THE ACCESS AND DELIVERY PARTNERSHIP

New Health Technologies for TB, Malaria and NTDs

The impact of WTO TRIPS Agreement on access to medicines

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UNDP

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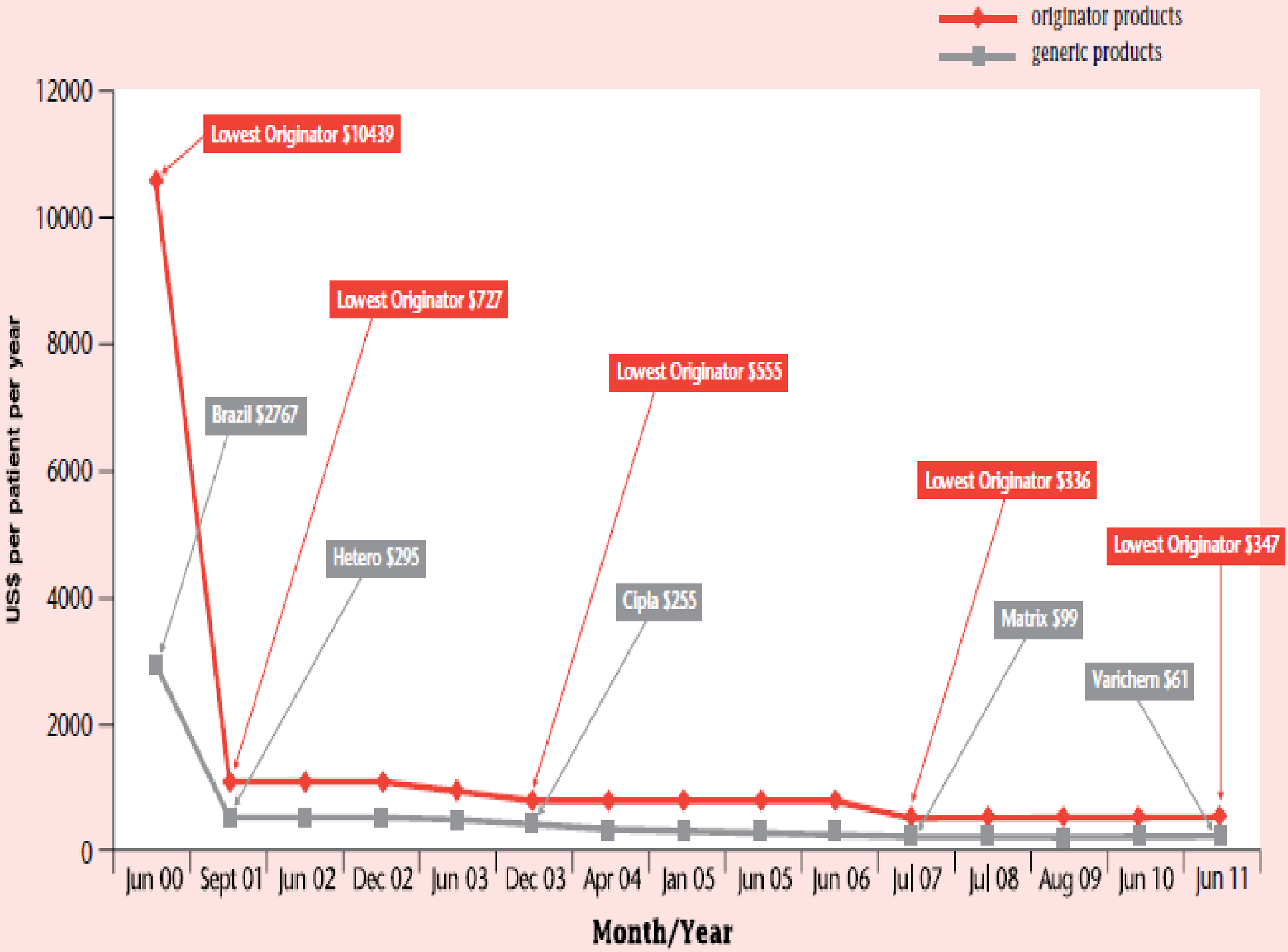
New Health Technologies for TB, Malaria and NTDs

Presentation Outline

- TRIPS, Doha and access to medicines
- What have we learnt?
- Future challenges and emerging issues
- An enabling environment for innovation and access
- Introducing the Access and Delivery Partnership


originator products
generic products
12000
10000
8000
6000
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2000
0
US$ per patient per year
Lowest Originator $10439
Lowest Originator $727
Lowest Originator $555
Lowest Originator $336
Lowest Originator $347
Brazil $2767
Hetero $295
Cipla $255
Matrix $99
Varichem $61
Jun 00
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Aug 09
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Jun 11
Month/Year

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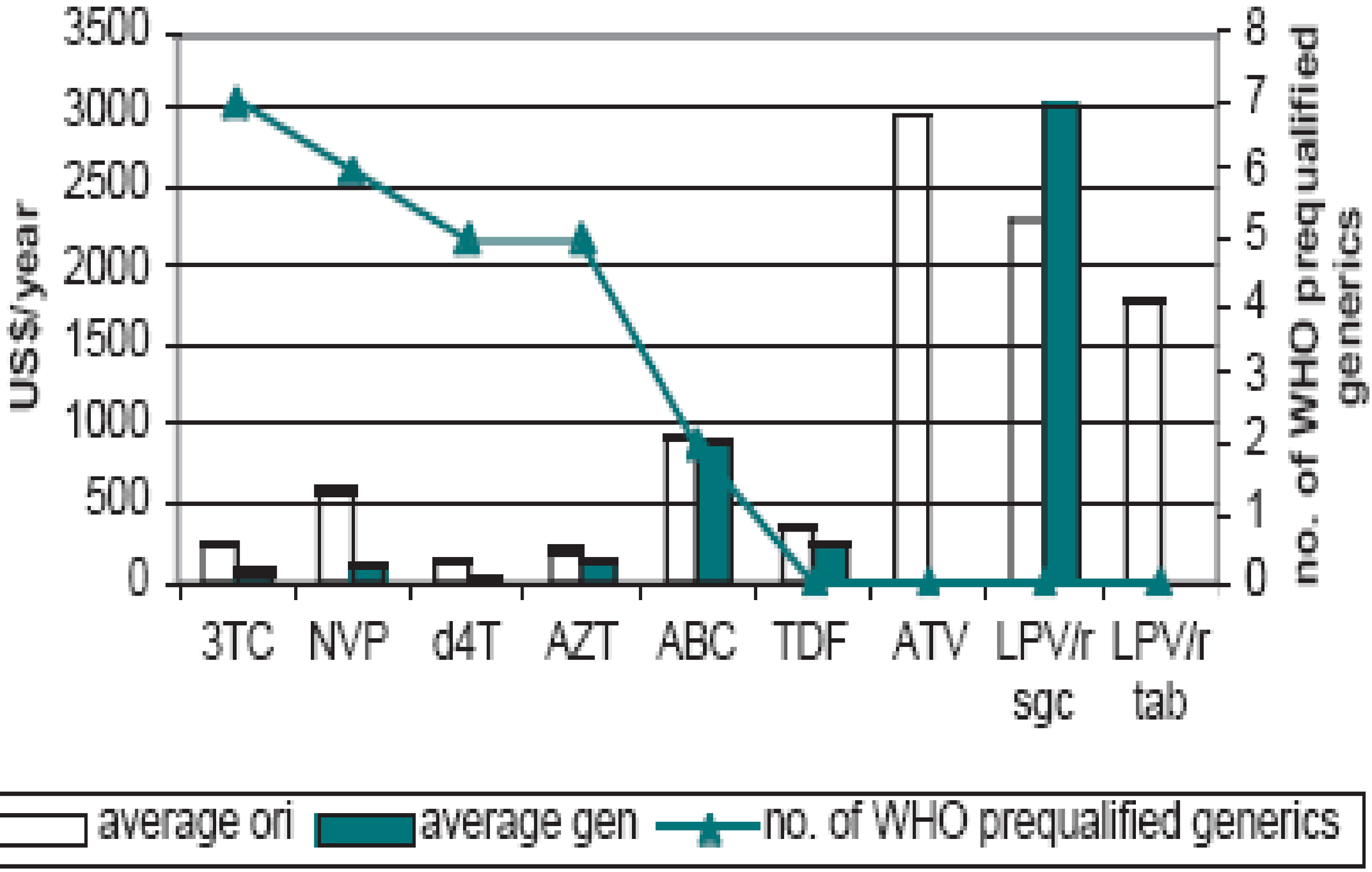
Patents and prices

- Cost of ARV treatment in 2000 = US$10,439 per year
- BUT in 2001, Indian company, Cipla, introduced generic ARVs at US$350 a year
- Introduction of generic ARVs have reduced prices up to 99% = $65 a year
- 22-fold increase in global ARV coverage has been possible due to competition from generic medicines
- **Introduction of generic medicines → market competition → reduced medicine prices**

The competition effect:
Prices drop with generic introduction



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Generic medicines

- The case of India demonstrates how strategic use of flexibility in TRIPS Agreement contributed to development of India's pharmaceutical industry
- Transition period under TRIPS allowed India not to grant patents for pharmaceutical products until 2005 ➔ permitted Indian manufacturers to produce **generic medicines**
- The 2005 transition period is an example of a flexibility available under TRIPS Agreement
- LDCs have another important flexibility – no pharmaceutical patents until 2016; no TRIPS implementation until 2021

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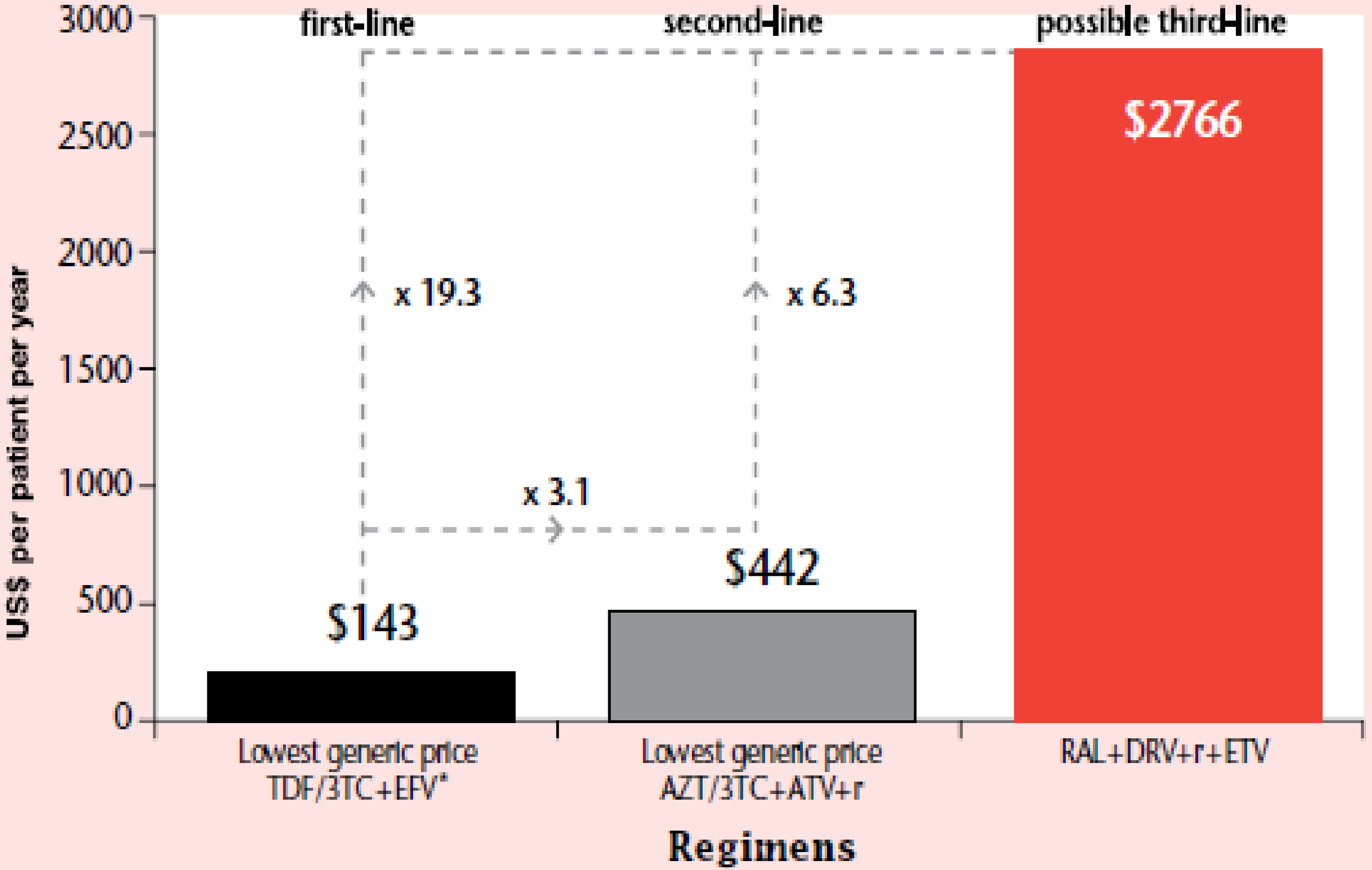
Generic competition

- The ability to produce and supply generic medicines will be limited in the future, as TRIPS Agreement implementation requires patent protection for pharmaceutical
- Majority of new medicines are now patented in many countries, including those with capacity to produce affordable ARVs and other generic medicines, such as India, Thailand and China
- **Use of TRIPS flexibilities will be crucial to ensure continued ability to produce generic medicines and ensure access to affordable medicines**

Price comparisons of first-line, second-line and possible third-line



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India's Patent Act: Impact on generic production and access

- India supplies over 80% of generic ARVs used in LMICs
- Patents on new medicines will affect ability of generic manufacturers to produce future ARVs and medicines to treat NCDs
- Drug resistance requires switch to second generation ARVs: some under patent 3.4 times more expensive, 3rd generation up to 23.4 times more expensive
- Exporting countries like India will need to maximise use of TRIPS Flexibilities
- Importing countries will need to take full advantage of safeguards and flexibilities
- This is especially important given eventual shift to 2nd & 3rd generation ARVs

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India's Patent Act: Impact on exports and patent grants

3520	1	0
Pharmaceutical patents granted in India, 2007-2012 (*Source:* Indian Patent Office)	Compulsory license for a German pharmaceutical product	Compulsory licenses for U.S. pharmaceutical Products

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Doha Declaration on TRIPS and Public Health

- Backdrop of HIV/AIDS epidemic
- Legal challenges to developing countries legislation
  - South Africa: Pharmaceutical company challenge of amendment to Medicines and Related Substances Act (1997)
  - Brazil: US complaint to WTO Dispute Settlement on local working provision (2000)
- The culmination of debate at WTO, arising from developing country proposal to examine impact of TRIPS on access to medicines – WTO 4th Ministerial Conference in Doha, 14 November 2001

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The Doha Declaration

*"We agree that the TRIPS Agreement **does not and should not** prevent Members from taking measures to protect public health … we affirm that the Agreement **can and should be** interpreted and implemented in a manner supportive of WTO Members' right to protect public health and in particular, to promote access to medicines for all"*

- Clarification that TRIPS Agreement does not prevent WTO Members from taking measures to protect public health
  - Interpretative guide to TRIPS
  - Affirmation of right to use flexibilities in TRIPS
  - Expeditious solution for countries with insufficient or no manufacturing capacities
  - Extension of LDC transition period (now up to 2016)

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Policy options for affordable medicines

Import of medicines

- **Compulsory licence** = government grants a compulsory licence to allow a drug company to import from a foreign produce. Example: Drug company or distributor in Country A imports generic medicine from India under a CL.
- **Government use licence** = government is licensed to import from foreign producer for “public use”. Example: MOH in Country A imports generic medicine from Thailand under GU licence for use in public hospital.
- **Parallel importation** from a country where the branded medicine is sold at a cheaper price. Example: Patented drug X is sold for $10 a tablet in Country A but sold for $5 in Malaysia. If national law in Country A allows for parallel import, drug X can be imported into the country at the cheaper price.

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Policy options for affordable medicines

Domestic R&D and local production

- **Patentability standards** = to ensure grant of high-quality patents
- **R&D exception** = to allow for research and development on patented chemical compounds
- **Bolar exception** = allows preparation and testing of patented product for drug regulatory approval, so that generic medicine can be ready for approval by FDA once patent expires
- **Compulsory licence** = a drug company is granted a CL to manufacture generic version of patented medicine in the country and to sell the generic version on the private market
- **Government use licence** = government grants a GU licence to a drug company in Country A to manufacture generic for use in the public sector

Year(s)	Nation	National Income Group	Disease	Disease Group	Total Products	Outcome
2001 (2007)	Brazil	UMIC	HIV/AIDS	HIV/AIDS	2	CL/discount
2001	Brazil	UMIC	HIV/AIDS	HIV/AIDS	1	Discount
2001	Canada	HIC	Anthrax	CD	1	Discount
2001–2003	South Africa	UMIC	HIV/AIDS	HIV/AIDS	8	VL/discount/none
2001	United States	HIC	Anthrax	CD	1	Discount
2002	Egypt	LIC	Erectile dysfunction	NCD	1	CL
2003–2004	Malaysia	UMIC	HIV/AIDS	HIV/AIDS	3	CL
2003, 2007	Brazil	UMIC	HIV/AIDS	HIV/AIDS	1	Discount
2003	Zimbabwe	LIC	HIV/AIDS	HIV/AIDS	All	CL
2004	Mozambique	LDC	HIV/AIDS	HIV/AIDS	3	CL
2004	Zambia	LDC	HIV/AIDS	HIV/AIDS	3	CL
2005–2006	Argentina	UMIC	Pandemic flu	CD	1	VL
2005–2007	Brazil	UMIC	HIV/AIDS	HIV/AIDS	1	Discount
2005–2009	Brazil	UMIC	HIV/AIDS	HIV/AIDS	1	Discount
2005	Ghana	LIC	HIV/AIDS	HIV/AIDS	All	CL
2005	Indonesia	LIC	HIV/AIDS	HIV/AIDS	2	CL
2005	Taiwan	HIC	Pandemic flu	CD	1	VL
2006–2007	India	LIC	Cancer	NCD	1	None
2006 (2010)	Thailand	UMIC	HIV/AIDS	HIV/AIDS	1	CL
2007	Rwanda	LDC	HIV/AIDS	HIV/AIDS	1	CL
2007 (2010)	Thailand	UMIC	HIV/AIDS, CVD	HIV/AIDS, NCD	2	CL
2007–2008	Thailand	UMIC	Cancer	NCD	1	Discount
2007–2008	Thailand	UMIC	Cancer	NCD	3	CL
2010	Ecuador	UMIC	HIV/AIDS	HIV/AIDS	1	CL

Totals: 24 Episodes, 17 Nations, 40 Unique Drug-Nation Combinations +2 Categorical CLs. Years in parentheses indicate CL renewals.
CVD, cardiovascular disease.
doi:10.1371/journal.pmed.1001154.t001

Beall R, Kuhn R (2012) Trends in Compulsory Licensing of Pharmaceuticals Since the Doha Declaration: A Database Analysis. PLoS Med 9(1): e1001154. doi:10.1371/journal.pmed.1001154
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001154

Price impact of compulsory licences

Source: Global Commission on HIV and the Law (2012), UNDP

Country	Type of License and medicine	Impact on prices
Malaysia (November 2003)	Government-use order for the production of combination of generic stavudine + didonasine + nevirapine	Resulted in price reduction of 83%
Indonesia (October 2004)	Government-use order to locally manufacture generic lamivudine, nevirapine	Resulted in price reduction of 53.3%
Thailand (January 2007)	Government-use order to import or locally produce generic lopinavir/ritonavir	Projected price reductions of 80.2%
Brazil (May 2007)	Compulsory licence issued by Government to import generic efavirenz	71.8% price reduction
Ecuador (April 2010)	Compulsory license to import and, if necessary, locally produce generic ritonavir	Patent holder reduced price of branded medicine by 70%
India (March 2012)	Compulsory license to locally produce sorafenib tosylate to treat kidney cancer and liver cancer	Price set by Patent Controller will result in 97% reduction

Indonesia – Government use licence

- 2004: Indonesian Presidential Decree authorised local production of nevirapine and lamivudine
- 2013: Indonesian Presidential Decree authorising local production of 6 medicines to meet the availability and urgent need of the Antiviral and Antiretroviral Medicines for the treatment of Human Immunodeficiency Virus-Acquired Immune Deficiency Syndrome (HIV / AIDS) and Hepatitis B.

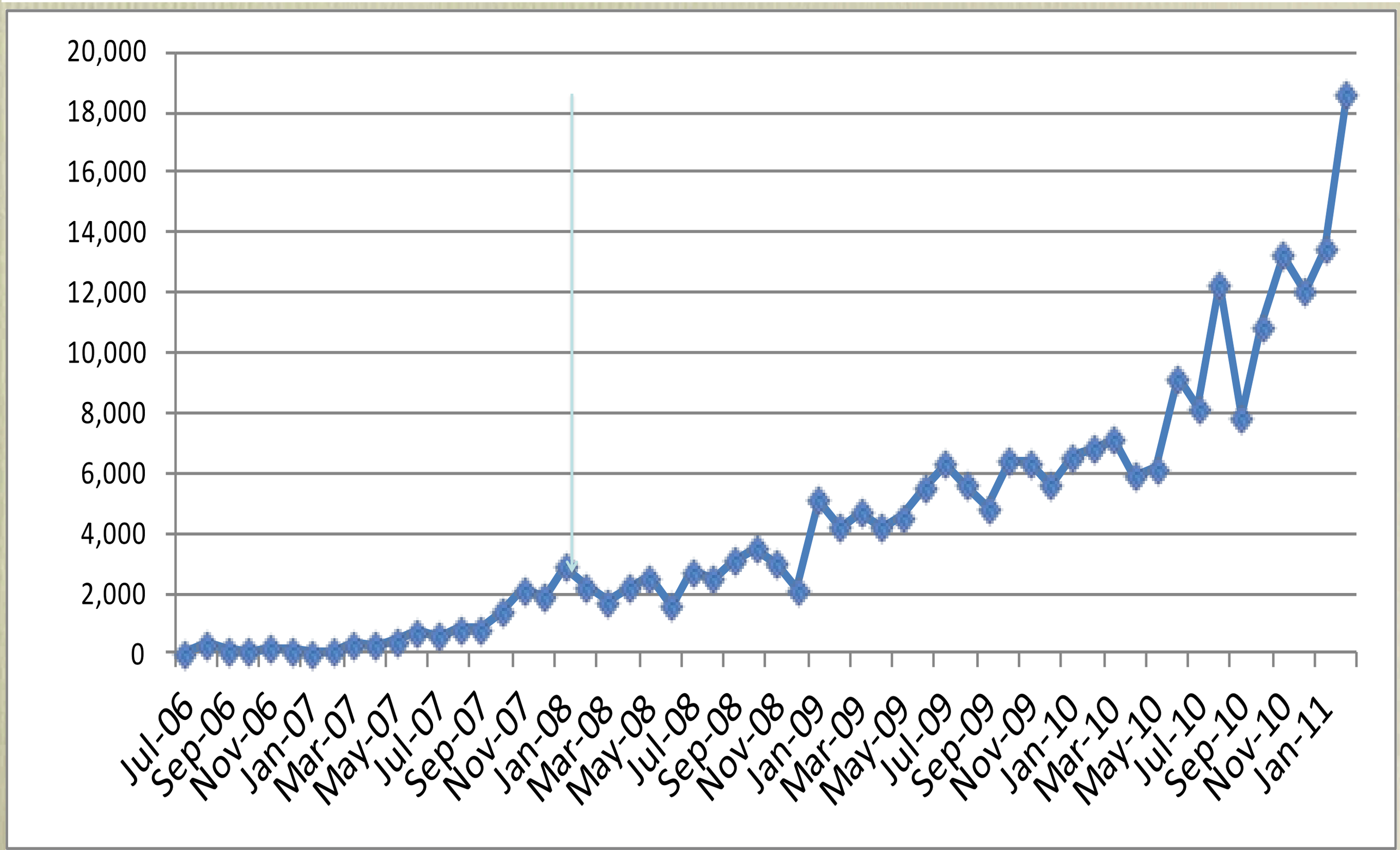
No	NAME OF ACTIVE SUBSTANCES	NAME OF PATENT HOLDER	PATENT NUMBER	TERM OF THE PATENT
1	Efavirenz	Merck & Co, INC	ID 0 005 812	Until the end term of the Patent , August 7, 2013
2	Abacavir	Glaxo Group Limited	ID 0 011 367	Until the end term of the Patent , May 14, 2018
3	Didanosin	Bristol – Myers Squibb Company	ID 0 010 163	Until the end term of the Patent , August 6, 2018
4	Combination of Lopinavir and Ritonavir	Abbot Laboratories	ID P 0023461	Until the end term of the Patent , August 23, 2018
5	Tenofovir	Gilead Sciences, Inc	ID 0 007 658	Until the end term of the Patent , July 23, 2018
6	Combination of Tenofovir and Emtrisitabin -Combination of Tenofovir, Emtrisitabin and Eyafirenz	Gilead Sciences, Inc	ID P0029476	Until the end term of the Patent , November 3, 2024

Comparison of originator vs. generic drug prices

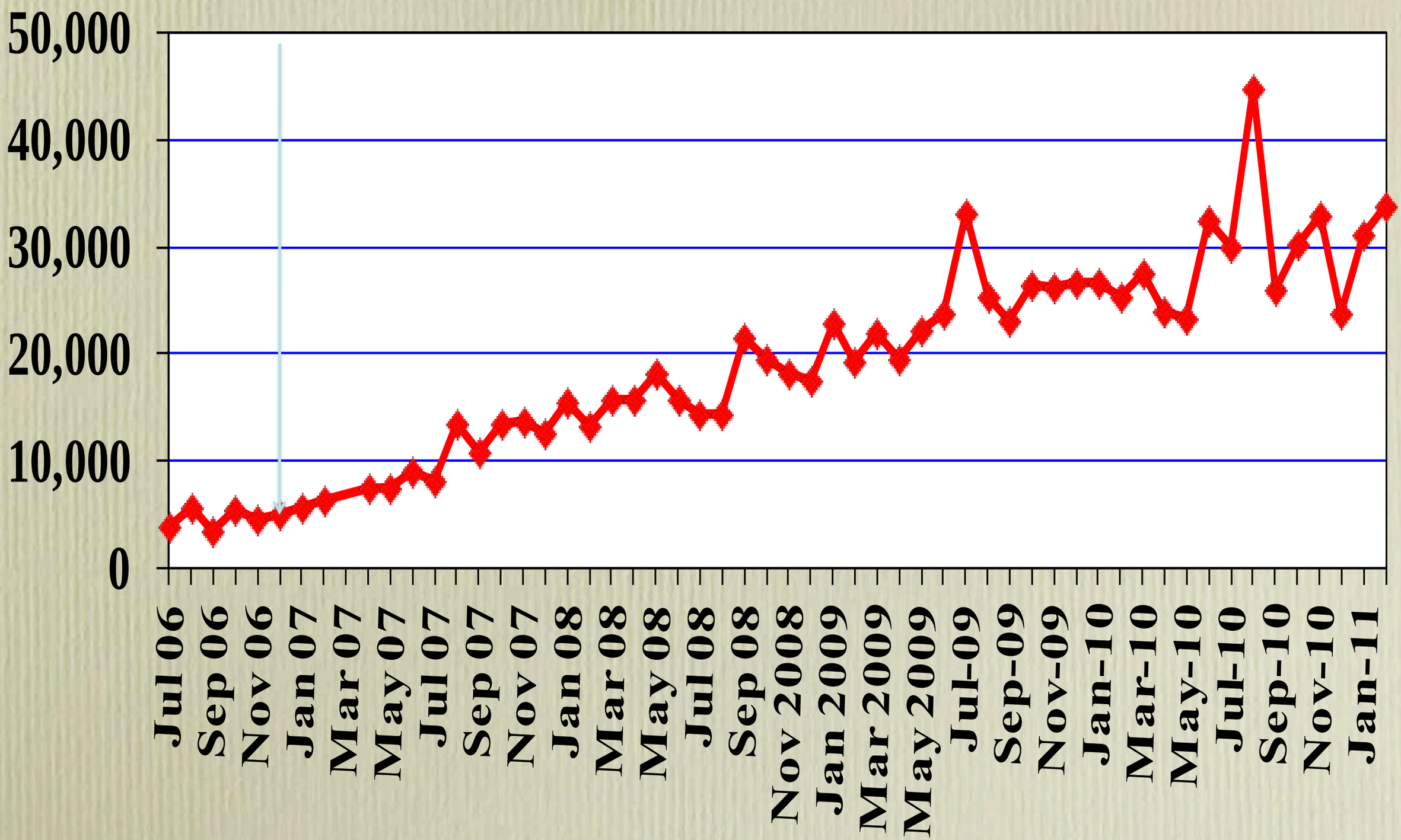
Drug specification	Price (USD)		% of price reduction
	Original	Generic	
1. EFV 600mg	2.0	0.7	66%
2. LPV/r 133mg/33mg	2.1	-	70%
LPV/r 200mg/50mg	-	0.6	
3. Clopidogrel 75mg	2.3	0.1	98%
4. Letrozole 2.5mg	7.0	0.2	97%
5. Docetaxel 80mg	863	37.9	96%
Docetaxel 20mg	237.71	9.1	96%
6. Erlotinib 150mg	83.7	22.4	73%
7. Imatinib 400mg	111.6	-	-

Source: HITAP (2009) Assessing the Implications of Thailand's Government Use Licences issued in 2006-2008 http://www.hitap.net/backoffice/news/news_display2_en.php?id=3750

Rate of use of Lopinavir/Ritonavir,200/50mg (bottles) under Universal Health Coverage scheme



Rate of use of Efavirenz, 600 mg. (bottles) under Universal Health Coverage Scheme



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Impact of patents on innovation and access

Triple therapy ARV FDCs:

- 2003 WHO Treatment Guidelines advocated use of FDCs to promote adherence and limit resistance, as a strategy for WHO 3x5 campaign
- FDCs from originator companies at the time did not reflect WHO-recommended regimens for first-line treatment - difficulties posed by patents on each component held by different parties
- Absence of product patents enabled Indian manufacturers to produce required FDCs - WHO prequalified first triple ARV FDCs from Indian generic manufacturers
- By 2009, USFDA and WHO PQ approved 57 adult FDCs, 31 paediatric ARVs from Indian generic manufacturers, compared to 8 adult FDCs and 14 paediatric ARVs by non-Indian and originator companies

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New Health Technologies for TB, Malaria and NTDs

- Global campaign against HIV/AIDS
- Lessons learnt?
  - Impact of patents on medicine prices
  - Generic competition enabled access
  - Impact of patents on innovation and access
- Going beyond HIV/AIDS

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Dearth of R&D for NTDs

"Is this going to have a big effect on our business model? No, because **we did not develop this product for the Indian market, let's be honest. We developed this product for Western patients who can afford this product, quite honestly.**"

Marijn Dekkers, Bayer CEO December 2013, referring to a decision by an Indian patent court that granted a compulsory license to a local company to reproduce Bayer's drug. Under Indian patent laws, if a product is not available locally at a reasonable cost, other companies may apply for licenses to reproduce those products at a more affordable price. Nexavar costs an estimated $69,000 for a full year of treatment in India, 41 times the country's annual per capita income.

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New Health Technologies for TB, Malaria and NTDs

Dearth of R&D for NTDs

- January 2014, AstraZeneca announces withdrawal from all early R&D for TB, Malaria and NTDs to focus efforts on drugs for cancer and hypertension
- Pfizer stopped R&D into all anti-infective drugs in 2012
- In 2012, only a third of funding required to undertake R&D for new TB products was made available

New drugs for diseases that disproportionately affect developing countries	New drugs to replace ineffective or toxic treatments	New drugs for emerging diseases
The "10/90 gap": **5% of global resources being applied to low and middle-income countries, where 93% of preventable deaths occur** **Only 1% drugs in last 25 years for tropical diseases and TB (which make up 11% of the GDB)** **Vaccines for HIV/AIDS, malaria, etc. are still**	**Drug resistance to existing HIV, TB, malaria treatments** **More effective HIV, TB and malaria drugs and combinations still needed** **New drugs are needed to replace current toxic treatments for diseases, such as trypanosomiasis and leishmaniasis**	**Over 20 diseases have emerged in past decade; including new strains of cholera, SARS, avian flu, H1N1** **Urgent need for new treatments and vaccines**

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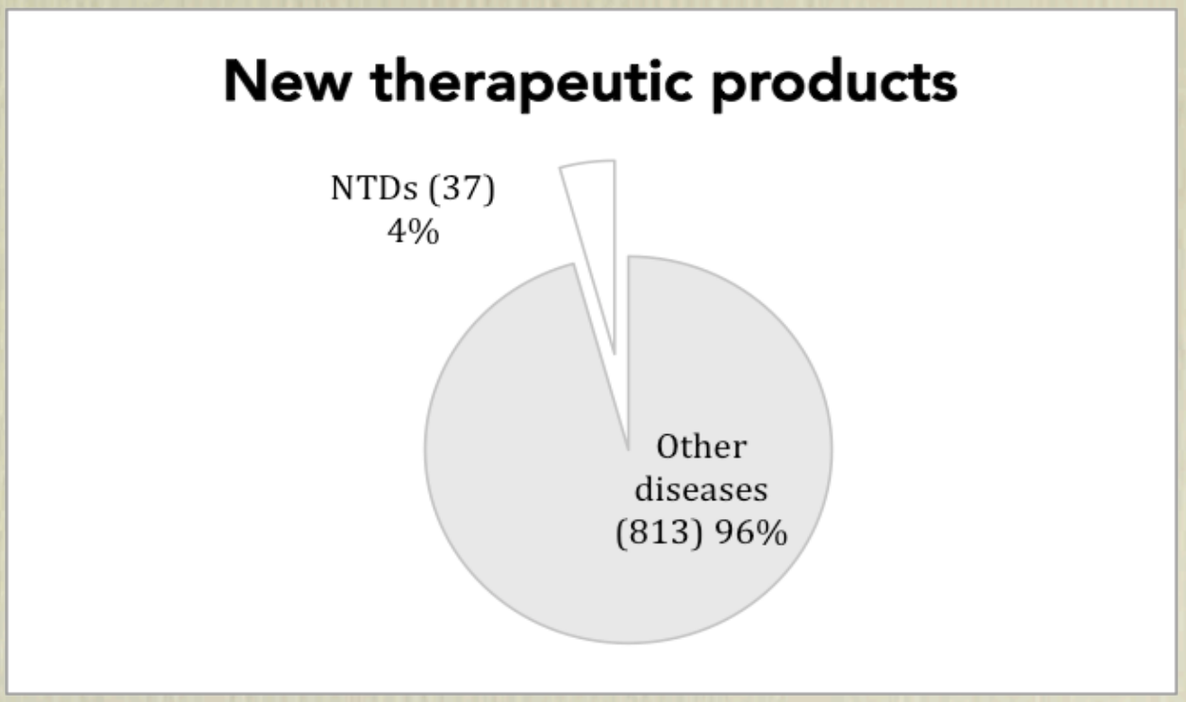
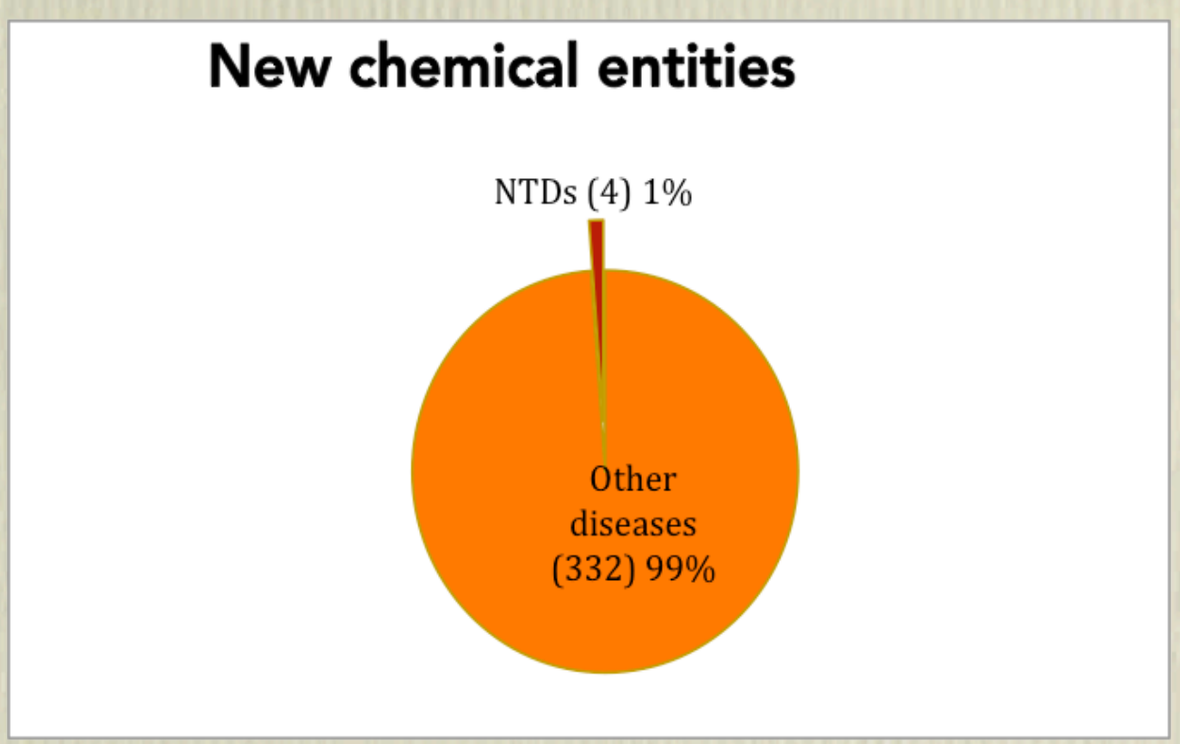
New Health Technologies for TB, Malaria and NTDs

R&D Landscape for TB, Malaria and NTDs 2000 – 2011

- 850 new therapeutic products registered in 2000-2011
- 37 (4%) were indicated for neglected diseases
- 336 new chemical entities
- only four ***new*** chemical entities (1%) were approved for neglected diseases (three for malaria, one for diarrhoeal disease)
- 148,445 clinical trials registered
- only 2016 (1%) were for neglected tropical diseases





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New Health Technologies for TB, Malaria and NTDs

Emerging Issues

Re-examining IP, innovation & public health

- Recognition that current system for stimulating R&D has failed to deliver, particularly for diseases disproportionately affecting poor people
- IP protection alone does not guarantee innovation
- International policy debate over the past decade on the twin problems of market failure and dearth of health technologies for diseases of the poor
- Global process at WHO ➔ CIPIH, WHO GSPOA, WHO CEWG
- What are the alternative mechanisms for increasing R&D and innovation?

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New Health Technologies for TB, Malaria and NTDs

Global Commission on HIV and the Law

Report of the Commission, 2012

- TRIPS has failed to encourage and reward the kind of innovation that makes more effective pharmaceutical products available to the poor, including for neglected diseases
- Countries must therefore develop, agree and invest in new systems that genuinely serve this purpose, prioritising the most promising approaches including a new pharmaceutical R&D treaty and the promotion of open source discovery

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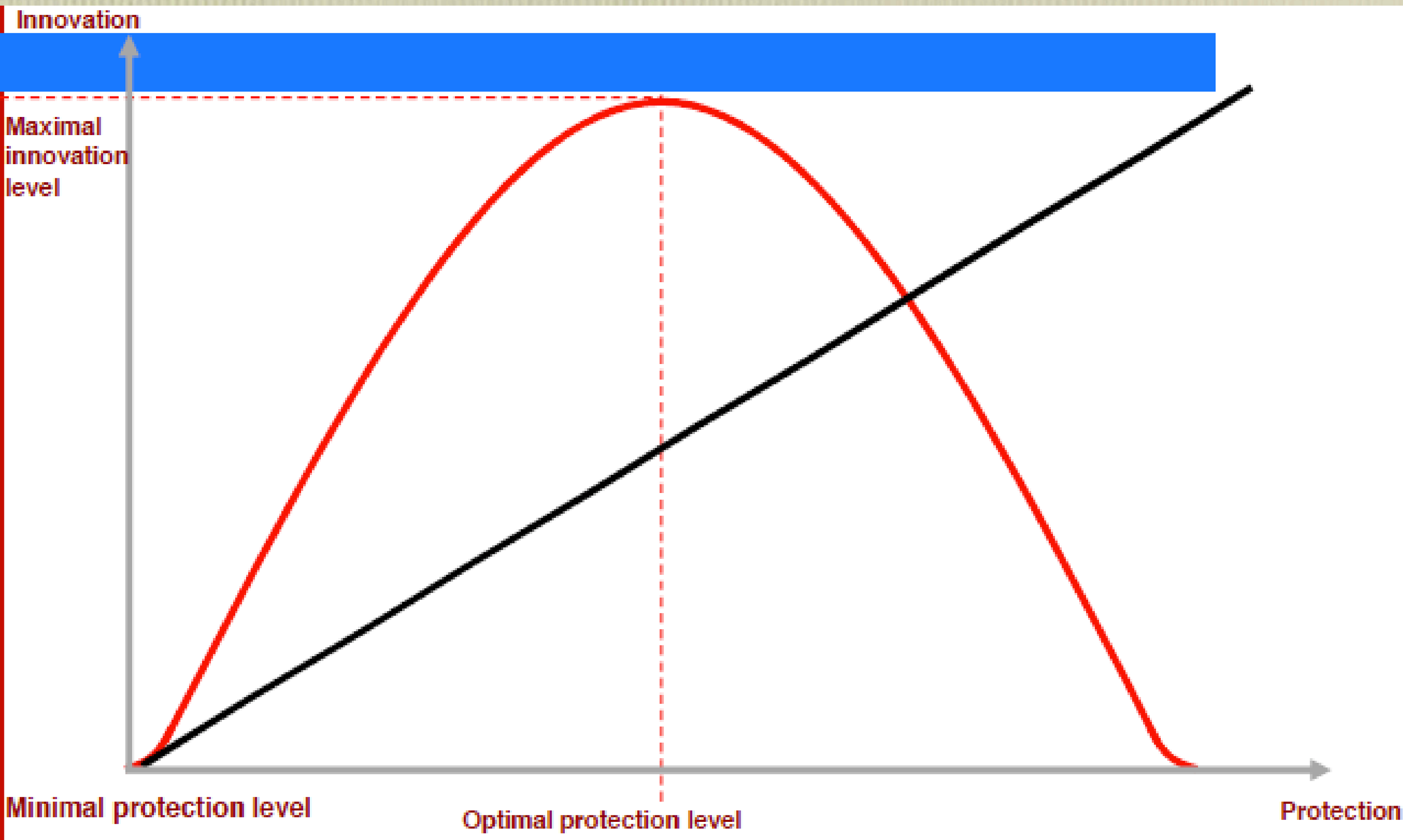
IP and innovation

Source: Swiss Federal Institute of Intellectual Property, October 2006



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New Health Technologies for TB, Malaria and NTDs

Impact of TB, Malaria and NTDs on development outcomes

- Tuberculosis kills 1.3 million people per year
- 207 million cases of malaria globally every year, resulting in more than 620 000 deaths per year
- The 17 NTDs identified by WHO are endemic in 149 countries
  - at least 100 countries are endemic for two or more diseases
  - 30 countries are endemic for six or more NTDs
- NTDs kill fewer people than HIV/AIDS, TB and malaria
- BUT they account for 11.7% of the global disease burden
- And are responsible for high morbidity and premature death and disability in developing countries

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New Health Technologies for TB, Malaria and NTDs

NTD treatments, outdated & ineffective

- MDR-TB treatment takes 2 years and includes:
- 8 months of daily injections
- 14 000 tablets to swallow
- Toxic side effects (deafness, psychosis and severe nausea) AND
- Less than 50% of patients are cured
- Treatment can still cost in excess of $5000 per patient per year
- Human African trypanosomiasis, Chagas disease, leishmaniasis all need new and safer medicines

- Innovation is one piece of the puzzle
- The other is the capacity of a health system to absorb a new product
- Depends on various factors:
  - Legal and policy environment
  - Sustainable financing mechanisms
  - Medicines regulatory capacity
  - Health care delivery systems
  - Supply chain management
  - Appropriate pricing policies
  - Adequate human resources

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New Health Technologies for TB, Malaria and NTDs

New partnerships for TB, malaria and NTDs

- The Government of Japan Global Health Policy, 2011-2015
- This calls for a “new approach” & new partnerships to stimulate R&D in TB, malaria and NTDs

2 complementary and synergistic projects:

- GHIT Fund: GOJ partnership with BMGF & Japanese research organizations to create a fund to promote engagement of Japanese research organizations in product development for global health
- Access & Delivery Partnership : GOJ funding to strengthen capacities of LMICs to access and absorb new health technologies as they become available

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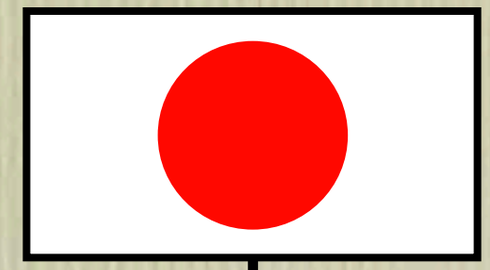
New Health Technologies for TB, Malaria and NTDs



JAPANESE PHARMACEUTICAL SECTOR

BMGF

WHO TDR

PATH

NATIONAL PARTNERS

UNDP

GLOBAL HEALTH INNOVATION TECHNOLOGY (GHIT) FUND

ACCESS AND DELIVERY PARTNERSHIP

TECHNICAL AND POLICY ADVICE

CAPACITY BUILDING FOR ABSORPTION

PDPS FOR NEW HEALTH TECHNOLOGIES

PPPs FOR NEW HEALTH TECHNOLOGIES

IMPROVED ACCESS AND DELIVERY OF NEW HEALTH TECHNOLOGIES FOR TB, MALARIA AND NTDS

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New Health Technologies for TB, Malaria and NTDs

Access and Delivery Partnership

- Government of Japan funded:
- US$3.5 million per annum over 2013-2018
- Comprising 3 implementing global initiatives bodies + partner LMICs + other stakeholders
  - UNDP (HIV, Health and Development Unit, BDP)
  - WHO (The Special Programme for Research and Training in Tropical Diseases)
  - PATH

Aims:

- To provide technical and policy advice on how to improve access and delivery of health technologies in LMICS and to strengthen capacity in LMICs to achieve this result
- To develop relevant capacity in LMICs to absorb new health technologies

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New Health Technologies for TB, Malaria and NTDs

Access and Delivery Partnership

Strategic Objectives:

- Promoting appropriate linkages between innovation and access
- Promoting an enabling environment for innovation in developing countries
- Facilitating strategic South-South collaboration
- Ensuring sustainable and affordable access to health technologies
- Building synergies and adding value to existing initiatives

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Capacity Strengthening Across the Value Chain of Access and Delivery

Integrated public health, innovation and industrial policies

Disease control programmes & drug regulatory frameworks

Financing for procurement & innovation

Procurement and supply chain management

OUTPUT 1
Policy & legal frameworks

OUTPUT 2
Evaluation of epidemiological studies

OUTPUT 3
Monitoring of Phase IV clinical trials

OUTPUT 4a
Financing for new health technologies

OUTPUT 4b
Commercialization pricing and supply

OUTPUT 5
Supply chain and delivery systems

Led by UNDP

Led by WHO/TDR

Led by PATH

IMPROVED ACCESS AND DELIVERY FOR TB, MALARIA AND NTDs

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New Health Technologies for TB, Malaria and NTDs

17 Neglected diseases as identified by WHO

- Buruli Ulcer (*Mycobacterium ulcerans* infection)
- Chagas disease
- Dengue/Severe dengue
- Dracunculiasis (Guinea-worm disease)
- Echinococcosis
- Foodborne trematodiases
- Human African Trypanosomiasis (Sleeping sickness)
- Leishmaniasis
- Leprosy
- Lymphatic filariasis
- Onchocerciasis (River blindness)
- Rabies
- Schistosomiasis
- Soil transmitted helminthiases
- Taeniasis/Cysticercosis
- Trachoma
- Yaws (Endemic treponematoses)