS treatment success rate in India is high (84 percent) and the country is expanding its DOTS coverage rapidly. In Russia, to take a second example, TB case notification rates are quite high, but less than 2 percent of smear-positive cases were notified and treated under DOTS in 1999.

The goal of the GPSTB is for all countries to achieve DOTS coverage of 100 percent of their population by 2005, and that 70 percent at least of all new TB cases will be detected and managed by DOTS programmes. The plan projects that DOTS case detection and treatment in each country will increase on a straight-line basis from current DOTS detection and treatment rates to the 2005 target rates, except in countries where credible projections show that targets will be met earlier. But, as noted, this study does not attempt to predict how quickly or to what extent the existing cost structure for TB control in specific countries will change with the increasing use of DOTS.

If DOTS programmes expand as projected and successfully treat 85 percent of patients, they could save some 3.4 million patients who will otherwise die of TB. As noted above, of the additional patients treated in expanded DOTS programmes, 6.9 million will be the result of increased case detection capability. Roughly 3.6 million of these patients will be SS+, and absent treatment, 65 percent of these patients will likely die, as will roughly 40 percent of the remaining, non-infectious TB patients. These figures alone, adjusted for mortality rates of SS+ patients within DOTS programmes (4 percent), yield a conservative estimate of 3.4 million lives that could be saved through DOTS expansion.

DOTS expansion in the 22 high-burden countries is projected to cost $6.2 billion over five years, an increase of $1.66 billion over what is now being spent for TB control. If these cost projections prove accurate, the incremental cost of detecting an additional 6.9 million cases and of treating these patients would thus be $240/patient, and the incremental cost per life saved would be $485. Assuming 24 years of life per death averted produces a cost for DOTS expansion of over $20 per year of life gained, on average.

[5]For comparison, in the Global Tuberculosis Control Report 2002, WHO estimates that an extra 330,000 SS+ cases will need to be treated each year if control targets are to be met. The fact that the 2 figures are very similar strengthens the validity of both estimates."

ADAPTING AND IMPROVING DOTS

Cost estimates for adapting and improving DOTS to cope with multidrug-resistant TB (MDR-TB) and with TB-HIV co-infection are preliminary. Strategies to deal with these health threats are still evolving. Furthermore, epidemiological data on these enormous challenges is more uncertain than that available for routine tuberculosis.

Table 3: Cost Projections for Adapting and Improving DOTS (in $ millions)

	5-Year Cost
TB-HIV Country Needs	**630**
• Voluntary Counselling ans HIV Testing	290
• TB Testing, Screening, and Programme Costs	330
• Drug Cost—INH Preventive Therapy	10
MDR-TB Country Needs	**1,070**
• Drugs	650
• Other Costs	420
Total	**1,700**

TB-HIV Co-infection TB-HIV co-infection is a terrible and complex problem confronting patients and health workers around the world. There still are too few programmes confronting the deadly synergy of these two diseases, and reliable data on those that are being implemented is still scarce. As a result, predicting the cost of widespread intervention is extremely difficult. Yet a Global Plan to Stop TB could not possibly pass over this central problem of TB control.

The GPSTB begins to estimate the costs of responding—shown above in Table 3— by drawing on preliminary cost information and promising results from ProTEST projects in sub-Saharan Africa and from other preliminary studies. Costs have been projected for voluntary counselling and testing (VCT) of roughly 28 million people in twelve sub-Saharan countries. The twelve countries are four that have established ProTEST projects (Malawi, Uganda, South Africa, and Zambia), four in which ProTEST projects are being established (Mozambique, Ethiopia, Kenya, and Tanzania) and four others (Rwanda, Congo DR, Cote D'Ivoire, and Senegal). An estimated 3.3 million of these patients (12%) are projected to be HIV-positive, and then half of these are projected to be co-infected with TB. These co-infected patients are assumed to receive INH preventive therapy to prevent the onset of active TB.

There are considerable limitations in these estimates. ProTEST provides an excellent model for how TB-HIV co-infection will have to be addressed, but reliable cost data from the projects is not yet available. There are also uncertainties regarding the extent of co-infection, the willingness of patients to volunteer for testing and the extent of the synergy between these two diseases. In addition, treating TB-HIV co-infection will likely require a larger set of

interventions. Cotrimoxazole, for example, is now being used by a number of African countries to prevent bacterial and parasitological complications of HIV. It will likely be used more extensively in the future, as further evidence on its effectiveness is assembled. As a result, the summary table at the end of Chapter 3 notes other likely components of TB-HIV control, even though they have no cost associated with them, in order to highlight their importance and the need for more complete cost information.

MDR-TB: Two scenarios were used in estimating the proportion of all TB cases that are multidrug resistant—one providing an MDR-TB rate of 3.2 percent and the second a rate of 4.6 percent. This study assumed the worse incidence, which would result in 1.9 million cases of MDR-TB. The GPSTB urges the rapid expansion of capacity to treat MDR-TB, yet it is very difficult to predict how rapid this DOTS-Plus expansion will be. Hence, we have made a necessarily tentative assumption that 40 percent of all MDR-TB cases detected will be appropriately treated over the next five years (494,000 of the 1.2 million estimated cases detected). This assumption will need to be reviewed in light of the progress of countries in initiating DOTS-Plus programmes.

Table 4: MDR-TB-Control Projections for 2001–2005 in Low- and Lower-Middle Income Countries (cases in millions).

	Current Level of TB Control	Stop TB Goals
Number of New Cases (Incidence)	**1.9**	**1.9**
Cases Detected and Treated	**0.9**	**1.2**
• Covered by DOTS-Plus	0.06	0.5
• Not Appropriately Treated	0.9	0.7

Cost estimates for MDR-TB treatment must be derived from very limited data. We have relied mostly on data from programmes in Peru, and have extrapolated those known costs to all other countries with likely MDR-TB problems. As further data is available from Peru and elsewhere, these estimates of treatment costs will need to be revised.

Expensive second-line drugs account for roughly 60 percent of the projected five-year cost estimate of $1.1 billion. The projected per patient cost for drugs is $1,317, on average, at current levels for standardized regimens. Other DOTS-Plus costs consist of programme costs of $170 million ($344/patient) and general health service system costs of $250 million ($507/patient), reflecting likely difficulties of initiating and scaling up DOTS-Plus programmes. These projections will be revised as further data becomes available.

[6] There are now roughly 7,000 patients worldwide being treated for MDR-TB under approved DOTS-Plus programmes.

Annex 2 Stop TB Working Group Plans and Budgets

Stop TB Working Groups	Lead Agency	Working Group Chair
DOTS Expansion	WHO	Dr. Mario Raviglione (WHO) raviglionem@who.ch
TB-HIV	WHO	Dr. Gijs Elzinga (RIVM) gijs.elzinga@rivm.nl
DOTS-Plus for MDR-TB	WHO	Dr. Jim Yong Kim (Partners in Health) jimkimpih@pih.org
TB Diagnostics	TDR	Dr. Carlos Morel (TDR) morelc@who.int
TB Drug Development	Global Alliance for TB Drug Development	Dr. María Freire (Global Alliance) maria.freire@tballiance.org
TB Vaccine Development	WHO/TDR	Dr. Ann Ginsberg (NIAID/DMID) AGINSBERG@niaid.nih.gov

Working Group on DOTS Expansion

Lead Agency: ***World Health Organization***
Chair: **Dr. *Mario Raviglione, Coordinator, WHO STB/TBS***

Summary 5-Year Work Plan

Objectives	Targets	Activities	Budget ($)
Objective 1: Ensure that countries are provided with technical and strategic assistance for comprehensive DOTS expansion	• Medium-term: To achieve year 2005 global TB-control targets (70% case detection rate and 85% cure rate) • Short-term: By end 2001, at least all high-TB-burden countries will have developed medium term DOTS expansion plans	• Further develop and refine interim targets, one year and five year plans • Address key challenges to TB-control effectiveness in specific countries through technical assistance, coordination, capacity building, and human resource development • Promote and monitor community involvement in TB control by providing guidelines and training material for such programmes • Promote and disseminate examples of policies and experiences of engagement of private sectors and other sectors in TB control	207,000,000
Objective 2: Support and coordinate national, regional, and global TB control	• Establish regional advisory groups and inter-agency coordinating committees • Impact of TB control on health sector and poverty	• Monitor DOTS expansion progress at global, regional, and country level and define next steps to achieve the global targets by 2005. • Monitor the effects of TB control in health sector development and poverty reduction by promoting development and use of outcome indicators.	16,080,000
Objective 3: Monitor and report annually on DOTS expansion and on the progression of the disease	• Annual updates on country places of action, country needs, and gaps	• Organized annually - DOTS Expansion Working Group meeting.	1,150,000
Objective 4: Advocate to increase commitment and financial resources	• Significant increase in resources to support DOTS expansion	• Advocacy campaign and social mobilization	1,000,000
TOTAL			**225,230,000**

Working Group on DOTS Expansion

2001 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Technical Assistance		**39,000,000**	**16,000,000**	**23,000,000**
• Capacity building and human resources development for DOTS implementation	• International training courses including training of consultants • Training material, coordination of training • In-service training	23,000,000	10,000,000	13,000,000
• Direct NTP assistance, advisors, missions and tools	• Medium-term plans including budget • DOTS coverage	16,000,000	6,000,000	10,000,000
Objective 2: Support and Coordination		**1,000,000**	**500,000**	**500,000**
• Regional strategic plans to cover endemic countries	• Meeting held	100,000	100,000	0
• Regional Advisory Groups and Inter-agency Committee		600,000	300,000	300,000
• Updating plans, country needs and gaps for 22 HBC	• Plans updated	200,000	50,000	150,000
• Updating of plans and budget for agencies (WHO/partners) supporting countries in DOTS expansion	• Budget available for agencies	100,000	50,000	50,000
Objective 3: Monitoring and reporting		**230,000**	**200,000**	**30,000**
• DOTS Expansion WG meeting	• Meeting held	180,000	150,000	30,000
• DOTS Expansion report No. 1	• Global DOTS Expansion Plan published	30,000	30,000	0
• DOTS Expansion report	• Global DOTS Expansion Plan published	20,000	20,000	0
Objective 4: Advocacy		**200,000**	**100,000**	**100,000**
TOTAL YEAR 2001		**40,430,000**	**16,800,000**	**23,630,000**

Working Group on DOTS Expansion

2002 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Technical Assistance		**42,000,000**	**21,500,000**	**20,500,000**
• Capacity building and human resources development for DOTS implementation	• International training courses including training of consultants • Training material, coordination of training • In-service training	24,000,000	12,000,000	12,000,000
• Direct NTP assistance, advisors, missions and tools	• Medium-term plans including budget • DOTS coverage	18,000,000	9,500,000	8,500,000
Objective 2: Support and Coordination		**3,770,000**	**1,370,000**	**2,400,000**
• Regional action plans for 50% of endemic countries	• Complete December 2002	1,000,000	500,000	500,000
• Regional Advisory Groups and Inter-Agency Committees	• TAG & ICC meetings	600,000	300,000	300,000
• Update action plans, country needs/gaps, and budgets for agencies supporting countries in DOTS expansion	• GDEP report published	170,000	70,000	100,000
• National inter-agency committees	• Established in regional priority endemic countries	2,000,000	500,000	1,500,000
Objective 3: Monitoring and Reporting		**230,000**	**130,000**	**100,000**
• DOTS Expansion WG meeting in Canada	• Meeting held	200,000	100,000	100,000
• DOTS Expansion report No. 3	• Report published	30,000	30,000	0
Objective 4: Advocacy		**200,000**	**0**	**200,000**
TOTAL YEAR 2002		**46,200,000**	**23,000,000**	**23,200,000**

Working Group on DOTS Expansion

2003 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Technical Assistance		**42,000,000**	**21,500,000**	**20,500,000**
• Capacity building and human resources development for DOTS implementation	• International training courses including training of consultants • Training material, coordination of training • In-service training	24,000,000	12,000,000	12,000,000
• Direct NTP assistance, advisors, missions, and tools	• Medium-term plans including budget • DOTS coverage	18,000,000	9,500,000	8,500,000
Objective 2: Support and Coordination		**3,770,000**	**1,370,000**	**2,400,000**
• Action plans all of endemic countries	• Complete by December 2003	1,000,000	500,000	500,000
• Regional Advisory Groups and Inter-Agency Committees	• TAG & ICC meetings	600,000	300,000	300,000
• Update action plans, country needs/gaps and budgets for agencies supporting countries in DOTS expansion	• GDEP report # 3	170,000	70,000	100,000
• National inter-agency committees	• Established all countries	2,000,000	500,000	1,500,000
Objective 3: Monitoring and Reporting		**230,000**	**130,000**	**100,000**
• DOTS Expansion WG meeting in late 2003	• Meeting held	200,000	100,000	100,000
• DOTS Expansion report No. 4	• Report published	30,000	30,000	0
Objective 4: Advocacy		**200,000**	**0**	**200,000**
TOTAL YEAR 2003		**46,200,000**	**23,000,000**	**23,200,000**

Working Group on DOTS Expansion

2004 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Technical Assistance		**42,000,000**	**21,500,000**	**20,500,000**
• Capacity building and human resources development for DOTS implementation	• International training courses including training of consultants • Training material, coordination of training • In service training	24,000,000	12,000,000	12,000,000
• Direct NTP assistance, advisors, missions, and tools	• Medium-term plans including budget • DOTS coverage	18,000,000	9,500,000	8,500,000
Objective 2: Support and Coordination		**3,770,000**	**1,370,000**	**2,400,000**
• WG missions for evaluation of progress (2000-2003) in all endemic countries	• Evaluation report (see below) Reports of visits	1,000,000	500,000	500,000
• Regional evaluations, Advisory Groups and Inter-Agency Committees	• AG & ICC meetings	600,000	300,000	300,000
• Update country needs/gaps and budgets for agencies supporting countries in DOTS expansion	• GDEP report updated	170,000	70,000	100,000
• National inter-agency committees	• National ICC meetings report TB control evaluation	2,000,000	500,000	1,500,000
Objective 3: Monitoring and Reporting		**230,000**	**130,000**	**100,000**
• DOTS Expansion WG meeting in late 2004	• Meeting held	200,000	100,000	100,000
• DOTS Expansion report No. 5	• Report published	30,000	30,000	0
Objective 4: Advocacy		**200,000**	**0**	**200,000**
TOTAL YEAR 2004		**46,200,000**	**23,000,000**	**23,200,000**

Working Group on DOTS Expansion

2005 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Technical Assistance		**42,000,000**	**21,500,000**	**20,500,000**
• Capacity building and human resources development for DOTS implementation	• International training courses including training of consultants • Training material, coordination of training • In-service training	24,000,000	12,000,000	12,000,000
• Direct NTP assistance, advisors, missions, and tools	• Medium-term plans including budget • DOTS coverage	18,000,000	9,500,000	8,500,000
Objective 2: Support and Coordination		**3,770,000**	**1,370,000**	**2,400,000**
• Review of action plans for sustainability in all endemic countries	• Plans by December 2005	1,000,000	500,000	500,000
• Regional Advisory Groups and Inter-Agency Committees	• AG & ICC meetings	600,000	300,000	300,000
• Update country needs/gaps and budgets for supporting agencies	• GDEP report updated	170,000	70,000	100,000
• National inter-agency committees	• National ICC established in all countries	2,000,000	500,000	1,500,000
Objective 3: Monitoring and Reporting		**230,000**	**130,000**	**100,000**
• DOTS Expansion WG meeting in late 2005	• Meeting held	200,000	100,000	100,000
• DOTS Expansion report No. 6	• Report published	30,000	30,000	0
Objective 4: Advocacy		**200,000**	**0**	**200,000**
TOTAL YEAR 2005		**46,200,000**	**23,000,000**	**23,200,000**

Working Group on TB-HIV

Lead Agency: ***World Health Organization***
Chair: **Dr. *Gijs Elzinga, The Netherlands***

Summary 5-Year Work Plan

Objectives	Targets	Activities	Budget ($)
Objective 1: Develop effective new strategies to combat TB in HIV-infected people	• New technical framework to guide country strategies, endorsed by WHO & UNAIDS by end 2001 • Disseminate guidelines on phased implementation of TB & HIV programme collaborations (mid-2002)	• Develop framework • Model impact of interventions • Develop prioritised essential package • Develop and disseminate guidelines	**965,000**
Objective 2: Promote implementation and scale-up of control programmes responding to the deadly synergy of these diseases	• Initiate implementation of collaborative activities in 8 sub-Saharan sites (PIA-TB/HIV*), and expand to other high-burden countries by end 2004	• Establish pilot projects and coordinate project network	**10,520,000**
Objective 3: Promote global partnership for collaboration between TB- and HIV-control programmes	• Promote national and regional strategies for control of TB in high HIV-prevalence settings linked with DOTS expansion (end 2003) • National strategies adapted and scaled up in most high HIV-prevalence countries (end 2005)	• Promote international and national partnerships to maximize synergies in health service treatment of co-infected people	**645,000**
Objective 4: Advocate for increased resources	• Raise $10.25 million by end 2005	• Target advocacy and fundraising	**220,000**
TOTAL			**12,350,000**

** The phased implementation of TB/HIV activities (PIA-TB/HIV) is the name for the planned collaborative activities to control TB (and HIV) in high-burden countries. It is the successor to the WHO-coordinated ProTEST projects, which are ongoing and which have provided much of the experience on which PIA-TB/HIV is based.*

Working Group on TB-HIV

2001 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Develop and Adapt TB/HIV Strategy • Development of strategic framework for TB/HIV • Commence modelling impact of interventions to inform development of prioritised essential package • Produce revised TB/HIV estimates	• Draft finalised, 2001 • First draft, 2001 • Complete paper, 2001	**125,000**	**125,000**	**0**
Objective 2: Promote Implementation • Develop ProTEST project evaluation framework • Plan implementation of post-ProTEST activities (PIA-TB/HIV) • First draft of technical guidelines for establishment of PIA-TB/HIV projects (including a generic protocol) • Coordinate network of ProTEST pilot projects • Monitor existing projects in Africa • Plan development of training tools and education materials	• Completed 2001 • First workshop, Feb. 2002 • Concluded 2001 • Regional plan ready • Regional plan ready End 2001	**730,000**	**730,000**	**0**
Objective 3: Form Global Partnership • Hold 1st annual meeting of Global TB/HIV Working Group • Appoint Working Group Coordinator	• Met April 2001 • WG Coordinator appointed Oct 2001	**25,000**	**25,000**	**0**
Objective 4: Advocacy for Increased Resources • Advocacy for ProTEST projects	• Plan complete mid-2002	**20,000**	**20,000**	**0**
TOTAL YEAR 2001		**900,000**	**900,000**	**0**

Working Group on TB-HIV

2002 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Develop and Adapt TB/HIV Strategy		**290,000**	**260,000**	**30,000**
• Complete, develop consensus on, publish, and disseminate strategy, technical, and clinical guidelines	• By end 2002	80,000	80,000	0
• Adapt framework for different regions	• By end 2002	50,000	50,000	0
• Two meetings of scientific panel (guidelines on recurrence of TB among HIV+ patients and operational research)	• Draft by end 2002	60,000	30,000	30,000
• Complete modelling of, focus for, and impact of interventions to inform development of prioritised essential package	• By end 2002	100,000	100,000	0
• Publish new TB/HIV estimates (no cost)	• By mid 2002			
Objective 2: Promote Implementation		**1,390,000**	**1,005,000**	**385,000**
• Establish PIA-TB/HIV projects in four additional countries	• Implement mid-2003	1,000,000	665,000	335,000
• Coordinate network of PIA-TB/HIV projects	• Consultant visits 'Q4	200,000	200,000	0
• Monitor existing ProTEST projects	• Ongoing	40,000	40,000	0
• Completion of ProTEST project evaluation	• Report, end-2002	80,000	80,000	0
• WHO regional office support	• AFRO TB/HIV plan, end-2002	20,000	20,000	0
• Develop human resource plan	• End, 2002	50,000	0	50,000
Objective 3: Form Global Partnership		**155,000**	**55,000**	**100,000**
• Five virtual and one actual meeting for core group of Working Group	• As scheduled	30,000	30,000	0
• Hold 2nd annual meeting of Global TB/HIV Working Group	• As scheduled	75,000	25,000	50,000
• First meeting of inter-agency collaboration group	• As scheduled	50,000	0	50,000
Objective 4: Advocacy for Increased Resources	• $1.25 million raised	**50,000**	**0**	**50,000**
TOTAL YEAR 2002		**1,885,000**	**1,320,000**	**565,000**

Working Group on TB-HIV

2003 Annual Plan*

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Develop and Adapt TB/HIV Strategy		**230,000**	**0**	**230,000**
• Adaptation of framework and guidelines for different regions	• Adapted for 3 regions, early 2003	50,000	0	50,000
• Dissemination of guidelines		20,000	0	20,000
• Two meetings of scientific panel	• As scheduled	60,000	0	60,000
• Economic modelling to compare interventions	• Report by mid-2003	100,000	0	100,000
Objective 2: Promote Implementation		**2,800,000**	**0**	**2,800,000**
• Establish new PIA-TB/HIV projects	• 9 new projects by end 2003	1,000,000	0	1,000,000
• Technical support to existing PIA-TB/HIV projects	• Consult reports, end 2003	1,000,000	0	1,000,000
• Maintain and coordinate network of PIA-TB/HIV projects	• Report to WG 2003	250,000	0	250,000
• Monitor and evaluate country-level PIA-TB/HIV projects	• Mentors reports to WG 2003	250,000	0	250,000
• Support implementation of human resource development plan	• Training plan implemented, end 2003	200,000	0	200,000
• Report and publish results on country projects	• As scheduled	100,000	0	100,000
Objective 3: Form Global Partnership		**155,000**	**0**	**155,000**
• Five virtual and one actual meeting for core group of WG	• As scheduled	30,000	0	30,000
• Hold 3rd annual meeting of Global TB/HIV WG	• As scheduled	75,000	0	75,000
• 2nd meeting of TB/HIV interagency collaboration group	• As scheduled	50,000	0	50,000
• Coordinate with regional and national inter-agency coordination groups (no cost)	• TB/HIV integrated with DOTS expansion plans			
Objective 4: Advocacy for Increased Resources		**50,000**	**0**	**50,000**
• Advocacy for ProTEST projects	• Various ($2 million raised)			
TOTAL YEAR 2003		**3,235,000**	**0**	**3,235,000**

** Estimates as of January 2002. At least $1.3 million will likely be obtained from existing sources, but as yet there are no firm pledges.*

Working Group on TB-HIV

2004 Annual Plan*

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Develop and Adapt TB/HIV Strategy		**160,000**	**0**	**160,000**
• Two meetings of scientific panel	• As scheduled	60,000	0	60,000
• Further mathematical modelling for strategic decision-making	• Reports published	100,000	0	100,000
Objective 2: Promote Implementation		**2,800,000**	**0**	**2,800,000**
• Technical support to existing PIA-TB/HIV projects	• Project and consultant reports for each country, end 2004	2,000,000	0	2,000,000
• Maintain and coordinate network of PIA-TB/HIV projects		250,000	0	250,000
• Monitor and evaluate country-level PIA-TB/HIV projects		250,000	0	250,000
• Support implementation of human resource development plan	• Consultant and trainer reports end 2004	200,000	0	200,000
• Report preparation and publication of results	• 3 peer-reviewed publications	100,000	0	100,000
Objective 3: Form Global Partnership		**155,000**	**0**	**155,000**
• Five virtual and one actual meeting for core group of WG	• As scheduled	30,000	0	30,000
• Hold 4th annual meeting of Global TB/HIV WG	• As scheduled	75,000	0	75,000
• 3rd meeting of TB/HIV inter-agency collaboration group	• As scheduled	50,000	0	50,000
• Coordinate with regional and national inter-agency coordination groups	• Reports of these bodies			
Objective 4: Advocacy for Increased Resources	• $3 million raised	**50,000**	**0**	**50,000**
TOTAL YEAR 2004		**3,165,000**	**0**	**3,165,000**

** Estimates as of January 2002. At least $1.3 million will likely be obtained from existing sources, but as yet there are no firm pledges.*

Working Group on TB-HIV

2005 Annual Plan*

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Develop and Adapt TB/HIV Strategy		**160,000**	**0**	**160,000**
• Two meetings of scientific panel	• As activities	60,000		60,000
• Further mathematical modelling for strategic decision-making	• Reports for publication	100,000		100,000
Objective 2: Promote Implementation		**2,800,000**	**0**	**2,800,000**
• Technical support to existing PIA-TB/HIV projects	• Project & consultant	2,000,000	0	2,000,000
• Maintain & coordinate network of PIA-TB/HIV projects	reports for each country	250,000	0	250,000
• Monitor & evaluate country-level PIA-TB/HIV projects	end 2004	250,000	0	250,000
• Support implementation of human resource development plan		200,000	0	200,000
	• Consultant & trainer	100,000	0	100,000
• Report preparation and publication of results from countries	reports end 2004			
	• 3 peer-reviewed publications			
Objective 3: Form Global Partnership		**155,000**	**0**	**155,000**
• Five virtual and one actual meeting for core group of WG	• As scheduled	30,000	0	30,000
• Hold 4th annual meeting of Global TB/HIV Working Group	• As scheduled	75,000	0	75,000
• 3rd meeting of TB/HIV inter-agency collaboration group	• As scheduled	50,000	0	50,000
• Coordinate with regional and national inter-agency coordination groups	• Reports of these bodies			
Objective 4: Advocacy for Increased Resources	• $4 million raised	**50,000**	**0**	**50,000**
TOTAL YEAR 2005		**3,165,000**	**0**	**3,165,000**

** Estimates as of January 2002. At least $1.3 million will likely be obtained from existing sources, but as yet there are no firm pledges.*

Working Group on DOTS-Plus for MDR-TB

Lead Agency: ***World Health Organization***
Chair: ***Dr. Jim Yong Kim, Partners in Health***

Summary 5-Year Work Plan

Objectives	Targets	Activities	Budget $
• **Objective 1:** Initiate and support pilot projects, through partner organizations, for the diagnosis and treatment of MDR-TB	• Pilot project guidelines issued: 2000 • Continue to expand number of pilot projects at a rate of approximately 3-6 per year	• Six MDR-TB pilot projects underway • Nine new MDR-TB projects scheduled • Continue to revise and improve DOTS-Plus project guidelines • Provide ongoing technical advice on clinical issues of MDR-TB management	**7,800,000**
• **Objective 2:** Establish drug access system to provide and prevent misuse of high-quality, second-line drugs	• Prices reduced on many drugs • Two procurement mechanisms operating • GLC to meet 12 times p.a. on country applications, and to discuss operational activities	• Make recommendations for increasing access/lowering price of second-line drugs • Establish and monitor procurement mechanisms	**1,190,000**
• **Objective 3:** Coordinate and monitor implementation of DOTS-Plus pilots; assess data; and help produce policy recommendations	• Regular data collection and review of pilot projects at least once a year	• Pre-approval site visits to projects applying for GLC drugs • Monitoring visits for GLC-approved projects • Develop DOTS-Plus data clearinghouse • Coord. operational research studies from projects	**6,890,000**
• **Objective 4:** Advocacy and resource development for new DOTS-Plus projects	• Increase visibility of the GLC and the working group • Increased funding for projects	• Increase visibility of DOTS-Plus efforts • Work with funders to provide an evidence-based approach to drug-resistant TB	**600,000**
TOTAL			**16,480,000**

Working Group on DOTS-Plus for MDR-TB

2001 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Pilot Projects		**2,100,000**	**100,000**	**2,000,000**
• Establish three pilot projects ($200,000 per project)	Projects established (Philippines, Peru, Orel)	600,000	100,000	500,000
• Training sessions in clinical management	• 4 sessions held in HBCês	500,000	0	500,000
• Piloting of new diagnostic tools	• In-pilot projects	1,000,000	0	1,000,000
Objective 2: Drug Access System		**330,000**	**130,000**	**200,000**
• Technical assistance for GLC applications, and monitoring of projects	• Application training for 3 countries, and monitoring visits to 4 projects	200,000	100,000	100,000
• Evaluate drug-procurement process	• Procurement strategies developed	50,000	30,000	20,000
• Staff IDA for registration and procurement activities	• Drug prices down by over 90% • As placed	80,000	0	80,000
Objective 3: Monitoring and Policy Development		**1,650,000**	**200,000**	**1,450,000**
• Collect and analyse data	• Papers submitted on Peru programme	50,000	20,000	30,000
• Operational research	• Protocols implemented	1,500,000	150,000	1,350,000
• Annual meetings of working group	• Annual meeting held	100,000	30,000	70,000
• Preparation and publication of policy document				
Objective 4: Advocacy and Resource Development		**200,000**	**70,000**	**130,000**
• Advocacy for pilot projects	• Press releases and newsletters	100,000	20,000	80,000
• Advocacy for GLC	• Press releases and newsletters	100,000	50,000	50,000
TOTAL YEAR 2001		**4,280,000**	**500,000**	**3,780,000**

Working Group on DOTS-Plus for MDR-TB

2002 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Pilot Projects		**2,400,000**	**150,000**	**2,250,000**
• Establish three pilot projects ($200,000 each)	As established	600,000	100,000	500,000
• Training sessions in clinical management	• Hold sessions in 2 countries	500,000	0	500,000
• Piloting of new diagnostic tools	• In-pilot projects	1,000,000	0	1,000,000
• Support to ongoing pilot projects		300,000	50,000	250,000
Objective 2: Drug Access System		**330,000**	**130,000**	**200,000**
• Technical assistance for GLC applications, and monitoring of projects	• Training session at working group meeting and in-country training in 2 countries monitoring visits to 3 projects	200,000	100,000	100,000
• Evaluate drug-procurement process	• Report on drug-procurement progress	50,000	30,000	20,000
• Staff IDA registration and procurement	• As placed	80,000	0	80,000
Objective 3: Monitoring and Policy Development		**1,650,000**	**200,000**	**1,450,000**
• Collect and analyse data	• Establish data clearinghouse at WHO	50,000	20,000	30,000
• Operational research				
• Annual meetings of working group	• Protocols accepted and established	1,500,000	150,000	1,350,000
• Preparation and publication of policy document	• Annual meeting in Estonia	100,000	30,000	70,000
Objective 4: Advocacy and Resource Development		**200,000**	**70,000**	**130,000**
• Advocacy for pilot projects	• Press releases and newsletters	100,000	20,000	80,000
• Advocacy for GLC	• Press releases and newsletters	100,000	50,000	50,000
TOTAL YEAR 2002		**4,580,00**	**550,000**	**4,030,000**

Working Group on DOTS-Plus for MDR-TB

2003 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Pilot Projects		**1,800,000**	**50,000**	**1,750,000**
• Training sessions in clinical management	• Hold sessions in 2 countries	500,000	0	500,000
• Piloting of new diagnostic tools	• In-pilot projects	1,000,000	0	1,000,000
• Support to ongoing pilot projects		300,000	50,000	250,000
Objective 2: Drug Access System		**330,000**	**130,000**	**200,000**
• Technical assistance for GLC applications, and monitoring of projects	• Training session (at working group meeting); training in 2 countries. • Visits to 3 projects	200,000	100,000	100,000
• Evaluate drug procurement process	• Report on procurement progress	50,000	30,000	20,000
• Staff IDA registration and procurement	• As placed	80,000	0	80,000
Objective 3: Monitoring and Policy Development		**1,750,000**	**250,000**	**1,500,000**
• Collect and analyse data	• Establish clearinghouse at WHO	50,000	20,000	30,000
• Operational research	• Protocols accepted and established	1,500,000	150,000	1,350,000
• Annual meetings of working group	• As scheduled	100,000	30,000	70,000
• Preparation and publication of policy document		100,000	50,000	50,000
Objective 4: Advocacy and Resource Development		**100,000**	**50,000**	**50,000**
• Advocacy for GLC	• Press releases and newsletters	100,000	50,000	50,000
TOTAL YEAR 2003		**3,980,000**	**480,000**	**3,500,000**

Working Group on DOTS-Plus for MDR-TB

2004 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Pilot Projects		**1,500,000**	**0**	**1,500,000**
• Training sessions in clinical management	• Hold sessions in 2 countries and at working group meeting	500,000	0	500,000
• Piloting of new diagnostic tools	• In-pilot projects	1,000,000	0	1,000,000
Objective 2: Drug Access System		**200,000**	**100,000**	**100,000**
• Technical assistance for GLC applications, and monitoring of projects	• Training session (at working group meeting); training in 2 countries. • Visits to 3 projects	200,000	100,000	100,000
Objective 3: Monitoring and Policy Development		**1,750,000**	**240,000**	**1,510,000**
• Collect and analyse data		50,000	20,000	30,000
• Operational research	• Protocols accepted and established	1,500,000	150,000	1,350,000
• Annual meetings of working group		100,000	30,000	70,000
• Preparation and publication of policy document	• As scheduled	100,000	40,000	60,000
Objective 4: Advocacy and Resource Development		**100,000**	**50,000**	**50,000**
• Advocacy for GLC	• Press releases and newsletters	100,000	50,000	50,000
TOTAL YEAR 2004		**3,550,000**	**390,000**	**3,160,000**

Working Group on DOTS-Plus for MDR-TB

2005 Annual Plan

Activities	Indicators	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Pilot Projects		**0**	**0**	**0**
Objective 2: Drug Access System		**0**	**0**	**0**
Objective 3: Monitoring and Policy Development • Annual meetings of working group • Preparation and publication of policy document	 • As scheduled • As published	**90,000** 90,000	**30,000** 30,000	**60,000** 60,000
Objective 4: Advocacy and Resource Development		**0**	**0**	**0**
TOTAL YEAR 2005		**90,000**	**30,000**	**60,000**

Working Group on TB Diagnostics

Lead Agency: ***UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases***
Chair: ***Dr. Carlos Morel, TDR***

Summary 4-Year Work Plan

Objectives	Targets	Activities	4-Year Budget ($)
Objective 1: Facilitation To promote and facilitate the development, evaluation, and appropriate use of improved TB diagnostics to assist disease control in endemic settings, including: • Simpler, faster, or more sensitive case detection tools • Faster and less laborious drug susceptibility testing methods • More practical and more predictive latent infection detection tests	• At least 5 diagnostic candidates identified and evaluated in phase I/II trials by 2005 • Evidence base for best use of TB diagnostics (timing and target populations) for improved disease control developed by 2004 • Phase III trials of at least 1 case detection tool and at least 3 new drug susceptibility testing methods completed by 2005 • International system for evaluation of TB diagnostics in place by 2005 • Guidelines for use of new TB tests published by 2007	• Coordinating outputs of discovery research and facilitating commercial uptake • Multi-step facilitation of commercial R&D for TB diagnostics relevant for DECs • Providing reagents and technical support to enhance the quality of diagnostics being developed • Developing diagnostics trial capacity and coordinating evaluation of new tools • Streamlining and strengthening the diagnostics regulatory process • Advocacy and establishment of an information resource centre • Planning and coordination by working group and ad hoc task forces	**25,855,000**
Objective 2: Advocacy and Information			**600,000**
Objective 3: Coordinate Activities			**600,000**
TOTAL			**27,055,000**

Working Group on TB Diagnostics

2002 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1:Facilitation	**6,780,000**	**2,130,000**	**4,650,000**
• Develop consortium to evaluate sputum processing methods	60,000	30,000	30,000
• Develop antigen discovery and evaluation programme	400,000	150,000	250,000
• Maintain bank of clinical reference materials for case detection tool R&D	450,000	250,000	200,000
• Perform market analysis, global use portrait, and economic analysis	800,000	150,000	650,000
• Coordinate phase III trials of DST methods	750,000	250,000	500,000
• Coordinate laboratory evaluation of case detection tools	250,000	100,00	150,000
• Coordinate programme to strengthen DEC laboratory capacity to evaluate and use new diagnostics in a network of trial sites	1,600,000	350,000	1,250,000
• Develop MTB strain bank to facilitate R&D and testing of DST methods	550,000	300,000	250,000
• Model impact of new case detection tools	60,000	20,000	40,000
• Coordinate multinational measure of TB diagnostic delay and dropout	250,000	150,000	100,000
• Coordinate phase III trials of case detection tool	950,000	300,000	650,000
• Regulatory harmonization workshops	400,000	50,000	350,000
• Develop strategy for global evaluation system for TB diagnostics marketed in developing countries	60,000	10,000	50,000
• Develop a comprehensive advocacy and information strategy for new TB diagnostics	200,000	20,000	180,000
Objective 2: Advocacy and Information	**150,000**	**20,000**	**130,000**
Objective 3: Coordination • Annual working group meeting • Ad hoc meetings of regional task forces	**150,000**	**0**	**150,000**
TOTAL YEAR 2002	**7,080,000**	**2,150,000**	**4,930,000**

Working Group on TB Diagnostics

2003 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**6,210,000**	**1,300,000**	**4,910,000**
• Support consortium to evaluate sputum processing methods	60,000	0	60,000
• Develop antigen discovery and evaluation programme	300,000	100,000	200,000
• Maintain bank of clinical reference materials	400,000	100,000	300,000
• Complete market analysis, global use portrait, and economic analysis	800,000	150,000	650,000
• Coordinate phase III trials of DST methods	750,000	250,000	500,000
• Coordinate laboratory evaluation of case detection tools	200,000	100,000	100,000
• Coordinate programme to strengthen DEC laboratory capacity to evaluate and use new diagnostics in a network of trial sites	1,600,000	0	1,600,000
• Maintain MTB strain bank to facilitate R&D and testing of DST methods	250,000	100,000	150,000
• Model impact of new case detection tools	60,000	20,000	40,000
• Coordinate multinational measure of TB diagnostic delay and dropout	150,000	50,000	100,000
• Coordinate phase III trials of case detection tools	950,000	300,000	650,000
• Regulatory harmonization workshops	400,000	50,000	350,000
• Develop strategy for global evaluation system for TB diagnostics marketed in developing countries	150,000	40,000	110,000
• Complete a comprehensive advocacy and information strategy for new TB diagnostics	100,000	20,000	80,000
• Model early detection impaction disease transmission	40,000	20,000	20,000
Objective 2: Advocacy and Information	**150,000**	**20,000**	**130,000**
Objective 3: Coordination	**150,000**	**0**	**150,000**
• Annual working group meeting			
• Ad hoc meetings of regional task forces			
TOTAL YEAR 2003	**6,510,000**	**1,320,000**	**5,190,000**

Working Group on TB Diagnostics

2004 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**6,140,000**	**1,090,000**	**5,050,000**
• Maintain consortium to evaluate sputum processing methods	150,000	0	150,000
• Complete antigen discovery and evaluation programme	400,000	0	400,000
• Maintain bank of clinical reference materials	450,000	150,000	300,000
• Circulate market analysis, global use portrait, and economic analysis	200,000	0	200,000
• Coordinate phase III trials of DST methods	750,000	250,000	500,000
• Coordinate laboratory evaluation of case detection tools	250,000	100,000	150,000
• Coordinate programme to strengthen DEC laboratory capacity to evaluate and use new diagnostics in a network of trial sites	800,000	0	800,000
• Distribute MTB strain bank to facilitate R&D and testing of DST methods	250,000	0	250,000
• Coordinate phase III trials of case detection tools	1,000,000	300,000	700,000
• Regulatory harmonization workshops	300,000	50,000	250,000
• Implement strategy for global evaluation system for TB diagnostics marketed in developing countries	350,000	100,000	250,000
• Develop expert advisor team for diagnostics assistants to NTP	600,000	0	600,000
• Collect field data to determine kinetics of community TB transmission	600,000	120,000	480,000
• Model early detection impaction disease transmission	40,000	20,000	20,000
Objective 2: Advocacy and Information	**150,000**	**20,000**	**130,000**
Objective 3: Coordination	**150,000**	**0**	**150,000**
• Annual working group meeting			
• Ad hoc meetings of regional task forces			
TOTAL YEAR 2004	**6,440,000**	**1,110,000**	**5,330,000**

Working Group on TB Diagnostics

2005 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**6,725,000**	**1,440,000**	**5,285,000**
• Support technology transfer of improved diagnostics	700,000	130,000	570,000
• Maintain bank of clinical reference materials	250,000	50,000	200,000
• Coordinate phase III trials of DST methods	350,000	150,000	200,000
• Coordinate evaluation of latency surrogates	400,000	100,000	300,000
• Coordinate programme to strengthen DEC laboratory capacity to evaluate and use new diagnostics in a network of trial sites	800,000	0	800,000
• Distribute MTB strain bank to facilitate R&D and testing of DST methods	150,000	0	150,000
• Model impact of new case detection tools on transmission	60,000	20,000	40,000
• Coordinate phase IV trials of case detection tools	1,350,000	200,000	1,150,000
• Implement strategy for global evaluation system for TB diagnostics marketed in developing countries	750,000	100,000	650,000
• Model early detection impaction disease transmission	40,000	20,000	20,000
• Diagnostic trial support programme	300,000	200,000	100,000
• Develop usage guidelines for new diagnostics	75,000	50,000	25,000
• Develop expert advisor team for diagnostics assistants to NTP	600,000	200,000	400,000
• Collect field data to determine kinetics of community TB transmission	900,000	220,000	680,000
Objective 2: Advocacy and Information	**150,000**	**20,000**	**130,000**
Objective 3: Coordination	**150,000**	**0**	**150,000**
• Annual working group meeting			
• Ad hoc meetings of the regional task forces			
TOTAL YEAR 2005	**7,025,000**	**1,460,000**	**5,565,000**

Working Group on TB Drug Development

Lead Agency: ***Global Alliance for TB Development***
Chair: ***Dr. María Freire, Global Alliance***

Summary 4-Year Work Plan

Objectives	Targets	Activities	Budget ($)
Objective 1: Develop new drug(s) to: • Shorten and/or simplify the treatment of TB disease • Develop more effective treatment(s) for MDR-TB • Develop more effective treatment(s) of latent TB infection.	• Have at least 5 drug candidates through preclinical trials by 2005 • Have at least 3 drugs through phase I and II by 2007 • Have 2 drugs in phase III by 2010 • Have at least one new drug registered by 2010	• Map activities in TB Drugs R&D: establish and update drug database • Establish partnership with industry • Undertake studies to define surrogate markers • Develop High Endemic Countries Network for clinical trials • Promote introduction of surrogate markers in regulatory package	**27,300,000**
Objective 2: Advocacy and Information		• Advocacy for TB Drugs R&D	**2,000,000**
Objective 3: Coordination: Annual working group meeting		• Working group activities	**400,000**
TOTAL			**29,700,000**

Working Group on TB Drug Development

2002 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation /Enabling the Environment	**7,200,000**	**1,550,000**	**5,650,000**
• Map activities in TB drug R&D: establish and update drug data base	500,000	150,000	350,000
• Establish partnership with industry	200,000	100,000	100,000
• Undertake studies to define surrogate markers for clinical activity	3,000,000	350,000	2,650,000
• Develop HEC clinical trials network and strengthen laboratory capacity	3,000,000	700,000	2,300,000
• Promote introduction of surrogate markers within the regulatory harmonization process	500,000	250,000	250,000
Objective 2: Advocacy and Information	**500,000**	**250,000**	**250,000**
Objective 3: Coordination: Annual working group meeting	**100,000**	**0**	**100,000**
TOTAL YEAR 2002	**7,800,000**	**1,800,000**	**6,000,000**

Working Group on TB Drug Development

2003 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 3: Facilitation /Enabling the Environment	**7,200,000**	**1,550,000**	**5,650,000**
• Map activities in TB drug R&D: establish and update drug data base	500,000	150,000	350,000
• Establish partnership with industry	200,000	100,000	100,000
• Undertake studies to define surrogate markers for clinical activity	3,000,000	350,000	2,650,000
• Develop HEC clinical trials network and strengthen laboratory capacity	3,000,000	700,000	2,300,000
• Promote introduction of surrogate markers within the regulatory harmonization process	500,000	250,000	250,000
Objective 2: Advocacy and Information	**500,000**	**250,000**	**250,000**
Objective 3: Coordination: Annual working group meeting	**100,000**	**0**	**100,000**
TOTAL YEAR 2003	**7,800,000**	**1,800,000**	**6,000,000**

Working Group on TB Drug Development

2004 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation /Enabling the Environment	**6,700,000**	**1,300,000**	**5,400,000**
• Map activities in TB drug R&D: establish and update drug data base	500,000	150,000	350,000
• Establish partnership with industry	200,000	100,000	100,000
• Undertake studies to define surrogate markers for clinical activity	3,000,000	350,000	2,650,000
• Develop HEC clinical trials network and strengthen laboratory capacity	3,000,000	700,000	2,300,000
Objective 2: Advocacy and Information	**500,000**	**250,000**	**250,000**
Objective 3: Coordination: Annual working group meeting	**100,000**	**0**	**100,000**
TOTAL YEAR 2004	**7,300,000**	**1,550,000**	**5,750,000**

Working Group on TB Drug Development

2005 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation /Enabling the Environment	**6,200,000**	**500,000**	**5,700,000**
• Establish partnership with industry	200,000	0	200,000
• Undertake studies to define surrogate markers for clinical activity	3,000,000	0	3,000,000
• Develop HEC clinical trials network and strengthen laboratory capacity	3,000,000	500,000	2,500,000
Objective 2: Advocacy and Information	**500,000**	**250,000**	**250,000**
Objective 3: Coordination: Annual working group meeting	**100,000**	**0**	**100,000**
TOTAL YEAR 2005	**6,800,000**	**750,000**	**6,050,000**

Working Group on TB Vaccine Development

Lead Agency: ***World Health Organization/TDR***
Chair: ***Dr. Ann Ginsberg, US-NIH/NIAID***

Summary 4-Year Work Plan

Objectives	Targets	Activities	Budget ($)

Objective 1: Facilitation	• An improved TB vaccine to:
	  • provide long-lasting primary protection
	  • prevent disease in individuals already infected
	• Stimulate and support the study of 5 –10 vaccine candidates in phase I/II trials by 2005.
	• Launch phase III efficacy trials of at least one TB vaccine candidate by 2007
		• Pre-clinical evaluation of vaccine candidates
		• Preparation of clinical evaluation of candidate vaccines and correlates of protection
		• Validation and distribution of standardized reagents
		• Coordination of fast-track transition of vaccine candidates from academia to industry
			3,400,000

Objective 2: Advocacy and Information		• Advocacy and establishment of an information resource centre	**700,000**
Objective 3: Coordinate Activities		• Planning and coordination by working group and ad hoc task forces	**400,000**
TOTAL			**4,500,000**

Working Group on TB Vaccine Development

2002 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**850,000**	**250,000**	**600,000**
• Establish a primate TB vaccine testing network	400,000	100,000	300,000
• Identify potential clinical phase III testing sites	250,000	100,000	150,000
• Vaccino-economic analysis and cost-effectiveness modelling	50,000	0	50,000
• Coordinate/build international consensus on standardized reference reagents. Support development and distribution.	150,000	50,000	100,000
Objective 2: Advocacy and Information	**200,000**	**50,000**	**150,000**
• Develop a comprehensive advocacy and information strategy for new TB vaccines			
Objective 3: Coordination of Activities	**100,000**	**50,000**	**50,000**
• Annual meeting of the working group			
• Ad hoc meetings of preclinical and clinical task forces			
TOTAL YEAR 2002	**1,150,000**	**350,000**	**800,000**

Working Group on TB Vaccine Development

2003 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**1,050,000**	**200,000**	**850,000**
• Establish a primate TB vaccine testing network	100,000	50,000	50,000
• Validate primate testing facilities	300,000	50,000	250,000
• Establish network of potential phase III clinical testing sites	100,000	50,000	50,000
• Build capacity for clinical testing of vaccine candidates	200,000	0	200,000
• Develop Points-to-Consider document for clinical trial protocols	50,000	0	50,000
• Coordinate/build international consensus on standardized reference reagents.	150,000	50,000	100,000
• Identify available GMP manufacturing capacity for pilot lots of vaccine candidates	50,000	0	50,000
• Coordinate/facilitate transition of potential candidates from academia to private sector, as appropriate and necessary	100,000	0	100,000
Objective 2: Advocacy and Information	**150,000**	**50,000**	**100,000**
• Develop a comprehensive advocacy and information strategy for new TB vaccines			
Objective 3: Coordination of Activities	**100,000**	**50,000**	**50,000**
• Annual meeting of the working group			
• Ad hoc meetings of task forces			
TOTAL YEAR 2003	**1,300,000**	**300,000**	**1,000,000**

Working Group on TB Vaccine Development

2004 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**750,000**	**100,000**	**650,000**
• Validate primate testing facilities	100,000	50,000	50,000
• Build capacity for clinical testing of vaccine candidates	300,000	50,000	250,000
• Develop adult immunization strategy	150,000	0	150,000
• Coordinate fast-track transition of vaccine candidates from academia to industry	150,000	0	150,000
• Identify and support development of needed GMP manufacturing capacity	50,000	0	50,000
Objective 2: Advocacy and Information	**150,000**	**50,000**	**100,000**
• Develop a comprehensive advocacy and information strategy for new TB vaccines			
Objective 3: Coordination of Activities	**100,000**	**50,000**	**50,000**
• Annual meeting of the working group			
• Ad hoc meetings of task forces			
TOTAL YEAR 2004	**1,000,000**	**200,000**	**800,000**

Working Group on TB Vaccine Development

2005 Annual Plan

Activities	Budget ($)	Funding ($)	Resource Gap ($)
Objective 1: Facilitation	**750,000**	**100,000**	**650,000**
• Capacity building for clinical testing of vaccine candidates	300,000	50,000	250,000
• Coordination of fast-track transition of vaccine candidates from the academic/industrial interface	150,000	0	150,000
• Building awareness among national TB control staff	100,000	0	100,000
• Building in-country infrastructure for monitoring and ethical review of clinical trials	200,000	50,000	150,000
Objective 2: Advocacy and information	**200,000**	**50,000**	**150,000**
• Develop a comprehensive advocacy and information strategy for new TB vaccines			
Objective 3: Coordination of Activities	**100,000**	**50,000**	**50,000**
• Annual meeting of the working group			
• Ad hoc meetings of task forces			
TOTAL YEAR 2005	**1,050,000**	**200,000**	**850,000**

ANNEX 3
COUNTRIES INCLUDED IN THE GPSTB ANALYSIS

High-burden and low- and lower-middle income countries(1)

Clusters	All low- and lower-middle income countries, excluding 22 High-Burden Countries		22 High-Burden Countries
Sub-Saharan Africa	45	Angola, Benin, Botswana (2), Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo, CÙte d'Ivoire, Djibouti, Eritrea, Gambia, Ghana, Guinea, Guinea-Bissau, Guinea (Equatorial), Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique (b), Namibia, Niger, Rwanda, Sao Tome & Principe, Senegal, Sierra Leone, Somalia, Sudan, Swaziland, Togo, Zambia	Congo DR, Ethiopia, Kenya, Nigeria, Uganda, South Africa, Tanzania (United Rep. of), Zimbabwe
Middle East & Northern Africa	12	Algeria, Egypt, Gaza & West Bank, Iran, Iraq, Jordan, Libya, Morocco, Syria, Tunisia, Turkey, Yemen	
Eastern Europe and the Newly Independent States	19	Albania, Armenia, Azerbaijan, Belarus, Bosnia-Herzegovina, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Macedonia, Moldova, Romania, Tajikistan, Turkmenistan, Ukraine, Uzbekistan	Russian Federation
Latin America & the Caribbean	19	Belize, Bolivia, Colombia, Costa Rica, Cuba, El Salvador, Ecquador, Guatemala, Guyana, Haiti, Honduras, Jamaica, Nicaragua, Paraguay, Dominican Republic, St. Vincent & Grenadines, Suriname	Brazil, Peru (3)
Asia	19	Bhutan, Korea (DPRK), Laos, Maldives, Mongolia, Nepal, Papua New Guinea, Sri Lanka	Afghanistan, Bangladesh, Cambodia, China, India, Indonesia, Myanmar, Pakistan, Philippines, Thailand, Viet-Nam
Total	**114**	**92**	**22**

(1) Countries are grouped as shown only for the purpose of the GPSTB economic analysis.

(2) Botswana had a GNP/capita of $3,240 per year in 1999. However, it was included in the present evaluation given the very high burden of TB in the country (the highest incidence rate in the world as of 2000 with approximately 7% of its population being dually infected by MTB and HIV).

(3) Mozambique joined the 22 HBC list in 2001, replacing Peru. However, cost estimates used for the GPSTB are based on the list for the year 2000, which included Peru but not Mozambique.

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1 Cauvin HE. Zimbabwe's sad lack: Land to bury AIDS victims. *The New York Times*. March 1, 2000: A4.

2 UNAIDS. Epidemiological Fact Sheet on HIV/AIDS and Sexually Transmitted Infections, 2000 Update—Zimbabwe. 2000.

3 UNAIDS. Epidemiological Fact Sheet on HIV/AIDS and Sexually Transmitted Infections, 2000 Update—Zimbabwe. 2000; World Health Organization. *Anti-tuberculosis drug resistance in the world: the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 1994–1997*. Geneva: World Health Organization, 1997.

4 World Health Organization. *World Health Report. Health Systems: Improving Performance.* Geneva: World Health Organization, 2000; World Health Organization. Online Statistical Index. Accessed on: February 7, 2001. Internet communication at: http://www.nt.who.int/whosis/statistics/menu.cfm?path=statistics,basic&language=english.

5 Kenyon TA, Valway SE, Ihle WW, et al. Transmission of multidrug-resistant *Mycobacterium tuberculosis during a long airplane flight. N Engl J Med.* 1996;334:933–8.

6 Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant *Mycobacterium tuberculosis* during a long airplane flight. *N Engl J Med*. 1996;334:933–8.

7 World Health Organization. *Anti-tuberculosis drug resistance in the world: the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 1994–1997*. Geneva: World Health Organization, 1997; Zimmermann, T. Fighting TB: a second chance to do it right. *US News and World Report.* March 31, 1997.

8 Pablos-Méndez A, Raviglione MC, Laszlo A, et al. Global surveillance for antituberculosis-drug resistance, 1994–1997. World Health Organization–International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. *N Engl J Med.* 1998;338:1641–9.

9 Cave AJE. The evidence for the incidence of tuberculosis in ancient Egypt. British Journal of Tuberculosis. 1939;33:142.

10 Dye C; Scheele S; Dolin P; Pathania V, and Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. *JAMA*. 1999; 282(7):677–86; World Health Organization. *Global Tuberculosis Control: WHO Report 1999*. Geneva: World Health Organization, 1999.

11 Bloom BR, Murray CJ. Tuberculosis: commentary on a reemergent killer. *Science*. 1992;257:1055–64; Dolin PJ, Raviglione MC, Kochi A. Global tuberculosis incidence and mortality during 1990–2000. *Bull World Health Organ*. 1994;72:213–20; Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. *JAMA*. 1999;282:677–86; Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet*. 1997;349:1498–504; Raviglione MC, Snider DE Jr, Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. *JAMA*. 1995;273:220–6; World Health Organization. *Tuberculosis control: the DOTS strategy: an annotated bibliography compiled by the Global Tuberculosis Programme and the Regional Office for South-East Asia*. Geneva: World Health Organization, 1997.

12 World Health Organization. *Global Tuberculosis Control: WHO Report 2001*. Geneva: World Health Organization, 2001.

13 World Health Organization. *Global Tuberculosis Control: WHO Report 2001*. Geneva: World Health Organization, 2001.

14 Raviglione MC, Dye C, Schmidt S, Kochi A. Assessment of worldwide tuberculosis control. WHO Global Surveillance and Monitoring Project. *Lancet*. 1997;350:624–9; World Health Organization. *Tuberculosis and Sustainable Development: Report from the Ministerial Conference in Amsterdam*. Geneva: World Health Organization, 2000. WHO/CDS/STB/2000.6.

15 Dye C, Garnett GP, Sleeman K, Williams BG. Prospects for worldwide tuberculosis control under the WHO DOTS strategy. Directly observed short-course therapy. *Lancet*. 1998;352:1886-91; Murray CJL; Styblo K, and Rouillon A. Tuberculosis. In: Jamison DT, World Bank; *Disease Control Priorities in Developing Countries*. New York, N.Y.: Oxford University Press (published for the World Bank), 1993.

16 Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet*. 1997;349:1498–504.

17 de Jonghe E, Murray CJ, Chum HJ, et al. Cost-effectiveness of chemotherapy for sputum smear-positive pulmonary tuberculosis in Malawi, Mozambique and Tanzania. *Int J Health Plann Manage*. 1994;9:151–81; Jha P, Bangoura O, Ranson K. The cost-effectiveness of forty health interventions in Guinea. Health Policy Plan. 1998;13:249–62; World Bank. *World Development Report: Investing in Health.* Washington: World Bank, 1993.

18 Kochi A. Tuberculosis control—is DOTS the health breakthrough of the 1990s? *World Health Forum*. 1997;18:225–32; discussion 233–47.

19 World Health Organization. Global Tuberculosis Control: Surveillance, Planning and Financing. WHO Report 2002. Geneva, Switzerland, WHO/CDS/TB/2002.295.

20 Raviglione MC, Dye C, Schmidt S, Kochi A. Assessment of worldwide tuberculosis control.

21 Murray CJ, Salomon JA. Modeling the impact of global tuberculosis control strategies. *Proc Natl Acad Sci U S A*. 1998;95:13881–6.

22 Raviglione MC; Snider DE, and Kochi A. Global epidemiology of tuberculosis: morbidity and mortality of a worldwide epidemic. *JAMA*. 1995; 273(3):220–226.

23 González E, Armas L, Alonso A. Tuberculosis in the Republic of Cuba: its possible elimination. *Tuber Lung Dis*. 1994;75:188–94; Henderson DA. The challenge of eradication: lessons from past eradication campaigns. *Int J Tuberc Lung Dis*. 1998;2:S4–8; Kok-Jensen A. [When can tuberculosis be eradicated in Denmark?]. *Ugeskr Laeger.* 1995; 157(3):273–9; Ohmori M. [Estimating the year of eradication of tuberculosis in Japan]. *Kekkaku*. 1991; 66(12):819–28.

[24]Bloom BR, Murray CJ. Tuberculosis: commentary on a reemergent killer. *Science*. 1992;257:1055–64; Fatkenheuer G, Taelman H, Lepage P, et al. The return of tuberculosis. *Diagn Microbiol Infect Dis*. 1999;34:139–46; Nolan CM. Multidrug-resistant tuberculosis in the USA: the end of the beginning. *Tuber Lung Dis*. 1996;77:293–4; Nolan CM. Nosocomial multidrug-resistant tuberculosis—global spread of the third epidemic. *J Infect Dis.* 1997;176:748–51; Raviglione MC, Rieder HL, Styblo K, et al. Tuberculosis trends in eastern Europe and the former USSR. Tuber Lung Dis. 1994;75:400–16.

[25]Griffith DE. The United States and worldwide tuberculosis control: a second chance for Prince Prospero. *Chest*. 1998;113:1434–6.

[26]World Health Organization. *Economic Impacts of Tuberculosis.* Geneva: World Health Organization, 2000.

[27]Kamolratanakul P, Sawert H, Kongsin S, et al. Economic impact of tuberculosis at the household level. *Int J Tuberc Lung Dis*. 1999;3:596–602.

[28]Saunderson PR. An economic evaluation of alternative programme designs for tuberculosis control in rural Uganda. *Soc Sci Med*. 1995;40:1203–12.

[29]World Health Organization. *Tuberculosis and Sustainable Development: Report from the Ministerial Conference in Amsterdam*. Geneva: World Health Organization, 2000. WHO/CDS/STB/2000.6.

[30]Devi S, Ganapathy S, Sivasubramanian, MR, et al. *Behaviour pattern of chest symptomatics in urban and rural population*. Report submitted to WHO Regional Office for South-East Asia, n.d; Pathania V, Almeida J, and Kochi A. *TB patients and private for-profit health care providers in India.* TB Research No. 1. Geneva: The Global TB Programme, World Health Organization, 1997. WHO/TB/97.223.

[31]Murray CJL and Lopez AD. *Global health statistics: a compendium of incidence, prevalence and mortality estimates for over 200 conditions.* Cambridge: Harvard University Press, 1996; World Bank. *World Development Report: Investing in Health.* Washington: World Bank, 1993.

[32]Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. *Int J Tuberc Lung Dis.* 1998;2:96–104; Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. *Tuber Lung Dis.* 1996;77:391-400; Murray CJ. Social, economic and operational research on tuberculosis: recent studies and some priority questions. *Bull Int Union Tuberc Lung Dis.* 1991;66:149–56.

[33]Rajeswari R, Balasubramanian R, Muniyandi M et al. Socio-economic impact of tuberculosis on patients and family in India. *Int J Tuberc Lung Dis.* 1999;3:869–77.

[34]Pablos-Méndez A, Raviglione MC, Laszlo A, et al. Global surveillance for antituberculosis-drug resistance, 1994–1997. World Health Organization—International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. *N Engl J Med.* 1998;338:1641–9; *World Health Organization. Anti-tuberculosis drug resistance in the world: the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 1994–1997*. Geneva: World Health Organization, 1997.

[35]Dye C, Espinal M, Watt C, et al. *Worldwide incidence of multidrug-resistant tuberculosis*, unpublished; Espinal MA, Laszlo A, Simonsen L, et al. Global trends in resistance to antituberculosis drugs. World Health Organization—International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. *N Engl J Med.* 2001;344:1294–303; Mercedes Becerra (personal communication); World Health Organization, International Union Against Tuberculosis and Lung Diseases. *Anti-tuberculosis Drug Resistance in the World, Report n°2 Prevalence and trends. WHO–IUATLD Global project on anti-tuberculosis drug resistance surveillance.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000; Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis.* Boston: Harvard University and Open Society Institute, 1999.

[36]World Health Organization. *Anti-tuberculosis drug resistance in the world: the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 1994–1997.* Geneva: World Health Organization, 1997.

[37]Espinal MA, Kim SJ, Suárez PG, et al. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. *JAMA.* 2000;283:2537–45.

[38]Espinal MA, Kim SJ, Suárez PG, et al. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. JAMA. 2000;283:2537–45; Iseman MD. MDR-TB and the developing world—a problem no longer to be ignored: the WHO announces 'DOTS Plus' strategy. *Int J Tuberc Lung Dis.* 1998;2:867; World Health Organization. *Coordination of DOTS-Plus pilot projects for the management of MDR-TB*. Geneva: World Health Organization, 1999.

[39]Iseman MD, Cohn DL, Sbarbaro JA. Directly observed treatment of tuberculosis. We can't afford not to try it. *N Engl J Med.* 1993;328:576–8; Farmer PE; Bayona J; Becerra M; Kim JY, and Shin S. Reducing transmission through community-based treatment of multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 1998; 2(11 Suppl. 1):S190.

[40]Iseman MD. Tailoring a time-bomb. Inadvertent genetic engineering. *Am Rev Respir Dis.* 1985;132:735–6.

[41]Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis*. Boston: Harvard University and Open Society Institute, 1999.

[42]Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis*. Boston: Harvard University and Open Society Institute, 1999.

[43]Steenland K, Levine AJ, Sieber K, Schulte P, Aziz D. Incidence of tuberculosis infection among New York State prison employees. *Am J Public Health*. 1997;87:2012–4; Ikeda RM, Birkhead GS, DiFerdinando GT Jr, et al. Nosocomial tuberculosis: an outbreak of a strain resistant to seven drugs. *Infect Control Hosp Epidemiol.* 1995;16:152–9; Kimerling ME, Kluge H, Vezhnina N, et al. Inadequacy of the current WHO re-treatment regimen in a central Siberian prison: treatment failure and MDR-TB. *Int J Tuberc Lung Dis.* 1999;3:451–3; Valway SE, Richards SB, Kovacovich J, Greifinger RB, Crawford JT, Dooley SW. Outbreak of multi-drug-resistant tuberculosis in a New York State prison, 1991. *Am J Epidemiol.* 1994;140:113–22.

[44]Amnesty International. *Annual Report 1999: Russian Federation.* London: Amnesty International, 1999. Internet communication at: http://www.amnesty.org/ailib/aireport/ar99/eur46.htm.

[45]Walmsley, Roy. *World Prison Population List.* Home Office Research, Development and Statistics Directorate: 1999. Internet communication at: http://www.homeoffice.gov.uk/rds/pdfs/r88.pdf.

[46]Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis.* Boston: Harvard University and Open Society Institute, 1999.

[47] Curtis AB, Ridzon R, Novick LF, et al. Analysis of *Mycobacterium tuberculosis* transmission patterns in a homeless shelter outbreak. *Int J Tuberc Lung Dis.* 2000;4:308–13.

[48] Barclay DM 3rd, Richardson JP, Fredman L. Tuberculosis in the homeless. *Arch Fam Med.* 1995;4:541–6.

[49] Pavlovic M, Simic D, Krstic-Buric M, et al. Wartime migration and the incidence of tuberculosis in the Zagreb region, Croatia. *Eur Respir J.* 1998;12:1380–3; Houston S. Tuberculosis in refugees and displaced persons. *Int J Tuberc Lung Dis.* 1998;2:S94–7; Gibson N, Boillot F, Jalloh H. The cost of tuberculosis to patients in Sierra Leone's war zone Int J Tuberc Lung Dis. 1998;2:726–31.

[50] Kenyon TA; Valway SE; Ihle WW; et al. Transmission of multidrug-resistant *Mycobacterium tuberculosis* during a long airplane flight. *N Engl J Med.* 1996; 334(15):933–938.

[51] Agerton TB, Valway SE, Blinkhorn RJ, et al. Spread of strain W, a highly drug-resistant strain of *Mycobacterium tuberculosis*, across the United States. *Clin Infect Dis.* 1999;29:85–92; discussion 93–5; Bifani PJ, Plikaytis BB, Kapur V, et al. Origin and interstate spread of a New York City multidrug-resistant *Mycobacterium tuberculosis* clone family. *JAMA*. 1996;275:452–7; Casper C, Singh SP, Rave S, et al. The transcontinental transmission of tuberculosis: A molecular epidemiological assessment. *Am J Public Health*. 1996;86:551–3; Codina G, Vidal R, Martin-Casabona N, et al. Multidrug-resistant tuberculosis caused by 'W'-related strains in three immunocompetent foreign-born patients. *Int J Tuberc Lung Dis.* 1999;3:82–4; Kreiswirth, 1999. (Personal communication).

[52] Farmer, P. Social inequalities and emerging infectious diseases. *Emerg Infect Dis.* 1996 Oct-1996 Dec 31; 2(4):259–69.
International Chamber of Commerce. (1997). World business calls globalization a powerful force for economic progress. Press Release. 18 June 1997.

[53] International Chamber of Commerce. (1997). World business calls globalization a powerful force for economic progress. Press Release. 18 June 1997

CHAPTER 2

[1] Dye C, Scheeles S, Dolin P, Pathania V, Raviglione MC. Global burden of tuberculosis: Estimated incidence, prevalence, and mortality by country. *JAMA*, 1999; 282, 677-686

[2] Dye, C., Fengzeng, Z., Scheele, S., and Williams, B. (2000) Evaluating the impact of tuberculosis control: number of deaths prevented by short-course chemotherapy in China. *International Journal of Epidemiology*, 29(3), 558–64.

[3] World Health Organization. *Global Tuberculosis Control. WHO Report 2001*. Geneva: World Health Organization, 2001. WHO/CDS/TB/2001.287.

[4] Results of directly observed short-course chemotherapy in 112,842 Chinese patients with smear-positive tuberculosis. China Tuberculosis Control Collaboration. *Lancet*. 1996;347:358–62.

[5] Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. *N Engl J Med.* 1994;330:1179–84.

[6] Farmer P, Leandre F, Mukherjee JS, et al. Community-based approaches to HIV treatment in resource-poor settings. *Lancet.* 2001;358:404–9.

[7] World Health Organization. 105th *Session of the Executive Board of the World Health Organisation*. *Stop TB Initiative. Report by the Director General.* Geneva: World Health Organization, 1999. Internet communication at: http://www.stoptb.org/material/dgebreportstoptb.

[8] Results of directly observed short-course chemotherapy in 112,842 Chinese patients with smear-positive tuberculosis. China Tuberculosis Control Collaboration. *Lancet*. 1996;347:358–62.

[9] Khatri GR, Frieden TR. The status and prospects of tuberculosis control in India. *Int J Tuberc Lung Dis.* 2000;4:193–200.

[10] World Health Organization. Global Tuberculosis Control. *WHO Report 2000*. Geneva: World Health Organization, 2000. Internet communication at: http://www.who.int/gtb/publications/globrep00/index.html.

[11] Appaix, Olivier. *Tuberculosis Control: Financial Evaluation for the 2001-2005 Period (in Low- and Lower Middle-Income Countries). Economic Annex to the Global Plan to Stop TB* Boston: Partners In Health, to be published in 2002; World Health Organization. *Global Tuberculosis Control. WHO Report 2000.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.275.

[12] World Health Organization. *Global tuberculosis programme. Report of the ad hoc committee on the tuberculosis epidemic.* Geneva: World Health Organization, 1998.

[13] Hurtig AK, Porter JD, Ogden JA. Tuberculosis control and directly observed therapy from the public health/human rights perspective. *Int J Tuberc Lung Dis.* 1999;3:553–60.

[14] World Health Organization. *World Health Report 2000. Health systems: Improving performance.* Geneva: World Health Organization, 2000.

[15] Appaix, Olivier. *Tuberculosis Control: Financial Evaluation for the 2001-2005 Period (in Low- and Lower Middle-Income Countries). Economic Annex to the Global Plan to Stop TB* Boston: Partners In Health, to be published in 2002.

[16] World Health Organization. *Conference report: Tuberculosis and sustainable development, 22–24 March 2000*. Geneva: World Health Organization, 2000. Internet communication at: http://www.stoptb.org/conference/index.html.

[17] Dye C, Garnett GP, Sleeman K, Williams BG. Prospects for worldwide tuberculosis control under the WHO DOTS strategy. Directly observed short-course therapy. Lancet. 1998;352:1886–91.

[18] G8 Countries. Chair's Summary Okinawa International Conference on Infectious Diseases. Internet communication at: http://www.g8.gc.ca/2000/okinawa_infectious_diseases-e.asp; Watts J. G8 nations to set up infectious-disease fund (News). *Lancet.* 2000;355:2060; World Health Organization. *World Health Report. Health Systems: Improving Performance.* Geneva: World Health Organization, 2000.

[19] Bosman MC. Health sector reform and tuberculosis control: the case of Zambia. *Int J Tuberc Lung Dis.* 2000;4:606–14.

[20] World Health Organization. *Global TB Drug Facility Prospectus*. Geneva: World Health Organization, 2001. WHO/CDS/STB/2001.10a.

[21] World Health Organization. *Involving Private Practitioners in Tuberculosis Control*. Geneva: World Health Organization, 2001.

WHO/CDS/TB/2001.285.

22 Peruvian Ministry of Health. *Tuberculosis en el Perú, Informe 1999*. Lima: Programa Nacional de Control de la Tuberculosis, 2000.

23 World Health Organization. *Global DOTS Expansion Plan: Progress in TB control in high-burden countries, 2001*. Geneva: World Health Organization, 2001. WHO/CDS/STB/2001.11.

24 Espinal MA, Kim SJ, Suárez PG, et al. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. *JAMA*. 2000;283:2537–45.

CHAPTER 3

1 Mann JM, Tarantola D, Global AIDS Policy Coalition; *AIDS in the World II Global Dimensions, Social Roots, and Responses*. New York: Oxford University Press, 1996.

2 UNAIDS. *AIDS epidemic update: December 2000*. Geneva: UNAIDS, 2000.

3 International Federation of Red Cross and Red Crescent Societies. *World Disaster Report 2000*. Geneva: International Federation of Red Cross and Red Crescent Societies, 2000; Garrett L. Of epidemic proportions/UN report: AIDS deaths to surpass plague, Spanish flu. *Newsday*. November 29, 2000: A08.

4 Garrett L. (2000) Of epidemic proportions/UN report: AIDS deaths to surpass plague, Spanish flu. *Newsday*, 29 November A08.

5 Farmer PE, Walton DA, Furin JJ. The changing face of AIDS: implications for policy and practice. In: Mayer KH, Pizer H, American Public Health Association; *The Emergence of AIDS: The Impact on Immunology, Microbiology, and Public Health*. Washington: American Public Health Association, 2000.

6 Mocroft A, Vella S, Benfield TL, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. *Lancet*. 1998;352:1725–30; Moore RD, Chaisson RE. Natural history of HIV infection in the era of combination antiretroviral therapy. *AIDS*. 1999;13:1933–42; Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med*. 1998;338:853–60.

7 Moore RD, Chaisson RE. (1999). Natural history of HIV infection in the era of combination antiretroviral therapy. *AIDS*, 13(14), 1933–42.

8 Palella FJ, Delaney KM, Moorman AC et al. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *New England Journal of Medicine*, 338, 853–60.

9 UNAIDS Epidemic Update, December 2001. World Health Organization. Geneva. 2001 internet communication at: http://www.unaids.org/worldaidsday/2001/Epiupdate2001/Epiupdate2001_en.pdf

10 Raviglione MC, Snider DE Jr, Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. *JAMA.* 1995;273:220–6.

11 Cantwell MF, Binkin NJ. Impact of HIV on tuberculosis in sub-Saharan Africa: a regional perspective. *Int J Tuberc Lung Dis*. 1997;1:205–14.

12 De Cock KM, Soro B, Coulibaly IM, Lucas SB. Tuberculosis and HIV infection in sub-Saharan Africa. *JAMA*. 1992; 268: 1581-7.

13 Dye C, Corbett L, Watt C, Walker, N. B*urden of tuberculosis related to HIV: new estimates and projections*. Provisional estimates and projections presented during the first meeting of the Global TB/HIV working group. April 9–11, 2001. Geneva: World Health Organization, 2001.

14 Republic of South Africa Department of Health. *National Antenatal HIV Sero-Prevalence Survey in South Africa, Health Systems Research and Epidemiology, Department of Health, Republic of South Africa, final report*. Johannesburg: Department of Health, 1999.

15 Raviglione MC, Harries AD, Msiska R, et al. Tuberculosis and HIV: current status in Africa. *AIDS*. 1997;11 Suppl B:S115-23.

16 UNAIDS, *Report on the Global HIV-AIDS Epidemic*, June 2000, Joint United Nations Program on HIV-AIDS, Geneva

17 UNAIDS, "UNAIDS Epidemic Update. December 2001" UNAIDS, Geneva 2001.

18 Corbett EL, Watt CJ, Walker N, Maher D, Raviglione MC, Williams B, Dye C. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic (submitted for publication)

19 UNAIDS, *Report on the Global HIV-AIDS Epidemic*, June 2000, Joint United Nations Program on HIV-AIDS, Geneva

20 Lucas SB, Hounnou A, Peacock C, et al. The mortality and pathology of HIV infection in a West African city. *AIDS* 1993; 7: 1569-1579

21 Sawert H, Kongsin S, Payanandana V, et al. Costs and benefits of improving tuberculosis control: the case of Thailand. *Soc Sci Med.* 1997;44:1805–16.

22 Bechu, N. The impact of AIDS on the economy of families in Cote d'Ivoire: Changes in consumption among AIDS-affected households. In: Ainsworth M, Over AM. *Confronting AIDS : Evidence From the Developing World Selected Background Papers for the World Bank Policy Research Report, Confronting AIDS: Public Priorities in a Global Epidemic.* Brussels and Washington: European Commission and World Bank, 1998.

23 Ahlburg DA. *The economic impacts of tuberculosis.* Geneva: World Health Organization, 2000. WHO/CDS/STB/2000.5.

24 Stover J, and Bollinger L. *Current Opinion in Infectious Diseases.* 1999;12(3):271–315.

25 http://www.usaid.gov/pop_health/aids/Countries/africa/kenya.html

26 http://www.unaids.org/whatsnew/adf/files/eco_impact.pdf

27 Hansen K, Chapman G, Chitsike I, et al. The costs of HIV/AIDS care at government hospitals in Zimbabwe. *Health Policy Plan*. 2000;15:432–40.

28 World Health Organization. *Global TB Control: WHO Report 2001.* Geneva: World Health Organization, 2001.

29 Chaisson RE, Clermont HC, Holt EA, et al. Six-month supervised intermittent tuberculosis therapy in Haitian patients with and without HIV infection. *Am J Respir Crit Care Med.* 1996;154:1034–8; el-Sadr WM, Perlman DC, Matts JP, et al. Evaluation of an intensive intermittent-induction regimen and duration of short-course treatment for human immunodeficiency virus-related pulmonary tuberculosis. Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA) and the AIDS Clinical Trials Group (ACTG). *Clin Infect Dis.* 1998;26:1148–58;

Perriens JH, St Louis ME, Mukadi YB, et al. Pulmonary tuberculosis in HIV-infected patients in Zaire. A controlled trial of treatment for either 6 or 12 months. *N Engl J Med.* 1995;332:779–84; Small PM, Schecter GF, Goodman PC, Sande MA, Chaisson RE, Hopewell PC. Treatment of tuberculosis in patients with advanced human immunodeficiency virus infection. *N Engl J Med.* 1991;324:289–94.

30 Heymann SJ. Modelling the efficacy of prophylactic and curative therapies for preventing the spread of tuberculosis in Africa. *Trans R Soc Trop Med Hyg.* 1993;87:406–11.

31 Brazilian Ministry of Health, National STD/AIDS Programme. *Antiretroviral Therapy: Brazil's Experience*. Brasilia: Brazilian Ministry of Health, 2001.

32 http://www.unaids.org/hivaidsinfo/statistics/fact_sheets/pdfs/Argentina_en.pdf

33 Hirschel, Bernard, HIV/AIDS Unit, Hopital Cantonal, Geneva. *Reasons why treatment of TB must be combined with HAART.* Presented during the first meeting of the Global TB/HIV working group. April 9–11, 2001. Geneva: World Health Organization, 2001.

34 Nunn P, Brindle R, Carpenter L, et al. Cohort study of human immunodeficiency virus infection in patients with tuberculosis in Nairobi, Kenya. Analysis of early (6-month) mortality. *Am Rev Respir Dis.* 1992;146:849–54.

35 Farmer P, Leandre F, Mukherjee JS, et al. Community-based approaches to HIV treatment in resource-poor settings. *Lancet.* 2001;358:404–9.

36 Odhiambo JA, Borgdorff MW, Kiambih FM, et al. Tuberculosis and the HIV epidemic: increasing annual risk of tuberculous infection in Kenya, 1986-1996. *Am J Public Health*. 1999;89:1078–82.

37 Mukadi YD, Maher D, Harries A. Tuberculosis case fatality rates in high HIV prevalence populations in sub-Saharan Africa. *AIDS*. 2001;15:143–52.

38 Yanai H, Uthaivoravit W, Panich V, et al. Rapid increase in HIV-related tuberculosis, Chiang Rai, Thailand, 1990– 1994. AIDS. 1996;10:527–31.

39 Dye, C. (2000) Tuberculosis 2000-2010: control, but not elimination. *International Journal of Tuberculosis and Lung Disease* 4, suppl. 2, S146-S152

40 Farmer P, Leandre F, Mukherjee JS, et al. Community-based approaches to HIV treatment in resource-poor settings. *Lancet*. 2001;358:404–9.

41 United Nations Development Programme. *Human Development Report 2000*. New York: Oxford University Press (for UNDP), 2000.

42 World Bank. Poverty reduction and human development in the Caribbean: a cross-country study. World Bank Discussion Paper; WDP 366, 1997.

43 Deschamps MM, Pape JW, Williams-Russo P, Madhavan S, Ho J, Johnson W. A prospective study of HIV-seropositive asymptomatic women of childbearing age in a developing country. *J Acquir Immune Defic Syndr* 1993; 6: 446–51.

44 UNAIDS. *Report on the global HIV/AIDS epidemic, June 2000*. Geneva: UNAIDS, 2000.

45 Central Intelligence Agency. *The world factbook 2000.* Washington: CIA, 2000. Internet communication at: http://www.odci.gov/cia/publications/factbook/geos/ha.html.

46 Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med.* 1994;331:1173–80.

47 Centers for Disease Control and Prevention. Update: provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV. *MMWR Morb Mortal Wkly Rep.* 1996;45:468–80.

48 Farmer P, Leandre F, Mukherjee JS, et al. Community-based approaches to HIV treatment in resource-poor settings. *Lancet.* 2001;358:404–9.

49 Perriëns, Jos. Presented during the first meeting of the Global TB/HIV working group. April 9–11, 2001. Geneva: World Health Organization, 2001.

50 Maher D, Floyd K, Raviglione M. A strategic framework to decrease the burden of TB/HIV. WHO/CDS/TB/2002.296 World Health Organization, Geneva.

CHAPTER 4

1 Bureau of Tuberculosis Control. *Bureau of Tuberculosis Control Information Summary: 1998*. New York: New York City Department of Health, 1999.

2 Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City—turning the tide. *N Engl J Med.* 1995;333:229–33.

3 Nosocomial transmission of multidrug-resistant tuberculosis among HIV- infected persons—Florida and New York, 1988-1991. *MMWR Morb Mortal Wkly Rep.* 1991;40:585–91.

4 Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City—turning the tide. *N Engl J Med.* 1995;333:229–33.

5 Fujiwara PI, Larkin C, Frieden TR. Directly observed therapy in New York City. History, implementation, results, and challenges. *Clin Chest Med.* 1997;18:135–48.

6 Bureau of Tuberculosis Control. *Bureau of Tuberculosis Control Information Summary: 1998*. New York: New York City Department of Health, 1999.

7 Bureau of Tuberculosis Control. *Bureau of Tuberculosis Control Information Summary: 1998*. New York: New York City Department of Health, 1999.

8 Gasner MR, Maw KL, Feldman GE, et al. The use of legal action in New York City to ensure treatment of tuberculosis. *N Engl J Med.* 1999;340:359–66.

9 New York City Department of Health, unpublished data.

10 Tuberculosis among foreign-born persons entering the United States. Recommendations of the Advisory Committee for Elimination of Tuberculosis. *MMWR Morb Mortal Wkly Rep.* 1990;39:1–21.

[11] Crofton J, Chaulet P, and Mahler D. *Guidelines for the management of drug resistant tuberculosis.* Geneva: World Health Organization, 1996. WHO/TB/96.21 (Rev/1).

[12] Iseman MD. Tailoring a time-bomb. Inadvertent genetic engineering. *Am Rev Respir Dis.* 1985;132:735–6; Grzybowski S, Enarson D. [Results in pulmonary tuberculosis patients under various treatment program conditions]. *Bull Int Union Tuberc.* 1978;53:70–5; Fischer B. Epidemiology of mycobacterial resistance (especially *Mycobacterium tuberculosis*). *Chemotherapy* 1999;45:109–20.

[13] Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. *N Engl J Med.* 1994;330:1179–84; World Health Organization. *Global Tuberculosis Control: WHO Report 1999*. Geneva: World Health Organization, 1999.

[14] Beck-Sague C, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant *Mycobacterium tuberculosis* infections. Factors in transmission to staff and HIV-infected patients. *JAMA.* 1992;268:1280–6; Di Perri G, Cadeo GP, Castelli F, et al. Transmission of HIV-associated tuberculosis to health-care workers. *Lancet.* 1992;340:682; Pearson ML, Jereb JA, Frieden TR, et al. Nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis*. A risk to patients and health care workers. *Ann Intern Med.* 1992;117:191–6.

[15] World Health Organization, International Union Against Tuberculosis and Lung Disease. *Anti-tuberculosis drug resistance in the world: The WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 1994–1997*. Geneva: World Health Organization, 1997; *WHO. Global Tuberculosis control: WHO report 2000*. Geneva: World Health Organization, 2000; World Health Organization. *Anti-TB drug resistance in the world. Report n° 2*. Geneva: WHO/IUATLD Global Project on antituberculosis drug resistance surveillance, 2000. WHO/CDS/TB/2000.278.

[16] Dye C, Espinal M, Watt C, Mbiaga C, Williams B, *Worldwide incidence of multidrug-resistant tuberculosis*, unpublished; Espinal MA, Laszlo A, Simonsen L, et al. Global trends in resistance to antituberculosis drugs. World Health Organization—International Union against Tuberculosis and Lung Disease Working Group on Anti-Tuberculosis Drug Resistance Surveillance. *N Engl J Med.* 2001;344:1294–303; Mercedes Becerra (personal communication); World Health Organization, International Union Against Tuberculosis and Lung Diseases, *Anti-tuberculosis Drug Resistance in the World, Report n°2 Prevalence and trends, WHO–IUATLD Global project on anti-tuberculosis drug resistance surveillance*. Geneva: World Health Organization, 2000. WHO/CDS/TB/2000; Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis*. Boston: Harvard University and Open Society Institute, 1999.

[17] Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis*. Boston: Harvard University and Open Society Institute, 1999.

[18] Bifani PJ, Plikaytis BB, Kapur V, et al. Origin and interstate spread of a New York City multidrug-resistant *Mycobacterium tuberculosis* clone family. *JAMA.* 1996;275:452–7; Agerton TB, Valway SE, Blinkhorn RJ, et al. Spread of strain W, a highly drug-resistant strain of *Mycobacterium tuberculosis*, across the United States. *Clin Infect Dis.* 1999;29:85–92; discussion 93–5.

[19] Casper C, Singh SP, Rave S, et al. The transcontinental transmission of tuberculosis: A molecular epidemiological assessment. *Am J Public Health*. 1996;86:551–3; Codina G, Vidal R, Martin-Casabona N, et al. Multidrug-resistant tuberculosis caused by 'W'-related strains in three immunocompetent foreign-born patients. *Int J Tuberc Lung Dis*. 1999;3:82–4.

[20] Borchardt J, Kirsten D, Jorres R, et al. Drug-resistant tuberculosis in northern Germany: a retrospective hospital-based study of 1,055 patients from 1984 until 1993. *Eur Respir J.* 1995;8:1076–83; Lambregts van Weezenbeek CS, Jansen HM, Nagelkerke NJ, et al. Nationwide surveillance of drug-resistant tuberculosis in The Netherlands: rates, risk factors and treatment outcome. *Int J Tuberc Lung Dis.* 1998;2:288–95; Codecasa LR, Porretta AD, Gori A, et al. Tuberculosis among immigrants from developing countries in the province of Milan, 1993–1996. *Int J Tuberc Lung Dis.* 1999;3:589–95.

[21] CDC. (1999). Primary multidrug-resistant tuberculosis—Ivanovo Oblast, Russia, 1999. Morbidity & Mortality Weekly Report, 48(30):661–3.; Coninx, R., Mathieu, C., Debacker, M., Mirzoev, F., Ismaelov, A., de Haller, R., and Meddings, D.R. (1999). First-line tuberculosis therapy and drug-resistant Mycobacterium tuberculosis in prisons. Lancet, 353, 969–973.; Kimerling, M.E., Kluge, H., Vezhnina, N., Iacovazzi, T., Demeulenaere, T., Portaels, F., and Matthys, F. (1999). Inadequacy of the current WHO re-treatment regimen in a central Siberian prison: treatment failure and MDR-TB. *International Journal of Tuberculosis Lung Disease*,3(5), 451–453.

[22] Manalo F, Tan F, Sbarbaro JA, Iseman MD. Community-based short-course treatment of pulmonary tuberculosis in a developing nation. Initial report of an eight-month, largely intermittent regimen in a population with a high prevalence of drug resistance. *Am Rev Respir Dis.* 1990;142:1301–5; Mitchison DA, Nunn AJ. Influence of initial drug resistance on the response to short-course chemotherapy of pulmonary tuberculosis. *Am Rev Respir Dis.* 1986;133:423–30; Shimao T. Drug resistance in tuberculosis control. *Tubercle*. 1987;68:5–18; Espinal MA, Kim SJ, Suárez PG, et al. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. *JAMA.* 2000;283:2537–45; Hauer B, Serke M, Loddenkemper R, et al. Various polyresistant strains of *M. tuberculosis* in one patient (case report). *Int J Tuberc Lung Dis.* 1999;3(9 Suppl. 1):S122.

[23] Espinal MA, Kim SJ, Suárez PG, et al. Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. *JAMA.* 2000;283:2537

[24] Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City—turning the tide. *N Engl J Med.* 1995;333:229–33; Arno PS, Murray CJ, Bonuck KA, Alcabes P. The economic impact of tuberculosis in hospitals in New York City: a preliminary analysis. *J Law Med Ethics*. 1993;21:317–23.

[25] Appaix, Olivier. *Tuberculosis Control: Financial Evaluation for the 2001-2005 Period (in Low- and Lower Middle-Income Countries). Economic Annex to the Global Plan to Stop TB* Boston: Partners In Health, to be published in 2002.

[26] Geerligs WA, van Altena R, van der Werf TS. Antituberculosis-drug resistance. *N Engl J Med.* 1998;339:1079–80.

[27] World Health Organization. *Guidelines for the Management of Drug-Resistant Tuberculosis*. Geneva: World Health Organization, 1996. WHO/TB/96.210.

[28] Furin JJ, Mitnick CD, Shin SS, et al. Occurrence of serious adverse effects in patients receiving community- based therapy for multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2001;5:648–55.

[29] Kritski AL, Marques MJ, Rabahi MF, et al. Transmission of tuberculosis to close contacts of patients with multidrug-resistant tuberculosis. *Am J Respir Crit Care Med.* 1996;153:331–5; Raviglione MC, Snider DE Jr, Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a worldwide epidemic. *JAMA.* 1995;273:220–6; Snider DE Jr, Kelly GD, Cauthen GM, et al. Infection and disease among contacts of tuberculosis cases with drug- resistant and drug-susceptible bacilli. *Am Rev Respir Dis.* 1985;132:125–32; Teixeira L, Perkins MD, Johnson JL, et al. Infection

and disease among household contacts of patients with multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2001;5:321–8; Agerton T, Valway S, Gore B, et al. Transmission of a highly drug-resistant strain (strain W1) of *Mycobacterium tuberculosis*. Community outbreak and nosocomial transmission via a contaminated bronchoscope. *JAMA.* 1997;278:1073–7; Victor TC, Warren R, Beyers N, van Helden PD. Transmission of multidrug-resistant strains of *Mycobacterium tuberculosis* in a high incidence community. *Eur J Clin Microbiol Infect Dis.* 1997;16:548–9; Warren R, Hauman J, Beyers N, et al. Unexpectedly high strain diversity of *Mycobacterium tuberculosis* in a high-incidence community. *S Afr Med J.* 1996;86:45–9.

[30] Beck-Sague C, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant *Mycobacterium tuberculosis* infections. Factors in transmission to staff and HIV-infected patients. *JAMA*. 1992;268:1280–6; Di Perri G, Cadeo GP, Castelli F, et al. Transmission of HIV-associated tuberculosis to healthcare workers. *Infect Control Hosp Epidemiol*. 1993;14:67–72; Valway SE, Greifinger RB, Papania M, et al. Multidrug-resistant tuberculosis in the New York State prison system, 1990–1991. *J Infect Dis.* 1994;170:151–6; Transmission of multidrug-resistant tuberculosis among immunocompromised persons in a correctional system—New York, 1991. *MMWR Morb Mortal Wkly Rep.* 1992;41:507–9.

[31] World Health Organization. *Anti-tuberculosis drug resistance in the world: the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 1994–1997*. Geneva: World Health Organization, 1997; World Health Organization, International Union Against Tuberculosis and Lung Diseases. *Anti-tuberculosis Drug Resistance in the World, Report n°2 Prevalence and trends*. WHO-IUATLD Global project on anti-tuberculosis drug resistance surveillance. Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.

[32] Garrett L; *The Coming Plague: Newly Emerging Diseases in a World Out of Balance*. New York: Farrar, Straus and Giroux, 1994.

[33] Bifani PJ, Plikaytis BB, Kapur V, et al. Origin and interstate spread of a New York City multidrug-resistant *Mycobacterium tuberculosis* clone family. *JAMA*. 1996;275:452–7.

[34] Franzetti F, Gori A, Iemoli E, et al. Outcome of multidrug-resistant tuberculosis in human immunodeficiency virus-infected patients. *Clin Infect Dis.* 1999;29:553–60; Moro ML, Gori A, Errante I, et al. An outbreak of multidrug-resistant tuberculosis involving HIV-infected patients of two hospitals in Milan, Italy. Italian Multidrug-Resistant Tuberculosis Outbreak Study Group. *AIDS.* 1998;12:1095–102; Moro ML, Errante I, Infuso A, et al. Effectiveness of infection control measures in controlling a nosocomial outbreak of multidrug-resistant tuberculosis among HIV patients in Italy. *Int J Tuberc Lung Dis.* 2000;4:61–8.

[35] Weyer K, Groenewald P, Zwarenstein M, Lombard CJ. Tuberculosis drug resistance in the Western Cape. *S Afr Med J.* 1995;85:499–504; Weyer K, Lancaster J, Balt E, Durrheim D. Tuberculosis drug resistance in Mpumalanga Province, South Africa. *Int J Tuberc Lung Dis.* 1998;2(11 Suppl. 2):S332–3.

[36] World Health Organization. *Global Tuberculosis Control. WHO Report 2000*. Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.275.

[37] Cantwell MF, Binkin NJ. Tuberculosis in sub-Saharan Africa: a regional assessment of the impact of the human immunodeficiency virus and National Tuberculosis Control Program quality. *Tuber Lung Dis.* 1996;77:220–5; Cantwell MF, Binkin NJ. Impact of HIV on tuberculosis in sub-Saharan Africa: a regional perspective. *Int J Tuberc Lung Dis.* 1997;1:205–14; Richards SB, St Louis ME, Nieburg P, et al. Impact of the HIV epidemic on trends in tuberculosis in Abidjan, Cote d'Ivoire. *Tuber Lung Dis.* 1995;76:11–6; World Health Organization. *Global Tuberculosis Control. WHO Report 2000.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.275; World Health Organization. *Tuberculosis and Sustainable Development: Report from the Ministerial Conference in Amsterdam.* Geneva: World Health Organization, 2000. WHO/CDS/STB/2000.6.

[38] Sacks LV, Pendle S, Orlovic D, et al. A comparison of outbreak- and nonoutbreak-related multidrug-resistant tuberculosis among human immunodeficiency virus-infected patients in a South African hospital. *Clin Infect Dis.* 1999;29:96–101; Silber E, Sonnenberg P, Saffer D, Koornhof HJ. Multidrug-resistant tuberculous meningitis in a health care worker. *Int J Tuberc Lung Dis.* 1998;2:774; van Rie A, Warren R, Richardson M, et al. Transmission of drug-resistant *Mycobacterium tuberculosis* strains in an epidemic area. *Int J Tuberc Lung Dis.* 1999;3(9 Suppl. 1):S126.

[39] Becerra MC, Freeman J, Bayona J, et al. Using treatment failure under effective directly observed short-course chemotherapy programs to identify patients with multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2000;4:108–14; Becerra MC, Freeman J, Bayona J, et al. Using treatment failure under effective directly observed short-course chemotherapy programs to identify patients with multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2000;4:108–14.

[40] Primary multidrug-resistant tuberculosis—Ivanovo Oblast, Russia, 1999. *MMWR Morb Mortal Wkly Rep.* 1999;48:661–4; Cegielski JP, Repina E, Laserson K, et al. Preparation for DOTS-Plus pilot project in Ivanovo, Russia. *Int J Tuberc Lung Dis.* 1999;3(9 Suppl. 1):S86; Kimerling ME, Kluge H, Vezhnina N, et al. Inadequacy of the current WHO re-treatment regimen in a central Siberian prison: treatment failure and MDR-TB. *Int J Tuberc Lung Dis.* 1999;3:451–3; Farmer, P.E., Kim, J.Y., Mitnick, C., Timperi, R. Responding to outbreaks of MDR-TB: Introducing "DOTS-Plus". In: Reichman LB, Hershfield ES. *Tuberculosis a Comprehensive International Approach.* New York: Marcel Dekker, 2000.

[41] World Health Organization. *Global Tuberculosis Control: WHO Report 2000.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.275.

[42] Kim SJ, Bai GH, Hong YP. Drug-resistant tuberculosis in Korea, 1994. *Int J Tuberc Lung Dis.* 1997;1:302–8.

[43] Kim SJ, Hong YP. Drug resistance of *Mycobacterium tuberculosis* in Korea. *Tuber Lung Dis.* 1992;73:219–24.

[44] Park SK, Kim CT, Song SD. Outcome of chemotherapy in 107 patients with pulmonary tuberculosis resistant to isoniazid and rifampin. *Int J Tuberc Lung Dis.* 1998;2:877–84; World Health Organization, International Union Against Tuberculosis and Lung Diseases. *Anti-tuberculosis Drug Resistance in the World, Report n°2 Prevalence and trends. WHO–IUATLD Global project on anti-tuberculosis drug resistance surveillance.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.

[45] World Health Organization, International Union Against Tuberculosis and Lung Diseases. *Anti-tuberculosis Drug Resistance in the World, Report Number 2 Prevalence and trends. WHO–IUATLD Global project on anti-tuberculosis drug resistance surveillance.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000; World Health Organization. *Global Tuberculosis Control. WHO Report 2000.* Geneva: World Health Organization, 2000. WHO/CDS/TB/2000.275.

[46] Kim JY, Bayona J, Furin JJ, et al. Making DOTS-Plus work: Laboratories, drug procurement, planning, and evaluation. In: Programme in Infectious Disease and Social Change. *The global impact of drug-resistant Tuberculosis*. Boston: Harvard University and Open Society Institute, 1999.

[47] Banatvala N, Matic S, Kimerling M, et al. Tuberculosis in Russia. *Lancet*. 1999;354:1036.

[48] Farmer P, Kim JY. Community based approaches to the control of multidrug resistant tuberculosis: introducing "DOTS-plus". *BMJ*. 1998;317:671–4; Farmer PE, Kim JY, Mitnick C, Timperi R. Responding to outbreaks of MDR-TB: Introducing "DOTS-Plus". In: Reichman LB, Hershfield ES; *Tuberculosis a Comprehensive International Approach*. New York: Marcel Dekker, 2000; Becerra MC, Freeman J, Bayona J, et al. Using treatment failure under effective directly observed short-course chemotherapy programs to identify patients with multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2000;4:108–14.

[49] Farmer PE, Bayona J, Shin S, et al. Preliminary results of community-based MDR-TB treatment in Lima, Peru. *Int J Tuberc Lung Dis.* 1998;2(11 Suppl. 2):S371; Farmer P, Kim JY. Community based approaches to the control of multidrug resistant tuberculosis: introducing "DOTS-plus". *BMJ*. 1998;317:671–4; Farmer PE, Bayona J, Becerra M, et al. Poverty, inequality, and drug resistance: Meeting community needs. *Proceedings of the International Union Against Tuberculosis and Lung Disease North American Region Conference.* Chicago, February 27–March. 2, 1997. Chicago: International Union Against Tuberculosis and Lung Disease, 1997, pp. 88–102; Farmer PE, Bayona J, Becerra MC, et al. International Working Group on Multidrug-Resistant Tuberculosis. The emergence of MDR-TB in urban Peru: A population-based study using conventional, molecular, and ethnographic methods. *Int J Tuberc Lung Dis.* 1997:1(5, S1);S44.

[50] Farmer P, Kim JY. Community based approaches to the control of multidrug-resistant tuberculosis: introducing "DOTS-plus". *BMJ*. 1998;317:671–4; Farmer PE, Kim JY, Mitnick C, Timperi R. Responding to outbreaks of MDR-TB: Introducing "DOTS-Plus". In: Reichman LB, Hershfield ES; *Tuberculosis a Comprehensive International Approach*. New York: Marcel Dekker, 2000; Grosset PJ. Systematic drug susceptibility testing: a necessary component of the "DOTS plus" strategy? *Int J Tuberc Lung Dis.* 1999;3:549–50; Iseman MD. MDR-TB and the developing world--a problem no longer to be ignored: the WHO announces "DOTS Plus" strategy. *Int J Tuberc Lung Dis.* 1998;2:867; Portaels F, Rigouts L, Bastian I. Addressing multidrug-resistant tuberculosis in penitentiary hospitals and in the general population of the former Soviet Union. *Int J Tuberc Lung Dis.* 1999;3:582–8; World Health Organization. *Coordination of DOTS-Plus pilot projects for the management of MDR-TB*. Geneva: World Health Organization, 1999. WHO/CDS/CBC/TB/99.262.

[51] Farmer P, Kim JY. Community based approaches to the control of multidrug resistant tuberculosis: introducing "DOTS-plus". *BMJ*. 1998;317:671–4; Farmer PE, Kim JY, Mitnick C, Timperi R. Responding to outbreaks of MDR-TB: Introducing "DOTS-Plus". In: Reichman LB, Hershfield ES; *Tuberculosis a Comprehensive International Approach*. New York: Marcel Dekker, 2000; World Health Organization. *Coordination of DOTS-Plus pilot projects for the management of MDR-TB*. Geneva: World Health Organization, 1999. WHO/CDS/CBC/TB/99.262.

[52] World Health Organization. Coordination of DOTS-Plus pilot projects for the management of MDR-TB. Geneva: World Health Organization, 1999. WHO/CDS/CBC/TB/99.262.

[53] Program in Infectious Disease and Social Change. *The global impact of drug-resistant tuberculosis*. Boston: Harvard University and Open Society Institute, 1999; Farmer P, Kim JY. Community based approaches to the control of multidrug-resistant tuberculosis: introducing "DOTS-plus". *BMJ*. 1998;317:671–4.

[54] Iseman MD. Treatment of multidrug-resistant tuberculosis. *N Engl J Med.* 1993;329:784–91; Furin JJ, Mitnick CD, Shin SS, et al. Occurrence of serious adverse effects in patients receiving community- based therapy for multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis.* 2001;5:648–55.

[55] World Health Organization. *Anti-tuberculosis drug resistance in the world: the WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance 199—1997.* Geneva: World Health Organization, 1997; Laszlo A, Rahman M, Raviglione M, Bustreo F. Quality assurance programme for drug susceptibility testing of *Mycobacterium tuberculosis* in the WHO/IUATLD Supranational Laboratory Network: first round of proficiency testing. *Int J Tuberc Lung Dis.* 1997;1:231–8.

CHAPTER 5

1 Ryan F. *The Forgotten Plague: How the Battle Against Tuberculosis Was Won--and Lost.* Boston: Little, Brown, 1993.

2 Fox W, Ellard GA, Mitchison DA. Studies on the treatment of tuberculosis undertaken by the British Medical Research Council tuberculosis units, 1946–1986, with relevant subsequent publications. *Int J Tuberc Lung Dis*. 1999;3 (10 Suppl 2):S231–79.

3 Michaud C and Murray CJL. Annex 5. Resources for health research and development in 1992: A global overview. In: *Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to future intervention options.* Geneva: World Health Organization, 1996.

4 Nunn P and Linkins J. *The Global Tuberculosis Research Initiative: Research to make a difference.* Geneva: World Health Organization, 1998. WHO/TB/98.248.

5 Cole ST, Brosch R, Parkhill J, et al. Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence. *Nature*. 1998;393:537–44.

6 Foulds J and O'Brien R. New tools for the diagnosis of tuberculosis: the perspective of developing countries. *Int J Tuberc Lung Dis.* 2000;10;778–83; Perkins MD. New diagnostic tools for tuberculosis. *Int J Tuberc Lung Dis.* 2000;12 (Supplement):S182–8.

7 Chang-Blanc D, and Nunn P. *Incentives and disincentives for new anti-tuberculosis drug development: situational analysis*. Geneva: World Health Organization, 2000. WHO/TDR/PRD/TB/00.1.

8 Global Alliance for TB Drug Development, *The Economics of TB Drug Development.* New York: Global Alliance for TB Drug Development, 2001.

9 Boston Consulting Group, for the Global Alliance for TB Drug Development, 2000 (personal communication).

10 Sachs J. Helping the world's poorest. *The Economist.* August 12, 1999; Sachs J. A new map of the world. The Economist. June 24, 2000.

11 Salaniponi F, Harries AD, Nyirenda T, et al. *Putting research into policy and practice: The experience of the Malawi National Tuberculosis Programme.* Geneva: World Health Organization, 1999. WHO/CDS/CPC/TB/99.268.

12 Crofton J. Sputum conversion and the metabolism of isoniazid. *American Review of Tuberculosis.* 1958;77:869–871.

13 Styblo K, Chum HJ. Treatment results of smear-positive tuberculosis in the Tanzania National Tuberculosis and Leprosy Programme: standard and short-course chemotherapy. In: *Proceedings of the XXVI IUAT World Conference on Tuberculosis and Respiratory Diseases*. Tokyo: Professional

Postgraduate Services, 1987:122–6.

[14]The International Network for the Rational Use of Drugs (INRUD), 2000. Internet communication at: http://www.msh.org/inrud/ ; Hogerzeil HV, Bimo, Ross-Degnan D, et al. Field tests for rational drug use in twelve developing countries. Lancet. 1993;342:1408–10.

[15]WHO. *Report of the Ad Hoc Committee on the tuberculosis epidemic, London*. Geneva: World Health Organization, 1998. TB/98.245.

[16]WHO. *Report of the First Meeting of the Global TB Research Initiative*. Geneva: World Health Organization, 1998. TB/98.245.