Opinion Piece Topic: Positioning the local API industry as a regional development and manufacturing hub for the African Continent – policy considerations.

Focus: Unlocking opportunities for the local API industry to stimulate sector growth and improve the quality of health care in South Africa and the Continent.

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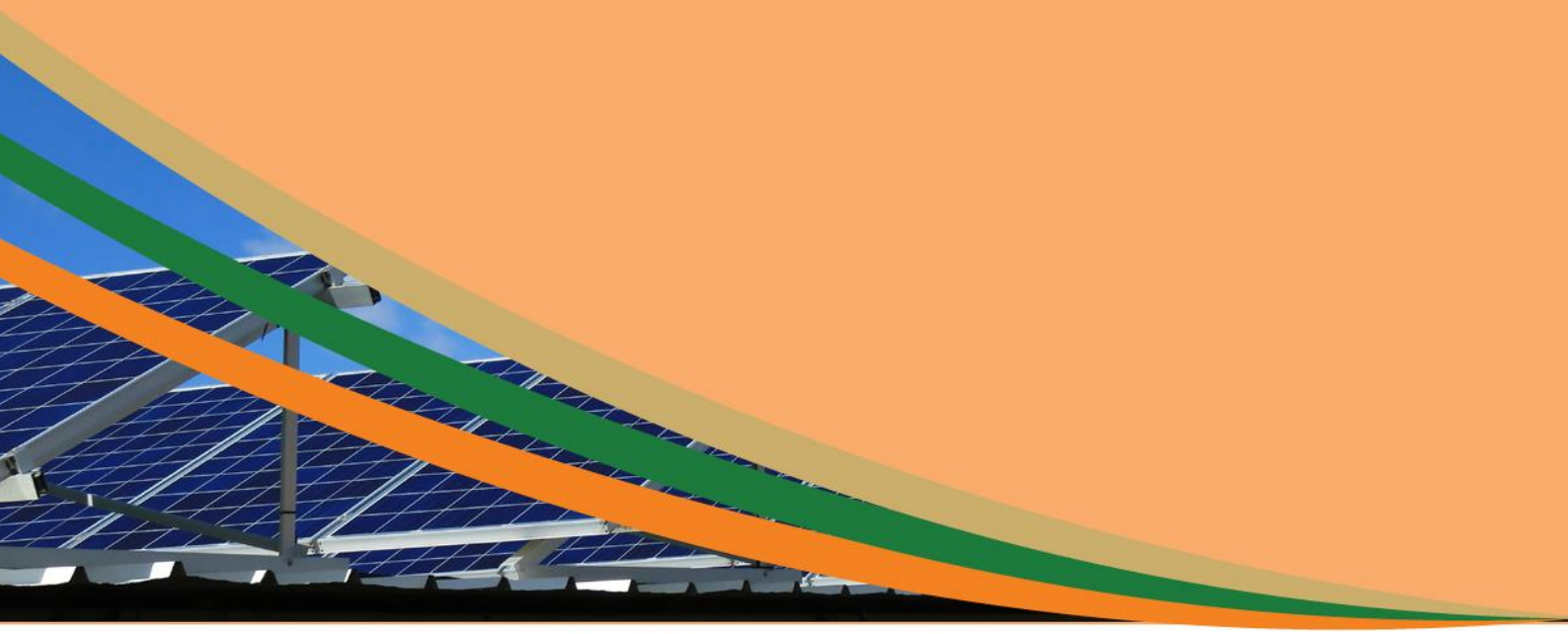

South Africa (SA) has a well-developed pharmaceutical formulating industry. Even though more than 60% of pharmaceutical products sold in SA are formulated locally, approximately 98% of Active Pharmaceutical Ingredients (APIs) used in local formulation are imported. APIs are the active healing substances in a drug that have a direct effect in treating diseases. They are at the very heart of modern medicine, and form the basis for many of the effective and innovative treatments available. They also account for between 60%-80% of the cost of production. Currently, India and China are global leaders in the manufacture of APIs and related intermediates.

What is most concerning is the fact that SA imports approximately R15 billion worth of APIs on an annual basis. This is an opportunity cost in that SA has the largest number of people living with HIV compared with other countries (8.2 million people in SA were living with HIV in 2021 according to Statistics SA), the majority of which rely on the government ARV Programme for their treatment. Currently, 100% of APIs used to formulate ARVs are imported. Furthermore, there is also a growing demand for pharmaceutical products used in the treatment of various types of cancer and other non-communicable diseases such as diabetes. This is putting additional strain on the public health sector resources.

Secondly, the problem with this heavy reliance on imported APIs/formulated medicines, over and above increasing the trade deficit in the pharmaceutical sector, is the fact that it also poses a major healthcare risk in instances when it becomes difficult to source such pharmaceutical products. A case in point is the recent covid-19 outbreak where global economies, including SA, were left shaken. SA and the entire African Continent were on the receiving end of export bans placed by India and China on pharmaceutical products (including APIs), which meant shortages of much needed medical supplies. The pandemic clearly exposed flaws in the entire global supply chains of vaccines, drugs and diagnostics, and thus served as a wake-up call for SA and the Continent.

Lastly, we cannot ignore the issues around international regulatory manufacturing standards. This is because a considerable amount of medicines consumed in Africa for the treatment of HIV, TB and malaria are procured by international donor organizations (e.g. Global Fund). The procurement of such medicines is currently restricted to manufacturers with the World Health Organization (WHO)'s prequalification (PQ). The attainment of acceptable good manufacturing practices certification (cGMP) and WHO PQ is often a lengthy and costly exercise, which requires substantial investment on the side of the manufacturers. Once the investment is made, it can inherently increase the cost of goods sold (COGS), thus making manufacturers less competitive (from a price point of view) in the public markets that do not require WHO PQ. This discourages manufacturers from pursuing such international accreditation, which in turn closes them out from accessing donor and other international markets. International manufacturers from countries like India often receive incentives, which make it competitive for them to export pharmaceutical products and to dominate the African market. This also puts African manufacturers and new entrants at a disadvantage.

Government, through its Re-Imagined Industrial Strategy (2019) and the South African Economic Reconstruction and Recovery Plan (2020) (ERRP), has identified the pharmaceutical industry as one of the strategic industries for the country, which need to be supported and strengthened. The ERRP programme for industrialization through localization, for example, highlights the importance of import replacement measures covering critical medical equipment, health stocks/APIs and key food products. These, together with the Health MasterPlan which is currently being developed by **the dtic**, industry, and other social partners, is a testament to government's efforts in working towards measures that will help strengthen the health sector and related industries, in order to minimize associated risks.

The Department of Science and Innovation (DSI) established an API Innovation Cluster in 2019 with the sole purpose of strategically driving API initiatives in the country, all the way to implementation. This development has subsequently led to the recent establishment of the API Cluster Technology Development Laboratory facility launched in March 2022. The facility is utilized to harness the ingenuity and expertise of the academic fraternity as well as other stakeholders, in order to develop API technologies and capabilities that will demonstrate improved API synthesis processes. This has the potential to unlock enormous opportunities for industry, such as building critical mass of local intellectual property (IP) which will enable SA to manufacture API molecules cost-effectively. The IP itself is in fact an important policy instrument that can be applied to foster innovation, technology transfer, and industrial development. An urgent move towards a Substantive Search and Examination (SSE) system can therefore contribute to increased R&D of new and follow-on products in this industry.

Secondly, there will be massive opportunities in establishing a commercial pipeline for local API manufacturing, which could be achieved through innovation, technologies, molecular formulations and the development of Drug Master Files (DMF) for competitive manufacturing of APIs emanating from the API Cluster initiatives. Thirdly, there are localization opportunities that could be unlocked for the country. Local companies like Chemical Process Technologies (Pty) Ltd (CPT) have already begun to develop technologies focusing on API molecules for TB, ARVs and malaria. These APIs once developed and approved by the South African Health Products Regulatory Authority (SAHPRA), should be used to manufacture drugs for the local SA market. This will help to build critical mass and local expertise, which are key factors for industry expansion. Lastly, the Continent in general also faces a range of public health challenges; and similarly, the risks associated with overreliance on imported pharmaceutical products (including APIs) also amplify the need for Africa to be more self-sufficient. A developed and vibrant local API industry has the potential to benefit not only SA but also the SADC region and the entire African Continent. The manufacture of strategic APIs (i.e. for HIV, TB and malaria), can position SA as a regional API manufacturing hub for the Continent. Access to bigger markets coupled with economies of scale will help drive down prices, thus making locally produced API competitive, even for the African market. The correlation between API price and purchase volumes means that long-term offtake agreements and pooled procurement in the region will become very crucial. These can contribute towards unlocking further investments in API/pharmaceuticals manufacturing in the Continent.

From a strategic point of view, if indeed we want to position the local API industry as a regional hub, it will be important, firstly, for local API/pharmaceuticals manufacturers to attain WHO PQ. Considering the additional investment required to manufacture APIs/pharmaceuticals at international standards, appropriate incentives (e.g. capital/innovation incentives, interest-free loans) and tariff remedies may be required to address key investment decision drivers. Secondly, strategic partnerships enabled through the Health MasterPlan (once finalised), will also play an important role in taking this industry forward. These measures will help to level the playing field and unlock future export markets for local API manufacturers.

Thirdly, a multipronged strategy with short, medium and long-term goals is required to address key issues such as R&D spending in API development, strategic partnerships in API manufacturing, IP SSE system, pooled procurement, long-term offtake agreements, WHO PQ accreditation, etc. Lastly, in a truly collaborative fashion, and as part of a multipronged strategy, the Continent must decide on key value-chains to pursue, as well as the infrastructure and incentives necessary to stimulate investments in API/pharmaceuticals development and manufacturing. Quick wins in the short-term can, for instance, include identifying intermediates that can easily be produced and used as input material to manufacture APIs. This can also help to provide the traction needed to grow the local API

industry in the medium to long-term. Finally, targeting local production of strategic APIs (e.g. for HIV, TB) presents a huge opportunity for import replacement, which can significantly contribute towards reducing the trade deficit in the pharmaceutical sector. This will, to some degree, help mitigate the risks associated with global supply chains, bring down the price of medicines, and improve access to medicines and the provision of healthcare in SA and the rest of the African Continent in the long-run.

There is a great need for a harmonized regulatory system in SA and the Continent as this would expedite approvals and stimulate investments in this space. This is a possibility now that the African Continental Free Trade Area (AfCFTA) is operational. The outbreaks of global pandemics (current and possible future pandemics) and their devastating consequences should propel the African Continent to move with speed in working towards achieving these strategic objectives. Well thought-through policy interventions and strategies can promote synergies and help the local API industry find alignment with other related initiatives within SADC and the African Union (AU).

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