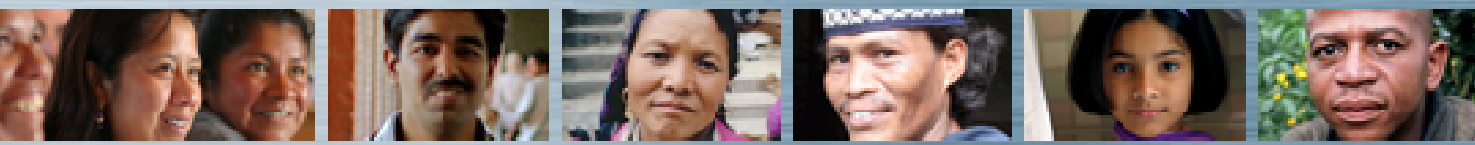


Analysis of the Global TB Drug Market and Country-Specific Case Studies of TB Drug Distribution Channels

US Case Study

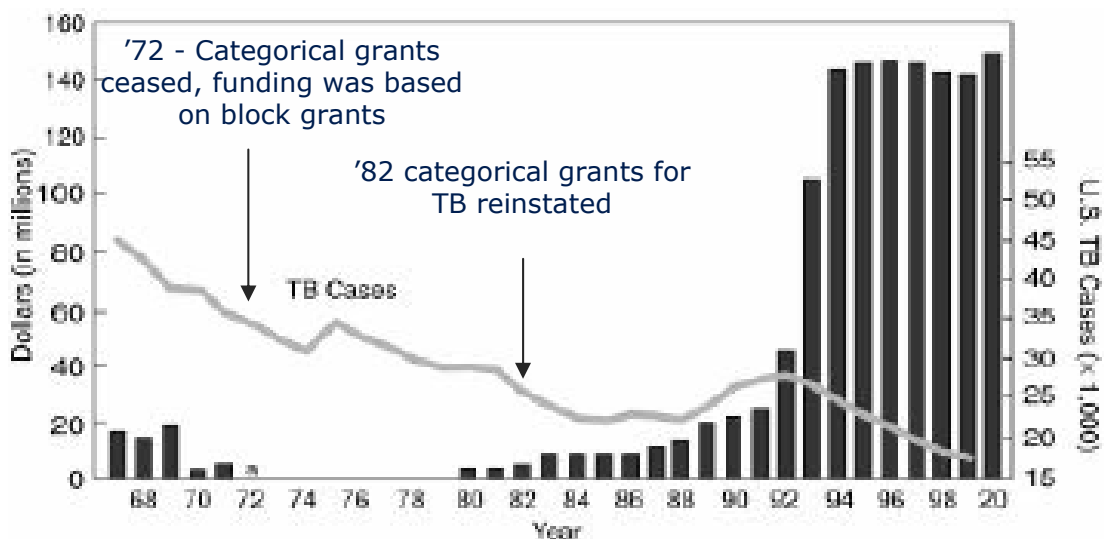


US Table of Contents

- TB Control in the US
- Procurement and distribution of TB Drugs in the US
- Value and Volume of the US TB Market
- Appendix

After a resurgence of TB cases between 1989-1993, the TB incidence has substantially been reduced

CDC Funding vs. Total TB Cases 1967-2000*

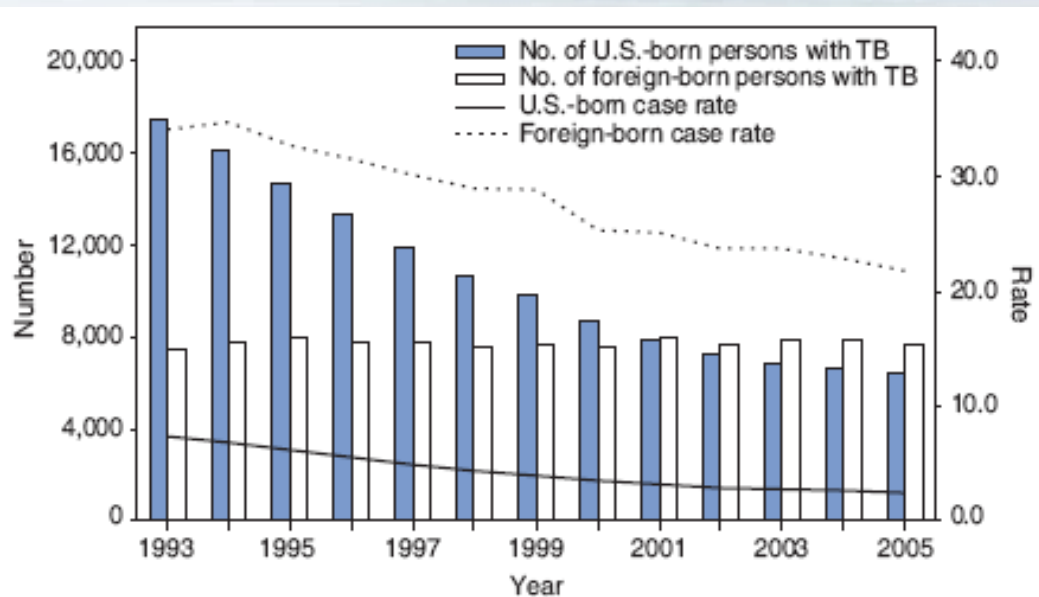


- 14,093 cases documented in 2005
- Overall number of cases in the US has dropped 41% since peak in 1992
- Resurgence of TB cases between 1985 and 1992 due to expansion of:
 - HIV infection,
 - Nosocomial transmission of *M. tuberculosis*
 - Increased immigration from countries with a high incidence of TB
- The fed re-established categorical grants specific for TB in 1992
- Funding increased drastically after resurgence in 1992 and 1993

Note: Source did not indicate whether or not the funding was adjusted for inflation
 Source: Institute of Medicine, Ending Neglect- The Elimination of Tuberculosis in the United States

TB cases in foreign-born persons have remained fairly constant

Number and rate of persons with TB by origin of birth and year (US 1993-2005)



- In 2005, the rate of TB in foreign born persons was 8.7 times that of US born making up 54% of total cases
- Ratio of foreign born to US born increased at a steady rate of 6.6% /yr between 1993-2002, but has dropped to only 0.5%/yr since
- Over half of all foreign born cases were reported in immigrants from Mexico(25.2%), Philippines (10.8%), Vietnam (7.5%), India (7.4%), and China (5.1%)

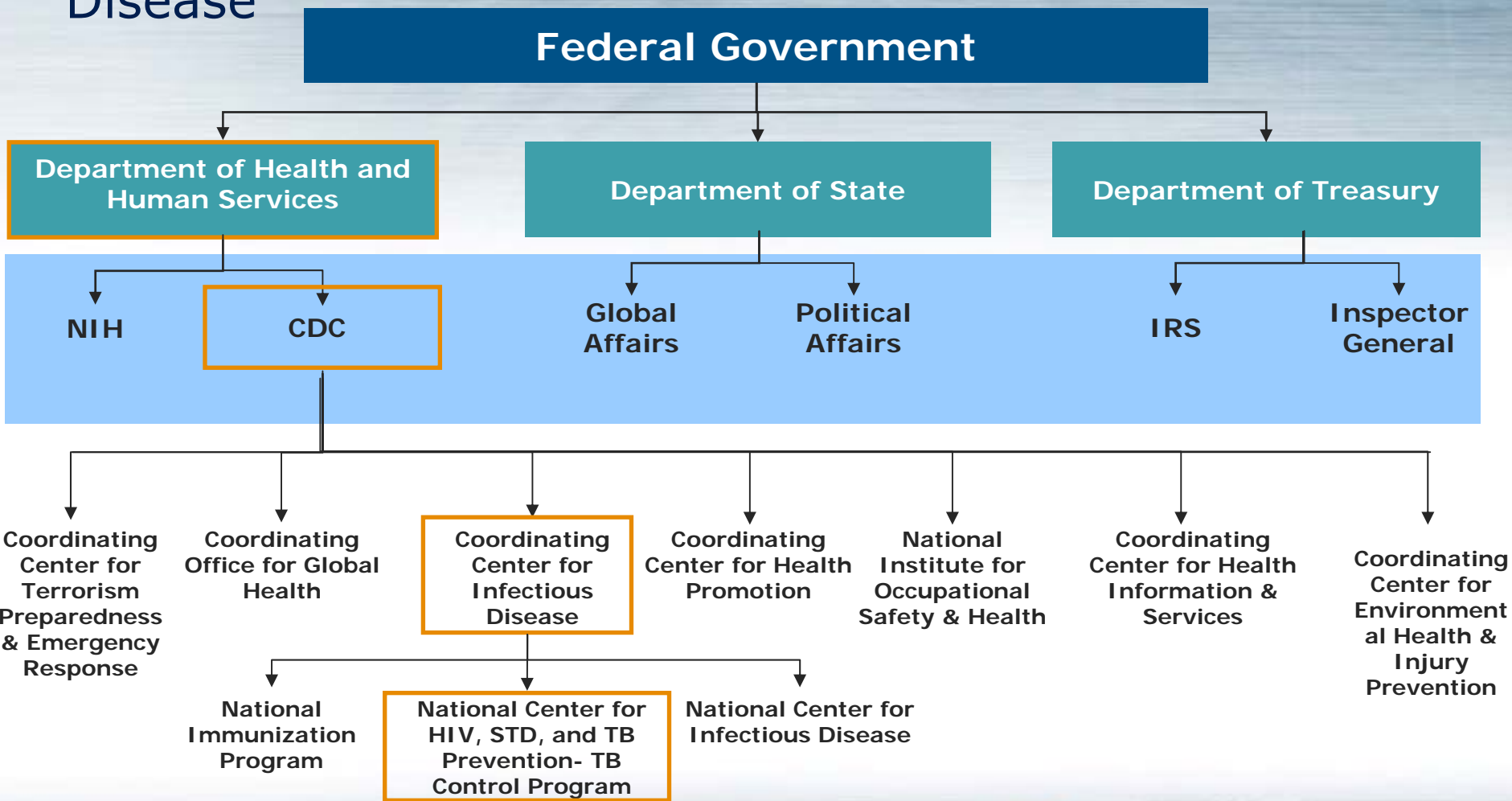
* Per 100,000 population.
 † Data for 2005 are provisional.

The National CDC and State Health Departments are the two critical entities for TB control and funding in the US

Role	National CDC	State Department of Health
Funding for Drugs	No drug funding	State funded procurement or funds distributed directly to local health departments for procurement
Funding for treatment and case detection	Fund states based on a weighted algorithm including case detection rate and severity of cases	Fund case detection, treatment, and contact screening
Monitoring and Reporting	Analyzes data across the US for guideline changes and funding distribution	Responsible for monitoring all TB cases and implementing DOT when necessary- send periodic reports to CDC
Guidelines/Policy establishment	Establish national guidelines to provide consistent case detection and treatment across the country	Follow the CDC guidelines – create state specific guidelines
Drug Procurement	Not involved	Some states procure their own drugs, others relegate it to local health departments
Education and Outreach	Main advocates and funders for education and case management programs- fund out-reach workers	Provide training to local health care workers; responsible for assigning treatment partners*

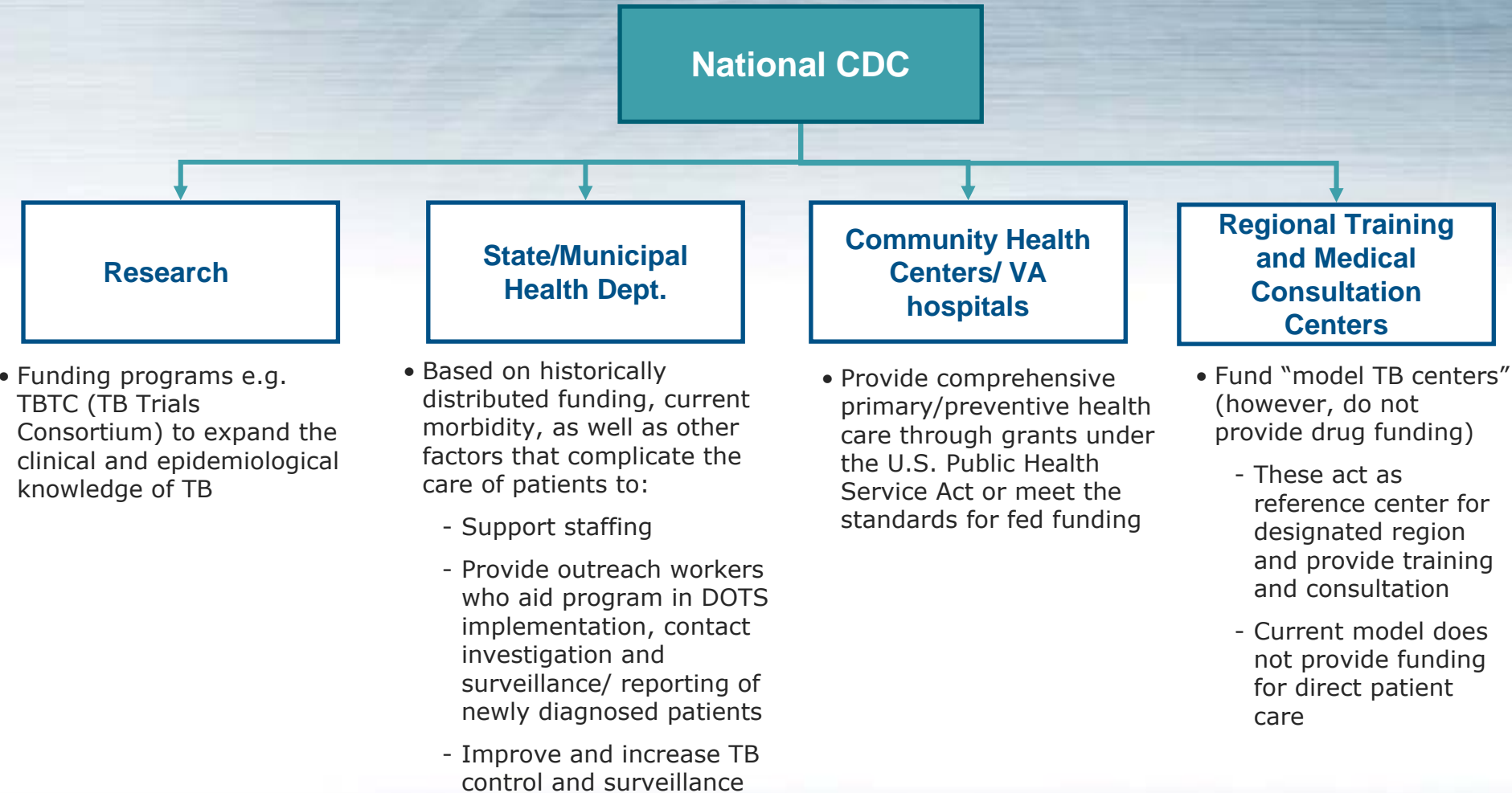
Note: Treatment partners can be out-reach workers or family members who support and monitor patient throughout therapy

The National TB Program falls under control of the CDC as a subpart of the Coordinating Center for Infectious Disease



Source: National Coalition for the Elimination of Tuberculosis – Federal Task Force on Tuberculosis Summary Fact Sheet; www.cdc.gov

Although the CDC funds a variety of NTP control activities, it is not involved in drug procurement



The CDC developed a set of guidelines for the use of funding and treatment regimens

CDC national recommendations:

1. Use of funding

- Federal funding should supplement local funding based on disease burden and control of TB - increase of federal funding should not result in any loss of state funding
- Federal funding may not be used for drug procurement

2. Treatment

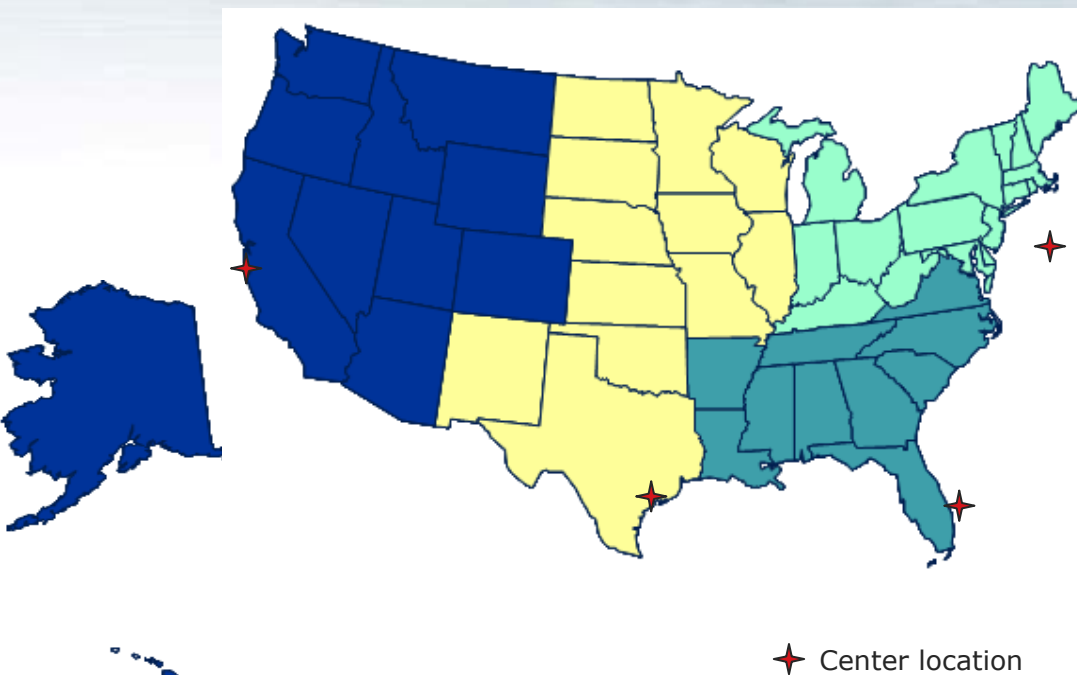
- All states should impose regulations that mandate completion of therapy
- All treatments should be administered in the context of patient-centered programs that consider the individual patient needs and characteristics
- Services should never be denied due to a patient's inability to make co-pay

3. Billing for Reimbursement

- Public and Private health insurance programs should be billed for TB diagnosis and treatment

As well as four regional centers providing training and medical consultation

Regional Coverage of 4 Regional Training and Medical Consultation Centers

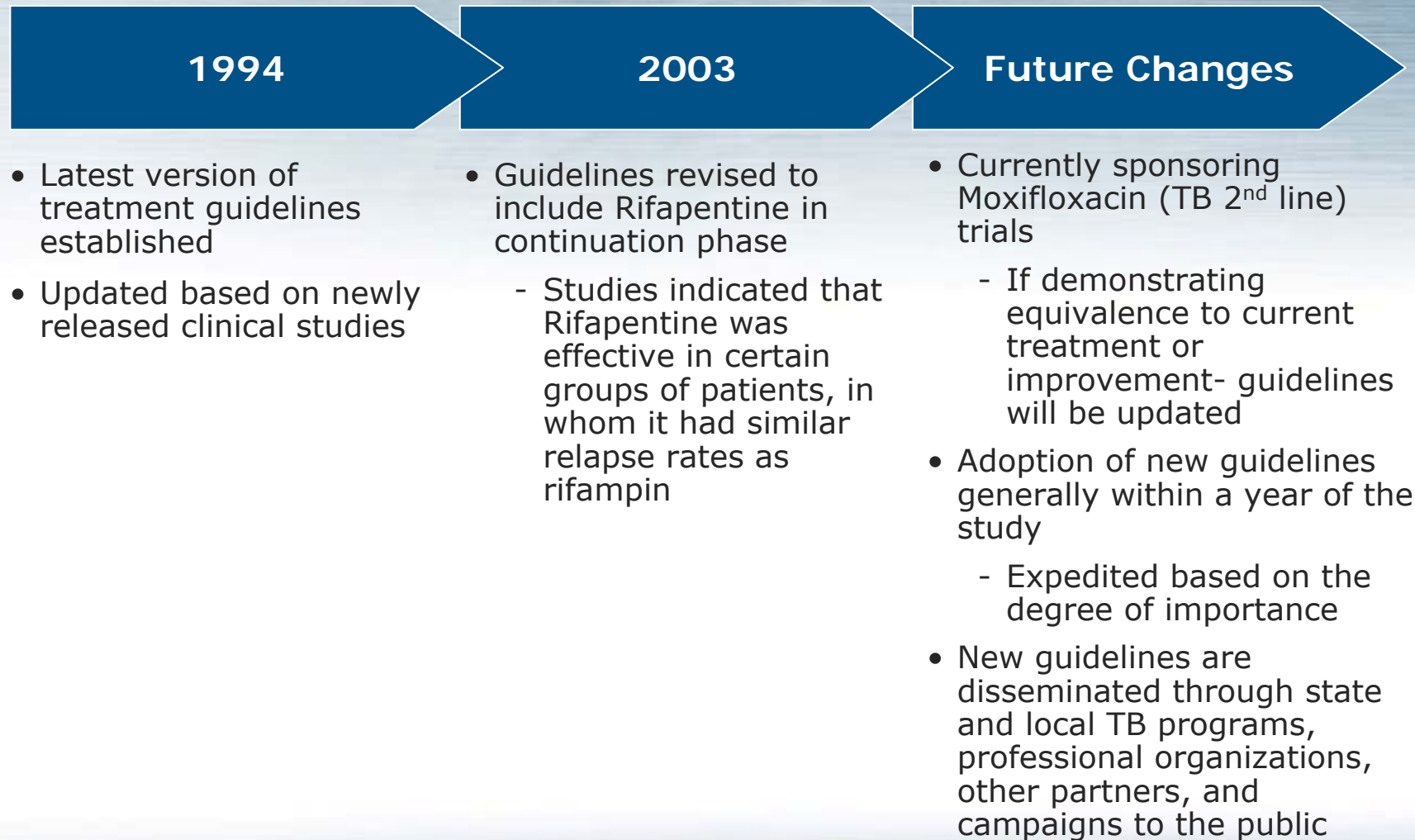


- 4 Regional Training and Medical Consultation Centers (RTMCC) established in CA, TX, FL, and NJ to:
 - Provide training and technical assistance to increase human resource development in TB programs;
 - Develop TB educational materials; and
 - Provide medical consultation to TB programs and medical providers
 - Current model does not provide funding for direct patient care
- Particularly important for areas who see little TB and particularly low MDR-TB
- CDC is the major funder for these centers but does not provide funds for drug procurement

Source: CDC Interviews;

Source 2: <http://www.cdc.gov/nchstp/tb/rtmcc.htm>

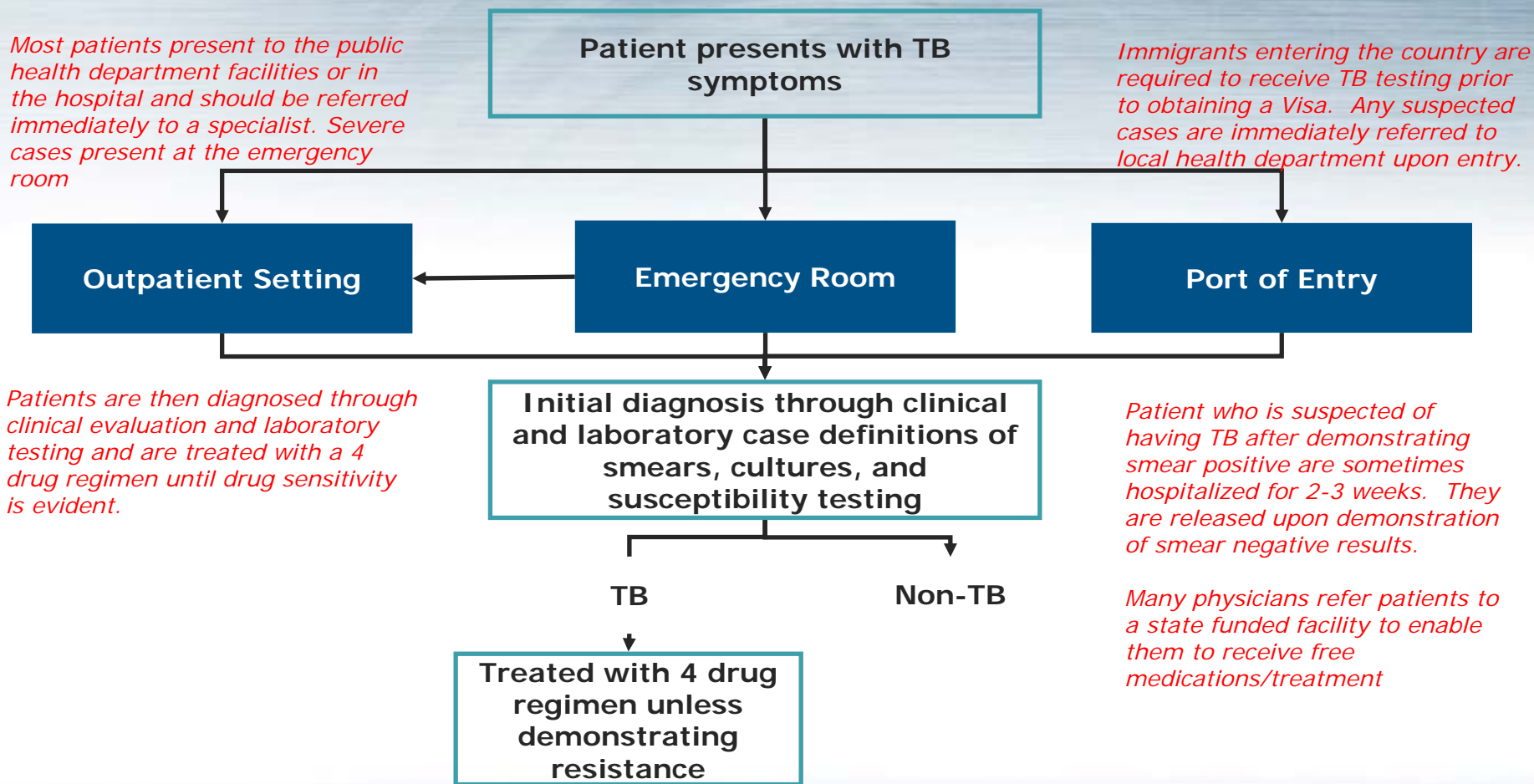
All treatment guidelines are evidence based and frequently updated with newly released clinical results



Source: CDC Interviews

Patient flow for initial diagnosis

Patient flow through the public/private sector



Source: CDC Guidelines, Interviews

Patients are then typically treated in an outpatient setting...

Patient flow through the public/private sector

Person at high risk of TB or with symptoms of TB disease is evaluated

Patients with latent TB are evaluated for treatment and high risk individuals are recommended to receive treatment

Documented cases are reported to the local health department and assigned a case manager to follow up with treatment, ensure no adverse reactions or resistance, and enforce compliance

Latent TB*

Active TB

Drug resistant TB

Under exceptional circumstances e.g. homeless or acutely ill patient will be isolated in the hospital

Assigned Case Manager

Assigned Case Manager

Hospital out-patient

State funded facility

Hospital In-patient

Retail pharmacy

Outpatient pharmacy

Patients can collect their drugs from State or City Health Department Clinics, hospital outpatient or retail pharmacies on a monthly basis to ensure regularly scheduled follow-up

*Treatment for Latent TB is not mandatory

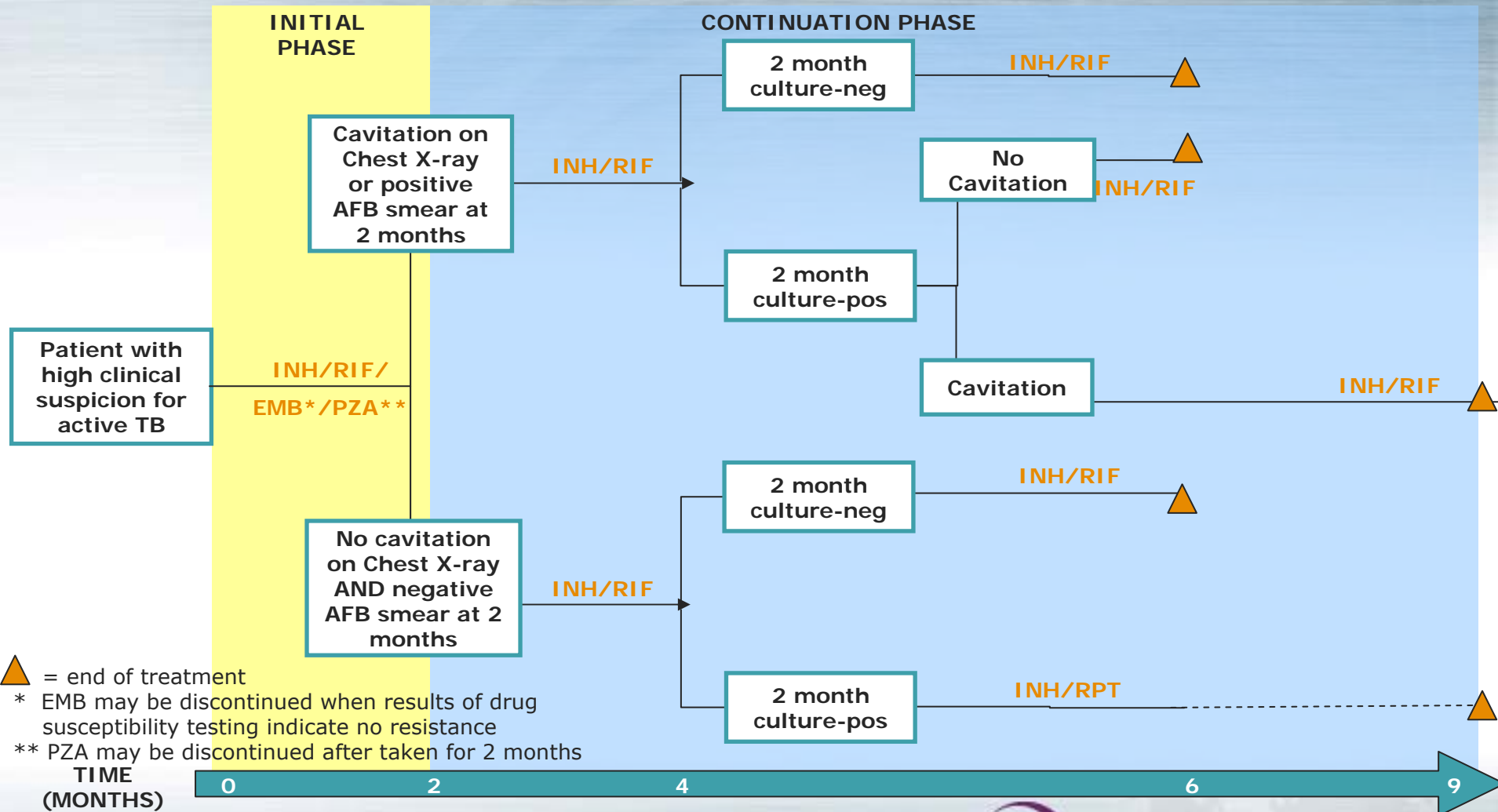
Source: CDC guidelines, Interviews

...following guidelines established by the CDC, the American Thoracic Society and the Institute of Medicine

Treatment options	Length of Time	Indications	Initial Phase of treatment	Continuation Phase
Option 1	6 months	Pulmonary and extra pulmonary TB in adults and children	<u>Daily for 8 weeks:</u> Isoniazid , rifampin, pyrazinamide + ethambutol or streptomycin	<u>Daily or 2 or 3 times/week for 16 weeks:</u> Isoniazid + rifampin
Option 2	6 months	Pulmonary and extra pulmonary TB in adults and children	<u>Daily for 2 weeks and then 2 times/week for 6 weeks:</u> Isoniazid , rifampin, pyrazinamide + ethambutol or streptomycin	<u>2 times/week for 16 weeks:</u> Isoniazid + rifampin
Option 3	6 months	Pulmonary and extra pulmonary TB in adults and children	<u>3 times/week for 6 months:</u> Isoniazid , rifampin, pyrazinamide + ethambutol or streptomycin	NA
Option 4	4 months	Pulmonary and extra pulmonary TB in adults	<u>Follow option 1,2, or 3 interval and duration for 8 weeks:</u> Isoniazid , rifampin, pyrazinamide + ethambutol or streptomycin	<u>Daily or 2 or 3 times/week for 8 weeks:</u> Isoniazid, rifampin, pyrazinamide, +ethambutol or streptomycin
Option 5	9 months	For smear and culture negative pulmonary TB in adults	<u>Daily for 8 weeks:</u> Isoniazid, rifampin + ethambutol or streptomycin	<u>Daily or 2 times/week for 24 weeks:</u> Isoniazid + rifampin

Source: CDC Report- Best Practices of Medicine- TB

These guidelines include treatment algorithms to ensure consistent therapy across the country



Source: Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America, June 20, 2003

As well as suggested regimens for latent and drug resistant cases

Type of TB	Length of Treatment	Treatment Regimen
Latent TB	9 months	INH daily or Twice weekly under DOT
	4 months	Rifampin daily
INH (\pm SM) resistance	6 months	Rifampin, Pyrazinamide + Ethambutol (a Fluroquinolone may strengthen regimen for those with extensive disease)
INH and RIF (\pm SM) resistance	18-24 months	Fluroquinolone, Pyrazinamide + Ethambutol, Injectable Agent, + Alternative Agent*
INH, RIF, (\pm SM) + EMB/PZA resistance	24 months	Fluroquinolone (Ethambutol or Pyrazinamide if active), Injectable Agent, +2 alternative agents*
RIF resistance	12-18 months	Isoniazid, Ethambutol, Fluroquinolone, supplemented with PZA for 1 st two months (an Injectable Agent may be included for the first 2-3 months for patients with extensive disease)*

*Injectable Agent: Includes aminoglycosides (streptomycin, amikacin, kanamycin) or polypeptide capreomycin
Alternative Agents: Ethionamide, Cycloserine, PAS, clarithromycin, amoxicillin-clavulanate, linezolid

Source: CDC TB Treatment Guidelines

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm>

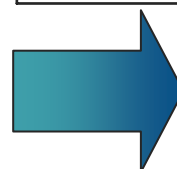
Source 2: CDC Targeted TB Testing and Treatment of Latent TB infection <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>

Treatment guidelines also provide recommended and maximum daily doses for 1st and 2nd line drugs

<u>1st line drug</u>	<u>Daily max (dosage)</u>	<u>Thrice weekly dosage</u>
Isoniazid	300mg (5mg/kg)	900mg (15mg/kg)
Rifampin	600mg (10mg/kg)	600mg (10mg/kg)
Pyrazinamide	No max (20-25mg/kg)	NA
Ethambutol	No max (15-20mg/kg)	NA

<u>2nd line drug</u>	<u>Daily max (dosage)</u>
Streptomycin	1 gram (15mg/kg)
Amikacin	1 gram (15mg/kg)
Capreomycin	1 gram (15mg/kg)
Kanamycin	1 gram (15mg/kg)
Ethionamide	1 gram (15-20mg/kg)
Cycloserine	1 gram (10-15mg/kg)
PAS	No max (8-12g/day)
Levofloxacin	500-1000mg daily
Moxifloxacin	400mg daily (not yet FDA approved for TB)
Gatifloxacin	400mg daily (not yet FDA approved for TB)

<u>FDC</u>	<u>Dosage per unit</u>	<u>Dose per day</u>
Rifamate	Rif-300mg, INH-150mg	2 capsules
Rifater	Rif-120mg, INH-50mg, PZA 300mg	≤44kg = 4 tablets 45-54kg = 5 tablets ≥55kg = 6 tablets



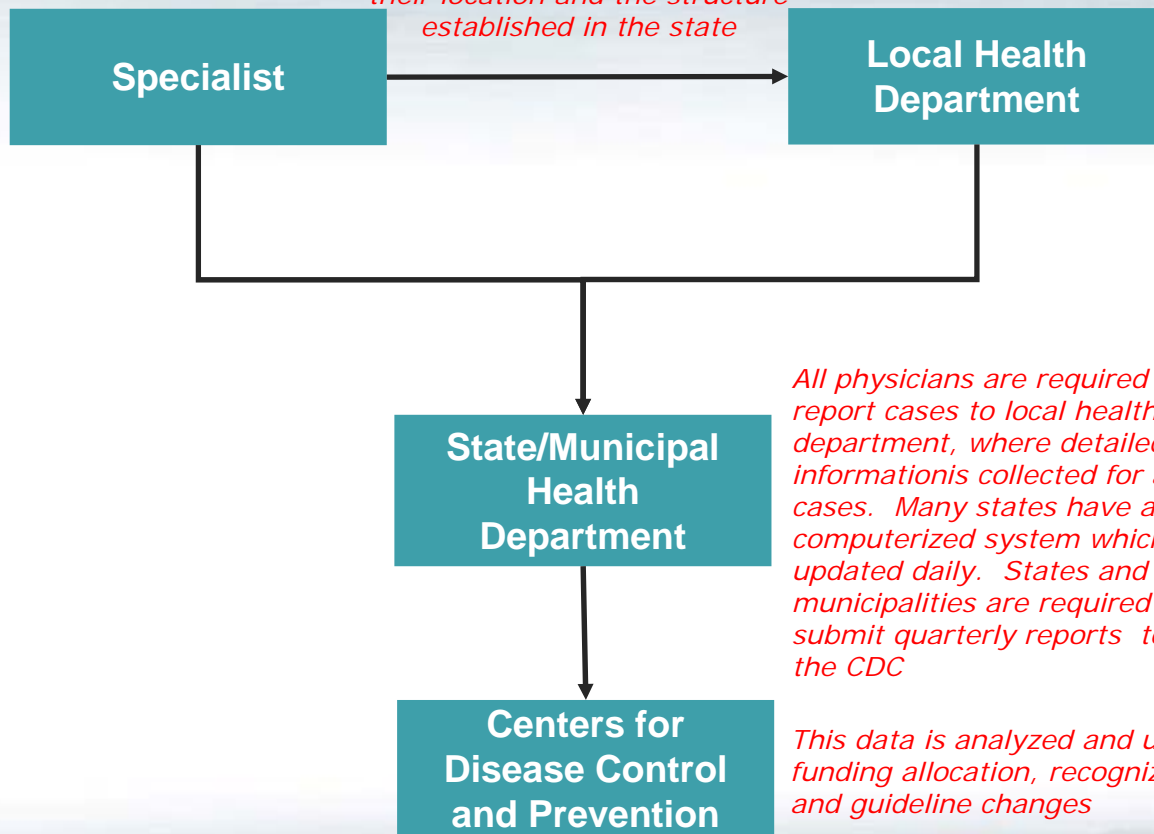
FDCs are rarely used in the US; most physicians utilize the 4 drug regimen (separate pills) for all TB patients

Source: CDC TB Treatment Guidelines
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm> 17

In an effort to maintain records, all state/municipal health departments are required to submit periodic reports

Flow of reporting

Physician sends all sputum smears to either their local health departments or the state department depending on their location and the structure established in the state

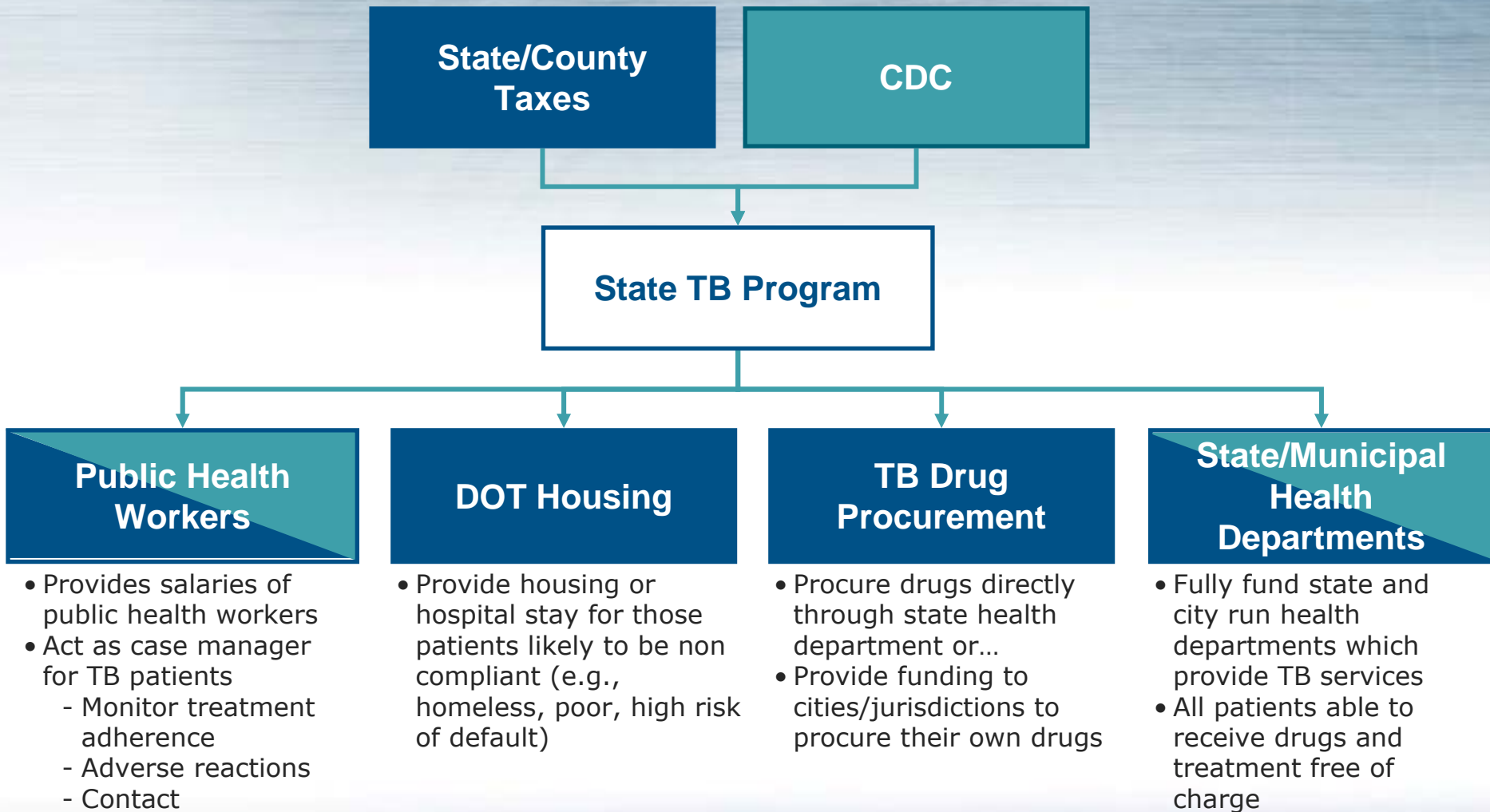


All physicians are required to report cases to local health department, where detailed information is collected for all cases. Many states have a computerized system which is updated daily. States and municipalities are required to submit quarterly reports to the CDC

This data is analyzed and used for funding allocation, recognizing trends, and guideline changes

Source: Interviews

Although receiving some federal funding, state TB programs are also heavily self-supporting...



Source: Interviews

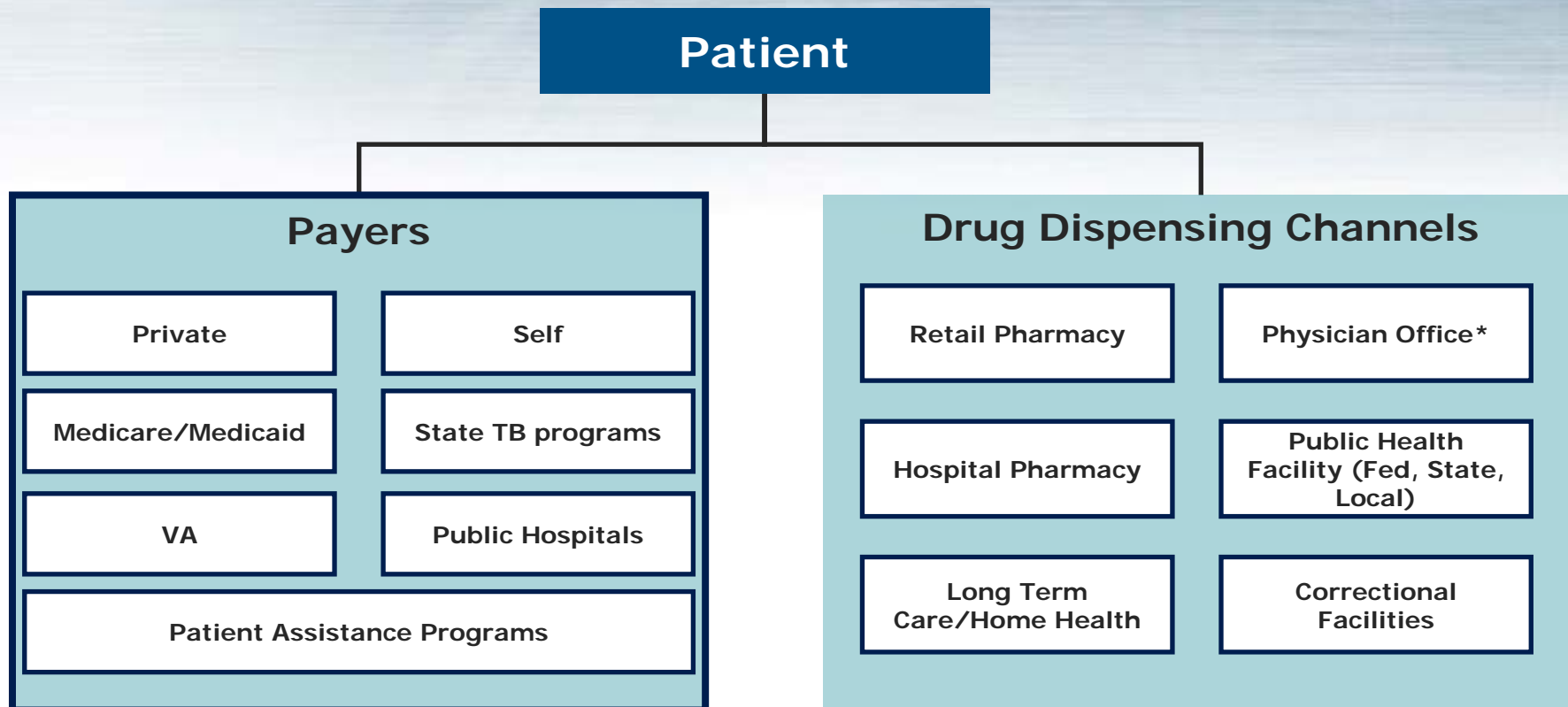
...and have autonomy in determining how to implement their own TB programs

Illustrative

State	Guideline Implementation	Funding allocation	DOTS mandated
California	Each city and jurisdiction is responsible for TB guidelines and implementation	State funds distributed to cities based on morbidity SF, SD, LA all receive direct CDC funding as well	No- case by case based on risk level
Massachusetts	Cities and counties follow state set guidelines	State distributes funding to city/county health depart and will reimburse drug costs for <u>public hospitals with TB clinics</u>	No- case by case based on risk level
New York- NYC	NYC established guidelines and implementation	NYC receives direct CDC funding in addition to state and local funds and allocates 60% of total funds to case contact/management activities- the remaining to city health clinics	No- Case by Case For ss+ over 80% receive DOT
Texas	Each region and local health department is responsible for TB guidelines and implementation	Previously allocated to region/local health dept based on morbidity Now use a formula based on risk factors Houston receives direct CDC funding as well	Yes- policy mandated by the state

Source: Interviews

Regardless of where patients receive their TB medication, there are a variety of payers responsible for coverage



**Injectables only*

Source: Interviews

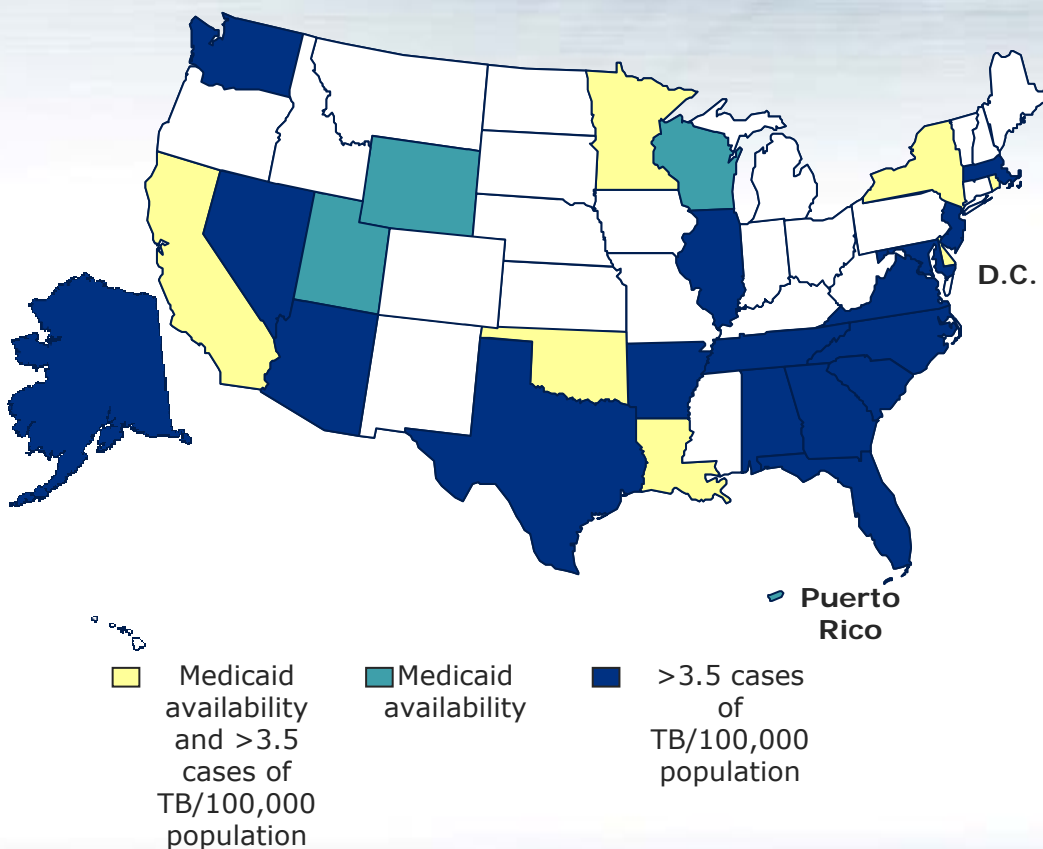
Insurance schemes include private insurance, Medicare, Medicaid, and VA with additional payment out-of-pocket

	Private	Medicare	Medicaid	VA
Funded	Employer/Employee premium	Federal Funding	State and federal funding	Federal Funding
Patient type	Employed individuals, Self-employed and those with no employer based health care, dependants	US citizens 65 or older, specified people under 65 with long-term disabilities	Indigent population-families w/ dependant children, the aged, the blind, and disabled who meet established poverty level	Active and retired members of the uniformed services and veterans of the Armed forces -includes their dependants and any survivors
Drug Coverage and Costs	Monthly premium and additional co-pays typically \$5-10 as most are generic	As of 2006 drug benefit program with monthly premium and co-pays typically \$5-10 as most are generic	Full coverage of Medicaid preferred drugs with minimal to no co-pay	All products available on VA hospital/center formulary provided for free to patients who are "service connected"
Location	All facilities	All facilities	All facilities	Only VA Hospitals and clinics

Source: IMS Research

Some states opt to include supplemental Medicaid coverage for TB patients who could not otherwise qualify

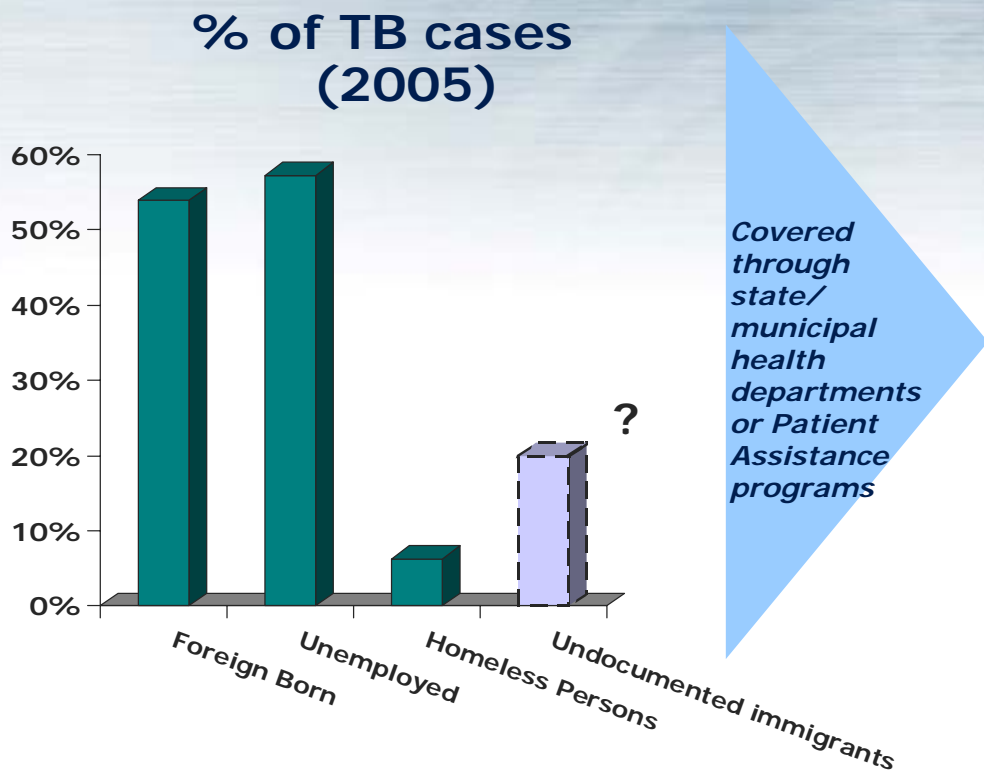
Supplemental Medicaid coverage by State
(US, 2005)



- Omnibus Budget Reconciliation Act of 1993 (OBRA '93), enabled states to offer supplemental Medicaid coverage
 - Available to low income individuals infected with TB not typically qualified for Medicaid
 - In 2005 only 9 states along with D.C., and Puerto Rico offered this service
- This coverage, however is limited to the following services:
 - Prescribed drugs
 - Physician/clinic services (hospital outpatient, rural health clinics and federally qualified health center services)
 - Laboratory and x-ray services
 - Case management services and those services included in the extended DOTS program

Source: CMS- Medicaid at a glance 2005

Despite available coverage in the current insurance schemes, many patients are still uninsured



The majority of these patients are not insured through either Employer Private Insurance, Medicaid, or Medicare

Note: Categories are not mutually exclusive

Source: Reported Tuberculosis in the United States 2004 – CDC Surveillance Report

Source 2: Trends in Tuberculosis 2005

- States **must** ensure treatment to all TB patients regardless of their ability to pay
 - Services provided either for free or based on a sliding scale of income
- Hospitals typically refer patients who cannot afford treatment to the state health departments or,
- Assist patients unaware of qualified status for health benefits
 - Typically through emergency Medicaid coverage
- Public hospitals not funded through the state ultimately must pay for patients unable to obtain coverage- these costs typically made up through “disproportionate payment system”
- Many 2nd line drugs provided free through Patient Assistance Programs i.e. Lilly Cares

US Table of Contents

- TB Control in the US
- Procurement and distribution of TB Drugs in the US
- Value and Volume of the US TB Market
- Appendix

A variety of payers are involved in negotiating contracts directly with manufacturers for TB meds

Payer	Customers	Negotiation	Price
Federal Government	Federally covered entities (i.e. Federal Prisons, state clinics, VA hospitals...)	Typically bidding process- fed price level is set at or below the "best price" manu offers to commercial plans Manufacturers must place bid with that price or lower	Federal Supply Schedule Price Veteran's Association FSS price 340 B public health rate
State Government	Medicaid	States negotiate separately or in small groups with manu to obtain rates at/below the "best price" for drugs on their preferred drug list	Medicaid Rate
Pharmacy Benefit Managers	Health Plans, Hospitals, Retail Pharmacy	Use member size to leverage volume power with manufacturers to obtain lower rates Formularies are used to increase negotiating power	Typically obtain access or performance based rebate at years end Around WAC*
Health Plans	Self-employed, hospitals, LTC, retail pharmacy, employers, employees	Use member size to leverage volume power with manufacturers to obtain lower rates Formularies are used to increase negotiating power	Typically obtain access or performance based rebate at years end Around WAC*
Group Purchasing Organization	Small hospitals or retail pharmacies	Use size of hospital base, patient volume, and formulary access to leverage negotiation power	Volume based discounts for formulary access Around WAC*

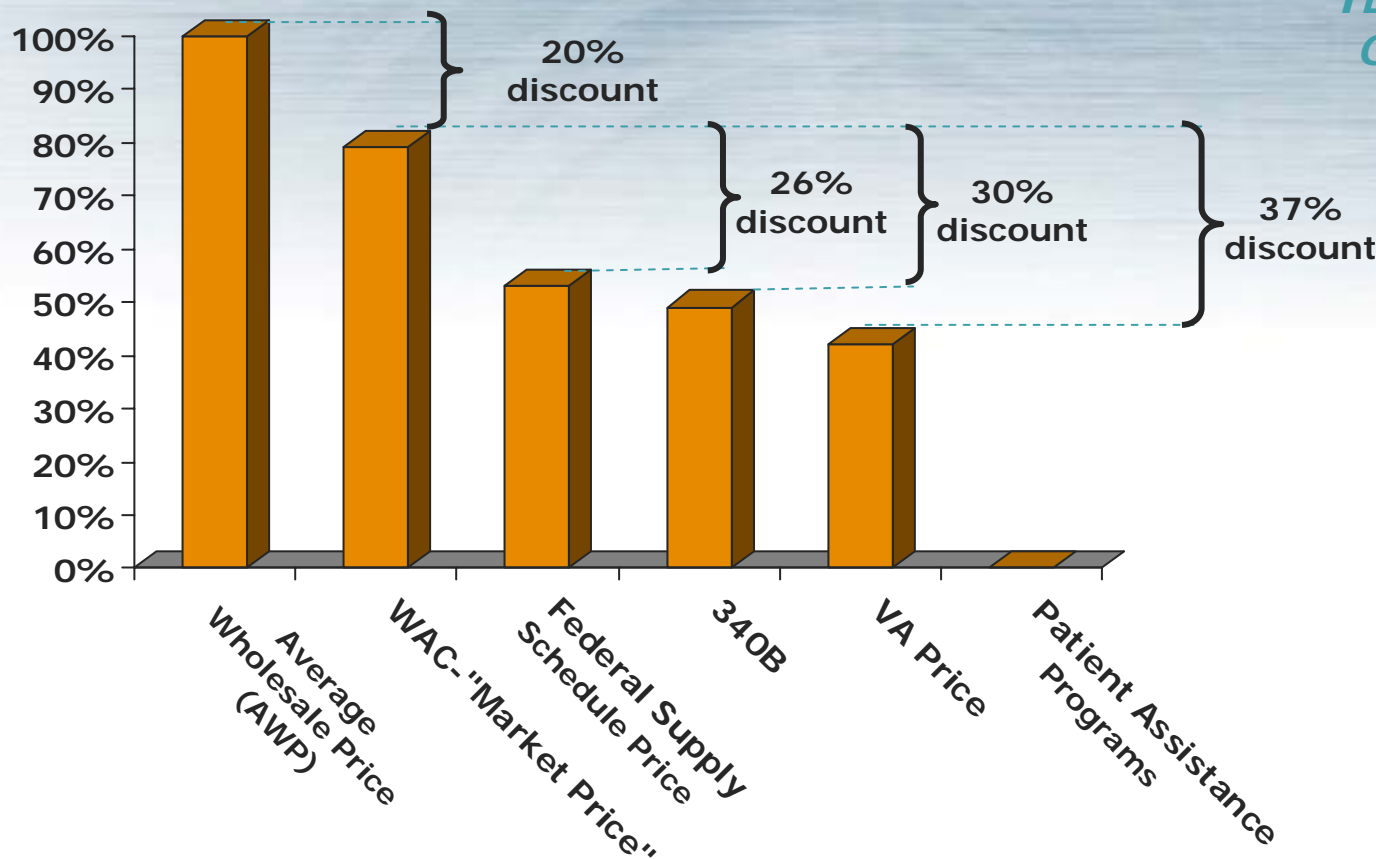
Source: IMS Research

*WAC stands for Wholesaler Acquisition Cost and is typically set at 20% below Average Wholesale Price



There are ultimately a range of costs for agents across the different settings

ILLUSTRATIVE OF BRANDED AGENTS



The industry standard sets Wholesaler Acquisition Cost (WAC) at 20% below Average Wholesale Price (AWP) however the AWP is only a published price used to negotiate discounts and is never the actual acquired price

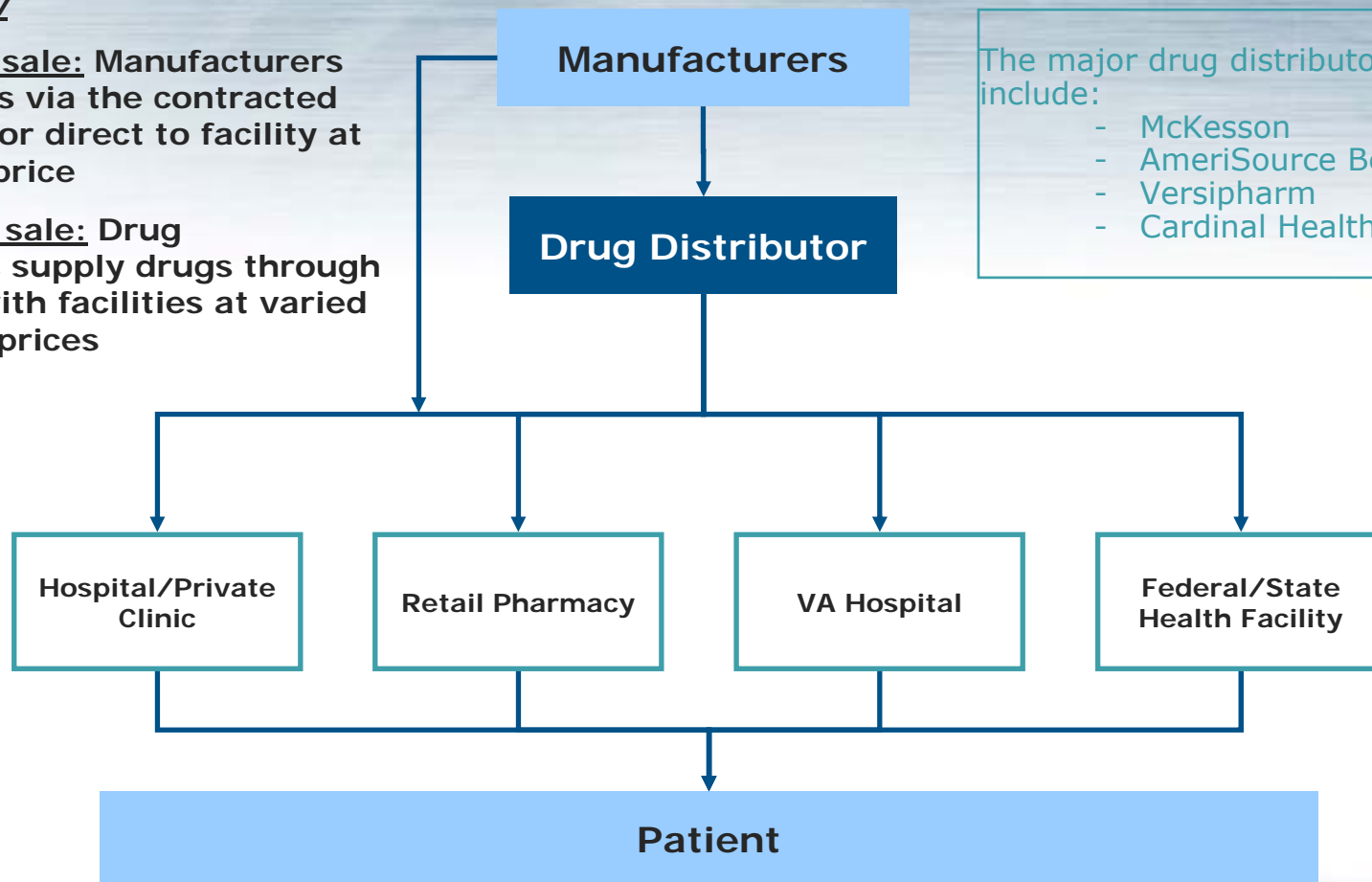
Source: <http://www.nfprha.org/pac/factsheets/340b.asp>; States and the 340B Drug Pricing Program, 2006 edition

The main distribution mechanism of TB drugs is identical to all other pharmaceutical products

Drug Flow

1st point of sale: Manufacturers supply drugs via the contracted distributor or direct to facility at the agreed price

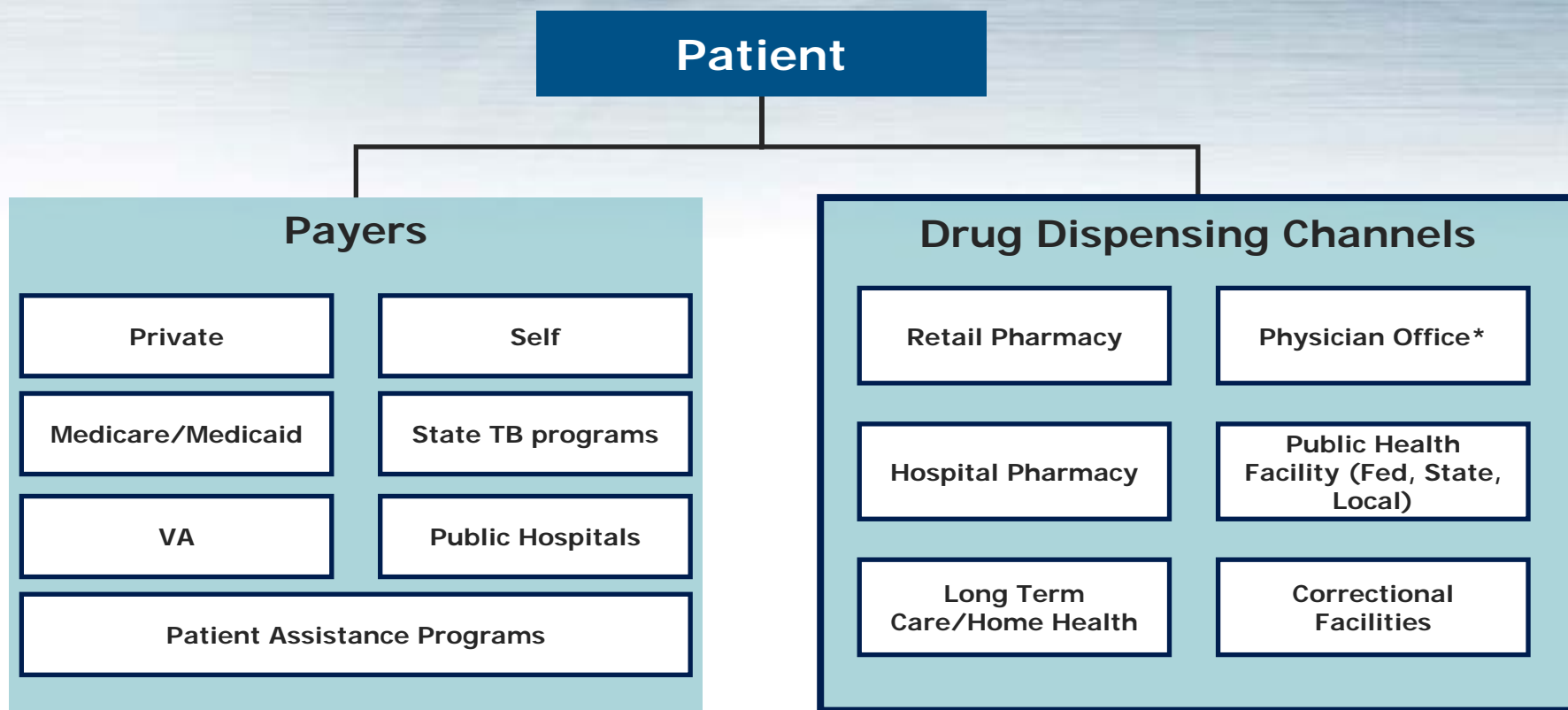
2nd point of sale: Drug distributors supply drugs through contracts with facilities at varied negotiated prices



The major drug distributors include:

- McKesson
- AmeriSource Bergen
- Versipharm
- Cardinal Health

TB meds are acquired and dispensed through numerous channels to insured and uninsured patients



**Injectables only*

Source: Interviews

All public/private hospitals and pharmacies typically acquire drugs at the determined “market price”

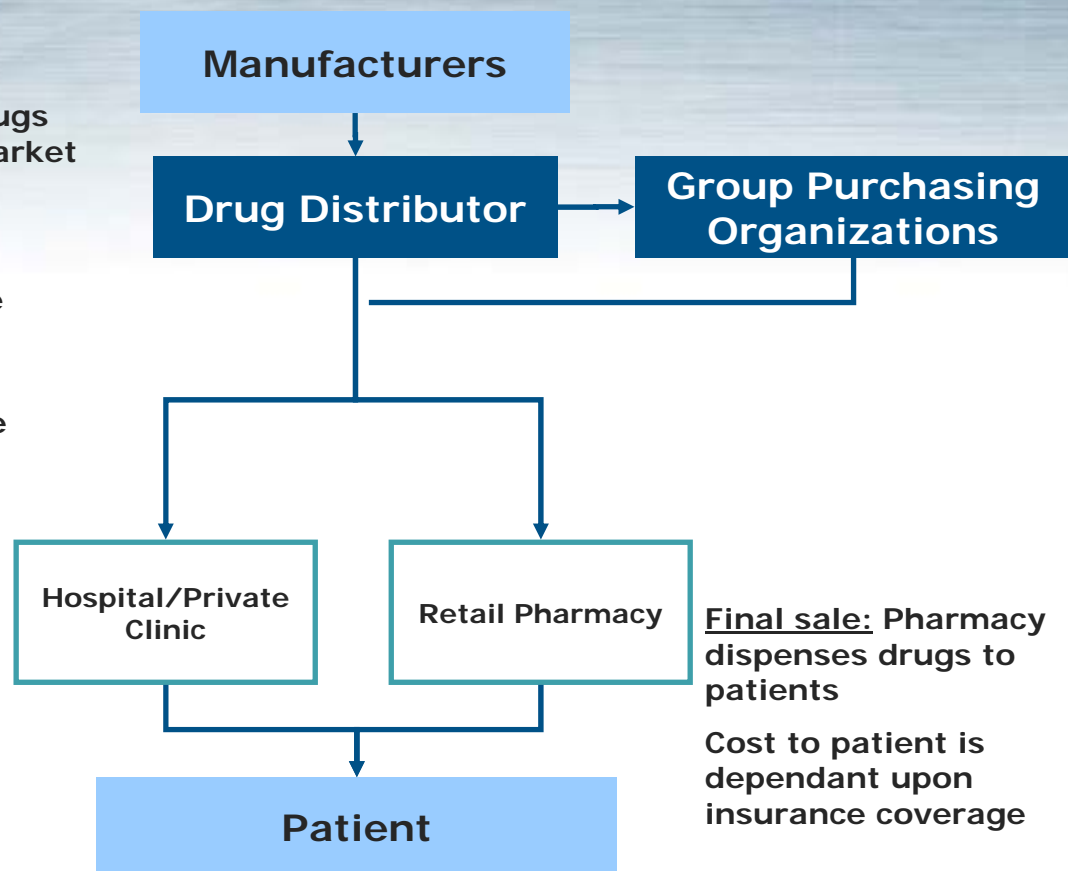
Drug Flow: Public/Private Hospitals

1st point of sale: Manufacturers supply drugs at Wholesaler Acquisition Cost (WAC)- “Market Price” to distributors

2nd point of sale: Hospital/Pharmacy Acquisition Cost is typically WAC +% price

Final sale: Drugs administered in hospital inpatient fall under the hospital DRG (case rate) at no direct cost to patient

Drugs dispensed in outpatient pharmacy where cost to patient is dependant on insurance coverage



Source: Kaiser; Follow the Pill- Understanding the US Commercial Pharmaceutical Supply Chain, interviews

Other entities are able to obtain drugs at the federal 340 B price, typically a 30% discount to WAC

What 340 B is

- A discounted drug program offering significant savings on outpatient drugs to specific federally funded "covered entities" serving the most vulnerable patient populations

How it works

- Manufacturers with drugs covered by the Medicaid program provide discounts on covered drugs purchased by "covered entities"
- The amount discounted is calculated using rebate formulas specified in OBRA '90
- Agreement prevents manufacturers from charging more than the 340B price regardless of procurement mechanism

Who it applies to

- **8,900 eligible covered entities participate including:** community health centers, non-profit disproportionate share hospitals owned by or under contract with state or local government, federally qualified health centers (FQHC), public housing primary care clinics, homeless clinics, and several others...

Source: <http://www.nfprha.org/pac/factsheets/340b.asp>;
States and the 340B Drug Pricing Program, 2006 edition

These entities include state and municipal health departments who then distribute free TB meds

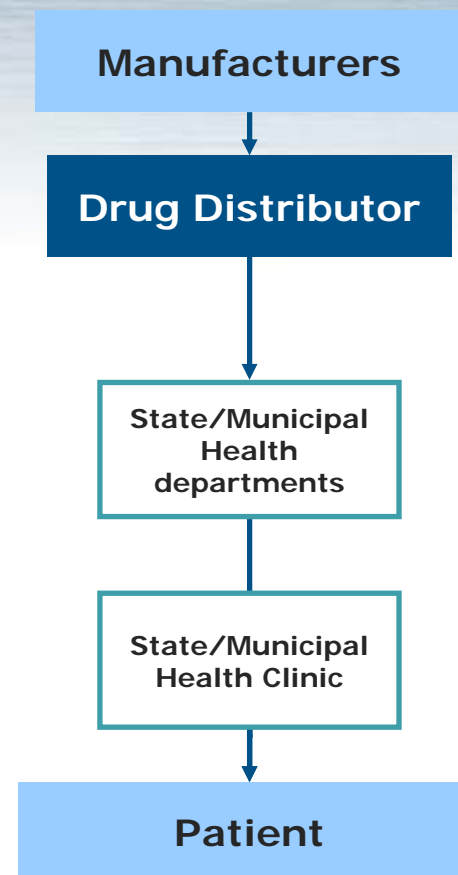
Drug Flow: State/Municipal Health Clinic

1st point of sale: Manufacturers supply drugs at 340 B price to all federally funded “covered entities”- typically through a major wholesaler

2nd point of sale: State health departments and clinics are able to acquire drugs at discounted rate

Final sale: These facilities provide drugs free of cost to their patients –typically dispensed on a monthly basis

Some facilities receive additional reimbursement through patient private and government insurance



The process of drug procurement and distribution can differ across states

Illustrative

State	Drug Procurement	Drug Distribution
California	<p>State does not procure any drugs- cities and counties are responsible for procuring and distributing own drugs</p> <p>Cities qualified for 340B price may procure drugs at this rate</p>	<p>Counties and cities have their own separate procurement mechanism</p> <p>Distributed directly to city or county clinics</p> <p>Typically maintain 3 month buffer stock in city/county health department</p>
Florida	<p>State procures drugs from one wholesaler based on bidding process</p> <p>Uses 340 B public health drug rate</p>	<p>State has central procurement mechanism</p> <p>Drugs are ordered monthly based on historical ordering patterns and stored in Tallahassee warehouse with 3 month buffer stock</p> <p>Distributed directly to state/locally funded health care facilities – for smaller counties without a pharmacy- drugs are mail ordered from central health dept</p>
New York- NYC	<p>NYC procures drugs through multiple wholesalers and repackaging suppliers through bidding process</p> <p>Uses 340 B public health drug rate</p>	<p>City has central procurement mechanism</p> <p>City Health Department order drugs on a bi-weekly basis to maintain adequate stock and distributes directly to local City TB clinics and community based organizations: 3-6 month buffer stock required depending on drug</p>
Texas	<p>State procures directly though one wholesaler through bidding process</p> <p>Uses 340 B public health drug rate*</p>	<p>State has central procurement mechanism</p> <p>Distributed through electronic system PIC (pharmacy inventory center) to local or regional health clinics- replenished based on need- required to maintain 3 month buffer stock</p>

*340 B Public Health drug rate is a discounted drug rate, based on negotiations between the federal government and manufacturers, that is available to federally funded “covered entities”

Source: Interviews

VA hospitals and federal prisons also receive TB drugs at a discount through the Federal Supply Schedule contracts

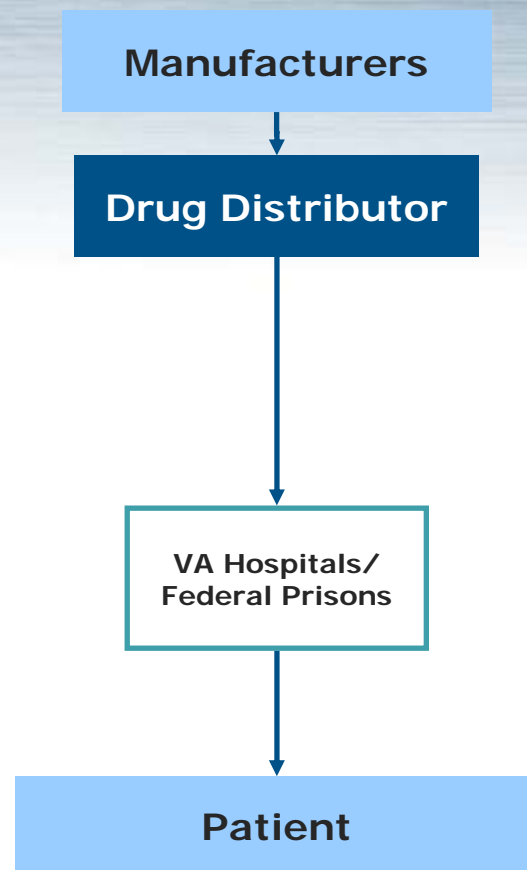
Drug Acquisition

1st point of sale: Qualified Manufacturers supply drugs at Federal Supply Schedule price to distributors (VA typically obtain a deeper discount than typical FSS)

2nd point of sale: VA Hospitals and Federal Prisons then obtain these products at the discounted price from wholesalers

Final sale: VA Hospitals dispense all drugs for free to patients that are service connected

Federal prisons provide drugs for free to inmates



US Table of Contents

- TB Control in the US
- Procurement and distribution of TB Drugs in the US
- **Value and Volume of the US TB Market**
- Appendix

There were several key data sources and assumptions incorporated into the TB market calculations

- **Data Sources:**

- NSP Sales Data: National Sales Perspective
 - Calculated through total prescriptions sold through manufacturers or wholesalers to each of the defined channels
 - Cost is based on the acquisition cost for the channel
- NPA Sales Data: National Prescription Audit
 - Provides total extended units based on a prescription audit capturing retail, LTC, and mail order pharmacies
- NDTI data: National Disease and Therapeutic Index
 - Provides % of each drug's prescription for TB use vs. prescriptions for all other use
 - Percentages were then applied to total NSP and NPA values

- **Topline Assumptions:**

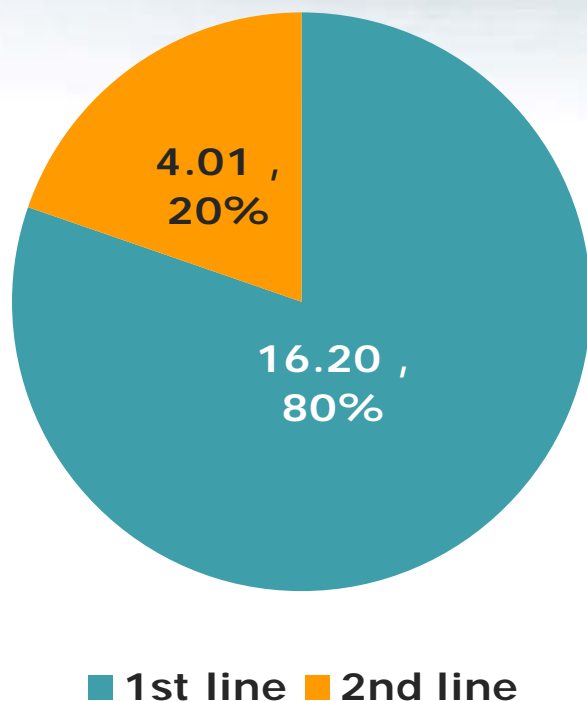
- NSP value data is based on acquisition cost for the channel (e.g., hospital/pharmacy/clinic), this would include any markups from the wholesaler. In order to align cost with the WAC price, a 10% markup was removed from the topline IMS figure
- In order to avoid overstatement of each product's use in TB, NDTI prescription % was applied to both the value and volume numbers for all TB meds

- **Bottom up Assumptions**

- Latent TB patients were provided by a quarterly report from the CDC reporting total states Latent TB cases completing treatment (only 75% reporting) – however it has been greater than 10 years since CDC collected these quarterly reports
- Public price utilized Florida and Texas 340 B Prices while Private price was stated at WAC pricing
- Included 85% completion and 10% re-treatment rate for 1st line
- Most facilities maintain at least a 3 month buffer stock for 1st line drugs and a 1-1½ month for 2nd line drugs that would be included in the total IMS value and volume. In order to align the top down and bottom up calculations a 25% buffer stock was added to the final 1st line bottom up value and a 10% buffer stock was added to the final 2nd line bottom up value figure

The total US market is valued at approximately 20.21 M USD, the majority of which is 1st line products

Total TB Market Value 2005
(Approximately 20.21M USD)

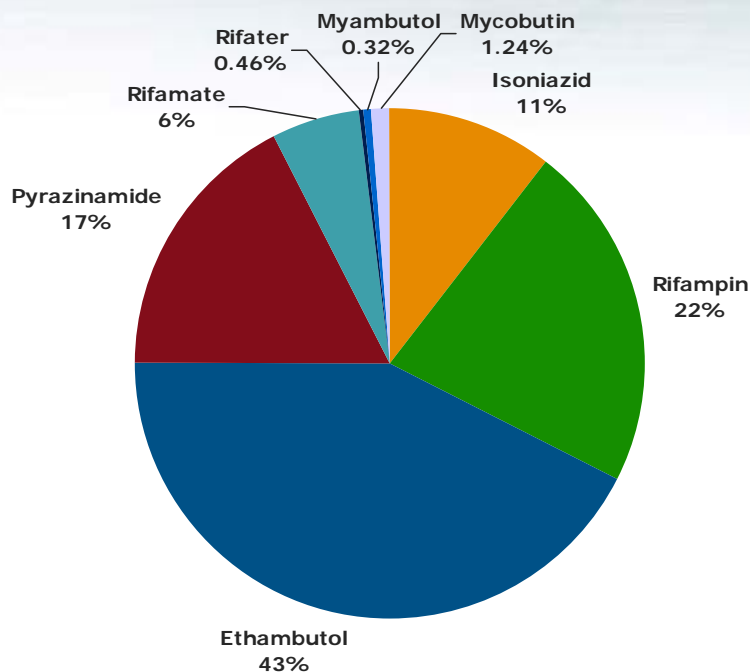


A predominantly first line market:

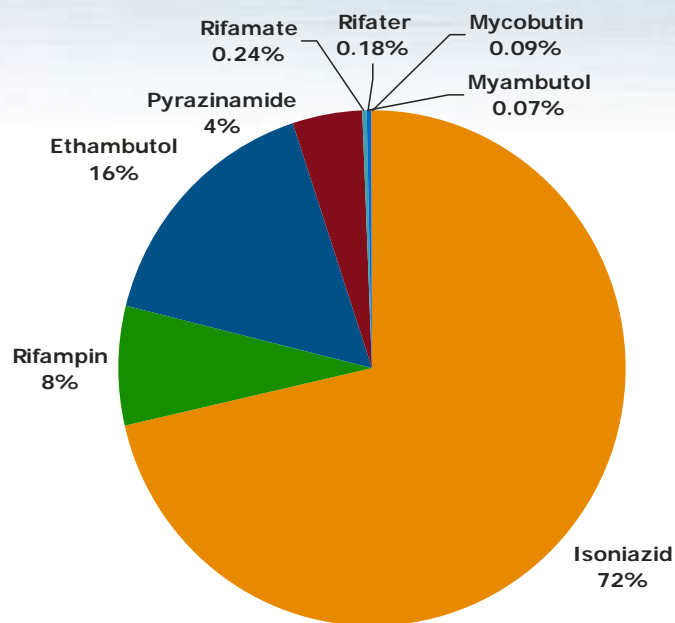
- The majority of TB cases are non-resistant with a total recorded 14,093 TB patients as of 2005
- Although MDR-TB represents a growing concern, it only affects about 1% of all TB cases, total of 128 patients in 2004
- The high costs of MDR-TB drugs results in a disproportionate value vs. first line drugs

The \$16M USD 1st line market is split between a range of products

Total 1st Line TB Market Value by Drug in 2005 (16.2M USD)



Total 1st Line TB Market Volume by Drug in 2005 (24.3M units)*

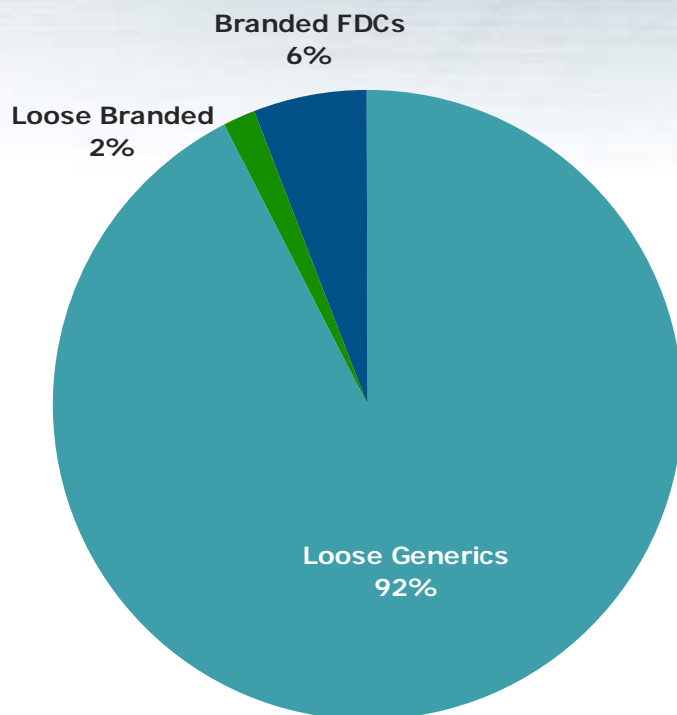


Note: Only covers retail market- does not include clinics or hospitals dispensing drugs
Volume refers to the number of units (e.g. tablets) dispensed*

Source: NSP/ NDTI -IMS Data

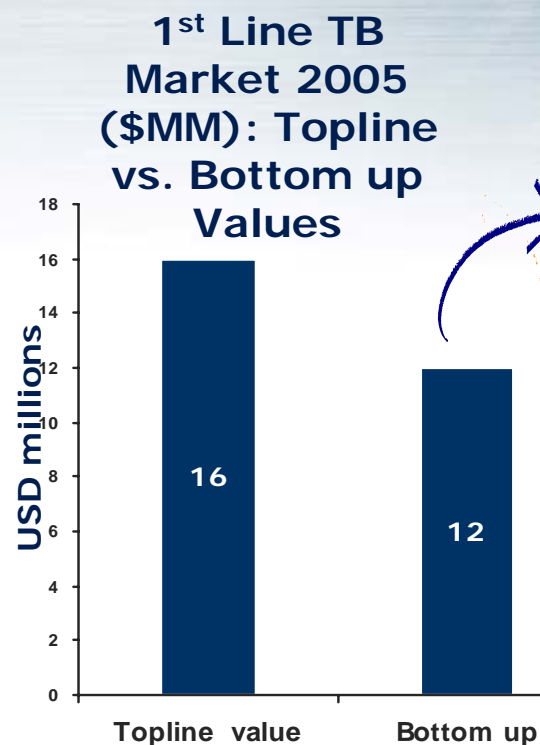
Within the 1st line market, the US relies on loose generic products

Total 1st Line TB Market Value by Drug in 2005 (16.2M USD)



- FDCs only account for 6% of the total market value – \$968 K USD
 - Rifamate (combination of rifampicin and isoniazid) accounts for \$893 K USD and 92% of FDC sales
 - Rifater (combination of rifampicin, isoniazid and pyrazinamide) – accounts for \$75K USD and 8% of FDC sales mainly because of its cost
- Physicians in the US tend to veer away from the FDCs for two reasons:
 - Compliance is not a high concern
 - Although FDCs are cheaper most patients are covered through insurance or the government and therefore cost is less of a problem

Although the bottom up calculations demonstrate a market size of 12.0 M...



Bottom Up Calculations

	Total Patients	Public Cost/Regimen (USD)	Private Cost/Regimen (USD)	Total Public Value	Total Private Value	Total
First line						
IR	123	\$188.60	\$586.97	\$13,798	\$29,474	\$43,273
IRZ	526	\$274.88	\$747.62	\$85,807	\$160,177	\$245,985
IRZE	7575	\$409.79	\$966.19	\$1,840,857	\$2,978,937	\$4,819,794
RZE- I resistant	838	\$830.40	\$1,665.74	\$539,798	\$737,032	\$1,276,830
IRE- ss negative	4245	\$364.51	\$933.13	\$917,681	\$1,612,381	\$2,530,062
Latent						
INH	14904	\$7.17	\$10.49	\$63,351	\$63,631	\$126,982
RIF	2630	\$55.61	\$176.02	\$173,459	\$376,842	\$550,301
Buffer Stock						
25%				\$908,688	\$1,489,619	\$2,398,306
Total				\$4,543,439	\$7,448,093	\$11,991,532

Public Price: Based on 340B Price obtained through Fla State Health Department and Texas State Health Department
 Private Price: MedImmune PriceRx- Based on WAC Prices

*See appendix for calculations of prices

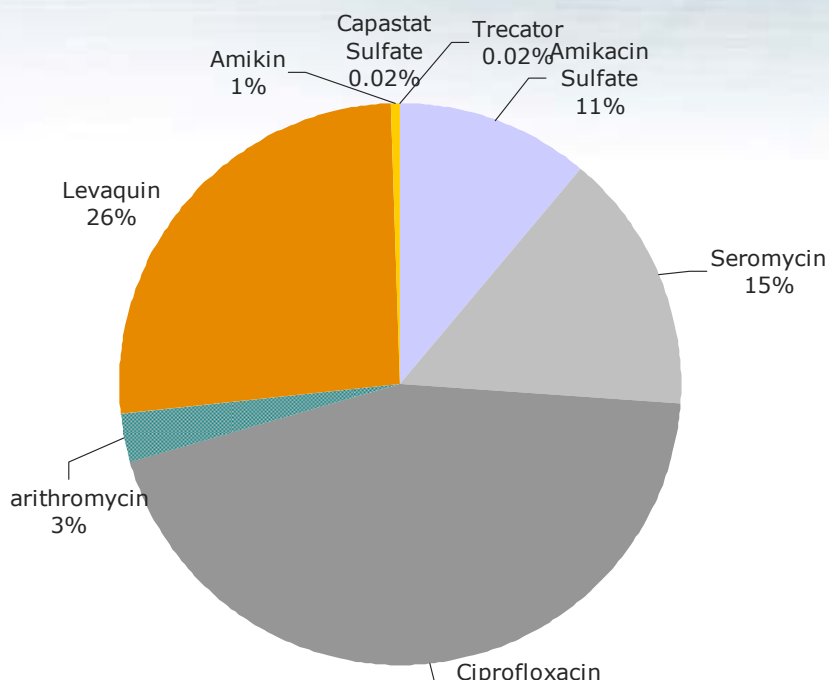
Source: DxTx: Interviews, DHHS report, Kenneth Castro Letter April 6, 2006; Kenneth Castro; Reported Tuberculosis in the United States 2004 - CDC Surveillance Report

...the discrepancy can be explained by several factors

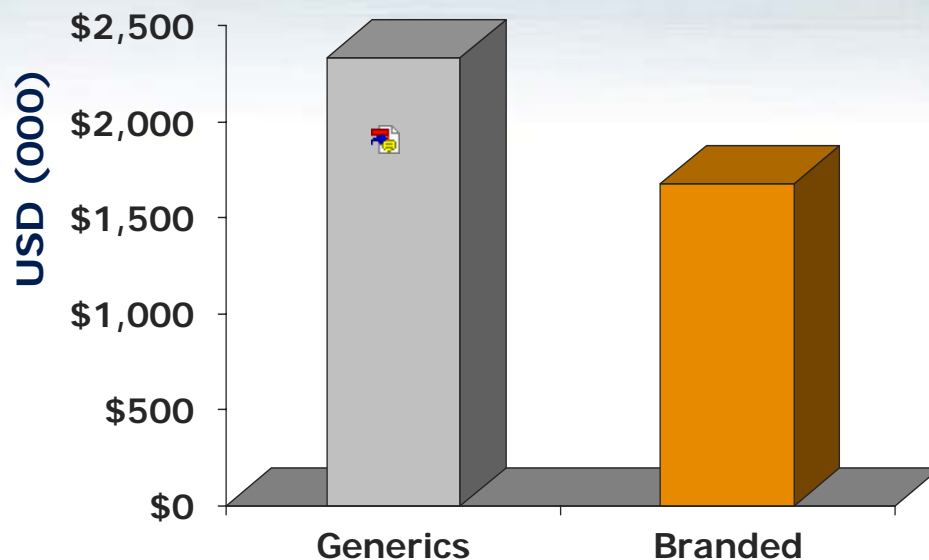
- In calculating bottom up value, we assumed an average weight of 55-60kg per person
 - This could be less than the average weight of patients and therefore is underestimating the dosing size and ultimately the total units of TB meds prescribe
- The bottom up approach does not account for treatment regimens deviating from the standardized guidelines
- Total latent prescribing may be greater than accounted for due to the 10+ year period that Latent TB reports have been collected
- WAC prices were based on the average prices procured through Versapharm (distributor) which may slightly differ from the median price of the private market.
- Florida and Texas state health department prices were utilized for the 340 B rate; however this may not be the same exact rate across the public market

The 2nd line market is valued at \$4.01M USD, also driven primarily by generic products

Total 2nd Line TB Market Value by Drug in 2005 (4.01M USD)



Total 2nd Line TB Market Value by Brand (2005)



- Generics include: Amikacin Sulfate (443K), Ciprofloxacin(1.78MM), and Clarithromycin (111K)
- Levaquin remains the major branded agent making up 62% of branded agent value and 1.04 MM

*Note: PAS is not included in total top line value due to lack of data through IMS NSP channel
Seromycin was not adjusted down due to lack of prescribing data from NDTI and may be over-accounted for Source: NSP/ NDTI -IMS Data*

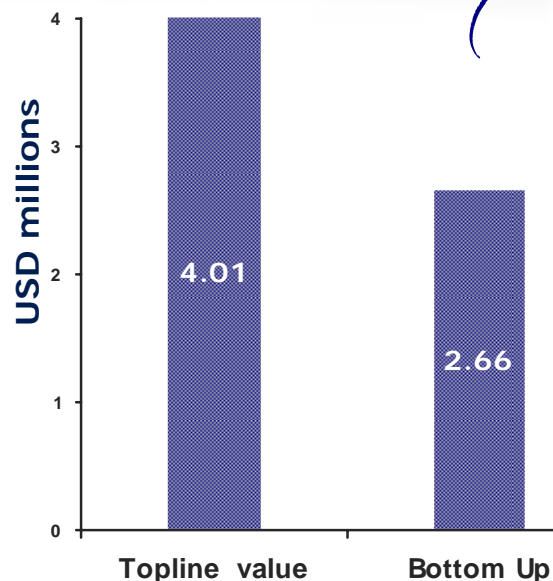
* Data was not available for all 2nd line drugs used in this country. Drugs listed do not comprise full 2nd line treatment regimen used in this country.

US Table of Contents

- TB Control in the US
- Procurement and distribution of TB Drugs
- Value and Volume of the US TB Market
- Appendix

Topline value figures and bottoms-up calculations suggest that the 2nd line TB market value is 2.66 to 4.01M USD

2nd Line TB Market 2005 (\$MM): Topline* vs. Bottom Up Values



Bottom Up Calculations

	Total Pts	Public Cost/Regimen (USD)	Private Cost/Regimen (USD)	Total Public Value	Total Private Value	Total
MDR-TB						
EZ+ Capreo, Ethio, Leva	115	\$12,744	\$21,164	\$870,580	\$992,322	\$1,862,901
4 drug Resistant						
Capreo, Ethio, Cyclo, Leva	13	\$13,698	\$21,624	\$103,974	\$112,653	\$216,628
XDR-TB						
Patient specific	6	\$30,000	\$45,000	\$227,712	\$109,714	\$337,426
Buffer Stock						
10%				\$120,227	\$121,469	\$241,695
Total				\$1,322,493	\$1,336,158	\$2,658,650

Note: PAS is not included in total top line value due to lack of data through IMS NSP channel
Seromycin was not adjusted down due to lack of prescribing data from NDTI and may be over-accounted for

*See appendix for calculations of prices

Private Price: MedImmune PriceRx- Based on WAC Prices

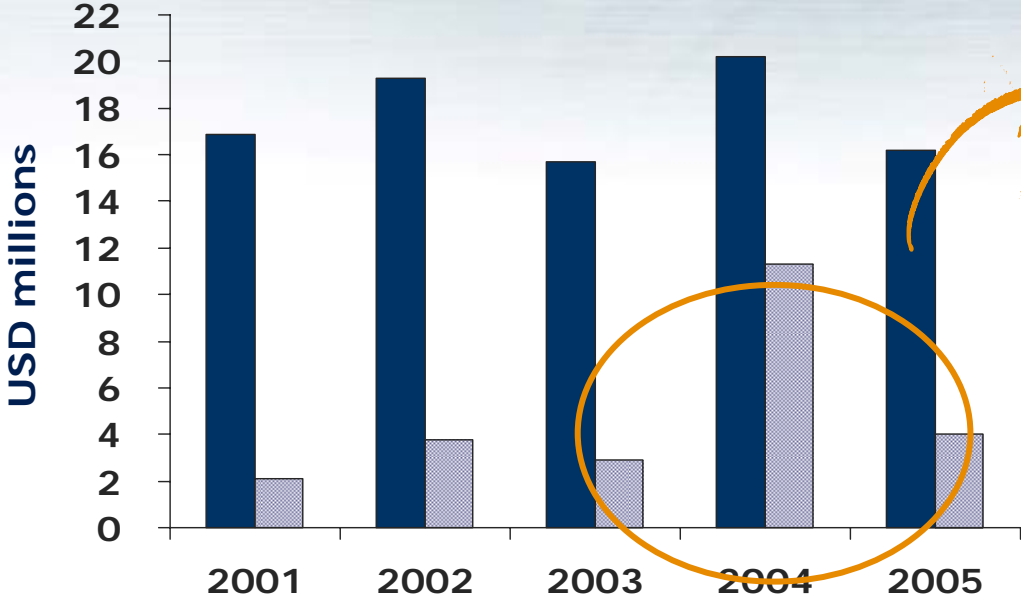
XDR-TB: U.S. Tuberculosis Rate at All-Time Low; California Healthcare Foundation 03/24/06

Source: DxTx: Interviews, Kenneth Castro; Reported Tuberculosis in the United States 2004 - CDC Surveillance Report
Public Price: Based on 340B Price obtained through Fla State Health Department and Texas State Health Department



Both 1st and 2nd line products have fluctuated over the past few years with a drastic 2nd line increase in 2004

Sales of 1st and 2nd line TB Drugs (2001-2005)



Ciprofloxacin	Total Extended Units	Total Value (USD)	Ave. Cost/Unit
2003	12,364,973	\$592,993	.048
2004	31,346,705	\$9,396,818	.300
2005	47,490,808	\$1,779,543	.038

The significant increase in 2004 second line value is likely due to the launch and initial high utilization of ciprofloxacin upon genericisation in late 2003 and the rapid drop in price with increased competition

Source: NSP/ NDTI -IMS Data

Note: PAS is not included in total top line value due to lack of data through IMS NSP Channel Seromycin was not adjusted down due to lack of prescribing data from NDTI and may be over-accounted for



Appendix: Price per Patient Calculations, 1st line Loose Drugs

First Line

	Drug	Formulation	Dose	Daily Units	Total Days Initial Phase	Total Days Continuation Phase	Total Units	Cost	
								340 B	WAC
First Line-Smear Positive	Isoniazid	300 mg tab	300 mg	1	56	128	184	\$5.89	\$8.62
	Rifampin	300 mg capsule	600 mg	2	56	128	368	\$182.71	\$578.35
	Pyrazinamide	500 mg tab	1500 mg	3	56		168	\$86.28	\$160.66
	Ethambutol	400 mg tab	1200 mg	3	56		168	\$134.91	\$218.57
	Total								\$409.79
INH resistant	Rifampin	300 mg capsule	600 mg	2		168	336	\$166.82	\$528.06
	Pyrazinamide	500 mg tab	1500 mg	3		168	504	\$258.84	\$481.98
	Ethambutol	400 mg tab	1200 mg	3		168	504	\$404.73	\$655.70
	Levaquin*	500 mg tab	1000mg	2		168	336	\$1,705.74	\$3,301.54
	Total								\$2,536.13
First Line-Smear Negative	Isoniazid	300 mg	300 mg	1	56	168	224	\$7.17	\$10.49
	Rifampin	300 mg	600 mg	2	56	168	448	\$222.43	\$704.08
	Ethambutol	400 mg	1200 mg	3	56		168	\$134.91	\$218.57
	Total								\$364.51

**Based on recommended dosing in CDC Treatment Guidelines
Assumes daily dosing for 60kg patient*

Appendix: Price per Patient Calculations, Latent and 2nd line

Latent TB

	Drug	Formulation	Dose	Daily Units	Total Days	Total Units	Cost	
							340 B	WAC
Latent	INH	300 mg tab	300 mg	1	224	224	\$7.17	\$10.49
	RIF	300 mg tab	600 mg	2	112	224	\$111.22	\$352.04

Second Line

	Drug	Formulation	Dose	Daily Units	Total Days	Total Units	Cost	
							340 B	WAC
4 Drug Resistance	Capreomycin	1g vial	1g	1	364	364	\$6,129.76	\$9,296.56
	Ethionamide	250 mg	500 mg	2	364	728	\$1,480.61	\$2,249.52
	Cycloserine	250 mg	500 mg	2	364	728	\$2,392.03	\$2,924.74
	Levaquin	500 mg	1000 mg	2	364	728	\$3,695.76	\$7,153.33
	Total							\$13,698.16
INH/Rif Resistance	Capreomycin	1g vial	1g	1	364	364	\$6,129.76	\$9,296.56
	Ethionamide	250 mg	500 mg	2	364	728	\$1,480.61	\$2,249.52
	Ethambutol	400 mg	1200mg	3	364	1092	\$876.91	\$1,420.69
	Pyrazinamide	500 mg tab	1500 mg	3	364	1092	\$560.83	\$1,044.28
	Levaquin	500 mg	1000 mg	2	364	728	\$3,695.76	\$7,153.33
Total							\$12,743.87	\$21,164.38
XDR-TB		multiple drugs - up to 250,000 per patient for 2 yrs					\$30,000.00	\$45,000.00

*Based on recommended dosing in CDC Treatment Guidelines
Assumes daily dosing for 60kg patient

Appendix: Interviewed Stakeholders

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