AFRICAN DIALOGUE ON TECHNOLOGY TRANSFER FOR LOCAL MANUFACTURING CAPACITY OF DRUGS AND VACCINES

TECHNOLOGY TRANSFER AND LOCAL MANUFACTURING OF PHARMACEUTICALS: THE SOUTH AFRICAN CASE

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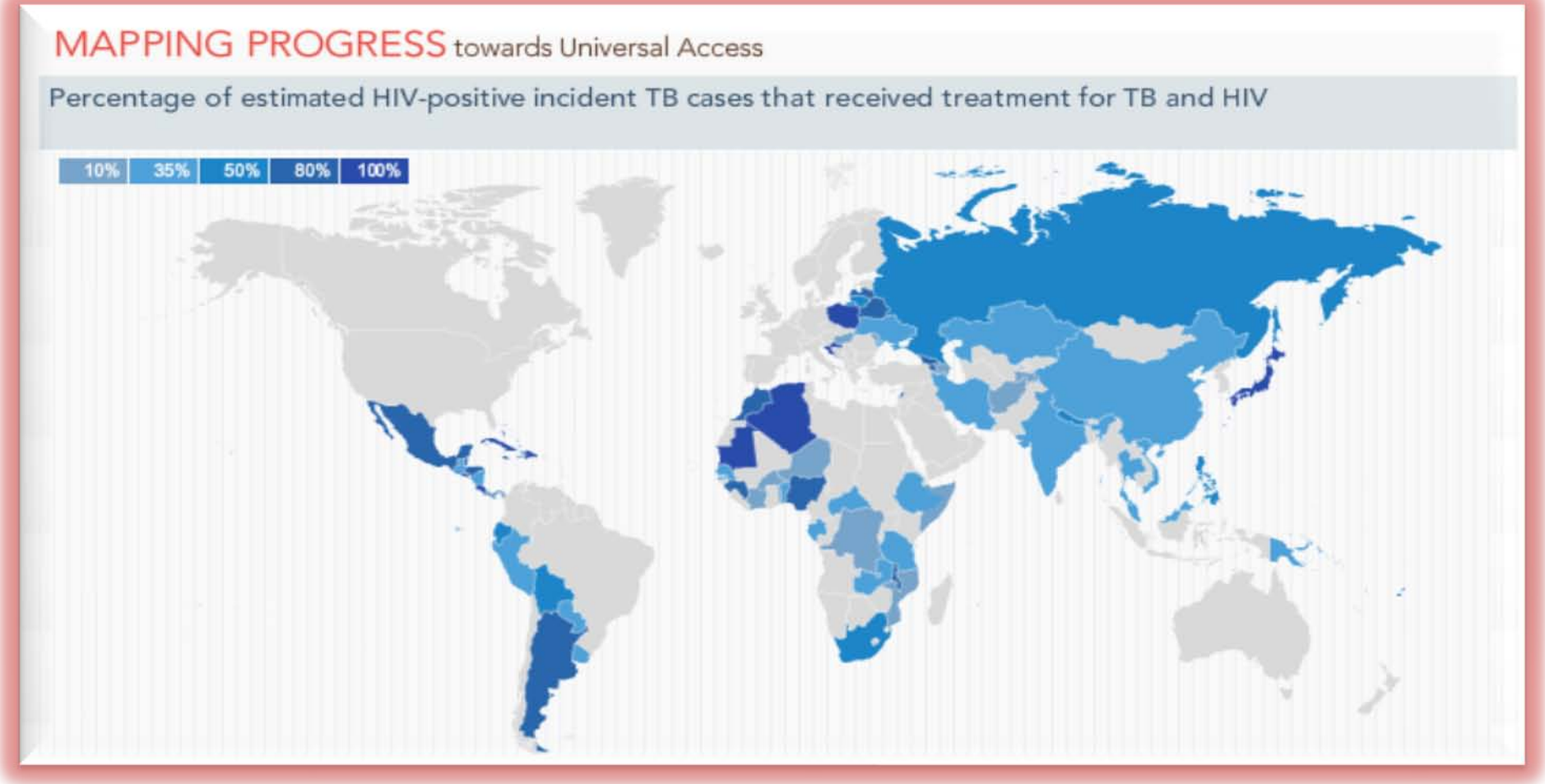
SLIDE BACKGROUND



Source: http://www.unaids.org/en/KnowledgeCentre/HIVData/mapping_progress.asp

PRESENTATION OUTLINE

- Introduction
- Pharmaceutical production in South Africa
- The regulatory environment
- Examples of technology transfer in South Africa
- Factors influencing technology transfer in South Africa
- Lessons learnt and recommendations

"... We believe that in the area of indigenous pharmaceuticals, there are untapped opportunities for economic growth, skills and job creation..."

Budget vote speech by the Minister of Science and Technology (18/06/2009)

INTRODUCTION

- Technology transfer (TT): converting scientific findings into useful products for society
- Pharmaceutical industry TT: processes needed for successful progress from drug discovery to product development to clinical trials to full-scale commercialization
- Also the process by which a developer of technology makes their technology available to a commercial partner that will exploit the technology
- Importance of pharmaceutical TT for health and economic improvement in developing countries demonstrated in article 66.2 of TRIPS & element 4 of GSPA

PHARMACEUTICAL PRODUCTION IN SA

(I) The Importance of the South African Pharmaceutical Industry

- Africa's medicine consumer market : 4 - 5 billion tablets – capsules (tab – cap)/year – only HIV/AIDS, Malaria and Tuberculosis (TB) symptoms.
- 36% accounted for by South Africa, Nigeria and Tanzania
- Great need for pharmaceuticals both within SA and the rest of Africa
- Urbanization in Africa (such as has occurred in South Africa) and its attendant life style diseases further complicate issues

(II) General Overview

- South Africa has he most developed pharmaceutical industry in Africa but numerous challenges regarding the provision of increased access to equitable and cost-effective healthcare
- Several mergers and take-overs due to restructuring to meet competitive challenges
- Various kinds of local production including primary production of chemicals and limited local production of generic APIs
- Over 90 registered pharmaceutical operations - majority of operating only as sales and marketing offices, with R&D and production being undertaken overseas
- Locally produced medicines are mostly generic, and the majority of the production facilities are privately owned; accounting for only a small proportion of national requirements

(III) Local Manufacturing & Distribution

- Limited local production of generic APIs. Drug formulation and last step synthesis common among the local subsidiaries of MNCs. Overall the value currently added across the pharmaceutical value chain in South Africa is relatively low

- 2005 WB study: locally owned SA manufacturers sourced 39% of AIs, 90% of packing materials & 49% of excipients locally. Local subsidiaries of MDCs sourced 1.5% of AIs, 36% of packing materials & 20% of excipients locally

- Takes 24 - 36 months for NCEs from local manufacturers to be registered, same for 1st generics. 12 – 18 months for new indications for already existing products - up to four times higher than international best practice

(IV) Recent Developments and Trends

- MNCs focus on low-cost units in logistically well-placed areas attractive to service major markets
- Recent pricing control policies, aimed at improving price equity and distribution, have been blamed by industry as compounding the already deteriorating drug manufacturing situation
- Other factors affecting local production include restrictions from IP rights and patent requirements; wide fluctuations in cost per unit; the high cost of bioequivalence tests for each product & the high cost of APIs when purchased in small quantities
- The DTI: The ratio of imported to exported pharmaceuticals ready for retail sale rose from approximately 8:1 in 1998 to 17:1 in 2006. Imports of pharmaceuticals in finished dosage form grew from 1.1 million USD in 2007 to 1.4 million USD in 2008

THE REGULATORY ENVIRONMENT

(I) SA's Natl. Drug Policy and Regulations

- Then highly skewed healthcare and pharmaceutical sector. E.g. 1990: private sector responsible for 80% of the SA's total expenditure on drugs, though 60 – 70% of the total volume of pharmaceuticals consumed in the public sector
- 1995: NDP aimed at addressing issues including developing an equitable pricing plan for drugs used in the public and private sectors and developing specific strategies to increase the use of generic drugs legislatively supported by the Medicines and Related Substances Control Act (101 of 1965)
- MCC is responsible for rationalising drug registration, controlling the registration of practitioners and the licensing of premises, enhancing the inspectorate and laboratory functions, and promoting other quality assurance measures
- As part of the NDP, sector-wide MPC monitors and regulates drug prices – including benchmarking of medicines as part of the pricing regulations of 2004
- NDP promotes the use of IMPP, using the INN or generic name; aimed at reducing drug costs and expenditure

(II) Impact of Policy on Society & Industry

- Current pricing proposal mandates benchmarking originator drug prices in SA against a basket of 4 comparator countries (Australia, Canada, New Zealand and Spain), and choosing the lowest price. Generic drugs to be priced at 40% of resulting originator price

- SA has already achieved up to 21% decrease in ex – manufacturer price level for the private market. But 20% of the population is served privately & consumes around 275 USD/capita per year, and 80% is served publicly & consumes 15 USD/capita per year

- Industry: pricing policies put in place by the MPC are “deeply problematic”, “lacking transparency and economic rationale” in addition to being “methodologically flawed”. NDP limits MNCs to sales and marketing, and renders segments of the industry economically unviable. MNCs estimate losses of 35% of their SA revenues with the pricing proposal. Generic manufacturers claim they are unable to make impact projections

(III) Legislation/Policies, TT, TRIPS & HIV/AIDS (1)

- 1997, President Nelson Mandela signed amended Medicine and Related Substances Control Act (Act 90) creating legal framework promoting availability of more affordable medicines (especially HIV/AIDS – related drugs) via parallel imports and compulsory license.
- National Health Act of 2003 & the BBEE Act to address issues of access and the plan to combat HIV/AIDS
- PMAs & MNCs filed lawsuits alleging TRIPS violations. Strong pressure from access campaigners, civil society and international public opinion led to withdrawal in April 2001

(III) Legislation/Policies, TT, TRIPS & HIV/AIDS (2)

- Provisions in Competition Act of 1998 have been used to address ARV pricing and voluntary licensing for local production. No compulsory licenses issued yet
- First voluntary licenses to Aspen Pharmacare Holdings Limited & others for the local production of generic ARVs including export to others SSA countries
- Following government's rollout of ARV's & implementation of various models of voluntary licensing it is estimated that some 110,000 – 115,000 SA patients can now access ARV's
- Thought to have been further enhanced by the full implementation of a Single Exit Price at manufacturer level

(III) Legislation/Policies, TT, TRIPS & HIV/AIDS (3)

Supply of ARVs to the South African Department of Health (through 2007)

Product	Pack size	Price (US$)	Quantity	Manufacturer
Stavudine 20 mg capsule	60 capsules	3.02	84,607	Aspen
Stavudine 30 mg capsule	60 capsules	3.02	2,192,400	Aspen
Stavudine 30 mg capsule	60 capsules	3.42	939,600	Cipla
Stavudine 40 mg capsule	60 capsules	3.34	1,879,200	Aspen
Stavudine 40 mg capsule	60 capsules	3.72	1,252,800	Cipla
Zidovudine 50 mg/5 mL syrup	200 mL	3.94	2,398,500	Aspen
Zidovudine 100 mg capsule	100 capsules	17.42	216,000	GSK
Zidovudine 300 mg tablet	60 tablets	11.93	103,200	GSK
Didanosine 25 mg tablet	60 tablets	10.52	5,069	Aspen
Didanosine 50 mg tablet	60 tablets	10.06	605,750	Aspen
Didanosine 100 mg tablet	60 tablets	11.12	3,564,000	Aspen
Lamivudine 10 mg/mL syrup	240 mL	3.77	2,649,600	Aspen
Lamivudine 150 mg tablet	60 tablets	5.54	5,030,400	Aspen
Nevirapine 200 mg tablet	60 tablets	6.79	1,879,200	Aspen
Nevirapine 50 mg/5 mL syrup	240 mL	30.69	1,152,000	BI
Stavudine 1 mg/mL powder	200 mL	13.54	727,200	Bristol-Myers Squibb

Source: South Africa Department of Health 2004.

Note: mg = milligrams. mL = milliliters.

All other orders were supplied as follows: lopinavir and ritonavir preparations from Abbott; efavirenz preparations from Merck Sharp & Dohme (MSD). All prices include 14 percent value added tax and are on a delivered basis.

EXAMPLES OF TECHNOLOGY TRANSFER IN SOUTH AFRICA

Examples of TT in SA (1)

- Mostly born out of years of contention between brand owners and civil society. Most arrangements made with local manufacturers do not include actual TT. Most ARVs produced locally from imported generic APIs
- License is granted, & local manufacturer conducts "reverse engineering" & register the product without the benefit of relying on the earlier registration of the originator product
- Example of hard-core TT – Eli Lilly and Aspen Pharmacare for manufacture of capreomycin and cycloserive, for the treatment of MDR TB for SA and regional markets
- Not many obvious situations where TT failed. Thembalami voluntarily recalled all its HIV/AIDS drugs in SA because of problems with bioequivalence

Examples of TT in SA (2)

TECHNOLOGY TRANSFER RECIPIENT (S)	TECHNOLOGY DONOR(S)	PRODUCT	TYPE OF TRANSFER
Aspen Pharmacare	Eli Lilly	Anti – TB drugs	Manufacturing
Aspen Pharmacare Enaleni – Cipla (formerly Cipla –Medpro) Feza Pharmaceuticals Biotech Laboratories	GSK, Boehringer Ingelheim (BI), Bristol Myers Squibb (BMS)	ARVs	Licences for manufacturing
Ranbaxy and Sonke (formerly Thembalami)	Merck & Co. (MRK)/MSD (Pty) Ltd	ARV	License to manufacture
Aspen Pharmacare	Gilead Sciences	ARV	License to Manufacture
Adcock Ingram	Baxter	Large Volume Parenterals	Manufacturing
Adcock Ingram Aspen Pharmacare	Merck & Co. (MRK)/MSD (Pty) Ltd	ARVs	License to manufacture

FACTORS INFLUENCING TECHNOLOGY TRANSFER IN SOUTH AFRICA

(I) Drivers/Incentives for TT

- Good business and manufacturing practices
- Potential for competitive pricing
- Strategic planning
- Strong economy, environment and civil society
- Transparent and efficient regulation
- Opportunities for contingency supply
- Public/investor pressure and corporate Image
- Access to new machinery, training, know-how and business partnerships

(II) Barriers/Disincentives for TT

- Lack of efficiency
- Focussing on the low end
- Low market share
- Cost of prequalification
- Labour Issues

LESSONS AND RECOMMENDATIONS (1)

- High-level Commitment and collaboration
- Form strategic partnerships with well – established pharmaceutical companies
- Provide technical assistance:
  - To member countries to examine the national patent laws
  - TRALAC – like organizations to support in the development of simple administrative structures and IP regimes addressing patent life, compulsory licensing, parallel importing etc.
  - More support from World Bank, WTO, and WHO
- Focus on sustainability which depends on relative competitiveness of the local manufacturing industry as well as the impact of external factors
- Take advantage of global trends towards for consolidation into centres of excellence

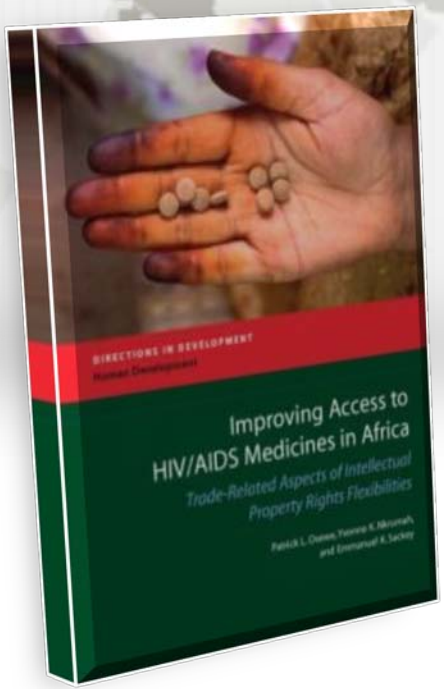
LESSONS AND RECOMMENDATIONS (2)

- Harmonization of regulations across Africa
- Build innovative capacity especially in clinical trials to stimulate growth R&D
- Recognize levels of interdependence between industrial policy and healthcare policy
- Be realistic, drug manufacturing companies are not charities


SIERRA LEONE!


BURUNDI!


GHANA!


DIRECTIONS IN DEVELOPMENT
Improving Access to
HIV/AIDS Medicines in Africa
Trade-Related Aspects of Intellectual
Property Rights Flexibilities

THANK YOU!