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Pharmaceutical Sector Profile: Zimbabwe

Global UNIDO Project: Strengthening the local production of essential generic drugs in least developed and developing countries



UNITED NATIONS
INDUSTRIAL DEVELOPMENT ORGANIZATION

PHARMACEUTICAL SECTOR PROFILE

Zimbabwe

Global UNIDO Project:
Strengthening the local production of
essential generic drugs in least developed and
developing countries



UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
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FOREWORD

Providing adequate healthcare to their populations remains a major challenge for governments in Africa. Unsatisfactory and inadequate access to essential drugs and other healthcare commodities is a key limitation that impacts on people’s health in most developing and Least Developed Countries (LDCs).

The increased funds now available for the procurement of medicines to treat the three pandemics (HIV/AIDS, malaria and tuberculosis) are a very valuable development and have reduced the suffering and extended the lives of millions of people in developing regions. However, reliance on donor funds is clearly not sustainable in the long term and there are many other diseases for which pharmaceuticals are key treatments and for which access to quality medicines is much less advanced. In response to these considerations, the African Union, subregional organizations such as the Southern African Development Community (SADC), and various individual countries in Africa have identified the local production of essential drugs as an important component of a long term solution to the provision of adequate healthcare in developing countries.

Adequate access to drugs is dependent on both the affordability and quality of the products. Unaffordable drugs are clearly not the solution but, equally, affordable low quality products are not the answer either. Therefore, an industry that produces high quality drugs at competitive prices must be the target when developing local manufacture of pharmaceuticals in Africa.

The pharmaceutical sector is a complex one, involving many different stakeholders such as the manufacturers themselves, national regulators, government ministries, wholesalers and others. Developing the industry requires concerted action across these stakeholders to create the environment in which industry can flourish and realize its full potential as an asset to economic and social development. An example of the role of different stakeholders can be seen with regard to the scourge of counterfeit drugs, which cause huge health problems and also represent a threat to legitimate manufacturers who effectively have to compete with these substandard products.

In the face of this situation, actions by, for example, regulators to reduce the penetration of these counterfeit products would, as well as being important from a health perspective, also benefit the local pharmaceutical industry. Furthermore, quality requires upgraded skills and equipment, so how can high quality products be produced at affordable prices? This challenge requires various government ministries to work together to establish the support to the industry that will enable efficient local companies to invest in high quality production. However, those companies that do invest in upgrading will need some form of protection from those that wish to produce products at a lower standard. Consequently, the establishment and enforcement of quality standards by regulators is a critical element in solving the conundrum.

Since 2006, UNIDO, with funding from the Government of Germany, has been conducting a project on strengthening the local production of essential generic drugs in developing and Least Developed Countries. The objective is to help the pharmaceutical sectors in developing countries realize their potential role of acting as a pillar of public health and contributing to economic and social development.

The project has carried out a number of different initiatives and will be continuing and ex-

panding on this work in the future. This series of reports, which describe the local pharmaceutical industry in individual countries, is one such initiative. They provide a comprehensive picture of the status and operating environment of the pharmaceutical sector and are designed to assist national level stakeholders and inform discussions on how local production fits into the strategy for improved supply of medicines. In parallel, this information will feed into the ongoing debate among the international development community on the local manufacturing of generic medicines in closer proximity to where they are actually needed.

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ACRONYMS

ACT	Artemisinin Combination Therapy
AIDS	Acquired Immune Deficiency Syndrome
API	Active Pharmaceutical Ingredient
ARCT	African Regional Centre for Technology
ARIPO	African Regional Intellectual Property Organization
ART	Antiretroviral Treatment
BE	Bioequivalence
BMI	Business Monitor International
BRI	Biotechnology Research Institute
CIF	Cost, Insurance and Freight
CIPIH	Commission on Intellectual Property, Innovation and Public Health
CIPR	Commission on Intellectual Property Rights
COHRED	Council on Health Research for Development
COMESA	Common Market of East and Southern Africa
CRO	Contract Research Organization
CTD	Common Technical Document
DCC	Drugs Control Council
DCs	Developing Countries
DFID	UK Department for International Development
DMF	Drug Master File
DOTS	Directly Observed Treatment, Short-course
DRA	Drug Regulatory Authority
ECSCA	East, Central and Southern African Health Community
EDLIZ	Essential Drug List for Zimbabwe
EOI	Expression of Interest
EPP	Epidemic Projection Package
ESP	Expanded Support Programme (HIV/AIDS)
FBTI	Food and Biomedical Technology Institute
FDA	Food and Drug Administration (US)
FDCs	Fixed Dose Combinations
FPP	Finished Pharmaceutical Product
GATT	General Agreement on Tariffs and Trade
GDP	Gross Domestic Product
GFATM	Global Fund to fight AIDS, Tuberculosis and Malaria
GMPs	Good Manufacturing Practices
GNP	Gross National Product
GNU	Government of National Unity
GPA	Global Political Agreement
GSPA	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HAI	Health Action International
HBC	High Burden Countries
HDPE	High Density Polyethylene
HIV	Human Immunodeficiency Virus
HSS	Health Systems Strengthening
HVAC	Heating, Ventilation and Air Conditioning
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICTSD	International Centre for Trade and Sustainable Development
IERC	Institutional Ethical Review Committee
IGWG	Intergovernmental Working Group on Public Health, Innovation and Intellectual Property
IPRs	Intellectual Property Rights
IRP	International Reference Price
ISI	International Scientific Information
LPG	Lowest Price Generic
MASCA	Medicines and Allied Substances Control Act
MCAZ	Medicines Control Authority of Zimbabwe
MCC	Medicines Control Council (of South Africa)
MDG	Millennium Development Goal
MIIT	Ministry of Industry and International Trade
MoHCW	Ministry of Health and Child Welfare
MPR	Median Price Ratio
MRCZ	Medical Research Council of Zimbabwe
MSG	Most Sold Generic
MSH	Management Science for Health
NAC	National AIDS Council
NATF	National AIDS Trust Fund
NCE	New Chemical Entity
NDA	New Drug Application
NDDS	Novel Drug Delivery System
NDP	National Drug Policy
NDTPAC	National Drug and Therapeutics Policy Advisory Committee
NEC	National Ethics Committee
NECF	National Economic Consultative Forum
NEPAD	New Partnership for Africa's Development
NGOs	Non Governmental Organizations
NHA	National Health Accounts
NTP	National Tuberculosis Programme
OAPI	African Intellectual Property Organization
OTC	Over The Counter
OVCs	Orphans and Vulnerable Children
PCD	Pharmaceutical and Chemical Distributors
PCT	Patent Cooperation Treaty
PEPFAR	(US) President's Emergency Plan for AIDS Relief
PI	Protease Inhibitor
PIC/S	Pharmaceutical Inspection Cooperation Scheme
PLHIV	People Living with HIV
PLWHA	People Living with HIV/Aids
PMA	Pharmaceutical Manufacturers' Association
PMPA	Pharmaceutical Manufacturing Plan for Africa
PMTCT	Prevention of Mother to Child Transmission
QbD	Quality by Design
QC	Quality Control
QOS	Quality Overall Summary
R & D	Research and Development
RBM	Roll Back Malaria
RCZ	Research Council of Zimbabwe
SADC	Southern African Development Community

SAGMA	Southern African Generic Medicines Association
SANAS	South African National Accreditation System
SESTAR	Strategizing for Economic Stabilization and Recovery
SIRDC	Scientific Industrial Research and Development Centre
SMEs	Small and Medium Enterprises
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
TRIPS	Trade Related Aspects of Intellectual Property Rights
UNCTAD	United Nations Conference on Trade and Development
UNIDO	United Nations Industrial Development Organization
VAT	Value Added Tax
WHA	World Health Assembly
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization
ZANU-PF	Zimbabwe African National Union-Patriotic Front
ZDV	Zidovudine
ZIA	Zimbabwe Investment Authority
ZINATHA	Zimbabwe National Traditional Healers Association
ZIPO	Zimbabwe Intellectual Property Office
ZNASP	Zimbabwe National HIV and AIDS Strategic Plan
ZRDCL	Zimbabwe Regional Drug Control Laboratory

EXECUTIVE SUMMARY

This report analyses the pharmaceutical manufacturing sector in Zimbabwe with a strong emphasis on generic essential medicines used in the management of Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), Malaria and Tuberculosis. Four companies namely, CAPS Private Limited, Datlabs, Plus Five Pharmaceuticals and Varichem Pharmaceuticals are profiled.

The pharmaceutical market in Zimbabwe is a relatively modest one with a balanced set of supply and demand fundamentals. Although there is a huge need for medicines used in the management of the three disease areas, the funding gap is too wide to meet this need. On the supply side, local generic manufacturing companies have relatively balanced product portfolios and are able to supply some 47 per cent of medicines by item on the Essential Drug List for Zimbabwe (EDLIZ). However, these portfolios are aged and highly commoditized resulting in poor export performance and intense competition from foreign suppliers, especially those of Indian origin.

Despite the balanced product portfolios of local generic pharmaceutical companies, the speed of generic drug product development and launch on the Zimbabwean pharmaceutical market is very slow as is evident from the absence of current therapies in local companies' portfolios for the management of malaria, tuberculosis and HIV/AIDS.

There are no up-to-date studies reviewing the prices of essential medicines, trends over time, affordability and availability. The last such study was carried out in 2004. However, research carried out in the framework of this report revealed that the prices of medicines in Zimbabwe are generally higher than international prices and that purchasing power for medicines among the population is very low.

With respect to local production of pharmaceuticals, at policy level there is a perceived conflict between industrial policy, which aims to promote local manufacture, and health policy, which aims for maximum access to essential medicines. In the area of antiretrovirals (ARVs), procurement of imported medicines by the Ministry of Health, thereby sidelining a local manufacturer of the same products, is an example of these conflicting objectives.

The overall importance of local pharmaceutical manufacturers cannot be overemphasized given their contribution to the production of essential medicines (47 per cent of items on the Essential Drug List for Zimbabwe). Nonetheless, there is a need to widen local manufacturers' product portfolios to cover combination tuberculosis and antimalarial drugs and certain specific ARVs which are not being locally manufactured.

An analysis of the pharmaceutical value chain in the pharmaceutical market in Zimbabwe reveals the need for local generic pharmaceutical manufacturers to embark on strategic alliances with selected partners in order to address weaknesses. Some of the main areas identified in this context are Research and Development tie-ups, strategic equity/loan investments and co-marketing activities.

With respect to the profiled local companies, the current business environment presents many challenges in the form of lack of funding - both short and long term, low disposable incomes among the population, aged and antiquated property, plant and equipment, an unfavourable tariff structure and other negative policies which are not pro-local production of pharmaceuticals.

The Patent Act of 1996, as amended in 2002, is in need of a complete overhaul in order to safeguard the interests of generic producers. In its present form, the Act allows for issuance of frivolous patents and use of patent thickets and follow-on patents. Provisions in the Act with respect to compulsory licensing need major revisions in order to facilitate exports of certain medicines. The Act also needs to provide comprehensive coverage of flexibilities as outlined in the Trade Related aspects of Intellectual Property Rights Agreement (TRIPS).

Although Zimbabwe has had a national drug policy since independence in 1980, its implementation has been erratic and, currently, there is no action plan for plan for this. The policy is also in need of constant updates.

Zimbabwe's drug regulatory machinery is relatively strong when compared with that of its counterparts in the African region. However, local pharmaceutical manufacturers feel that the regulatory authority, the Medicines Control Authority of Zimbabwe (MCAZ), is too strict. However, the authority has had its fair share of challenges especially in the areas of manpower and financial resources. Fees charged by MCAZ for various services, especially registration and retention of registered products, are considered prohibitive by the local industry especially in view of the prevailing lethargic business environment.

The local generic pharmaceutical industry needs to actively participate in the various international and regional activities which have a bearing on the industry. These include the Global Strategy and Plan of Action on Public Health, Intellectual Property and Innovation (GSPA), the Pharmaceutical Manufacturing Plan for Africa (PMPA) and the Southern African Development Community (SADC) Pharmaceutical Business Plan. These plans will have a huge impact on local pharmaceutical manufacturers yet, to date, their involvement has been minimal or non-existent.

The areas of pharmaceutical research, science and technology need strengthening if local generic pharmaceutical manufacturers are to keep ahead of the tide and be able to compete regionally and globally. Generally, Zimbabwe's pool of human resources skilled in science and technology has shrunk substantially as a result of brain drain to other countries and there is a need to address this area urgently in order to restore and increase this pool.

This is also the case with pharmacy education which feeds into the science and technology human resource pool. Pharmacy training has been hit hard by the mass exodus of teaching staff resulting in inadequate staff levels with repercussions on the quality of the pharmacist cadre. Lack of appropriate lecturers has also led to the decline in postgraduate activities. This obviously weakens the human resource base for the local pharmaceutical manufacturing industry.

The Pharmaceutical Manufacturers' Association needs a major overhaul in order to increase its effectiveness. Lobbying and advocacy activities have been very weak and, in many cases, lack the substantive evidence needed to support calls for the policy changes and new strategies and policies the industry needs if it is to be sustainable.

The National Pharmaceutical Company (NatPharm) of Zimbabwe, which is vital to the survival of local pharmaceutical manufacturers from a throughput perspective, has serious liquidity problems which have resulted in lack of procurement of much needed pharmaceuticals for the country. This has led to a serious business viability challenge for local producers of pharmaceuticals since it is orders from NatPharm which provide them with the necessary volumes to attain adequate levels of capacity utilization and economies of scale.

Whilst the World Health Organization (WHO) Prequalification of Medicines Programme has opened up opportunities for local manufacturers for increased business in the areas of antiretrovirals, antimalarials and tuberculosis drugs, these companies have struggled to attain WHO Prequalification for their products in these three disease areas and have thus been unable to access donor funded markets, most of which require WHO Prequalification.

One local company did obtain prequalification status for two of its ARVs at the end of 2010 but this is just one step towards meeting a major challenge to local pharmaceutical production. Moreover, local industry faces a myriad of other challenges, which include infrastructure, strategy, technical issues, liquidity, policy, the regulatory and legal environment, the trade association, human capital requirements, and NatPharm funding.

In order to strengthen capacity to produce pharmaceuticals in Zimbabwe, a number of initiatives are needed at various levels. Policy issues need to be addressed urgently in order to create a conducive business environment for the industry. In addition to an overhaul of the Zimbabwe Patent Act, additional training for staff members of the Zimbabwe Intellectual Property Office (ZIPO) and the African Regional Intellectual Property Rights Organization (ARIPO) is required in order to make the Zimbabwe patent system more water tight and to avoid the issuance of frivolous patents.

The Medicines Control Authority of Zimbabwe (MCAZ) and the School of Pharmacy require urgent assistance to strengthen their capacity to serve the local pharmaceutical manufacturing industry. Three of the four companies interviewed for this report, namely Datlabs, Plus Five and Varichem Pharmaceuticals, have identified capacity-building projects to assist them in their quest to increase local production of essential generic medicines for the country and the region. They are hoping to receive external assistance from development institutions in order to implement these projects.

The industry also needs support, through the Pharmaceutical Manufacturers Association, in the form of training in pharmaceutical technology, Good Manufacturing Practices and TRIPS. This would go a long way in assisting local industry to increase its knowledge base and thus build competencies that can enhance local production. Additional help in the areas of strategic management, pre-investment studies, business planning and business model synthesis and analysis will also be critical for the success of the local pharmaceutical producers.

1. INTRODUCTION

The Zimbabwean economy has been experiencing serious challenges over the last decade with unemployment and hyperinflation reaching unprecedented levels and extensive economic and political turmoil. In September 2008, the ruling party and the two main opposition parties signed a Global Political Agreement (GPA) whose intention, amongst other things, was the “Restoration of Economic Stability and Growth”¹. The GPA led to the formation in February 2009 of a Government of National Unity (GNU), a coalition government involving the three parties to the GPA.

Following the formation of this new Government, the Zimbabwean economy abandoned its national currency, the Zimbabwean Dollar, in favour of a foreign multicurrency system. Although this led to a degree of stabilization of the economy, it is still in desperate need of a very large injection of liquidity to kick start all sectors, especially manufacturing, whose base was seriously eroded during the years of economic turmoil.

The role of pharmaceuticals in the overall manufacturing sector was defined in the National Drug Policy, unveiled in December 1995, which states as one of its objectives: “To promote and encourage further the production of essential pharmaceutical products and raw materials required for these, thus achieving medicine self reliance in Zimbabwe. The Policy aims at promoting and encouraging the most cost effective local production of safe, effective, and good quality drugs in order to achieve optimal self reliance within the context of national development goals”.

The devastating effects of the three pandemics, namely Human Immunodeficiency Virus (HIV)/Acquired Immunity Deficiency Syndrome (AIDS), Tuberculosis (TB) and malaria have focused great attention on the pharmaceutical sector. It was mainly the HIV/AIDS pandemic which stimulated discussion and recognition of the need to tackle the disease swiftly. Zimbabwe has one of the highest incidences of HIV/AIDS in Sub-Saharan Africa and the urgent need to expand treatment in order to reduce the mortality rates was clear.

The Government of Zimbabwe declared a six month period of emergency on HIV/AIDS in May 2002. The notice from the Minister of Justice reads: “In view of the rapid spread of HIV/AIDS among the population of Zimbabwe, the Minister declared an emergency for a period of six months, with effect from the date of promulgation of this notice, for the purpose of enabling the State or a person authorized by the Minister under section 34 of the Act (Minister of Justice, Patent Act Chapter 26:03 as Amended in 2002, 2002):

1. To make or use any patented drug, including any antiretroviral drug, used in the treatment of persons suffering from HIV/AIDS or HIV/AIDS related conditions;
2. To import any generic drug used in the treatment of persons suffering from HIV/AIDS or HIV/AIDS related conditions.”

This period of emergency was then further extended for six years running from January 2003 to December 2008 as provided for in Statutory Instrument 32 of 2003 (Minister of Justice, 2003).

¹ Agreement between the Zimbabwe African National Union-Patriotic Front (ZANU-PF) and the two opposition parties, Movement for Democratic Change-Tsvangirai (MDC-T) and Movement for Democratic Change-Mutambara (MDC-M).

This declaration of a period of national emergency on HIV/AIDS in Zimbabwe paved the way for the Government to issue compulsory licences and/or government use orders to Zimbabwean companies for the importation or local manufacture of HIV/AIDS related medicines. Varichem Pharmaceuticals, one of the first companies in Sub-Saharan Africa to manufacture generic antiretrovirals (ARVs) was issued with a compulsory licence for the manufacture of generic ARVs (blanket licence) on 8 April 2003 and the company introduced its first generic antiretroviral in October 2003.

Against this background, Varichem and another local company, Datlabs, were given a special dispensation for three years to supply ARVs to the Government of Zimbabwe without prior calls for tender. However, the acute shortage of foreign currency prevailing in the country meant, in fact, that the government was unable to go ahead and procure these medicines on this preferential basis. CAPS, another local generic pharmaceutical company, was given approval from the Medicines Control Authority of Zimbabwe (MCAZ) to market its first generic ARV in October 2005.

All these developments were welcome in the Zimbabwean health sector. However, Zimbabwe as a nation has not benefited much from the local production of ARVs as a result of the severe and sustained deterioration in the national economy and the structure of financing of ARVs as outlined later in this report. In view of the extensive shortfalls in government revenue, public sector funding of Antiretroviral Treatment (ART) has been minimal with the result that, if ARVs are to be supplied to those who need them, then other funding sources are required.

Given the magnitude of the HIV/AIDS pandemic in the world, the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) was established to boost resources to fight three of the world's most devastating diseases and to direct those resources to the areas of greatest need. Since its creation in 2002, the Global Fund has become the main source of funds to fight the three pandemics. It provides a quarter of all international financing for AIDS globally, two-thirds for TB, and three-quarters for Malaria.²

In 2003, the (US) President's Emergency Plan for AIDS Relief (PEPFAR) was launched to combat global HIV/AIDS - the largest commitment by any nation to combat a single disease in history. In addition to GFATM and PEPFAR, various other organizations, such as UN Agencies, Non Governmental Organizations (NGOs) and the national level HIV/AIDS Expanded Support Programme (ESP) have been funding procurement of ARVs.

PEPFAR requires that any procurement of a product under this programme be either approved or tentatively approved by the US Food and Drug Administration (FDA). Moreover, GFATM, most NGOs and all United Nations (UN) agencies have similarly strict procurement requirements for ARVs, antimalarials and TB drugs.

GFATM requires that any product procured be either WHO prequalified³ or registered with a stringent regulatory authority or has been recommended for use by the Expert Review Panel⁴ (GFATM, 2009). A stringent drug regulatory authority means any regulatory authority which is (a) a member of the International Conference on Harmonization (ICH); or (b) an ICH observer, being the European Free Trade Association (EFTA), Health Canada and WHO (as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally binding mutual recognition agreement. Thus, the

² Global Fund Website.

³ Refer to section 6.5.5 on WHO Prequalification of Medicines Programme.

⁴ Where there are not enough prequalified products or stringent regulatory authority approved products.

Medicines Control Council (MCC) of South Africa is not considered to be a stringent drug regulatory authority.

Until late 2010, neither Varichem nor CAPS had any of their products WHO prequalified, approved or tentatively approved by the FDA or registered with stringent regulatory authorities (Varichem has just obtained prequalification for two of its ARVs).

No formal analysis has been carried out as to why, despite producing ARVs for many years, most local manufacturers have failed to have their products prequalified by WHO, although various constraints have been cited over the years. These include the high costs of carrying out bioequivalence studies, formulation challenges, especially for TB Fixed Dose Combinations (FDCs) and Artemisinin based Combination Therapy (ACT), outdated and antiquated equipment, and the challenges of compliance with Good Manufacturing Practices (GMP).

It is against this background that UNIDO wishes to help strengthen the local production of essential medicines in developing countries, particularly those used in the management of HIV/AIDS, TB and malaria. This report has been commissioned with a view to establishing the current status of the pharmaceutical sector in Zimbabwe with respect to the production of essential medicines, with particular emphasis on drugs against the three major pandemics of HIV/AIDS, TB and malaria.

The report is based on company responses to structured questionnaires, extensive literature reviews and personal interviews with important stakeholders in the private and public sectors. The findings will assist in formulating recommendations for the strengthening of local manufacturing of essential generic medicines through appropriate interventions. Local manufacturers need assistance from development institutions in order that those among them who already produce the relevant generic medicines can prepare themselves for WHO prequalification and to enable those companies not yet manufacturing these products to do so.

Some producers in Zimbabwe are not pursuing WHO prequalification of medicines as they see this as an expensive and difficult task upon which to embark. This mindset inevitably shuts out such companies from a lucrative pool of funding for the common diseases affecting the region. It is no surprise that they find themselves in a 'market deficiency crisis' as it is a recurrent feature of developing countries that a great disparity exists between the need⁵ for medicines to treat endemic diseases and the lack of purchasing power of (or for) those patients most at risk.

Any review of the growing importance of local pharmaceutical production in Zimbabwe inevitably leads to the intense ongoing debate on the commercial viability of local pharmaceutical production in developing countries given the international market dynamics (the political economy of the pharmaceutical industry). Many aspects of industrial development policy in developing countries seem, at first glance, to run counter to health policy objectives. This apparent incompatibility has led to tension between a health policy focusing on the objective of increasing access for patients to low cost and quality-assured medicines and an industrial (primarily private sector) policy of promoting economic growth and employment through local industry development even if the products involved are initially more expensive than those on the international market.⁶

⁵ The word 'need' has been used here in preference to demand as the word 'demand', technically speaking, implies that the purchasing power to finance these needs exists.

⁶ Local Production of Pharmaceuticals: Industrial Policy and Access to Medicines, Warren Kaplan and Richard Laing.

Against this background, UNIDO has been quite clear in defining its global project on ‘Strengthening the local production of essential generic drugs in the least developed and developing countries’ that the project will only support those enterprises which meet the following criteria:

1. The production is economically viable and sustainable in the long term
2. The local production increases access to drugs through local availability at current market prices or lower than current market prices
3. The products meet the highest quality standards of international GMP
4. Key personnel are familiar with GMP and ideally have experience in running a GMP-compliant facility
5. Staff are fully committed to supporting the efforts of consultants/experts and carry out assigned tasks in a self-reliant manner

It is therefore vital that individual companies and, above all, pharmaceutical business trade associations carry out studies which will provide a strong foundation for their arguments in favour of increased local production. Evidence-based advocacy will go a long way in clearing misconceptions and establishing the facts in this intense debate. Manufacturers and business trade associations need to ask themselves complex questions about their existence and about their sustainability. According to Kaplan and Laing, these questions should be informed by political and economic considerations, marketing strategies, human resource requirements, legal, regulatory and intellectual property constraints, as well as health-related considerations such as the country’s burden of disease, treatment guidelines and Essential Medicines List. The answers to these questions should lead to a realistic vision of the role of the local pharmaceutical industry.

2. THE PHARMACEUTICAL SECTOR IN ZIMBABWE

2.1 Overview of demand for medicines and health supplies

A country’s demographic and healthcare indicators shape its demand for medicines. Total healthcare expenditure by government is normally expected to be closely associated with total Gross Domestic Product (GDP). Given this association, a strong positive relationship is also expected between the value of local pharmaceutical production and GDP. In the case of Zimbabwe, however, a weak positive relationship between the value of local production and size of population was observed in a study by Kaplan and Laing.

Table 1 summarizes the key demographic and healthcare indicators for Zimbabwe. Apart from the disturbingly low absolute levels of total government expenditure on health, private sector expenditure is largely driven by out-of-pocket private expenditure. This makes private demand for pharmaceuticals very vulnerable to the vagaries of business and economic cycles. In periods of low economic activity, purchases of pharmaceuticals will be relatively low as households adjust their budgets to cater for the essentials of basic living. As at 2006, the level of out-of-pocket private expenditure on health as a percentage of total private health expenditure in Zimbabwe was 56.7 per cent versus, for example, a level of 17.1 per cent in South Africa during the same year.

The results of a survey carried out for this report using a structured questionnaire distributed to four pharmaceutical companies in Zimbabwe revealed that business activity is currently subdued as a result of the population’s low purchasing power and negligible expenditure on health by the Government. This latter phenomenon is evident from the lack of tenders issued by the National Pharmaceutical Company of Zimbabwe (NatPharm).

Table 1: Key Demographic and Healthcare Indicators for Zimbabwe

<i>Statistic</i>		<i>Year</i>	<i>Source</i>
Population (thousands)	13 349	2007	UN Population Division
Population growth rate (per cent)	1.3	2007	World Bank
Dependency Ratio (per 100)	79	2006	World Health Statistics
GDP (US\$ Billion, current X-rate)	11.98	2008	IMF database Apr 09
GDP growth rate (per cent)	-5.3	2005	World Dev. Indicators
Total annual expenditure on health (US\$ avg. exchange rate)	502 098 533	2006	National Health Accounts
Total expenditure on health as a percentage of GDP	9.3	2006	World Health Statistics
Government annual expenditure on health (US\$ avg. exchange rate)	244 602 837	2006	National Health Accounts
Total government expenditure on health as a percentage of total expenditure on health	48.7	2006	World Health Statistics

Statistic	Year	Source
Private expenditure on health as a percentage of total expenditure on health	2006	World Health Statistics
General government expenditure on health as a percentage of total government expenditure	2006	World Health Statistics
External resources for health as a percentage of total expenditure on health	2006	World Health Statistics
Social security expenditure on health as a percentage of general government expenditure on health	na	na
Out-of-pocket expenditure on health as a percentage of private expenditure on health	2006	World Health Statistics
Private pre-paid plans as a percentage of private expenditure on health	2006	World Health Statistics

2.2 HIV/AIDS - incidence and treatment

Table 2 shows the estimated number of adults and children living with HIV in Zimbabwe. Zimbabwe is one of the countries in Sub-Saharan Africa most severely affected by the HIV and AIDS epidemic. According to the national HIV estimates of 2007, the estimated prevalence among adults between 14 and 49 years was 15.3 per cent. An estimated 1,320,739 (adults and children) were living with HIV and AIDS and, of this population, an estimated 102,566 were estimated to be in urgent need⁷ of antiretroviral therapy (ART) by the end of 2007.

Table 2: Estimated number of adults and children living with HIV in Zimbabwe⁸

	2007	Low Estimate	High Estimate
Adults (15+) and children	1 300 000	1 200 000	1 400 000
Adults (15+)	1 200 000	1 100 000	1 300 000
Children (0-14)	120 000	110 000	140 000
Adult rate (15 – 49) (per cent)	15.3	14.6	16.1
Women (15+)	680 000	650 000	720 000

Source: United Nations General Assembly (UNGASS) report on HIV and AIDS, Zimbabwe Country Report. January 2006 – December 2007

⁷ ‘Urgent need’ means HIV positive clients who are likely to die in the absence of immediate treatment and ‘need’ means those who would die within two years without ART intervention.

⁸ Epidemiological Fact Sheet on HIV AIDS, Zimbabwe 2008. WHO, UNAIDS, UNICEF. Estimates are given in rounded numbers. Estimates are presented with ranges. These bounds reflect the certainty associated with each estimate; the wider the bounds, the greater the uncertainty surrounding the estimate.

Fortunately, however, the country has been experiencing a contraction in HIV prevalence which appears to have started in the late 1990s. A decline was observed in both sentinel surveillance of pregnant women and in the national HIV estimates based on available data using the Epidemic Projection Package (EPP) and Spectrum software. Among pregnant women (15 to 49 years), HIV prevalence declined from 25.8 per cent in 2004 to 17.7 per cent in 2006. In the general population, HIV prevalence in Zimbabwe was estimated to have been 26.5 per cent in 2001 and to have declined to 23.2 per cent in 2003, 19.4 per cent in 2005 and 15.3 per cent in 2007.

This decline is attributed to a combination of both mortality and a change in behaviour. The estimated number of HIV positive clients who were likely to die in the absence of treatment was 322,000 in 2005, 342,000 in 2006 and 102,566 in 2007. Realising the need to strengthen delivery of comprehensive HIV and AIDS services, the Ministry of Health and Child Welfare (MoHCW) developed the Plan for the Nationwide Provision of ART (2005-2007). The goal was to reduce related morbidity and mortality due to HIV and AIDS and to improve the quality of life of People Living with HIV/AIDS (PLWHA) in Zimbabwe.

Table 3: Estimated number of people needing antiretroviral therapy*

	2004	2005	2006	2007
Both Sexes	600 000	600 000	590 000	570 000
Low Estimate	460 000	460 000	450 000	440 000
High Estimate	720 000	720 000	710 000	690 000

Source: UNAIDS/WHO 2008

* based on UNAIDS/WHO methodology

Although a target was set to provide ART services to 60,000 PLWHA by December 2005, 150,000 by December 2006, and 250,000 by December 2007, these figures have to be revised downwards as a result of numerous challenges such as the fact that supplies of ART were insufficient to meet demand, skilled human resources were insufficient and there were acute shortages of foreign currency for the purchase of either ARVs or raw materials for their local manufacture. Nonetheless, the MoHCW made significant progress in improving adult ART coverage from less than 1 per cent in 2002 to 8.3 per cent in 2005, 17.5 per cent in 2006, and 38 per cent as of December 2007.

The provision of Co-trimoxazole and antiretroviral therapy to children has also improved. In 2006, of the 60,920 patients accessing ART, only 4,364 were children (0 to 14 years) but this figure increased to 10,000 by the end of 2007.

Table 4: Estimated number of people receiving antiretroviral therapy

	2004	2005	2006	2007	Current Estimate	Target December 2010
Both sexes	8 000	25 000	67 000	98 000	180 000	300 000
Low Estimates	7 500	22 000	64 000	93 000		
High Estimates	9 000	27 000	70 000	103 000		

Source: UNAIDS/WHO 2008

According to the MoHCW, the December 2010 treatment target was based on using funds from Zimbabwe’s allocation under Round 8 of the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM), the extended GFATM Round 5 grant, the (US) President’s Emer-

agency Plan for AIDS Relief (PEPFAR) and a basket funding mechanism to which donors contribute for various HIV and AIDS interventions known as the Expanded Support Programme on HIV/AIDS (ESP).

The choice of drug regime is based on the ‘essential drug’ concept and the rational use of medicine. In the Zimbabwe treatment guidelines, use of Fixed Dose Combinations (FDCs) is strongly encouraged to maximize adherence. The national ART programme uses FDCs in accordance with its interim policy, i.e. use of Stavudine in first line regime, although WHO no longer recommends the use of Stavudine, stating that “Stavudine (d4T) continues to play a critical role in the scaling-up of ART in low- and middle-income countries; however, its cumulative toxicity is unacceptable to PLHIV and to many healthcare providers. Newer, more patient friendly - but currently more expensive - ART regimes are available.”⁹ WHO has recommended that countries should progressively phase out Stavudine from their first line regime but such a shift is dependent on resource availability.

According to Waning and others, examination of purchase trends for first line ARVs strongly suggests that the WHO guideline recommendations play an important role in driving ARV demand. The five ARVs listed in the 2003 WHO treatment guidelines accounted for more than 98 per cent of ARVs purchased in 2004-2006. Shortly after the addition of Tenofovir Disoproxil Fumarate (TDF) and Emtricitabine (FTC) to WHO first line treatment guidelines in 2006, purchases of TDF increased more than 15-fold, from 16,000 person-years in 2006 to 240,000 person-years in 2008, while FTC purchases increased more than 20-fold over the same period to reach 162,000 person-years in 2008.

Similarly, purchase patterns appear to reflect 2006 WHO guidance away from Stavudine (d4T) containing regimes. From 2006 to 2008, demand for Stavudine increased less than twofold, from 515,000 person-years to 895,000 person-years, while demand for Zidovudine (ZDV), which is the lowest-cost substitute for d4T grew more than fivefold, from 139,000 person-years to 733,000 person-years, over the same time period. It is thus important for Zimbabwe’s treatment guidelines to follow as closely as possible those of WHO in order to assure local producers of a diversified regional market.

In first line treatment, once the starter pack for the first two weeks has been tolerated, the step up phase is started. If there are no adverse events, such as rashes, this is continued or, otherwise, the alternative first line therapy is initiated.

Table 5: First line treatment regimes for HIV/AIDS

<i>Standard first line treatment</i>	<i>Alternative first line treatment</i>
Starter Pack for the first two weeks	Starter Pack for the first two weeks
Morning Dose: Dual combination of Stavudine 30 + Lamivudine (Dual Fixed Dose Combination (FDC) -30)	Morning Dose: Dual combination of Zidovudine + Lamivudine
Evening Dose: Triple combination of Stavudine 30 + Lamivudine + Nevirapine (triple FDC-30)	Evening Dose: Triple combination of Zidovudine + Lamivudine + Nevirapine
Step up after the first two weeks	Step up after the first two weeks
Morning Dose: Triple combination of Stavudine 30 + Lamivudine + Nevirapine (triple FDC-30)	Morning Dose: Triple combination of Zidovudine + Lamivudine + Nevirapine
Evening Dose: Triple combination of Stavudine 30 + Lamivudine + Nevirapine (triple FDC-30)	Evening Dose: Triple combination of Zidovudine + Lamivudine + Nevirapine

⁹ WHO Rapid Advice on ART, November 2009.

It is envisaged that in the near future Tenofovir plus Lamivudine plus Nevirapine (or Efavirenz) may become the preferred first line regime. This will obviously necessitate a change in the currently recommended second line regime.

Assuming a Stavudine- or Zidovudine-containing first line regime, the following second line regimes are recommended:

Table 6: Second line treatment regimes for HIV/AIDS

<i>Preferred second line</i>	<i>Alternative second line</i>
<ul style="list-style-type: none"> Tenofovir 300mg orally once a day, plus Lamivudine¹⁰ 150mg orally twice a day, plus Lopinavir/Ritonavir combination two tablets twice a day 	<ul style="list-style-type: none"> Abacavir 300mg orally twice a day (or 600mg once daily), plus Didanosine 400mg once a day if weight is greater than 80kg (or 250mg once a day of the enteric coated Didanosine for those weighing less than 60kg), plus Lopinavir/Ritonavir¹¹ two tablets twice a day.

The recommended first line treatment for children is shown below:

Table 7: First line treatment regimes for children with HIV/AIDS

<i>First Line Treatment</i>		<i>Alternative First Line Treatment</i>	
<i>Nevirapine-exposed infants</i>	<i>Non-Nevirapine exposed infants</i>	<i>Nevirapine-exposed infants</i>	<i>Non-Nevirapine exposed infants</i>
Stavudine + Lamivudine + a protease inhibitor (PI)	Stavudine + Lamivudine + Nevirapine	Zidovudine + Lamivudine + a protease inhibitor (PI)	Zidovudine + Lamivudine + Nevirapine

Recommended second line treatment in children is that, if no protease inhibitor (PI) is used in the first line treatment, Abacavir plus Didanosine, plus Lopinavir/Ritonavir should be used. If a child has been using a PI, he or she will need to use a Nevirapine-based combination.

The adult treatment guidelines for Zimbabwe are not in line with those of WHO and this complicates the production plans of local producers of ARVs since, if they base their ARV product development only on the country’s guidelines, they will be unable to supply the markets of those countries which do follow the WHO guidelines. For example, South Africa has the largest ART programme in the world and its ART guidelines have been recently revised in line with those of WHO.

2.3 Tuberculosis - incidence and treatment

The tables below show the prevalence and mortality figures for tuberculosis (TB) based on the GFATM website, country statistics and disease indicators.

¹⁰ Lamivudine may be replaced by Emtricitabine 200mg once a day

¹¹ Alternative boosted PI, Atazanavir 300mg/Lopinavir 100mg once daily

TB is among the 10 most prevalent diseases in Zimbabwe and is a leading cause of death among adults. According to the WHO 2009 Global TB report, Zimbabwe is ranked 17th among 22 high burden TB countries in the world.¹²

Table 8: Summary of main tuberculosis TB indicators

<i>Incidence</i>	<i>Statistic</i>
All forms of TB (thousands of new cases per year)	104
All forms of TB (new cases per 100 000 pop/year)	782
New ss+ cases (thousands of new cases per year)	40
New ss+ cases (per 100 000 pop/year)	298
HIV+ Incident TB cases (percentage of all TB cases)	69%

Source: Zimbabwe Tuberculosis Strategic Plan 2010

ss+ = sputum smear positive

The report also states that Zimbabwe had an estimated incidence of about 40,000 new sputum smear positive TB cases (incident rate of 298 per 100,000) and an incidence of 104,000 of all forms of TB (incident rate of 782 per 100,000). The burden of all forms of TB disease has increased over sixfold from 121 cases per 100,000 population in 1991 to 782 cases per 100,000 population in 2007.

The most significant single contributing factor to the TB epidemic is the HIV/AIDS epidemic. The TB/HIV co-infection rate in Zimbabwe is estimated by WHO at 69 per cent and treatment success rates for the national TB control strategy over the past five years have generally been showing a decline. Although up to 74 per cent of TB patients diagnosed in 2007 were successfully treated, and that figure was up from 60 per cent in the previous year, it is still well below the global benchmark target of 85 per cent recommended by WHO.¹³

There are two main drug regimes for treating TB¹⁴, each with a combination of five first line drugs. Treatment is the same for HIV-infected and non-HIV infected patients but there are specific differences between regimes for adults and children in each category.

The following table provides a key to drug abbreviations used in the treatment of TB in Zimbabwe:

Table 9: Key to TB drug abbreviations

<i>Key to Drug Abbreviations</i>	
H = Isoniazid	Z = Pyrazinamide
R = Rifampicin	S = Streptomycin
E = Ethambutol	

Category I is for all new cases of TB, regardless of site, bacteriology or severity.

Table 10: Category I drugs used in the treatment of TB

<i>Adults</i>		<i>Children < 10 years</i>	
<i>Intensive phase</i>	<i>Continuation phase</i>	<i>Intensive phase</i>	<i>Continuation phase</i>
Two months FDCs of HRZE	Four months FDCs of HR if DOTS (six FDCs of HE for patients on Nevirapine-based ARV regime who cannot wait until end of treatment)	Two months FDCs of HRZ	Continuation phase: Four months FDCs of HR (six FDCs of HE for patients on Nevirapine-based ARV regimen)

DOTS = Directly Observed Treatment, Short-course

Category II is used for all retreatment of any form of TB.

Table 11: Category II drugs used in the treatment of TB

<i>Adults</i>		<i>Children < 10 years</i>	
<i>Intensive phase</i>	<i>Continuation phase</i>	<i>Intensive phase</i>	<i>Continuation phase</i>
Intensive phase: Two months of FDCs of SHRZE + one month of FDCs of HRZE (DOTS)	Five months of FDCs of HRE (DOTS)	Intensive phase: Three months of FDCs of HRZ (DOTS)	Five months of FDCs of HR (DOTS)

Daily doses by weight for both category I and category II regimes are contained in the guidelines.

2.4 Malaria: incidence and treatment

Malaria remains an important public health problem in Zimbabwe, with transmission being generally unstable and seasonal. Plasmodium falciparum continues to be the primary species of malaria parasite, accounting for 97 per cent of confirmed cases, with P. ovale and P. malariae occurring in the remaining 3 per cent of cases, sometimes in mixed infections. Complications only occur with P. falciparum and usually in young children, pregnant women, debilitated persons, adults in epidemic prone areas and people moving from areas of no malaria to areas with malaria, including immune-suppressed patients.

The main vector mosquito is Anopheles Arabiensis. The highest transmission occurs along international border areas, especially in the north (Zambia) and the east (Mozambique). The borders to the west (Botswana) and south (South Africa) support little transmission but are epidemic prone. The central highlands are largely malaria free.

National malaria incidence was 126 cases per 1,000 persons per year in 2007 based on the 2007 figure of 1,535,877 reported cases. This represents only a 7.5 per cent decline from the incidence of 136 in the Roll Back Malaria (RBM) baseline year of 2000. The number of cases of clinical malaria (fever) reported annually has not changed materially since 1996, ranging from approximately 1.5 million to 1.8 million cases per year.¹⁵ In 2007, the number of reported deaths was 1,916.

¹² Zimbabwe Tuberculosis Strategic Plan 2010.

¹³ Zimbabwe Tuberculosis Strategic Plan 2010.

¹⁴ 5th Essential Drugs List and Standard Treatment Guidelines for Zimbabwe 2006.

¹⁵ Roll Back Malaria: Country Needs Assessment, Zimbabwe Report November 2008

Table 12: Summary of main malaria indicators, 2007

	<i>Malaria</i>
Reported cases	1 535 877
Reported deaths*	1 916
Estimated deaths	1 342

* Reported deaths = actual deaths as opposed to estimated deaths which are calculated from the prevalence of the disease and population statistics

Source: Roll Back Malaria: Country Needs Assessment, Zimbabwe Report November 2008

The preferred long term first line treatment of uncomplicated malaria in Zimbabwe is Artemisinin Combination Therapy (ACT), such as Artemether-Lumefantrine (Co-artemether). The ACT options now recommended by WHO for treatment of uncomplicated falciparum malaria are (in alphabetical order):

- Artemether plus Lumefantrine
- Artesunate plus Amodiaquine
- Artesunate plus Mefloquine
- Artesunate plus Sulphadoxine-Pyrimethamine
- Dihydroartemisinin plus Piperaquine.

Second line therapy consists of oral Quinine plus Doxycycline or Clindamycin. In cases of severe malaria, treatment must be parenteral and the drug of choice is Quinine.

Pyrimethamine and Dapsone remain the drug combination of choice for prophylaxis in Zimbabwe. Those intolerant to Pyrimethamine and Dapsone should take Proguanil and Doxycycline orally. Pregnant women in regions of potentially year round and essentially seasonal endemics should use intermittent presumptive therapy based on a combination of Sulphadoxine-Pyrimethamine and Chloroquine.

2.5 Funding of HIV/AIDS, tuberculosis and malaria treatment in Zimbabwe

In order to understand the demand and need dynamics shaping the markets for medicines to treat HIV/AIDS, TB and malaria, it is important to look at the various funding mechanisms for these three diseases in Zimbabwe. The main sources of funding are outlined below but others exist so the discussion is not exhaustive.

2.5.1 The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM)

The main source of funding for HIV/AIDS worldwide is the Global Fund to fight AIDS, Tuberculosis and Malaria. Table 13 shows details of Global Fund Grants to Zimbabwe

from Round 1 through to Round 8. Zimbabwe's Round 9 (current) proposals were rejected by the Technical Review Panel of the Fund and, in practice, Zimbabwe has so far received funds only in Rounds 1, 5, and 8.

The total funding request for HIV/AIDS during Rounds 1, 5 and 8 amounted to US\$ 371,150, 446, with a maximum approval of US\$ 158,673,238, representing 42.75 per cent of the total requested. However, only US\$ 66,599,267 had been disbursed as at December 2009. During the same period, US\$ 172,114,681 was requested for the malaria programme and the approved maximum grant was US\$ 102,191,981, representing 59 per cent of the total sought. Disbursements for the malaria programme, for the three approved rounds, amount to US\$ 49,079,798 to date.

Table 13: Grants to Zimbabwe from the Global Fund to Fight AIDS, TB and Malaria (GFATM)

all figures in US \$

Round	HIV/AIDS		Malaria			Tuberculosis			
	Total Fund Request	Approved Maximum	Total Funds Disbursed	Total Fund Request	Approved Maximum	Total Funds Disbursed	Total Fund Request	Approved Maximum	Total Funds Disbursed
1	14 100 000	14 100 000	11 149 443	8 559 911	8 559 911	6 926 197	-	-	-
5	62 478 891	59 932 023	35 396 112	28 491 458	26 550 256	19 740 979	12 041 766	11 686 597	9 105 155
8	294 571 555	84 641 215	20 053 712	135 063 312	67 081 814	22 412 622	54 621 099	28 236 113	11 260 969
Totals	371 150 446	158 673 238	66 599 267	172 114 681	102 191 981	49 079 798	66 662 865	39 922 710	20 366 124

Requests to GFATM for TB funds during Rounds 5 and 8 totalled US\$ 66,662,865, of which US\$ 39,922, 710 – or 60 per cent – was obtained, with US\$ 20,366,124 disbursed by March 2010.

For comparison, Table 14 below shows a summary of Global Fund grants to a selected group of Southern African countries from Round 1 through to Round 8.

Table 14: Global Fund Grants to a group of Southern African countries

US dollars

Country	Rounds	Components	Approved Maximum	Total 5-year Maximum
Zimbabwe	1,5,8	HIV-AIDS/Malaria/TB	\$300 787 929	-
South Africa	1,2,3,6	HIV-TB/HIV-AIDS	\$271 254 474	\$384 693 868
Angola	3,4,7	HIV-AIDS/Malaria/TB	\$175 918 075	\$236 258 097
Zambia	1,4,7,8	HIV-AIDS/Malaria/TB	\$606 944 896	\$810 483 602
Malawi	1,2,5,7	HIV-AIDS/Malaria/TB	\$541 501 950	\$860 567 470
Mozambique	2,6,7,8	HIV-AIDS/Malaria/TB	\$410 421 899	\$640 595 427

It can be seen that Zimbabwe has not fared well in terms of its requests to GFATM, having so far received considerably less than Malawi, Mozambique and Zambia.

2.5.2 The (US) President's Emergency Plan for AIDS Relief (PEPFAR)¹⁶

The PEPFAR programme in Zimbabwe has played a critical role in supporting the country's national response to the HIV epidemic. The US Government supports vital ongoing activities to prevent HIV, including behaviour change programming, voluntary and provider initiated counselling and testing, and support for the national Prevention of Mother to Child Transmission (PMTCT) programme. It plays a key role in treatment programmes through capacity building for health workers in ART delivery and provides critical support for commodity logistics systems to ensure the reliable supply of ARV drugs and other related commodities. In addition, it works with the US Embassy in Zimbabwe to strengthen public outreach on HIV/AIDS, to lessen stigma through media and cultural programmes and to support Orphans and Vulnerable Children (OVCs).

Through PEPFAR, Zimbabwe received US\$ 23.5 million in Fiscal Year (FY) 2007 and US\$ 26.4 million in FY 2008. The FY 2009 approved funding was US\$ 26.5 million, of which US\$ 6.6 million was spent on treatment. Some of the achievements (there were many more) through direct PEPFAR support during FY 2009 include:

- 40,000 individuals receiving antiretroviral treatment
- 123,000 HIV positive individuals receiving care and support (including TB/HIV)
- 17,700 HIV positive pregnant women receiving antiretroviral prophylaxis for PMTCT

2.5.3 The Expanded Support Programme (ESP)

The Expanded Support Programme on HIV/AIDS (ESP) is a common fund supported by five bilateral donors and implemented through UN agencies working in partnership with the Ministry of Health and Child Welfare, the National AIDS Council (NAC) and NGOs. The project provides strategic support at national level and targeted support in 16 districts for behaviour change communication, treatment and care, procurement, coordination and management, and monitoring and evaluation. The project will run from 2007 to 2012 with a projected budget of US\$ 40 million.

The procurement component of the ESP is implemented through the United Nations Children's Fund (UNICEF), working in collaboration with the MoHCW, NatPharm, the Medicines Control Authority of Zimbabwe (MCAZ) and WHO. As of March 2009, achievements included - *inter alia* - the procurement of antiretrovirals for 58,000 children and adults.

2.5.4 The European Union (EU)¹⁷

The European Union remains a significant donor to the health sector in Zimbabwe, contributing more than Euro 40 million in the period 2007-2009 in health related projects. The two overarching goals of EU support are to contribute to the fight against the HIV pandemic and to the achievement of the Millennium Development Goals (MDGs).

¹⁶ PEPFAR website www.pepfar.gov/countries/zimbabwe/

¹⁷ EU Support to the Health Sector in Zimbabwe 2007-2009

The EU supports several international NGOs, each with their national partner organization, to implement HIV prevention or mitigation activities in 38 districts throughout the country. There is a wide range of care, treatment and support programmes, with activities ranging from prevention of mother to child transmission to support to orphans and vulnerable children, including the provision of ART for some 2,000 people.

2.5.5 The National AIDS Council (NAC)¹⁸

The National AIDS Council (NAC) was created in 1999 and started operations in 2000. Its mandate is to prevent the spread of HIV and AIDS and to promote, coordinate and implement programmes and measures to limit the spread of HIV and impact of AIDS.

The National AIDS Trust Fund (NATF), commonly known as the National AIDS levy, was introduced by the Government of Zimbabwe in 2000 through the National AIDS Council Act. The Act required individuals and companies in Zimbabwe to pay three per cent of their income and corporate tax into the NATF to finance various programmes in response to the HIV and AIDS pandemic. The first deductions for the AIDS levy were effected in January 2000.

The Government of Zimbabwe, through the Ministry of Finance, contributed US\$ 14,700,000 in 2005, US\$ 63,437,000 in 2006 and US\$ 86,256 in 2007. However, with the collapse of the national economy, the Fund became worthless and external support was urgently required. It was hoped that funds would come from the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) following the approval of the country's proposal under the inaugural Round One grant of 2002 but these funds were not, in fact, disbursed until 2005.

In order to further boost the procurement of drugs for the treatment of AIDS, as more people went for HIV testing due to increased awareness programmes, the Government adopted a new policy in 2006 which stipulated that 50 per cent of the AIDS levy would go towards the procurement of drugs.

Following the introduction of the multi-currency system in February 2009, NAC resumed procurement of ARVs and other commodities, drawing on US\$ 1.8 million from the National AIDS Trust Fund in 2009. Some of the items procured included ARVs purchased from an Indian generic manufacturer, an incident which became a subject of contention with local pharmaceutical manufacturers as discussed later in this report.

2.6 Needs gap analysis

The large gap between the need for medicines and the actual demand (i.e. people actually receiving treatment) means that Zimbabwe is very dependent on non-national funding mechanisms such as GFATM in order to try to meet the country's medicine requirements. Given the total collapse of the economy in Zimbabwe over the last decade, the country needs extensive external support to fund the fight against HIV/AIDS, tuberculosis and malaria. As noted earlier, demand has to be accompanied by the relevant purchasing power. Unless such funding or purchasing power is mobilized, needs will remain as needs and will never be translated into demand.

¹⁸ NAC website www.nac.org.zw

It is evident from the figures shown in Tables 3 and 4 above that there is a wide gap between the number of people living with HIV/AIDS who are in need of treatment and those actually receiving treatment. This gap could be in the region of some 400,000 patients. Assuming an average treatment course cost for one year of US\$ 150 per patient (based for argument's sake on the assumption that all patients need first line treatment), some US\$ 60 million per annum would be needed for treatment alone, excluding other interventions. Moreover, if second line therapy, alternative first line therapy, and therapy for children are included in the assumption, the total funding needs would be far in excess of US\$ 60 million per annum.

Under Round 8 of the GFATM, the project entitled "Addressing critical gaps in HIV Prevention, Treatment, Care and Support" has an approved funding grant of US\$ 84,641,215 out of a total funding request of US\$ 294,571,555. As of December 2009, a total amount of US\$ 20,053,712 had been disbursed for this project.

Even including other funding mechanisms such as PEPFAR, ESP, NAC, the extended Round 5 grant and others, the current funding for HIV/AIDS is grossly inadequate. It is clear that this gap in funding arising out of the difference between the amount requested and the amount disbursed under Round 8 of the GFATM and other funding sources will remain unless other mechanisms are urgently put in place or unless the GFATM increases its grants to the country.

Also during Round 8, the malaria project, "Scaling up effective malaria control interventions in Zimbabwe" received funding of US\$ 32,810,290 out of a total request of US\$ 135,063,312 (this figure includes a Health Systems Strengthening (HSS) component of US\$ 81,748,254). As of 15 December 2009, only US\$ 20,319,314 had been disbursed.

In the case of tuberculosis funding, under GFATM Round 8, the project "Towards universal access: Improving accessibility to high quality DOTS in Zimbabwe", an amount of US\$ 54,621,099 was requested, with a grant of US\$ 28,236,113 approved and disbursement of US\$ 11,260,969 as of 11 December 2009.

2.7 Supply of medicines

Generic medicines are widely accepted in the Zimbabwean pharmaceutical market, with large volumes imported, mainly from Indian pharmaceutical companies. According to a price survey carried out in 2005¹⁹, these drugs were being offered at a much lower price than locally produced drugs. The Median Price Ratios (MPRs) for the most sold generic (MSG) equivalents and lowest price generic (LPG) were four times and three times those of the Management Science for Health (MSH) International Reference Prices (IRPs). During this survey, innovator brands of 43 medicines investigated were almost non-existent in the distribution chain, underlining the predominantly generic nature of the Zimbabwean pharmaceutical market.

According to a position paper by the Pharmaceutical Manufacturers' Association (PMA) of Zimbabwe (see Annex 3), local manufacturers are currently capable of supplying almost 47 per cent of the country's essential drug requirements by listed item. The industry aims to supply at least 75 per cent of these requirements by 2015 through new product development efforts.

¹⁹ Medicines Prices in Zimbabwe, March 2005. WHO, MoHCW, European Commission.

The Zimbabwean pharmaceutical market is quite diverse and comprehensive, with all therapeutic classes of medicines available. The wholesale business has very low barriers to entry and, as a result, there are 70 wholesalers registered with the MCAZ. However, the wholesale business is dominated by Greenwood wholesalers, a sister company to Varichem Pharmaceuticals, and by Pharmaceutical and Chemical Distributors (PCD). PCD is largely a distributor of the products of the majority of top Indian generic manufacturers. According to the 2005 Medicines Prices in Zimbabwe Survey, the cumulative mark ups added to medicines to the final consumer were as high as 138 per cent.

That report reveals that the most significant mark ups added to medicines included an average 40 per cent at the wholesale level, a 50 per cent retail mark up, import duties and insurance and freight. For medicines imported through agents, additional mark ups included finance costs and an agent mark up of around 40 per cent.

2.7.1 Drugs to treat HIV/AIDS

A number of antivirals have received marketing authorization in Zimbabwe. As of January 2008, 80 different formulations of antivirals had been approved by the MCAZ, with 61 (76.25 per cent) of these being antiretrovirals.

The first ARV to be approved in the country was GlaxoSmithKline's Zidovudine 100mg capsule in January 1988. The first generic antiretroviral to be approved locally was Cipla's Zidovudine 100mg capsule in February 2000. The same formulation was only approved in the USA in May 2007 since the US Food and Drug Administration (FDA) does not approve generic equivalents until the patent of the originator product has expired or the generic company has successfully challenged the patent and won the patent litigation against the innovator.

Ranbaxy was the second company to gain approval of a generic antiretroviral with its Lamivudine/Zidovudine combination in April 2003. In fact, April 2003 was a landmark date for the Zimbabwean pharmaceutical market since it signalled the approval of six generic antiretrovirals from Ranbaxy and Cipla, with the introduction of the first locally produced antiretroviral, Lamivudine/Zidovudine, from Varichem in July 2003. From this date onwards, more generic antiretrovirals from various other generic companies were approved by the MCAZ, giving the Zimbabwean patient a wider choice of supply.

The advent of triple fixed dose combinations (FDCs), pioneered by Cipla, simplified and revolutionised the treatment regime for HIV/AIDS. Cipla was the first company to gain approval of its two triple FDCs containing Lamivudine/Nevirapine/Stavudine in October 2004. The first locally produced triple FDC from Varichem was approved by the MCAZ in October 2005.

CAPS was the second local company to manufacture antiretrovirals, following the approval of its first generic single ingredient product in October 2005. However, from a strategic perspective, this was an ill-conceived product concept as the country's treatment guidelines were emphasizing the use of FDCs in order to improve patient compliance by reducing the pill burden and thereby improving treatment outcomes.

Nonetheless, it is disturbing to note that the ARV pipeline for local manufacturers has not been strong enough to keep pace with global developments in the treatment of HIV/AIDS. Products like Didanosine, Efavirenz, Tenofovir, Abacavir and Ritonavir boosted Lopinavir do not appear in the MCAZ pending records and, consequently, with changes in treatment regimes, local manufacturers can find themselves with redundant ARV product portfolios.

In this situation, coupled with the lack of WHO prequalification or US FDA tentative approval for ARVs by local manufacturers with the exception of the very recent prequalification of Varichem, the supply of such products has been dominated by both Indian generic manufacturers and innovators, with local companies only supplying the miniscule private market at most.

According to a report compiled by the Zimbabwean consultancy StratGenIntelli on Global Fund purchases for Zimbabwe, some US\$ 11,661,087 has been spent for the purchase of ARVs and related medicines for the country. Of this total, a meagre US\$ 13,750 was spent on Co-trimoxazole from local company CAPS. The vast majority of the money was spent on ARVs manufactured by Ranbaxy and Cipla, with Hetero and Strides receiving small amounts of this GFATM grant money.

Local producers of pharmaceuticals need to track developments in the ARV markets and transfer such technology to their companies in a timely manner to enable them to keep pace with developments in this dynamic market. It is also noteworthy that, apart from the commoditization of ARVs on the local market, the number of ARVs prequalified by WHO and those which have received USFDA tentative/final approval is high from a competition perspective. Local companies need to do thorough pre-investment studies to ascertain the feasibility of local manufacturing of ARVs before they embark on substantial investment projects in this activity.

Given the large amounts of money spent by the Global Fund, mainly on ARVs, there is a huge potential for exports to other countries in the region if producers are competitive. These markets have not been accessible to Zimbabwean manufacturers mainly because they lack WHO prequalification status or FDA tentative/final approvals of their products. They are thus losing out on potential exports and local supply opportunities.

Aspen Pharmacare Holdings Ltd. of South Africa, the continent's largest pharmaceutical manufacturer, is a good example of what can be achieved in exporting within and outside the African continent. Between March 2006 and August 2008, Aspen supplied drugs worth US\$ 28,642,340 to South Africa and other countries, with ARVs dominating the list. With finance from the Global Fund, the company has supplied various ARVs to Gambia, Uganda, Zambia, Madagascar, Honduras, Burkina Faso, Morocco, Benin, Cote d'Ivoire, Ethiopia, Swaziland and the Russian Federation.

2.7.2 Drugs to treat tuberculosis

The treatment regime for TB is quite complicated, with a patient taking multiple drugs depending on the disease category and treatment phase. The multiple drugs to be taken, together with the prolonged treatment period, require that these medicines be formulated in Fixed Dose Combination (FDC) in order to reduce pill burden and increase compliance and treatment outcomes.

Of the 16 products approved by the Medicines Control Authority of Zimbabwe (MCAZ) for use in treating TB, only two are double FDCs of Isoniazid and Rifampicin and are supplied by generic manufacturers in India. However, it is encouraging to note that, in January 2008, the number of products pending registration with the MCAZ and containing two or more anti-TB molecules, i.e. FDCs, numbered 41, these being different formulations from different manufacturers. This is not surprising given the permutations and combinations which arise from different formulation strengths containing the four core ingredients, namely Rifampicin, Isoniazid, Ethambutol and Pyrazinamide.

One of the double FDCs, containing Isoniazid and Rifampicin, was from the local manufacturer Varichem. However, the application date of the dossier is September 2000, which points to difficulty in having this dossier accepted for marketing approval. The rest of the FDCs were from generic companies outside Zimbabwe. The long outstanding list of anti-tubercular drugs pending registration confirms formulation development issues which have been highlighted in the relevant literature. It is well known that such FDCs are complicated to formulate, especially in the presence of Rifampicin and Isoniazid. Currently, no local manufacturers produce TB FDCs and a business case to support development of such formulations should be made through appropriate pre-investment studies by local companies.

2.7.3 Drugs to treat malaria

The 2006 Essential Drug List for Zimbabwe (EDLIZ) indicates that the proposed and preferred long term first line treatment for uncomplicated malaria is the use of Artemisinin Combination Therapy (ACT)²⁰. The use of Chloroquine in combination with Sulphadoxine/Pyrimethamine was an interim treatment policy and the preferred ACT is currently a fixed dose combination (FDC) of Artemether and Lumefantrine, whose generic name is Co-artemether.

An analysis of the list of approved antimalarials in Zimbabwe as at the end of 2007 reveals that the list is dominated by drugs from the old treatment regime consisting of Chloroquine and Sulphadoxine/Pyrimethamine in combination. It is disturbing to note that this report shows only limited suppliers of Quinine oral and Quinine parenteral used in the treatment of complicated malaria. The report further reveals the dependency of the country on imports of the preferred first line and second line treatment regimes, namely Co-artemether and Quinine. There are currently no local producers of these two drugs nor are there any pending applications for them. Although Datlabs has registered an injectible Quinine preparation, this product is not being produced at the moment since the company stopped the manufacturing of small volume parenterals some years ago.

With the policy preference for ACTs, as listed in the latest version of EDLIZ, it would make sense for local manufacturers to embark on an aggressive product development exercise for Co-artemether whose patent in Zimbabwe expires in June 2011. In fact, Ranbaxy has filed a high dose oral pharmaceutical formulation patent for Co-artemether, which will reduce the pill burden experienced with the current innovator Co-artemether pharmaceutical composition. This development represents innovation from a generic pharmaceutical company similar to Cipla's invention of the triple FDC containing Lamivudine/Nevirapine/Stavudine.

²⁰ 5th Essential Drugs List and Standard Treatment Guidelines for Zimbabwe 2006 (latest version).

If they are to be successful, local generic pharmaceutical companies need assistance in formulation development for ACTs. It is well known that development pharmaceuticals for ACTs is relatively complex and this is demonstrated by the fact that, as of end 2009, there were only nine ACTs prequalified by WHO.

2.8 Prices of essential medicines, trends over time, affordability and availability

A study to measure the prices of essential medicines using the WHO/HAI (Health Action International) methodology was carried out in Zimbabwe in 2004 and published in 2005 (WHO, MoHCW, EU, 2005). Whilst this study is old, and no new ones on the same subject have been carried out since then, the general results are still worth looking at.

For the sake of evidence-based advocacy and the long term development of the local manufacturing pharmaceutical industry, the Pharmaceutical Manufacturers Association and the Directorate of Pharmacy Services in the Ministry of Health and Child Welfare could institutionalise this exercise. Without such studies, unsubstantiated claims of local manufacturers' price competitiveness will prevail.

It should be borne in mind that the 2005 study was carried out in the midst of Zimbabwe's extremely difficult and volatile economic situation. Nonetheless, the major conclusions worth noting are:

- The prices of medicines in Zimbabwe were generally higher than international prices
- There was a wide acceptability of generics in the country in line with the country's successful generic prescribing policy
- Very large cumulative mark-ups are added to medicines sold in the country, from the manufacturer through to the final consumer
- There is no transparency in the pricing of pharmaceuticals with the problem more acute in the private and dispensing doctors sectors
- The availability and use of innovator products was very limited
- There is a low level ²¹ of affordability of medicines in the general public in Zimbabwe (to obtain the lowest priced generic of Atenolol, the lowest paid government worker needed to work for 0.7 days, 1.3 days and 2.3 days if obtaining the medicine in the public, private and dispensing doctors sectors respectively)

It is recommended that the PMA should organise a study of medicine prices in the private sector in order to ascertain where local manufacturers' prices stand in relation to imported products. Mere claims without factual support will not hold water. This is supported by the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property²² under Element 6, 'Improving Delivery and Access', which states that "consider where appropriate, the development of policies to monitor pricing and to improve affordability of

²¹ The lowest paid government worker would need 4.5 days' wages to purchase asthma treatment in the private sector. The same government worker would need to work for nearly 3 days to get generic medicines for asthma in the public sector.

²² Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, 61st World Health Assembly, May 2008

health products; further support WHO's ongoing work on pharmaceutical pricing." Pricing studies carried out using the WHO/HAI methodology could also reveal the existence of an unlevel playing field in the supply and distribution chains and in the procurement of pharmaceuticals and inputs for manufacturing.

2.9 Supply gap analysis

It is evident from the discussions focusing on HIV/AIDS, tuberculosis and malaria that there is a big gap in the supply of locally manufactured medicines required to manage these diseases. It is important that local manufacturers tackle the need to fill this gap in a systematic manner. Decisions to widen local manufacturers' portfolios to meet the country's requirements should be backed up by appropriate pre-investment studies proving the economic viability of the project/s.

WHO prequalification or FDA approval or tentative approval is necessary but not sufficient for commercial success. Business viability must also be considered. Local manufacturers have so far failed to export meaningfully to countries in the African region, leaving these markets to Indian suppliers who continue to dominate in the supply of medicines for HIV/AIDS, TB, malaria and other disease areas.

3. LOCAL PHARMACEUTICAL PRODUCTION

3.1 Overall sector importance

The current ability of the local manufacturing industry to supply a considerable share (47 per cent) by item of Zimbabwe's essential medicine requirements positions the sector as a key partner in delivering health to the national population. In addition to direct employment of Zimbabweans, the pharmaceutical sector supports both downstream and upstream industries. The biggest upstream success has been the establishment and support of a relatively vibrant primary packaging manufacturing industry. On the downstream side, local manufacturers support a number of retail pharmacies and pharmaceutical wholesalers.

The current status of the manufacturing sector in terms of size, structure, level of capacity utilization and profitability levels of its various subsectors, contribution to Gross Domestic Product (GDP), Gross National Product (GNP), national value addition, formal employment, export revenues, and import costs, and its general linkages with the rest of the economy, is unknown given "a general lack of timely, sound and appropriate data for planning purposes in Zimbabwe, especially in the industry sector" (UNIDO, 2010).

No trade statistics are available with respect to the level of imports and exports of pharmaceuticals in Zimbabwe. The country is a net importer of pharmaceuticals *inter alia* because of the large import bill for raw materials used as inputs in the manufacture of local formulations. According to data provided by respondents to the survey carried out in connection with this report, on average 10 per cent of output is exported, with the rest being consumed locally. Export destinations cited include South Africa, Botswana, Swaziland, Namibia, Lesotho and the Caribbean. No actual values of exports were given.

3.2 Structural characteristics

The Zimbabwean pharmaceutical industry is characterised by a few manufacturers with a total of nine players according to the most recent Register of Licensed Pharmaceutical Manufacturing Premises published by the Medicines Control Authority of Zimbabwe (MCAZ). Of these nine companies, four are serious generic manufacturers whilst the rest are largely concentrating on trading and have narrow product portfolios. These four companies could easily account for 90 per cent of the secondary pharmaceutical manufacturing (formulation) business in the country.

The industry can be divided on the basis of pharmaceutical form and therapeutic application. Formulations constitute 100 per cent of the market, with no local manufacturing company carrying out primary manufacturing of bulk drugs. The anti-infective, cardiovascular and analgesic segments constitute the majority of the Zimbabwean retail formulations market.

3.3 Competitive environment

Given the paucity of strong local generic manufacturers and their limited portfolios, there is a lot of competition from other generic manufacturers, mainly from India. Generic drug competition from the African region is limited to two South African companies, Aspen and

Adcock Ingram. There is also competition, although at subdued levels, from innovator brands, especially in areas where generic companies have not been able to introduce an equivalent generic when the innovator patents expired.

Multinationals, both innovator and generic companies, and other generic competitor companies have no direct presence in Zimbabwe. They are all represented either by distributors or wholesalers. For example, a locally based pharmaceutical wholesaler and distributor, Pharmaceutical and Chemical Distributors Private Limited (PCD) represents 14 companies, including Indian generic companies and Pfizer as an originator company.

The competitive forces shaping the generic pharmaceutical industry in Zimbabwe can be analysed as follows:

- **Threat from New Players – Low to Medium:** The main barriers to entry in the generic pharmaceutical manufacturing industry are essentially high set up and compliance costs for green field projects. Moreover, there is price-based competition in most segments which reduces the industry's attractiveness. However, for new players in trading activities, set up and compliance costs are quite low and tariff barriers to finished products are non-existent, making entry into the industry attractive. Nonetheless, the number of existing players together with the economic crisis in the country make market entry unattractive for new traders except those with niche third generation generics.
- **Market Strength of Suppliers – High:** The consistent supply of high quality APIs with appropriate documentation, such as supplier quality agreements and drug master files or certificates of suitability, is threatened, especially in the areas of HIV/AIDS, malaria and TB where there is a high demand from both generic and innovator global and/or national players. There is a tendency for innovator and other big players to buy up all APIs coming from Drug Master File (DMF) quality facilities. Local manufacturing companies are also competing with the same suppliers of APIs in the finished pharmaceutical product business since most API suppliers have integrated downstream into this area. Where the API supplier acts in such a dual role, this tends to create a significant cost advantage over local manufacturers in view of economies of scale and the non-existence of tariffs on exported finished pharmaceutical products, together with export incentives that further lower final export product prices.
- **Market Strength of Buyers – High:** Buyers are price sensitive and therapeutically equivalent substitutes are available, giving buyers a wider choice of products.
- **Threat from Substitutes – High:** The number of available generics is high and price competition is intense; hence, the threat from substitutes is high.
- **Rivalry within the industry – High:** The large number of players, especially importers from emerging pharma markets, represents a high threat; marketing is aggressive and fighting for market share intense.

3.4 The pharmaceutical value chain and strategic alliances

The pharmaceutical value chain consists of the following stages:

- Research and Development
- Inbound logistics
- Manufacturing operations
- Market development, sales and distribution

3.4.1 Research and Development

Research and Development (R & D) in the generic pharmaceutical industry is mainly confined to the following activities:

- Formulation studies/development
- Assay method development and validation
- Stability studies
- Production processes/technology improvements

Not all local companies have separate approved R & D units. Some companies utilize commercial production and quality control facilities to carry out R & D activities. This is, however, not the optimum approach as best practices require that R & D be carried out at laboratory and pilot plant levels so that intensive work can be done with no limits imposed because of cost considerations. Development work carried out in commercial manufacturing facilities will tend to have a narrow scope and can lead to poor outputs. It is generally recognised that obtaining marketing approval from the regulatory authority depends largely on the quality of work carried out during the generic drug product development process.

The adoption by MCAZ of the WHO Guideline on Submission of Documentation for Registration of Multisource (Generic) Finished Pharmaceutical Products (FPPs) and the Common Technical Document (CTD), together with the Quality Overall Summary (QOS), means that local manufacturers need to have fully compliant R & D facilities, with equipment similar to that used in the commercial manufacturing facility. Failure to do so will, in all probability, lead to the development of poor products and low quality registration dossiers, resulting in a long approval process or no approval at all. The CTD and QOS emphasize the concept of Quality by Design (QbD). This concept is impossible to institutionalize where there is no fully equipped and compliant separate R & D facility.

There is no systematic approach in the industry to technology transfer from R & D to production sites and consequently there is a risk that this can lead to repeated failures of manufacturing processes and analytical methods for a variety of reasons commonly known as “non-robust processes and methods”.

R & D projects need to be assessed for business viability and, generally, the intricacies of generic drug product project management are not well understood by most local generic manufacturers. This is confirmed by the inability of local industry to develop and introduce key molecules in time at various molecule patent expiry dates.

Although some local companies are involved in the formulation of basic dosage forms, none of them is undertaking sophisticated formulation development activities involving ACTs, tuberculosis FDCs and novel drug delivery systems. One company cited the need for assistance in this area.

3.4.2 Inbound logistics

Active Pharmaceutical Ingredients (APIs) for the local manufacture of generics in Zimbabwe are imported mainly from China, India and Italy and are usually sourced directly from the manufacturer. In some cases, where volumes are small, intermediaries become the source. Inactive ingredients (excipients), primary packaging material and secondary packaging material are acquired both locally and through import.

Local pharmaceutical manufacturers have put in place systems for the qualification of suppliers of starting materials and other critical inputs. Audits of local suppliers' facilities are carried out regularly according to defined standard operating procedures. Foreign suppliers are required to provide documentary evidence to prove the quality of their materials. These include Drug Master Files (DMFs), validation reports, and certificates of analysis which are verified in-house on at least three different batches of the appropriate material, material safety data sheets, and supplier quality agreements detailing various aspects that ensure quality supplies. It is also common practice in the industry to source starting materials from approved suppliers only.

Duties on imported raw materials have been cited as a major obstacle to the development and competitiveness of the local generic pharmaceutical industry. There is no duty levied on finished pharmaceutical products used in the treatment of chronic diseases. However, various levels of duty are levied on the inputs used to manufacture such products locally. This situation is further exacerbated by Value Added Tax (VAT) which is levied on imported materials but can subsequently be reclaimed (VAT on imports of finished pharmaceutical products cannot be reclaimed). This procedure further disadvantages the local manufacturer as it ties up valuable working capital for long periods of time.

3.4.3 Manufacturing operations

Manufacturing operations are focused on the secondary manufacturing of finished pharmaceutical products using imported APIs, local and imported excipients and packaging materials. No primary manufacturing of APIs occurs in the country and companies have not indicated their intention to embark on such an activity. Issues like economies of scale, investment capital, technology and human capital need serious consideration.

Local producer Varichem has vertically integrated backwards and has started the manufacture of primary packaging material in the form of High Density Polyethylene (HDPE) bottles used in the primary packaging of various pharmaceuticals. This has resulted in considerable cost savings.

Manufacturing processes consist of various unit operations for different conventional dosage forms ranging from manual to automatic. However, processes are predominantly manual with very low levels of automation. No specialised technology such as extrusion-spheronization, melt-extrusion is used in the manufacturing process whereas one of the ARVs currently prescribed as second line treatment uses one of these technologies. If local companies are to make a difference in the management of HIV/AIDS in Zimbabwe, they need to embark on enhancing their skills in such complex formulation.

It is important to note that machinery and equipment in the country's generic pharmaceutical industry is fairly antiquated. In this situation, it would be very difficult to introduce concepts such as quality by design and to replicate processes. The industry is thus in dire need of equipment and machinery replacement. In addition, only one of the local manufacturing facilities is able to meet international clean room standards and current Good Manufacturing Practice (GMP) requirements for facility design and layout. These plants are in acute need of refurbishment or, preferably, new installations.

3.4.4 Market development, sales and distribution

Although the public sector would normally be expected to be the largest purchaser of pharmaceuticals, sales in Zimbabwe are currently heavily biased towards the private sector because of lack of funds in the public health system. In addition, a number of challenges are faced by local manufacturers, including:

- Intensive competition from cheaper Indian generics
- Liquidity problems, with no lines of credit available to companies
- Inadequate or non-existent purchasing power in the private sector
- Vast supplies of imported pharmaceuticals provided by donors
- Imports of non-registered products

The pricing of pharmaceuticals is distorted, with public prices much lower than those set for the private market. Currently, there are no price controls on pharmaceuticals. The Pharmaceutical Manufacturers' Association (PMA) could carry out regular pricing studies to help position local companies on a competitive level and as a tool to lobby against prohibitive policies such as tariffs on imported inputs. Various discounting policies are in operation and these include discounts for wholesalers and retailers, as well as cash discounts.

On average, some 50 per cent of total private market sales are made through wholesalers, with retailers taking some 10 per cent and the rest going to non-governmental organizations (NGOs), hospitals, mines and corporate clinics. Most companies distribute these supplies by using their own and contracted vehicles. The companies CAPS, Varichem, and Plus Five have vertically integrated downstream by establishing their own wholesale and retail pharmacy distribution units.

3.5 Product portfolio analysis

The current product portfolio of a company is critical to its success in the market. Table 15 shows a summary of product approvals over four consecutive five year periods, running from January 1988 to December 2007, for the four local companies reviewed in this report as well as Cipla, an Indian pharma company, and two South African companies, Aspen and Adcock Ingram.

Table 15: Product Portfolio Analysis of Four Local Manufacturers, Cipla, Aspen and Adcock Ingram

Company	Period	No. of Products Registered	No. of Antivirals incl. ARVs	No. of TB drugs	No. of Antimalarials
Varichem	1988 to 1992	25	0	0	0
	1993 to 1997	25	0	4	1
	1998 to 2002	35	3	0	1
	2003 to 2007	18	10	0	0
CAPS	1988 to 1992	26	0	2	1
	1993 to 1997	22	0	1	0
	1998 to 2002	12	2	0	0
	2003 to 2007	8	2	0	0
Datlabs	1988 to 1992	29	0	0	1
	1993 to 1997	13	0	1	0
	1998 to 2002	7	0	0	0
	2003 to 2007	14	1	0	0
Plus Five	1988 to 1992	6	0	0	0
	1993 to 1997	0	0	0	0
	1998 to 2002	5	0	0	1
	2003 to 2007	16	2	0	1
Cipla	1988 to 1992	0	0	0	0
	1993 to 1997	0	0	0	0
	1998 to 2002	4	2	0	0
	2003 to 2007	24	7	0	0
Aspen ²⁷	2003 to 2007	118	18	1	0
Adcock Ingram ²⁸	2003 to 2007	170	23	0	0

Source: StratGenintelli, Harare, Zimbabwe

²³ South African market

²⁴ South African market

From the figures, it is quite evident that local generic companies were very aggressive in introducing new products on the market especially during the first three periods under study although for three of the four the trend was downwards. However, local company Plus Five registered a record number of new products in the fourth five-year period.

Varichem, a company established in 1985, was very aggressive with impressive new product introductions in its early stages (first three periods) but this fizzled out in the fourth period. This last period saw the introduction of 10 ARVs by Varichem and marked the end of their aggressive new product introduction capabilities. It seems that the company was now concentrating on ARVs and neglecting the other therapeutic areas which had earlier made it a shining star on the Zimbabwean generic pharmaceutical market.

Table 15 also shows that local manufacturers have not been successful in the antimalarial and antitubercular therapeutic areas, having introduced very few product lines in these two areas. It is also noticeable that Cipla entered the local market during the third period under study and registered a massive 24 products, including seven ARVs in the fourth period when most local generic companies' approved product portfolios were weakening.

If the analysis were to be extended to a fifth period, covering the years 2008 to present, this trend would be maintained, i.e. dwindling product introductions by local manufacturers and increased registrations by foreign firms, especially from India. The table also shows the relatively high number of registrations by the top two South African players, Aspen and Adcock Ingram.²⁵ These companies are very aggressive in new product introductions and local companies, at their present rate, will not be able to compete with them on the South African market. Given the fact that local companies need to register their products with the local regulatory authority before registering with a foreign authority (for locally developed products), this means that they will have to start their development cycles earlier than, for example, South African producers, if they are to compete successfully.

A review of the product portfolios of the four local companies, CAPS, Datlabs, Plus Five and Varichem as at the end of 2007 shows that these product portfolios are characterized by aged molecules (common to most companies) whose patents expired many years ago (except for ARVs) and the portfolios are generally commoditized. When compared with the product portfolios of the South African companies over the same period, it is evident that these are healthier with a relatively high number of new molecules. It is thus not surprising that local manufacturers will struggle to compete with these companies on the South African market.

3.6 Late stage product pipeline analysis

Both the future and the credit ratings of a pharma company are determined by its product pipeline. Table 16 shows a summary of the late stage product pipelines of four local companies, together with those of some selected Indian firms, over two consecutive five year periods spanning the years 1998 to 2007. It can be seen that local companies are relatively weak when compared with their Indian counterparts in terms of new product development. The weaker pipelines of local manufacturers are demonstrated by the declining trends in product approvals as shown in the table.

²⁵ South African companies typically register at least two dossiers on the same product but with a different brand name so there is inevitably some double counting in the figures presented.

Table 16: Late Stage Product Pipeline Analysis of Local Manufacturers and Selected Indian Companies

Company	Period	No. of Pending Products	No. of Antivirals incl. ARVs	No. of TB Drugs	No. of Antimalarials
Varichem	1998 to 2002	5	1	1	0
	2003 to 2007	2	2	0	0
CAPS	1998 to 2002	7	0	0	0
	2003 to 2007	3	2	0	0
Datlabs	1998 to 2002	1	0	0	0
	2003 to 2007	16	13	0	0
Plus Five	1998 to 2002	1	0	0	0
	2003 to 2007	5	0	0	0
Cipla	1998 to 2002	6	0	0	0
	2003 to 2007	51	17	0	2
Ranbaxy	1998 to 2002	0	0	0	0
	2003 to 2007	13	6	0	0
Glenmark	1998 to 2002	2	0	0	0
	2003 to 2007	8	0	0	0
Ipca	1998 to 2002	11	0	3	0
	2003 to 2007	13	0	0	1
Torrent	1998 to 2002	4	0	0	0
	2003 to 2007	10	0	0	0

Source: StratGenintelli

The quality of the product pipelines is also weak as it is dominated by aged molecules, whereas the pipelines of the Indian companies contain a relatively high number of new molecules. The Cipla product pipeline in the period under analysis is relatively strong and includes new molecules for the management of HIV/AIDS and malaria.

3.7 Company profiles

Four of the nine pharmaceutical manufacturers listed in the MCAZ Register have been reviewed in detail for this report. Company profiles were prepared based on a comprehensive 60 page questionnaire distributed to all members of the Pharmaceutical Manufacturers Association of Zimbabwe.

The companies studied and profiled are CAPS Private Limited, Datlabs, Plus Five Pharmaceuticals, and Varichem Pharmaceuticals. The other licensed companies did not participate in the review as they felt that the roles they play in the local manufacture of generic essential medicines was very minimal²⁶. The ninth company, Reckitt Benckiser, is not involved in the manufacture of generic pharmaceuticals but mainly produces two Over-the-Counter (OTC) products.

Company Profile No. 1: CAPS

²⁶ Pharmanova, Zimbabwe Pharmaceuticals, Meditech and Graniteside Chemicals

Company Overview

CAPS (Private) Limited is a wholly owned subsidiary of CAPS Holdings and was founded in 1952 as a small manufacturing and pharmaceutical wholesale business. In 1958, CAPS took a major decision to cease general wholesaling operations and to focus on the manufacture and marketing of pharmaceutical preparations. CAPS was the second pharma company in Zimbabwe to manufacture ARVS locally.

Basic Company Statistics

Year of establishment:	1952
Ownership:	Parent company Public, listed on the ZSE
No. of employees:	200
Facility manufacturing licensing:	Approved, MCAZ, MCC, Namibia NMRC, Botswana DRU
Last GMP inspection:	MCAZ, March 2010
Product range:	204 items (as at end 2007, including registrations under Geddes*)
ARVs; antituberculars; antimalarials:	Acyclovir; Nevirapine, Lamivudine; Pyrazinamide, Ethambutol, Streptomycin Sulphate, Streptomycin; Chloroquine Phosphate
Facility design & layout:	Recently refurbished, requires HVAC
Average age of equipment:	n.a.
Additional equipment required:	n.a.
Capital needed for additional equipment:	n.a.
Capacity utilization (2009):	20 per cent to 30 per cent
Location:	Harare, Zimbabwe

Vision – To be Africa's leading household name in generic pharmaceuticals and health care

Mission – To create and maintain a continuous demand for our products and services. To achieve this, we will continuously strive to provide customer oriented products and services using relevant technology, systems and nurturing an entrepreneurial culture to sustain and enhance our business.

Core Values – Ethics and Integrity, Mutual Respect of Individuals, Value and recognize Good Performance, Continuous Development of our People, Quality Products and Services, Good Corporate Governance and Responsible Corporate Governance

Recent Company Activities

CAPS completed a new facility in order to meet increasing GMP requirements. However, this facility was temporarily shut down by the regulatory authority in December 2009 but re-opened in mid-March 2010. The authority had not sanctioned the operation of the new facility.

SWOT Analysis

Strengths

- Over 200 products registered in 16 Sub-Saharan African countries
- Well established, has been in operation since 1952
- Strong brand equity
- Large pool of installed capacity
- Qualified and experienced senior management

Weaknesses

- Negative publicity in home country
- Lack of financial resources to satisfy markets and introduce new products
- Technology used in production has room for improvement
- Inadequate resources for new product development

Opportunities

- Increased product portfolio
- Growing attention to health sector at national and international level
- Saturation point of market entry is far away
- Widespread use of generics
- New markets opening up

Threats

- Low cost Asian generic producers
- Intense rivalry
- Stricter registration procedures and high cost of introducing new products
- Brain drain and high cost of sales and marketing

Comments

Whilst there is a perceived strength within CAPS that the company has a strong product portfolio, this portfolio is old and heavily commoditized. This is supported by the huge decrease in export activity. At its high point, CAPS derived at least 20 per cent of its turnover from exports, i.e. when the product portfolio was still young and prone to less competition. New product introductions have been minimal.

Contact

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n.a. = not available * Geddes is a subsidiary of CAPS Holdings, the holding company of CAPS Pharmaceuticals

Company Profile No. 2:

Datlabs

Company Overview

Datlabs is a 100 per cent subsidiary of Pharmed Labs Jersey Limited, domiciled in the Channel Islands, and was established in the early 1950s in Bulawayo. The company has links with the Adcock Ingram Group through technology agreements. The company has a strong portfolio of consumer health care products which it uses to its advantage on the local market.

Basic Company Statistics

Year of establishment:	1950s
Ownership:	100 per cent private foreign
No. of employees:	175
Facility manufacturing licensing:	Approved, MCAZ, Namibia
Last GMP inspection:	22 May 2005, 22 August 2007
Product range:	137 items (as at end 2007)
ARVs; antituberculars; antimalarials:	Acyclovir; Rifampicin; Chloroquine Phosphate, Chloroquine, Quinine Hydrochloride, Dapsone, Pyrimethamine
Facility design & layout:	Requires upgrade, no heating, ventilation or air conditioning (HVAC)
Average age of equipment:	16.5+ years (Range: 1 yr to 30+ years)
Additional equipment required:	24 pieces
Capital needed for additional equipment:	US\$ 1.5 million
Capacity utilization (2009):	32 per cent
Location:	Bulawayo, Zimbabwe

Vision – To be the preferred supplier of quality branded health and personal care products

Mission – Datlabs is in the business of manufacturing and marketing health and personal care products in Zimbabwe

Core Values – Passion, Respect, Integration, Development and Execution

Recent Company Activities

None

SWOT Analysis

Strengths

- Well established company
- Enjoys favourable quality manufacturer image
- Tie ups with a renowned pharmaceutical company with up to date R & D facilities

Weaknesses

- Narrow generics portfolio
- High cost of production
- Reliance on external R & D
- Old and outdated equipment

Opportunities

- Expansion of generics portfolio
- Development of tuberculosis FDCs
- Exploitation of SADC and COMESA markets

Threats

- Regulatory censure for slow compliance with latest cGMP and WHO guidelines
- Cheaper imports from Asia

Comments

Datlabs does not have its own R & D facilities and acquires dossiers from a technical partner from South Africa. However, regulatory differences in certain requirements between the two countries strongly disadvantage the company in its business development activities. The issue of technology transfer is also a huge compliance hindrance to first mover advantage.

Contact

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Company Profile No. 3:

Plus Five

Company Overview

Plus Five Pharmaceuticals Private Limited (Plus Five) is the youngest, local, wholly owned generic pharma company in Zimbabwe having started operations in August 1996. The start-up was a joint venture partnership between two Zimbabweans and the Venture Capital Company of Zimbabwe which exited the company in 2001, offloading its shares to two local shareholders and promoters of the project.

Basic Company Statistics

Year of establishment:	1996
Ownership:	100 per cent local private
No. of employees:	91
Facility manufacturing licensing:	Approved, MCAZ
Last GMP inspection:	6 October 2009
Product range:	28 items
ARVs; antituberculars; antimalarials:	Acyclovir; Chloroquine Phosphate
Facility design & layout:	Requires upgrade, no HVAC
Average age of equipment:	8.25 years (Range: 0.5 yrs to 20 years)
Additional equipment required:	30 pieces
Capital needed for additional equipment:	US\$ 1.5 million

Capacity utilization (2009): 17.5 per cent (plant shut down for upgrade for 9 months)

Location: Bulawayo, Zimbabwe

Vision – To make the Plus Five brand the leading one in the health delivery system of Zimbabwe and the region

Mission – To provide effective and affordable health solutions and to enhance the quality of life through the production, marketing and distribution of quality, safe, efficacious and essential drugs to Zimbabwe and the region at affordable prices

Core values – Innovativeness, Professionalism, Customer Satisfaction, Integrity and Social Responsibility

Recent Company Activities

Plus Five embarked on a nine month plant refurbishment in 2009 to upgrade to GMP standards. A second phase of the upgrade was due in 2010 covering utilities upgrading and construction of a QC laboratory.

SWOT Analysis

Strengths

- Unique niche in finished pharmaceutical products
- Innovativeness
- Vertically integrated
- Low cost base
- Low gearing
- Niche markets

Weaknesses

- Lack of R & D capabilities
- Lack of a QC laboratory including microbiology
- Marketing skills non-availability
- Narrow product range
- Lack of WHO prequalification
- Poor IT system

Opportunities

- 55 per cent of essential medicines imported
- 95 per cent of specialist medicines imported
- Regional trade blocs
- HIV/AIDS pandemic

Threats

- Long registration approvals
- Political and economic risk
- Lack of credit lines and low liquidity levels
- Unfavourable tariff structure
- Bio-similars
- Counterfeit and substandard medicines

Comments

The company does not have an independent compliant R & D facility. Development activities are carried out in commercial manufacturing facilities and the company does not have its own fully GMP compliant QC laboratory. Microbiology activities are outsourced.

Contact

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Company Profile No. 4: Varichem Pharmaceuticals

Company Overview

Varichem Pharmaceuticals, established in 1985, was the first private, wholly locally owned generic pharmaceutical company in Zimbabwe. The company was one of the leading pioneers in the manufacture of generic antiretrovirals in Africa, having introduced its first generic ARV in October 2003 and, in the last quarter of 2010, it became the first local pharma company to obtain WHO prequalification status for two ARVs. Initially, it was the fastest growing pharmaceutical manufacturing company in the country and remained so up until late 2006 when it lost steam and its product pipeline and new approvals significantly declined.

Basic Company Statistics

Year of establishment: 1985
Ownership: 100 per cent private local
No. of employees: 110

Facility manufacturing licensing: Approved, MCAZ, MCC, Namibia NMRC, Botswana DRU

Last GMP inspection: 27 July 2009, 21 Jan 2004, 28 Nov 2003, 31 March 1999

Product range: 103 items (as at end 2007)

ARVs; antituberculars; antimalarials: Lamivudine+Zidovudine, Lamivudine + Nevirapine + Stavudine; Rifampicin, Isoniazid, Pyrazinamide, Ethambutol

Facility design & layout: GMP compliant, recently refurbished

Average age of equipment: 9.6 years (Range: 2 yrs to 30+ years)

Additional equipment required: 18 pieces

Capital needed for additional equipment: US\$ 1.0 million

Capacity utilization (2009): 30 per cent to 60 per cent

Location: Harare, Zimbabwe

Vision – To become a research-based, world class integrated pharmaceutical company

Mission – To manufacture and market internationally competitive generic and related products for the Zimbabwean and export markets.

Core Values – Integrity, Good Corporate Governance, Professionalism, Innovation and Continuous Improvements, Fairness, and Teamwork

Recent Company Activities

Varichem upgraded its facility in 2006 in order to meet international GMP standards including WHO prequalification project requirements with the assistance of UNDP. In the last quarter of 2010, Varichem obtained WHO prequalification for Lamivudine+Zidovudine Tablets (150 mg+300 mg) and for Lamivudine + Nevirapine + Stavudine Tablets (150mg + 200mg + 30mg). The facility is, however, in need of certain pieces of equipment in order to complement its facility upgrade and enhance its GMP.

SWOT Analysis

Strengths

- Strong corporate brand
- Wide product portfolio
- WHO prequalification for ARVs
- Dynamic top management
- Committed staff
- Vertically integrated, core packaging material
- Excellent support from foreign suppliers
- Quality customer service

Weaknesses

- Product development skewed and slow
- Lack of financial resources
- Lack of management development and empowering programmes

Opportunities

- Expansion in regional and local markets
- Product outsourcing
- Joint venture projects

Threats

- Lack of economies of scale
- Political instability
- Unfair tariffs and restive labour force
- Unavailability of credit facilities and low purchasing power

Comments

Although Varichem has the strongest R & D amongst local generic manufacturers, the R & D facility needs to be upgraded to meet GMP requirements. The facility will also require additional equipment and machinery, especially on the manufacturing side. Their current equipment is more biased towards the analytical side of development.

Contact

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3.8 Bio-Equivalence (BE) studies

Since the advent of ARVs in Zimbabwe, manufacturers of generic pharmaceutical products are required to prove interchangeability of their products with innovator products through tests called bioequivalence (BE) studies. Varichem was the first - and so far the only - local company to sponsor a bioequivalence study through an Indian Contract Research Organization (CRO) in 2002. To date, the company has sponsored a total of 10 such studies. However, with a major policy shift in favour of BE studies for certain molecules, especially for drugs used in the management of HIV/AIDS, TB and malaria, local companies intending to enter these market segments will have to carry out such studies in order to obtain market authorization of their products. No such studies are currently carried out locally in Zimbabwe.

The biggest barrier to carrying out BE studies is the high cost and the high risk of failure, especially in view of the poor R & D capabilities of local companies. A feasibility study carried out for the establishment of a BE centre in East Africa estimates the following prices for carrying out commercial BE studies in the designated countries/regions (Ali, 2009):

Table 17: Cost of carrying out BE studies according to geographical location

Country	Bioequivalence cost range (US\$)
USA	150,000 to 200,000
Canada	140,000 to 180,000
Western Europe	120,000 to 160,000
Eastern Europe	80,000 to 160,000
South Africa	40,000 to 100,000
India	50,000 to 120,000

The actual cost depends on the study design and the product being investigated. From the table above, it can be seen that carrying out BE studies at foreign facilities is very costly and out of reach of local pharmaceutical companies. It would thus be an option for local manufacturers to carry out a feasibility study for the establishment of a local bioequivalence centre in order to establish the viability and price competitiveness of such a local facility.

3.9 The public health versus local pharmaceutical sector development debate

Local production may not be the path of choice if a country’s priority is to improve access to medicines. Countries need to go through a process of reflection in order to assess their position with respect to the health policy versus industrial policy arguments against and for local production respectively.

Increased competition, for example, through local production and importation, can help to bring down prices²⁷. A practical example which reflects this ‘pro access’ health policy versus industrial policy argument is that of a local generic manufacturer of ARVs versus the National AIDS Council (NAC). NAC procured ARVs from an Indian generic company rather than locally on the grounds that the imported drugs were far cheaper than the locally produced ones. An argument was raised that the funds utilized by NAC to purchase drugs

²⁷Global Strategy on Public Health, Innovation and Intellectual Property , Element 6

from India were raised locally (local tax on Zimbabweans) and should therefore have been used to procure drugs produced locally. However, NAC raised a health policy argument (access) in that it had been able to provide ARVs to a wider client base than would have been possible had the Council purchased locally produced drugs.

The overall lesson is that companies in Zimbabwe should ultimately strive to become competitive. Measures towards helping the sector overcome current disadvantages should be formulated in conjunction with the industry and the responsible government bodies and should include a phase out strategy. If this were to be achieved, public health and industrial development considerations would no longer be a contradiction.

4. THE BUSINESS ENVIRONMENT FOR PHARMACEUTICAL SECTOR PERFORMANCE AND DEVELOPMENT

4.1 Industrial policy

Zimbabwe's Industrial Development Policy (2004 - 2010) aimed at establishing the country as a major producer of industrial goods and services within the region, with a vision of "transform(ing) Zimbabwe from a producer of primary goods into a producer of processed value added goods for both the domestic and export markets". The policy focuses on attracting both domestic and foreign investment with the main emphasis on the manufacturing sector.

This policy identifies strategic sectors - of which pharmaceuticals is one - which can play a pivotal role in turning around the economy. The pharmaceutical sector is identified as crucial in ensuring a healthy nation and the control and eradication of diseases. The policy document states:

"The sector has a highly trained labour pool and produces high quality drugs which are competitive on the export market. It also boasts of modern production methods. There are great investment opportunities in the production of various medicinal, veterinary and skin products. Research and Development in the sector will also enhance the utilization of locally available resources. The Government will encourage the production of medicines under licensing. In this regard, it will facilitate partnerships between local and international partners."

Whilst great importance is attached to the pharmaceutical sector in the policy document, the situation on the ground is very different. Pharmaceutical manufacturers in Zimbabwe must confront a number of unfavourable practices and high import tariffs on their inputs. This is not the case with imported finished pharmaceutical products, which enjoy tariff free import status whilst imported inputs for local manufacture incur duty which ranges from 5 per cent to 15 per cent of the c.i.f value of the inputs.

Moreover, local pharmaceutical manufacturers pay value added tax (VAT) on imported inputs whilst imported finished products do not carry VAT. Although the VAT can be reclaimed, reimbursement is only made some 60 to 80 days from point of claim and this has an adverse effect on the cash flows of local businesses. Manufacturers have also been further squeezed in recent years by some negative export policies which mean that most of their hard earned foreign currency has had to be deposited with the central bank. This has eroded local industry's ability to use its export proceeds to re-equip and fund further imports of inputs.

Another sensitive issue is the conflicting aim of industrial policy versus health policy. Whilst, on paper, the Ministry of Industry and International Trade (MIIT) seeks to promote the local pharmaceutical industry, the policy objective of the Ministry of Health and Child Welfare (MoHCW) is to ensure access to medicines for all. As pointed out earlier (see 3.9), the National AIDS Council (NAC) opted to procure ARVs from outside Zimbabwe with the aim of maximising access to these drugs but this argument was not well received by the local industry. Manufacturers argue that the funds used to procure ARVs externally are generated locally through a tax, the AIDS levy, imposed on local Zimbabweans and so should

benefit local industry which is creating economic value through its manufacturing activities.

Based on a position paper submitted to Government by the Pharmaceutical Manufacturers Association of Zimbabwe (PMA) (see Annex 3), the National Economic Consultative Forum (NECF) Health Task Force, which falls under the MIIT, issued recommendations to the Ministry in July 2009 on measures needed to resuscitate the pharmaceutical industry. They included:

- Assisting the sector with short term lines of credit at concessionary rates and reasonable grace and repayment periods
- Offering a 25 per cent local preference on all locally produced products in all public and government tenders
- Removal of duties and VAT on pharmaceutical raw and packaging materials
- Preference to local sourcing of all national medicine requirements
- Reduction in utility tariffs which are currently extremely high and out of line with regional and international charges
- Access to pre-shipment financing
- Long term credit for capital investment
- Tax allowances and rebates
- Special skills retention allowances
- Import bans on products which are manufactured locally (as in Nigeria)
- Strengthening the policing capacity of the Medicines Control Authority of Zimbabwe (MCAZ) in order to protect local manufacturers against imports of unregistered products
- Export incentives
- A complete overhaul of the Patent Act in order to make it TRIPs compliant and to remove TRIPs plus provisions

To date, despite these recommendations and the inclusion of pharmaceuticals as a priority sector in MIIT's industrial development policy, no specific pharmaceutical sector plan or actual action on the ground has been forthcoming. Consequently, the sector continues to be constrained, especially in relation to the value added tax levied on imported raw materials.

4.2 Investment policy

The Zimbabwe Investment Authority (ZIA) promotes and facilitates both foreign and local direct investment. Its mission is to contribute to sustainable economic development and growth through the timely promotion and facilitation of value added investments.

The Authority's functions include to:

- Plan and implement investment promotion strategies for the purpose of encouraging investment by foreign and domestic investors
- Identify sectors of the economy with potential for investment for the purpose of attracting domestic and foreign investors
- Facilitate and process investment applications for approval
- Promote decentralization of investment activities in accordance with the development policy of the Government
- Promote and coordinate investment activities in enterprises or sectors of the economy which are of strategic importance to national development

In line with the Industrial Development Policy, ZIA has targeted investment in the manufacturing sector as the growth engine of the economy. It also intends to strategically target companies in various subsectors which are key to the whole economy. The pharmaceutical sector has been identified as one of the critical components of the investment strategy, which aims at boosting economic output by stimulating industrial production and reducing the output gap that has led to the import of so many products that the country has the capacity to produce and which could also be exported thus generating foreign currency.

The Authority aims to support the manufacturing sector through the establishment of an external credit facility for importing raw materials and equipment for retooling, amongst other necessities. This facility needs funding in excess of US\$ 1 billion for an initial period of 12 months and is estimated to have the potential to raise capacity utilization from 10 per cent to about 60 per cent. However, no funding has yet been mobilized and many observers feel that the Indigenization and Economic Empowerment Act, which seeks to empower indigenous Zimbabweans by ensuring a minimum 51 per cent indigenous ownership in any business with a minimum asset base of US\$ 500,000, may also act as a deterrent to potential investors.

Local indigenous businesses are having serious problems in funding their current operations and capital expenditure because of the liquidity crisis in the country. These firms are in great need of external credit lines or foreign direct investment. However, the risk of expropriation, which is used to promote "indigenization," is high.

Nonetheless, this policy does open up equity investment opportunities for locals in companies like Datlabs (see 3.7).

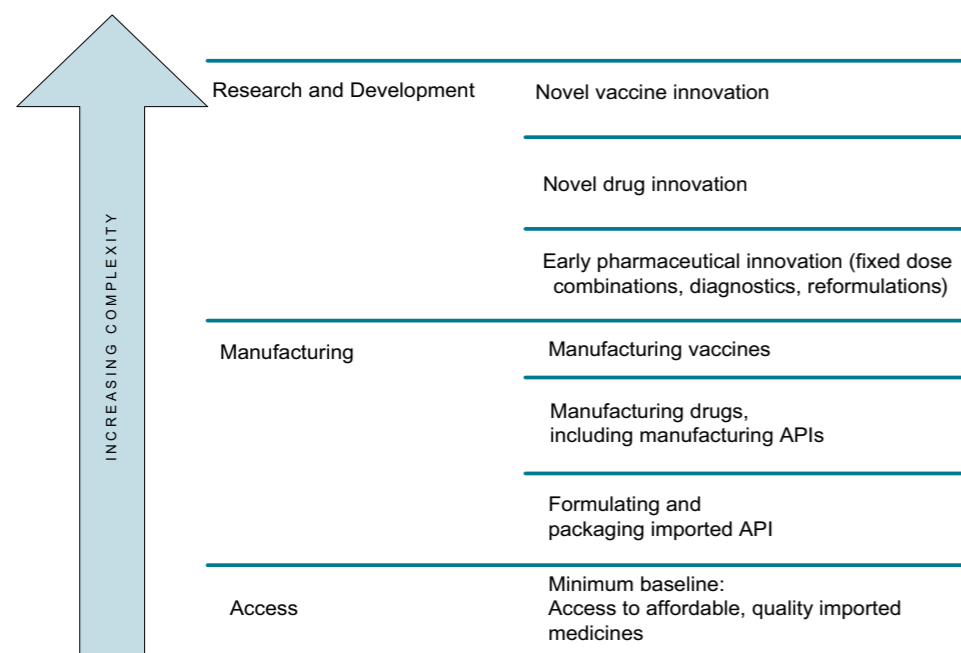
4.3 National pharmaceutical innovation strategy

Two mechanisms have emerged that aim to put countries in the driving seat to determine and manage research, production of and access to medicines, and to promote innovation. They are the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA) adopted by the 61st World Health Assembly in May 2008 and the African Union's Pharmaceutical Manufacturing Plan for Africa (PMPA) on which work started in 2005 in the framework of the New Partnership for Africa's Development (NEPAD).

Together, these two plans constitute the first comprehensive framework and promise of long term funding to support African countries’ strategies for pharmaceutical innovation. According to NEPAD and the Council on Health Research for Development (COHRED), many African countries have the potential to engage in pharmaceutical innovation but, if this is to become a reality, decision makers and planners need to be clear on how to get started, what skills are needed in the country, and what issues they need to better understand in order to design strategies and action plans to deliver better access to medicines.

Seven critical complexity levels in the innovation process have been identified according to NEPAD-COHRED thinking on pharmaceutical innovation. These are illustrated in Figure 1 below.

Figure 1: Pharmaceutical Innovation Milestones: seven critical complexity levels



Source: NEPAD-COHRED

Based on these levels, countries need to determine their priority needs for pharmaceutical innovation, namely, providing access, producing medicines, and discovering new drugs. A country then needs to assess its current potential to deliver in response to the needs and to assess the capacity which needs to be developed in order to achieve this goal. This will form the basis for a national pharmaceutical innovation strategy and plan.

One of the companies profiled in this study has a vision to become a research-based world class integrated pharmaceutical company. This vision is based on a higher level complexity and will require substantial resources. Matching this vision with the country’s skills and potential (financing, infrastructure, etc.) will show what is realistic and possible. It is recommended that this company progress along the innovation milestone grid systematically. To help attain this vision, there is a need for national involvement through the development of a national pharmaceutical innovation strategy and action plan along the lines discussed above. Such a plan can help countries negotiate with potential donors and partners in the pharmaceutical industry with a view to obtaining assistance in its operationalization.

4.4 Health policy, strategy and the health system

The Primary Health Care (PHC) approach was adopted at Independence in 1980 as the government strategy for achieving the “Health for All” targets by 2000. In the early 1990s, the Ministry of Health and Child Welfare (MoHCW) embarked on a Health Sector Reform Programme, which included decentralization, health financing, regulation of the private sector, management strengthening and contracting out of non-core activities.

In 1997, the Ministry launched its National Health Strategy for Zimbabwe: “Working for Quality and Equity in Health”, covering the period 1997 to 2007. This was followed by the National Health Strategy for Zimbabwe: “Equity and Quality in Health: A People’s Right”, covering the period 2009 to 2013. The objective of these plans was and is to clearly define the policy framework and the values that guide national investment towards improving the health and quality of life of all citizens.

Most health services are provided by the public sector, which consists of the MoHCW, the Ministry of Defence, the Ministry of Home Affairs (police), the Ministry of Justice (prison services), local authorities and mission health services. Management and administration of this sector is divided into four functional levels: national, provincial, district, and ward, with the following responsibilities:

- The national level is responsible for policy formulation, regulation, resource mobilization, disbursement of resources for programme implementation, training, coordination of research activities and monitoring and evaluation
- The provincial level provides technical and management support to the district level, including coordination of planning; overseeing implementation of national standards and guidelines, and training, monitoring and evaluation. The overall responsibility for these activities lies with the Provincial Health Executive
- The district level supports, supervises and coordinates the implementation of primary health care in the district. The overall responsibility for these activities lies with the District Health Executive
- Essential primary health care is provided at the primary or rural health centre level, the first point of contact between the community and the health sector

Many mines, large estates, and industrial complexes run their own health delivery services. There is a well developed private health sector, comprising mainly independent medical practitioners and private hospitals/clinics, found in almost all towns in the country. Traditional healers also have an important role in health delivery. The Zimbabwe National Traditional Healers Association (ZINATHA) was formed in 1980 to regulate their activities.

The loss of experienced managers at all levels of the health system in the last decade has reduced management capacity, negatively impacting on basic health care, particularly at the lowest level. This has contributed to the breakdown of the referral chain and to the increasing use of referral hospitals as primary care providers.

4.4.1 The Zimbabwe National HIV and AIDS Strategic Plan (ZNASP) 2008-2011

In line with its mandate, the National AIDS Council (NAC) has developed guiding national policies which have been regularly reviewed in response to emerging trends. Currently, the national response is articulated in the Zimbabwe National HIV and AIDS Strategic Plan (ZNASP-2008 - 2011), which is based on the “Three Ones” principle. The “Three Ones” are:

- one agreed HIV/AIDS action framework that provides the basis for coordinating the work of all partners
- one national AIDS coordinating authority with a broad-based multi-sectoral mandate; and
- one agreed country-level monitoring and evaluation system

NAC is responsible for coordinating the one-agreed HIV and AIDS action framework and has developed the national HIV and AIDS monitoring and evaluation system.

The ZNASP provides the policy and strategic framework for all sectoral and national responses, articulates the shared sense of direction and targets for the national response and provides the basis for advocacy, resource mobilization and programming. Specific strategic programmes to prevent new HIV infections, increase access and utilization of treatment and care services, improve support for individuals, families and communities, including orphans and other vulnerable children infected and affected by HIV and AIDS, have been developed and are being implemented.

4.4.2 The National Tuberculosis Programme (NTP)

The National Tuberculosis Programme (NTP) was established in the 1960s. In 1983, the government integrated policy on all TB activities into the general health services. In 1997, the NTP officially adopted the Directly Observed Treatment, Short-course (DOTS) strategy and, in 2006, also adopted the new Stop TB Control Strategy.

The three key points are:

- Sputum smear microscopy is the basis for case identification and follow up and is provided free of charge in the public health sector at the point of access
- All TB cases are provided with a standardized short course of chemotherapy free of charge; and
- TB services are available at all levels of the health delivery system and are integrated into the primary health care system to ensure efficient case finding, particularly for smear positive patients, and successful completion of treatment

The Zimbabwe Strategic Plan for Tuberculosis Control 2010 – 2014 provides a roadmap for strengthening NTP planning, coordination and effective implementation with the aim of attaining the national and global TB targets. It also facilitates the coordination of inputs from various sectors, including NGOs and donors, and hence provides a platform for effective coordination of partners by the NTP.

The vision of the Strategic Plan is to attain a TB-free Zimbabwe and its mission is to develop and implement TB control activities through effective, efficient and evidence-based strategies that contribute to the attainment of national and global TB control targets, as well as Millennium Development Goals (MDGs). The goal is to dramatically reduce the mortality, morbidity and transmission of tuberculosis in line with the MDGs and the Stop TB Partnership targets.

It is expected that the Strategic Plan will contribute to the strengthening of the overall health system and also act as an instrument for resource mobilization.

4.4.3 The National Drug Policy (NDP)

Shortly after Independence in 1980, Zimbabwe embarked on the formulation of a National Drug Policy (NDP) based on the WHO concept of essential drugs. In 1981, a provisional essential drugs list was issued for comment and in 1985 the first definitive Essential Drugs List for Zimbabwe (EDLIZ) was published. In 1987, the NDP was further developed to include all the major elements of a drug policy: selection of essential drugs, quantification of needs, financing, procurement, storage, distribution and rational use, as well as quality assurance.

The 1987 NDP contained provisions for promoting the use of generic drugs. This was done through the use of generic names when prescribing medicines in both the public and private sectors and this policy was a first for Africa. This strategy has been so successful that the level of genericization in Zimbabwe is relatively high when compared with other countries in the region. It is further strengthened by a legal provision within the Medicines and Allied Substances Control Act which permits generic substitution at dispensing level unless otherwise explicitly prohibited by the prescriber.

The NDP was initially designed to be linked with the national development plan and the national health policy but, at present, such linkages seem to have blurred or are non-existent. Specific provisions in the NDP aimed at advancing local manufacturing of essential drugs are as follows:

- Promoting and encouraging the most cost effective local production of safe, effective, and good quality drugs in order to achieve optimal self-reliance within the context of national development goals. As already pointed out, this issue of public health versus industrial policy has been debated and continues to be debated in global pharmaceutical circles
- Ensuring that only drugs and medical supplies of good quality, safety and efficacy are used in the population. The quality assurance infrastructure will be in accordance with internationally accepted standards, as specified under the Medicines and Allied Substances Control Act and Regulations

- The drug regulatory authority will, without compromising its own standards, collaborate with authorities in other countries with a view to the harmonization of control, registration requirements, exchange of information and ratification of international conventions
- Public sector prescribing and dispensing will be by generic name only and will be in accordance with the standard treatment guidelines contained in the EDLIZ. The MoHCW will continue consistently and vigorously to advocate the use of generic names and the EDLIZ in the public and private sectors. The MoHCW will collaborate with the pharmaceutical and medical associations, medical aid societies, consumers, general practitioners and other interested parties in Zimbabwe in order to promote generic substitution and to reduce the overall cost of drugs
- The aim of the policy is to promote and support drug research and development activities in Zimbabwe. Government will encourage and facilitate drug research and development in the local pharmaceutical industry, including efforts in the development of local raw materials of good quality. Government will promote and support cooperation and collaboration between national and international institutions involved in drug research
- The Government will encourage technical cooperation within the region, especially within the Common Market for Eastern and Southern Africa (COMESA) and the Southern African Development Community (SADC), as well as the East, Central and Southern African Health Community (ECSA)

The quality assurance aspect of the NDP is implemented through the MCAZ and the Regional Medicines Quality Control Laboratory, which falls under the MCAZ. Zimbabwe remains one of the few countries in the African region where there is strict control of medicines. Although counterfeiting is a cause for concern, recorded incidences remain sporadic, with fewer than five reports per year being recorded according to the MCAZ. It is, in fact, individuals smuggling medicines into the country, whether registered or not, who present the most risk to patient safety and regulatory enforcement.

The NDP does not contain any provisions for pharmaceutical pricing controls and thus the industry currently enjoys free pricing. One of the findings of the 1985 medicines prices study was that there is no transparency in the pricing of pharmaceuticals in any sector in Zimbabwe although the problem was more acute in the private and dispensing doctors sectors. In contrast, in South Africa, prices are controlled through the single exit price legislation and an annual list of single exit prices is freely available through the Department of Health website.

The subject of generic prescribing and dispensing in both the private and public sectors is generally accepted. One of the major conclusions of the 1985 prices study was that “There is wide acceptability and usage of generic medicines in the country in line with the country’s successful generic prescribing policy”.

Currently, there is no action plan for the implementation of the National Drug Policy. It was initially designed to link the national health and development policies consistently. However, recent developments seem to favour national health policy over industrial development.

4.5 Regional health initiatives

The local regulatory authority, MCAZ, has been actively involved in regional harmonization initiatives although there appears to have been little progress so far. The MCAZ is one of the strongest regulatory bodies within the SADC and COMESA regional economic communities and it is an active participant in all regional regulatory bodies’ activities, including:

- Harmonization of registration of pharmaceuticals
- Harmonization of regulation of clinical trials
- Harmonization of laws to combat counterfeit drugs
- Harmonization of Good Manufacturing Practice

With respect to Research and Development (R & D), not much success has been achieved by way of R & D of locally produced raw materials, technical cooperation and collaboration between national and international companies. To date, there has been no collaboration or technical cooperation within the regional economic communities although there are some ongoing activities within the African Union and SADC. Regional harmonization initiatives have yielded little success other than the issuance of guidelines covering various areas.

4.6 Legal framework

The two main pieces of legislation and agreements framing Zimbabwe’s pharmaceutical industry are the Patents Act of 1996, as amended in 2002, and the accompanying regulations, and the Trade and Related aspects of Intellectual Property Rights (TRIPS) Agreement.

The TRIPS Agreement addresses, *inter alia*, the subject of patents and establishes that all member states of the World Trade Organization (WTO) – created in January 1995 – should grant patents for inventions in all technological fields, including pharmaceutical products and processes. Zimbabwe has been a member of WTO since 5 March 1995.

Developing countries like Zimbabwe were given a transition period of five years, i.e. until January 2000, to adapt national legislation to the TRIPS Agreement and then had an additional five year period (until 2005) to recognize patents in technological sectors not protected before the TRIPS Agreement.

Within the scope of TRIPS, the following are some of the main flexibilities which countries can use (Chaudhuri, 2005):

- Provide exemptions from grant of patents in certain cases
- Provide exceptions to product patent rights in certain cases
- Limit data protection
- Provide for government use and
- Provide for compulsory licences to non-patentees

4.6.1 The patent system

Zimbabwe is a member of the African Regional Intellectual Property Organization (ARIPO) and is a party to the Patent Cooperation Treaty (PCT). The country amended its patent act, Patent Act (Chapter 26:03) Revised Edition of 1996, through the Patent Amendment Act of 2002 in line with its obligations under the TRIPS Agreement.

The main features of the amendments are as follows:

- Inclusion of parallel importation
- Inclusion of the Bolar provision
- Change of the term of a patent to 20 years in line with the TRIPS Agreement
- Permission to remedy a practice determined to be anti-competitive according to Article 31 (k) of the TRIPS Agreement
- Inclusion of a section on compulsory licensing in respect of dependent patents, Article 31 (l) of the TRIPS Agreement
- Addition of Anton Piller orders (an order by the court to secure the preservation of documents or objects as evidence in cases of infringement proceedings)
- Patent Cooperation Treaty (PCT) Provisions
- Restriction of the use of compulsory licences for the Zimbabwean market
- Making compulsory licences non-exclusive

4.6.1.1 Exemptions from Patentability

Under Article 27.1 of TRIPS, patents will have to be provided for inventions, which are “new, involve an inventive step and are capable of industrial application” (Chaudhuri, 2005). The agreement, however, does not define these terms. This provides some flexibility and it has been suggested that developing countries can interpret these terms so as to restrict the number of patents (the first flexibility cited above).

Zimbabwe amended its 1996 Patent Act in 2002 in order to meet the TRIPS Agreement obligations. Unlike the Indian Patent Act of 1970, whose scope of patent protection for pharmaceuticals was limited, the scope of patent protection under this 1996 Act was very wide and open (very liberal patent standards as followed by developed countries).

Article 27.3 (a) of the TRIPS Agreement, Patentable Subject Matter, reads “Members may also exclude from patentability: diagnostic, therapeutic and surgical methods for the treatment of humans or animals”.

The Patent Amendments Act of 2002, Section 3, provides for such exclusion from patentability by the addition of a new section “Inventions for which patents may not be granted”.

Chaudhuri further argues that, if patentability standards are so broad that the terms “new” and “inventive” are defined to include all new forms of the same New Chemical Entity (NCE) then, effectively, the patent life can be extended beyond the 20 year period. Zimbabwe should thus exercise discretion in this regard. Stricter patentability criteria are important to prevent patent owners from ‘evergreening’, i.e., extending the life of patents beyond the original 20 year period. Based on the three criteria for patentability, i.e. novelty, non-obviousness and utility (industrial application), the term ‘stricter criteria’ implies, for example, worldwide novelty and concrete industrial purpose rather than undetermined, multiple purposes and obviousness not for local but for an international person skilled in the art.

According to Paragraph 4 of the Doha Declaration on the TRIPS Agreement and Public Health: “while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO members’ rights to protect public health and, in particular, to promote access to medicines for all.”

Legally, (Osewe, 2008) member countries, according to paragraph 4 of the Declaration, have the opportunity, and indeed the obligation, to interpret and implement the provisions of Article 27.1 of the TRIPS Agreement with respect to the patentability of “new use” of medicines in a manner that seeks to protect public health and ensure access to medicines. The same argument can also be applied to the term “inventive step and novelty and industrial application.”

The Commission on Intellectual Property Rights (CIPR) has pointed out that there is no compulsion under the TRIPS Agreement for developing countries to follow the liberal patent standards of developed countries (CIPR, 2002). The aim should be to ensure that patents are granted for true technical contributions and not for blocking innovation and legitimate competition by generic producers (Chaudhuri, 2005).

When a patent application is filed directly with ARIPO, the examination of the patentability criteria of the product in question is the sole responsibility of the regional organization (Osewe, 2008). In the case of ARIPO countries, for instance, it is that Organization which examines the application as to substance (for patents) and decides whether a patent can be granted. Osewe further points out, however, that member states which have the capacity to examine the substance can examine applications that are filed at their offices and are based on the applicable national patent law for patentability. Moreover, a member state reserves the right to refuse to ratify a patent granted by ARIPO, thus making the patent non-operational in its own territory. Thus, the decision on patentability of the product in question lies with ARIPO.

The Africa Bureau – Quadripartite Agreement is a cooperation agreement among:

- The World Intellectual Property Organization (WIPO)
- The African Regional Intellectual Property Organization (ARIPO)
- The African Regional Centre for Technology (ARCT)
- The African Intellectual Property Organization (OAPI)

The purpose is to promote cooperation among the four organizations with a view to promoting the technological development efforts of their member states. Osewe points out that under this quadripartite framework it might appear that both OAPI and ARIPO function as *de facto* registration agencies for patents filed and granted in the developed countries without recourse to any meticulous examination of such patents with regard to new and second uses of existing pharmaceutical products. A related concern is that, in contrast to the prevailing situation in Sub-Saharan Africa, patent challenges are very frequent in the developed world and sometimes result in the withdrawal of granted patents.

Under the current system, patents can be withdrawn in the developed world yet remain in force within OAPI and ARIPO. To take advantage of the flexibility provided for under Article 27.1 of the TRIPS Agreement, it would be advisable to specifically exclude secondary patenting in the legal instruments of ARIPO as well as in domestic legislation.

4.6.1.2 Limited exceptions to exclusive rights

According to Chaudhuri, patents basically confer on the patentee the right to prevent others from using an invention. But such rights are not absolute. Most patent laws usually provide some qualifications to such exclusive rights.

Article 30 of TRIPS permits member countries to “provide limited exceptions to the exclusive rights conferred by a patent ...”. This article does not list the specific acts for which exceptions can be provided. What it says is that such exceptions should satisfy certain conditions such that it does not “unreasonably conflict with a normal exploitation of the patent and do(es) not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties”. According to Chaudhuri, the three most significant and common exceptions provided for by national legislation in many countries when TRIPS came into effect are:

- Early working
- Parallel imports
- Research and experimental use

It is generally understood that individual countries have some flexibilities in interpreting these terms and incorporating some exceptions to exclusive rights of the patentees in national patent laws.

The “early working” provision is popularly referred to as the “Bolar” provision or exception, as it is known in the USA. The exception allows a company to complete all the procedures and tests necessary to obtain market approval for a generic drug product before the original patent expires. Given the long generic drug product development and approval process, generic companies need to roll out such developments years before the patent expires so that they are in a position to market generics immediately after patent expiry.

Under Article 28 of TRIPS, the patent owner has the exclusive right to prevent others not only from making, using or selling the invented product or process in the country but also from importing from other countries. This is, however, subject to Article 6 on “exhaustion”. What this basically means, according to Chaudhuri, is that the patent holder in a country cannot legally stop imports of patented products offered for sale in another country. Such imports of patented products without the consent of the patent holder in the importing country are known as parallel imports. This is important in the pharmaceutical industry because the same patented medicine is often sold at different prices in different countries. Hence parallel imports permit a country to shop around for the lowest cost price.

The underlying justification for allowing parallel imports is that, since the innovator has been rewarded through the first sale of the product, its exclusive distribution rights under the patent have been “exhausted” and hence it should have no say over the subsequent resale. Under Article 6 of TRIPS, as clarified by the Doha Declaration (paragraph 5(d)), each country is “free to establish its own regime of such exhaustion without challenge”.

4.6.1.3 The Bolar (early working) provision

It is disturbing to note that, in the case of Zimbabwe, the Bolar provision as per the Patent Amendments Act, 2002 is not practical and does not serve its intended purpose. Section 7 of the Patent Amendment Act, 2002, states that:

“The principal Act is amended by the insertion after section 24 of the following sections-
24B Test batches of patented products

- (1) Test batches of a patented product may be produced without the consent of the patentee six months before the expiry of the patent: provided that the test batches shall not be put on the market before the expiry date of the patent.
- (2) Where test batches of a patented product have been produced in terms of subsection (1) the patent term of the original product shall not be extended”.

Given the above amendments and the citation on the Bolar exception, the inclusion of a time limit in the Patent Act Amendments of 2002 is a clear indication of ignorance of the generic drug product development and approval process and the purpose of the exception.

It is surprising that the local industry has done nothing to have this obvious flaw in the Patent Act rectified. Indeed, those involved in the R & D of generic drug products still protected by patent in Zimbabwe are infringing patent rights of others if they are carrying out these activities prior to the six months stated in the legislation which, to all intents and purposes, should be happening for those local generic companies which have a strategic perspective.

The second provision of the Bolar exception states that “provided that the test batches are not put on the market before the expiry of the patent”. It is common knowledge to those in the pharma industry that such test batches will never be put on the market. Therefore, the clause is obsolete.

Within the same amendment, there is a provision which states that “where test batches of a patented product have been produced, the term of the original patent shall not be extended”. This prevents evergreening of patents, which is expressly provided for in some OECD countries, from being applied in Zimbabwe.

4.6.1.4 Parallel importation

It is important to note that the Medicines and Allied Substances Control (Import and Export of Medicines) Regulations, 2008, limit the interpretation of parallel importation according to TRIPS and state that:

“No person shall import into or export from Zimbabwe any registered medicine, for the purpose of wholesale dealing, unless he is duly appointed as an authorized importer or exporter by the principal in respect of that medicine.

Any pharmacist, veterinary surgeon, dental practitioner or medical practitioner may import into Zimbabwe any medicine, for no other purpose than except for resale, from authorized premises, to his or her customers, patients, or clientele, as the case may be.”

These regulatory provisions have been made necessary by the need to control the influx of registered, unregistered and counterfeit medicines into the country. From a regulatory point of view, medicines are registered by source of the manufacturing country and this makes it difficult to parallel import from an import source of choice, which might not necessarily be the registered source. This runs contrary to public health policy initiatives. There is thus a need to find a solution to this conflict in the overall interests of public health.

4.6.1.5 Research and experimental use

The Zimbabwe Patent Act as amended does not make provision for the use of patented inventions for research and experimental use. As UNCTAD-ICTSD have pointed out, exceptions may be granted for scientific research, that is, for acts made without a commercial intent but merely to generate new knowledge. They also point out that it may also be possible to exempt acts of experimentation on the invention even if made with commercial purposes such as in order to “invent around”, improve on the protected invention, evaluate an invention in order to request a licence, or for other legitimate purposes, such as to test whether the invention works and the patent granted is valid.

Chaudhuri points out that, in order to avoid ambiguity, it should be clearly understood that the non-patentee can experiment with the invention and develop its own process of manufacturing for commercial purposes (although it may not be able to actually use this unless it is authorized to do so). This is a powerful flexibility as it provides an opportunity to use an invention for R & D purposes, thus enabling indigenous firms in developing and least developed countries to be ready with efficient processes and to use these when they are permitted to do so.

4.6.2 Data protection

Zimbabwean law does not provide for data exclusivity, that is the granting of exclusive rights to innovator companies to prevent subsequent applicants from using data submitted for the registration of new molecule entities. Article 39.3 of TRIPS is being interpreted by multinational corporations and some developed countries, particularly the USA, to mean that WTO member states are required to grant data exclusivity for a specified period of time (Chaudhuri, 2005).

Data exclusivity provisions have implications for generic entry and hence for competition and prices. They imply that a regulatory authority cannot make use of innovator submitted data on safety and other relevant clinical data for marketing approval purposes for a generic submission during this period of exclusivity. Thus Zimbabwe has been able to use an important TRIPS flexibility with positive implications for generic competition and prices. However, due to the flawed Bolar exception, if the drug substance is patented at the same time, a generic competitor cannot use it until six months before patent expiry, thus limiting the flexibility on test data.

4.6.3 Compulsory licensing

Article 31 of the TRIPS Agreement regulates the practice commonly known as compulsory licensing. TRIPS does not use the term “compulsory licence” but refers to “use without authorization of the right holder” and includes both use by third parties (usually referred to as compulsory licences) and use by government (Chaudhuri, 2005).

Article 31 of TRIPS does not place any restriction on the grounds under which compulsory licensing can be undertaken. The Declaration on the TRIPS Agreement and Public Health adopted at the Doha Ministerial Conference states:

“Each member has the right to grant compulsory licences and the freedom to determine the substantive grounds upon which such licences are granted.” However, according to Article 31 of TRIPS, certain conditions of a procedural nature need to be satisfied.

In the amended Patent Act, an application for a compulsory licence can be made under two sets of circumstances:

- 1) Under Section 30A, where the working of a patent (referred to as a dependent patent) without infringement of a prior patent is dependent upon the obtaining of a licence under that prior patent, the proprietor of the dependent patent may, if agreement cannot be reached as to such licence with the proprietor of the prior patent, apply to the Registrar for a licence under the prior patent.
- 2) Under Section 31, subject to subsection (15), any person interested who can show that he/she has been unable to obtain a licence under a patent on reasonable terms may, within a period of six months from the initial request for a voluntary licence, apply for a compulsory licence on the grounds that the reasonable requirements of the public with respect to the invention in question have not been met or will not be satisfied.

According to Chaudhuri, what is often critical for an effective compulsory licensing system is to have straightforward, transparent and fast procedures. A patent holder will naturally be opposed to any compulsory licences. The Zimbabwean procedure is open-ended without any time limit imposed for the granting of compulsory licences. According to subsection (3) (b) of Section 31, the applicant is required to advertise the application in the Patents and Trademarks Journal after the Registrar of Patents is satisfied that the applicant has a *bona fide* interest and that a *prima facie* case for relief has been made out. However, this is not a requirement under TRIPS. The patentee or another person may oppose the grant and will have to be given time for doing so. The process is excessively cumbersome and provides the patentees the opportunity to buy time through litigation. This might dissuade generic companies from applying for licences because of the anticipated legal costs of litigating the patentee.

4.6.3.1 Government use

Article 31 of the TRIPS Agreement dealing with non-voluntary uses provides for special provisions “in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use”. Public use of patents or “government use” is a standard feature of patent laws in many countries (Chaudhuri, 2005) and it is embodied in Section 34 of the Zimbabwe Patents Act.

Section 35 of the Act makes special provisions as to state use during emergency as follows:

“During any period of emergency the powers exercisable in relation to an invention by a department of State or a person authorized by the Minister under Section thirty four shall include the power to make, use, exercise and vend the invention for any purpose which appears to the Minister necessary or expedient.”

The patent owner can challenge such use or the terms of such use under Section 36 of the Act, ‘Reference of Disputes as to State Use’. The ability of the government to use such provisions to enhance the affordability of drugs will be crucially dependent on proper administrative and judicial systems being put in place (Chaudhuri, 2005).

4.6.3.2 Compulsory licensing for exports

Article 31 (f) of the TRIPS Agreement places a limitation on the export of products manufactured under a compulsory licence. Under this article, the production will have to be “predominantly for the supply of the domestic market of the member authorizing such use” (unless the compulsory licence was issued to remedy anticompetitive practices under Article 31 (k)).

Many developing and least developed countries cannot produce either active ingredients or formulations due to lack of technology, equipment, human resources or the economic (non)

viability of domestic production (Correa, 2004). To mitigate this problem, a decision was only reached in August 2003. The solution takes the form of a temporary waiver (pending amendment of TRIPS) of the obligation under Article 31 (f) of TRIPS that a compulsory licence can be granted predominantly for the supply of the domestic market. The decision permits countries producing patented drugs under compulsory licence to export these to countries with no manufacturing capacities. Chaudhuri points out that conditions that have been attached to this decision raise serious doubts about the extent to which it can be used at all. Rather than facilitating exports of drugs to countries which urgently need them, unnecessary procedural complications and limitations were introduced.

The Patent Act of Zimbabwe needs to be amended in line with this decision. The amendment will need to permit exports to those countries lacking manufacturing capacity.

4.6.3.3 The situation on the ground

Zimbabwe initially declared a period of national emergency on HIV/AIDS in 2002 for a period of six months in terms of section 34, as read with section 35, of the Patents Act. This period was not long enough to enable implementation of the provisions of the Act under section 34, i.e. the use of patented inventions in the service of the State. Having recognized the shortcomings in the initial emergency declaration, the Government then extended it for a five year period.

The Declaration of the Period of Emergency on HIV/AIDS Notice, 2003 reads:

“2.The Minister hereby declares an emergency period of five years with effect from 1st January, 2003 to 31st December, 2008 for the purpose of enabling the State or a person authorized in writing by the Minister under section 34 of the Act:

- a) To make or use any patented drug, including any antiretroviral drug, used in the treatment of persons suffering from HIV/AIDS-related conditions;
- b) To import generic drugs used in the treatment of persons suffering from HIV/AIDS or HIV/AIDS-related conditions.”

In April 2003, Varichem Pharmaceuticals, one of the pioneers in the manufacture of generic antiretrovirals in Africa, was given authority by the Minister of Justice, Legal and Parliamentary Affairs to make, use or exercise any invention disclosed in any specification lodged at the Patent Office for the service of the State.

The authority was issued subject to the following conditions:

- a) The applicant shall produce antiretroviral or HIV/AIDS-related drugs and supply three-quarters of its produced drugs to State-owned health institutions.
- b) The prices of the drugs shall be fixed subject to price control mechanisms to be determined by the Minister.
- c) The applicant shall prove the veracity of the figures it has used to present the price differentials between the patentee’s drugs and its own manufactured drug.

It is evident from condition (a) above that there are some contradictions as to the authority compliance with TRIPS. Whereas section 34 of the Act deals solely with the use of patented inventions for the service of the state, the authority allows Varichem to supply a quarter of its produced drugs for non-state use (commercial uses). In fact, prior to Varichem obtaining WHO prequalification for two ARVs in late 2010, and because of the inability and/or unwillingness of the state through NAC to procure from Varichem, the authority was being used for purposes other than for the service of the state.

This obviously compromises both the State and Varichem with respect to the obligations of the country insofar as the TRIPS Agreement is concerned. This also compromises endeavours by local companies to do business in ARVs outside Zimbabwe when they seek to obtain voluntary licences or immunity from suit since, to date, most countries in the region, and especially South Africa, have opted for voluntary licences as opposed to compulsory ones.

The Minister should have dealt with Varichem's request for a compulsory licence in terms of Section 31 of the Act and, to safeguard the interests of the state, should have issued a separate government use order under section 34 of the Act as read with section 35. The current authority makes it difficult for Varichem to benefit from the provisions of the Doha Declaration and the subsequent 30 August 2003 Decision as the current authority is not a valid compulsory licence. As previously mentioned, a compulsory licence is directed to an identified patent and the current authority is blanket.

Datlabs was also granted authority by the Minister to import generic medicines from Ranbaxy for treatment of HIV/AIDS and related diseases. The position of local firm CAPS with regard to the grant of a compulsory licence is not known.

The declaration of a second period of emergency expired at the end of December 2008 and seems not to have been renewed. Thus, all the activities being carried out under this declaration are null and void. It is surprising that the interested party, the local pharma industry, has not raised the need for an extension of the period with the Minister.

4.7 Regulatory environment

The principal statutory instruments which regulate the pharmaceutical industry in Zimbabwe are the Medicines and Allied Substances Control Act (MASCA) [Chapter 15:03] and the Dangerous Drugs Act [Chapter 15:02], together with their corresponding regulations.

MASCA is basically "An Act to establish a Medicines Control Authority of Zimbabwe and to confer on such Authority in relation to the registration of medicines; to provide for the Zimbabwe Regional Medicines Control Laboratory and for its functions; to provide for the appointment of a Director-General of the Authority and for the keeping of a Medicines Register; to provide for certain prohibitions, controls and restrictions relating to medicines and other substances; and to provide for matters connected with or incidental to the foregoing." (Medicines and Allied Substances Control Act [Chapter 15:03], 1969)

The main activities regulated under MASCA are:

- Conduct of clinical trials
- Registration of medicines
- Licensing and control of pharmaceutical premises and persons
- Quality Control of medicines

All medicines to be sold in Zimbabwe (human and veterinary) must be registered as stipulated in the Medicines and Allied Substances Control Act and Regulations. A Medicines Register is maintained with particulars of any medicine which has been registered by the Authority and any cancellation of the registration (market authorization) or variation of the conditions of registration of any medicine in the terms of the Act. The Medicines Register has two parts; the first relates to medicines which are not for veterinary use and the second to veterinary medicines. The registers are freely available to the public in hard copy or in electronic format after payment of a prescribed fee. As at the end of 2007, the Medicines Register contained 1,604 separate medicine items, both generic and new chemical entities.

The MCAZ also keeps a register of all medicines pending registration and this is also available at a fee in both electronic and hard formats.

In addition to MASCA, the Authority develops and publishes guidelines on various topics covered by the Act. The MCAZ is currently working on the implementation of Guidelines on Submission of Documentation for Registration of Multisource (Generic) Finished Pharmaceutical Products (FPPs) which capture the latest developments in generic pharmaceutical pre-approval best practice. With these guidelines, the structure and format of the product dossier will conform to the International Conference on Harmonization (ICH) Common Technical Document (CTD).

Medicines in Zimbabwe may only be registered in the following conditions (MCAZ, 1991), (MASCA Section 30):

- "1) The Authority shall approve the registration of a medicine if it considers that:
- a) The availability of that medicine is in the public interest; and
 - b) The safety, quality and therapeutic efficacy of that medicine:
 - i. In the case of a medicine which is not a veterinary medicine, in relation to its effect on the health of man;
 - ii. In the case of a veterinary medicine, in relation to its effect on the health of animals;

warrant its registration; and
 - c) In the case of a medicine manufactured in Zimbabwe, the premises at which it is manufactured and all processes of manufacture are satisfactory.

- 2) Notwithstanding subsection (1), the Authority shall not approve the registration of any medicine manufactured outside Zimbabwe unless a valid certificate of registration in respect of such medicine issued by the appropriate authority established for the registration of medicines in the country of origin of that medicine has been produced to the satisfaction of the Authority.”

In practice, it has been taking a minimum of two years to register a medicine in Zimbabwe. This time lag has been largely attributed to the poor quality of dossiers submitted for market authorization by manufacturers and also staff shortages at MCAZ to review the dossiers. The Authority’s target is to register a product within a period of six months from the date of submission of a dossier, provided all the required information is supplied.

The table below gives a summary of the number of registrations or marketing authorizations on a yearly basis by the MCAZ compared with those of South Africa’s Medicines Control Council (MCC). The number includes both generics and new molecules. The table also includes data on tentative approvals per year by the US Food and Drug Administration (FDA) since these can be taken as a proxy for generic innovation in the USA.

Given the size of the Zimbabwean market and the resources of the MCAZ relative to the South African market and the MCC respectively, the number of annual marketing authorizations issued is quite commendable despite the declining numbers.

Table 18: Annual Marketing Authorizations by the MCAZ and South Africa’s MCC and USFDA Tentative Approvals²⁸

<i>Year</i>	<i>Number of Marketing Authorizations MCAZ</i>	<i>Number of Marketing Authorizations MCC</i>	<i>USFDA Tentative</i>
Approvals			
2003	111	436	13
2004	110	254	33
2005	73	644	71
2006	78	441	90
2007	26	392	172
2008			124

It would have been more instructive had it been possible to separate these marketing authorization statistics into generic and new molecular entities. It would also have been interesting to analyse both the MCAZ and the MCC authorization data in terms of generics approved but still on patent in the respective national territories. These statistics would have been the comparable figure with the USFDA tentative approvals and would have facilitated a comparison of the level of generic innovation in the three countries relative to their levels of development. It is not surprising that the level of generic innovation in the USA has been showing an upward trend. Success in the generic pharmaceutical industry is highly dependent on the rate at which a company introduces new generic products near to patent expiry.

²⁸ The actual number of market authorizations for MCAZ may differ from those reported because of product deregistration. The MCC database was compiled manually using MCC notifications for registration and so might not give a true reflection of the actual situation on the ground.

Premises and persons dealing in pharmaceuticals are licensed in accordance with the Medicines and Allied Substances Control Act and Regulations and a register of such licensed premises and persons is kept by the Authority.

Despite the severe economic and political difficulties in the country over the last decade, Zimbabwe still has a well regulated pharmaceutical sector. Unsupervised premises, especially pharmacies, have been closed by the regulatory authority when there is no continuous personal supervision of a pharmacist. It is the general policy of the MCAZ that local pharmaceutical manufacturers be inspected every two years. However, this has not been possible due to the shortage of both human and financial resources at MCAZ. Nonetheless, “the big five” pharma companies have all been inspected in the last five years.

4.8 The Global Strategy and Plan of Action on Public Health Innovation and Intellectual Property (GSPA) and the local pharmaceutical industry

In May 2008, the 61st World Health Assembly adopted Resolution WHA 61.21: the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA). The GSPA aims to promote new thinking on innovation and access to medicines. Based on the recommendations of the Commission on Intellectual Property, Innovation and Public Health (CIPIH) report, it also aims to provide a medium term framework for securing an enhanced and sustainable basis for needs-driven essential health research and development relevant to diseases which disproportionately affect developing and least developed countries, proposing clear objectives and priorities for R & D, and estimating funding needs in this area (WHO, 2008).

The GSPA covers seven elements:

- (1) Prioritizing research and development needs
- (2) Promoting research and development
- (3) Building and improving innovative capacity
- (4) Transfer of technology
- (5) Application and management of intellectual property to contribute to innovation and promote public health
- (6) Improving delivery and access
- (7) Establishing monitoring and reporting systems

The Plan is a prerequisite for the systematic development of the pharmaceutical industry although no concrete steps have yet been taken in this direction by Zimbabwe. The local pharmaceutical industry should be actively involved in its implementation and, for example, the Pharmaceutical Manufacturers Association (PMA) could set up a standing committee specifically to handle this issue.

Without a sound and solid national innovative capacity, movement of the industry up the pharmaceutical value chain will be impossible. Companies like Varichem have set their sights on drug discovery but are unlikely to achieve this objective unless they are backed by a national innovative capacity.

4.9 The Pharmaceutical Manufacturing Plan for Africa (PMPA)

The African Union developed a Pharmaceutical Manufacturing Plan for Africa (PMPA) in 2007 with the objective of promoting the local production of generic medicines on the continent and of making full use of the flexibilities within the TRIPS Agreement and the Doha Declaration on TRIPS and Public Health.

The major concern of the Union, then and now, is the reliance by most countries in Africa on China and India for the supply of generic medicines. The overall aim is to consolidate local production of the much needed generic medicines in Africa while ensuring economic and technical viability. In October 2007, a technical committee on the Pharmaceutical Manufacturing Plan was inaugurated as the first phase. Its members are:

- North Africa (Egypt and Libya)
- West Africa (Ghana, Nigeria and Senegal)
- Central Africa (Burundi, Cameroon and Gabon)
- East Africa (Kenya and Ethiopia)
- Southern Africa (South Africa)

In May 2008, the committee met to map out phase two plans and recommendations were made on the elaboration of a concrete plan of implementation comprising six themes:

- Mapping
- Situation analysis and compilation of findings
- Manufacturing agenda
- Intellectual property issues
- Political, geographical, and economic considerations
- Financing

A special meeting of the African Union's Extended Technical Committee on the Pharmaceutical Manufacturing Plan for Africa was convened in South Africa in February 2010. It gave strong support to the development and implementation of a business plan for the PMPA and invited partners to assist in development and implementation by providing resources and ensuring synergies with the private pharmaceutical sector.

To date, the most active players in the drafting and implementation of the PMPA have been government officials, together with their nominated experts on the technical com-

mittee. Private sector involvement has been minimal except for the South Africa meeting. The local industry in Zimbabwe needs to take an active role in the PMPA initiative through the Pharmaceutical Manufacturers Association (PMA) and the Southern African Generic Medicines Association (SAGMA).

The PMPA project should be integrated with the implementation of the GSPA in Zimbabwe and other countries in order to generate synergies. The recent study by the Council on Health Research for Development (COHRED) entitled "Strengthening Pharmaceutical Innovation in Africa – designing strategies for national pharmaceutical innovation: choices for decision makers and countries" could be used by the principals of the PMPA and the GSPA as an implementation tool at national and company level. Whilst the PMPA is the basis for a more coordinated approach to regional pharmaceutical production, the GSPA seeks to make pharmaceutical innovation for Africa, based on the health needs of the continent, a reality.

One of the major weaknesses in the pharma business in Africa has been the lack of backward vertical integration into the large scale manufacture of competitively priced APIs. Pharmaceutical innovation and technology transfer is urgently required in the area of Active Pharmaceutical Ingredients (API) manufacturing. The potential market represented by the combined populations of member countries of the African Union could make this initiative a reality. Regional pharmaceutical players should seek to collaborate with partners in the region to initiate regional production of APIs.

Local companies with the vision to position themselves in the drug discovery arena have an opportunity to achieve this through international partnerships. However, there is a need to develop both national and individual company innovation strategies before regional partnerships can be pursued.

On the secondary manufacturing side, local companies should, through PMA and SAGMA as previously suggested, keep track of developments with respect to the implementation of phase II of the PMPA, as this has serious business implications, both locally and regionally. Priority areas to watch are the mapping, situation analysis, manufacturing agenda and financing exercises. Local companies need to be kept up to date and involved as they form an integral part of African secondary manufacturing capacity.

4.10 The SADC Pharmaceutical Business Plan

In 2007, the Southern African Development Community (SADC) unveiled a SADC Pharmaceutical Business Plan for the period 2007 – 2013 with the objective of ensuring availability of essential medicines, including African traditional medicines, and reducing the disease burden in the region.

The Plan states that:

"Its main objective is to improve sustainable availability and access to affordable, quality, safe, efficacious essential medicines including African traditional medicines. In order to achieve the overall goal and the main objective, the following strategies will be pursued:

- i. Harmonizing standard treatment guidelines and essential medicines lists;
- ii. Rationalizing and maximizing the research and production capacity of local and regional pharmaceutical industry in generic essential medicines and African traditional medicines;
- iii. Strengthening regulatory capacity, supply and distribution of basic pharmaceutical products through ensuring a fully functional regulatory authority with an adequate enforcement infrastructure;
- iv. Promoting joint procurement of therapeutically beneficial medicines of acceptable safety, proven efficacy and quality to the people who need them most at affordable prices;
- v. Establishing a regional databank of traditional medicine, medicinal plants and procedures in order to ensure their protection in accordance with regimes and related intellectual property rights governing generic resources, plant varieties and biotechnology;
- vi. Developing and retaining competent human resources for the pharmaceutical programme;
- vii. Developing mechanisms to respond to emergency pharmaceutical needs of the region; and
- viii. Facilitate the trade in pharmaceuticals within SADC.”

A quick comparison of the SADC Pharmaceutical Business Plan and the Pharmaceutical Manufacturing Plan for Africa reveals that there are common goals within these documents but with a somewhat different scope. The PMPA defines much broader activities than the SADC Pharmaceutical Business Plan. The common feature of both documents is that they are politically derived plans with little or no involvement or consultation of/with the pharmaceutical private sector. It would be sensible to integrate the two plans in some way since, failing this, confusion is likely to reign.

Whilst the Directorate of Pharmacy Services in the Ministry of Health and Child Welfare in Zimbabwe has been involved through WHO in the compilation of the document entitled “Country Data Profile on the Pharmaceutical Situation in the Southern African Development Community (SADC), Zimbabwe”, to serve as an input to the SADC Pharmaceutical Business Plan, local industry has not been consulted in either the drafting or implementation of the plan. It is consequently vital that local companies, as very important stakeholders, should seek involvement, through the PMA, in the implementation of the SADC Pharmaceutical Business Plan.

5. THE INSTITUTIONAL ENVIRONMENT FOR PHARMACEUTICAL PRODUCTION AND DEVELOPMENT

5.1 The Medicines Control Authority of Zimbabwe (MCAZ)²⁹

The Medicines Control Authority of Zimbabwe (MCAZ), which became operational in 1997, is a successor to the Drugs Control Council (DCC) and the Zimbabwe Regional Drug Control Laboratory (ZRDCL). It is a statutory body established by The Medicines and Allied Substances Control Amendment Act (MASCA) (No. 1 of 2006) [Chapter 15:03] with the aim of enabling the Authority to operate as a business entity capable of sustaining itself financially whilst also fulfilling a statutory mandate.

MCAZ’s mandate is to protect public health by ensuring that medicines and medical devices on the market are safe, effective and of good quality. This is achieved by:

- Evaluation and registration of all medicines and allied substances and medical devices
- Control of manufacture, distribution and storage of medicines and medical devices
- Inspections and post marketing surveillance
- Quality control testing of medicines and medical devices
- Administration of the Dangerous Drugs Act on behalf of the Ministry of Health and Child Welfare

The vision of the MCAZ is to be an effective medicines regulator in Zimbabwe and a leading regulatory authority in the world. Its mission is to protect public and animal health by ensuring that accessible medicines, allied substances and medical devices are safe, effective and of good quality through enforcement of adherence to standards by manufacturers and distributors.

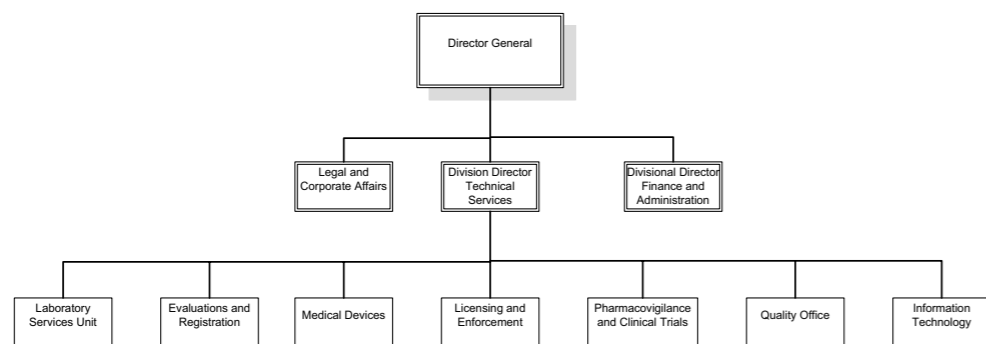
Authority members, who cover working committees as detailed below, are appointed by the Minister responsible for health to serve for periods of up to five years, with the possibility of renewal. The Authority discharges its functions through working committees which have decision making powers and such decisions are ratified by the Authority at its quarterly meetings. Each committee is chaired by a member of the MCAZ and the other members are informed of the activities of each committee by way of minutes. The Authority has eight such committees, namely: Executive, Registration, Licensing and Advertising, Veterinary, Legal, Adverse Drug Reactions and Medicines Review, Finance, and Laboratory. Committee members are selected by the Authority on the basis of their expertise.

²⁹ Brochures from the MCAZ, and website www.mcaz.co.zw

5.1.1 Organizational structure

The MCAZ is headed by a Chief Executive Officer, who is the Director General. The organization consists of two divisions, Technical Services and Finance and Administration, each headed by a divisional director. The Legal and Corporate Affairs Unit falls under the Director General's office.

Figure 2: MCAZ Organizational Structure



The **Technical Services Division** consists of seven units, namely: Evaluations and Registration, Laboratory Services, Medical Devices, Licensing and Enforcement, Pharmacovigilance and Clinical Trials, Quality Office and Information Technology.

The **Laboratory Services Unit** is the testing arm of MCAZ for medicines and allied substances. It has two sections, chemistry and microbiology, and its main objective is to ensure that medicines distributed on the market meet international standards and comply with WHO specifications. Tests are carried out according to both pharmacopoeial and validated in-house methods. Analysis of complementary medicines is a recent development in this unit and is intended to verify safety by testing for the absence of heavy metals and pathogenic microbes. As a service to the local pharmaceutical industry, the unit also produces secondary chemical reference standards at affordable costs.

The **Medical Devices Unit** carries out quality control testing of condoms and gloves in line with international standards. Physical tests are carried out on medical devices as well as checks for poor workmanship.

The **Evaluations and Registration Unit** is responsible for:

- Evaluation of applications for registration of human and veterinary medicines
- Evaluation and control of complementary medicines and allied substances

All new products that have not been registered with the MCAZ have to go through the Evaluations and Registration Unit for approval.

The **Licensing and Enforcement Unit** is responsible for:

- Enforcement of the Import and Export Regulations for Medicines and Allied Substances and Medical Devices
- Post marketing surveillance
- Licensing of premises and persons
- Good Manufacturing Practice Inspections
- Control of Narcotics and Psychotropic Substances

The **Pharmacovigilance and Clinical Trials Unit** carries out the following activities:

- Clinical trial protocol evaluation
- Monitoring of clinical trials
- Training and consultancy in clinical trials
- Pharmacovigilance on medicines
- International and regional liaison
- Harmonization, information and research
- Post registration control of medicines

The **Quality Office** is responsible for the development and implementation of the ISO 17025 Quality Management System. It ensures that all activities in the organization are carried out in accordance with international standards.

The **Information Technology Unit** ensures the smooth running of the authority's information technology systems and implementation of current global IT developments.

The MCAZ has three laboratories covering Chemistry, Microbiology, and Medical Devices whose role is to analyse and assess the quality and efficacy of all medicines, allied substances, complementary medicines and medical devices that are distributed on the Zimbabwean market.

MCAZ obtained ISO 17025 accreditation with the South African National Accreditation System (SANAS) in October 2010 in respect of chemical and microbiology analysis. Nonetheless, all the laboratories are in need of new equipment in order to replace antiquated equipment and to keep pace with technological developments.

The benefits of ISO 17025 accreditation to MCAZ are as follows:

- Establishes minimum competency standards
- Identifies laboratory's specific competencies
- Documents non-conformities

- Improves performance
- Enables continuous improvement
- Meets procurement requirements
- Assures acceptance of data
- Overcomes barriers to international trade

The benefits of accreditation to MCAZ’s customers are:

- Worldwide recognition of data
- Legitimacy
- Assurance of meeting quality requirements of consumers
- Reduced risk

The Authority charges fees for the registration of a medicine on application and levies an annual retention fee thereafter, as shown in Table 19.

Table 19: Schedule of fees applicable to local manufacturers

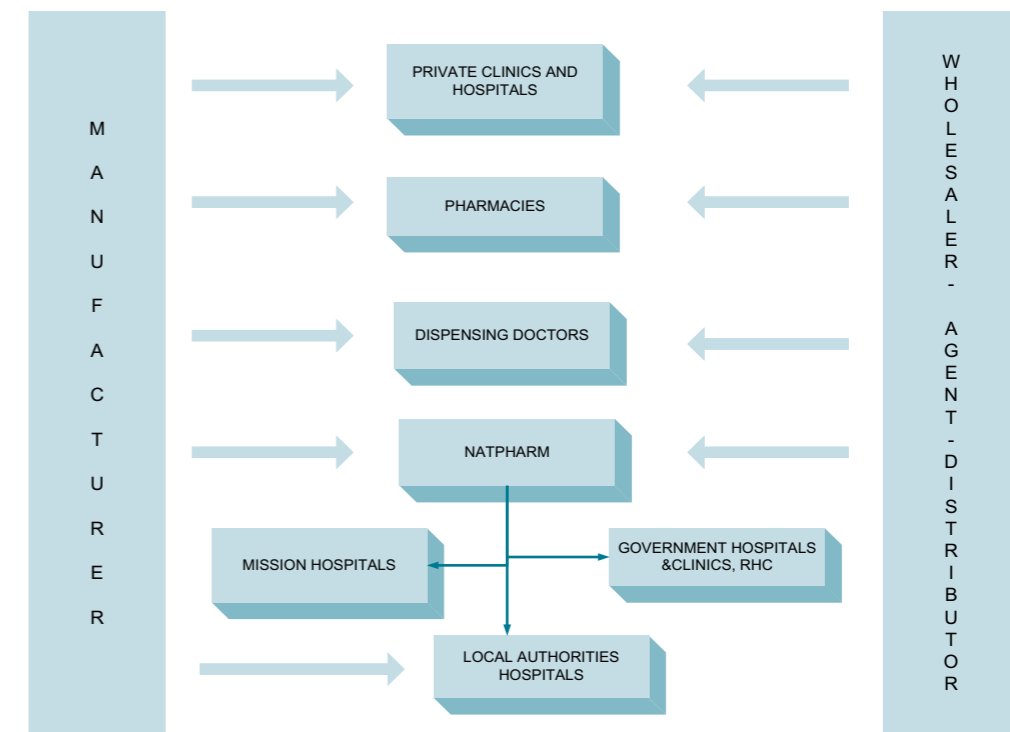
Activity	Fee (US\$)
Application for a licence for a pharmaceutical manufacturer’s premises	5 000
Application for the renewal of a licence for a pharmaceutical manufacturer’s premises lodged not more than two months and not less than one month before the expiry of such licence	3 750
Application for the registration of a locally manufactured medicine:	
Human medicine	900
Veterinary medicine	600
Application for reinstatement of registration of a previously registered product locally manufactured	1 000
Retention of a registered medicine, locally manufactured, annually:	
Human medicine	200
Veterinary medicine	150
Application to conduct a clinical trial funded by a local sponsor:	
Human medicine	2 000
Veterinary medicine	1 000

Other fees are levied, including on amendments to original applications, advertising and promotional material, etc. The local industry views these fees as prohibitive and as a deterrent to their development.

5.2 The National Pharmaceutical Company of Zimbabwe (NatPharm)

The National Pharmaceutical Company of Zimbabwe (NatPharm) is the national drug and medical commodities and equipment procurement and distribution body for all government hospitals and clinics. Private procurement and distribution is carried out through private wholesalers/agents/distributors and retail pharmacies.

Figure 3: Pharmaceutical Procurement and Distribution Channels in Zimbabwe



The Government Medical Stores was privatised and renamed the National Pharmaceutical Company of Zimbabwe (NatPharm) in 2002. NatPharm sources medicines and health commodities through open and closed tenders. Open tenders normally call for international competitive bidding to ensure price competitiveness. All pharmaceutical products procured by NatPharm should be registered with the MCAZ prior to actual procurement. Bidders of unregistered products are given a chance to submit their registration dossiers at the time of submission of tenders and such applications are given priority for evaluation by the MCAZ.

NatPharm is funded by the Government of Zimbabwe through budgetary allocations. However, the current economic difficulties have made this type of funding non functional. Consequently, over the past two decades, NatPharm procurement of pharmaceuticals has been funded by external bodies, including the World Bank, the European Union, the UK’s Department for International Development (DFID) and many others. This lack of funding at NatPharm has had a substantial negative impact on the sustainability and viability of the local pharmaceutical manufacturing industry since the public sector is by far the largest consumer of pharmaceuticals. In addition, donor organizations have been channelling finished pharmaceutical products into the country through NatPharm and this has further worsened the precarious position of local industry.

Moreover, although NatPharm was set up largely to serve the public sector, in some disturbing developments some years ago, the organization started selling excess tender stock to retail pharmacies. In this way, local pharmaceutical manufacturers found themselves competing with the same products on the private market, as NatPharm prices were much lower than theirs because of economies of scale due to the large volumes in which it purchases. This underlines once more the tension between health and industrial policies. This dubious practice was carried out under the guise of providing private market patients access to medicines for chronic diseases at subsidised levels. Such *ad hoc* practices are detrimental to the local pharmaceutical manufacturing industry.

In the private sector distribution system, manufacturers give discounts to wholesalers and pharmacies based on *de facto* industry levels. Wholesalers are awarded discounts of 10 to 15 per cent on gross sales and retail pharmacies a level of 5 to 10 per cent. Within the retail pharmacy sector, there has long been an unwritten agreement that mark-ups be set at 50 per cent while the level of mark-ups at wholesale level varies. As pointed out earlier, during the medicines prices survey carried out in 2004 and published in 2005, it was concluded that there was no transparency in the pricing of pharmaceuticals with the problem being more acute in the private and dispensing doctors sectors.

5.3 WHO prequalification of medicines

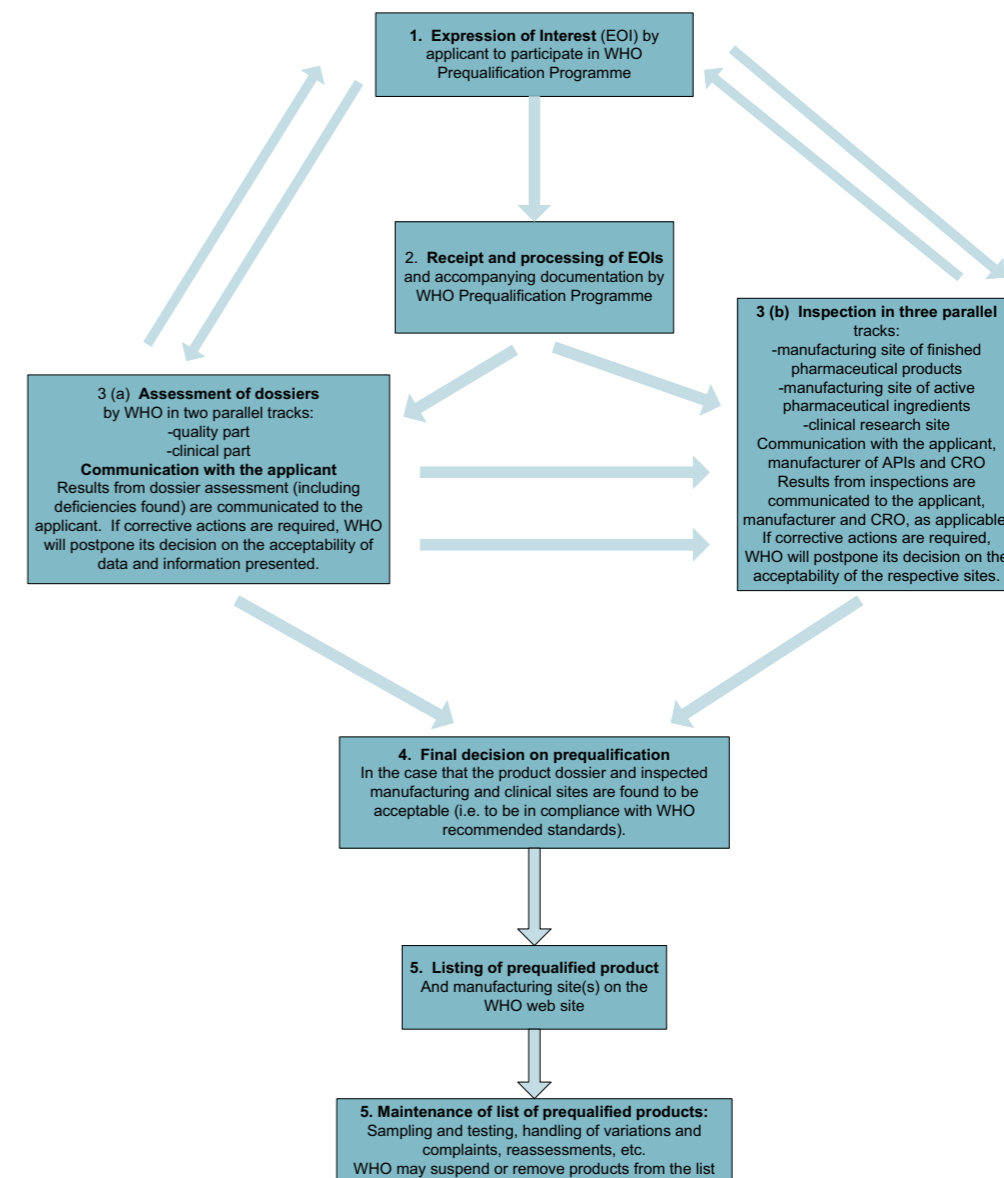
The World Health Organization (WHO) provides United Nations agencies with advice on the acceptability in principle of pharmaceutical products for procurement, the aim being to facilitate access to priority essential medicines that meet WHO-recommended norms and standards of acceptable quality.

The quality of pharmaceutical products is of crucial importance for the safety and efficacy of such products. WHO undertakes a comprehensive evaluation of the quality of pharmaceutical products based on information submitted by the manufacturers or other applicants and on inspection of the corresponding manufacturing facilities and clinical sites. This is done through a standard procedure based on WHO-recommended quality standards. Pharmaceutical products found to meet the WHO-recommended quality standards are included in the list of medicines considered acceptable, in principle, for procurement by UN agencies. The list of prequalified pharmaceutical products is mainly intended to guide procurement decisions taken by these agencies, which include the United Nations Programme on HIV/AIDS (UNAIDS), the United Nations Children’s Fund (UNICEF) and the United Nations Population Fund (UNFPA).

The growing list of pharmaceutical products which meet WHO-recommended standards may also be of interest to other organizations and countries wishing to engage in the bulk procurement of pharmaceutical products. The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) is one such organization. In fact, most organizations involved in the procurement of ARVs have also opted to require WHO prequalification for these products. Figure 4 below shows a flow chart of the procedure for obtaining WHO prequalification of pharmaceutical products. The purpose is to evaluate whether certain pharmaceutical products (considered by WHO as vital for the prevention and treatment of HIV/AIDS, tuberculosis, malaria and other diseases, or for reproductive health) meet the requirements recommended by WHO and are manufactured in compliance with current Good Manufacturing Practices (cGMP).

Inclusion in the WHO prequalification list does not imply any approval by WHO of the pharmaceutical products and manufacturing sites in question (which is the sole prerogative of national authorities). Moreover, inclusion in the list does not constitute an endorsement or warranty by WHO of the fitness of any product for a particular purpose, including safety and/or efficacy in the treatment of specific diseases.

Figure 4: Flowchart of WHO prequalification of pharmaceutical products



Source: Procedure for prequalification of pharmaceutical products, WHO Technical Report Series. No. 953, 2009

5.4 Pharmaceutical research bodies

There are no specific pharmaceutical research institutions in Zimbabwe but there are other research bodies with activities which include pharmaceutical research. Examples are:

5.4.1 The Research Council of Zimbabwe (RCZ)³⁰

The Research Council of Zimbabwe (RCZ) is a statutory body established under the Research Act of 1986. It is mandated to promote, direct, supervise and coordinate research in Zimbabwe. One major function is advising government on issues of research for sustainable development. RCZ also provides a forum for interaction and discussion for the mutual benefit of government, academia and industrialists.

The Council's role is that of a catalyst. Having identified broad areas of concern, it consults and brings together relevant experts to define a programme of work and to seek sources of funds. The RCZ operates through standing committees and other committees. Standing committees of relevance to this project are:

- **Industrial Development:** Promoting industrial support research in areas such as metrology and standardization, biotechnology, micro-electronics, and material sciences, especially in relation to natural resources, including conventional and renewable energy technologies
- **Health Sciences:** Promoting research in preventive health services, nutrition, sanitation, vaccines and pharmaceutical drug development. Emphasis is on strengthening epidemic preparedness through the use of epidemiology information systems, disease prevention and control strategies for top priority diseases such as HIV/AIDS.

The RCZ has approval procedures for carrying out research in Zimbabwe. Applications for research in the medical field should be approved by the Medical Research Council of Zimbabwe (MRCZ) prior to RCZ approval.

5.4.2 The Medical Research Council of Zimbabwe (MRCZ)

The Council's mandate is to provide independent ethical advice on research into health matters conducted by researchers or by/within institutions. The MRCZ is supported by the Government of Zimbabwe through the Ministry of Health and Child Welfare and is composed of scientists, medical experts, ethicists, patient representatives, and community representatives.

The Council's main functions are:

- To provide guidance, advice, and decisions (in the form of 'approval/disapproval') of specific research protocols intended for implementation in Zimbabwe by researchers and health institutions
- To provide ethical guidance and advice on research programmes undertaken within Zimbabwe
- To provide ethical guidance and advice on specific issues presented to it by the Institutional Ethical Review Committees (IERCs) and other interested parties

³⁰ Research Council of Zimbabwe website: www.rcz.ac.zw

- To develop and/or review, as requested, ethical guidelines for conducting medical research in Zimbabwe

The MRCZ is particularly concerned with research that addresses issues of relevance to Zimbabwe. The Council presents the conclusions of its reflections to the applicants (principal investigators) in the form of an independent decision which may be an approval, a disapproval, or negative advice.

5.4.3 The Scientific Industrial Research and Development Centre (SIRDC)

A notable institutional development in Zimbabwe was the creation of the Scientific Industrial Research and Development Centre (SIRDC) in 1993 and its 10 constituent institutes. The Centre's mission, through its various institutes, is to provide Zimbabwe and the region with technological solutions for sustainable development.

Two of SIRDC's institutes of particular relevance to this report are the Food and Biomedical Technology Institute (FBTI) and the Biotechnology Research Institute (BRI). The FBTI was established in 2002 as an autonomous technical department of the SIRDC. It undertakes focused research and development to promote growth and sustainable expansion in the food and biochemical industries and to discover new compounds and techniques of pharmaceutical and medical importance through scientific and technological exploration of Zimbabwe's vast biodiversity.

The FBTI's main objectives are:

- To develop and lead into practice technologies and processes that will promote food, pharmaceutical and biochemical industries in the country
- To provide technical consultancy and training services to food, chemical, biochemical and pharmaceutical industries
- To offer analytical services to food, chemical, pharmaceutical and biomedical industries

5.4.4 Human capital in science and technology³¹

The UNESCO Science Report of 2005 estimated that Zimbabwe had 1,100 staff in higher education and 600 full time researchers in 1999. All researchers were in the public sector with no or negligible research activity in the private sector. With 30 researchers per million inhabitants, Zimbabwe has a very low score when compared with other African countries, as shown in the table below.

³¹ Study carried out by Mziwandile Madikezela of High Impact Innovation, Johannesburg

Table 20: The science workforce of Zimbabwe in comparison with selected African countries

Country	Staff in Higher Education	Researchers full time in the public sector	Researchers full time in private sector	Full Time Equivalent Researchers	Researchers per million inhabitants
Kenya	1 800	600	0	1 000	35
South Africa	17 000	8 500	5 000	13 000	350
Tanzania	1 400	0	0	600	70
Tunisia	9 000	800	400	3 000	350
Zimbabwe	1 100	300	0	600	30

0 = negligible

During the first 25 years of Independence, the Government of Zimbabwe, in partnership with local communities, made great strides in the building of schools, teacher training and resource improvement. As a result, the country boasts one of the highest literacy rates in Sub-Saharan Africa. Yet despite the outstanding progress, especially in the area of education and access to education for the otherwise underserved groups, a number of gaps and constraints have been identified. These include:

- Inadequate funding levels for overall human resource development where existing levels of supply cannot meet demand
- Shortage of lecturers at technical colleges and at universities largely due to poor conditions of service
- Skills shortages exacerbated by the emigration of highly trained technical staff to neighbouring countries offering better conditions of service
- Shortage of equipment and staff resulting in the postponement of the introduction of technical and science subjects in schools

'Brain drain' is the main cause of the skills crisis in Zimbabwe and this trend has accelerated in the last 15 years, with most professionals going to countries such as the United Kingdom, Australia, New Zealand, Canada, South Africa and Botswana. It is estimated that professionals account for one third of the estimated 1.5 million Zimbabweans living outside the country. Similarly, universities face a considerable challenge in retaining highly qualified lecturers and can only do so by improving their salaries and conditions of service.

5.4.5 Research and Development funding

Government and private sector expenditure on research and development in Zimbabwe is only about 0.2 per cent of Gross National Product. As a way to promoting R & D, the Government has approved the following incentives to industry and individuals promoting research:

- A government budgetary allocation
- A double deduction on expenses incurred in promoting research
- Tax deduction on donations to R & D institutions

There are no data available on the level of international donor funding which has been channelled to R & D in Zimbabwe.

5.5 Business membership organizations

The Pharmaceutical Manufacturers' Association (PMA) is a trade organization which represents Zimbabwean generic manufacturing companies and has a total of eight members as detailed below. Currently, the PMA does not have a secretariat and this impairs the level of the Association's effectiveness.

Major activities include collective bargaining in the areas of employee wage and benefit negotiations; advocacy in relation to sector specific issues such as tariffs on inputs, the pharmaceutical tendering system, liquidity, and general support to the industry, medicine regulations and registration, and intellectual property rights. This work mainly involves face to face interactions with appropriate stakeholders and the presentation of position papers with the aim of influencing policy and other relevant issues.

In July 2009, the Association presented a paper entitled: "Pharmaceutical Manufacturers' Association Position Paper on the Resuscitation of the Pharmaceutical Manufacturing Industry in Zimbabwe", (Annex 3). This document has been widely circulated to various authorities and influential organizations, including the National Economic Consultative Forum, the Ministry of Health and Child Welfare, the Ministry of Industry and International Trade, the Confederation of Zimbabwe Industries and the Medicines Control Council of Zimbabwe. The paper advocates certain policy changes and the introduction of incentives for the local pharmaceutical manufacturing industry as outlined in section 4.1 on industrial policy.

The following pharma firms are members of the PMA:

- Plus Five Pharmaceuticals (current Chair)
- Varichem Pharmaceuticals
- Datlabs
- CAPS
- Pharmanova
- ZimPharm
- Graniteside Chemicals
- Ecomed

The PMA is currently in need of a major overhaul. Its constitution dates back to the colonial era and the organization has not been very successful in its lobbying and advocacy activities. It is felt that the Association places its main focus on routine issues like collective bargaining and has not put in place appropriate structures to enable it to successfully engage and lobby for pro-active policies which would lead to industry growth.

Once endowed with the appropriate structures, the Association should actively participate in the following national and regional activities:

- Implementation of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA) in Zimbabwe
- Implementation of the Pharmaceutical Manufacturing Plan for Africa
- Implementation of the SADC Pharmaceutical Business Plan
- Drafting and implementation of a National Pharmaceutical Innovation Strategy and Plan for Zimbabwe

The PMA could strengthen its performance by using existing tools developed by such organizations as WHO and Health Action International Global, details of which are in the public domain. These tools are of particular relevance for:

- Measuring medicine prices, availability, affordability and price components
- Measuring transparency in the public pharmaceutical sector
- Using indicators to measure country pharmaceutical situations: Fact Book on WHO Level I and Level II monitoring indicators

The information gathered using these tools can constitute an independent knowledge base for advocacy, policy recommendations and other changes sought by the PMA.

5.6 Training institutions and pharmacy education

The College of Health Sciences was established in 1963 and is still the only training centre for medical doctors and pharmacy in Zimbabwe. It currently offers degree programmes in Medicine, Dentistry, Pharmacy, Nursing Science, Medical Laboratory Sciences, Rehabilitation, Radiology, and Health Education and Promotion.

The School of Pharmacy was established in 1974 and offers a three year pharmacy degree programme. It has the responsibility of training pharmacists for Zimbabwe and also for the Southern African region. The first intake of 11 students graduated in 1976 and since then student numbers have increased steadily to the current 50 per year.

The School offers a Bachelor of Pharmacy Honours degree, which is designed so that, on completion, a graduate will have sound scientific training which will enable him/her to practice in the main professional areas of pharmacy. The degree programme is currently a four year one and its breadth is sufficient for a career in all areas of pharmacy-related employment.

Industrial pharmacy is covered under the course 'Pharmaceutics and Pharmaceutical Technology'. In Pharmaceutics, lectures and practical experience are offered. The laboratory classes are designed to present the principles and practical aspects of the syllabus at experimental level and to impart the necessary manipulative skills. The laboratory work is also designed to provide hands on experience in the use of modern equipment and techniques.

The course includes Drug Development workshops, in which small groups of students look at the stages of development of a drug from the bench to the market place. Participants are given the opportunity to evaluate a typical drug registration dossier and to make the appropriate recommendation for registration of the drug or rejection of the application. Sterile products practical sessions introduce the students to special manipulative techniques.

6. CHALLENGES AND OPTIONS FOR STRENGTHENING LOCAL PHARMACEUTICAL PRODUCTION

Between 2000 and December 2007, the national economy contracted by as much as 40 per cent, inflation soared to over 66,000 per cent and there were persistent shortages of hard currency. Industrial production contracted by 47 per cent. Zimbabwean generic pharmaceutical manufacturing companies have thus been facing various serious challenges for the past 10 years, with the situation deteriorating at an even faster rate from around 2008.

Initially, the major challenge was a marked lack of foreign currency to fund both working capital and capital expenditure. Despite the presence of acceptable levels of both domestic and export order books, the industry was failing to respond because of the non-availability of foreign currency to fund purchases of inputs. Foreign currency was largely available on the informal market but the exchange rate was very volatile, thus necessitating regular price adjustments. With a shortage of working capital, it was impossible for companies to fund equipment and machinery maintenance and replacement and this led to a huge stock of antiquated and dilapidated machinery.

Notwithstanding these constraints, the Zimbabwean pharmaceutical industry has managed to survive in the face of a high burden of policy, regulatory, legal and economic challenges. This can be attributed to its strong historical base and the fact that it has traditionally been able to supply the country with almost half of its essential medicines requirements.

Below, we summarize the major challenges currently being faced by Zimbabwean generic pharmaceutical manufacturers.

6.1 Issues at the policy level

The ‘health versus industrial policy’ tension is a reality in Zimbabwe, as demonstrated by the National AIDS Council’s procurement of imported ARVs. This puts local industry at a clear disadvantage. This is an area which the Ministry of Health and Child Welfare and the Ministry of Industry and International Trade need to address, together with local manufacturers.

Moreover, imports of finished pharmaceutical products used for the management of chronic diseases do not face any tariffs. In contrast, inputs for the manufacture of pharmaceuticals carry import duty which varies from as low as 5 per cent for active pharmaceutical ingredients to as high as 15 per cent for other materials and value added tax which is currently pegged at 15 per cent of the c.i.f. value of imports. This issue of the duty levied on imported inputs is perennial and has been debated for almost two decades, if not longer.

Local manufacturers are also of the opinion that there should be a policy which prohibits the import of those generic medicines which are commonly produced locally, in line with the current policy in Nigeria.

The industry also feels that the Government of Zimbabwe lacks commitment to the promotion of local production of pharmaceuticals despite its pledge in the National Drug Policy. Although some local preference is awarded to local manufacturers on local tenders and some foreign financed tenders, these are not considered adequate by the local industry, which would like to see preferences raised from 15 per cent to 25 per cent.

Through the National Economic Consultative Forum, the industry has put forward some recommendations on the policy changes required to resuscitate the pharmaceutical manufacturing sector but there has been very little positive response from the relevant policymakers. There is a need for interested parties, including the Pharmaceutical Manufacturers Association, the Ministries of Finance, Economic Planning and Development, Industry and International Trade, and Health and Child Welfare to form a pharmaceutical working group responsible for examining policy issues affecting the industry. In this way, early involvement of policymakers may ensure commitment from them when industry advocates policy changes or policy formulation through this working group. The National Drug Policy clearly articulates support for the local pharmaceutical manufacturing industry but implementation is non-existent. It would be possible, through the proposed working group, to strive to achieve integration and to eliminate inconsistencies and conflicts in existing policies on health, industry and the NDP.

Within the global and regional context, there are certain initiatives which have an impact on the local pharmaceutical manufacturing industry. These include the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA), the Pharmaceutical Manufacturing Plan for Africa (PMPA) and the SADC Pharmaceutical Business Plan. These initiatives have largely been developed and carried out without the involvement of the local industry yet they should serve as an input to the industry's planning process. Without the industry's participation and involvement, such global and regional initiatives could be counterproductive to the development of the pharmaceutical manufacturing sector.

6.2 Issues at the regulatory level

The Medicines Control Authority of Zimbabwe (MCAZ) is the body responsible for regulating the pharmaceutical industry in Zimbabwe. The Authority has the responsibility for approval and registration of medicines and this aspect of its mandate is critical for the local manufacturing industry as it governs and controls new product introductions into the market.

The drug approval or registration process and subsequent market authorization is currently taking at least two years. This limits the capacity of companies to compete both locally and on export markets. Moreover, before a product is approved for sale in foreign markets, the authorization of the relevant authorities is necessary in most countries, adding more waiting time to the whole process.

Registration fees are one time fees levied on applications for the registration of a Finished Pharmaceutical Product (FPP). Thereafter, a yearly retention fee is levied per FPP. Service fees charged by the MCAZ, especially in the areas of product registration and retention, are viewed as prohibitive by local pharmaceutical manufacturers, all the more so in view of current business viability and liquidity problems being experienced in the country. Some local manufacturing companies are even having to negotiate terms in order to settle their

retention fees bills.

The Medicines Control Authority of Zimbabwe (MCAZ) is currently working on the implementation of Guidelines on Submission of Documentation for Registration of Multisource (Generic) Finished Pharmaceutical Products (FPPs) in order to capture the latest developments in generic pharmaceutical preapproval best practices. With these Guidelines, the Authority has adopted the Common Technical Document (CTD) for submission of information for generic drug product development. It is hoped that the use of these new procedures will result in an overall improved quality of dossiers, subsequent shorter review cycles and faster registration of generic drug products.

The use of the CTD with its quality overall summary (QOS) component indirectly calls for the adoption of the quality by design (QbD) principle. This will present many challenges for the local manufacturing industry from the perspective of the generic drug product development process. No local company has a compliant, fully equipped, R & D facility. This will make it impossible for these companies to follow the QbD principle and generate the submission data required by the quality overall summary portion of the CTD. This will increase the risk attached to obtaining regulatory approval and further slow down the introduction of new products by local companies.

Moreover, bioequivalence studies, especially for drugs used in the management of the three pandemics are required for marketing approval by regulatory authorities. Dossiers without a bioequivalence study will not be accepted for filing with regulatory authorities. The current costs of conducting *in vivo* bioequivalence studies are prohibitive for the majority, if not all, of the local manufacturing companies. It is probable that only Varichem has experience of contracting out these studies since it has already sponsored a number of bioequivalence studies for its ARVs currently on the market and these were carried out by a Contract Research Organization (CRO) in India. However, with the increased products in the pipelines of Varichem and other companies, the cost of funding multiple bioequivalence studies becomes prohibitive. There is a need for alternative, cheaper bioequivalence CROs in addition to the currently available ones.

6.3 Issues at the legal level

The protection of Intellectual Property Rights (IPRs) provided to pharmaceutical products has a bearing on the structure of the industry and the nature of competition. The appropriate legislation protecting IPRs in Zimbabwe is the Patent Act of 1996, as amended in 2002. It is felt that this legislation is not sufficiently watertight to prevent 'evergreening' and the patenting of frivolous inventions. In the developed world, a number of pharmaceutical patents have been challenged by generic manufacturers and found to be non-patentable and subsequently cancelled. Lack of an adequate foolproof patent legislation is an obstacle to local manufacturers in Zimbabwe introducing essential generic medicines at a pace similar to that of their peers in developed nations.

In its current form, the Patent Act presents many challenges, in many respects, to the local pharma manufacturing industry. The legislation is in need of a complete overhaul in order to safeguard the interests of the local industry. Section 4.5.1 dealt in detail with the weaknesses arising from the current Act. Industry needs to influence the revision of this piece of legislation in order to address the weaknesses outlined above. However, given the concerns already expressed in relation to the lack of adequate and immediate attention to

policy changes and/or formulation by policymakers, redressing the legal inadequacies of the current Patent Act would be particularly challenging for the local pharma industry.

Another legal challenge facing the industry is the lack of transparency with respect to the status of pharmaceutical patents nationally. Unlike countries such as the USA, where it is a legal requirement for applicants to disclose all patents other than process patents covering any New Drug Application (NDA) filed with the US FDA, there are no such provisions within the Medicines and Allied Substances Control Act (MASCA). This makes it very difficult for local manufacturers to verify the validity and enforceability of patents when preparing for generic drug product development activities. There is a need for governments to make available, through appropriate legislation, full and reliable information on patents granted.

6.4 Issues at the institutional level

6.4.1 Business associations

The Pharmaceutical Manufacturers Association (PMA), which is the trade association for the local generic pharmaceutical manufacturing industry, does not have a full time secretariat and is run on a part time basis by its various members. Such an arrangement is not sustainable and weakens the Association. The PMA should carefully study and thoroughly analyse how it can strengthen its advocacy and policy influencing activities. Without a full time secretariat, this could be impossible.

The PMA needs to reinvent itself by building a new vision and mission and by coming up with a new constitution, together with creating the appropriate internal structures. However, funding constraints limit such a reorganization. A number of development institutions offer financial assistance to trade associations and may be able to support the PMA. There will, however, be a need for a strong business case validation of such support.

6.4.2 NatPharm Funding

With the current lack of funding for NatPharm, the viability of the country's generic pharmaceutical manufacturing industry is at stake. Local industry depends on access to public sector business through NatPharm in order to maintain its volume of activity and economic survival. Without this business, plant utilization will remain low and threatens the continuing existence of local manufacturers. Donated pharmaceutical products are flowing into the country, further exacerbating this situation.

Without such large volume domestic business, exports would seem to be the next business option for local companies. However, the export market, both public and private, is extremely competitive. Whilst the product portfolios of some local companies contain essential medicines utilized in regional markets, competition in public sector tenders is fierce and subject to questionable business practices. As mentioned earlier, the product portfolios of local companies are heavily commoditized for meaningful business in the export private market.

6.5 Issues at the enterprise level

6.5.1 Access to finance

Zimbabwe's current investment policy, together with the troubled political and economic situation, is not conducive to any form of investment, whether direct foreign investment or equity foreign investment and investment flows into the country have all but evaporated in recent years.

Local manufacturers are finding it difficult to source appropriate financing mechanisms to fund either working capital or capital expenditure. Currently, companies are receiving credit from suppliers, mostly local, with a few foreign suppliers also extending credit to Zimbabwean companies. Short term financing (30 to 90 day loans) is being accessed from local commercial banks at annual interest rates of around 15 per cent. Given the long cash conversion cycle (period between purchase of inputs, receipt thereof, conversion into finished pharmaceutical products, subsequent sale and collection of proceeds) in the pharmaceutical industry, the 30 to 90 day loan financing facility is not suitable since the loans are called in before the borrower has generated any cash and the amount advanced is, in any case, usually inadequate for the company's needs.

In view of the short term nature of the funds, local companies are finding it difficult to re-equip in order to modernize their manufacturing operations. The average age of equipment/machinery in the industry is about 10 years, with a range of 0.5 years to 30 plus years. Local pharmaceutical manufacturers need long term loan facilities and/or credit lines to finance capital expenditure. Short term financing, of an appropriate nature for the pharmaceutical industry, is also needed to finance working capital.

6.5.2 Infrastructure at plant level

The local generic pharma industry is in urgent need of infrastructure investment at the commercial, laboratory and pilot plant levels. Without this, local companies will not be able to access existing sources of funds for medicines to treat HIV/AIDS, tuberculosis and malaria. Given the ongoing economic turmoil in Zimbabwe, such investment will be very difficult to attract and local companies will need to innovate around this problem as, without upgrading, the industry risks irreparable decline.

6.5.3 Strategic management

Strategic management receives little, if any, attention from local generic manufacturing companies although it is a fundamental requirement for success. The nature of a company's product portfolio is a key success factor in the generic pharmaceutical industry and it needs to be revised on a yearly basis as new molecules lose their patent lives. This can only be done with a strong strategic management approach to new generic drug product develop-

ment and marketing.

This fact has not been taken seriously by the local industry as evident in its *ad hoc* and non systematic product development and introductions at a very slow pace with redundant molecules. There is thus a need for local companies to re-invent themselves and institutionalize strategic management in their business operations. It is well known that cultural changes are the hardest to implement in any organization and the introduction of strategic management is certain to be a cultural shock which would be met with much resistance, especially from top management who would view this as a challenge to its leadership.

6.5.4 Technical challenges

Over and above the non-existence of GMP compliant R & D facilities, equipment and machinery in the companies taking part in this report, there is a need for technology transfer in formulation development for sophisticated formulations since local companies lack the ability to develop such products. ACTs and TB FDCs are currently being used in the management of malaria and TB respectively and it is well known that these products present serious formulation challenges. This is confirmed by the relatively small number of WHO prequalified ACTs and TB FDCs.

In addition to ACTs and TB FDCs, sophisticated technologies like melt extrusion are being used in ARVs, a typical example being the heat stable combination of Lopinavir and Ritonavir (Kaletra, Alluvia from Abbott), the so called Meltex formulation, which uses this melt extrusion technology. Cipla launched its version of a heat stable combination of Lopinavir and Ritonavir, called Lopimmune, in 2007 using a melt granulation technology. These technologies are currently beyond the reach of local manufacturers who need some form of technology transfer in order to access these sophisticated formulations.

It is also well known that both generic and innovator pharma companies have used Novel Drug Delivery Systems (NDDS) to extend product life cycles and to gain competitive advantage over other players. This is another area which local companies need to pursue through strategic alliances and technology transfer.

6.5.5 WHO prequalification

Two local manufacturers, Varichem and CAPS, are currently producing ARVs. Varichem's first antiretroviral was approved for marketing by the MCAZ in July 2003 and that of CAPS in October 2005. These two companies have since broadened their ARV portfolios, with Varichem's range comprising nine items and that of CAPS two items at the end of 2007.

In a breakthrough for local pharmaceutical manufacturers in the last quarter of 2010, Varichem obtained prequalification for two of its ARVs, Lamivudine/AZT FDC and Lamivudine/Nevirapine/Stavudine. However, CAPS has not submitted an Expression of Interest in WHO prequalification for any of its products and it is evident that most dossiers require additional information if they are to be positively evaluated. Dossier quality thus presents a big challenge in the WHO prequalification programme in general.

6.5.6 Datlabs

Datlabs is one of the oldest pharmaceutical companies in Zimbabwe and was set up in 1950. The company has a relatively modern GMP compliant large volume parenteral facility in which products are manufactured under licence from Baxter Healthcare International. As with Plus Five, Datlabs intends to upgrade or build a completely new facility in order to achieve GMP compliance. This project will entail:

- Construction of a modern tableting suite
- Construction of a modern encapsulation suite
- Construction of a modern fully automated liquids unit
- Provision of complete service units

6.5.7 Plus Five Pharmaceuticals

Plus Five Pharmaceuticals is the second largest indigenous pharmaceutical company in Zimbabwe after Varichem Pharmaceuticals. It is also the youngest, having been established in 1996 and, as such, is one of the most receptive companies in terms of new thinking in the industry and willingness to learn new things.

Despite the financial constraints faced by many local companies, Plus Five has recently refurbished its facility located in Bulawayo in order to improve GMP compliance and it intends to carry out a phase two expansion of its facility. This will include the following activities:

- Construction and equipping a new modern laboratory
- Construction and equipping a new R & D facility
- Construction of an administration block and training facility
- Extension of the current Oral Solid Dosage form manufacturing unit
- Extension of the warehouse and addition of a sampling booth
- Installing a heating, ventilation and air conditioning (HVAC) system
- Expansion of the finished goods warehouse and quarantine area
- Construction and equipping of a facility to cater for external dosage forms

To date, the company has been financing its capital expenditure from its reserves. The second phase of the expansion programme will be partly financed from an offshore facility

being negotiated with a regional bank.

6.5.8 Varichem

Varichem Pharmaceuticals was the first indigenous pharmaceutical company established in Zimbabwe in 1985. Together with Aspen, it was one of the first companies in Southern Africa to pioneer local production of generic antiretrovirals and it introduced its first generic ARV in October 2003. The company embarked on a facility upgrade in 2007 with the assistance of the United Nations Development Programme (UNDP) and, to date, the Varichem commercial manufacturing facility is the only GMP compliant OSD facility in Zimbabwe.

6.6 Issues at the human capital level

Brain drain to neighbouring countries and international destinations has left the country with a huge void in its human capital base. Industries, training institutions and other critical organizations such as hospitals have been badly affected. Currently, the local pharma manufacturing industry is battling to satisfy its needs for well skilled and trained personnel. In addition, the quality of the pharmacist graduates from the College of Health Sciences has been compromised due to the shortage of highly qualified lecturers.

Zimbabwe does not have abundant PhD scientists in fields such as process chemistry and other critical areas required for pharmaceutical primary manufacturing and drug discovery research. This presents enormous challenges for the national pharmaceutical innovation strategy and industry ambitions to venture into API manufacturing and drug discovery research. Despite the relatively high number of scientific papers published by Zimbabweans, the number of patent applications filed by residents and patents granted to residents remains minimal. This indirectly confirms the lack of quality scientists in the country in various disciplines.

6.7 Options for strategic alliances

Based on the value chain analysis, key factors for success in the generic drug product industry, product portfolio analysis, late stage pipeline analysis and the analysis made in section 2.7 on the supply of medicines in Zimbabwe, suggestions are made in this report in terms of pharmaceutical strategic alliances which could be embarked upon by local manufacturers in order to strengthen their market position.

As already noted, local generic pharmaceutical companies are behind their Indian counterparts in terms of new product development, especially in the disease areas of the three pandemics. Local companies' current portfolios, discussed earlier in section 3.5, consist of aged molecules which cannot compete locally or in export markets with those of Indian generic companies. Based on the MCAZ pending list, pipeline products are also weak. Further analysis of the products in the pending register also shows Indian companies like Cipla to be aggressive, based on the number and quality of pending applications and their therapeutic coverage.

During the first medicines prices survey of its kind carried out in the country in 2004/2005, there was a general observation that prices in Zimbabwe at that time were generally higher than international reference prices. In addition, it is generally recognised that, because of poor product portfolios and a poor sales and distribution network, export prospects for local companies are generally weak as evidenced by the fact that the Global Fund ARVs market in selected African countries is dominated by Indian companies. In addition, there is an urgent need for local companies to embark on extensive equipment and machinery investment.

Against this background, the following strategic alliances are recommended:

Research and Development tie-ups

In order to reduce marketing time and regulatory risks, improve product portfolios and pipelines for new generic drug products, local generic pharmaceutical companies should consider R & D tie-ups with appropriate partners. The value chain analysis in this report points to weak generic drug product development as a result of weak infrastructure and technical capacity when compared with peers from the Indian generic fraternity. Development tie-ups have been utilized successfully by South African companies like Aspen Pharmacare and can take many forms, including:

- Outright purchase of existing dossiers
- Purchase of existing dossiers with supply agreements
- Contracting out of dossier development based on own molecule identification

There is obviously a need to carry out the necessary due diligence and pre-investment studies before embarking on any of the above proposed alliances. Such strategic alliances will reduce the challenges of market entry for both the local and export markets and enhance local companies' capacity to enter lucrative highly competitive markets and build cash reserves to finance organic or acquisitive growth. The current position, where local companies think they can do it alone, has put a brake on their growth and confined them to lower quality export markets which are insufficient to sustain their operations.

Co-marketing

Co-marketing alliances act as engines for growth in markets where it is difficult to invest capital resources. They help in overcoming the need to establish a strong brand by utilizing local firms that already enjoy significant brand equity in a particular market. Success stories in this area include those of Dr. Reddy's in the US, Ranbaxy and Mallinckrodt in India, Aspen and GlaxoSmithKline in various emerging markets and many others. For a co-marketing arrangement to be meaningful, one of the partners will need a strong product pipeline and portfolio and the other partner a strong marketing and distribution network, two of the key success factors mentioned earlier.

Although local companies mention that their exports as a percentage of turnover are in the range of 10 to 20 per cent, these values are insignificant (although no actual turnover figures have been disclosed), given the current lethargic demand prevailing in the local market. Moreover, given the high import intensity of the pharmaceutical industry, if exports are to make a significant contribution to the foreign currency reserves required to sustain local

companies, export sales should account for a substantial portion of annual turnover as they do in India. In that country, exports account for as much as half of total sales of some major companies like Ranbaxy and Dr. Reddys (Athreya).

For market entry into lucrative markets like South Africa, local manufacturing companies cannot expect great success with their aged product portfolios. Products selected for export market entry should meet market requirements in terms of product therapeutic profiles and molecule age. Co-marketing needs to be heavily supported by aggressive strategic new product development activities.

Joint ventures

Firms use joint ventures in order to enter new markets or product areas where they can create greater value by leveraging the combination of their core competencies rather than going it alone.

Given the importance of generic drug product development and the nature of a company's product portfolio and product pipeline as key success factors in the generic pharmaceutical industry, local companies should strongly consider partnering with each other and other stakeholders, private or public, to set up a Contract Research Organization (CRO) specializing in generics Research & Development. Such a CRO could cover a very wide scope of generic drug product development activities including conventional formulation development, analytical method development and stability studies. No one local company will be able to fund such an entity on its own and the most appropriate model will only be arrived at after some thorough investigation and studies.

This approach should also be adopted in the case of establishing a bioequivalence CRO after carrying out the appropriate pre-investment studies. One of the major obstacles for local companies wishing to expand their product portfolios is the increased requirement for bioequivalence studies for newer molecules and other products like ARVs, TB FDCs and ACTs which are required for life threatening conditions. However, given the current cost of carrying out these studies at facilities in India, Europe or South Africa, local companies will not be able to fund the bioequivalence requirements for a sizeable product portfolio. A home grown solution complying with international standards is required.

Strategic equity/loan investments

Strategic equity and/or loan investments are of great importance for the resuscitation and eventual growth of the industry, particularly in view of the antiquated state of equipment and machinery and the fact that most pharmaceutical manufacturing facilities in the country do not comply with international clean room standards and GMPs.

However, given the current political and economic risks associated with Zimbabwe, raising this investment could be a mammoth task for the local pharmaceutical industry. Properly conceived investment projects supported by the right pre-investment studies covering the dimensions of business viability are needed in order to mobilize the assistance of development banks/institutions.

7. STRENGTHENING LOCAL PHARMACEUTICAL PRODUCTION: RECOMMENDATIONS FOR ACTION

If local production of generic pharmaceuticals is to move forward in Zimbabwe, the challenges facing the industry discussed in chapter 6 of this report need to be adequately addressed. Intervention is required at policy, institutional, sector and enterprise levels. One company, Varichem, has recently succeeded in obtaining WHO prequalification for two ARVs, thus demonstrating that the local industry has some strong members. With some assistance, local pharmaceutical manufacturers are capable of increasing production of essential medicines for the domestic and export markets. Below, some interventions are outlined which could strengthen local pharmaceutical production at different levels.

7.1 Support at the policy level

A development strategy for the pharmaceutical sector

It is important that policy issues impacting on the local production of pharmaceuticals be addressed in order to make the business environment more conducive. For this to happen, a strong trade association with appropriate structures to influence the political environment is required. Without evidence-based advocacy, it will be difficult to influence policymakers in the required direction.

Faced with this situation, it is recommended that technical support should be given to the Pharmaceutical Manufacturers Association (PMA) to enable it to engage effectively in the public-private dialogue process (see also 7.3). The approach suggested could be similar to that taken in Ghana and Kenya and involve a multi-stakeholder sector strategy building process. To date, policy advocacy efforts have been very erratic and have not yielded any positive results due to the fragmented approach adopted.

A pharmaceutical sector strategy building process would systematically involve all stakeholders, including policymakers, in a consultative process. All stakeholders would be apprised of the situation on the ground and the need to change or implement new policies which encourage the development of the local generic pharmaceutical manufacturing industry.

The Patent Act

The Patent Act is very basic and out of date. It needs to be revised and re-drafted, taking into account relevant developments since the introduction of the Act and also to provide a more encouraging legal framework for the local production of pharmaceuticals. It is therefore recommended that Zimbabwe revise the patent legislation and draw up a comprehensive TRIPS compliant patent legislation. Technical assistance to this effect would probably be required.

7.2 Support at the institutional level

Restructuring of the Pharmaceutical Manufacturers Association

The PMA would benefit from an institutional overhaul. This could involve drawing up a new constitution and bylaws and designing a new structure which would, in particular, include a permanent secretariat. This would enable PMA to engage better in ongoing policy processes as discussed below.

Promoting private sector involvement in the Pharmaceutical Manufacturing Plan for Africa, the SADC Pharmaceutical Business Plan and the GSPA

To date, the most active players in the drafting and implementation of the Pharmaceutical Manufacturing Plan for Africa (PMPA) have been government officials, together with their nominated experts on the technical committee. Private sector involvement has been minimal except for the meeting of the extended technical committee in South Africa in 2010.

Similarly, local industry has not been consulted in either the drafting or implementation of the Southern African Development Community Pharmaceutical Business Plan. It is consequently vital that local companies, as very important stakeholders, should seek involvement in the implementation of this regional plan.

The local industry in Zimbabwe could take an active role in both these initiatives through the Pharmaceutical Manufacturers Association (PMA) and the Southern African Generic Medicines Association (SAGMA), particularly with respect to the implementation of phase II of the PMPA, as this has serious business implications, both locally and regionally. Priority areas to watch are the mapping, situational analysis, manufacturing agenda and financing exercises. Local companies need to be kept up to date and involved as they form an integral part of African secondary manufacturing capacity.

Another initiative in which the involvement of the local pharmaceutical manufacturing sector is of great importance is the implementation of the Global Strategy and Plan of Action on Public Health Innovation and Intellectual Property (GSPA). Without a sound and solid national innovation capacity, movement of the industry up the pharmaceutical value chain will be impossible. In this respect, the Pharmaceutical Manufacturers Association (PMA) could set up a standing committee to specifically handle this issue.

Strengthening of the School of Pharmacy

There has been a massive flight of skills from the School of Pharmacy in the College of Health Science at the University of Zimbabwe. As a result, the quality of the pharmacist cadre coming out of the institution is hardly adequate for the ever dynamic generic pharmaceutical manufacturing industry. In many countries, there is extensive collaboration between generic pharmaceutical companies and pharmacy schools in the area of product development and quality control, among other activities. In order to strengthen local production of essential medicines in Zimbabwe, it is particularly crucial to support the strengthening of the School of Pharmacy. Assistance could take the form of:

- Strengthening the School's staff through secondments to the schools of various pharmacy disciplines in universities overseas
- Equipping the School with basic machinery and equipment required for laboratory and pilot scale production of generic pharmaceutical products
- Equipping the School with basic equipment required for quality control of generic pharmaceutical products

Facilitating access to a national or regional bioequivalence unit

One of the most significant barriers to local producers attaining WHO prequalification is the financing of bioequivalence studies, which currently need to be carried out outside the country by foreign Contract Research Organizations (CROs). Local companies need to have access to a national or regional bioequivalence unit whose fees for bioequivalence studies are more affordable than those currently charged by companies from Europe, India and South Africa. Consequently, the local pharmaceutical industry and Zimbabwe as a whole would benefit immensely from the establishment of a local bioequivalence CRO.

In the course of interviewing local companies, both Varichem and Plus Five expressed the wish for technical assistance in the establishment of a bioequivalence CRO in Zimbabwe. A pre-feasibility study would be the first step. Also of interest would be access to the East African Community Bioequivalence Centre when it is functional.

Training in pharmaceutical patenting

The Zimbabwe Intellectual Property Office (ZIPO) is the legal body which administers all intellectual property legislation in Zimbabwe. The African Regional Intellectual Property Organization (ARIPO), of which Zimbabwe is a member, is also based in Harare. Consequently, interested parties can file patents at either the national level through ZIPO or through ARIPO by designating the relevant nationality. However, the final decision on grant of patents on a patent filed with ARIPO which designates a particular country still lies with the national authority of that country.

In view of this, it is important that patent examiners at national level are conversant with pharmaceutical patent claims. It is thus recommended that both ZIPO and ARIPO patent examiners should be trained in pharmaceutical patenting, which is particularly complicated. This would help to prevent the issuance of frivolous patents which in turn retard the development of the local generic pharmaceutical industry.

7.3 Support at sector level

Training: Advanced industrial pharmacy for the staff of PMA member firms

Company staff members need to improve their general Good Manufacturing Practices (GMP) knowledge and obtain more specialised skills in generic drug product development. These include formulation skills, analytical method development and validation skills and

statistical tools. With this in mind, it is recommended that PMA members participate in courses such as those included in the Advanced Industrial Pharmacy Training Programme organized by the Kilimanjaro School of Pharmacy in Tanzania.

Training: Specific aspects of the TRIPS Agreement

The level of understanding among manufacturing firms of the provisions of the TRIPS agreement as it relates to the local production of generic pharmaceuticals is very low, as revealed by the responses to requests for information in the framework of preparing this report. In view of this, it would be useful to enhance the understanding of the TRIPS provisions that affect the generic manufacturing industry.

Training: Generic drug product development and technology transfer

The Zimbabwean generic pharmaceutical industry is capable of producing the majority of the country's essential medicines if given the necessary support in terms of training in generic drug product development and technology transfer for difficult to formulate products. Currently, two companies (Varichem and CAPS) are producing ARVs. However, no company is producing TB Fixed Dose Combinations or antimalarial ACTs. With appropriate technical support in the area of formulation development, local generic pharmaceutical manufacturers are capable of expanding their portfolios to include ACTs, TB FDCs, as well as those ARVs currently not manufactured and other essential medicines.

Business development and strategic management

The current product portfolios of the local industry are mature and, as a result, firms cannot compete effectively on either the domestic or the export markets. The identification and verification of business opportunities at company level and professional business planning are preconditions for the development of a viable pharmaceutical industry. To strengthen the local pharmaceutical industry, strategic business development is an important component. This could involve product portfolio development and competitiveness benchmarking as well as considering strategic alliances and business partnerships.

Facilitating the manufacture of APIs at regional level

One of the major weaknesses in the pharma business in Africa has been the lack of backward vertical integration into the large scale manufacture of competitively priced APIs. Pharmaceutical innovation and technology transfer is urgently required in the area of Active Pharmaceutical Ingredients (API) manufacturing. The potential market represented by the combined populations of member countries of the African Union could make this initiative a reality. Regional pharmaceutical players should seek to collaborate with partners in the region to investigate the feasibility of initiating regional production of APIs.

7.4 Increased financial support from external donors

Although there is a very serious need for generic medicines in Zimbabwe, expenditure on health still remains very low. This situation has led to the shrinkage of business activity in the local pharmaceutical manufacturing industry. The country has been supported financially through the Global Fund, PEPFAR, the EU and other organizations but the volume of financial support has been very low in comparison with other countries in the region. Consequently, there is a need to develop the market for medicines and consider local procurement that improves access to medicines due to the shortened supply chain.

ANNEX 1. Persons, Institutions and Enterprises interviewed

Basopo Victor	New Business Development Manager	Datlabs
Bepe Nyasha	Pharmacist - Production	Plus Five
Chapanga Lloyd	Quality Assurance Manager	Varichem
Chimuma Archibald Taurayi	Regulatory Affairs Director	Varichem
Chinyama Naison	Head Quality Management Unit	Plus Five
Dlamini Mtonzima	Maintenance Manager	Datlabs
Hove Ropafadzai	Director; Pharmacy Services	Ministry of Health and Child Welfare
Kufa Nyasha	Pharmacist - R & D	Plus Five
Majaka Justice	General Manager	CAPS
Makura Tsurai Daniel	Technical Director	Datlabs
Masea Tafara	Pharmacist - Quality Assurance	Plus Five
Mashavave Stanley	Production Manager Pharmacist	Plus Five
Mavere Brian	Maintenance Engineer	Plus Five
Motsi Leonah	Quality Control Manager	Plus Five
Muchabaiwa Alois	Technical Director	Varichem
Mudzimu Forward	Pharmaceutical Expert	Ministry of Health and Child Welfare
Mujuru Emmanuel	CEO	Plus Five
Mutseyekwa Denford	Production Manager	Datlabs
Nyamangara Pasi	Compliance Manager	CAPS
Rukwata Richard	Assistant Director; Legal and Corporate Affairs	MCAZ
Sibutha Mafika	QA Manager	Datlabs

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ANNEX 3. Position Paper of the Pharmaceutical Manufacturers' Association (PMA)

Resuscitation of the Pharmaceutical Manufacturing Industry in Zimbabwe

1.0 PREAMBLE

- 1.1 The Zimbabwe pharmaceutical manufacturing industry is a major player in the country's health delivery system through the provision of affordable, safe, effective and quality medicinal drugs. To this end it is a key component in the restoration of the country's health delivery system to its past glory.
- 1.2 There are 260 drugs in the latest edition (2006) of the Essential Drug List of Zimbabwe ("EDLIZ"). The Zimbabwe pharmaceutical manufacturing industry is capable of supplying more than 122 products which represents 46.9% of the country's essential drugs requirements. Efforts are being made through new product development to increase the local component to 75% in the next five years.
- 1.3 Access to essential medicines in poor countries is hindered by low availability and unaffordable prices. Duties, taxes, VAT add to the cost of medicines. Local manufacture of generic drugs not only improves the availability of essential medicines but also lowers the cost.
- 1.4 Government committed itself through the Zimbabwe National Drug Policy to "promote and encourage the most cost effective local production of safe, effective, and good quality drugs in order to achieve optimal self-reliance within the context of national development goals". In the same document section 4.2 state that, "Government will support the pharmaceutical industry, especially in their production of drugs in EDLIZ, by means of various incentives".
- 1.5 The local pharmaceutical industry, in terms of development and sophistication, is second, only to South Africa in the SADC region.
- 1.6 The industry is a major contributor to the country's economic growth and GDP through exports, import substitution, tax revenues and employment. The industry exports its products to the following countries; Botswana, South Africa, Namibia, Zambia, Malawi, Angola, DRC, Tanzania, Uganda, West Indies among others.
- 1.7 There are 9 licensed pharmaceutical manufacturing companies in Zimbabwe which, in alphabetical order, are as follows:
 - i. CAPS
 - ii. Datlabs
 - iii. Graniteside Chemicals
 - iv. Meditech
 - v. Plus Five Pharmaceuticals (Pvt.) Ltd.
 - vi. Pharmanova
 - vii. Reckitt & Colman
 - viii. Varichem Pharmaceuticals
 - ix. Zimbabwe Pharmaceuticals

2.0 KEY ROLE PLAYED BY THE LOCAL PHARMACEUTICAL MANUFACTURING INDUSTRY

The following are the critical roles played by the local pharmaceutical manufacturing industry:

- 2.1 **Availability of essential drugs:** The local industry manufactures at least 46% of the country's essential drug requirements for the country. A vibrant industry will be able to contribute significantly to the availability of essential drugs. Ready availability of essential drugs is also assured through location advantages.
- 2.2 **Prices of Essential Drugs:** The local pharmaceutical manufacturing industry produces drugs at prices cheaper than imported products as shown by its competitiveness in all tenders floated by the government and non-governmental organisations (NGO's).
- 2.3 **Protection from Counterfeits:** The increased piracy in counterfeit drugs is of major concern to most regulatory authorities hence the heightened surveillance by WHO and local regulatory authorities. Counterfeits will be reduced through local production.
- 2.4 **Quality, Safety and Efficacy:** This is assured through local production because the production facilities can easily be monitored and effectively policed by the regulatory authorities. Liability can easily be enforced as opposed to foreign companies which are under different jurisdictions.
- 2.5 **Employment:** The local pharmaceutical industry provides employment to more than a thousand employees at current capacity utilisation. It is a key employer and training ground for degreed graduates and technicians in the following disciplines: pharmacists, chemists, accountancy, engineering, marketing, management and human resources, among others.
- 2.6 **Economic:** Economic benefits derived by the country from the local pharmaceutical industry includes: economic growth, income tax, PAYE, exports, import substitution and employment creation among others. The local industry exports its products to the following countries: South Africa, Botswana, Zambia, Malawi, West Indies, Angola, and Tanzania among others. The industry also supports other industries that include the packaging industry, retail and wholesale industry, engineering and tool making industry, ICT and the building industry. Some big companies in these industries are highly dependent on the local pharmaceutical industry for their survival and growth.
- 2.7 **Scientific and Technological Advancement:** The pharmaceutical industry is one of the most scientifically and technologically advanced disciplines in modern times. Development in this sector is also very rapid. To this end the local industry continuously adopts new technology and scientific methods in manufacturing, formulation development, analysis and quality assurance systems. One of the local companies was the first to produce generic ARV's in sub-Saharan Africa. The industry also provides material support and conducts collaborative research with the School Pharmacy at the University of Zimbabwe and other research institutions in the country.

3.0 CHALLENGES CONFRONTING THE PHARMACEUTICAL MANUFACTURING INDUSTRY

- 3.1 The Zimbabwe pharmaceutical manufacturing industry is currently confronted by the following challenges which are preventing local companies from playing a significant role in improving the availability of affordable essential medicines to the public.
- 3.1.1 Low capacity utilisation is currently averaging at below 25%.
- 3.1.2 Lack of short term credit lines to finance the purchase of starting materials (raw materials and packaging materials) which is central to increased capacity utilisation and availability. Prices will significantly come down if product availability and capacity utilisation increases. For example since the beginning of the year prices have gone down by more than 50% and continue to fall as capacity utilisation increases and competition intensifies.
- 3.1.3 Some procurement policies for the public sector favour foreign producers at the expense of local producers. For example foreign suppliers are given irrevocable letters of credit before they supply while local suppliers are required to supply on open credit ranging from 30 to 60 days. A case in point being the last tender floated by NatPharm on 27 March 2009. Given the country's poor credit rating and unavailability of credit lines for local financial institutions the local manufacturers will be unable to finance the procurement of raw materials and packaging materials and other input costs. This to a great extent affects the performance of local producers. However, foreign suppliers will be able to use the LC as security deposit to raise pre-shipment finance for the orders they would have won.
- 3.1.4 Old or antiquated plant and machinery is in urgent need of replacement to improve production efficiencies and product quality. This will make the industry more competitive not only locally but also in the regional markets especially against South African and Indian companies that have been the main source of essential drugs in the region.
- 3.1.5 Higher import tariffs in the form of customs duty and VAT on pharmaceutical raw materials and packaging that increase the cost of drugs, thus making them less affordable to the general public. Pharmaceutical raw materials and packaging materials attract higher duties than imported finished pharmaceutical products. VAT is charged on raw and packaging materials while it is not levied on imported finished products. There is therefore urgent need to at least level the playing field.
- 3.1.6 Whilst humanitarian assistance in the form of drug donations is welcome given the critical shortage of essential medicines in the country, it will be much helpful if wherever possible priority was given to the sourcing of these drugs from the local pharmaceutical manufacturing industry. This will be doubly beneficial to the country, not only will this improve availability and price but also contribute significantly to the reviving of the local manufacturing industry. Government will also benefit from the expanded tax base.
- 3.1.7 Lack of state support in the form of preference for locally produced pharmaceutical products in government tenders.

It goes without saying that a vibrant local pharmaceutical manufacturing industry capable of meeting the bulk of the country's essential drug requirements will play a significant role in the restoration of the country's health delivery system.

4.0 REQUIREMENTS TO RESUSCITATE THE INDUSTRY

4.1 Immediate Term Requirements

The pharmaceutical manufacturing industry recommends the following requirements which will have an immediate impact in resuscitating the industry and greatly improve the accessibility of essential drugs to the general public.

- 4.1.1 **Lines of credit:** Short term lines of credit at concessionary interest rates with reasonable grace periods (3-6months) and repayment periods (12-36 months) to finance the following working capital requirements:
- raw materials and packaging materials;
 - production consumables, laboratory reagents, protective clothing;
 - spare parts and repairs and maintenance of plant and machinery;
 - production, marketing, distribution, administration and other operational costs.
- 4.1.2 **25% Local preference** should be given to locally produced products in all public and government tenders administered by public institutions such as Natpharm (National Pharmaceutical Company) and EU funded tenders. We propose that locally produced pharmaceutical products should be given at least 25% price up from the current 10% to effectively protect the local industry against dumping and give it time to recover. This is also mindful of the fact that the National Drug Policy lists the promotion of local production of medicinal drugs as one of its major policy objective.
- 4.1.3 **Removal of duties and VAT** on pharmaceutical raw materials and packaging materials to reduce the cost of locally produced drugs. This will go a long way in improving the availability and affordability of essential drugs. It will also level the playing field against competition from imported finished products which currently enjoy lower duties and are VAT free.
- 4.1.4 **Local Sourcing:** Whenever logistics and resources permit priority should be given to sourcing of essential drugs from local manufacturers for humanitarian purposes by non-governmental organisations. This will be greatly beneficial to the revival of the industry, employment creation and economic growth.
- 4.1.5 **Importation of unregistered drugs:** The industry is grateful to the humanitarian organisations for their crucial role in alleviating the current critical shortage of drugs in the face medical emergencies such as cholera, HIV/Aids, TB, and Malaria among others. However, the industry strongly feels that such importation should cover short-term requirements and when available products should be sourced from local companies.

4.1.6 **Electricity, Water & Telephone Charges:** Whilst we appreciate the need to increase Electricity, Water and Telephone tariffs to ensure commercial viability for the providers of these vital services. The increase must be gradual and consistent with the recovery of the industry. Tariffs currently being charged by some of these institutions are above the regional average. This does not bode well for the competitiveness of the local industry and has a direct impact on the cost of locally produced drugs. Bills, especially telephone bills that have been received by our member are too high and unaffordable.

4.1.7 **Pre-shipment Finance:** Support in the form of pre-shipment finance is required. Pre-shipment finance should be given to the local pharmaceutical manufacturing industry to assist in securing raw materials and packaging materials for these orders. Flexible financial instruments such as irrevocable letters of credit and bankable guarantees should be made available to local manufacturers who would have won public tenders to assist them in raising financing for raw materials, packaging materials and other input costs. At a minimum the same payment terms should be made available to both local and foreign suppliers to level the playing field.

4.1.8 **Ban on the export of sanitary products** manufactured locally should be lifted.

4.2 Short Term Requirements:

The local pharmaceutical manufacturing industry is asking for the following requirements in the short term period (3-12 months):

4.2.1 **Long Term Lines of Credit:** Promotion of capital investment in the pharmaceutical manufacturing industry such as retooling, procurement of plant and machinery, factory refurbishments and upgrades by providing extended lines of credit at concessionary interest rates and long repayment periods of 3 to 10 years.

4.2.2 **Adoption of the Rand:** Joining the Rand monitoring area. Adoption of the Rand as the official anchor currency, whilst rehabilitating the local currency, will increase liquidity, price stability and promote immediate lines of credit from South African banks operating in Zimbabwe.

4.2.3 **Tax allowances and rebates:** Reduction of company taxation for all locally based pharmaceutical manufacturing companies to on average 15% as is the case in Botswana. Tax allowances and rebates for: Research and development, skills training and development.

4.2.4 **Special skills retention allowances:** Introduction of special skills retention allowances or tax rebates for professional and highly skilled personnel will assist in the development and recovery of the pharmaceutical industry. This should also be extended to supporting institutions such as the College of Health Sciences and School of Pharmacy at the University of Zimbabwe and Medicines Control Authority of Zimbabwe (MCAZ). The industry is highly skills intensive.

4.2.5 **Importation of locally produced drugs:** Banning of the importation of commonly produced pharmaceutical products (e.g. Aspirin, paracetamol, co-trimoxazole, amoxicillin etc.) should be considered. This was done in Nigeria to the great benefit of the local pharmaceutical manufacturing industry.

4.2.6 **Medicines Control Authority of Zimbabwe:** Strengthening of the local regulatory authority, Medicines Control Authority of Zimbabwe (MCAZ), to protect the local industry from infiltration by unregistered drugs, counterfeit drugs and poor quality products. MCAZ needs to be fully funded for it to fully discharge its mandate and retain staff.

4.2.8 **Compulsory Licensing:** Introduction of the necessary legislation to allow compulsory registration for local manufacture of essential drugs protected by international patent for public health reasons. This can be accomplished through the use of the flexibilities compatible with the TRIPS Agreement of the World Trade Organisation (WTO), as reaffirmed in the 2001 Doha Declaration on the TRIPS Agreement and Public Health for the purpose of "promoting access to medicines for all". One of these flexibilities is Member States' ability to issue compulsory licenses for public health reasons in relation to any pharmaceutical product under patent in the country. For example, the government can permit the local production of generic versions of patented medicines for purposes of public health.

4.2.9 **Compulsory local representation:** Introduction of legislation that will make it compulsory for all externally owned pharmaceutical companies marketing and distributing pharmaceutical products in Zimbabwe to have a local agent which is locally incorporated and majority owned. This is meant to effectively enforce accountability and prevent the distribution of counterfeit drugs. Such a requirement is now mandatory internationally and in some countries in the SADC that include South Africa and Namibia.

4.2.10 **Authorised Port of entry:** Lobby South Africa to designate Beitbridge/ Musina Boarder Posts as an authorised port of entry for drugs being imported into South Africa. Currently OR International port of entry is the only designated port of entry into South Africa. This means that all drugs entering South Africa will need to flown into that country which is proving to be very expensive for the local industry. This to some extent constitutes a trade barrier.

4.2.11 **Export Incentives:** Incentives for the promotion of exports which might come in the form of tax rebates, export subsidies, etc.

4.0 BENEFITS TO BE DERIVED FROM THE ABOVE

4.1 Capacity utilisation will increase from below 25% to 50% in the next 6 months and more than 75% in 12 months time.

4.3 Improved availability of essential drugs.

4.2 Prices of locally produced products will come down drastically consistent with the increase in capacity utilisation and concomitant reduction in cost of production.

4.3 Local pharmaceutical manufacturers will be able to sell on credit to credit worthy customers in the private and public sector, to great improvements in product availability.

- 4.3 Increased availability of locally manufactured products. Local companies will be capable of producing more than 46% of the country's essential drugs requirements within the next 6 months. 4.4 Employment enrolment will increase significantly by more than 150% not only for the pharmaceutical manufacturing industry but also other associated industries such as manufacturers of packaging, pharmaceutical wholesalers and retail pharmacies.
- 4.5 Regional exports will increase significantly by more than 120% due to increased competitiveness in prices. 4.5 More resources will be channelled into product Research and Development, thereby promoting growth of the industry through the continuous introduction of better products ahead of competition. Through this, the industry's contribution to the provision essential drugs list (EDLIZ) and specialist essential drugs list (SEDLIZ) will be increased significantly to more than 75% and 40% respectively.
- 4.6 More revenues to the fiscus through expansion of the taxes base that include PAYE, Income tax etc.
- 4.7 Growth of the local pharmaceutical manufacturing industry will contribute significantly to economic growth and improvements of the welfare and standard of living of the general population.
- 4.8 Strengthening of the local regulatory authority, MCAZ, to enable it to effectively police, control and enforce the country's pharmaceutical industry and thus protecting its market base from infiltration by poor quality, unregistered and counterfeit drugs.

5.0 POLICY RECOMMENDATIONS

We are humbly recommending the following policies which we strongly believe will not only revive the local pharmaceutical manufacturing industry but will also improve the availability and affordability of essential drugs.

- 5.1 Removal of import duties and VAT on imported raw materials and packaging materials. This will reduce the cost of locally produced pharmaceutical products thereby improving the availability and cost of essential drugs to the population.
- 5.2 Local preference of 25% on all public tenders in order to promote the local production of medicinal drugs and protect the local industry against dumping by foreign companies. This will also promotes technological transfer as multinational companies will be enticed to license local companies to produce their products or set up facilities for local production. Multinational companies such as Johnson & Johnson, Pfizer, Roche, and GSK among others have moved and are no longer producing locally.
- 5.2 Introduction of higher import tariffs for all finished pharmaceutical products that are commonly produced locally.
- 5.4 Aggressively launch buy Zimbabwe theme or proudly Zimbabwean to restore confidence in local products and increase local demand.

- 5.5 Government should come up with long term policies that promote development of the pharmaceutical manufacturing industry. This can be in the form of a National Industrial Policy Framework covering the pharmaceutical industry amongst others. Policy consistency is important for confidence building and long term investment decision making.
- 5.6 Adoption of the Rand as the official currency as a short gap measure in the immediate term to improve liquidity, stabilise prices, reduce inflation and build confidence in the economic environment.
- 5.7 Removal of trade barriers and tariffs between all SADC and COMESA member states and move towards a free trade zone similar to the European Union in the next five years. This will open the local pharmaceutical manufacturing industry to a market of more than 250 million people.
- 5.8 Harmonisation of the drug registrations in the SADC and COMESA member countries.
- 5.9 Government should come up with long term policies that will transform the country from being agriculture driven to being based on industrial production and service provision.
- 5.10 Review pertinent labour laws which make it difficult to hire and dismiss poor performers.
- 5.11 Introduce legislation that will facilitate compulsory licensing for local production medicinal drugs under patent within the flexibilities offered by WTO's TRIPs agreement for public health purposes. (See 4.2.8)
- 5.12 Export incentives in the form of either export subsidies or tax rebates of up to 25% of export value. This will accelerate exports growth through price competitiveness and levelling of the playing field with other countries offering the same facilities.
- 5.13 Put in place a revolving special fund (US\$50 million or more), managed by a local banks, for on lending to the local manufacturing industry at concessionary interest rates and manageable repayment periods. This could have a grace period of up to 3 years consistent with the estimated recovery period for the industry. The fund could be used to finance capital expenditure, plant upgrades and renovations, product development among other short to long term requirements.

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