



The viability of pharmaceutical manufacturing in Ghana to address priority endemic diseases in the West Africa sub-region

2007

Publisher:

Deutsche Gesellschaft für
Technische Zusammenarbeit (GTZ) GmbH
Dag-Hammarskjöld-Weg 1-5
65760 Eschborn
Internet: <http://www.gtz.de>

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This study has been commissioned by BMZ and GTZ, Germany. The views expressed in this study are those of the authors only and should not be attributed to BMZ and GTZ.

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ACRONYMS

ACT	Artemisinin-based Combination Therapy
ADR	Adverse Drug Reaction
API	Active Pharmaceutical Ingredient
ASNAPP	Agribusiness in Sustainable Natural African Plant Products
ART	Anti Retroviral Therapy
ARV	Anti Retroviral drug
AU	African Union
BMZ	German Federal Ministry for Economic Cooperation and Development
BP	British Pharmacopoeia
CIM	Centre for International Migration
CL	Compulsory Licensing
COA	Certificate of Analysis
CSRPM	Ghana Council for Scientific Research into Plant Medicine
CTD	Common Technical Document
DC	Developing Country
DFID	UK Department for International Development
DOT	Directly Observed Therapy
DRA	Drug Regulatory Authority
ECOWAS	Economic Community of West African States
eCTD	Electronic Common Technical Document
EDL	Essential Drugs List
EMA	European Medicines Agency
EPI	Extended Programme of Immunisation
FDA	US Food and Drug Administration
FDB	Food and Drugs Board (of Ghana)
FP	Finished medicinal Product
GCG	Global Cooperation Group of ICH
GDP	Good Distribution Practice
GDP	Gross Domestic Product
GHS	Ghana Health Service
GIPC	Ghana Investment Promotion Centre, Office of the President
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GNDP	Ghana National Drugs Policy
GTZ	German Agency for Technical Cooperation
HAN	Health Access Network
HPLC	High Performance Liquid Chromatography
ICB	International Competitive Bidding
ICH	International Conference on Harmonisation (of Technical Requirements for Registration of Pharmaceuticals for Human Use)
IDA	International Dispensing Association
InWEnt	Capacity Building International
IP	International Pharmacopoeia
IPR	Intellectual Property Rights
IR	Infra Red
ISO	International Standards Organisation
ITN	Insecticide Treated Net
KNUST	Kwame Nkrumah University of Science and Technology
LDC	Least Developed Country
MA	Marketing Authorisation
MAA	Marketing Authorisation Application

MCC	Medicines Control Council of South Africa
MHRA	UK Medicines and Health Product Regulatory Authority
MOH	Ministry of Health
MRP	Mutual Recognition Procedure
MSF	Medecins Sans Frontieres
NCB	National Competitive Bidding
NDP	National Drug Policy
NGO	Non Governmental Organisation
NHIS	National Health Insurance Scheme
NTD	Neglected Tropical Disease
NEPAD	The New Partnership for Africa's Development
NHP	National Health Policy
OPIC	US Overseas Private Investment Corporation
OTC	Over the Counter Product
PED	Priority Endemic Disease
PEPFAR	President's Emergency Plan for HIV/AIDS Relief
PLWHAs	People Living with HIV/AIDS
PMAG	Pharmaceutical Manufacturers' Association of Ghana
PMS	Post Marketing Surveillance
POM	Prescription only Medicine
PPME	Department of Policy, Planning, Monitoring and Evaluation of Ghana MoH
PPP	Public Private Partnership
PPT	Parallel Pharmaceutical Trade
PSF	Pharmaciens Sans Frontieres
QA	Quality Assurance
QC	Quality Control
QCL	Quality Control Laboratory
R&D	Research and Development
RHI	Regional Harmonisation Initiative
RPA	Retail Pharmacists Association
SADC	Southern African Development Community
SME	Small and Medium sized Enterprise
SP	Sulphadoxine-Pyrimethamine
STG	Standard Treatment Guideline
SWOT	Strengths, Weaknesses, Opportunities and Threats
TB	Tuberculosis
TGF	The Global Fund to fight AIDS, Tuberculosis and Malaria
TRIPS	Trade Related Aspects of Intellectual Property Rights
UNCTAD	United Nations Conference on Trade and Development
UNIDO	United Nations Industrial Development Organisation
USAID	US Agency for International Development
USD	US dollar
USP	United States Pharmacopoeia
VL	Voluntary Licensing
WAHO	West Africa Health Organisation
WAPMA	West Africa Pharmaceutical Manufacturers Association
WTO	World Trade Organisation

EXECUTIVE SUMMARY

Major tensions and reiterating vicious cycles exist concerning the issue of developing local pharmaceutical production in the context of addressing Priority Endemic Diseases in Developing (DC) and Least Developed (LDC) countries: the tensions of (i) globalisation and localisation (buying or making) and (ii) public health goals and profits; and two vicious cycles exist that need breaking in Africa as a whole: (i) the poverty-sickness cycle, and (ii) the dependency cycle. As the recent Ghana National Health Policy states, the priority should be on creating 'Wealth through Health'.

There are a number of Ghana-specific and sub-region 'Access to Drug initiatives' operating that address communicable and non-communicable disease problems, but it is beyond the scope of this report to examine these initiatives, how they are coordinated at a national and sub-region level and how they contribute toward an overall public health strategy.

In the context of the aforementioned tensions and vicious cycles, this report examines the viability of pharmaceutical manufacturing in Ghana to address Priority Endemic Diseases in Ghana specifically and with reference to the West Africa sub-region as a whole. This report also examines the operating environment of the local pharmaceutical manufacturing industry including some issues that have West Africa (ECOWAS) sub-region relevance, particularly pharmaceutical regulation.

Severe difficulties with financing and implementing development projects in the African pharmaceutical industry undermine sustainable development across Africa. However, Ghana has a well established and developing pharmaceutical manufacturing base and this report provides profiles of six of the major Ghana pharmaceutical manufacturers. The profiles provide some interesting contrasts in manufacturing strategy against the background of many common constraints for local pharmaceutical manufacturing development in Ghana.

In the absence of accurate pharmaceutical market statistics, it is estimated that the Ghana pharmaceutical market (both for non prescription – OTC and prescription medicines) is made up of approximately 30% locally produced and 70% imported products that originate mainly from India and China, the latter arguably being of better quality and certainly cheaper than those locally produced. Pharmaceutical market supply is divided approximately 50/50 between the private sector and the public donor sector. The local manufacturing sector is focused largely on providing OTC products in a saturated local OTC market (which exists for several reasons), while the public donor sector (particularly The Global Fund to Fight Aids, Tuberculosis and Malaria) provides the majority of products that address Priority Endemic Diseases.

While there is no shortage of pro-activeness on the part of many of the local major pharmaceutical manufacturers, some of which are beginning to produce drugs that address Priority Endemic Diseases, the Ghana pharmaceutical manufacturing industry faces a number of barriers and constraints (weaknesses and threats) for its future rational development which theoretically is founded on the supply of essential drugs to Ghana and the sub-region. A major symptom of the constraints that the local industry is facing is significant under utilisation of manufacturing capacity, often by more than 50%.

The major constraints facing the development of the local pharmaceutical industry consist of:

- (i) a chaotic and unregulated pharmaceutical distribution chain that leads to high prices and which seriously compromises pharmaceutical supply chain security;
- (ii) a focus of local production on OTC product manufacturing in a highly saturated local OTC market against the background of an 'ad hoc' local pharmaceutical market;

- (iii) inability to produce essential medicines that meet the standards for international tenders (i.e. WHO prequalification with its emphasis on manufacturing and product international regulatory compliance);
- (iv) relatively high manufacturing costs, for a number of reasons, of locally manufactured pharmaceutical products compared for example to imports from China and India;
- (v) absence of a local 'enabling business environment', i.e. effective and coordinated incentives and support for local pharmaceutical production of essential drugs according to international pharmaceutical standards;
- (vi) difficult access to cost-effective investment;
- (vii) limited attention and support for pharmaceutical R&D, when clear opportunities exist;
- (viii) weaknesses and gaps in implementation of IPR issues relating to TRIPS flexibilities and inefficiencies in the usage of in-licensing – whether by voluntary or compulsory means;
- (ix) inadequate and in-coordinated sub-region pharmaceutical regulatory framework;
- (x) arguably poor perception of sub-region produced medicinal products;
- (xi) the growing threat of counterfeit and diverted medicines – both for finished dosage forms and for active pharmaceutical ingredients (from India and China in particular);
- (xii) local inaction and in-coordination leading to increasing reliance on imported medicines (from international donors, China, India and from elsewhere in Africa and the sub-region); and
- (xiii) unmet professional human resource development / capacity building needs.

For a number of reasons, there are strong grounds for encouraging local pharmaceutical manufacturing that addresses the 'double burden of disease' in Ghana and the sub-region (Priority Endemic Diseases and chronic degenerative illnesses such as cardiovascular disease). It is probably neither sustainable nor desirable for West Africa to rely to a large degree on its drug supply (including the import of manufacturing materials) from outside sources such as China and India. The latter two countries have received a lot of investment and development incentives from their national governments to develop their growing pharmaceutical industries, and indeed perhaps can provide good case studies for the development of the African pharmaceutical industry. Although it is in the interest of vertically integrated Chinese and Indian pharmaceutical manufacturing companies with large manufacturing economies of scale to supply West Africa, this is not ultimately in the long term interest of West Africa.

Given the increasing economic and political stability in Ghana and several other countries in the sub-region, the time appears to be right to address local pharmaceutical industry development issues full on and in a way that deals with the cycles of poverty-sickness and dependency that exist in Africa.

This report presents a number of detailed recommendations that can potentially address the barriers and constraints facing local pharmaceutical production in the context of supporting better long term sustainable and cost effective health care and wealth creation in Ghana and the sub-region.

1 INTRODUCTION

1.1 Report Purpose

The purpose of this report funded by GTZ (the German Agency for Technical Cooperation) is to provide a review and analysis of pharmaceutical manufacturing capability in Ghana and its operating environment, and its ability to provide medicinal products for the priority disease areas of HIV/AIDS, malaria, tuberculosis and neglected tropical diseases for the Ghana population in addition to the populations of the sub-region of West Africa as a whole.

The task of ensuring the population's access to quality essential drugs at affordable prices is among the prime challenges facing many governments in the management of public health systems in developing countries. In recent years considerable progress has been made, with for example support from The Global Fund to Fight Aids, Tuberculosis and Malaria (TGF), in the supply of essential medicines to combat the three pandemic diseases of HIV/AIDS, malaria and TB. However, the gap between the type and volumes of such drugs required on the one hand and those that are affordable by the poor segment of the population on the other hand remains substantial.

One option available to LDCs in addressing this shortage against the background of tightened international intellectual property or patenting rules and regulations (TRIPS Agreement) is to stimulate the domestic manufacturing of essential generics. It is thus that the extended deadline granted to LDCs for TRIPS compliance (until 2016) is being looked at as a window of opportunity.

According to the WTO classification, Ghana is not considered to be a LDC but a DC which complicates the situation for Ghana with respect to implementation of TRIPS flexibilities. Ghana as a developing country cannot profit from the transition period for LDCs until 2016. However, Ghana can take advantage of all other TRIPS flexibilities (e.g. definition of patentable subject matter, scope of patentability criteria, compulsory licensing). Therefore, Ghana can make use of most TRIPS flexibilities.

This report provides detailed analysis and recommendations for technical assistance and capital investment needs for assisting the Ghana pharmaceutical manufacturing industry and its operating environment.

1.2 Report in the Context of GTZ Support (and other donor initiatives that address the same area)

The GTZ/ BMZ / UNIDO Programme

The GTZ/ BMZ / UNIDO programme to support local pharmaceutical production in Africa began in 2005, against the background of the fact that developing countries (such as India and China as important producers of generic medicines) had to implement the TRIPS agreement by 2005, and that the least developed countries have a transition period in 2016 to do so. The initiative aims at assisting selected developing countries in the establishment and upgrading of local capacities for pharmaceutical production. It includes capacity building and advisory activities to enable developing countries to make full use of the flexibilities provided by the World Trade Organisation (WTO) Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS), the Declaration on the TRIPS Agreement and Public Health of 2001, and the Decision of 30 August 2003 on the Implementation of Paragraph 6 of the Doha Declaration on TRIPS and Public Health. Within the context of this initiative GTZ, the United Nations Conference on Trade and Development (UNCTAD) and the United

Nations Industrial Development Organisation (UNIDO) have been carrying out activities in selected countries since 2005, so far in East African countries (mainly Tanzania, Ethiopia, Kenya) and South/ Southeast Asia (Bangladesh, Cambodia, Lao).

Other donor and sub-region initiatives

ECOWAS, the African Union, UK DFID and the international research-based pharmaceutical manufacturing industry have also recently implemented initiatives in this sector and a summary of their findings are provided in this report and examined in the context of providing overall coordinated technical assistance and funding to the sector.

1.3 Methodology for the Ghana Pharmaceutical Sector Assessment

The methodology used in the pharmaceutical sector scan for Ghana consisted of literature review, stakeholder interviews including focus group discussions and manufacturing site visits.

The stakeholders interviewed included:

- 6 local pharmaceutical manufacturers (including site visits): Ayrton (CEO and Marketing and Sales Manager), Danadams (CEO and production staff), Ernest Chemists (CEO and production staff), Kinapharma (International sales Manager), LaGray Chemical Company (Directors and production staff), and Phytoriker (Production Manager)
- the Pharmaceutical Manufacturers Association of Ghana (PMAG);
- the West African Pharmaceutical Manufacturers Association (WAPMA);
- the Food and Drugs Board of Ghana (FDB) – Departments of (i) Inspection, (ii) Drug registration and evaluation, (iii) Import and export control, (iv) quality control laboratory, (v) Tema port FDB control office;
- the Ministry of Health - departments of (i) Policy, Planning, Monitoring and Evaluation; (ii) Information, (iii) Procurement, (iv) Traditional and Herbal Medicines, (v) Chief Pharmacist, (vi) Central Medical Stores; (vii) Ghana National Drugs Programme;
- Ghana National Health Insurance Scheme (NHIS);
- the Ministry of Trade, Industry, Private Sector Development and the President's Special Initiatives;
- Ghana Investment Promotion Centre (GIPC);
- Ghana Customs and Excise authority;
- Ghana Ministry of Justice – Office of the Attorney General;
- Ghana Health Access Network (HAN);
- WHO Ghana office (programmes for HIV/AIDS, malaria, tuberculosis and neglected tropical diseases);
- the head of the Ghana narcotics control board (who is seconded from FDB);
- Ghana pharmacy faculty at Kwame Nkrumah University of Science and Technology
- UNAIDS office, Accra
- Interviews with senior representatives from regional African banks (e.g. Ecobank)
- Interviews with pharmacy stores and patients at pharmacies
- National Health Insurance Council Secretariat
- Noguchi Memorial Institute for Medical Research

Annex 1 to this report provides a fuller list of organisations and persons interviewed for this assignment.

Site visits were conducted to 6 of the principle pharmaceutical manufacturing facilities in Ghana.

1.4 Issues Examined

In the context of analysing the viability of Ghana pharmaceutical manufacturing to address Priority Endemic Diseases in Ghana and the West Africa sub-region, and its 'operating environment' a number of related issues are examined:

- the local/sub-region political and economic situation (and investment environment);
- public health;
- Intellectual property rights (including the issues of compulsory and voluntary licensing);
- local pharmaceutical sector policy and management;
- the functioning of the local pharmaceutical sector;
- the local pharmaceutical manufacturing situation (a SWOT analysis is provided);
- issues that concern the sub-region - pharmaceutical regulatory and manufacturing standards and coordination

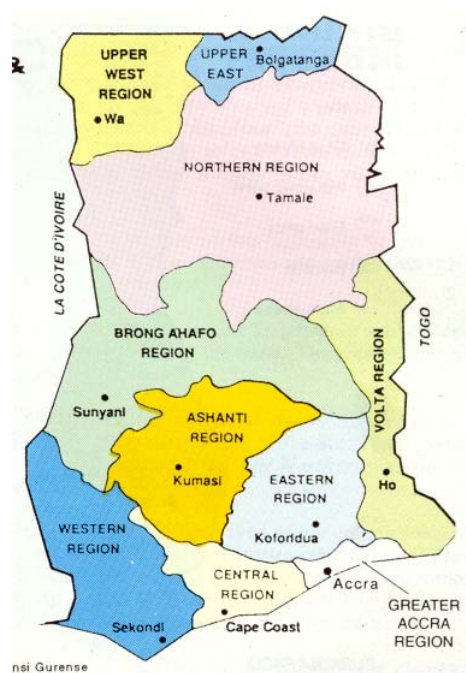
2 GHANA PROFILE

2.1 Demographics

Ghana is a tropical country in West Africa which is bordered on the north by the Gulf of Guinea and to the north by Burkina Faso to the west by La Côte d'Ivoire, and to the east by the Republic of Togo. There are two major weather seasons, namely the rainy and dry seasons (harmattan). The total land area of Ghana is 238,533 km square with an Exclusive Economic Zone of 110,000 km square of the sea. Ghana has a population of 20 million people and is divided into 10 regions.

Ghana's has an estimated population of 20.5 million in 2004. The level of fertility has remained very high, with a current rate of about 4.2¹. Infant mortality and under 5 mortality have worsened to 64 and 111² deaths respectively per 1,000 live births compared to 57 deaths and 108 deaths in 1998 respectively. Ghana has a pyramidal age structure due to its large numbers of children below 15 years of age: 44% of the population is below age 15 while only 5% is above age 65. There are slightly more women (53%) than men (47%) in the overall population. Life expectancy at birth for a Ghanaian is estimated at 57.7 years: 55 years for males and 59.2 years for females.

Map of Ghana, showing the regions



The Ghana Living Standard Survey estimated that about 40%³ of Ghanaians are living below the national poverty line. Finally, Ghana was ranked 131 out of 177 countries in 2004's Human Development Index measure.

¹ Ghana Demographic and Health Survey (2003)

² Ghana Demographic and Health Survey 2003

Demographic, Social and Economic Indicators		
Estimated Population (thousands)		22 113
Population Growth Rate		2.1%
Life expectancy at birth	Men	Women
	56	58
Human Poverty Index	Rank	Value
	62	35.1
Human Development Index		138
Percentage of people living with less than US\$2 a day		78.5%
Per Capita Gross National Income, ppp, Intl dollar rate		US \$ 2280
Per Capita Government Expenditure on health at Intl dollar rate		31

Source: UNAIDS

2.2 Economic and Political Overview of the ECOWAS / West Africa Sub-Region

In the context of providing an assessment of local pharmaceutical production capability to address priority endemic diseases and its ability to attract investment, it is important to provide an analysis of current and future estimated political and economic stability in Ghana and the sub-region.

While African countries are governed nationally by the respective national governments, cooperation between these governments is fostered by the African Union (AU), established in 1999. At a sub-region level economic cooperation is fostered by regional organisations; for the West Africa sub-region cooperation is fostered by the Economic Community of West African States (ECOWAS).

The West Africa sub-region consists of 16 states – all of which belong to ECOWAS (except Mauritania) - and is divided politically into 5 Anglophone⁴ and 11 Francophone speaking countries, a legacy of colonialism. This divide still presents political difficulties for economic cooperation in the sub-region. For example, France is a major sponsor of the Francophone states and the pharmaceutical supply to these countries is highly reliant on France. Arguably, this has contributed towards the lack of pharmaceutical regulation and pharmaceutical industry development in the West Africa francophone countries.

The political stability in the West Africa sub-region is highly variable; Ghana is considered to be one of the most politically stable countries in the sub-region (see box below), however countries such as Liberia, Sierra Leone and Cote D'Ivoire have had recent conflicts and have unstable political regimes, which undermines the possibilities of achieving sub-region integration in key areas such as public health.

Africa Risk Assessment - Ghana

Political Risk: Low Security Risk: Low

In spite of the 1998 drought, Ghana has initiated a program of privatisation within its state-owned enterprises. However, the government divestiture of parastatal organisations has been delayed, despite announcing plans to privatise the energy sector. In 2002, Ghana made improvements in its governance, financial sector and tax administration, its terms of trade with higher gold and cocoa prices, and in the water and electricity sectors. "The nation is proving itself a mature and united, indeed a beacon of democracy with a peaceful, stable and secure environment," Ghana's President John Kufuor told the nation.

Source: www.times-publications.com/risk-assesment/risk-assesment.html

⁴ The Gambia, Ghana, Liberia, Nigeria, Sierra Leone

In view of its relative political and economic stability, Ghana is reportedly the first country in the sub-region to establish an official government ministry dedicated to dealing with sub-region economic integration.

3 THE PRIORITY ENDEMIC DISEASE SITUATION IN GHANA AND RELEVANT DRUG TREATMENT PROTOCOLS

This section of the report provides an overview of the Priority Endemic Disease (PED) situation in Ghana. Ghana suffers from a *double burden of disease*. An examination of the 2002 Global burden of disease WHO report shows the top causes of death in Africa to be HIV/AIDS, respiratory tract infections, cardiovascular disease, and malaria. In fact it has been recently reported that hypertension is the number one killer in Ghana.

Common communicable diseases in Ghana include malaria, HIV/AIDS, pulmonary tuberculosis, pertussis, tetanus, measles, and infectious hepatitis. The non communicable disease burden in Ghana consists of hypertension (and resulting cardiovascular diseases), diabetes and others. Added to these are a number of neglected diseases of public health importance e.g. trachoma and schistosomiasis

Acute respiratory infections, diarrhoea, malnutrition, anaemia, and measles continue to be major health challenges. These health problems account for about 50% of all childhood admissions to health facilities and for 30% of childhood deaths.

There are a number of local and sub-region 'Access to Drug initiatives' operating in Ghana that address the communicable disease and non communicable disease problems, but it is beyond the scope of this report to examine these initiatives and how they are coordinated at a national level.

3.1 HIV/AIDS

Although the HIV / AIDS epidemic is less severe in West Africa relative to other parts of sub-Saharan Africa, the rate at which it is spreading across the sub-region creates the urgency for action on the part of all stakeholders. It is thus likely that the demand for ARVs is going to increase. West Africa has an estimated 4.96 million people infected with HIV. Of this number an estimated 2.9 million are in Nigeria, 750,000 in Cote d'Ivoire and 350,000 in Ghana (a 2.3% prevalence rate). Approximately 20% of this population (980,000) requires Anti Retroviral (ARV) treatment (UNAIDS, December 2006), but only 13% of those who require ARVs are currently receiving them.

HIV / AIDS cases are located in 2 corridor areas in Ghana. 11,534 (MoH Sept 2007) patients are accessing ARV treatment representing 15% of those in need of ARVs from the state and private sector, this this number is far short of the total population in need of these life-prolonging drugs.

The following 2 tables summarise (i) the HIV/AIDS estimates and (ii) HIV/AIDS progress indicators for Ghana based on the most recent information available from UNAIDS.

Ghana HIV/AIDS Estimates	
Number of people living with HIV	350 000 [270 000 – 380 000]
Adults living with HIV/AIDS	320,000
Adult HIV/AIDS Prevalence Rate	3.1%
Adults aged 15 to 49 HIV prevalence rate	2.3 [1.9 – 2.6]%
Adults aged 15 and up living with HIV	320 000 [250 000 – 350 000]
Men aged 15 and up living with HIV	140,000
Women aged 15 and up living with HIV	180 000 [150 000 – 210 000]
Deaths due to AIDS	29 000 [21 000 – 36 000]
Children aged 0 to 14 living with HIV	25 000 [9800 – 48 000]
Orphans aged 0 to 17 due to AIDS	170 000 [130 000 – 210 000]

Source: UNAIDS

Ghana HIV / AIDS Progress Indicators

Expenditures

National funds spent by governments from domestic sources	US \$ 9 267 783
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National Programmes

Percentage of pregnant women receiving treatment to reduce mother-to-child transmission	1.3%
Percentage of HIV-infected women and men receiving antiretroviral therapy	7.0%
School attendance among orphans	65.0%
non-orphans	81.0%

Knowledge and Behaviour

Percentage of young people aged 15 to 24 who correctly identify ways to prevent HIV	Men	Women
	44.0%	38.0%
Percentage of young people aged 15 to 24 who had sex with a casual partner in the past 12 months	Men	Women
	83.0%	50.0%
Percentage of young people aged 15 to 24 who had sex before 15	Men	Women
	3.9%	7.4%
Percentage of young people aged 15 to 24 who used a condom last time they had sex with a casual partner	Men	Women
	52.0%	33.0%

Source: UNAIDS

According to the Ghana AIDS Commission, Ghana's HIV infection rate has dropped for the first time in five years, and is now down countrywide to 3.2 percent from 3.6 percent in 2004, according to a sentinel survey released in 2007. *"It's not conclusive proof of an overall decline, but the findings at least suggest that the epidemic is slowing down. We need a consistent fall over three years,"* (Nii Akwei Addo, programme manager of the National AIDS Control Programme - NACP).

Patients receiving treatment is gradually scaling up, but the Ghana MoH considers that TGF may not be able to cover all the Ghana ARV needs over the next few years. The Government of Ghana has committed to scaling up HIV treatment and will use the \$15 million given over two years by TGF for the distribution of Anti Retroviral drugs (ARVs).

While ARV treatment (ART) is only a part of the continuum of care for People Living with HIV/AIDS (PLWHAs) it obviously forms an import part. The Standard Treatment Guidelines (STGs) for HIV / AIDS treatment for Ghana are summarised as follows:

(i). Post Exposure Prophylaxis (PEP) for potential occupationally-acquired infection

Zidovudine and Lamuvudine (for low risk exposure) and Zidovudine, Lamuvudine and Nelfinavir (for high risk exposure).

(ii). The national ART Guideline

This recommends the use of two nucleosides and one non-nucleoside analogue. In the START program common regimens in use are: Zidovudine, Lamivudine and Nevirapine; Zidovudine, Lamivudine and Efavirenz; Stavudine, Lamivudine and Nevirapine; Stavudine, Lamivudine and Efavirenz. Zidovudine is replaced by Stavudine in case of severe adverse drug reaction or vice versa, Nevirapine is switched for Efavirenz or vice versa.

(iii). First and second line ARVs

The following first and second line drugs are recommended:

First Line Drugs: Lamivudine / Zidovudine / Nevirapine / Nelfinavir or Stavudine

Second Line Drugs: Abacavir / Didanosine / Indinavir

* Effavirenz is designated for treatment switch option

* products can be presented as either single or combination (double / triple)

It is estimated that 95% of the population receive first line drugs, while only 5% receive second line drugs.

3.2 Malaria

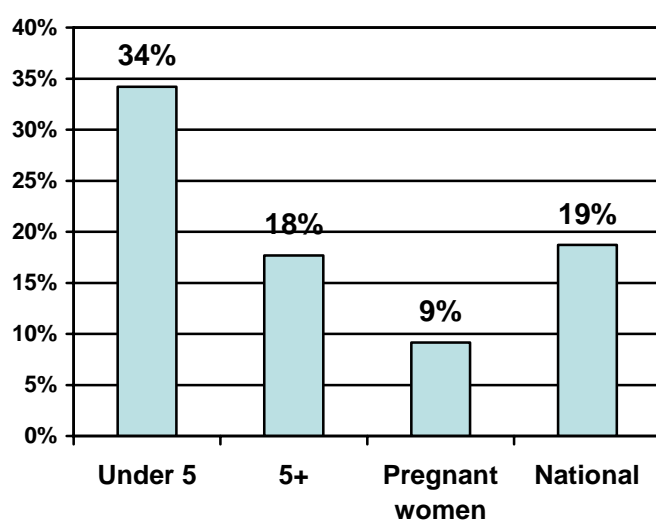
Malaria is still one of the leading causes of morbidity and mortality in developing countries and is the number one killer among children. The best estimate of malaria statistics for Ghana comes from the WHO and is summarised in the following table.

Ghana Malaria Statistics	
Malaria Cases (2003)	3,552, 869
Malaria Case Rate (2003)	170
Malaria Deaths (2003)	3,245

Source: WHO

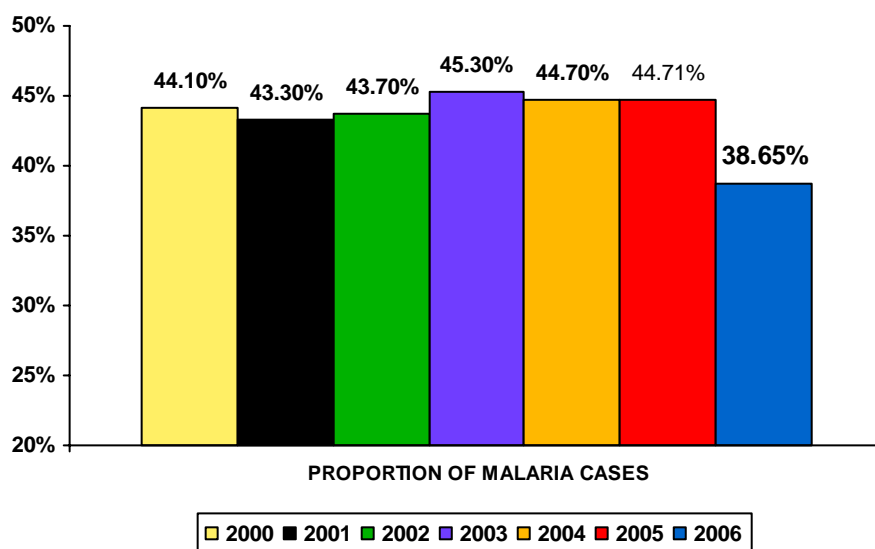
The age proportion of deaths resulting from malaria in Ghana in 2006 is summarised in the following graph:

Proportion of deaths attributed to Malaria in Ghana by target groups in 2006



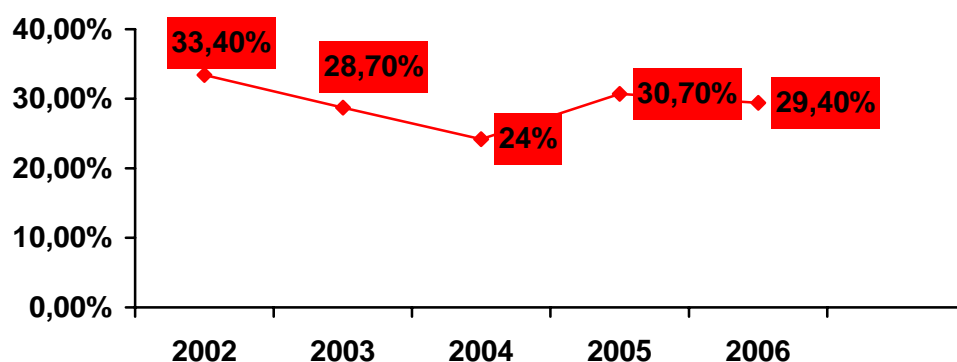
The following graph presents an estimation of Ghana clinic out patient department cases reported due to Malaria between 2000 and 2006

Proportion of Out Patient Department Cases attributed to Malaria in Ghana (2000 – 2006)



The proportion of under 5 deaths attributed to malaria in Ghana (2002-2006) is presented in the following graph:

Proportion of under 5 deaths attributed to Malaria in Ghana (2002-2006)



The cost of controlling malaria in Ghana is estimated as follows:

- malaria contributes to US\$ 2.63 of per capita income which translates into US\$ 13.51 per household (per month);
- on average the cost per case to the MOH/GHS was estimated at US\$2.94;
- this is equivalent to 9.74% of per capita government expenditure on healthcare.

As a result of recent interventions an impact assessment of achievements in malaria control is summarised as follows:

- Malaria deaths in children dropped from 4/100 to 2/100 children admitted for malaria;
- Malaria deaths in pregnancy women reduced especially in the initial 20 GF supported districts;
- Mothers and caretakers who can recognize early signs and symptoms of malaria and responded correctly increased from 30.2% to 75.5%;
- Case Fatality rate in under-five years has dropped from 3.26 in 2003 to 2.0 in 2006;
- In the 20 Round 2 supported districts, admissions due to malaria reduced from 39, 497 in 2003 to 19,000 as at the end of 2006 where as outpatient department cases dropped from 554,000 to 392,000 (30% drop);

- ITNs use in children under-five years has also increased from 26.4% in 2003 to 33.0% in districts with Round 4 support and 38.6% in Round 2 supported districts with by the close of 2006;
- ITNs use in pregnant women has also increased from 38.5% in 2003 to 46.5% in Round 2 supported districts;
- IPT coverage also increased from 0% as at beginning of 2003 to 71.9% as 2006 (IPT started in 2003).

The percentage of the population receiving treatment is hard to determine given the self medication programme in operation.

The cost and time of obtaining blood tests for malaria is prohibitive for the local population (e.g. in private sector 20 USD cost and half hour wait and in public sector 5 USD and 3 hour wait).

One of the major challenges facing Africa in the fight against malaria is drug resistance of *plasmodium* strains to cheap and commonly used anti-malarial drugs such as Chloroquine and Sulphadoxine-Pyrimethamine (SP). Consequently, the WHO has recommended a major shift from the monotherapies to Artemisinin based Combination Therapy (ACT), a treatment policy that Ghana is implementing. By hitting different biochemical targets on the malaria parasite, drug combinations are more effective, allow for shorter treatment courses, and protect each individual drug from resistance. It is now widely agreed that the best current treatment solution is ACT. Artemisinin derivatives, which are extracted from a Chinese plant (*Artemisia*), are fast-acting, highly potent and complementary to other classes of treatment. To date, no resistance to ACT has been reported, although the problem of counterfeiting (provision of low level active ingredients and in the wrong combinations is causing particular international public health concern, e.g. the situation in South East Asia).

The Amodiaquine-Artesunate combination is currently the ACT of choice for the treatment of uncomplicated malaria in Ghana. Where treatment failure occurs or in the case of cerebral malaria then Quinine is recommended. For the treatment of malaria in pregnancy, under the Intermittent Preventive Treatment (IPT) regime, SP is recommended utilising the Directly Observed Therapy (DOT) method.

The provision of Insecticide Treated Nets (ITNs) is also a large part of malaria prevention in Ghana and the supply of which relies largely on international donations.

3.3 Tuberculosis

According to the Ghana Ministry of Health, tuberculosis (TB) is the most common cause of lost healthy lives due to premature deaths. An estimated 10,000 deaths due to tuberculosis occur in Ghana each year. In 2003, Ghana projected more than 40,000 new cases of tuberculosis in its population of 20 million people. The following table presents the latest available TB statistics for Ghana:

Ghana Tuberculosis Statistics	
New TB Cases (2003)	N/A
People living with TB (2003)	79,466
TB Prevalence Rate (2003)	380
TB Deaths (2003)	10,572
TB Death Rate (2003)	N/A
DOTS Coverage (2003)	60%
DOTS Detection Rate (2003)	40%
DOTS Treatment Success (2002)	N/A

Source: [Stop TB: Http://www.stoptb.org](http://www.stoptb.org)

Currently, private health facilities lag behind the public sector in the management of this disease. A TGF grant of more than USD 2 million has been aimed to promote equitable access to prevention, care, support and treatment for all people affected by tuberculosis. Supporting private-sector participation in the national tuberculosis control program and improving the quality of directly observed treatment, short-course, (DOTS) programmes within the private sector are chief goals of the program supported by TGF.

To enable the expansion of DOTS coverage, TGF financing has underwritten the training of 450 metropolitan and private sector health-care workers, improvements to private-sector laboratory facilities, the renovation of 60 DOTS centres, the introduction of home visits to tuberculosis patients and the coordination of public and private-sector activities to combat tuberculosis.

By using incentives such as providing equipment and training, the Ministry of Health hopes to encourage the private sector to coordinate with the National Tuberculosis Control Programme. It is anticipated that within five years, 95 percent of all private facilities will be coordinated with the national program. This will promote a more uniform approach to treatment and care, consistent with the work of the Stop TB Partnership.

By the end of two years, Ghana expects to have used TGF grant to increase case detection rates by 10 percent and increase cure rates from 50 percent to 70 percent at private health-care facilities in Ghana's two largest cities, Accra and Kumasi. This program builds upon a strategy now used by the Metropolitan Health Services and the National Tuberculosis Control Programme, which improves detection of tuberculosis, manages the implementation of DOTS and provides quality care for tuberculosis patients.

As one of the first countries in the world to receive TGF financing, Ghana is already using more than 40 percent of the funds committed for two years to train health-care workers and to provide DOTS. The box below summarises the Ghana TB STGs:

Ghana Tuberculosis Standard Treatment Guidelines

1. Short Course – Direct Observed Therapy (DOT) for new cases(8 months treatment duration)

S (2 months), H (6 months), R (6 months), Z (2 months) plus continuation phase of 6 months with H + T (or H + E where HIV co-infection is suspected).

Rifinah (Isoniazid + Rifampicin) is recommended as a combined preparation so as to reduce the risk of drug resistance.

2. Standard course for negative pulmonary TB (12 months treatment duration)

S (2 months), H+T (2 months), H+T (10 months continuation phase)

3. Retreatment regimen (for treatment failure or relapse)

RHZE (3 months) and S (2 months), RHE (5 months continuation phase)

The standard TB drugs are Rifampicin (R), Isoniazid (H), Pyrazinamide (Z), Ethambutol (E), Streptomycin (S) and Thiacetazone (T)

However, the current 2004 Ghana guidelines for TB treatment do not concur with international recommended guidelines and thus this has led to a problem of TB drug provision and dispensing – for example, the following types of TB patient treatment kits are supplied by international donors:

Category 1 + 3 patient kit: RHZE (2 months), RH (4 months);

Category 2 patient kit: S+RHZE (2 months), RHZE (1 month), RHE (5 months).

Thus this situation leads to procurement and dispensing confusion.

Ghana has a TB immunisation and prevention programme based on BCG immunisation of new-born or at first contact and Isoniazid prophylaxis.

3.4 Neglected Tropical Diseases

Neglected Tropical Diseases (NTDs) include diseases such as buruli ulcer, guinea-worm disease, leishmaniasis, lymphatic filariasis, onchocerciasis (river blindness), schistosomiasis, soil-transmitted helminthiasis, trachoma, trypanosomiasis and yaws.

It is estimated that onchocerciasis affects two thirds of Ghana; other stated NTD problems in Ghana include guinea-worm disease, leishmaniasis, trypanosomiasis and yaws. It is estimated that two thirds of the population take the anti-parasite medicine Ivermectin and all children receive Albendazole, or Mebendazole.

A related problem is meningococcal meningitis - Ghana is in the Africa 'meningitis belt'). Chloramphenicol is required for treatment but this is not produced in West Africa.

Many of the medicines required to treat NTDs are not produced in West Africa and provision of NTD medicines is reliant on sources such as TGF. The WHO Ghana office states that there is also a need for products such as West Africa viper anti-toxin, laboratory reagents for diagnosis and vaccines to be produced in the sub-region.

4 INTELLECTUAL PROPERTY RIGHTS: TRIPS, COMPULSORY AND VOLUNTARY LICENSING

The 'TRIPS agreement (Agreement on Trade-Related Aspects of Intellectual Property Rights) and 'Doha Declaration' provides provisions for Ghana and other countries in the sub-region to develop their local pharmaceutical production. The issue of TRIPS pertaining to local and sub-region pharmaceutical production in Africa has been well covered by several other reports and publications, so this report does not go into detail on these issues (good summaries of the TRIPS flexibility issues are provided by the following reference: *UNCTAD 2007: Reference Guide to Intellectual Property and Pharmaceutical Production in Developing Countries*.) This section of the report provides an overview of IPR issues concerning African local pharmaceutical production, licensing issues and the existing situation in Ghana.

4.1 Overview of IPR Issues for Ghana and West Africa

Resolving pharmaceutical intellectual property rights (IPR) issues is considered to be a vital measure for the provision of essential drugs to Africa. The issue of IPR and pharmaceutical production in Africa, with particular respect to the implementation of TRIPS flexibilities, is highly complex and controversial due to the interplay of a number of global and local economic and public health factors. Much of the text and legal interpretation in this overview is drawn from the presentation made by *Christoph Spennemann, Legal Expert, Policy Implementation Section/Intellectual Property Division on Investment, Technology and Enterprise Development (DITE), UNCTAD* on 24 October 2007 at the "Regional Workshop on Pharmaceutical Production in West and Central Africa" in Dakar, Senegal.

The TRIPS Agreement requires that all World Trade Organization (WTO) members should adopt certain minimum standards regarding IPR including rules on patents for pharmaceutical products. There is an initial challenge relating to the scope and interpretation of the policy, especially flexibilities embodied in the Agreement that could be used to improve availability and access to essential patented medicines.

There is an important interface between exclusive rights (IPRs) concerning international patented medicines and public health access to essential medicines, particularly for medicines that address PEDs. There is a 2016 window of opportunity for LDCs to not require or enforce international pharmaceutical patents due to the WTO waiver provided by the DOHA agreement.

Under the TRIPS agreement, governments in LDCs and DCs are provided tools ('flexibilities') to promote access by local producers to patented pharmaceutical ingredients and also to the know-how and the technology to produce patented pharmaceuticals. The importance of TRIPS flexibilities for investment in local pharmaceutical production in LDCs / DCs in Africa are that they increase the amount of knowledge in the public domain, limit exclusive rights and promote competition; TRIPS flexibilities enable generic producers not only to access essential materials but also knowledge (e.g. through re-engineering on a legal basis); thus allowing them to enter the market.

The Doha Declaration 'on the TRIPS Agreement and Public Health' appears as an opportunity to resolve the challenge on the provision of patented medicines to DCs and LDCs as it provides a window for DCs and LDCs to take advantage of the 'Flexibilities' for public health considerations.

According to UNCTAD, the future investment in Africa DC/LDC production depends on implementation of TRIPS flexibilities by host countries, for example the Indian

Pharmaceutical Alliance has stated that TRIPS flexibilities be fully implemented in the West Africa sub-region before its members can invest in DC/LDC production sites.

The transition periods for LDCs to implement TRIPS Flexibilities are until 1 July 2013 for all TRIPS obligations and until 1 January 2016 for patents and 'trade secret' protection of pharmaceuticals. In the interim transition period LDC-based producers may use substances that would otherwise be patented and LDC-based traders may import and sell patented ingredients. However, according to the Bangui Agreement (revised 1999) as applied to OAPI countries there is no requirement to define an exact transition period - pharmaceutical product patents are available and local producers need to check patent status of needed substances and seek product licenses.

However, given that the ECOWAS sub-region consists of both DCs and LDCs, then this issue needs addressing in terms of developing and implementing a common IPR approach for the sub-region.

4.2 Licensing Agreements – Voluntary and Compulsory Licensing

The implementation of Voluntary Licensing (VL) agreements for production in African countries of patented medicines has in recent years been brought under the microscope in view of a 'market failure'. Thus the practice of Compulsory Licensing (CL) has been introduced and advocated by the international community (e.g. WHO and UNCTAD). Concerning the WTO, its Secretariat has been very reluctant to openly promote CL (due to pressure from some countries such as the US).

Which or either system of licensing actually is or will contribute to public health in Africa is open to debate.

Licensing involves a local producer paying for the rights to manufacture, distribute and use patented ingredients or final dosage forms. Ideally, a foreign patent holder and a local producer, under fair licensing conditions, should be able to enter into an agreement to take advantage of lower local production costs and new markets as well as delivering essential products to the diseased population that needs them. But this ideal situation has been difficult to achieve for a number of reasons resulting in a lose-lose situation for all parties.

Concerning international guidelines for implementation of licensing agreements, TRIPS provides a framework for control of abusive terms to safeguard licensee's interests and the Bangui Agreement contains rules on unfair competition, but these rules do not address the issue of restrictive licensing. According to UNCTAD, there is a need to develop rules on: excessive pricing of patented ingredients, predatory pricing to avoid competition, refusals by the right holder to license, and the anti-competitive effects of patent pools & cross-licensing. UNCTAD also considers that there is a need for government or civil society involvement in terms of supervising licensing agreements.

In terms of being able to obtain favourable local licensing terms it has been noted that there are 'exceptions to granted patent rights' – a patented ingredient may be used for (i) marketing approval of generic products (as approved by WTO jurisprudence), and (ii) research & development (as used in developed country legislation – the main purpose must be research/promotion of technological progress, and the ultimate commercial consequences should be accepted by developed country jurisprudence (e.g. as is the case in Germany)).

Compulsory Licensing (CL) concerns the authorisation by the government of a third party or a government agency to use an invention without the consent of the right holder. Governments are free to determine the grounds for issuing Compulsory Licences, although

the reason for doing so is often based on public health emergency reasons, and the CL issue normally concerns countries lacking domestic manufacturing capacities.

Compulsory licensing is considered to be a powerful negotiating tool for government to influence international drug prices (e.g. the Brazil and Thailand experience), to involve generic producers in reasonable licensing terms (e.g. the South Africa and Thailand experience). In 2006/2007, the Thailand Government issued 3 Compulsory Licences, in 2007, the Brazilian Government issued 1 Compulsory licence.

In August 2003, the WTO made the decision to facilitate export of drugs produced under CL to other countries (for example under a regional trade agreement framework), waive compensation requirements in importing countries with the intention of facilitating regional cooperation within the framework of LDC-dominated trade agreements so as to attract foreign investment. According to the August 2003 decision, any country can issue a compulsory license for the production of generics that can then be exported to any other country, provided that this country has also issued a compulsory licence for the import. For example, Rwanda will import generic drugs from Canada under this decision soon.

In terms of CL implementation there are several weaknesses in international law. Under the Bangui Agreement: important grounds for CL are not included, i.e. the need to rectify violations of competition law; to remedy patent abuse, and the need to issue a CL either for or on behalf of government.

4.3 Case Studies of Voluntary and Compulsory Licensing in Africa

This section provides a brief overview and discussion of the VL and CL issue based on some recent case studies in Africa.

The Canadian Government has formerly endorsed third party manufacturing by its pharmaceutical industry within the framework of CL through its 'Pledge to Africa Act' and has become the first country to notify the WTO that it has allowed a Canadian company to make generic medicines for export. The box below summarises this recent Canadian government intervention:

Canadian government intervention with Compulsory Licensing

Canada has become the first country to notify the World Trade Organization that it has agreed to allow a Canadian company to make generic medicines for export.

"The WTO received from Canada, on 4 October 2007, the first notification from any government that it has authorized a company to make a generic version of a patented medicine for export under special WTO provisions agreed in 2003," the WTO said in a statement.

The triple combination AIDS therapy drug TriAvir will now be made in Canada by the Canadian company Apotex and exported to Rwanda. Earlier this year, Rwanda informed the WTO that it intended to import some 260,000 boxes of the drug from Canada over the next two years. "Canada's notification completes the circle. Both notifications were required for the medicine to be exported to Rwanda under an important agreement among WTO members reached on 30 August 2003," the WTO said.

Under the terms of the WTO accord, a country can issue a "compulsory license" to a national company allowing it to reproduce patented medicines for export to meet emergency needs such as AIDS, malaria and tuberculosis.

However, the implementation of CL can be a fraught business with political and economic consequences in spite of the TRIPS CL provisions. To the extent that the international

research-based industry cannot provide countries such as Ghana with their essential medicine needs at a fair price directly, there is initially the option of using VL (as opposed to first resorting to the use of CL) to enable the local pharmaceutical manufacturing industry to provide the essential medicine needs of its citizens.

A number of important questions have to be posed concerning the product licensing process. What has CL so far achieved in terms of obtaining better health care for Ghana and the sub-region? Is there real evidence that CL has contributed towards local public health and pharmaceutical industry development? What is the experience with VL in Africa and in ECOWAS sub-region? Are there successful models for introducing VL and effective technology transfer (and which companies have succeeded in doing this) and what are the constraints to introducing VL Agreements?

A recent example of successful technology transfer with respect to ARV production to pharmaceutical manufacturers in Ethiopia and Zimbabwe is provided in the following box and which highlights the potential of a well conceived technology transfer / VL approach for developing local pharmaceutical manufacturing capacity:

Pharmaceutical company [Roche](#) on Tuesday announced that it has signed agreements with Addis Pharmaceutical Factory in Ethiopia and Varichem Pharmaceuticals in Zimbabwe to train the companies on how to develop generic antiretroviral drugs, *AFX News* reports. Under the agreements, which are part of Roche's 2006 Technology Transfer Initiative, the two African companies will be provided with no-cost technical training and guidance to manufacture generic anti retrovirals based on the processes used to develop Roche's second-line antiretroviral saquinavir (*AFX News*, 29/5/2007).

Roche researchers will work onsite at the manufacturing facilities in Ethiopia and Zimbabwe and from the company's headquarters in Switzerland. Through the initiative, the African companies will be able to produce saquinavir for distribution in Ethiopia and Zimbabwe, as well as any country within sub-Saharan Africa. The drug also can be distributed in any country defined as least developed by the United Nations, according to Roche. Roche has Technology Transfer agreements with five African companies. Thirty-two manufacturers in 15 eligible countries -- including Ghana, Kenya, Nigeria and Zimbabwe -- have expressed interest in participating in the initiative. Roche is working with the companies to assess production over the coming weeks (*Roche May 2007 Press Release*)

Further examples of successful VL Agreements include the GSK cooperation with Aspen (South Africa) and Cosmos (Kenya).

It has been argued though that VL agreements made with local private sector producers in Africa have led to the products produced through such agreements being more expensive than international reference prices (partly because the VL terms of reference has been between two companies and may not be disclosed to a third party).

The ultimate success of implementing licensing agreements very much relies on the willingness of all parties concerned (patent holders, third party country governments, health authorities and local generic manufacturers) to enter into faithful agreements that result in fair market prices. Very often the need to implement CL can be seen as being a result of 'market failure' and arguably it closes the door for effective technology transfer. However there is good evidence that the potential threat of implementing CL has resulted in favourable VL agreements being implemented.

4.4 Related IPR Issues – Scope of Patents and Protection of Pharmaceutical Test Data

The *scope of patents* in the future can be limited for a number of potential reasons, e.g.:

- (i) reference can be made to the Swiss draft patent law that has introduced the innovative concept of ‘experimental use exception’ – this covers both scientific and commercial activities, provided research leads to new knowledge about patented products (the patent is limited to existing know-how, but does not obstruct follow-on innovation);
- (ii) exclusions from patentability due to new medical uses of natural substances – either qualify as no invention, but discovery (n.b. there is no TRIPS definition of ‘invention’); or qualify as invention, but not patentable due to methods of medical treatment (Article 27.3 (a), TRIPS);
- (iii) strict patentability requirements to address ‘ever-greening’ – avoidance of patenting of new uses of known substances; and avoidance of patenting of minor changes of existing drugs (trivial patents restricted by 2007 US Supreme Court decision);

The Bangui Agreement states that methods of medical treatment are not patentable, but mentions new use patents. In Ghana, there is no reference to new uses or trivial changes of known products; a patent may be rejected through the strict application of the inventive step requirement (e.g. by requiring that structural similarity indicates obviousness of new product).

Concerning *Protection of Pharmaceutical Test Data* (i.e. data submitted to DRAs for marketing approval purposes) - TRIPS authorises different approaches:

- (i) data exclusivity approach: the DRA may not rely on original data for examination of subsequent submissions (e.g. in the USA and EU);
- (ii) non-exclusive approaches: reliance by the DRA on original data which speeds up market entry of generic competitors.

The Bangui Agreement: prohibits dishonest use of confidential data, however a DRA may rely on originator data for subsequent approvals, as reliance is not considered to be ‘dishonest use’. In Ghana, according to data protection provisions under the Protection Against Unfair Competition Act (2000), its DRA may rely on originator data for subsequent approvals.

4.5 The Situation in Ghana with Respect to Pharmaceutical IPR

Ghana is a developing country (DC) under the WTO classification of countries that must comply with the TRIPS Agreement by 2005, compared to many countries in the sub region that are classified as Least Developed Countries (LDCs).

The problem that Ghana faces with the provision of drugs for the treatment of Priority Endemic Diseases (PEDs) with respect to IPR issues are summarised as follows:

- (i). according to the Ghana National Drug Programme, Ghana as a member state of the World Health Assembly has subscribed to the generic policy and Ghana’s essential drug requirements for the public sector are covered within the essential medicines list of 2004. The major constraint concerns patented ACTs and second line ARVs;

(ii). Ghana's patent regime pertaining to pharmaceuticals is currently considered to be TRIPS 'Plus' compliant, therefore the Ghana Attorney General considers that there is a need to revise the Patent law to make it 'TRIPS normal'. A draft amendment to the Ghana patent law exists that takes this point into consideration (30th August Decision);

(iii). there is a need to incorporate into the Ghana patent Law framework the 'Bolar provisions' concerning permitting generic product development prior to the date of originator patent expiry. Currently there are no exceptions for marketing approvals in Ghana - submission of generic copies can only occur after patent expiry which is an unfavorable situation for generic producers;

(iv). the current CL procedure in Ghana requires a waiting period of 3 years from initial patent granting and 4 years from initial patent application. It is unclear if prior negotiations are required in case of government use;

(v). there is a degree of unclarity at a senior government level concerning the interpretation of and necessity for TRIPS provisions for the implementation of Compulsory Licensing. Related issues raised by senior government staff is the ability (or the desire) of the ECOWAS sub-region as a whole to enact a Compulsory License and the opportunity for technology transfer from the third party manufacturer to local producers. Thus the Ghana MoH is currently in the process of creating Compulsory Licensing guidelines (including terms for compensating the patent holder). The MoH also considers that there is a need to create harmonised Compulsory Licensing guidelines in the sub-region.

In Ghana, Compulsory Licenses are issued by the Ministry of Justice (Attorney General) on the advice of the Minister of Health.

Ghana in 2004 initiated Anti-Retroviral Therapy (ART) for People Living with HIV/AIDS at four sites. There was the need to scale up to ten more sites by the end of 2005. A patent search revealed that four antiretroviral medicines on the national treatment protocol had patents designated in Ghana by the Africa Regional Intellectual Property Organization (ARIPO). However, Ghana's Patent Act 657, 2003 has provision for the exploitation of Patent for Government use and compulsory licensing. In November 2005, Ghana took advantage of the provisions under Government use to enable her to import 4 ARVs - Efavir (Lamivudine), Retrovir (Zidovudine), Combivir (Lamivudine/Zidovudine), Ziagen (Abacavir) from sources outside Ghana. This was mainly due to the fact that the pharmaceutical industry in Ghana at the time had insufficient capacity to locally manufacture the quantity of ARVs required and also the Fund used for the ARV procurement requires that the company providing the ARV medicine must be WHO pre-qualified.

The ARVs listed above were supplied from Indian companies and at the time the products were not patented in India. By this action Ghana made savings on 60% on the four anti-retroviral procured through the issuance of a Compulsory License for Government use.

5 PARALLEL PHARMACEUTICAL TRADE

Parallel Pharmaceutical Trade (PPT) has been proposed as an option to provide cheaper medicines to the local population in Ghana based on the assumption that parallel importation of a patented medicine from a country where it is sold at a lower price will enable more patients in the importing country to gain access to cheaper drugs (whether international exhaustion applies to medicines produced under compulsory licensing, however, is still a lively debate). Paragraph 5(d) of the Doha Declaration explicitly reaffirms members' freedom to determine their own regimes for the exhaustion of intellectual property rights without challenge. Ghana's 2003 Patent Act finally facilitates this by incorporating this provision; it allows parallel importation only under the condition that the product to be imported is already "put on the market in any country by the owner of the patent or with the owner's consent."

The European Commission's (EC) May 2003 Regulation to facilitate differential pricing is considered by some observers to be an option for encouraging PPT including reducing the concerns of the research-based pharmaceutical industry with this practice. The EC regulation in theory provides anti-diversion measures against specific pharmaceutical products and requires manufacturers to reduce their essential medicines export prices to developing countries by '75% off the average ex-factory' price in OECD countries, or at the cost of production plus 15%.

Although in theory PPT may provide savings and be a force for sub-region price harmony, the best evidence shows that the costs outweigh the benefits. How for example, is it possible to enforce EU regulatory guidance internationally? The European Union experience (which has a unified pharmaceutical regulatory system and a developed single market for pharmaceuticals, contrary to the situation in West Africa) is that PPT provides marginal economic benefit at best (even that is debatable) while it certainly increases regulatory administrative costs and the risks to patient safety (substandard products, counterfeit and diverted medicines, repackaging and re-labelling problems, batch recall problems etc). The benefits of PPT largely accrue to intermediary traders who complicate the already complicated pharmaceutical supply chain.

If this is the experience with PPT in the European Union, what are the benefits and repercussions for introducing such a policy in the West Africa sub-region? The following statement is provided recently by a leading European expert on drug safety with respect to pharmaceutical trade in Kenya:

"Kenya by its own reckoning has 30% counterfeits in its drug supply chain which translates into a huge problem with unregulated and unlicensed medicines. Dr Fred Siyoi, Chief Pharmacist of the Kenya Health Ministry, speaking in Nairobi about unlicensed and herbal medicines, implored citizens as follows:

"I would therefore urge members of the public not to be hoodwinked by these unscrupulous people and instead liaise with my board to verify if the medicines have been tested and registered for use in the country,"

Given that Kenya is awash with unlicensed, spurious and counterfeit medicines, is it impolite to suggest that perhaps it might be a better use of the regulatory authority's time to get those particular problems sorted out before importing another in the form of parallel pharmaceutical trade."

In the absence of a harmonised international standard system of pharmaceutical regulation in the West Africa sub-region and an unregulated pharmaceutical distribution system, in the opinion of the author it could result in a public health disaster in the short term to introduce a parallel pharmaceutical trade policy.

6 PHARMACEUTICAL SECTOR POLICY AND MANAGEMENT OVERVIEW

6.1 National Health and Drug Policy

The foundation stones of government policy concerning pharmaceutical management (and medical devices) are the Ghana National Health Policy and its subsidiary National Drug Policy.

The Government of Ghana *National Health Policy* is outlined in the Ministry of Health's annually produced Programme of Work⁵. The objective for 2007 is to *Create Wealth through Health*. The major thrust of health care delivery in 2007 is based on four areas:

- Healthy Lifestyles and Environment;
- Health, Reproduction and Nutrition Services;
- General Health System Strengthening; and
- Governance and Financing.

Concerning the health industry, the Programme of Work states – ‘the policy thrust for 2007 is to create a better understanding of the health industry as a basis for enhancing the capacity and sustainability of the health system and contribute to the national economy’. In terms of health industry policy, the Programme of Work outlines a number of broad activities as follows:

- In collaboration with the Ministry of Trade and Industry, map and analyse the health industry to understand the components, structure, size, barriers and contribution to the national economy;
- Create an understanding of the importance of health and the health industry to the national economy among key stakeholders;
- Collaborate with the Ministry of Trade and Industry to support the development of micro-enterprises for production of health commodities;
- Strengthen collaboration with private sector and NGOs in health delivery.

An important sub component of Ghana National Health Policy is its National Drug Policy (NDP). The Ghana NDP objectives for 2008 are summarised below:

- Collaboration with WHO and other relevant partners on prequalification of locally manufactured medicines;
- Update Standard Treatment Guidelines and Essential Medicines List and harmonise with the National Health Insurance Scheme;
- Continuous orientation of health workers in the national procurement laws and procedures to ensure full implementation of the law within the health sector;
- Computerisation of stock management and establishing a data base link between regional and central medical stores;
- Developing a strategy for debt collection and increased medicines availability;
- Instituting systems for continuous monitoring and assurance of quality, efficacy and safety of medicines including traditional medicines;
- Continuing with the implementation of the administrative guidelines for issuing compulsory licensing, parallel importation, exploitation of TRIPS flexibilities, particularly with regard to certain ARVs, and advocacy for amendment of the Patent law 2003⁶.

⁵ Ministry of Health 2007 Programme of Work

⁶ Ghana Health Sector Programme of Work 2007

The Ghana National Drug Policy is informed by regular WHO Baseline pharmaceutical Studies (that provides a number of indicators on pharmaceutical sector development).

In the opinion of some senior members of the MoH, Ghana is not fully implementing its NDP due to a lack of political will; the Essential Drug List (EDL) is reportedly the only implemented part of the policy. However, the Ghana NDP programme has also produced a very comprehensive set of Standard Treatment Guidelines (last edition 2004).

It has been stated that there is a need for the MoH to encourage local manufacturers to produce drugs on the EDL and to gain greater coordination between public health objectives and health manufacturing policy.

Ghana has had some problems with implementing health policy with respect to anti-malarials. One particular problem that occurred with health-oriented manufacturing policy was for the local production of the anti-malarial (Artesunate + Amodiaquine) in 2005 which resulted in many drug side effects due to formulation problems. The box below summarises the case:

Food and Drugs Board Takes Action On Artesunate Amodiaquine

2005-12-19

The health authorities announced on Friday that single tablets of the new malaria drug, artesunate-amodiaquine, which contain 600 mg of amodiaquine and 200 mg of artesunate formulations, should be withdrawn until additional safety tests are done. The decision was reached at a meeting convened by the Minister of Health, Major (Rtd) Courage Quashigah on Thursday following concerns expressed by the media and individuals about the safety and efficacy of the new drug combination for the management of uncomplicated malaria. The policy change took off in January this year.

A statement signed by Mr Samuel Owusu-Agyei, Deputy Minister of Health, said representatives of local manufacturers, the Food and Drugs Board (FDB), the Pharmaceutical Society of Ghana, Noguchi Memorial Institute for Medical Research, the Pharmacovigilance Centre of the University of Ghana Medical School, among other bodies attended the meeting. The statement said the Ministry had taken these concerns seriously and as part of the implementation process instituted an independent pharmacovigilance system to follow-up on all reported adverse reactions. It said the Ministry would continue to monitor the safety, efficacy and quality of the new drug combination in the implementation of its malaria treatment policy.

"The Ministry of Health wishes to emphasise that the efficacy of the artesunate-amodiaquine drug in the treatment of uncomplicated malaria is not in question and local as well as international efficacy studies confirm this. We wish to indicate that the adverse reactions reported so far appear to be linked to the formulations containing 600mg amodiaquine and 200mg artesunate as single tablets.

The statement said studies from 10 sites spread across the country over the last year provided further confirmation of the efficacy of the combination therapy over chloroquine.

"The Ministry further wishes to advise all prescribes and dispensers not to prescribe and dispense the single tablet formulations containing 600mg amodiaquine and 200mg artesunate and also to adhere strictly to the guidelines provided by the National Malaria Control Programme in the management of uncomplicated malaria. In the meantime, the Food and Drugs Board has initiated the process of withdrawing all the single tablet formulations containing 600mg amodiaquine and 200mg artesunate."

The decision to change the drug in the treatment of malaria started in 2002 when it was noticed that the efficacy of chloroquine had reduced significantly. A series of multi-sectoral meetings was held to discuss the policy change and it was not until 2004 that the final decision on the new anti-malaria policy change was concluded. A number of systems, including safety, quality and efficacy monitoring were put in place to support the implementation process.

"It must be noted that more than 13 African malaria-endemic countries are already using artesunate-amodiaquine combination following their drug policy change," the statement said.

Source:

<http://www.ghanahealthservice.org/articles.php?nd=33&tt=Food%20and%20Drugs%20Board%20Takes%20Action%20On%20Artesunate%20Amodiaquine>

A reviewed anti-malaria medicine policy is being worked on, the final draft exists and requires submitting to the Minister of Health for approval.

The Ghana MoH now desires the need to obtain a clearer picture of what drugs are produced locally and the extent to which local pharmaceutical production addresses public health needs.

6.2 Public Health Sector Human Resource Development Plan

Human resources forms a critical mass in moving technology transfer for local manufacture as well as assuring quality in this sector. The following matrix provides information on the overall human resource capacity for health delivery in Ghana.

Indicator	2006 Performance	2007 Target
<i>Health professional density</i>		
Medical Officers	2057	2238
Pharmacists	1550	1645
General Nurses	7,304	11,459
Midwives	2810	2962
Community Health Nurses	3246	4375
Medical Assistant	500	600
Health care assistants	0	0
Trained Herbal Practitioner	0	15
<i>Output of training institutions</i>		
Medical Officers	250	275
Pharmacists	90	100
General Nurses	1500	1650
Midwives	200	399
Community Health Nurses	1173	1388
Medical Assistant	50	103
Health care assistants	0	0
Trained Herbal Practitioner	15	15
<i>% Communities with trained volunteers in IMCI</i>		
Percentage of facilities with 100% tracer drug availability		
% Districts with appointed Health Information Officer	33%	51%
District level capacity index (to be defined based on standards)	Not Available	Baseline to be established
% Districts with minimum health infrastructure (Access to health services)	Not Available	Establish baseline including definition of minimum health infrastructure

Source: PPME 2007 Programme of Work

The Ghana public health sector has a well considered human resource development plan which has public health financing and delivery logic behind it. However, it does not address the needs for pharmaceutical manufacturing in the context of providing publicly funded training.

6.3 Drug Procurement and Supply Management

Public sector drug procurement is managed by the MoH Procurement Department and the supply of publicly procured drugs and medical devices is administered by the MoH Central Medical Stores based in Tema port. Public sector procurement is conducted according to the traditional and rational procedure of lower level needs assessment (rural areas and communities) -> higher level needs assessment (district level) -> central authorities (procurement assessment and tendering).

Public sector drug procurement for Ghana is carried out via four processes:

(i). International Competitive Bidding (ICB)

ICB is conducted for drugs that address the local Priority Endemic Diseases (PEDs) and which are defined by and financed through TGF. Medicinal products for PEDs in Ghana are largely funded by TGF and procured through ICB.

In order to qualify for ICB a manufacturer needs to first technically pre-qualify its products with the WHO based on meeting international product regulatory standards as well as obtaining product registration with the Ghana Food and Drugs Board (FDB).

A national procurement assessment is performed every third annual quarter which is followed by tender announcements for international and national competitive bidding, followed by a process of public bid opening.

Drug needs assessment under the ICB TGF process is carried out as follows:

- ARVs and drugs for AIDS opportunistic infections: assessment is made by the Ghana office of UNAIDS and WHO;
- Anti-malarials (ACTs): assessment is made by the Ghana national malaria control programme;
- TB drugs: Assessment is made by the Ghana national TB programme and WHO;
- NTD drugs: assessment is made by the Ghana MoH and WHO.

Based on these inputs, a final drug needs assessment is made by the Ghana MoH public procurement department in conjunction with the Central Medical Stores. The USAID introduced 'quantimed system' is used to assess procurement requirements.

(ii). National Competitive Bidding (NCB)

NCB is conducted for essential drugs that are not provided through TGF. The product qualification requirements for NCB are FDB product registration and GMP certification. Approximately 1% of national ARV and anti-malarial drug needs are procured through the NCB process.

(iii). Donations

A large number of vaccines and medical devices (e.g. disposables and condoms) are donated through UNICEF and USAID as well as ITNs through various NGOs. In addition the research-based industry also reportedly donates a large amount of medicines, although the exact types and quantities are not clear.

(iv). 'Shopping'

The MoH Central Medical Stores maintains large supplies for medicines and medical devices that address PEDs (and which are procured through ICB and NCB), however from time to time it faces serious shortages and needs to conduct local 'shopping'. The 'shopping' procurement procedure refers to the necessity for the MoH to fulfill drug procurement orders as a result of often lengthy delays in receiving products requested through the ICB and NCB

procurement processes. As a result, a significant percentage of essential drugs are procured through the 'shopping' procedure.

The public procurement ICB process for essential medicines in Ghana is extremely lengthy. It is only now that drug procurement estimates for November 2005 are being delivered to Ghana through the ICB process. It is the case that the MoH Central Medical Stores has to make frequent supplementary orders through 'shopping'. Although it is estimated that the ICB/NCB process can save 50% over restricted tenders, the length of time to receive the products reportedly undermines the savings made through ICB and NCB procedures. The Ghana MoH states that it has had serious problems dealing with the International Dispensing Association (IDA) which has resulted in supply shortfalls, even reportedly resulting in street demonstrations in Accra.

A particular recent crisis they faced was the ability to supply TB drugs, as the international orders take many months to deliver and there is no local capacity to produce TB drugs locally. The logistic problems that the MoH Central Medical Stores face include the lack of a computerised inventory management system, adequate cold storage facilities and guaranteed electrical supply.

The MoH recognises that there is a need for modernisation and re-engineering of the public procurement, stores management and distribution systems. The MoH states that the poor functioning of Central Medical Stores has led to shortages of essential drugs and supplies and is further compounded by non patronage by health facilities leading to wastages. The indebtedness of district medical stores to the Central Medical Stores remains a challenge.

6.4 ARV Prices

The MoH / Central Medical Stores Procurement manager estimates that international prices for ARVs are falling rapidly over the last year, but the Ghana MoH is constrained in making an accurate international drug price evaluation due to the absence of MoH systems for being able to check international drug prices. However, according to a recent summary report by the WHO/AMDS Global Price Reporting Mechanism (GPRM), prices of ARVs continue to decline for the first-line regimen.

WHO/AMDS Global Price Reporting Mechanism (GPRM) Report 2007 – ARV Prices

Median prices of the most commonly prescribed ARVs in fixed dose combination (stavudine 30 mg + lamivudine 150 mg + nevirapine 200 mg) continued to decline during the period from January to June 2007. They are now available for less than US\$ 100 per patient per year (pppy) with a median price of US\$ 77 in low-income countries and US\$ 99 in middle-income countries.

The same trend is being observed with ARVs for children. However, the costs of oral solutions for infants/young children still remain high. For instance, the median cost of the most widely prescribed regimen as oral solution (zidovudine 10 mg/ml + lamivudine 10 mg/ml + nevirapine 10 mg/ml) for a five kg infant is now US\$ 174 (pppy) in low-income countries and US\$ 235 (pppy) in middle-income countries.

Second-line treatment is still significantly more expensive than the first-line treatment in both low- and middle-income countries and continues to be disproportionately more expensive in the latter. Prices of second-line treatment have been very stable and the limited decrease observed in both low- and middle-income countries in recent months is mostly due to the new price of lopinavir/ritonavir announced by Abbott Laboratories for low-income countries and lower middle-income countries.

One of the many challenges in scaling-up towards universal access is the increasing need for individual countries to include more second-line drugs in their national procurement plans as greater number of patients will be expected to become eligible for second-line treatment

due to the failure of the first-line treatment. National programmes will soon be confronted with dramatic budget increases in order to meet treatment programme requirements, thus theoretically putting these programmes at risk. Potential price reductions for second-line treatment, thanks to increased generic competition, are therefore of paramount importance to ensure sustainability of treatment programmes.

6.5 Pharmaceutical Distribution

(i). Pharmaceutical distribution system overview – Ghana and the sub-region

The private sector pharmaceutical distribution system in Ghana (and elsewhere in the sub-region) can best be described as chaotic. The number of intermediaries involved in pharmaceutical distribution is hard to determine, but is likely to number 1000's. There can be little doubt that this chaotic system impacts adversely on the availability, product security and the final price of pharmaceutical products and undermines the possibility of consumers to obtain medicines as and when they need (i.e. accessibility). Given this chaotic situation, introducing parallel pharmaceutical trade is likely to make matters worse.

Local pharmaceutical manufacturers face serious constraints in the distribution of their products throughout the sub-region as a result of a lack of regulation and the chaotic nature of the pharmaceutical distribution supply chain. Very often it is necessary for major local producers to create their own distribution companies in order to secure the supply of their products at fair prices in their own national markets.

If national private sector distribution in the sub-region is chaotic, then the export / import distribution of products is even worse. For example, reportedly it is very often necessary for manufacturers in Ghana and Nigeria to export products first to France which then are reimported back into Francophone West Africa as there is no rational cross sub-region pharmaceutical distribution system. It is very difficult to further comment on the private sector pharmaceutical distribution system which can only be described as a public health disaster.

However, drugs procured publicly via ICB/NCB in Ghana rely on a public sector system of distribution organised by the MoHs Central Medical Stores. This involves transportation of publicly procured drugs to Ghana district distribution centres (district medical stores) managed by district health authorities from where publicly procured drugs are delivered to public dispensing centres (i.e. health facilities). This system of distribution of publicly funded medicines is vital in view of the failure of private sector pharmaceutical distribution.

(ii). Distribution of products procured via the ICB/ NCB process

- *Anti-Malarials:*

Global initiatives are taking place to ensure access to essential medicines, particularly Artemisinin based combination therapy (ACTs). One of the initiatives being distribution of subsidised ACTs through the private sector (particularly drug shops).

Malaria in Ghana is now largely treated outside of the public health system and through chemist shops due to traditional consumer health seeking behaviour and costs of accessing qualified medical practitioners. ACT anti-malarials were recently removed from the Ghana Prescription only Medicine (PoM) list and declassified to Over the Counter (OTC) for this reason, so as to enable better population access to medicines including the promotion of home-based care.

However, due to a lack of medical supervision, a number of challenges are faced with this initiative: (i). unqualified dispensing staff (i.e. with no medical/pharmaceutical background)

running drug shops, (ii). inappropriate dispensing of medicines, (iii). poor regulatory mechanisms at the grassroot level and (iv). poor storage capacity. The potential consequences of this situation is poor dispensing practice and irrational use of medicines in the community that can ultimately lead to increased drug resistance. An illustration of a potential problem with unsupervised anti-malarial therapy is provided in the case where a product defect may exist. Ghana experienced this problem 2 years ago when a new locally produced combination anti-malarial resulted in many side effects due to over dosage (the dosage form provided a daily dose in a single dose as opposed to dosage being evenly spread over the day). As the product was being provided OTC this hindered detection of adverse events and timely product recall.

However, the problems associated with unsupervised provision of ACTs can be addressed, for example some work has been done in Tanzania related to improving quality of services offered by drug shops (through accreditation, training, community mobilization and improving regulations). The Program in Tanzania is known as the Accredited Drugs Dispensing Outlets (ADDO).

The provision of ITNs forms a large and necessary part of addressing malaria in Ghana and currently these are all imported largely from donors.

- *ARVs, TB and NTD medicines*

Given the need for expert medical supervision, medicines for HIV/AIDS and TB are only provided via the public sector and which is confirmed by the Ghana Standard Treatment Guidelines. Some NTD medicines are produced in country but the rest are imported via ICB/NCB and distributed via the public sector.

6.6 Pharmaceutical Retail

The pharmaceutical retail business in Ghana is fully privatised and is conducted by (i). Pharmacies that employ registered pharmacists and which can dispense PoMs; and (ii). Chemist shops, managed by pharmacy technicians and which dispense OTC products solely. Given the high popularity and 'cash cow' nature of OTC products in Ghana, reportedly even the principle teaching hospital in Accra has commenced selling OTC products. Pharmacies are regulated by the Ghana Pharmacy Council, but it is not clear who regulates Chemist shops.

Many countries in the sub-region have a problem with street peddling of pharmaceuticals. According to the Ghana FDB, Ghana has a 'relatively' safe retail pharmaceutical supply chain and does not have a major problem with street trading of pharmaceuticals, although this does occur to some extent in rural and peri-urban areas.

6.7 Health Insurance, Drug Financing and Pricing

(i). The Ghana National Health Insurance Scheme (NHIS)

Traditionally Ghana has relied on a 'cash and carry' system of health funding. The Ghana NHIS set up in 2005 covers as of September 2007 approximately 50% of the Ghana population. The scheme reimburses based on the benefits package which is managed by district scheme managers.

A challenge for the NHIS has concerned the unstandardised prices of medicines reimbursed. The NHIS Secretariat however has recently set up a system for reviewing the prices and tariffs of products and services. A related challenge the Council faces concerns the technical capacity of scheme managers and IT issues to ensure rapid processing of claims and also

reduce fraud. The NHIS is attempting to introduce a co-payment system and reimbursement list for essential drugs, and hopes to introduce this system in 2008.

Barriers to achieving greater national health insurance coverage include the patient costs involved of signing up to the scheme and the fact that the NHIS does not cover all diseases which is seen as a major disincentive to the local population for signing up to the NHIS scheme. Many drugs that are intended to treat PEDs (e.g. ARVs) are not covered by the NHIS as they are paid for by TGF and hugely subsidised to patients in designated health facilities (Patients pay five Ghana cedis for all services including laboratory investigations and medicines).

(ii). Drug Financing and Pricing

The Ghana MoH Programme of Work 2007 provides a detailed analysis of health sector funding requirements in terms of sources and allocation of funds. The budget line for pharmaceuticals and non drug consumables is presented in the following table:

Ghana Ministry of Health 2007 Budget for Pharmaceuticals and Non drug consumables

ITEM	Need	GoG	H Fund	NHIF	IGF	Earmarked	Total Funding	Gap	Not Filling Gap
Pharmaceuticals & non drug consumables	358,909			40,000	318,909		358,909		187,729
Vaccine (EPI)	150,000		20,000	20,000		74,931	114,931	35,069	
Vaccines (Rabies)	2,500			2,500			2,500	0	
Anti snake Scum	9,800		2,300	7,500			9,800	0	
Contraceptives	45,200		15,000	15,000			30,000	15,200	
ART	104,887		10,000			94,887	104,887	0	
Malaria (ITNs)	30,000		10,174			9,000	19,174	10,826	
Malaria (ACTs)	30,000		10,200	15,000		2,904	28,104	1,896	
TB drugs	10,200	5,174	5,026				10,200	0	
Psychiatric drugs	5,200		5,200				5,200	0	

Notes:

Currency is in million Cedis (n.b. Ghana recently devalued its Cedi by a factor of 1,000)

Need – the estimated amount of funding required to provide the Ghana population with essential drugs from publicly funded sources

GoG – Government of Ghana

H Fund –MoH public funds

NHIF – National Health Insurance Fund (NHIS)

IGF – i.e. The Global Fund to Fight Aids, Tuberculosis and Malaria (TGF)

The MoH considers that the public sector drug budget for Ghana is adequate but it is beyond the scope of this report to analyse the MoH drug financing plan presented above, how it addresses real population public health needs and how the financial figures for estimating population public health needs were derived.

According to a recent pricing survey carried out in Ghana approximately 45% of the population lives on less than one USD per day, and the lowest paid government worker earns one USD, thus the prices of medicines are high, making essential medicines unaffordable for many.⁷ Results of this study showed that there was no relationship between prices paid by patients and procurement prices in the public and mission sectors. In the public sector, retail prices were found to be between 110% - 300% over the public procurement price. In the mission sector patient prices were on the average 12% percent higher than the public sector patient prices (Median MPR of 2.73 as compared to 2.43 for the public sector of the Lowest Priced Generic).

Private sector prices were considerably higher resulting in higher treatment costs for many people who use this sector. The prices of innovator brands were extremely higher than their generic equivalents. For a basic monthly treatment for peptic ulcer⁸ in the private retail pharmacy, for example, the price was as high as requiring 86.6 days' wages for an innovator brand and only 6.4 days for a generic equivalent.

Duties, tariffs and markups significantly contribute to the prices of medicines paid by patients (it is estimated that 30-40% for taxes and tariffs and 50-200% for markups that contribute to a final drug price).

There are major weaknesses in drug pricing controls due to an uncontrolled distribution system and absence of an enforced drug price mark up system for distributors and retailers which clearly has an adverse impact on essential drug access in Ghana.

6.8 Pharmaceutical Regulation

Pharmaceutical regulation in Ghana is the responsibility of the Ghana Food and Drugs Board (FDB) which has recently celebrated its 10 year anniversary.

The FDB is an executive agency of the MoH and its organisational and operational model is based on that of the US FDA. It is overseen by an executive board representing various stakeholders and is operationally autonomous (according to the FDB, rarely does Ministerial involvement become necessary in the carrying out of its activities; reportedly only when it may be necessary to close down a manufacturing facility). The FDB is largely self financing (for services and equipment, although staff are paid according to Ghana civil service scales) through the application of service fees. Currently the FDB has a total staff of approximately 300. Control of legal narcotics and psychotropic substances in Ghana is performed by the FDB. Ghana has a separate recently formed Narcotics Control Board that is responsible for the control of illegal dealings in Narcotics, psychotropic substances and precursor chemicals.

The various FDB departments (Executive Administration, Technical, Laboratory and Support Services) are spread over 4 different sites in Accra (due to the rapid growth of the organization and lack of space in the originally allocated offices) and thus the FDB has a 5 year investment and operational plan which includes construction of a new centralised facility that combines all the various units of the FDB in one location. The FDB new facility is

⁷ Ghana Drug Pricing Survey 2004

⁸ Using ranitidine 150mg I twice a day for 30 days (60 tablets)

currently approximately 40% finished and due to lack of government funding the FDB is requesting external funding support to complete its new facility.

(i). FDB Inspectorate Department (and GMP / GDP compliance)

The FDB Inspectorate consists of the following units: premise inspection post market surveillance and industrial support (the latter was previously known as operational research). In the central Accra office there are 14 staff. The types of inspections carried out consist of:

- pre-licensing inspections (for applicant manufacturers and their warehouses (Inspection of pharmaceutical distributors is carried out separately by the Ghana Pharmacy Council);
- routine annual premise inspections (with an unannounced follow up to see if recommendations have been implemented);
- Post Marketing Surveillance (PMS); and
- Advertisement monitoring and enforcement.

The FDB does not have a system for regulation of pharmaceutical distribution (neither public nor private distribution) in the absence of any national legislation governing this activity. However the Inspectorate states that it is very active in elimination of the growing medicines street trading problem. The FDB states that Ghana, compared to other countries in the sub-region, has a relatively lesser problem of street pharmaceutical trading as a result of locally introduced strong medicines market enforcement.

Concerning licensing and inspection of pharmacies and 'chemical stores' (and ensurance of Good Pharmacy Practice), this is the sole responsibility of the Ghana National Pharmacy Council. But there are sometimes joint task teams organised between the FDB and Pharmacy Council to conduct particular operations. The FDB inspectorate also operates a public complaints service which is functional.

The FDB Inspectorate is making many and growing seizures of unregistered medicinal products which largely seem to originate from China (e.g. particularly copies of Viagra, the contents of which are hard to determine in view of the constraints for testing faced by the FDB Quality Control Laboratory - QCL). At the same time, the FDB Inspectorate has identified many product quality problems due to improper storage conditions and product non compliance with region climatic zone requirements for drug stability. In terms of making batch recalls for drug quality problems, only one voluntary recall was made this year (Viracept manufactured by Roche).

The FDB assessment of GMP standards of local pharmaceutical manufacturing is that standards are gradually improving. The FDB Inspectorate has stated that it is drafting a 'road map' for local manufacturer GMP in order to achieve WHO GMP standards. However, some local manufacturers that state they have introduced international GMP (through investment and training) are concerned that several local pharmaceutical manufacturers are not operating to international GMP standards and are not fully supervised by the FDB to ensure that international GMP is achieved.

The constraints faced by the FDB Inspectorate concern (i) ad hoc training in GMP inspections (e.g. they recently received a 1 week course from FIP, but there has been no follow up), (ii) the inability of district and border inspectorates to perform quality control checks (they are requesting support for wider introduction of the 'minilab system'), (iii) lack of funding for Post Marketing Surveillance (PMS) activities.

(ii). FDB Drug Evaluation and Registration Department

The department operates with 10 staff. The drug registration application (Marketing Authorisation Application – MAA) dossier format is based on the WHO model. Dossier documentation requirements are gradually increasing as the Ghana pharmaceutical regulatory system develops. The eventual plan is to implement the ICH Common Technical

Document (CTD) and eCTD dossier format and requirements, although when is not yet certain. However the department sometimes does receive applications in CTD format (for example they recently received two eCTD drug registration applications from Pfizer). Since 2004 the department has been using the WHO SIAMED database drug registration system (which inter alia greatly assists tracking the drug registration process).

The number of medicinal products registered by the Ghana FDB is approximately 4,000 (including different dosage forms). Following an analysis of the FDB drug register by the author of this report, it can be said that the level and type of drug registrations corresponds with anticipated public health demands.

99.9% of MAA applications to the department do not get approved in the initial application (first submission) process. Thus there is a lot of 'back and forth' between the department and applicants before a drug registration application is finally accepted or rejected. The minimum time frame for granting an MA is 3 months (a similar time frame exists elsewhere in the sub-region), but can take over 1 year with 'problem dossiers', the occurrence of which is very high with respect to all MAA submissions. 'Problem dossiers' result from the following types of problems:

- incomplete or missing data (e.g. no process validation, no or delayed CPP, no pharmacological analysis of raw materials, no bioequivalence studies, stability studies conducted with inappropriate climatic conditions for the region, no Drug Master File (DMF – closed and open parts)⁹ and no batch production records);
- proposed packaging and labelling problems ('requested legal changes', e.g. because of the potential for brand name confusion); and
- MAA drug sample quality problems.

The FDB operates a temporary (provisional) registration system for incomplete drug registration dossiers submitted – a full licence (MA) is only issued after complete documentation is submitted.

Concerning MAAs by pharmaceutical manufacturers from Ghana, typical problems consist of incomplete and inadequate dossier submissions, stability testing problems and lack of provision of batch production records. Because of the problems associated with incomplete dossier submission, very often the department has to rely largely on the FDB QCL product quality testing and GMP inspections to make evaluations and marketing approval of locally produced drugs.

Concerning Pharmacovigilance, the FDB has recently created a National Pharmacovigilance Centre which replaces and updates the previous system jointly managed by the FDB and the Ghana medical school. The introduction of this system was motivated by the drug safety problem in 2005 with the introduction of the Artesunate-Amodiaquine combination product into Ghana's market (see box in section 6.1 above - *Food and Drugs Board Takes Action on Artesunate Amodiaquine*).

The recently introduced Ghana pharmacovigilance system operates on a well thought out and practical system of utilising clinical pharmacists to assist prescribers in reporting of Adverse Drug Reactions (ADRs). The FDB has a Technical advisory committee on safety and monitoring which reviews ADR reports every 3 months and which are passed on to the WHO Uppsala Monitoring Centre for collation in the global database.

⁹ For example, some international research-based manufacturers refuse to submit a full DMF for patented medicines due to lack of confidence with data confidentiality issues in Africa as a whole.

The FDB Drug Evaluation and Registration department operates a system of continuous improvement. For example, the drug evaluation process is now conducted using the formula of 'retreats' whereby the various staff responsible for quality, preclinical and clinical evaluation can combine effectively together in making individual registration application assessments. Furthermore, the department is gradually introducing more stringent requirements for drug registration applications. For example, they have recently introduced new application guidelines concerning stability studies, climatic zone specificities to Ghana and drug solvency. According to the department, their drug registration requirements are more stringent than those employed elsewhere in the sub region.

The FDB Drug Evaluation and Registration Department is also now providing training and guidance to local manufacturers on documentation submission, e.g. Certificate of Analysis (CoA), stability data and production and batch records. In June 2007, the department held its first documentation seminar for local manufacturers. Three local companies have applied for WHO prequalification, and there is a need to have regulatory advisory support to the applicants in the light of the problems local manufacturers are facing in obtaining WHO prequalification. The department recognises there is a need to introduce the same regulatory standards as are required by the WHO prequalification process so as to avoid duplication of drug registration between local DRAs and the WHO system.

Training support to the department has until recently been provided by WHO on an ad hoc basis but this has recently terminated for reasons not clear to the author. Reportedly, in many drug evaluation and registration training events, Ghana has been the only country from the sub-region participating, which indicates a real need to provide an impetus for the provision of sub-region pharmaceutical regulatory training support under a sub-region context.

Company sponsored clinical trials are increasing rapidly in Ghana. The trials conducted concern mainly malaria vaccination, the Extended Programme of Immunisation (EPI) and ARV trials. The department also considers that the increasing number of clinical trials being performed in Ghana is partly a response to the problems of trial patient recruitment in developed countries as a result of some highly publicised clinical trial failures with respect to volunteer safety, e.g. the recent UK TGN1412 trial¹⁰. The governance of clinical trials in Ghana is performed by the Ghana National Ethics Committee in conjunction with the FDB Safety and Monitoring Committee – thus Ghana has an international standard framework for clinical trial governance.

The FDB Drug Evaluation and Registration Department has identified a number of training needs concerning in particular regulation of (i) clinical trials, (ii) biological and biotechnology-derived products, and (iii) local manufacturer WHO regulatory prequalification requirements so as to obtain harmonisation of Ghana regulatory requirements with those of the WHO.

(iii). FDB Import and Export Control Department

The FDB operates offices in the 10 districts of Ghana as well as at Accra Kotoka international airport (4 staff) and at Tema seaport (10 staff), the only legal entry points for imported medicines and medicines manufacturing materials into Ghana. The FDB considered it necessary to open offices at these entry access points as the Ghana customs and excise is not equipped to deal with the public safety control of imported food and medicines. The Ghana Customs and Excise is also reportedly solely interested in meeting 'quota seizure' requirements and has little interest in exercising its duties for public health and safety protection reasons.

For example, a large number of so called 'personal use' medicinal products are imported into Ghana, but the customs service is unable to deal with this problem. The FDB is in the

¹⁰ see <http://en.wikipedia.org/wiki/TGN1412>

process of also opening border town offices (particularly at its East and North borders) so as to tackle the problem of illicit border trade in counterfeit, adulterated and diverted medicines, medical devices and consumer health products.

Ghana is considered to be a principle importation destination for the sub-region for several reasons. The problems associated with the control of drug importation (both manufacturing materials and finished products) into Ghana are reported by the FDB Import and Export Control Department to be quite considerable (high number of counterfeit, adulterated and diverted medicines and consumer health goods) and which is complicated by sub-region political instability (e.g. an ongoing war in Cote D'Ivoire).

The largest problem that the FDB Import and Export Control Department faces is dealing with imported 'unlicensed' medicinal products (by their estimation 5-10 % of medicinal products on the Ghana market are unlicensed). 'Unlicensed', in the terms used by the FDB, covers (i). medicinal products brought into the Ghana market which may have acceptable manufacturing quality and are registered outside of Ghana, (ii). mislabelled (deliberately or otherwise), or (iii). substandard ingredients. These 'unlicensed' / substandard products reportedly largely originate from China and transit through Cote D'Ivoire and Nigeria. The concept of 'unlicensed medicines' is perhaps better stated as 'pharmaceutical crime and medicines counterfeiting'. In addition, the department has to monitor the large transit through Ghana of intermediate manufacturing materials and narcotic and psychotropic precursors.

The FDB has to re-export detained or seized products, but as far as possible the FDB attempts to bring into compliance products that are substandard as a result of either mislabelling or the absence of an FDB packaging tag. The department states that, compared to other countries in the sub region, 'it is difficult to bring medicinal products into Ghana' and as a result of this they are providing import, export and transit control advice to other countries in the sub-region.

The FDB Import and Export Control Department is gradually introducing more sophisticated information systems that allow for better coordination and tracking of activities; e.g. (i) Oracle database and GCNet system (that links the FDB, customs and other relevant government departments and which will be fully operational in October), (ii) electronic import / export licensing system (linking the central office with the FDB offices at the airport and seaport), and (iii) electronic system for market data collection which will be operational in 2008.

The FDB Import and Export Control Department is requesting financial and technical support for implementation for the introduction of the following activities and systems:

- a mobile inspection unit to identify inter alia unauthorised trade routes;
- given the increasing number of seizures of 'unlicensed' medicinal products, the FDB now requires a bonded warehouse for detained products;
- creation of a market Intelligence unit to be jointly operated by the FDB import/export and inspectorate departments (akin to intelligence units operated by DRAs in Europe, e.g. UK MHRA) and a network for sub region market intelligence collaboration; and
- Data gathering and analysis system including customs coding for medicines.

(iv). FDB Quality Control Laboratory

The FDB Quality Control Laboratory (QCL) has been operating since 2002 and consists of physico-chemical, microbiology and medical device departments and currently has 33 staff. Activities are split between food and medicines testing. The QCL is reportedly operated according to Good Laboratory Practice (GLP) standards with respect to QCL standards (that

are also defined under international GMP guidelines.) and is accredited to ISO 17025¹¹ standards and audited via WHO proficiency testing.

The following types of QC tests are carried out by the FDB QCL (using International Pharmacopoeia, US Pharmacopoeia and British Pharmacopoeia monograph references):

- every consignment of imported medicines is tested;
- drug registration applications – a full pharmacopoeial analysis is conducted (approximately 1,000 MAA pre-registration and re-registration samples are tested per year, of which approximately 8% are found to be substandard. Previously the QCL was performing analytical checks on every product MAA, but due to resource constraints it is now focusing now on carrying out analytical checks on so-called ‘problem companies’ and ‘problem products’);
- samples taken in GMP inspections;
- post marketing surveillance (PMS) sampling of medicines. In 2005 antimalarials were sampled and in 2006 a detailed study of all the different ciprofloxacin and co-amoxiclav products on the Ghanaian market was carried out (non conforming products based on dissolution testing failure were 12 out of 33 and 5 out of 15 respectively). Non conforming products were mainly imported. In 2007 no PMS testing was performed due to financing difficulties and the national electricity supply crisis; and
- Medical device testing – condoms, HIV testing kits, and other medical devices are routinely checked by the FDB irrespective of source.

According to the FDB QCL Director, Ghana and Nigeria are the only countries in the region that do full medicines QC testing. In terms of regional medicines QC collaboration, the QCL cooperates to some extent with South Africa, but there is currently no collaboration / exchange of information between the ECOWAS countries.

The major constraints that the FDB QCL is facing consist of (i). a severe shortage of space (currently they are unable to operationalise new equipment as a result of space shortage), (ii). servicing of equipment (given the distances involved of supplier to user, it is nearly impossible to get servicing of equipment and it is often cheaper to completely replace malfunctioning equipment), (iii). financing for new equipment, (iv). inability to conduct full and necessary PMS activities (due to funding shortages and operational constraints), and (v). insufficient staff training (although the staff have received some training from the WHO and by UK MHRA, training is conducted on an ad hoc basis, conducted abroad and there is no possibility to implement a long term continuous training programme).

The new FDB facility under construction will be able to alleviate the physical constraints that the FDB QCL is facing, but it is not sure when the new facility will be completed or how it will obtain the remaining necessary finance. An inventory audit for the new QCL has been conducted by WHO which lists the full equipment needs.

6.9 Civil Society and NGO Pharmaceutical Sector Technical Support Activity in Ghana

The Civil Society NGO sector provides important support for pharmaceutical sector development in Ghana including providing leverage and raising issues with politicians. For example, the Health Access Network (HAN), a key pharmaceutical sector Civil Society NGO, provides advocacy for civil society with respect to essential drugs and provides drug management services to the public sector consisting of support for: (i) pharmacy and hospital

¹¹ ISO 17025 concerns Laboratory Accreditation – it is the criteria for laboratories to demonstrate the technical competence to carry out specific test methods; generate valid calibration data, test results, and operate an effective quality system.

IT systems, (ii) mission facilities, and (iii) a pharmaceutical sector training and information support strategy.

The HAN considers there is a need to have several studies conducted to support evidence-based pharmaceutical sector policy and development (see the report recommendations section) with which the report authors concur. For example, The HAN recently conducted a joint study with the FDB on “small scale local production” which is intended to act as a Training Needs Assessment for the local pharmaceutical production sector. The report is not yet finalised but is intended to feed into the overall GTZ / UNIDO programme for support to the local pharmaceutical industry.

Irrespective of the problems faced by developing local pharmaceutical production, the HAN faces problems of sustainability in view of the need for continual funding of Civil Society advocacy.

7 ASSESSMENT OF PHARMACEUTICAL MANUFACTURING CAPABILITY IN GHANA AND IN THE CONTEXT OF THE WEST AFRICA SUB-REGION

The last 5 years has seen a major upsurge in the development of pharmaceutical manufacturing in Ghana, but the local industry faces several constraints as well as opportunities. At the same time the pharmaceutical market in Ghana and the sub-region is quickly developing in response to pharmaceutical market globalisation and the serious attempts being made by the international donor community to address the priority endemic diseases in the sub-region.

7.1 The Ghana (and Sub-Region) Pharmaceutical Market

In order to provide the context for an assessment of local pharmaceutical production in Ghana, it is first necessary to examine the situation and trends in the local and sub-region pharmaceutical market, as well as the threats posed to its normal functioning.

In the absence of a pharmaceutical market statistical information collection system in West Africa (different stakeholders are collecting different sets of market information, but the type of information collected needs to be developed more and coordinated), it is difficult to gather accurate data on the value, volume, imports and exports in both Ghana and the sub-region, but some general trends can be surmised.

The Ghana pharmaceutical market is made up of approximately 30% locally produced and 70% imported products; the latter originating mainly from India and China. It is estimated that 30% of the sub-region market is supplied by Nigerian manufacturers although Ghana-based manufacturers also export significant quantities to the sub-region. In contrast, Francophone countries are heavily reliant on imported medicines (local production is estimated to be approximately 5% in these countries; e.g. 94% of medicines in Cote D'Ivoire are imported), particularly from France, and reportedly this reliance on imports from France has reduced the motivation to develop a local pharmaceutical industry in the Francophone countries.

The OTC sector in Ghana is considerable and consists of drugs popular with consumers such as tonics and combination analgesics. Why Ghana has a very large OTC sector is due to several reasons, including the traditional population reliance on OTC medicines (due to inaccessibility issues concerning prescription medicines), the very recent introduction of a health insurance system in 2005 that provides prescription drug coverage, local industry focus on OTC production at the expense of essential drug production as well as heavy advertisement of OTC drugs.

However, with the introduction in the past few years of major donor funding for the provision of essential drugs (and the creation of a MoH essential drug list), the local pharmaceutical market is becoming more rational in terms of addressing the priority endemic diseases and population morbidity.

Concerning the supply of medicines for priority endemic diseases to Ghana through TGF financing and the ICB procedure, the supply of:

- (i). ARVs is heavily dependent on suppliers from India, e.g. Cipla, Ranbaxy, Haya, Emcure, Hetero, Aurobindo, and Gokals (the latter a Ghana India-owned local distributor). In addition Ghana receives patented ARVs from Roche, GSK, BMS and Abbott. Only a few companies in the sub-region are producing ARVs;
- (ii). Anti-malarial ACTs are largely supplied from India and China;

- (iii). TB drugs are largely supplied through the IDA; and
- (iv). Drugs for NTDs are principally imported.

Ghana has a local capacity for the production of parenteral fluids (two companies are producing - San Bao Company Limited and Intravenous Infusions Limited), however the supply of vaccines and parenteral medicines to Ghana is provided via imports through MoH ICB and NCB as well as drug donations (e.g. quinine, parenteral antibiotics such as benzyl penicillin and ampicillin).

Ghana, like every other country in the World, also has a problem of ensuring pharmaceutical supply chain security in the face of the growing threat from counterfeit and unregistered medicines. Unregistered products are estimated to account for approximately 5% of the Ghana pharmaceutical market. The extent of counterfeit medicines present on the Ghana pharmaceutical market is hard to estimate as no local market surveillance studies on this issue have been performed.

However many products are imported from China and India (which have a well documented fake drug industry) and also which transit through the Middle East and Nigeria; the latter which notoriously has a very large counterfeit medicine problem (a few years ago the Nigeria market was estimated to consist of over 50% counterfeit medicines, but recently this has been reduced to around 30% as a result of proactive action by the Nigerian National Agency for Food and Drug Administration and Control - NAFDAC).

The Consultant was able to view a large batch of counterfeit medicines imported from China recently seized by the Ghana FDB. The standard of the fakes was of a very poor standard and easily detectable by the authorities. The situation whereby poor fake products are targeted at West Africa implies that counterfeiters consider the West African market to be an easy target in view of relatively weak pharmaceutical regulation in the sub-region.

7.2 Overview of the Ghana Pharmaceutical Manufacturing Industry

Within the sub-region Ghana has a comparatively strong pharmaceutical industry. Ghana has 32 registered pharmaceutical manufacturers (compared to, for example, Nigeria which has approximately 90 pharmaceutical manufacturers) producing oral and topical finished dosage forms¹², of which six are considered to be major producers and 14 medium scale producers. Annex 2 (profiles of the principal pharmaceutical manufacturing companies in Ghana) presents detailed profiles of these six companies, namely Ayrton Drugs, Danadams Ltd, Ernest Chemists Ltd, LaGray Chemical Company, Kinopharma and Phytoriker. One company, LaGray, has the capacity to produce Active Pharmaceutical Ingredients (APIs) and is reportedly so far the only producer of APIs in the West Africa sub-region.

Ghana is now beginning to see investment in local pharmaceutical production from some Indian companies, which has been partly motivated by issues relating to TRIPS and its flexibility provisions.

Ghana's national market is rather small to absorb its pharmaceutical production capacity. A local pharmaceutical manufacturer producing drugs for HIV/AIDS, TB and malaria is therefore compelled to look beyond national borders in order to sell its products. This requires building a sales and distribution network if the private retail sector is targeted, or participating in international tenders where there is much competition¹³. Large scale

¹² Ghana does have the capability to produce parenteral fluids via 2 companies, but so far has limited capacity for the production of parenteral medicines (except topicals).

¹³ DFID health resources Centre 2004 'Process issues for increasing access to medicines : the evidence for domestic production and greater access to medicines

manufacturers exist within Ghana but are producing under capacity for a number of reasons, particularly because of the fact that the local pharmaceutical industry is largely focused on producing OTC non essential products that compete in the heavily supplied Ghana OTC pharmaceutical sector.

Thus, given the limited market size of Ghana, local production and product marketing is increasingly being developed to serve the sub-region pharmaceutical market. For example, compared to the situation elsewhere in the sub-region, the prevalence of HIV/AIDS in Ghana is relatively low at 3%; therefore, to the extent that Ghana wishes to develop a local ARV production capacity, this has to be reliant on also supplying the entire sub-region.

Traditionally, local pharmaceutical manufacturers have focused on the provision of OTC medicines that are considered to be 'cash cows', which is partly due to the fact that they have had little incentive to invest in the production of essential drugs. However this situation is now changing in response to the increasing public health crisis and the donor response (e.g. via TGF) and local manufacturers are beginning to produce medicines that address priority endemic diseases.

In response to the HIV/AIDS pandemic that afflicts the sub-region, a few manufacturers located in the sub-region have entered recently into the business of manufacturing ARVs. Of the 3 companies that have commenced ARV production - Danadams (Ghana), Fidsons (Nigeria) and Pharmaquick (Benin) - only Danadams is reportedly actually still producing ARVs (Fidsons and Pharmaquick have reportedly seized production due to the difficulties in obtaining WHO pre-qualification for ICB). A few local manufacturers are now producing anti-malarial ACTs, but there is almost no local production of TB drugs, drugs that address NTDs and cardiovascular illnesses.

7.3 Local Pharmaceutical Manufacturer Coordination - Pharmaceutical Manufacturers Association of Ghana (PMAG)

(i). Background

The Pharmaceutical Manufacturers Association of Ghana (PMAG) was born from the consultancy of the Centre for Development of Enterprises (CDE) in 1998. The association began with the setting up of a six member committee charged to develop a constitution. PMAGs role is to unite pharmaceutical manufacturers, to become a strong lobbying group as well as providing self auditing of processes to improve on manufacturer quality assurance systems. The constitution was adopted in 1999 by fourteen member companies. PMAG was inaugurated the same year and currently membership is at 34 with 22 active members.

(ii). PMAG Initiatives

PMAG working, with other stakeholders, has successfully lobbied for VAT exemption for imported raw materials to be increased from 34 to the current level of 66 items (out of an approximate total of 200 raw material items used in local pharmaceutical manufacturing). PMAG has also succeeded in lobbying Government for zero rating of pharmaceutical items (i.e. VAT is paid but refunded once documentation processes have been completed).

PMAG has also been at the forefront working with the Malaria Control Programme, during the Malaria Drug Policy Change and its subsequent review, and has been involved with the Medicines Transparency Alliance to ensure prices of medicines have been affordable by the majority of Ghanaians. PMAG has been collaborating with the Kwame Nkrumah University of Science (KNUST) in the training of Pharmaceutical Technologists.

(iii). Constraints

The main constraints for PMAG have concerned its financing, the lack of funding available to employ a full time professional pharmaceutical policy expert and lobbyist and gaining active involvement of its members.

According to PMAG, members lack access to funds to support the expansion of their businesses and capacity building due to high interest rates. Members have difficulty with qualifying for Governmental purchases of ARVs and anti-malarials because of funding clauses attached to ICB. Utility costs, especially energy, have made manufacturing costs uncompetitive and this is affecting company liquidity. PMAG considers that the donor community has made many unfulfilled promises and therefore is reluctant to be involved in donor initiated programmes.

(iv). Cooperation

PMAG is a major contributor to the West African Pharmaceutical Manufacturers Association (WAPMA), which was inaugurated in Accra in October 2005, and PMAG hosts the WAPMA Secretariat.

7.4 Assessment of Local Pharmaceutical Good Manufacturing Practice

Reportedly according to the ECOWAS secretariat, within the sub-region Ghana currently has the best quality locally produced pharmaceutical products due to (i) the stringent criteria, inspection and enforcement procedures of the Ghana FDB, and (ii) the recent efforts made by local manufacturers to meet the Ghana FDB requirements.

However, within the Ghana pharmaceutical manufacturing industry, there is clearly a variation of GMP standards between manufacturers which leads to the perception (which may often be incorrect) that products from Ghana are of inferior quality than those imported from India or China for example.

Judging and enforcing GMP standards in Ghana is a fraught business for the Ghana FDB, given the understandable need to give both space for local industry development to improve GMP (which is dependent on investment, training etc) and the absolute need to meet international GMP standards. However, reportedly the space given to local producers by the Ghana FDB to meet international GMP standards has led to a disincentive for some local manufacturers to improve their GMP as they consider that their current level of GMP is acceptable (this is a problem of moral hazard). Local manufacturers that are seriously attempting to meet international GMP through large investments feel that this is an unfair situation.

According to the GMP assessment of local manufacturers made by the Ghana FDB, local industry can be classified into good, average and poor. With the exception of one company, all are considered to be below international GMP and have problems meeting GMP compliance. Furthermore, it has been stated by some parties that cheap imported manufacturing material sourcing often leads to product quality problems.

However on the plus side, the failure to reach GMP standards by many local manufacturers are considered by the FDB to be minor infringements in addition to the fact that the majority of local manufacturers are making efforts to improve their GMP. Also, increasing local competition as well as the WHO pre-qualification process has both acted as a stimulus for local manufacturers to meet international GMP standards.

7.5 Local Pharmaceutical Industry Barriers and Constraints

In spite of some major investment efforts made in the last few years by the local pharmaceutical industry, it is not able to operate to full production capacity. The reasons for this are several and which are presented below:

(i). Local manufacturer focus on supplying OTC products (ass opposed to prescription essential drugs) in a saturated and intensely competitive OTC market

Local manufacturers tend to focus on producing comparable OTC products which results in high market competition for this market segment.

(ii). WHO Prequalification

Essential drugs are largely funded by international donors, thus one of the major disincentives for local manufacturers to focus on essential drug production is the WHO prequalification requirement for ICB. The prequalification requirement is founded on both product and manufacturing compliance with international standards.

(iii). Local manufacturing costs – the price differential between locally produced and imported generic drugs

Locally produced drugs tend to be more expensive than imported equivalents from India and China (which make up the vast majority of imported drugs). Although local labour costs are comparatively low in Ghana, the country suffers a competitive price disadvantage for local pharmaceutical production for the following reasons:

- VAT on the majority of imported manufacturing materials;
- High local cost of borrowing and inadequate access to competitive investment capital;
- Comparatively high local utility costs (electricity, water, transport);
- Inconsistent supply of utilities (i.e. failures in the supply of water and electricity);
- Unfavourable material (APIs, excipients and packaging materials) and equipment sourcing and supply – prices and reliable / timely delivery (the international supply system and distance of Ghana from main supply sources leads to local manufacturers paying high prices and having to create large stocks of manufacturing materials. To obtain competitive prices, buyers have to purchase considerable quantities of material, holding unnecessarily high levels of stock and tying up capital. This is a contributory factor to the proliferation of cheaper OTC medications such as paracetamol and ibuprofen. The older antibiotics such as ampicillin are also reasonably priced but anti-infectives that have recently come off patent cost several hundred dollars per kilogram and at minimum purchase quantities of 100 kilograms are out of the reach of most manufacturers;
- Unfavourable in-licensing conditions - arguably, the local industry has to rely on unfavourable VL conditions (as opposed to using CL that may provide fairer licensing conditions) in terms of in-licensing of products that address PEDs.

Therefore for a number of reasons, imported products from, for example, India and China are more price competitive.

(iv). Unfair competition in terms of product formulations – climatic zone product stability

New drug entities developed in temperate climates are usually subjected to stability studies that show the degradation pattern of drug product at different temperatures and humidity and are approved for sale based on the data. The extreme condition of 40 C and 75% relative humidity is used for accelerated stability studies and approval is given if data shows no significant degradation in 6 months. This is extreme for those regions but is the common storage condition encountered in a typical pharmacy in Accra, Dakar or Lagos. These expensive imports are approved and sold throughout the continent with few questions asked by African regulatory agencies. The label may say 'store below 30 C' but there is no mention of what happens at 40 C and 75% relative humidity. The fact is that many drug formulations will break down under these conditions to give degradation products that are ingested by the

unsuspecting patient. The dangers of remaining or getting sick from these approved and expensive medicines from the major pharmaceutical companies are minimally the same as that of fake drugs, considering that some of these fake drugs are merely placebos while degraded drug product may contain harmful related impurities.

(v). Difficulties exporting products to other countries in the sub-region

Local manufacturers have major problems exporting their products to other countries in the sub-region due to a complex and irrational supply chain.

(vi). Absence of adequate incentives

The absence of incentives and support for production of essential drugs is a major constraint for local manufacturers.

(vii). Inadequate Human Resource Development / Capacity Building access

Current cost effective opportunities for Human Resource Development / Capacity Building for local manufacturers is limited.

7.6 Incentives for Local Pharmaceutical Production, Access to Credit and Investment Attraction

Given the constraints presented above that the local pharmaceutical industry is facing to supply the essential medicines needs of Ghana, it is important to examine the existing incentives available for local pharmaceutical production and the ability for the local pharmaceutical industry to both access credit and to attract investment.

(i). VAT exemptions on imported manufacturing materials

Zero VAT exemptions currently exist for 66 of a total of approximately 200 different materials used for local pharmaceutical manufacturing. However even where VAT exemptions exist, there is often a lengthy bureaucratic procedure involved in reclaiming VAT payments (including a 1% administrative fee for reclaiming VAT). Several local manufacturers feel that the time and cost of reclaiming VAT entirely negates available VAT exemptions. PMAG is currently lobbying to resolve the VAT exemption issue and the Ministry of Finance is reviewing VAT on materials.

(ii). Drug procurement marginal preference scheme for local producers

A system of 'marginal preference', based on a 15% discount incentive, is given to local manufacturers for participation in both the ICB and NCB public procurement tenders. However for several reasons (including inability of local manufacturers to pre-qualify) this system is not working.

(iii). Ghana industry development incentive schemes

The Ghana Ministry of Trade, Industry, Private Sector Development and the President's Special Initiatives operate an incentive scheme for the development of local industry. Under the President's Special Initiatives scheme, a number of sectors have been targeted by the President of Ghana where Ghana has potential for local industrial development; for example, production of garments, salt, oil palm, kasava and starch as well as areas aimed at developing human capacity for example distance learning.

Criteria for qualification of support from the scheme include existence of a local resource base, ability for local development, local and export market potential and the need for technology transfer. The scheme consists of the following types of incentives: fund security, available market and political support.

Given the importance of the Ghana pharmaceutical industry to produce drugs that address priority endemic diseases, it is not clear why the Ghana pharmaceutical industry has not yet applied for qualification for the President's Special Initiative Scheme.

(iv). Local manufacturer access to finance – borrowing and equity investment

Two local pharmaceutical manufacturing companies are floated on the Ghana stock exchange - Ayrton Drugs (which is profiled in Annex 2 of this report) and Starwin Products. According to a senior director of a major African bank looking to invest in the West Africa sub-region, the extent of capital attracted towards local pharmaceutical manufacturing through the Ghana Stock Exchange is not substantial as the sector is seen to be undermined by the reliance on international imports. In his opinion there are also 'business cultural reasons' why local companies do not like to attract outside private equity.

Bank lending rates are extremely high in Ghana – the cost of borrowing is at least 20%. Some local financial institutions have declared a willingness to provide short term working capital, others would finance the procurement of equipment only, but very few are willing to consider financing a pharmaceutical production venture in its entirety, building the requisite infrastructure or even sharing the risk as local guarantors of foreign loans.

According to LaGray Chemical Company, while the return on investment for pharmaceutical production ventures is high enough to ensure profitability and sustainability, it is not high enough to merit the perceived risk by foreign venture capitalists. What about local financial institutions? Most local financial institutions tend to invest in local banks in order to increase access to capital to entrepreneurs. Surprisingly, many of these 'local' banks are even more risk averse.

The opinion of some major banks operating in Ghana, and which recognise the high cost of obtaining short or long term loans within country, the local pharmaceutical industry should look at a number of alternative funding sources, namely:

- Africa Development Bank (ADB);
- Islam Development Bank (IDB);
- Exim Bank (IBRD);
- BMZ (Germany);
- US Overseas Private Investment Corporation (OPIC); and
- Venture capital funding companies.

The LaGray Chemical Company managed to obtain significant financing from OPIC which had also financed the rejuvenation of the largest pharmaceutical manufacturing concern in West Africa. The reliance on local manufacturers for investment from overseas sources begs the question, is Africa getting the message that health is wealth and that it should be a domestic policy objective to finance innovations aimed at improving the region's health situation? Or will Africa continue to look to others to provide the financing?

It should be noted that Ghana has an Investment Promotion Centre (www.gipc.org.gh), but the effectiveness of this organisation is open to debate, as it appears to be very difficult to obtain investment credits at internationally competitive rates in Ghana. At the same time, major banks that operate in the region (given that Ghana has a relatively good political, economic, investment risk assessment) would like to see investment proposals from the Ghana pharmaceutical manufacturing industry.

(v). International examples of successful local pharmaceutical industry development policy – the case of India

The growth of the Indian pharmaceutical industry is of course nothing short of phenomenal and sub-Saharan Africa as a whole, being a collective developing economy, needs to look at India as an example. The Indian industry currently represents USD 6.5 billion of the USD 550

billion global pharmaceutical markets and is the fourth largest with its share increasing by 10% a year. Up to 70% of the products on the Indian market are manufactured by the 250 – 300 companies in the organised sector. The success of the Indian pharmaceutical sector is due in large part to the policies of the government which continues to give tax related incentives and institute regulatory reforms in an effort to bolster quality and improve the image of the local industry globally, hence promoting exports.

The question then is what are African governments such as Ghana doing to support the financing and establishment of such a vital industry? Drug discovery and development is an extremely costly undertaking. The current approach of berating the major pharmaceutical concerns, asking them to give drugs away in Africa or encouraging the violation of their patents may be politically popular but is poorly conceived, unsustainable and unfair considering the billions of dollars spent by these companies to come up with innovative new drugs. There are basic drugs available to treat most of the diseases in the world and these can be manufactured locally. A win-win situation is to support a private-sector initiated approach in which locally built-up capacity can be leveraged in the acquisition of voluntary licenses and technology to enable patented drugs to be manufactured locally.

The health strategy document for The New Partnership for Africa's Development (Nepad) notes that 'Africa remains far too dependent on importation of essential drugs' and calls for support to be given for local production of essential drugs as well as for members to advocate and leverage support for the development of drugs and vaccines needed in Africa. The paper notes that beside the potential to make drugs more affordable is the benefit of industrial development. However, there are no specific suggestions as to how this can be achieved.

'Give a man a fish, he feeds for a day, teaches him to fish and he feeds for a lifetime'. These sentiments were echoed in 2005 by Professor Dame Julia Higgins (Vice President and Foreign Secretary of the UK Royal Society), who asked the UK government to invest in building a domestic pharmaceutical industry in developing countries, particularly in sub-Saharan Africa. She emphasised the crucial difference between investing in relief aid alone and investing in both aid and long term development. She stressed that 'relief aid keeps developing countries dependent on the developed world to tackle the problems they face today. Long term development allows countries to build their capacities in science and technology so that they can solve the problems of tomorrow themselves' (reference: *Graham A, Lartey P. Health is Wealth. Partnerships for Prevention and Cure. GBC Corporate Africa Ghana Health Conference 2007. 16-17 April 2007*)

7.7 Herbal Medicines: The Opportunity for Development of Local Research & Development and Production

The international interest in the potential for Ghana and the West Africa sub-region in general to exploit its natural wealth in herbal plants for medicinal uses commenced in the mid 1980's - the time when the potential for drug discovery of new medicines derived from herbal substances that address major endemic diseases was realised. For example, UNIDO conducted a study in 1986 of the herbal medicine industry in Africa that looked at conversion of traditional liquid forms into modern dosage forms.

A number of recently identified herbal substances originating from Ghana have reportedly been shown to have anti-bacterial, anti-viral and anti-malarial activity. Concerning anti-malarials, 20 plant substances have been identified so far that have potential to be developed into medicinal products. As a consequence of the research and development that Ghana is conducting on identification of active herbal substances that can potentially be converted to finished medicinal products, the Ghana MoH is in the process of developing guidelines for IPR protection for such substances.

Thus Ghana recognises the role of herbal medicines in meeting the pharmaceutical needs of the population. The Ghana herbal medicine industry is growing with increasing activities in cultivation, extraction, substance identification, preclinical assessment, and monograph development. There is increasing retail of herbal medicines in Ghana, particularly through the growing number of herbal medicine centres.

The health sector for many years has placed a lot of emphasis on the provision of allopathic medicine with little attention to traditional and alternative medicine which is used by about 60% of Ghanaians, especially people living in rural areas. The health services over the years have been supply driven and the MoH now realises that the time has come for the sector to provide services that the people need and accept.

The sector has taken steps to recognise the role of non-allopathic providers by setting up a Traditional Medicines Practice Council to oversee regulation of the sector. The Kwame Nkrumah University of Science and Technology (KNUST) has started a programme to train herbal medicine graduates with the intention of increasing in country capacity for the assessment, regulation and provision of herbal medicines. The first batch of students has completed their internships and currently a second batch is undergoing internships at the Ghana Council for Scientific Research into Plant Medicine (CSRPM) and the FDB.

In addition a Directorate of Herbal and Traditional Medicines has also been set up within the MoH¹⁴ and which has a number of tasks including (i). provision of support to herbal practitioners, (ii). sensitisation of allopathic health providers on the integration of services, (iii). organisation of research and development into herbal medicines, (iv). assessment of herbal medicines, and (v). creation and maintenance of a list of essential herbal medicines.

On the basis of scientific evaluation, clinical evidence and experience of usage the list of essential herbal medicines has been reduced to 200 medicines from an original total of 400. The Ghana authorities have not yet completed this list as they require reports and monographs from other African countries so as to avoid duplication of work.

The CSRPM is engaged in screening and scientific assessment of herbal medicines and has improved its capacity for conducting and evaluating preclinical and clinical trials (which are regulated by the FDB). In this context, it has produced a *'Manual of harmonised procedures for assessing the safety, efficacy and quality of plant medicines in Ghana'* (2005).

Approximately 1,000 active herbal substances have been identified and documented. 500 of these are FDB registered (of which 300 are locally developed and produced and 200 are imported). Of the approximate 1,000 identified active herbal substances, 550 have been thoroughly pharmacologically researched and compiled into the national pharmacopoeia. The Center for Scientific and Industrial Research (CSIR) is examining the rest and compiling the monographs.

One research project of note in the field of herbal medicines in Ghana is that of *'Artemisia Annua* cultivation, production, extraction and purification of artemisinin for the manufacture of Artesunate Based Combination Therapy (ACT) in Ghana'. As a result of the WHO recommendations for a shift in malaria treatment to ACTs, there has been a huge increase in demand for artemisinin-based products globally and a resulting attendant shortage of artemisinin supply, thus the need for Ghana to create a dependable local supply of artemisinin.

The above project is sponsored by WHO and UNICEF and is being conducted jointly by Agribusiness in Sustainable Natural African Plant Products (ASNAPP) and KNUST. It is

¹⁴ PPME Programme of Work of Herbal Medicines

designed to be carried out in three phases over a 5 year period: 2006-2010. It is envisaged that the achievement of this goal will position Ghana as a prime *Artemisia annua* supplier, a producer of artemisinin and a manufacturer of ACTs. This in turn, will contribute significantly to enhanced human health and reduction of deaths from malaria, particularly among children and pregnant women.

7.8 The Potential for Local Production of Medical Devices That Address the Priority Endemic Diseases

Medical devices required for the control of PEDs are practically all imported and mainly rely on donations from USAID etc. The principle medical devices required are Insecticide Treated Nets (ITNs) and condoms. In view of the donor reliance on the supply of these types of products, it has perhaps not been surprising that so far there has been no local incentive to initiate local manufacture. Given the relatively rudimentary nature of the manufacturing technology for these types of products, a scheme needs to be created for the conversion of donor dependency to local manufacturing capacity for these types of effective low technology devices.

8 PHARMACEUTICAL REGULATION AND MANUFACTURING COORDINATION IN THE ECOWAS SUB-REGION

8.1 Coordination and Harmonisation of Pharmaceutical Regulation in the Sub-Region

The sub-region suffers from a lack of sufficient pharmaceutical regulatory coordination and harmonisation to allow it to better meet international standards and which acts as an impediment to local producers. The inability for local producers to obtain WHO pre-qualification illustrates the problem clearly. While each country in the sub-region may be addressing individually their own needs to meet international regulatory standards, there is a lack of a process to deal with the 'the mechanics of sub-region pharmaceutical regulatory integration'.

In order to achieve effective and efficient pharmaceutical production in the sub-region, it is important to have coordinated and harmonised regulatory structures and systems that are developed in a way that ultimately results, in the shortest time possible, in international regulatory standards being implemented. At the same time, the ability of local pharmaceutical manufacturers to achieve international regulatory compliance is limited by the absence of sub-regional specialised medicinal product preclinical and clinical testing/trial facilities and the lack of opportunity to be able to conduct clinical bioequivalence studies locally in the sub-region.

The barriers to achieving sub-regional regulatory coordination and harmonisation include (i) the Anglophone-Francophone divide, (ii) variations within the sub-region in drug registration processes (arguably none meet international standards), and (iii) differences in regulatory structures.

Concerning the latter point, Ghana and Nigeria have a similar drug regulatory structure model based on the US FDA system. Francophone countries have not so far adopted the internationally widely adopted model of a Drug Regulatory Authority (DRA). In the Francophone countries drug registration and inspection tends to be carried out by MoH departments and other aspects of pharmaceutical regulation are carried out by other structures, e.g. drug QC is conducted by public health laboratories. For example, Sierra Leone operates a 'quasi-government model' of regulation. However, The Gambia and Liberia, for example, reportedly may shortly introduce a DRA.

An ECOWAS pharmaceutical sector coordinator exists in the person of Dr. Marianne Ngoulla, at the ECOWAS secretariat in Abuja, who is coordinating a number of initiatives on local production (especially of ARVs) and harmonisation of regulatory systems and procedures. WAHO is reportedly working on sub-regional regulatory harmonisation issues and WAHO is discussing the possibility of creating a sub-regional DRA.

In terms of achieving sub-region regulatory harmonisation, an issue that needs urgently addressing is the creation of an ECOWAS pharmaceutical regulation group (with involvement of regulatory professionals from the various countries of the sub-region) that can participate in the ICH Global Cooperation Group (GCG) Regional Harmonisation Initiatives (RHIs). Other sub-regions of Africa have already done so, e.g. SADC¹⁵. SADC in recent years has made great progress in adopting and implementing international pharmaceutical regulatory procedures and standards as a result of its participation within the ICH GCG framework.

¹⁵ See for example, SADC – ICH 6 presentation (Osaka, Japan November 2005) and SADC Harmonisation Initiatives (ICH GCG Meeting Brussels, 2007)

The driving force for ECOWAS sub-region pharmaceutical regulatory coordination and harmonisation appears to come from Ghana in the shape of one of the key developers of the Ghana FDB, Mr Ben Botwe. The latter is working with the ECOWAS secretariat and WAHO to establish ECOWAS subgroups in the following pharmaceutical regulatory areas (based on the ICH GCG model):

- GMP;
- medicines QC;
- drug evaluation (including drug registration dossier format, e.g. CTD and dossier assessment standards);
- clinical trials;
- traditional herbal medicines; and
- Pharmacovigilance.

Mr Botwe is in the process of identifying experts in the sub-region to make up the proposed various ECOWAS pharmaceutical regulatory subgroups. The philosophy behind this process, notwithstanding the need for sub-region harmonisation and collaboration, is also based on the need to combine sub-regional expertise in the field of pharmaceutical regulation given the limited in country expertise and experience that may exist in the sub-region. There is a clear need to pool regional pharmaceutical regulatory expertise.

In August 2007, Mr Botwe hosted a Francophone plus Mauritania (11 country) meeting and study tour on pharmaceutical regulation (covering legislation, inspection, import and export control, manufacture and registration procedures) and 'sensitisation' to why it is important for sub-region regulatory systems to be harmonised. This activity funded by the EC through the EC/ECOWAS project on public health and pharmaceuticals based in Benin (Cotonou). The EC project concerns the 'macro phase' of regional harmonisation in public health issues. Mr Botwe considers that international funding support is a stimulus for motivating Francophone countries to participate in regional regulatory harmonisation initiatives. At the end of October 2007 there was an ECOWAS and Mauritania DRA meeting in Abidjan to follow up on project developments and discuss the way forward for regulatory harmonisation issues.

Ultimately ECOWAS needs to introduce a sub-region drug registration Mutual Recognition Procedure (MRP) which should be based on the introduction of international drug dossier standards (i.e. CTD format and dossier requirements that also take account of abridged application procedures). But while there exists a large disparity in sub-region drug registration requirements (for both the registration process and the expertise to conduct it) this is not possible. For example, Nigeria has stated that it is reluctant to introduce an ECOWAS MRP procedure given the current situation of large divergence between pharmaceutical regulatory standards and practices in the sub-region (although Ghana and Nigeria have similar drug registration procedures and standards).

As a step towards achieving eventual mutual recognition of drug registrations in the ECOWAS sub-region, it has been proposed that a cross sub-region country working group (review team) be initiated comprising representative country experts in drug evaluation and registration. There is a recognition of the need to create a sub-region harmonised drug registration procedure and dossier format which requires as a first step harmonisation between (i) the Anglophone West Africa countries and (ii) between the Francophone West African countries. The second step is then considered to be harmonisation of the respective Anglophone and Francophone drug registration procedures and drug registration dossiers.

Ultimately there is the possibility of creating an ECOWAS sub-region DRA, based for example on the EU EMEA model. The proposal by local experts of such a model of sub-region pharmaceutical regulatory integration is very worthy and needs serious consideration, but there are a lot of prior steps to go through before this objective can be achieved.

A practical regulatory weakness in the sub-region is the absence of any facility to conduct clinical bioequivalence studies which are a vital part of ensuring the quality, safety and efficacy of any generic medicine compared to the original authorised medicinal product (which can either be an originator product in terms of patented medicines or a national / sub-region accepted reference generic product). Many stakeholders in Ghana consider there is a vital need to create a sub-region clinical bioequivalence centre that can perform the necessary studies for local producers. There is a debate about where such a centre should be located, but the current local expert opinion suggests that this centre could be located in both Ghana and Nigeria (with a split of activities, for example chemical and biological drug entity testing, between the two countries). The creation of such a centre is considered to be a key area for Public Private Partnership Support.

8.2 Coordination of Pharmaceutical Manufacturers Based in the Sub-Region

In addition to national manufacturer associations, pharmaceutical manufacturers in the West Africa sub-region are also represented by a regional association: the West African Pharmaceutical Manufacturers Association (WAPMA) which was established in October 2005.

The WAPMA President is the Director of the company Nimeth (Nigeria) and the Vice President is the Director of the company Ayrton (Ghana) and the Secretariat is based in Accra at the same premises where PMAG is located. WAPMA was set up with support from the Centre for the Development of Enterprise (CDE), an institution of the Africa, Caribbean and Pacific (ACP) Group of States and the European Union, in the framework of the Cotonou Agreement) (see www.cde.int). An association draft constitution has recently been created. Major issues for WAPMA are harmonization of DRA practice and procedures in the sub-region and the introduction of a sub-region drug registration MRP. Other related issues include harmonisation of customs, VAT, tariffs as well as harmonisation of STGs for priority endemic diseases.

9 DISCUSSION AND CONCLUSIONS

The report of the WHO “Sachs Commission on Macroeconomics and Health” (*Macroeconomics and Health: Investing in Health for Economic Development, 2001*), for the first time, quantified the relationship between poverty and disease in macroeconomic terms. The report showed a striking correlation between the economic development of a country and the quality of its healthcare system. The bottom line is, those who seek economic development must invest strategically in healthcare.

Two tensions exist concerning the issue of developing local pharmaceutical production in the context of addressing Priority Endemic Diseases: (i) globalisation and localisation (buying or making) and (ii) public health goals and profits.

A rational long term strategy for dealing with the Priority Endemic Disease (PED) problem in Ghana and the ECOWAS sub-region is to develop local manufacturing of products that address these diseases. This premise is based on several logical grounds:

- there is a serious endemic disease and chronic degenerative disease problem in the sub-region (double burden of disease);
- breaking the cycles of dependency (for example, TGF will not exist for ever) and poverty-sickness;
- enhancing economic self-sufficiency and increased local employment;
- fostering national/sub-region scientific and technological capacity (long term sustainable conditions for local R&D, especially herbal medicines);
- investment in local manufacturing can be a focal point for a knowledge and skill-oriented society and a transition into value added manufacturing;
- there is increasing political and economic stability in Ghana and other countries in the sub-region; and
- local manufacturing diminishes both the reliance on often expensive manufacturing material and unreliable supply sources and the growing threat of counterfeit and diverted drugs that (results from major global pharmaceutical supply chain insecurity problems).

In the short term, self-sufficiency in drug development and manufacturing ensures that such drugs are available and affordable. In the medium term partnerships forged with innovator companies for the local production of drugs for HIV/AIDS. In the long term, pharmaceutical research capabilities will enable the discovery of new drugs and drug combinations for fighting uniquely local diseases, such as malaria, through local initiatives.

In terms of the ability of Africa as a whole to introduce local pharmaceutical production to address PEDs (‘South-South cooperation’) there is the conundrum of South Africa which has strong (i). international standards of pharmaceutical manufacturing (e.g. Aspen), (ii). pharmaceutical regulation (including international standard clinical laboratory services), and (iii). sub-region regulatory collaboration (i.e. SADC ICH GCG). But at the same time South Africa has one of the largest HIV/AIDS problems globally. Thus, in terms of the need to encourage development of local pharmaceutical production, there are broader issues involved that rely on models of society development and ‘Access to Essential Medicines’.

A key question is, what level of local and sub-region manufacturing does the ECOWAS sub-region want to see (with respect to the production of medicines that address PEDs) and what is the development plan for this? West Africa has to break the cycle of dependency, but in this respect it is of some concern that there is a noticeable difference between Anglophone and Francophone West Africa; the former appears to be considerably more developed in terms of its pharmaceutical sector than the latter.

An important area that needs addressing in Ghana and the wider sub-region concerns IPR issues. TRIPS provide important tools/flexibilities to promote access to pharmaceutical substances, technology transfer and local production. TRIPS flexibilities are useless if they are not implemented in domestic legislation. It is important to note that implementation of TRIPS flexibilities potentially attracts investment by foreign generic firms. In terms of licensing strategy, it is important to make effective use of both CL and VL procedures.

The Ghana and wider sub-region pharmaceutical market is far from being rational in terms of imported and locally produced medicines and the pharmaceutical regulatory system across the sub-region is having problems dealing with this, although Ghana in the opinion of the report writer, has a comparatively strong pharmaceutical regulatory system in place. The local and sub-region pharmaceutical market is undermined by counterfeit, adulterated, diverted and unregistered medicines. However, there are considerable difficulties in being able to obtain informative pharmaceutical market data for Ghana and the wider sub-region which undermines health policy and local manufacturing strategy.

In the absence of a sub-region harmonized, coordinated and enforced pharmaceutical regulatory system, against the background of a chaotic pharmaceutical distribution system and the increasing global threat from counterfeit and diverted medicines, it arguably would be irresponsible to introduce a sub-region parallel pharmaceutical trading system at this time. In the short to medium term, Ghana and the wider sub-region need to focus on introducing harmonised and coordinated international pharmaceutical regulatory standards, including regulation of pharmaceutical distributors, to protect public safety and to support development of local pharmaceutical production to international standards (pharmaceutical manufacturing and pharmaceutical regulatory development go hand in hand). Regional harmonisation and cooperation create bigger markets and economies of scale for pharmaceutical production

Despite the fact that the Ghana pharmaceutical industry is largely focused on the production of non-essential medicines (in fact local producers often duplicate their production in terms of types of products produced which adds to OTC market saturation) that do not address local public health issues, it has a comparatively strong pharmaceutical manufacturing base in the sub-region that provides a platform for future pharmaceutical industry development and which deserves investment attention. Ghana also has a strongly developing pharmaceutical regulatory and civil society infrastructure as well as a favourable investment risk assessment. However, the local pharmaceutical industry faces a number of barriers and constraints for its future development.

What is missing are a coordinated (cross-ministry and inter-governmental) policy implementing framework supported by technical assistance, cost-effective investment, effective measures to eliminate the many barriers and constraints that the local industry faces and strong incentives to encourage local producers to invest in the production of essential medicines.

The Ghana pharmaceutical manufacturing industry has the potential to produce drugs that address PEDs, but it faces a number of specific local industry weaknesses and operating environment constraints and inefficiencies.

Ghana has a pharmaceutical manufacturers association (PMAG) that can potentially play a strong role in galvanising action for development of local pharmaceutical production. In the report writer's experience, well developed and motivated local pharmaceutical manufacturer associations are a vital driving force for pharmaceutical sector development (e.g. the case of Bosnia Herzegovina – the single most important intervention in terms of rationalising the pharmaceutical sector in a post conflict and developing country situation, within the framework of EC pharmaceutical sector assistance in 2000-2001, was the creation of a local pharmaceutical manufacturers association which could effectively represent the local

industry as well as acting as a major force for development and implementation of effective MoH policy).

The following table presents an overall summary analysis of the Strengths, Weaknesses, Opportunities and Threats (SWOT) that face the Ghana (and sub-region) pharmaceutical industry with respect to both its capacity for production of drugs that address PEDs and operating environment.

Strengths
An established as well as a developing local pharmaceutical production base exists
The local industry has the capacity to supply the sub-region
Some local pharmaceutical manufacturers are now introducing products into their portfolios that address PEDs
Emerging international GMP standards – there is a demonstrated commitment by the much of the local pharmaceutical industry to achieve international GMP standards
Ghana arguably has one of the strongest pharmaceutical industries in the ECOWAS sub-region (Nigeria is also reportedly strong)
A well-functioning pharmaceutical regulatory system is in place
A public budget for products that address PEDs and which meets local health needs exists
A core cadre of pharmaceutical manufacturing and regulatory expertise exists in country
Ghana is considered to have a high degree of economic and political stability (and so should in theory be able to attract investment)
Weaknesses
Several local pharmaceutical manufacturers are under utilising their production capacity (often under utilised by 50%), which is perhaps not surprising as many companies are producing competing non- essential medicines (the OTC market in Ghana is saturated)
There are limited incentives for PED drug production and thus local industry largely concentrates on producing OTC drugs
Many companies have set up light industry local manufacturing or the repackaging of essential drugs
Local pharmaceutical manufacturing industry is not yet full international GMP standard (there is reportedly some variation in GMP standards between Ghana manufacturers and a ‘moral hazard’ situation for GMP development)
Regulatory documentation of local pharmaceutical manufacturers does not meet local / international regulatory standards
Local pharmaceutical industry is unable to conduct the bioequivalence studies necessary for WHO pre-qualification
High cost of locally manufactured products compared to the cost of imported products (for a number of reasons)
Health product manufacturing and health policy in-coordination (private health industry sector not engaged in health policy)
Arguably non effective local industry lobbying and member support capacity, e.g. non utilisation of the President’s Special Initiative Programme to gain incentives for local production of essential drugs
Where local incentive schemes exist, they are inefficient e.g. the ‘marginal preference’ clause for tenders
There is a large variation in local ex-manufacturing prices for comparative products
Incomplete implementation of TRIPS flexibilities
Weak consumer protection (particularly in a society pharmaceutical supply model that is based on OTC product provision). Although Ghana has a ‘Patient Health Charter’, Ghana also requires a consumer protection law
Opportunities
The local and sub-region pharmaceutical market for the manufacture and supply of drugs that address priority endemic diseases exists
WHO pre-qualification (allows better access of local producers to international markets)
Utilisation of the ‘marginal preference’ scheme applied to tenders
Accessing the President’s Special Initiative Programme

Access to external funding sources and technical assistance (e.g. BMZ, GTZ, UNIDO)
Technology transfer and effective use of CL / VL
Development of a local pharmaceutical R&D potential based on herbal medicines
Creation of local API, excipient and packaging material production locally
PMAG and WAPMA effective lobbying on important local industry issues
South-South Cooperation (in Africa as a whole, not just ECOWAS)
Threats
Inability for local pharmaceutical producers to attain WHO prequalification standards
Inaccessibility and non cost-effectiveness of bioequivalence testing
Non harmonisation of sub-region pharmaceutical regulatory system to international standards
Non sub-region coordination on TRIPs issues and failure to fully implement TRIPs flexibilities
Continuing focus of local pharmaceutical manufacturing on the production of OTC products
Lack of attention to pharmaceutical R&D issues
Imported pharmaceutical products are cheaper (and arguably better quality) than locally produced products
The ex-factory price of Ghana produced products is higher than the ex-factory price of similar products produced elsewhere in the sub-region
Imported raw material expense and supply shortages
VAT on imported manufacturing materials (and continuing difficulties reclaiming VAT)
High cost of obtaining local capital (short and long term loans etc)
Sub-region production of medicines for PED products is conducted in another sub-region country (e.g. Nigeria)
Growing threat of counterfeit and diverted medicines
Continuing chaotic and unregulated pharmaceutical distribution system
Parallel pharmaceutical trade
Inter Ministry in-coordination and weak information dissemination
Unmet human resource development needs
Stakeholder inaction (e.g. no follow up action to 2005 DFID report)

So what has been achieved in recent years and what is being done to address current barriers and constraints? What is Ghana's role in creating a sustainable self reliant pharmaceutical supply situation for itself and the sub-region? Based on good evidence, Ghana appears to have a strong local pharmaceutical production, regulatory capacity and investment environment in the context of the West Africa sub-region as a whole. In several areas and for several reasons Ghana is providing pharmaceutical manufacturing sector leadership for the sub-region.

Ghana and the sub-region require effective coordinated international support (by both donors and the private sector) to assist the transition from dependency to local sustainability. Cost-effective international support requires well managed coordination and implementation of recommendations.

To illustrate the point, in 2005, the UK DFID provided a detailed report entitled 'Improving Access to Medicines: The Case of Local Production and Greater Access to Medicines for Ghana' that provided a number of well considered recommendations. However there appears to have been little impetus for the implementation of the recommendations made by DFID since this time. It is beyond the scope of this report to examine the reasons why DFID recommendations have not been implemented, but several have been incorporated under this report.

BMZ, GTZ, UNIDO and UNCTAD have affirmed their commitment to supporting the development of local pharmaceutical manufacturing in Ghana and the sub-region that addresses PEDs and through their extensive network they can facilitate technology transfer and South-South cooperation.

10 RECOMMENDATIONS

A broad number of recommendations can be made that address the viability of pharmaceutical (health product) manufacturing in Ghana and the environment in which it operates and which are sub-divided into the areas of:

- (1) Pharmaceutical regulation,
- (2) Human Resource Development/Capacity Building,
- (3) IPR issues,
- (4) Technology Transfer,
- (5) Manufacturer and regulator equipment needs,
- (6) Studies to inform policy and action,
- (7) Trade incentives and investment promotion,
- (8) Pharmaceutical R&D (particularly herbal medicines),
- (9) Production of raw materials: APIs, excipients and packaging,
- (10) Medical device production,
- (11) Local industry coordination and lobbying – strengthening of PMAG,
- (12) Drug pricing, and
- (13) Health industry policy ‘road map’ and creating an enabling environment

11 SEVERAL OF THE RECOMMENDATIONS WILL REQUIRE FUNDING SUPPORT, WHILE SOME REQUIRE LOCAL ACTIONS TO IMPLEMENT WHICH MAY ALSO REQUIRE TECHNICAL ASSISTANCE. IN ADDITION TO THE POTENTIAL ASSISTANCE THAT GTZ CAN PROVIDE, IT IS UNDERSTOOD THAT BMZ HAS TRUST FUNDS WITH UNIDO AND UNCTAD FOR THE SUPPORT OF PHARMACEUTICAL PRODUCTION IN DEVELOPING COUNTRIES, AND OTHER GERMAN IMPLEMENTING AGENCIES SUCH AS INWENT ARE PREPARING ACTIVITIES STARTING IN 2008. IT HAS BEEN ADVISED THAT THE GHANA MINISTER OF HEALTH PROVIDE A LETTER TO THE GERMAN AMBASSADOR TO LOBBY FOR DONOR SUPPORT FOR LOCAL PHARMACEUTICAL PRODUCTION.

The recommendations have been refined, and some preliminary commitments, made as a result of the joint *BMZ / GTZ / UNIDO Regional Workshop on Pharmaceutical Production* held in Dakar Senegal on 23-24 October 2007. The box below summarises the preliminary commitments made, the local institutions to be involved and the international agencies that will support the activities (and with some indicative dates):

No	Activity	Local Partners	International agencies	Preliminary Dates
1	National round table on local pharmaceutical production [1]	Ministries, PMAG	UNIDO	Jan-March 2008
2	National conference on IPR and TRIPS flexibilities [2]	Ministries, PMAG	UNIDO	Latest – Summer 2008
3	IPR capacity building training course [3]	Ministries, PMAG	UNCTAD / InWEnt	2008
4	Quality infrastructure development [4]	Industry, regulators	UNIDO / GTZ	2008 - tbd
5	Feasibility study on Sub-region Bioequivalence Testing Centre (in Ghana or Nigeria or joint split of activities) [5]	University/ PMAG / WAPMA / ECOWAS	GTZ SVAIDS / NRW county / German enterprises	2008 - tbd
6	Preparation of project proposal for the extraction and derivitisation of Artemisia and production of ACT APIs [6]	Ghana MoH, LaGray, N.N.	Action Medeor, GTZ	2008 - tbd
7	Provision of a long term expert in industrial pharmacy for KNUST School of Pharmacy [7]	PMAG / KNUST	GTZ/ CIM	2008 - tbd
8	Capacity building for DRAs [8]	FDB	GTZ SVAIDS	2008 - tbd
9	Funding proposal for activities supporting sub-region regulatory coordination and harmonisation [9]	FDB / other ECOWAS DRAs	GTZ	Early 2008
10	Proposal for an R&D centre – galenic essential drugs and pre-clinical/clinical trials [10]	NOGUCHI Memorial Institute for Medical Research	GTZ	2008 - tbd
11	National conference on local pharmaceutical production [11]	President of Ghana Ministries, PMAG	UNIDO / GTZ	2008 – 2 nd half

Notes:

[1] Discussion of this report and define detailed implementation plan to foster local pharmaceutical production in terms of a national health production strategy See 13 (i) below

[2] See 3 (i) below

[3] See 3 (ii) below

[4] Quality Infrastructure development concerns strengthening human resources via consultancies and capacity building - see 2. Human Resource Development below

[5] See 1. 1 below

- [6] See 8 (ii) below
- [7] See 2.1 (i) below
- [8] See 2.2 below
- [9] See 1.3 below
- [10] See 8 (iii) below
- [11] See 13 (i) below

Several of the recommendations made in this report as detailed below were not covered by the *Regional Workshop on Pharmaceutical Production* held in Senegal, but should also be fully considered.

In addition, ECOWAS and the African Union have initiatives in the area of local pharmaceutical production too. So the recommendations presented in this report need to be considered between all the donors and supporting institutions involved with this sector.

It is worth noting that many of the recommendations are similar to those proposed for Nigeria and thus some economies of scale in terms of effectiveness of donor intervention can possibly be achieved through coordination (and in some cases combination) of support to both Ghana and Nigeria. It is also necessary to define which support activities can be conducted directly at the ECOWAS level so as to foster a common sub-regional approach for sector support.

1. Pharmaceutical Regulation

1.1 The pharmaceutical distribution chain – regulation/supervision and distribution effectiveness

The pharmaceutical distribution system in Ghana and the sub-region is chaotic - hundreds of unregistered and/or unsupervised distributors exist which undermines the entire healthcare system. It is a highly complex process to import and export pharmaceuticals between countries in the sub-region which is subverted by the many intermediary traders resulting in increased costs of medicines and compromising of supply chain security. There is an urgent need to provide legislation for and stronger enforced regulation of pharmaceutical distribution at both the national and sub-region level.

There are good grounds for limiting the number of distributors nationally and in the sub-region as a whole in order to rationalize the existing system; for example it can be proposed to provide ECOWAS level licensing for a limited number of sub-region level full line pharmaceutical wholesalers (that can operate across the sub-region borders and which manufacturers can trust).

Given the existing chaotic and largely unregulated system of pharmaceutical distribution in the sub-region and increasing global supply chain security concerns it is not recommended to introduce the practice of parallel pharmaceutical trade in the sub-region at this time.

Recommendation 1: Regulation and supervision of pharmaceutical distribution. – Creation of legislation and adequate enforcement provisions to support a rational pharmaceutical distribution system

Recommendation 2: Creation of a list of authorised ‘whole line’ pharmaceutical distributors / wholesalers that can operate nationally and at the sub-region level (the latter issue requires an ECOWAS consultation and agreement process)

Recommendation 3: Avoid introducing parallel pharmaceutical trade until satisfactory sub-region harmonised regulation and distribution is put in place

1.2 Creation of a Sub-Region Clinical Bioequivalence Centre

The current inability for local pharmaceutical manufacturers to conduct bioequivalence testing (and climatic zone stability testing) of their products is a major constraint for local production (i.e. not just being able to obtain WHO pre-qualification, but also in guaranteeing the quality, safety and efficacy of locally produced products in general). Currently some local manufacturers that wish to achieve WHO pre-qualification are seriously constrained through the absence of such a sub-region centre and are required to submit products for testing in South Africa. The cost of doing so is prohibitive to the local industry.

However, there is a political willingness in the sub-region to establish such a centre. A major issue for discussion has been where it should be located within the sub-region. Following a WAHO (under the Agency of the West Africa Health Community) meeting at the beginning of 2007 (in Abidjan, Nigeria) with participation from WAHO, WAPMA and ECOWAS and regional MoH ministers, the recommendation was made to locate the proposed centre in Accra (probably at the KNUST). In the opinion of the WHO the proposed Centre should be located in either Ghana or Nigeria. A credible sub-region expert opinion is that such a Centre could be split between Ghana and Nigeria (for example, with a split in chemical and biological testing).

Although an initial approach has been made to the ADB for funding of such a Centre, there has been no follow up on this. Thus the various sub-region stakeholders are requesting funding support via BMZ/GTZ/UNIDO.

An Initial investment is required, but the intention is that the centre will be sustainable through the application of service user fees. It is intended that the Centre would be managed by an ECOWAS pharmaceutical secretariat, although the exact details of this need to be clarified. It has been further proposed that the centre could be set up as a PPP – the introduction of a foreign joint venture partner potentially makes the project more credible and sustainable.

According to a local expert, the total cost for creation of this Centre is estimated to be 3 million USD, but so far no Business plan / Feasibility study has been created. Therefore there is a need for donor funding to (i) conduct a feasibility study / create business plan, and (ii) provide financing for the proposed centre.

Recommendation 4: Feasibility study for the creation of a sub-region clinical (and preclinical) bioequivalence centre (a combined feasibility study for both Ghana and Nigeria is ideally required)

1.3 Achieving sub-region pharmaceutical regulatory coordination and harmonisation

There is a need to establish a harmonised pharmaceutical registration regime for locally manufactured drugs. The establishment of a harmonised regime accomplishes several things: it reduces the cost of registration and time to register. Uniform standards of drug quality and safety can be established and enforced and local manufacturers would have the potential to engage in bigger and more attractively sized markets.

There appears to be a political willingness in the sub-region to achieve pharmaceutical regulatory coordination and harmonisation and Ghana is playing a driving role towards achieving this objective. Pharmaceutical regulatory coordination and harmonisation in the sub-region should realise both sector efficiency gains as well assisting achievement of international pharmaceutical regulatory standards. There is an identified need to have technical support, provided by both international and sub-region experts, to achieve sub-region pharmaceutical regulatory harmonisation. International pharmaceutical regulatory

expert support could be conducted by the expert proposed for providing specific Ghana regulatory capacity building support (see recommendation 16 below). The rest of this section identifies specific areas where assistance is requested and which require conversion into a full funding proposal.

Recommendation 5: Creation of a full funding proposal for activities supporting sub-region regulatory harmonisation (to be conducted jointly by FDB, other sub-region DRAs, ECOWAS Secretariat and GTZ)

(i). ECOWAS sub-region membership of ICH Global Cooperation Group¹⁶ and establishment of ECOWAS ICH GCG office, secretariat and working groups

In order to achieve sub-region pharmaceutical regulatory harmonisation, the ECOWAS sub-region needs to become a member of the ICH GCG. The recent SADC ICH GCG presentation in Brussels in May 2007¹⁷ presents a good overview of the tasks that are required to be implemented by ECOWAS within the ICH GCG framework. This requires ECOWAS to establish a sub-region office and technical secretariat to facilitate the pharmaceutical regulatory coordination and harmonisation process. It has been proposed that such an office should be established in Accra, perhaps within the FDB office facilities. There are a number of good arguments as to why Ghana should host the ECOWAS ICH GCG secretariat *inter alia*, the reported regional perception of Ghana having strong infrastructure, regulatory competence, and political and economic stability. Ghana also has experience in acting as an effective interface between Anglophone and Francophone West Africa. Although Nigeria represents the largest economy in the sub-region, reportedly Nigeria itself agrees that Ghana should host such a secretariat.

Thus there is an identified need to have funding support to establish a sub-region ECOWAS ICH GCG office, secretariat and establishment of sub-region working groups (e.g. based on the model provided by SADC) so as to assist in achieving sub-region pharmaceutical regulatory coordination and harmonisation. An outline funding proposal is being prepared by a Ghana sub-region pharmaceutical regulation expert - Mr Ben Botwe (see report section 8.1 above) and which can be submitted to GTZ upon request.

Recommendation 6: Establishment and implementation of ECOWAS ICH GCG group with office and secretariat

(ii). Establishment of reference products for generics and products deemed to have well-established medicinal use

It is necessary for Ghana (and the sub-region) to establish reference medicinal products in terms of meeting international pharmaceutical regulatory requirements.

Recommendation 7: Creation of local and sub-region agreed list of reference medicinal products (and medical devices)

(iii). ECOWAS Common Drug Regulatory Dossier

There is a need to introduce a drug regulatory dossier format and content that meets international regulatory standards. There is only one international standard now which is the Common Technical Document (CTD). Ghana and the sub-region has to introduce this format as soon as possible.

¹⁶ ICH GCG – International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use – Global Cooperation Group

¹⁷ SADC_Presentation_Brussels,_May_07[1].ppt (available on www.ich.org)

Recommendation 8: Introduction of ECOWAS common drug registration dossier format and supporting guidelines

(iv). Implementation of sub-region drug registration Mutual Recognition Procedure and Abridged drug registration procedures

Based on (i), (ii) and (iii) above it should be possible to implement a sub-region drug registration MRP and abridged drug registration procedures. There is a need to identify sub-region experts.

Recommendation 9: Implementation of a sub-region Mutual Recognition Procedure for drug registration

(v). Creation of a 5 year plan for sub-region international standard GMP implementation

Given the varying standards of international GMP implementation in Ghana and the sub-region, there ideally needs to be a 5 year plan for ensuring that all sub-region pharmaceutical manufacturers attain international GMP standards.

Recommendation 10: Creation of a 5 year plan for GMP implementation in Ghana and the sub-region

(vi). Establishment of an ECOWAS level Drug Regulatory Authority

An eventual step in developing effective sub-region pharmaceutical regulation could be the creation of a sub-region ECOWAS DRA. However, this involves first solving (i) sub-region issues with respect to political and economic integration and (ii) sub-region pharmaceutical regulatory harmonisation measures as described above.

Recommendation 11: A detailed examination of feasibility of introducing a sub-region DRA

(vii). Elimination of substandard and counterfeit medicines from the local and sub-region market

The presence of what is likely to be a significant proportion of substandard (including medicines not suitable to local climatic conditions) and counterfeit medicines is a major threat to the local industry that is attempting to reach international standards of manufacturing.

Recommendation 12: Establish a sustained effort to rid the region of fake or adulterated drugs and drugs not suitable for the region climatic conditions, be they imported or locally produced

(viii). Ghana Government lobbying to reduce stringency of WHO prequalification requirements for ICB and FDB authorisation of ICB products

The aim of TGF is to support countries such as those in West Africa concerning their fight against PEDs. Several local producers are able to supply products funded by TGF, however they are not able to qualify for the ICB process for reasons explained elsewhere in this report. The Ghana FDB regulatory standards are comparatively strong for the sub-region and ideally it should be possible to allow the FDB to authorise products for ICB purposes. It also assists the development of the FDB to be able to participate in the prequalification evaluation process. In this respect it would be ideal for WHO to provide the FDB with some technical support.

Recommendation 13: Prequalification of local producers for ICB - Ghana government lobbying to WHO and FDB to conduct prequalification process (with technical support from WHO)

2. Human Resource Development / Capacity Building

2.1 Manufacturer Human Resource Development (Quality infrastructure development /Capacity building) – training in pharmaceutical production, regulation, management/marketing

Human Resource Development is a fundamental necessity for the development of the local pharmaceutical manufacturing industry. Training support to date for the Ghana pharmaceutical manufacturing and regulatory sector has largely been performed on an Ad Hoc basis, out of country and very often instigated by local companies individually (as opposed to having relevant training provided on a pooled basis for several local companies simultaneously). Ad hoc training provided either outside of country or within country at large individual company expense is not a long term cost effective solution. An in-country training programme for the sector (for example to be conducted over a 3 year period) needs to be created (based on pooled training and individual company consultancies) which has adequate and appropriate funding support and that addresses local training needs in a cost-effective manner and which sustains future sector development.

There is an identified need to provide Human Resource Development support in the following areas:

(i). *manufacturing* - e.g. pharmaceuticals and GMP (quality assurance/control, ISO 9000/9001 compliance etc)

Specifically the need was identified to place a long-term expert in industrial pharmacy at Kwame Nkrumah University of Science & Technology, School of Pharmacy. It has been agreed that this expert will be identified by GTZ/CIM and jointly funded with PMAG.

(ii). *regulatory affairs* - e.g. regulatory documentation (WHO / international standard dossier compilation), bioequivalence, stability testing and batch sample testing issues

(iii). *management / marketing* – e.g. product licensing, gaining export markets, achieving more cost effective production and economies of scale maximisation (effective cost control, procurement, contract manufacturing), business plan development

In terms of potential *training methods*: (i) cost effective training is best provided in country and to all relevant parties simultaneously, (ii) there is also a need for company-specific training needs assessment and consultation support – individual company consultancies, and (iii) in order to achieve long term local training capacity and sustainability there is a need to provide 'Training of Trainers' and university pharmacy curricula strengthening and reorientation.

Recommendation 14: A sector human resource development plan with adequate and appropriate funding support is required that addresses local needs in a cost-effective manner

Recommendation 15: Placement of a Long-term Expert in Industrial Pharmacy at Kwame Nkrumah University of Science & Technology, School of Pharmacy (via GTZ/CIM and PMAG).

2.2 Drug Regulatory Authority Human Resource Development (Quality infrastructure development /Capacity building)

There is also a need to provide capacity building support to the national DRA – the Ghana FDB. The FDB has stated that what they need is funding for human resource development, systems development, market surveillance activities – for quality and safety, and further decentralisation of regulatory functions.

Training for FDB staff is currently conducted on an ad hoc basis, abroad and is limited by financial constraints. The FDB has thus requested a more sustainable and longer term approach to providing training support and in a way which can be conducted in country. One option is to place a long term international pharmaceutical regulatory expert within the FDB that can provide directed training support following a training needs assessment (concerning the latter the FDB has indicated that it is ready to develop a comprehensive capacity building proposal with anticipated budget based on the assumption that it will capacity building support). Such an expert can also provide training support in regulatory affairs to local manufacturers (see 2.1 above).

Recommendation 16: DRA capacity building - training needs assessment and placement of a long term international pharmaceutical regulatory expert

In terms of systems development, there is a need for the *creation of a 5 year plan for introduction of international GMP manufacturing standards for local manufacturers* (see section 1.2 (v) above). The Ghana FDB needs to introduce a clear and well communicated 5 year plan to assist the local industry in achieving international GMP standards. Ideally such a plan should be coordinated with other countries in the sub-region so as to attain a common standard of pharmaceutical manufacturing in the sub-region.

Post market surveillance activities - the FDB Inspectorate and QCL are requesting support for the conduct of enhanced Post Marketing Surveillance activities. This includes funding for QC laboratory testing and material needs (e.g. reagents) and the purchase of minilab systems for field product testing in the outlying districts of Ghana. Their request is entirely appropriate given the increasing concerns over global pharmaceutical supply chain security.

Recommendation 17: Funding support for the Ghana FDB to conduct full post market surveillance activities

3. IPR Issues

Major issues that need addressing include *inter alia* the TRIPS 'plus' status of the Ghana IPR law, competition law, intergovernmental licensing, patent holder remuneration, and voluntary versus compulsory licensing.

(i). National conference on IPR and TRIPS flexibilities

It is proposed to hold a national conference on IPR issues, including TRIPS flexibilities, at the latest by the Summer of 2008 and to be supported by UNIDO. The intended participants are the various relevant Ghana ministries, PMAG and individual manufacturers.

Recommendation 18: National conference on IPR and TRIPS flexibilities

(ii). IPR capacity building training course

As a follow up to the national conference described above, it is proposed to conduct an IPR capacity building training course by the end of 2008 organised jointly by UNCTAD and InWent. The intended participants are the various relevant Ghana ministries, PMAG and individual manufacturers

Recommendation 19: IPR capacity building training course

(iii). Guidelines for effective licensing strategy

In an ideal situation, voluntary licensing should be achieved as opposed to compulsory licensing, however this may not always be possible. Guidelines for product in-licensing need to be created, particularly concerning the conditions for implementing compulsory licensing. For example, there is a need to develop rules on restrictive terms (refusals to deal, etc.),

extend grounds for granting of CLs (as outlined in the Bangui Agreement) and to abolish waiting periods

Recommendation 20: Guidelines for effective licensing strategy

(iv). *Ghana patent law revision to 'TRIPS 'normal' and inclusion of 'Bolar provisions' (Bangui agreement), 'experimental use exception' and limiting the scope of future patents*

The Ghana patent law requires revising to TRIPs 'normal', and inclusion *inter alia* of the Bolar provisions, extending the experimental use exception (e.g. with reference to the Swiss draft law on this issue), and limiting the scope of future patents (i.e. exclude product patents for new uses and apply the strict inventive step standard to trivial changes).

Recommendation 21: Revision of Ghana patent law

(v). *Sub-region coordinated conversion of TRIPS / DOHA into a workable legal framework that addresses sub-region public health.*

A sub-region coordinated legal framework (unified patent regime) that effectively interprets TRIPs flexibilities needs to be created and which should take account of the fact that the ECOWAS sub-region is made up of both LDCs and DCs (i.e. the latter includes Ghana and Nigeria).

Recommendation 22: Creation of a sub-region legal framework/ unified patent regime (and guidelines) that effectively interpret TRIPS

4. Technology Transfer

Technology transfer is vital for the future development of the local pharmaceutical industry, particularly in the production of new locally manufactured product forms that address PEDs. Very often technology transfer fails because the concerned parties cannot understand or communicate their objectives satisfactorily. Most often, it is the human factors that undermine the process. However, there are now examples of successful technology transfer initiatives appearing between the international research-based industry and local manufacturers in sub Sahara Africa.

A number of mechanisms can be proposed to better enable the technology transfer process.

Local manufacturers require assistance in how to create business trust, identifying suitable partners and the legal options for ensuring effective technology transfer, e.g. confidentiality agreements, material transfer agreements, Deed of assignment, License agreement, Joint Ventures / Strategic Alliances (Co-marketing agreements), etc.

The World Intellectual Property Organisation has an extensive website with a wealth of information about intellectual property and technology transfer at <http://www.wipo.int/index.html.en>.

The National Institutes of Health has an excellent technology transfer training site which provides introductory on line web based training on aspects of technology transfer. It does focus upon NIH processes, but nevertheless provides a good introduction. The on line training can be accessed at <http://ttraining.od.nih.gov/>

Recommendation 23: Training workshop and follow up technical assistance to implement effective technology transfer for the local pharmaceutical industry

5. Local Manufacturer and Regulator Equipment Needs

5.1 Local manufacturer equipment needs

The equipment needs of local producers, in terms of developing local production are company-specific. This varies from the need to procure individual items (e.g. IR spectrophotometer, HPLC) to the need to invest in equipment for new production lines.

To the extent that the relevant donors wish to provide funding support for local producer equipment needs, then this should be contingent on the equipment being utilised for production of drugs that address PEDs. Individual companies need to submit their individual equipment needs for donor assessment and approved equipment should be procured through an international tender.

Ideally equipment needs should be specified under a specific company project, therefore there is a need for companies to develop and submit appropriate business plans.

Recommendation 24: Creation of a full inventory of local producer and regulator equipment needs created against strict criteria including submission of company specific business plans

5.2 FDB equipment needs

These include completion of the new Ghana FDB facility, equipping the new QCL, bonded warehouse for detained products and mobile inspection units.

- the new FDB facility is approximately 40% complete - the FDB is requesting funding support for completion of the new FDB facility;
- equipping the new QC laboratory;
- given the increasing number of seizures of 'unlicensed' drugs, the FDB now requires a bonded warehouse for detained products; and
- mobile inspection units equipped with 'minilab' systems to conduct in the field product testing and to identify *inter alia* unauthorised trade routes.

The FDB is able to provide a detailed funding needs assessment upon request.

Recommendation 25: Funding support to the Ghana FDB for various equipment needs

6. Studies to Inform Sector Policy and Action

In Ghana and the sub-region regular WHO pharmaceutical sector baseline surveys and drug pricing surveys are conducted. However, these surveys do not capture all the data necessary to make informed manufacturing and related sector policy. There is a need to perform further relevant pharmaceutical sector studies to inform policy with respect to local / sub-region pharmaceutical production. Some studies are one off, while others need to be institutionalised and conducted on a regular basis. Such studies should be coordinated between MoH, FDB, WHO, PMAG, WAPMA, Civil Society etc. The funding for such studies needs to be discussed between local stakeholders and donors.

The types of studies that need to be conducted include, *inter alia*:

(i). Coordinated system for providing local and sub-region pharmaceutical market statistics

The absence of accurate pharmaceutical market statistics both locally and in the sub-region leads to difficulties in creating informed manufacturing policy and market assessment. Thus a coordinated market audit system in Ghana and the sub-region is required to provide better market information that builds upon the WHO annual sector baseline studies. In theory, this

could be a task of the PMAG and WAPMA to organise such a system of pharmaceutical market information.

(ii). A full pharmaceutical regulation assessment of the ECOWAS sub-region.

Given that pharmaceutical regulatory issues are a major barrier for local industry development, a full sub-region pharmaceutical regulation assessment is required. The assessment should examine the current situation and sector development challenges that so far have not been identified so as to provide recommendations for the creation of harmonised pharmaceutical regulation in the sub-region and in a way that encourages stronger local pharmaceutical production.

(iii). Supply chain security: counterfeit, sub standard and unregistered medicine base line study (with sub-region comparisons)

Information on the counterfeit, sub standard and unregistered medicine situation is variable between the countries of the sub-region (information is particularly weak in the conflict affected countries of the sub-region such as Liberia and Sierra Leone).

(iv). Comparison of GMP standards in the sub-region (and policies for developing GMP in the sub-region)

Ideally a full study of the GMP standards of sub-region manufacturers needs to be conducted to act as a baseline for further interventions so as to assist the sub-region to meet international GMP standards.

(v). Evaluation of sub-region manufacturer ex-factory prices in the sub-region

The ex-factory price cost calculus for drugs manufactured in the sub-region requires detailed examination, in view of the high ex-factory prices of sub-region produced drugs in comparison to imports from Asia and China.

(vi). Evaluation of drug registration (Marketing Authorisation) requirements (particularly registration dossiers) used by the various authorities in the sub-region

In order to harmonise pharmaceutical regulatory practice in the sub-region, it is necessary to fully examine the drug registration dossier requirements utilised in the countries of the sub-region.

(vii). Comparison and evaluation of Standard Treatment Guidelines for Priority Endemic Diseases used in the sub-region.

There is a requested need to compare and evaluate Standard Treatment Guidelines for Priority Endemic Diseases in the sub-region so as to inform local / sub-region pharmaceutical manufacturing policy.

(viii). Overall comparison of pharmaceutical sector development in Africa (particularly local pharmaceutical industry development and pharmaceutical regulation – comparison of the sub-regions)

It is of concern that some sub-regions in Africa are developing less quickly than others with respect to developing international standards of pharmaceutical production. For example, East Africa and South Africa sub-regions are more developed than West Africa in terms of pharmaceutical production. Why is this the case? It is necessary to provide some sub-region comparisons to assist West Africa to develop its local pharmaceutical manufacturing industry.

(ix). Provision of case studies on Compulsory Licensing, Voluntary Licensing & Technology Transfer in sub-Sahara Africa

There is a real need to provide case studies on Compulsory Licensing, Voluntary Licensing and Technology Transfer in the Sub-Sahara Africa pharmaceutical sector so as to inform future policy and actions. GTZ has stated that Pharmaciens Sans Frontieres (PSF) is the best organisation to provide such case studies.

Recommendation 26: Implementation of studies to support sector policy and actions

7. Trade Barrier Reduction, Incentives and Investment Promotion.

A certain number of trade barriers exist that lead to higher than necessary local production costs which require elimination or minimisation so as to make locally produced drugs more competitive with imported drugs. At the same time, there is scope to provide greater and more coordinated incentives for investment in the manufacturing of drugs that address PEDs and in a way that the local pharmaceutical industry can easily comprehend and take action on. Any incentives that are created have to be clearly linked with the production of essential drugs, particularly those that address PEDs.

(i). Elimination of VAT, duties and levies on all raw materials (APIs, excipients, packaging) and equipment used for manufacturing of drugs that address PEDs

There is a need to extend VAT exemption to all materials used in manufacturing (currently only a third of materials are covered) of drugs that address PEDs (and essential drugs in general). At the same time there is a need to rationalise and increase the efficiency of the VAT reclaims procedure.

Recommendation 27: Elimination of VAT, duties and levies on all raw materials and equipment needed for pharmaceutical production and rationalisation of VAT reclaim procedure

(ii). More effective use of the 'marginal preference scheme' for ICB and NCB

There is scope for more effective functioning of the marginal preference scheme that offers a 15% price offer advantage for local producers that wish to supply products through ICB and NCB procedures. For several reasons, local pharmaceutical manufacturers are currently not able to take advantage of the marginal preference scheme applicable to the ICB process (due to *inter alia* WHO pre-qualification problems and government inefficiencies). In the case that local manufacturers are having a problem with utilising 'marginal preference', then this surely has to be a major task of the PMAG to resolve the issues obstructing its correct implementation.

Recommendation 28: More effective use of the marginal preference scheme

(iii). Implementation of effective pooled procurement of raw materials

Local pharmaceutical manufacturers face both high imported raw materials costs and lengthy delivery times, in the absence of any significant local production of raw materials. Market shortages of certain key APIs can also occur in view of high global demand (e.g. artesunate). It is recommended that there should be implementation of a centralised pooled procurement system, based on international tender procedures, that covers all local pharmaceutical manufacturer raw material needs so as to secure better cost and supply terms.

Centralised pooled procurement of raw materials could be organised via PMAG, and would require them employing probably a full time procurement manager who would have a number of tasks, including for example, organising supply tenders, making contractual supply arrangements, monitoring international material prices, handling price and supply negotiations etc.

Recommendation 29: Pooled procurement of raw materials

(iv). The President of Ghana's Special Initiatives Scheme (including provision of tax incentives)

The President's Special Initiatives Scheme operates to support local industry regarded as having development potential and already a number of sectors are covered (e.g. textiles and some food products). However, perhaps surprisingly, so far the scheme does not cover the sector of manufacturing of drugs that address PEDs.

There are some historically successful models for providing an enabling environment in countries where the pharmaceutical industry is considered to be a strategic sector for development. For example Ireland in the 1980s which was able to attract a lot of investment in developing its pharmaceutical industry through a number of government targeted incentives (e.g. concessional loans, tax holidays, etc) as well as the more recent case of India (highlighted above in the report). If the Government of Ghana is able to provide a similar enabling environment, then this would be of enormous benefit for the local pharmaceutical industry to become competitive and provide the drugs that the population needs.

In view of the importance of addressing the sickness-poverty cycle, there would appear to be a good case for inclusion of local pharmaceutical manufacturing for drugs that address PEDs under the President's Special Initiatives Scheme. It is proposed that PMAG, with technical assistance if required, produce an outline plan to be submitted to the Scheme.

Certainly there is a need to provide tax incentives to pharmaceutical manufacturers who: (i) build facilities to international GMP standards, (ii) invest in primary drug discovery and process development efforts.

Recommendation 30: Inclusion of pharmaceutical manufacturing of drugs that address PEDs under the President's Special Initiatives Scheme and provision of tax incentives

(v). Access to cost competitive investment capital

Local bank short and long term lending interest rates are prohibitive making it difficult for local manufacturers to obtain bank financing to provide both short term working capital and long term investment needs. For several reasons, one new local manufacturer in Ghana has been able to attract significant competitively priced investment funding via the US Overseas Private Investment Corporation (OPIC) bank (see LaGray Chemical Company Ltd company profile). Another local company (see Danadams Ltd company profile) has recently commissioned a feasibility study by an international management consulting company to obtain investment in ARV production.

There also exists the option of attracting private equity funding through the Ghana Stock Exchange and receiving assistance through the Ghana Investment Promotion Council (GIPC). But neither of these options for various reasons appears to work in practice.

There needs to be a brokerage facility for providing local pharmaceutical manufacturers with access to cost competitive investment capital (perhaps even interest free and other types of concessional loans). Given that there is a potential capacity in Ghana for local industry to address PEDs, the Central bank and other state financial institutions should accord priority to loan facilities for pharmaceutical production and at lower than prevailing interest rates. Favourable banking terms should also rely on local manufacturers providing the necessary investment plans / feasibility studies.

Recommendation 31: Establishment of brokerage and priority loan facilities to enable access to cost competitive investment capital for local producers that are intending to invest in production of drugs that address PEDs

(vi). Other trade barriers that need eliminating

There is a need to abolish export tariffs for locally-manufactured drugs exported elsewhere and to enact policies for protecting the local drug manufacturing sector from unfair foreign competition, such as product dumping.

Recommendation 32: Abolish export tariffs and address unfair foreign competition practices, e.g. dumping

8. Pharmaceutical Research & Development (particularly herbal medicines)

Ghana is not passive in its desire to eventually be able to contribute towards global pharmaceutical R&D. Activities have already commenced in the field of identifying potential herbal substances.

(i). Establishment of a national pharmaceutical R&D programme - particularly focusing on herbal substances

Reportedly, Ghana has a wealth of active plant substances that can potentially be converted into effective and safe APIs for the manufacture of drugs that address PEDs. The MoH and academic institutions have a number of ongoing initiatives in this area that require coordinating into an effective overall R&D programme with participation from local pharmaceutical manufacturers.

Areas where assistance for pharmaceutical R&D is required include:

- identification of reports and monographs on herbal medicines from other African countries
- development of cross-Africa R&D collaborations
- technology transfer for conversion of herbal substances into APIs (e.g. artemisinin);
- development of new formulations – innovations in the area of formulation development are needed such as formulation of heat resistant drugs;
- preclinical and clinical development (e.g. via local university / company – international CRO joint venture)

Recommendation 33: Creation of a national pharmaceutical R&D programme (particularly based on herbal substances)

(ii). Assistance for a specific identified R&D project – Artemisia conversion to APIs

Ghana has already commenced cultivation of artemisia with the eventual intention of producing Artemisinin APIs. Support is requested for the extraction and derivitisation of Artemisia and production of APIs. The Ghana API manufacturer (LaGray Chemical Company – the first API producer in West Africa) has the manufacturing capacity to eventually produce ACT APIs, but requires some technical assistance. Thus it is proposed that a specific project proposal for this activity be prepared, perhaps based on a PPP joint venture.

Recommendation 34: Preparation of a project proposal for the extraction and derivitisation of Artemisia and production of ACT APIs (local partners: Ghana MoH, LaGray Chemical Company, N.N.; international partners: Action Medeor, GTZ)

(iii). Pharmaceutical Preclinical and Clinical Development – public sector technical and management capacity building based on public-private partnerships

Based on the strong assumption that there is a need to strengthen pharmaceutical R&D capacity in the sub-region, there is a real need to develop a sector pharmaceutical (pre-clinical and clinical) R&D capability in terms of both technical and management capacity. The public-private sector partnership approach, as advocated and supported by GTZ, is an ideal mechanism for achieving this objective.

The Ghana NOGUCHI Memorial Institute for Medical Research is an ideal candidate for consideration in terms of investing in sub-region public sector R&D. The institute would like to establish a galenic essential drug R&D Centre and develop the capacity to conduct pre-clinical and clinical trials, separate of industry.

Recommendation 35: Technical and management assistance for supporting the Ghana NOGUCHI Memorial Institute for Medical Research to become a sub-region public pharmaceutical R&D centre

9. The Potential for Local and Sub-region API, Excipient and Packaging Production

The local reliance on often monopolistic and distant inconsistent supply of APIs, excipients and packaging materials is a major constraint for local manufacturers in terms of prices, delivery times as well as potential raw material quality problems – the often poor quality of raw materials produced in Asia and China is of major concern).

The reliance of local manufacturers on imported materials is a major contributory factor to the high prices of locally produced medicinal products. Very often the quality of imported manufacturing materials cannot be checked which is a major point of concern.

In the short term these constraints can be better addressed through pooled procurement (see recommendation 29 above), however in the medium to long term the local and sub-region pharmaceutical industry should consider the option of entering into production of raw materials.

The potential for local and sub-region production of raw materials for pharmaceutical production requires a detailed feasibility study in view of the likely heavy investment required. It is necessary to examine a number of factors in detail, for example the future local / sub-region pharmaceutical manufacturing demand for raw materials, future guarantees of supply, a detailed cost /benefit calculation, sub-region manufacturing coordination, identification of companies that can backward integrate into raw material production or identification of new business opportunities for new players to enter the local / sub-region market etc.

Recommendation 36: Feasibility study for local / sub-region raw material production (APIs, excipients, packaging) and conversion of feasibility study into actual sub-region production

10. Medical Device Production

Ghana is reliant on imports from public procurement and donations for medical devices that address the PEDs; for example Insecticide Treated Nets (ITNs) against malaria, condoms, diagnostic devices, diagnostic reagents and antitoxins (for example). The local regulatory capacity exists to determine the quality of medical devices, but the local manufacturing capacity does not.

A local manufacturing strategy and investment plan have to be put in place to provide the necessary medical devices on a long term basis, as the country cannot rely on receiving donations of medical devices that are considered to be relatively easy to manufacture locally and which are also expensive to import from outside the sub-region.

Recommendation 37: Feasibility study for local production of medical devices that address PEDs and conversion of feasibility study into actual sub-region production

11. Local Industry Coordination and Lobbying – Strengthening of PMAG

Ultimately, the effectiveness of donor actions for the sector relies largely on the local industry achieving greater coordination between its members and effective lobbying. Donors cannot support individual companies without a context for sector development. The local industry association – PMAG – is a vital platform for future local industry development.

Thus it is incumbent on the local manufacturing industry to organise itself to create its sector strategy, lobby for sector objectives (i.e. replacement of imports via local production) and to recommend the plans for doing so. In this way, donor funding can be allocated more effectively.

In this respect, it is a great step forward that the Ghana pharmaceutical manufacturing industry has organised its representative association PMAG in 1998, as well as the recent formation of the West Africa Pharmaceutical Manufacturers Association (WAPMA) in 2005. PMAG now has to start working to support its members and to interact with WAPMA so as to support a sub-region strategy for pharmaceutical production (including the manufacture of raw materials).

Recommendation 38: Creation of PMAG (and WAPMA) pharmaceutical manufacturing strategy and plan for implementation

However, PMAGs ability to be able to effectively work on behalf of its members has so far been limited by the absence of a professional staff pharmaceutical policy expert/lobbyist due to financial constraints. Thus PMAG (and WAPMA) is requesting funding support in order to hire a professional staff member.

Recommendation 39: Funding support for full time PMAG (and WAPMA) professional pharmaceutical policy expert / lobbyist

12. Pharmaceutical Pricing

Drug pricing key recommendations include: (i) the need to develop transparent and enforced national reimbursement and co-payment system and supporting guidelines for medicines provided through the NHIS, (ii) define and enforce compliance with maximum mark-ups for wholesale and retail of medicines (notwithstanding the fact that import duties, taxes, port charges and facility markups also contribute greatly to the final price of medicines and thus are issues which also need addressing), (iii) the drug mark up system for wholesalers and retailers needs revising (i.e. an inverse mark up system with percentage margins in accordance with international standards should be introduced) and enforcing.

Recommendation 40: Introduction of transparent pharmaceutical price guidelines that are enforced and revise the mark up system in accordance with international standards

Recommendation 41: Introduce a pharmaceutical pricing inspection system that is enforced

13. Health Industry Policy ('road map') and Creating an Enabling Environment

The Ghana government, for understandable reasons in terms of its needs to drive the economy to meet international standards, needs to apply a 'top down approach' of Ministry interventions to support local economic development. It is necessary that the Government of Ghana create a long term plan for health industry development. There is a recognition by the Ghana MoH, that the health industry section of its Programme of Work (2007) requires updating in future editions and needs attention to how health industry policy can be implemented.

(i). Health industry policy – creation of a 5 year health industry development plan (targets and objectives)

This report, as well as the 2005 DFID report (*‘Improving Access to Medicines: The case of local production and greater access to medicines for Ghana’*), provide templates and concrete suggestions for introduction of a health industry policy for Ghana. The issues now come down to ‘what, when, where, who, how?’ International donors have an important role to play in the development and implementation of such a plan; but it is necessary for local stakeholders and donors to sit down together to determine the correct approach based on informed reports. It is proposed to hold in 2008 an initial round table to prepare an outline health industry policy followed later in the year by a national conference where the policy is formally presented. In the initial policy formulation stage it would be helpful for donor support to provide sharing of experience from pharmaceutical industry development in East Africa (as donor activities in this field have so far been more developed than in West Africa).

(ii). Creating an ‘enabling environment’ for the local health industry

A fundamental issue that needs addressing in order to support a health industry policy is that of creating an ‘enabling environment’. There are many ‘locally created’ barriers that the local health industry faces in its attempt to achieve international competitiveness which need to be addressed. In particular, establishing effective inter-ministry coordination on local health industry development is vital.

<i>Recommendation 42: Creation of a health industry development plan (road map)</i>

ANNEXES

ANNEX 1: LIST OF GHANA INTERVIEWEES

1. Local pharmaceutical manufacturers

- (i). Ayrton Drugs: Samuel Adjavon, CEO; Belinda Opoku, Marketing and Sales Manager
- (ii). Danadams Pharmaceuticals Ltd: Dr Yaw Gyamfi, CEO
- (iii). Ernest Chemists Ltd: Ernest Sampong, CEO; Ossaka Abdel-Kasim, General manager manufacturing
- (iv). Kinapharma: Mr Louis Nortey, International sales Manager
- (v). LaGray Chemical Company: Dr Paul Lartey, CEO; Dr Alexandra Graham, Chief operating officer
- (vi). Phytoriker: Kaustubh Dharkar, CEO; Caroline Asante; Nunno Humphery; Faustina Sackey; Eric Addae –Sekyi

2. Pharmaceutical Manufacturers Association of Ghana (PMAG): Mrs Gerda Kankam-Sulemana; Dr Mike Addo

3. West African Pharmaceutical Manufacturers Association (WAPMA) representative

4. Food and Drugs Board of Ghana (FDB)

- (i). Chief executive: Kyeremateng Agyarko
- (ii). Inspectorate: Samuel Kwakye, Senior regulatory officer and other representatives
- (iii). Drug evaluation and registration department: Mimi Darko, Head
- (iv). Import and export control department representatives
- (v). Quality control laboratory: Cheetham Mingle and other representatives
- (vi). Administration: Jones Ofose, Head
- (vii). Tema port FDB control office representatives

5. Ministry of Health

- (i). Policy, Planning, Monitoring and Evaluation department: Dr Edward Addai, Head
- (ii) Information department: Isaac Adams, Head
- (iii) Procurement department: Sam Boateng, Head
- (iv) Traditional and Herbal Medicines department: Peter Arhin, Director; George Agyemfra
- (v) Chief Pharmacist Pharmacy Council: Felix Yellu
- (vi) Central Medical Stores: Peter Gyimah, Head
- (vii) Ghana National Drugs Programme: Martha Gyansa-Lutterodt*

6. Ghana National Health Insurance Scheme (NHIS): Mr O.B Acheampong, NHIS-Secretariat

7. Ministry of Trade, Industry, Private Sector Development and the President's Special Initiatives: Kofi Larbi, Chief commercial officer

8. Ghana Investment Promotion Centre (GIPC): Abdel Mahama, Deputy Director

9. Ghana Customs and Excise authority: representatives

10. Ghana Ministry of Justice – Office of the Attorney General: Joseph Tamako, Principal State Attorney

11. Ghana Health Access Network (HAN): Charles Kallotey, Director

12. WHO Country office for Ghana: Country advisors for HIV/AIDS, malaria, tuberculosis and neglected tropical diseases

13.UNAIDS office, Accra

14. Kwame Nkrumah University of Science and Technology (KNUST), Pharmacy Faculty, Kumasi: Prof. Mahama Duwuieja, Dean

15. Noguchi Memorial Institute for Medical Research: Prof. Alexander Nyarko, Director

16. Senior representatives from regional African banks (e.g. Ecobank)

17. Interviews with pharmacy stores and patients at pharmacies

18. Independent experts: Mr Ben Botwe (Head of FDB Drugs division, currently seconded as consultant to Ghana narcotics control board); Dr Emmanuel Mensah

* Martha Gyansa-Lutterodt also acted as the local consultant for researching and producing this report

ANNEX 2: PROFILES OF THE PRINCIPLE PHARMACEUTICAL MANUFACTURING COMPANIES IN GHANA

This Annex provides a summary company profile of six of the major pharmaceutical manufacturers in Ghana (there may also be other key pharmaceutical manufacturers in Ghana):

1. Ayrton Drugs Manufacturing Company
2. Danadams Pharmaceutical Industry (Ghana) Ltd
3. Ernest Chemists Ltd
4. Kinapharma
5. LaGray Chemical Company
6. Phytoriker

The company profiles provide a summary of (i). Company background, (ii). Product portfolio overview, (iii). Company initiatives and development plans, (iv). Company constraints, (v). Summary of company assistance needs, and (vi). Overall company assessment.

Ayrton Drug Manufacturing Company

(i). Company Background

Ayrton began as a small family business manufacturing pharmaceuticals in 1965 with 15 workers and later expanded to their current location at Tesano on the Abeka Road in 1969. Ayrton in 2005 floated shares of the company and got listed on the Ghana Stock exchange. Ayrton was the second pharmaceutical company after Starwin Industries to be listed. The company continues to enjoy high patronage at the Ghana stock exchange being the company most traded in as of Friday 12th October 2007.¹⁸

The current staff strength is 430 with a turnover of 25-30%. The company's expansion programme is evidenced by a new block being built behind the current factory and another one on the Spintex Road. Currently the MD Mr. Samuel Adjavon is the chair for West African Pharmaceutical Manufacturers Association (WAPMA).

(ii). Product Portfolio Overview

Ayrton currently produces generic products including analgesics (both tablets and syrups) and anti-infectives (capsules, tablets and suspensions) and the old anti-malarial chloroquine. Ayrton does not produce any drugs that address the priority endemic diseases (i.e. TB, HIV/AIDS and current treatment for malaria). Ayrton sources APIs from India, China and the EU.

(iii). Company Initiatives and Development Plans

The company has currently three regional depots i.e. Bolgatanga, Kumasi and Takoradi in addition to Accra. This is to reduce the wholesaler interface so Ayrton could penetrate the market directly thereby reducing the long credit period that wholesalers take and the high prices patient pay because of high wholesaler margins.

(iv). Company Constraints

Ayrton face a number of constraints including: (i) challenged with production space and thus not being able to meet local market needs, (ii) debt management difficulties and long credit periods resulting in the lock up of capital, (iii) the presence of middle men (wholesalers) that results in the retail prices of their products being relatively expensive, (iv) regulatory documentation remains a challenge, and (v) manufacturing constraints, i.e. currently their antibiotics, especially the beta lactamases, are produced in the same area of production and they do not have a microbiologist on site and thus have to contract this function out to the Noguchi Memorial Institute for Medical research and Standards Board.

(v). Summary of Company Assistance Needs

Capacity building for the staff and a bioequivalence centre would go along way to support their expansion programme. The issue with energy, although almost solved, affected the company greatly and it would be grateful if there is support in this area in the future.

(vi). Overall Company Assessment

The company is taking advantage of the Ghanaian financial markets for expansion and the company's drive for expansion is laudable and market penetration good.

Danadams Pharmaceutical Industry (Ghana) Ltd

(i). Company Background

Danadams, founded in May 2004, is a wholly Ghanaian owned company and is a subsidiary of the Danpong Group of Companies. The company is governed by a twelve member Board of Directors with diverse backgrounds. Danadams has a total equity value of approximately

¹⁸ JOY FM Business and Financial news @7pm of 12/10/07

3,300,000 USD with the Managing Director as the sole shareholder. The shareholding structure of the company is not expected to change; rather, the company intends to secure loan financing which is expected to change the capital structure to 32% equity and 68% debt.

The company is made up of the following business units: finished product manufacturing, wholesaling and pharmacy retail. It also operates patient clinical laboratory services. The total staff employed as of September 2007 is 85 split between the functions of operations, quality assurance & regulatory affairs, sales & marketing and finance & administration. The Managing Director considers the company to have the requisite expertise and experience to manage each function.

Danadams is one of the few companies in West Africa that is championing the cause for locally produced ARVs. The Managing Director estimates that the company has invested approximately 5 million USD into ARV production so far.

(ii). Product Portfolio Overview

Since 2005, their product portfolio consists of a number of ARVs, anti-malarials and other miscellaneous anti-infectives. They are planning for API and also parenteral production. Danadams is the only ECOWAS manufacturer currently producing ARVs (there were 2 other regional manufacturers producing ARVs until recently – Fidsons in Nigeria and Farmakwik in Benin, but these 2 producers have reportedly stopped producing ARVs due to the problem of qualifying for international tenders).

(iii). Company Initiatives and Development Plans

Danadams is planning to expand its ARV product sales to other countries in the West Africa region, given the need to address the HIV/AIDS sub-region endemic. The company has authorisation to market ARVs in Burkino Faso, Sierre Leone, Liberia, Cote d'Ivoire and Ghana. The Company states that it has the network and structures to be able to provide the regional demand for ARVs.

The company has created a human resource development strategy as a part of its expansion process to prepare the Company to tap the opportunities in the West African pharmaceutical market that will entail regular training and employee development programmes.

Danadams considers that it has the capabilities and adequate plant capacity for its current operations. The company stated that it has secured a reliable source of raw materials (ingredients and packaging) and manufacturing equipment. However the current manufacturing facilities and the equipment available to it can only produce tablets and capsules. The Company wishes to invest in ARV drug oral liquid form production and is requesting investment for the creation of a liquid line manufacturing facility that can supply the entire West Africa sub-region.

Danadams has recently (in August 2007) had a 'Feasibility Study for the Production and Supply of Antiretroviral Drugs' conducted by the international management consultancy firm KPMG. The study has assessed the resources and capabilities Danadams has to produce ARVs in the quantities that are required to meet the increasing demand for these drugs as well as what is required to enable Danadams to meet the demand.

(iv). Company Constraints

The Danadams production facility is currently not operating at full capacity and is thus not making full use of its qualified staff. The principle constraints that Danadams faces are as follows:

(a). The WHO prequalification process.

Local producers, even if they are of 'internationally acceptable GMP standard' are finding it difficult to qualify for ICB due to some key constraints¹⁹²⁰:

- drug registration (MAA) dossier format and content problems;
- the cost of obtaining a Certificate of Analysis (CoA) by an 'international standard DRA'. For example Danadams has obtained satisfactory CoAs for all its products submitted to the ICB process according to analysis performed by the Research Institute for Industrial Pharmacy, North West University in South Africa;
- the cost of conducting necessary clinical bioequivalence studies (for example, conducting the necessary studies in South Africa costs on average 30,000 USD per dosage form). For Danadams this means a total cost of approximately 500,000 USD for the products they would like to include in the ICB tender.

Thus although Danadams ICB tender portfolio may well meet acceptable international quality, safety and efficacy standards; it is currently unable to prequalify in its view because of the administrative cost of meeting WHO prequalification standards, as opposed to any inherent lack of production quality standards. However it is able to supply some ARVs and anti-malarials to the Ghana MoH via the process of 'shopping' when product shortages arise due to delays or procurement miscalculations in the ICB procurement process.

The fact that the company is unable to supply their products through donor funded international competitive bidding (which is the principle method of purchasing drugs for priority diseases in Ghana) is a major threat to the future viability of the company.

(b). Obtaining short term credit for funding of the need to obtain large stocks of imported raw materials

It is practically impossible in Ghana, even for credible manufacturing companies, to obtain the necessary short term bank credit for funding of the large amount of manufacturing supplies they require to maintain a secure manufacturing material stock (given both the high costs and the length of the supply chain for importing manufacturing materials from distant sites based in Europe and Asia). Securing timely imported packaging and API material at international prices is a fraught problem for local producers.

(c). Access to investment capital and government support schemes

A major problem that Danadams faces is being able to obtain internationally competitive priced capital and loans due to the high cost of obtaining capital in Ghana (in Ghana, loan interest rates are extremely high – at least 20% p.a.). Despite the statement made by the President of Ghana on the occasion of the commissioning of the Danadams pharmaceutical production facility in June 2005 that 'the factory is strategic for Ghana's fight against endemic diseases like malaria and HIV/AIDS and should be supported by the government and the entire nation', the company has reportedly received limited government support.

(v). Summary of Company Assistance Needs

Danadams is requesting the following type of assistance to support its programme for production of medicines that address local endemic priority diseases:

- pharmaceutical regulatory support: WHO prequalification, drug dossier upgrading to international standards (i.e. CTD format) and the creation of a regional clinical bioequivalence laboratory;
- investment in the creation of a liquid ARV drug production line;

¹⁹ WHO prequalification letter sent to Danadams; Tender for procurement of Sulfadoxine Pyrimethamine Addendum No.1 MoH letter ('The product must have been WHO prequalified or authorized by a stringent regulatory authority such as the EU, Japan and the US FDA')

²⁰ See Certificates of Analysis of Danadams products performed in South Africa

- investment in back-up manufacturing facility support; and
- access to competitive loan funding.

(vi). Overall Company Assessment

In the opinion of the GTZ consultants, Danadams is a motivated company but faces constraints in achieving full international GMP, adequate regulatory documentation and the ability to conduct cost effective bioequivalence studies.

Danadams should be considered as an investment opportunity for ARV production based on the following premises:

- the company has experience in the manufacturing of solid ARV drug dosage forms (i.e. capsules and tablets) and it considers that this experience can be leveraged for the production of ARV liquid drug dosage forms;
- availability of current factory space for production of liquid ARVs (the Company also owns 5 acres of land in the Accra region that is earmarked for future production expansion of liquid ARVs); and
- the company's establishment of good relationships with suppliers of raw manufacturing materials.

Ernest Chemists Ltd

(i). Company Background

Ernest Chemists Ltd was founded in 1986 as a sole proprietorship and in 1993 was converted into a limited liability company. It is a wholly owned Ghanaian company. It has diversified from retail and distribution into manufacturing. It commenced manufacturing operations in the early 2000s at Tema. The manufacturing facility located at Tema has a total of 177 staff.

The company also provides local representation for several international research-based companies. In addition, it also produce under license several OTC products the from Seven Seas company UK.

The company has recently commenced exporting to other countries in the West Africa sub-region (e.g. Sierra Leone and Senegal).

(ii). Product Portfolio Overview

The company's product portfolio consists of a broad range of coated tablets, capsules, oral liquids and suspensions for paediatric use, medicines for external use and oral rehydration therapy powder. Therapeutic areas covered include:

- a broad range of antibiotics;
- vitamins, minerals and tonics;
- analgesics;
- anti-malarials (artesunate, chloroquine and Sulfadoxine Pyrimethamine);
- miscellaneous (e.g. anti helminthics, sedatives, antipsychotics, diuretics, hypoglycaemics);
- antiseptics.

(iii). Company Initiatives and Development Plans

Ernest Chemists is currently constructing a separate penicillin-based production facility for oral and parenteral forms.

(iv). Company Constraints

The company's manufacturing facility is not operating at full capacity (currently operating a single shift system) and is thus not making full use of its qualified staff. The principle constraints that Ernest Chemists faces are as follows:

- *High loan interest rates* (20% bank base rate, but can be as high as 25-30% annually);
- *The need to maintain large material stocks.* All manufacturing materials are imported (APIs, excipients and packaging). Sources of supply are far away (e.g. APIs, excipients and packaging are imported from India, China, UK, Denmark, Germany and Portugal) although some packaging is now produced locally. It can take 3 months or more for materials to reach the manufacturing site, therefore the company needs to maintain large material stocks (approximately 4-5 months worth of stock is stored in the company warehouse which is full to capacity);
- *High manufacturing material costs.* The need to import materials from large distances and difficulties in obtaining materials at international competitive prices leads to a comparative price disadvantage for locally produced products vis a vis finished products imported from India and China (where the principle API, excipient and packaging suppliers are located);
- *Unreliable and expensive manufacturing utilities.* The water supply is inconsistent (sometimes it is necessary for the company to purchase tanked water) and high electricity costs;
- *High local transport costs.* This affects the import of manufacturing materials and transit / export of the company's products (high costs associated with freight via air, road and sea and storage costs while materials are undergoing customs clearance);
- *Time and expense for customs clearance.* There is reportedly a lengthy customs clearance procedure for imported materials, equipment (and spare equipment parts). The company considers that various unnecessary customs inspection procedures are implemented and that there are more effective ways for checking that materials and equipment parts are actually being used for local production. In addition a 2% tax is levied for customs clearance procedures;
- *VAT on imported materials.* The company has to pay VAT of 12.5% (plus 2.5% that goes to the National Health Insurance Scheme) on imported materials but it cannot charge VAT on its finished products. Therefore the company has to pass the cost on to the customer. 66 of approximately 200 materials required for drug manufacturing are VAT exempt, but the procedure for reclaiming VAT payments is extremely lengthy and the costs incurred, in terms of time and effort, of reclaiming VAT offset the money reclaimed;
- *Doing business in the sub-region.* The company has experienced difficulties doing business in the sub-region outside of Ghana; e.g. problems of contractual law and the honouring of contracts by exporting / importing agents from other countries in the sub-region (e.g. Nigeria);
- *Difficulties qualifying for procurement of essential drugs through International Competitive Bidding.* In the company's opinion, the Ghana FDB should be responsible for conducting prequalification and not the WHO, particularly as the company considers the FDB to be a high standard regulatory authority in the sub-region. The need for the company to register products (that address priority diseases and which are designated for the local market) with two different authorities duplicates the regulatory approval process and leads to extra cost;
- *Perception of locally produced medicinal products.* Medicinal products from India are perceived to be of higher quality than locally produced products.

(v). Summary of Company Assistance Needs

Ernest Chemists requires assistance in the following areas:

- access to competitive loan funding;
- creation of a regional bioequivalence centre;
- provision of in-country training for its manufacturing and regulatory personnel;

- purchasing of equipment for its in house QCL (e.g. IRR, HPLC);
- Investment for infrastructure development (i.e. the penicillin manufacturing facility);
- introduction of pooled procurement for manufacturing materials required by local producers (this could be implemented via the Pharmaceutical Manufacturers Association of Ghana);
- elimination of VAT on all drug manufacturing materials;
- Simplification and rationalisation of customs clearance procedures for imported materials and manufacturing equipment. The Ghana FDB should provide evidence to customs that manufacturing materials are actually being used for local production and are not being traded once arriving in Ghana (which should be possible since the FDB maintains records of pharmaceutical imports and exports).

(vi). Overall Company Assessment

Ernest Chemists is considered locally to be a strong local pharmaceutical manufacturer in terms of both manufacturing quality standards and production capacity. The company has a very large product portfolio some products of which address priority endemic diseases in Ghana (e.g. anti-malarials, anti-helminthics and oral rehydration therapy). The company has a product portfolio that consists of a large number of OTC products as manufacturing OTCs is the 'cash cow' for local producers.

Ernest Chemists has several antibiotics and anti-helminthics in its product portfolio which are largely repackaged on site. Given that the company has already invested money in creating a separate antibiotic manufacturing facility, it requires further support for completing its production plans in this respect.

Although the company is currently focused on supplying OTC products, it has the potential to manufacture antibiotics that address priority endemic diseases.

Kinapharma

(i). Company Background

Kinapharma was founded July 1988 as a limited liability company and is an executive member of PMAG. The vision of the company is to become the largest indigenous producer and marketer of high quality reliable and affordable pharmaceutical product in the West African sub-region. The company employs a total of five hundred (500) employees with key technical staff of about sixteen pharmacists, two chemists three in IT, one mechanical engineer and seven mechanical technicians with administrators.

The company has won several awards such as Ghana's Marketing man of the year 2003 and the Ghana media describe Kinapharma as "the most popular local company in Ghana".

(ii). Product Portfolio Overview

Kinapharma is one of the first local companies to produce Ghana's recommended ACT's Amodiaquine–Artesunate. The company produces anti-infectives, multivitamins, analgesics etc. Sources of APIs include India, France UK and Germany.

(iii). Company Initiatives and Development Plans

The company has diversified into other areas, for example, tyre retreads (heavy-duty truck tire retreading), telecommunications, security services and fruit juice processing.

Kinapharma also has implemented a large scale social responsibility programme. The company has been training shop owners and managers in collaboration with the Pharmacy Council in 136 districts throughout the country and also operates a continuous education programme for chemical sellers in all districts. The company sponsors sports development in Ghana and is a member of Ghana's prestigious CLUB 100.

Kinapharma states that it has maintained a great community spirit from its inception seventeen years ago by making donations and sponsor support in cash and drugs to diverse causes, charities, local organizations and district support groups. Kinapharma's budget in rural/peri-urban community health program product donations alone now amounts to \$50,000 annually excluding cash.

(iv). Company Constraints

The major constraints that the company faces are new product development and regulatory issues, e.g. WHO prequalification.

(v). Summary of Company Assistance Needs

Company requires support for training of technical staff and support for bioequivalence studies in anti-malarials.

(vi). Overall Company Assessment

The company is largely self supporting but requires assistance for Human Resource Development / Capacity Building.

LaGray Chemical Company

(i). Company Background

LaGray Chemical Company is a fully vertically integrated pharmaceutical manufacturing company with the technology to manufacture both active pharmaceutical ingredients (APIs) and finished dosage forms. LaGray is reportedly the first API manufacturer in West Africa. The venture commenced in 2001 with the construction of a greenfield manufacturing facility. The facility is located at Nsawam in the Eastern Region of Ghana. The total number of employees is 55 and commercial production commenced in July 2007.

The two Founders and Directors of the company are Ghanaian and Nigerian American who worked in industrial chemistry and infectious disease research & development at the Executive level for the research-based pharmaceutical industry (Abbott and Pfizer) in the USA for many years. The principle investments for the creation and operationalisation of the facility have come from the directors' own resources and a significant loan received from the US Overseas Private Investment Corporation (OPIC).²¹ Although it took LaGray 5 years to search for the necessary financing eventually they succeeded. Access to external capital (through tenacity and conviction) has been an advantage for LaGray given the extremely high cost and difficulty of obtaining capital investment loans in Ghana.

The company's strategy is to manufacture most products, starting from synthetic intermediates and starting materials, through the APIs to the finished dosage forms, in a vertically integrated fashion. This, the company believes, enables the control of quality from start to finish and positions the company for voluntary licenses and technology transfer that will enable the company to manufacture many products in a self-sufficient manner.

The facility is built to US FDA cGMP standards. From concept to implementation, the aim was to build the company's facility in accordance with the latest international guidelines for the design of premises for pharmaceutical manufacturing.

Some of these are:

- Control of man and material entry into the manufacturing areas;
- 10 air handling units with HEPA filters to control the air quality; and
- RO water loop system to control the quality of water used in manufacturing.

The company's quality control function consists of fully equipped analytical chemistry, instrumentation and microbiology laboratories. Equipment includes HPLCs, Fourier transform infrared spectroscopy (FTIR) and atomic absorption spectrometer.

The company has installed a comprehensive treatment plant for gas emissions and aqueous effluent from manufacturing and laboratory operations, in compliance with its environmental protection plan.

The objective behind using US FDA guidelines for facility design and implementation is to position the company for product prequalification by international regulatory agencies such as the WHO. This will, in turn, enable the export of the company's products throughout the sub-region and beyond.

The company's manufacturing capacity is 10 metric tons of API for a single shift operation, 8 million laminated aluminum tubes of dermatological products and 300 million filled hard gelatin capsules per year. The company's objective for the near future is to increase API manufacturing capacity and to complete its oral dosage form manufacturing facility. The

²¹ OPIC is an agency of the US government and offers US investors political risk insurance as well as long-term financing, directly or through guarantees, for commercially viable overseas projects that support US foreign policy objectives.

company's long term goal is to build a healthcare company with capabilities in pharmaceuticals, vaccines and diagnostics.

(ii). Product Portfolio Overview

The company's strategy for finished products is to focus on local and sub-regional unmet drug demand and is planning to export to the rest of West Africa.

In the current phase of project implementation, the company's current focus is on the production of dermatologicals, oral anti-infectives and anti-hypertensives. The next project implementation phase (2008) consists of the production of a number of antibiotics and related medicines, including, for example, drugs for HIV/AIDS opportunistic infections and azithromycin.

In two years time the company intends to start producing (i) ARVs, and (ii) anti-malarials. The latter includes the conversion of *Artemisia annua* (cultivated and isolated in Ghana and Nigeria) into API (artemisinin conversion to artemether and artesunate), and the production of halofantrin (this previously required a 15 step synthesis, now, through development work that the company did with Howard University (US), it is possible to do with 5 steps, therefore the production cost is cheaper). There has been well documented problems concerning halofantrin and QTc interval prolongation; however the company believes it is possible to alter the molecule in a way that does not lead to this adverse reaction while still retaining anti-malarial activity).

(iii). Company Initiatives and Development Plans

- Building up API production capacity
- Increasing product portfolio by completing oral solid dosage plant
- Acquiring voluntary licenses and technology transfer in vertically integrated ARV manufacturing.

(iv). Constraints

Constraints the company is facing include:

- the ability to provide cost-effective staff professional training. The company has to a large extent so far had to rely on expensive training support from the USA.
- identification and recruitment of qualified professional staff. The company faces difficulties in identifying and recruiting professional staff for functions such as API manufacturing and regulatory affairs.
- either weak and 'difficult to apply' or absence of trade incentives for the local pharmaceutical industry interested in producing drugs for endemic priority diseases.
- attracting equity or donor funding to finance development plans.

(v). Summary of Company Assistance Needs

LaGray is requesting assistance in the following areas:

- *Funding (equity or donor) for capacity building in its API production.* The company's current API manufacturing capabilities need to be expanded in order for it to meet the needs of the region.
- *Coordinated and sustainable training in the areas of pharmaceutical regulation, inspection, GM .etc.* There is a need to have a co-funded (i.e. by both local industry and donors) programme of long term sustainable training of professional staff for both local producers that have demonstrated serious intention to manufacture medicinal products that address priority endemic diseases, and the local pharmaceutical regulatory authorities. There is a need to address professional pharmaceutical manufacturing and regulation training simultaneously to both local manufacturers and the regulatory authorities. For example, this could be conducted through 2-3 day workshops.

- *Creation of more explicit national incentives for local pharmaceutical production that addresses priority endemic diseases.* The current situation of incentives for the local manufacturing of medicinal products that address priority endemic diseases is weak in Ghana. There needs to be a system whereby there are incentives and support for plant improvement, expansion, discovery research and achieving voluntary licensing (as opposed to compulsory licensing). This will support the growth of the industry and will ensure a fair process of technology transfer from the international research-based industry (e.g. API synthesis, formulation, pharmaceuticals etc).

(vi). Overall Company Assessment

The Company has made a large investment into vertically integrated international standard (i.e. US FDA approved) pharmaceutical manufacturing. For a number of reasons, the company has been able to attract internationally competitive loan funding. Reportedly the company is the first API producer in West Africa and furthermore has the expertise and facilities to conduct industrial chemistry research & development. The company strategy for product in-licensing is based on the principle of Voluntary Licensing as opposed to Compulsory Licensing. The company considers the latter approach to be non optimal as it is contentious, there is often a need to reinvent the production process and regulatory documentation (e.g. Drug Master File), and it closes the door to technology transfer and future cross border pharmaceutical industry collaboration.

Phytoriker

(i). Company Background

Phyto-Riker (GIHOC) Pharmaceuticals Ltd (PRG) was established in 1998 when the state owned Ghana Industrial holding Cooperation was acquired by Phyto-Riker Pharmaceuticals Inc. through a competitive privatization process. GIHOC Pharmaceuticals Ltd, formerly the State Pharmaceutical Cooperation was established in 1962 and completed in 1967. The factory is situated at Dome near Achimota on a 104 acre site off the Accra-Nsawam road and employs 250 staff. The main production facility for solid dosage forms was commissioned by the German government in 1991. The Company has a beta-lactamase plant which was commissioned in 2002 separately from the other solid dosage forms production facility. The liquid production facility was commissioned in 2003. The company has a microbiologist in house and the company is GMP and ISO 9001-2000 certified.

Currently the company is being managed by the Overseas Private Investment Corporation (OPIC) and other US investors holds 25% shares in the company whilst TransAfrican Pharmaceuticals Ltd owns majority shares of 65% , with the Government of Ghana retaining 10% interest.

(ii). Product Portfolio Overview

The company produces anti-inflammatory, antipyretic, analgesics and anti-infective agents especially antibiotics and anti-malaria agents as well as drugs used in the treatment of common tropical diseases. The company produces a wide range of essential pharmaceutical products to meet the drug requirements within Ghana and the entire West Africa sub-region and even beyond. Many of their products had been registered in 18 countries mainly in West and Central Africa; The Company has product registrations in major markets like Nigeria, Senegal, Cote D'Ivoire, Niger, Mali and Benin amongst others.

The company also undertakes contract development, production and analysis for other companies within the industry.

(iii). Company Initiatives and Development Plans

Phytoriker is collaborating with the major South Africa pharmaceutical manufacturer Aspen, which is WHO pre-qualified.

(iv). Company Constraints

The major constraints the company is facing include:

- WHO prequalification (batch sample submission procedure in particular);
- since the new management take over in 1998 there has been only 35% company growth;
- difficulties in obtaining cost effective financing of working capital;
- competition with cheap Indian and Chinese imports in the sub-region;
- ISO certification renewal due in 2008;
- the non enforcement of GMP standards by the Ghana Food and Drugs Board (in the opinion of the company director, pharmaceutical companies such as Phytoriker that invest in achieving international GMP standards are unfairly penalised by the Ghana FDB allowance of pharmaceutical manufacturers to operate at different degrees of GMP standards²²;
- the irrational insecure pharmaceutical distribution system in Ghana and the sub-region that results in the need for manufacturers to set up their own distribution companies and to export products via France in order to distribute products to Francophone West Africa in a way so as to guarantee product security and competitive retail pricing.

²² The Phytoriker company director's opinion is supported by several other companies and senior Ministry of Health officials

(v). Summary of Company Assistance Needs

Phytoriker requires:

- new equipment to replace ageing existing equipment;
- the government needs to implement the 'marginal preference scheme' to support local manufacturers;
- technical assistance for the regulatory documentation issues concerning WHO prequalification;
- Access to cost effective working capital to enable company growth.

(vi). Overall Company Assessment

PhytoRiker has the capacity to grow itself and has a huge infrastructure to satisfy the sub-region local pharmaceutical manufacturing needs. The Company is currently producing under capacity. The company already has a strong presence in the sub-region pharmaceutical market and with some assistance could provide quality products to the entire sub-region.

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