

# Will a state owned pharmaceutical manufacturing company solve the shortage of medicines?

*Dr Skhumbuzo Ngozwana MBChB, MPharm Med, MBA  
President & CEO - Kiara Health*

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# PHARMACY

SHAPING THE FUTURE



# Disclaimer

The views and opinions expressed herein are solely those of the author and do not necessarily represent those of any company.



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# Introduction



## Framing the Debate

**"In the future, regional and global power and national stability will be determined not by who controls arms, but by who controls access to medicines".**

Michel Sidibe: Addressing the African heads of State and Government on June 6, 2012



# South Africa Pharma at a Glance

- ❑ Valued at ZAR 42.6 billion (IMS / ImpactRx August 2016)
- ❑ Only 35% (volume) of our pharmaceutical consumption (FF) is locally produced
- ❑ Closure of ~ 40 pharmaceutical plants in ~ 15 years
- ❑ Pharma is a 5th leading driver of the trade deficit
- ❑ Highest HIV / AIDS burden in the world – 3.4 million on Rx: totally dependent on imported API (FF to some extent)
- ❑ High incidence of medicine stock- outs at health facilities (Public & Private) undermines Section 27 (c)

# Access to medicines is a Constitutional Right & Imposes an Obligation on State

- ❑ The new constitution enshrined a bill of Rights, with section 27, which reads as follows:
  - Sec (1) (a); everyone has the right to have access to healthcare services, including reproductive health
  - Sec(2): the state must take all reasonable legislative and other measures within its available resources, to achieve the progressive realisation of each of these rights.



# Suppliers get blame for drug stockouts

May 25, 2015 | Andile Makholwa

Health Minister Aaron Motsoaledi cuts short overseas trip, but denies wide shortages — including antiretrovirals

HEALTH Minister Aaron Motsoaledi has hit back after reports that state hospitals and clinics are suffering severe "stockouts" of essential drugs, including antiretrovirals, shifting the blame for the shortages to suppliers.



# Factors Influencing Access to Medicines



## FACTORS LIMITING ACCESS

Supply side issues (Institutional & system)

- ✓ **Pharmaceutical (e.g. Production, QSE)**
- ✓ Registration inefficiencies
- ✓ Shortage of trained professionals
- ✓ Rationale Use

Socio-political

- ✓ Poverty & unemployment
- ✓ Cultural & linguistic
- ✓ Poor governance & management
- ✓ Lack of political will
- ✓ **Huge disease burden**

Economic

- ✓ Inadequate budgets
- ✓ **Lack of distribution chain**
- ✓ **Health infrastructure**

Demand side issues (Regulatory and policy)

- ✓ **Health financing policies**
- ✓ **Industrial imperatives**
- ✓ **Procurement policies**
- ✓ IRP laws
- ✓ Cross-border inefficiencies

Source: Metanoia Pharma Consulting

# The coming challenge of Affordability and Supply

- ❑ **India's significant cost advantage is eroding fast**
  - cost of compliance is going up
  - salary hikes
  - cost of putting up new plants now approximating in the west
  - the changing IP policy and its implications for second /third line drugs
  - current export incentives slowly falling off - price hike inevitable.
  - DPCO and slowing R&D & fewer generic product introductions – “Oligopolistic behavior” danger according to IMS report
- ❑ Indian companies are increasingly looking to the lucrative markets of the west, and also shifting production capacity to more lucrative products which attract better margins.
- ❑ In the (near) future Africa will have to procure drugs at the same price as the western world.

# Medicine Shortages: The Causes



# Causes of Medicine Shortages

## ❑ Manpower

- Lack of human resources
- Inadequate supply chain
- Poor planning
- Delays in amendment approvals for new API sources

## ❑ Money

- Financial distress (production cost versus selling price)
- Exchange rate fluctuations
- Delayed payments (reluctance to supply)

## ❑ Materials

- Disruption of raw material supply (API, Excipients, Packaging – Beijing Olympic etc.)
- Vulnerabilities linked to breakdowns in global supply chains (e.g. Cyclone Hudbud)
- Production interruptions (e.g. equipment breakdown)

# Causes of Medicine Shortages

## ❑ Markets

- Supply and demand issues (surge in demand, short term more profitable business / insufficient profits)
- Erratic ordering
- Therapeutic & other substitution
- Unreliable reporting (consumption etc.)

## ❑ Manufacturing difficulties

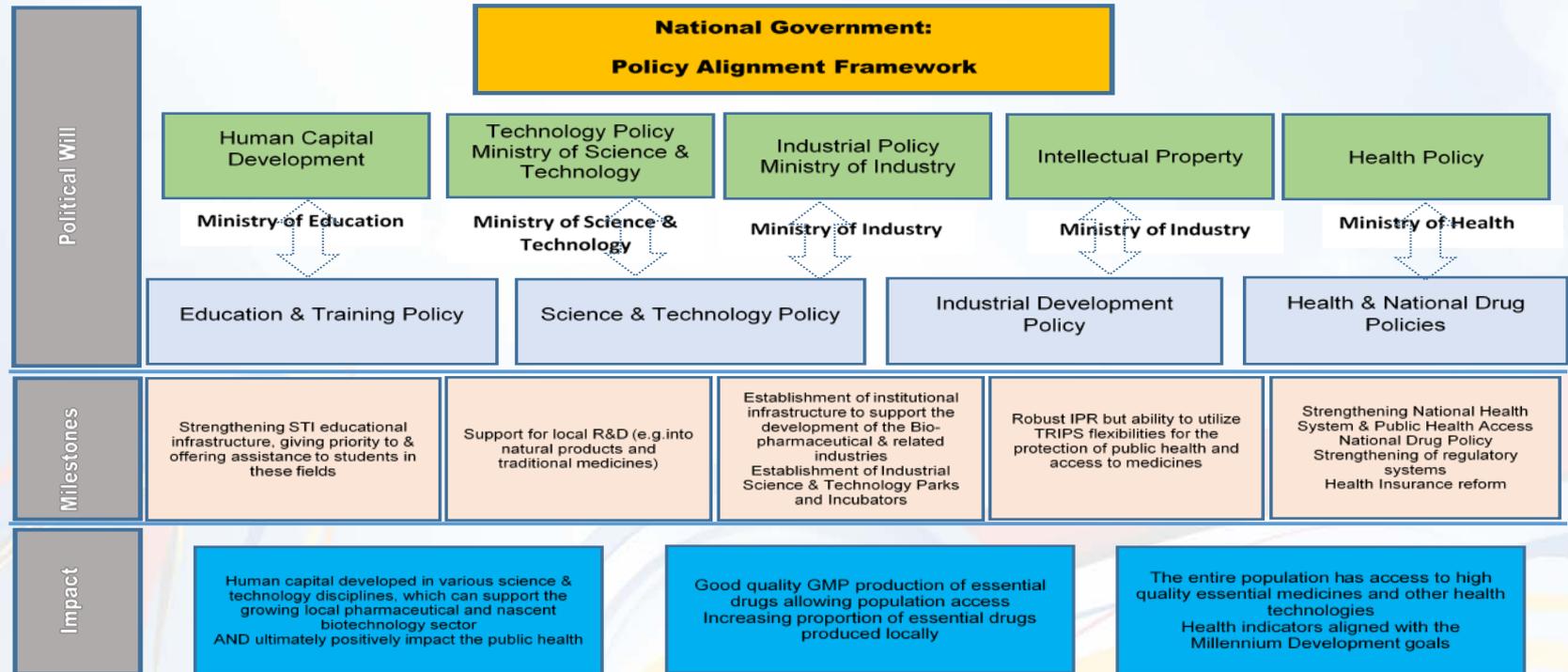
- Regulatory issues
- Lack of capacity (intention vs. ability to supply) < 10 companies supply the total market
- Utilizing capacity for more profitable lines (National Pharmaceutical Pricing Authority (NPPA) DPCO has over 800 drugs under price controls)
- Financial strain
- Formulation changes
- Product discontinuation



What does Government have to do to address the shortages – realize the provisions of Section 27 (C); & ensure SECURITY OF SUPPLY



# Policy Alignment Framework



# National Development Plan 2030

- ❑ The plan articulates the vision for healthcare in South Africa as follows:
  - “We envisage that in 2030, South Africa has a life expectancy of at least 70 years for men and women..., the quadruple burden of disease have been markedly reduced compared to the two previous decades”.
- ❑ The NDP also aspires to:
  - Ensure that the population of under 20’s free of HIV / AIDS increases
  - Progressively improve TB prevention and cure by 2030
  - Reduce maternal, infant and child
  - Significantly reduce prevalence of non-communicable chronic diseases
- ❑ Calls for the government to invest in technological revolutions of the 21st century - specifically highlighting biotechnology and nanotechnology

# Dept. of Science and Technology's Bioeconomy Strategy

- ❑ The key Strategic priorities as outlined in the Bioeconomy strategy include the following:
  - to develop improved therapeutic and drug delivery systems to address priority diseases
  - to develop new and improved vaccines and biologics
  - develop improved diagnostics
  - develop improved medical devices
  - strengthen clinical research and development capabilities, and
  - establish pharmaceutical manufacturing in the country
- ❑ Specifically, the Bioeconomy strategy calls for the prioritization of drug development and proposes that this be pursued via public-private partnerships (PPPs).



# Department of Trade and Industry's Industrial Policy Action Plan (IPAP)

- ❑ IPAP purpose is to expand production in value-adding sectors with high employment and growth multipliers that compete in export markets as well as in the domestic market against imports.
- ❑ Pharmaceutical sector is one of the prioritized sectors. The key growth opportunities identified (by IPAP) in the pharmaceutical sector are:
  - Domestic production of active pharmaceutical ingredients (API) for key ARVs
  - Local production of reagents for AIDS / HIV diagnostics, under license.
  - Domestic production of vaccines under license.
  - Domestic production of biological medicines such as erythropoietin and monoclonal antibodies.
  - Removing regulatory barriers and constraints to clinical research in South Africa.

# National Dept. of Health's Strategic Plan

- ❑ **Mission:** To improve health status through prevention of illness, disease and promotion of healthy lifestyles, and to consistently improve the healthcare delivery system by focusing on access, equity, efficiency, quality and sustainability
- ❑ Core focus on improving access to affordable, safe, efficacious medicines, including to newer therapies
- ❑ Has five key priority areas: HIV / AIDS, TB, Cancer, Maternal & Child Health and Diabetes

**What else can government do?**



# Lead the adoption of leap-frogging technologies & Create Conducive env.

- ❑ Government's role is to LEAD /CATALYSE the "Adoption of Leap-Frogging Technologies" for API / Biosimilars and other priority product for local production:
  - Reduced Capital Investment, smaller, "greener" footprint versus competitors who already have huge installed capacities;
- ❑ Government role is to create a conducive environment for the Private sector (incentives, SEZ's etc) e.g.
  - European API Producer Sterling's Euro 25 million API project (Dube Trade Port)
  - Cipla Biotech's ~ ZAR 800 million Biosimilar project Dube Trade Port

# Create a window of opportunity

- ❑ Government's role is to "Create a window of opportunity for local manufacturers" & utilize public procurement as a financial asset for local companies:
  - Price preference for local companies (15-32.5%) – IDC Study
  - Restriction on imports of certain drugs if produced in sufficient quality and quantity to meet local demand (Bangladesh, Algeria, Ghana, Algeria, Nigeria, Tunisia etc.)
  - 25% pre-payment for awarded tenders
  - Enter into long term contracts (5 years) with local companies to improve competitiveness (scale economies in procurement, better production planning, lean manufacturing, and cash flow management.)
  - Expedite registration for products to be produced locally & approval of variations for new API sources

# Generation of TT packages

- ❑ Government's role is to "catalyze the development of local industry through centralized generation of Technology Transfer Packages" for critical products, serving national and continental needs
  - Diffuse to industry at a nominal rate
  - High-quality, low-investment, high-return support for new product launch and SRA approvals
  - Leverage resources that are scarce at African Pharmas

# Case Study: India



**“A dwarf standing on the  
shoulders of a giant can see  
further than the giant”**

*Sir Isaac Newton – private correspondence to Robert Hooke*

# Indian Pharma Historical Context

- ❑ Dominance by foreign companies
- ❑ Poor access (pricing, focus by companies)
- ❑ Largely dependent on imports – Finished Product (FF) & all raw materials
- ❑ Lack of the requisite skills needed for Pharma manufacturing
- ❑ Lack of access to capital – huge capital requirements
- ❑ No government incentives in place
- ❑ Constrained by IP issues that ignored the need on the ground

# The Indian Government Takes DELIBERATE CORRECTIVE Action

# 1 (a). Government Entered the Fray

- ❑ 5 government-owned BULK DRUG companies were created:
  - 1954 - The Hindustan Antibiotic Ltd. (HAL) with the assistance of the WHO and UNICEF;
  - 1961 - Indian Drugs and Pharmaceutical Ltd. (IDPL) with assistance from the former USSR;
  - (1972)- Smith Stanistreet Pharmaceutical
  - 1930 (1977) – The Bengal Chemical & Pharmaceutical Works; India's 1st state drug manufacture
  - (1984)- Bengal Immunity Ltd;

# 1 (b). Government Entered the Fray...

- ❑ Hindustan Antibiotics Limited (HAL)
  - 1st drug manufacturing company to be set up with the assistance of WHO and UNICEF.
  - 1st drug manufacturing unit in India to undertake commercial production of antibiotics like Penicillin, Streptomycin, Gentamicin, Ampicillin & Amoxicillin etc.
  - Diversified into formulation and has facilities to manufacture various dosage forms - Injectables, capsules, tablets, large volume Parenterals, liquid orals, etc. conforming to pharmacopoeial standards.
  - HAL has also diversified into agro-vet products.

# 1 (c). Government Entered the Fray...

- ❑ Indian Drugs and Pharmaceutical Ltd. (IDPL)
  - Largest Central Pharma Public Sector Undertaking in India
  - Set up with the assistance of the USSR
  - Established as part of healthcare infrastructure with the following main objectives
    - To create self-sufficiency in essential life saving medicines,
    - To free the country from dependence on imports and
    - To provide affordable medicines to the millions
  - Played a pioneering infra-structural role in the growth of Indian Drug Industry base (spin offs – e.g. Dr Reddy's founder)

## 2. Investment in the Right Education

Parameter / Country	West	India
Number of Graduates	215,000 UK	3,000,000
	222,000 USA	
Number of Science graduates	500,000 EU	700,000
	US400,000 USA	
Number of Chemistry MSc's	3000 Germany	150,000
	3500 UK	
Number of Chemistry PhD's	1,500 Germany	12,000
Number of Pharmacists	?	50,000

Source: KPMG, Deutsche Bank & others

India has 389 universities, 14,169 colleges and 1,500 research institutions – Source: University Grants Committee; Accessed 2010

### 3. Investment in R&D (diffusion to private sector)

- ❑ National Chemical Laboratory (NCL)
- ❑ Indian Drugs & Medical Research Institute
- ❑ All India Institute of Medical Sciences
- ❑ Indian Institute of Chemical Technologies
- ❑ Institute of Human Genetics
- ❑ Centre for Biotechnology
- ❑ Institute of Microbial Technology
- ❑ Indian Institute for Metallurgy, Ceramics etc amongst others

# The Role of the NCL put in Perspective

"This was the start of a very useful and productive partnership between NCL and the pharmaceutical industry. Our collective effort in the post Indian Patents Act 1970 era laid the foundation on which was built the API manufacturing industry as it exists today.

Dr. Y. K. Hamied, Chairman, Cipla Limited in his speech at IICT, Hyderabad delivered on 2 April 2005

# 4. Creating an Enabling Regulatory env.

Parameter / Year	< 1970	1970-2005	2005 -
IP	Product patent 14 yr term	Process patent only 7 yr term	Product patent 20 yr term
Pricing	Limited price ceilings	DPCO – strict controls	DPCO – some drug withdrawals from market: Oligopoly (IMS)
% Indian product	FF < 20% API < 10%	FF ~ 80% API ~ 75%	FF ~ 95% API ~ 85%
% Indian Imports	~ 90%		~ < 15%

# A Virtuous Cycle is Created: Evolution to Innovation

# Evolution: 1930 – 1995+

1930's - 50

Foreign dominance & only FF

1950's - 70

State enters the fray:

- API starts in 1960's
- Technology acquired through public sector efforts & infused into private sector

1970's - 95

- Entrepreneurs spin off from state & other companies to form own firms.
- DPCO forces entrepreneurs to innovate & to increase efficiencies in order to improve margin

1995 -

- World's pharmacy migrates up the value chain – original R&D

# Current Picture

## Volume & values globally

- ✓ 3<sup>rd</sup> largest by **volume** & only 13<sup>th</sup> by **value**
- ✓ 5<sup>th</sup> largest in bulk drugs after US / EU / Japan & China
- ✓ 20-25% of the world's generic drugs produced in India
- ✓ 22 Billion USD market

## Volume & values domestically

- ✓ More than 20000 registered units, +/- 10,000 active
- ✓ Top 250 companies control 70% of the market
- ✓ Top 10 companies have ~ 30% of the market
- ✓ Market leader has ~ 6 % market share

## Quality

- ✓ World leader in DMF filings with US-FDA – 27% of all Type 2's
- ✓ Largest # of US-FDA approved plants outside of the US
- ✓ 25% of all ANDA filings & Tentative approvals at US-FDA
- ✓ Highest # of Certificate of Suitability granted by EU Directorate of Quality Medicine
- ✓ Destination of first choice for CRAMS / CRO's

# Current Picture

## Tier1 Firms

- ✓ 50-100 large firms
- ✓ Majority wholly owned Indian firms
- ✓ R&D (typical scientific pool of +/- 1200, >200 or more PhD's)
- ✓ Global exports – FDA / MHRA / TGA / EMEA / MCC

## Tier 2 Firms

- ✓ 200-250 mid sized firms
- ✓ Limited investment capability
- ✓ Primarily serve domestic market
- ✓ Experts in reverse engineering & formulation
- ✓ Niche players who specialize in CRAMS
- ✓ Mostly export only to semi-regulated and unregulated markets

## Tier 3 Firms

- ✓ +/- 5800 small firms
- ✓ Contract manufacture for Group 1&2 companies or MNC
- ✓ Do not meet GMP for export
- ✓ Serve domestic and unregulated markets

# Case Study – India & Dr Reddy's

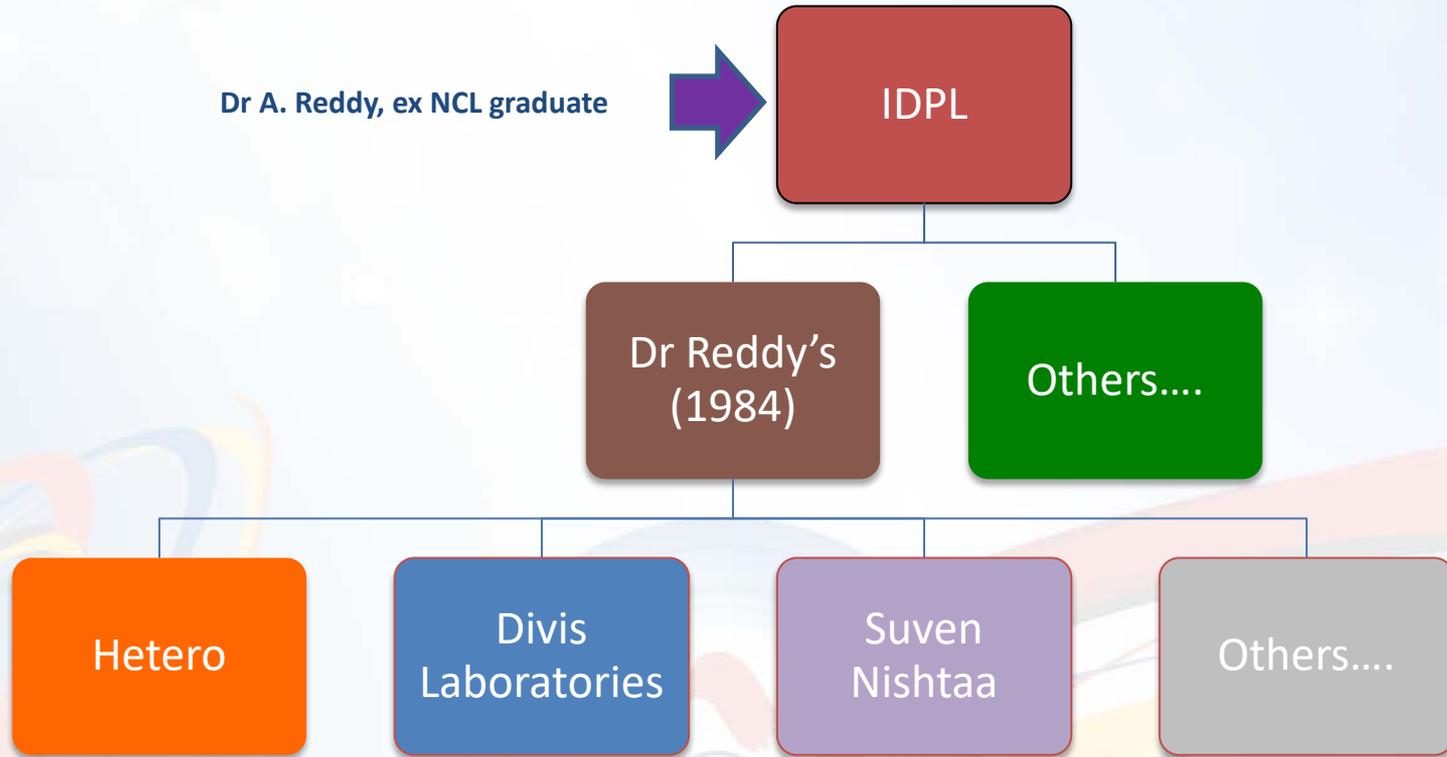
**“No Indian company can make an  
API that meets our specifications”**

*Global R&D company in letter to Dr Reddy's in 1984*

*The establishment of IDPL was a major step in bringing a large range of bulk drug technologies into the country*



# A Virtuous Cycle - entrepreneurs take off



Source: DRL Moments, Memories & Molecules. 2010

# Dr Reddy's Laboratories

- ❑ Founded 1984 by Dr Anji Reddy (PhD NCL & ex- IDPL)
- ❑ Global leader in Methyldopa (1985), Ibuprofen (1987) & Naproxen (1988)
- ❑ Training ground for Indian pharma – entrepreneurs spin off to form
  - Hetero / Divis Laboratories / Suven Nishtaa Pharma / Symbio Labs / Kareus Therapeutics / Shodhana Labs, BRR Pharmaceuticals etc
- ❑ Original R&D – first NCE patent filed in 1995

The price of doing nothing is too ghastly to contemplate...

**"In the future, regional and global power and national stability will be determined not by who controls arms, but by who controls access to medicines".**

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# Conclusion

- ❑ A state-owned company CAN HELP solve the problem of medicine shortages – investing in API's, technology creation & diffusion to local manufacturers; and by creating a window of opportunity for local manufacturers to thrive!!!
- ❑ If government does this, it can create a sustainable competitive industry.....

# Thank You!!!

[Skhumbuzo@kiarahealth.com](mailto:Skhumbuzo@kiarahealth.com)

Cell: +27 (0) 82 829 3832