

PHARMACEUTICAL MANUFACTURING PLAN FOR AFRICA

INTRODUCTION:

1. Pursuant to the AU Assembly decision 55 taken during the Abuja Summit in January 2005 which mandated the AU Commission to develop a Pharmaceutical Manufacturing Plan for Africa with the framework of NEPAD, the AU Conference of Ministers of Health undertook “to pursue, with the support of our partners, the local production of generic medicines on the continent and to making full use of the flexibilities within the Trade and Related Aspects of Intellectual Property Rights (TRIPS) and DOHA Declaration on TRIPS and Public Health {Gaborone Declaration Doc. CAMH/Decl.1(II) 3 (10 – 14 October 2005)}. They further requested the AU Commission to “accelerate development and facilitation of the implementation of a Pharmaceutical Manufacturing Plan for Africa” {CAMH/Decl.1 (II) 13(ii)}. The AU Commission conducted a drug production capacity mapping exercise in line with the Assembly decision on local drug production in the continent in collaboration with the World Health Organization.

2. At the WHO-AFRO 56th Regional Committee Meeting that was held in Maputo (AFR/RC55/10), discussions on strengthening local production of essential medicines emphasized that policy decisions about whether to import essential medicines from reputable sources or to promote local manufacturing should be based on careful situation analysis and realistic appraisal of the technical feasibility and financial viability underpinned by sound regulatory systems. A market size that would ensure sustainability as well as technical and financial viability was considered imperative. The WHO Regional Committee for Africa adopted resolutions AFR/RC/49/R5 and AFR/RC38/R19, which emphasize essential medicines, local production of essential medicines and African traditional medicines.

3. Pharmaceutical production occurs at three levels, primary, secondary and tertiary. The primary level includes the manufacture of active pharmaceutical ingredients and intermediates from basic chemical and biological substances. Secondary production includes the production of finished dosage forms from raw materials and excipients. The tertiary level is limited to packaging and labelling of finished products or repackaging of bulk finished products. (WHO AFRO, SADC).

4. A number of countries in the continent largely rely on India and China for imports of affordable generics and raw materials. The fact that India and China had to comply with both process and product patent laws by 2005 was seen as a potential threat to affordability and access essential drugs in Africa.

5. Unreliable medicine supply systems continue to hamper access. Some of the **perceived** benefits of local production include: -

- i. Local production will save foreign exchange,
- ii. Local production creates jobs, thus alleviating poverty and promoting social development,
- iii. Local production facilitates technology transfer,

- iv. Local production will stimulate exports,
- v. Raw materials produced locally will be readily available and cheaper,
- vi. Local production will improve/ enhance self-sufficiency in drug supply.¹

6. The leadership of the African Union is committed to ensuring access to essential medicines for countries in need, irrespective of their level of technological development and manufacturing capacity.

SITUATIONAL ANALYSIS

7. Assessment of local production of medicines in some African countries (in the WHO African Region) indicated that out of 46 countries, 37 have pharmaceutical industries, 34 have secondary level production and 25 have tertiary production. Only **one** has limited primary production. Nine countries have no production capacity (WHO AFRO, Aug 2005). Self-reliance in local production seems to be a priority strategy in a number of Eastern Mediterranean countries. The national capacity for production has increased in Egypt, the Islamic Republic of Iran, Jordan, Morocco, Pakistan, Syrian Arab Republic and Tunisia to between 60% and 95% of their national requirements for essential medicines.¹ Though no one country, whatever its size and level of economic development, is entirely self-sufficient in pharmaceuticals, the negative trade balance of most countries in the continent is of concern.

ISSUES TO BE CONSIDERED

8. Pharmaceutical production is **capital, technology** and knowledge intensive/ driven. **Technical expertise** is absolutely critical, both in terms of sufficient numbers and appropriate skills. The continent will have to invest in the production of different skilled scientists (biology, chemistry, process engineering, medical engineers, biochemistry, bio-computer science, physics, medical engineers, clinicians, pharmaceutical scientists, technicians etc.). The critical factor is the ability of education system to produce sufficient numbers of skilled personnel in a sustainable manner. It will be necessary to form strong linkages with universities and funders to ensure a sustainable supply of required skills. **Academicians often have more interest in basic research compared with clinical research**, as the former is a faster route to promotions.³ The balance between the two must be properly promoted and nurtured. Africans in the diaspora can probably assist in this regard. Incentives may have to be identified. At this moment there are very few technical experts with the appropriate qualification and experience to enable the Continent to go into large scale primary manufacturing.

9. At national and regional level, **the legislative framework** needs to be conducive to regionalised local production. This extends beyond legislation that ensures Good Manufacturing Practice (GMP), Good Distribution Practice (GDP), Good Laboratory Practice (GLP), Good clinical Practice (GCP) and other aspects of product regulation but also extends to legislation **regulating related duties on imported raw materials and intermediates and related taxes**. In-country procurement legislation and guidelines may also need to be amended. The continent

is not homogeneous and has varying legislative frameworks and enforcement capacity.

10. Pricing policies and legislation linked to market size also have an impact on the extent to which local production can be expanded. **TRIPS flexibilities and national patent laws also have an impact.**

PROMOTION OF TECHNOLOGY TRANSFER

11. A strong link between academic and industrial research needs to be fostered. Technology transfer can meaningfully occur when there is a level of primary production. It is also highly dependant on the willingness of the technology owner, who may be losing a market in the process. Innovative manufacturing is in the hands of a few multinationals that have drastically reduced the number of manufacturing sites to a few niche areas around the globe, ideally located close to the more lucrative markets. Location is also influenced by favourable labour costs. **Would these innovators realistically be willing to transfer technology?** A few examples of technology transfer from the north have been for diseases of the developing world, and old technologies that are no longer profit-making eg. Treatment for Tuberculosis.

PHYSICAL INFRASTRUCTURE

12. Other than manufacturing plant and laboratory equipment, reliable, sustainable, reasonably priced **electricity and water** supplies, and modern IT and **telecommunication** technologies are critical. Reliable distribution networks are also important. Singapore has used some of these strategies to promote pharmaceutical production.²

PARTNERSHIPS

13. The assistance of development partners may be required in the following areas: -

- i. The World Bank and DFID have done some economic analyses of pharmaceutical production in developing countries and these may be focused on the continent or used as a benchmark / comparators.
- ii. WHO AFRO has also done a study on local production. WHO can be used to draw or source specific expertise as and when required.
- iii. Other development partners can be used to support Research and Development, particularly in the areas of Indigenous knowledge systems and neglected diseases.
- iv. Development partners may also be used to channel seed funding at the beginning.
- v. Public private partnerships may need to be explored

² Footnote to be completed

14. Production in the continent is in the hands of the private sector. WHO advises that this may be the best arrangement so that governments concentrate on regulatory mechanisms.

TENSION BETWEEN HEALTH OBJECTIVES AND TRADE OBJECTIVES

15. There is tension between industrial policy and health policy. A manufacturer would decide to make a commodity if:-

- i The desired quality is unavailable
- ii Suppliers are unreliable,
- iii There is desire to maintain intellectual property rights,
- iv There is need to develop a local employment base
- v There is need to reduce reliance on imports and manage foreign exchange flow
- vi There is desire to produce for export
- vii There is desire to increase technology transfer.¹

16. On the other hand, health policy objectives' aim is to improve access to affordable medicines of good quality, without constraints like access to foreign currency, long lead times and inability to negotiate affordable prices. Some developing countries have embarked on pro-poor policies by capping prices for the domestic market, granting a range of incentives for local manufacturers etc. Some trade policies have encouraged investment by foreign innovative companies, with built-in safeguards for technology transfer to improve their global competitiveness. A balance has to be found to manage this tension. Both health and trade policies should be explicit and consistent with the overall development strategy.³

WHAT TO MANUFACTURE

17. The plan must investigate and suggest criteria for determining **what is to be produced**. Though the primary focus may understandably be on the diseases which contribute more to the burden of disease, like HIV and AIDS, TB and malaria, an investigation needs to be made whether concentrating only on these priority conditions will lead to sustainability. A decision needs to be made as to which medicines will be produced by whom. Essential Medicines Lists are not harmonised and there may be need to negotiation on which products to produce. Few medicines are however currently used to manage TB, malaria and AIDS.

18.

19. Criteria will need to be developed for deciding **which manufacturing plants will be eligible**. These may be linked to sustainable financing, compliance with GMP standards, sound regulatory systems, availability of appropriate human resources, reliable sources of electricity and water, technical feasibility and a viable market size.

20. Decisions also need to be made on intra-regional choice of **which country or group of countries will produce which commodity**.

21. Resources required need to be identified. Sources of funding will have to be identified up –front for both the producers and the purchasers. **Human resources**

need special attention both at inception and to ensure continuous supply and sustainability.

22. An honest appraisal of **when regulatory systems can be adequately strengthened** is a key milestone. Several models to strengthen regulatory systems may be explored. **Countries within a region may pool their resources together and form a regulatory system similar to the EU.** Countries with weaker regulatory systems would then eventually up-scale their regulatory skills within this umbrella. Post –marketing surveillance forms part of the regulatory system strengthening. The proliferation of counterfeits and substandard medicines in the market and the recent withdrawal of Cox2 inhibitors manufactured by reputable companies make this imperative. Regulation of clinical trials is equally important. Efficient and effective distribution systems are necessary to ensure that quality medicines reach the intended beneficiaries. It will be important to analyse whether mark-ups through the value chain do not compromise affordability, thus hampering access.

ADDITIONAL FACTORS TO BE CONSIDERED

POLITICAL

23. The plan must have safeguards against monopolistic tendencies by the approved centres. Tools to measure efficiency and fairness / competitiveness of prices must be developed, implemented and continuously monitored. A strategy needs to be developed for countries that do not have manufacturing capacity to share benefits and tasks from the plan, other than medicines. (Manufacturing packaging material, etc.)

24. Will the plants manufacture only medicines that address HIV and AIDS, malaria and TB only or will other medicines e.g. antibiotics, analgesics; OTC also form a basket of manufactured products? Viability will determine the model.

25. Will markets be segmented to cater for lower technology-driven and high-technology driven production? Where will centres of R&D be situated?

26. Will production be limited to generics or will an attempt be made to create space for development of innovative technologies including African Traditional Medicines and other indigenous knowledge systems. Will the plan include investigations of better medicine delivery systems more suitable to our climate and conditions?

27. A number of countries have recently entered into joint ventures with manufacturers from India to manufacture antiretrovirals. How will these plants be accommodated?

28. What strategies will be used to compete with China and India that historically have lower labour costs and bigger markets?

29. Acceptability of locally produced generics by both providers and consumers may be a challenge unless marketing is done.

30. As countries in the continent are at different levels of development, labour costs will not be the same and they will impact on the final price of commodities.

SOME SOBERING THOUGHTS

31. Local production may not save foreign currency at entry. Active pharmaceutical ingredients account for 60% or more of the final cost of the product. Until primary manufacturing becomes a reality, there will not be meaningful savings of foreign currency. Production equipment, laboratory equipment and reagents etc. will be paid for in foreign currency.

32. Manufacturing requires highly skilled scientists, engineers, technicians etc. Modern production is technology –driven and may not create many entry - level jobs. There are however possibilities of job creation across the value chain if we begin at research through development, production and distribution. Jobs can be created in public research organisations, small and medium biotech companies, upstream in engineering and downstream in public health services.³

33. Export markets can only be achieved with innovation, competitive prices and quality. Government – driven procurement often protects local products through preference margins in government tenders. This may distort the market, as local small companies may not even attempt to be competitive.

Raw materials and intermediates are manufactured by a few players and the quantities produced are not too large. An analysis would have to be made to establish whether manufacturing raw materials is cheaper than importing them. Patent and TRIPS issues also play a significant part in this area.

34. The response of big PhRMA (The Pharmaceutical Research and Manufacturers of America) and other similar structures to the plan and their geopolitical influence may need to be analysed, particularly with regard to the donor community.

CONCLUSION

35. Local production can be successfully done in the continent. However there is need for the African countries to reassess the realities, possibilities and the feasibility of the programme so that it moves from being a political slogan to a reality after good ground work .The time needed to do thorough scientific analyses in the continent , together with WHO and other bodies that can add value, is certainly longer than two years . An economic analysis however needs to be done to ensure appropriate planning.

36. It may be recommended for the African Union Conference of Ministers of Health to mandate a technical body well versed with manufacturing to do a “skill search” and appoint all the relevant expertise (taking care of all the regional groupings i.e. geographical, linguistic) to study the detailed implications and come out with a suggested plan to advise the ministers in the following areas:

- Capabilities of the regions ,
- Legislative reforms needed –TRIPS
- Products and level of Manufacturing (primary ,secondary and tertiary)
- Infrastructure, capital and market analysis
- Issues of equitable benefits for all countries per region
- Sustainability possibility of new inventions
- This group may be mandated to bring a firm proposal/informed advice to the Ministers on this highly technical issue within a few months

PLAN OF ACTION

This plan of action is being presented in phases to allow intense assessment of the feasibility and modality of local manufacturing of medicines in Africa.

PHASE I

It is recommended that Health Ministers are requested to appoint a committee of experts that will have regional and linguistic representation in the continent with the following expertise:-

- i. Pharmaceutical production including technology transfer
- ii. Health Economists
- iii. Bio-engineers
- iv. GMP Experts
- v. Academia
- vi. Epidemiologists
- vii. Intellectual Property Rights and TRIPS
- viii. Procurement
- ix. African Traditional Medicine
- x. Biotechnology
- xi. Development partners in Health
- xii. Legal

This group should be able to co-opt experts as and when necessary.

2. TERMS OF REFERENCE OF THE GROUP OF EXPERTS

- 1) Definition of regions
- 2) Mapping of pharmaceutical plants
- 3) Skills audit
- 4) Human resource needs identification
- 5) Infrastructure assessment
- 6) Identification of products to be manufactured by different regions
- 7) Level of manufacturing (primary, secondary, tertiary)
- 8) Market prospecting within the continent and beyond
- 9) Identify opportunities for new technological inventions
- 10) Financial resource needs.

3. The group should work with the support of AU Commission and present an informed plan of action to the Ministers of Health within six months.

TIME FRAME	April 2007 CAMH 3	May to October 2007	November 2007
ACTIVITIES	<p>Appointment of group of experts with the following skills:-</p> <ul style="list-style-type: none"> i. Pharmaceutical production including technology transfer ii. Health Economists iii. Bio-engineers iv. GMP Experts v. Academia vi. Epidemiologists vii. Intellectual Property Rights and TRIPS viii. Procurement ix. African Traditional Medicine x. Biotechnology xi. Development partners in Health xii. Legal 	<p>Group of experts does its work guided by (but not limited to) the following TORs</p> <ul style="list-style-type: none"> 1. Definition of regions 2. Mapping of pharmaceutical plants 3. Skills audit 4. Human resource needs identification 5. Infrastructure assessment 6. Identification of products to be manufactured by different regions 7. Level of manufacturing (primary, secondary, tertiary) 8. Market prospecting within the continent and beyond 9. Identify opportunities for new technological inventions 10. Financial resource needs. 	<p>Report and submit informed plan of Phase II plan of action to Ministers.</p>

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**THIRD SESSION OF THE AFRICAN UNION CONFERENCE
OF MINISTERS OF HEALTH
9– 13 APRIL 2007
JOHANNESBURG, SOUTH AFRICA**

CAMH/MIN/7(III)

Theme: ***“Strengthening of Health Systems for Equity and
Development in Africa”***

**MINISTERS’ MEETING
10-13 APRIL 2007**

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