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Biotechnology and the bioeconomy—Towards inclusive and sustainable industrial development

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ABSTRACT

To transform developing and least developing countries into industrialised ones, biotechnology could be deployed along the value chain, to provide support to the development of the bio-based industries in such a way to ensure sustainability of the sector and to reduce negative environmental impacts that might otherwise occur. In agribusiness development, for instance, interventions could start from inputs and agricultural mechanization, modern processing technologies, packaging of perishable products, the promotion of food safety in the processing and regulatory environment; and interventions to improve competitiveness and productivity. Worth over USD 300 billion in revenue, the role of the biotechnology goes beyond industrial growth, since it provides opportunities for progress towards many of the UN sustainable development goals (SDGs). This paper reviews the status of industrial biotechnology as it relates to inclusive and sustainable industrial development.

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Introduction

Key industrial sectors that derive their raw material and/or key components along the value chain from natural resources and biological processes constitute the bio-based economy or bioeconomy. The world faces a number of major environmental, economic and social challenges which have to be properly addressed if future generations are to enjoy a safe, healthy and prosperous future. The solutions we arrive at will change the way we live and work and – if we make the right choices – these changes will generally be for the better. The transition from a dependence on fossil fuels to a situation where agriculture not only will continue to provide food security but also biomass as a renewable raw material for industry will be the basis of the integrated bioeconomy. The bioeconomy is already making substantial contributions to sustainable development and this

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contribution will increase in the future: higher quality, renewable raw materials will be produced sustainably, and food security and a healthy environment will continue to be assured. Conversion to a wider range of end products, whether food, feed, fuel, fibre or other healthcare or industrial products, is also sustainable, being efficient, producing little or no waste, and often using biological processing. Developing all sectors of the bioeconomy in concert will provide global food security, improve nutrition and public health, make industrial processing cleaner and more efficient and make a significant contribution to the effort to mitigate climate change. For maximum benefit, the various sectors of the bioeconomy must be properly linked, since they are all interdependent. Concerted action will not only create strong individual sectors, but strong and effective links are needed to create a bioeconomy web. This inter-connectedness means that all sectors must be equally strong; one weak link could significantly reduce the overall effectiveness of the web and limit competitiveness.

In recent years, biotechnology is revolutionizing industrial and agricultural practices by improving quantity and quality of products. In addition, the number of commercial biotechnology products is increasing each year [1]. In the agriculture and agribusiness sector for instance, biotechnology applications play a significant role, from increasing productivity to value addition and product diversification of agriculture produce, while reducing their environmental impact. In the manufacturing sector, biotechnology is used to produce a wide range of bulk and fine chemicals; and the biotechnology derived "*cold water enzymes*" allow effective washing at room temperature. The production of plastics and fuels from biomass is now also well-established globally. Global bioplastics production is estimated to increase from 1.7 million tons in 2014 to approximately 7.8 million tons by 2019 [2].

The economies of many developing countries are based on agriculture and other natural resources. Biotechnology therefore presents unique opportunities for sustainable industrial development. The use of appropriate technology in processing and manufacturing will not only improve efficiency of production and quality of products, but also facilitate trade and international development cooperation.

Agricultural biotechnology in industrial value chains

Underlying all human societies is the need for food security. The modern bioeconomy has its roots in providing both food and non-food products from managed agricultural, aquaculture and forestry ecosystems. Based as it is on continuously renewable resources, it provides an ideal platform from which to tackle 21 st Century challenges. Major issues such as water usage, land management, efficient use of nutrients like nitrogen and phosphorus, maintaining carbon sinks and socio-economic development must be tackled in a systematic and holistic way across all the interconnected sectors. Managing natural resources sustainably is a vital start, but the whole supply chain must also be sustainable, to ensure food security, supply sufficient quantities of renewable raw materials and energy, reduce environmental footprints and promote a healthy and viable rural economy. Beyond this, it is also important to avoid unnecessary waste and to recycle unavoidable waste in useful and efficient ways. The ideal is to have closed loop systems of production and by-product reuse. The bioeconomy already does this adequately, but the ambition is always to use by-products from one sector in another part of the web if they cannot be used directly.

Biotechnology as applied in agriculture, offers a wide variety of scientific approaches to improve plants, animals and micro-organisms aiming at developing solutions to agriculture productivity and sustainability. These scientific tools are very diverse and include for example tissue culture, molecular breeding, genetic engineering, molecular diagnostic tools. They assist breeders in delivering high quality new varieties, assist the farmers to detect diseases or serve the industry to produce molecules of high added value for food or health improvement.

The uptake of these technologies has been very fast in agriculture and numerous crop varieties have been ameliorated or engineered with the help of biotechnology, being it conventional or genetically engineered varieties. Thus, several millions hectares of agriculture land over the globe today have been in hands of biotechnology to ensure their quality and success in the field. However, only some parts of the world have benefited from the availability of these technologies and the poorest parts of the world often have only limited access to such technology.

For the propagation and conservation of most important crops and especially those with a vegetative way of propagation, tissue culture (TC) is the biotechnological tool of choices since many decades. Tissue culture (TC) is the cultivation of plant cells, tissues, or organs on specially formulated nutrient media [3]. Commercial plant tissue culture is now a key component of the horticulture and seed industries, as well as in management of forest resources. The transfer of TC to the private sector mainly through development of SME's has permitted to farmers to get access to clean planting material which is a key element for a good harvest whereas farmers traditionally propagated themselves in the field under uncontrolled growth conditions. In India, for example, 93 commercial TC production units have been recognized by the Department of Biotechnology, Govt. of India under the National Certification System for Tissue Culture Raised Plants [4].

The production of biological products for plant growth-promotion and disease suppression is another important aspect of biotechnology in the agribusiness sector. This includes: 1) biopesticides which fight against stresses caused by pests and diseases through predatory, parasitic, or chemical relationships, soil improvers; 2) biofertilizers which are substances that contain living microorganisms which, when applied to seeds, plant surfaces, or soil, colonizes the rhizosphere or the interior of the plant and promotes growth by increasing the supply or availability of primary nutrients to the host plant; and 3) biostimulants [5]. Biostimulants/biofertilizers include the nitrogen fixers, phosphorus solubilizers, phosphorus mobilizers, micro-nutrient (Silicate and Zinc) solubilizes and plant growth promoting Rhizo bacteria (PGPR) [6].

The worldwide turnover of biopesticides is approximately USD 1.8 billion and the market availability of different types of microbial cultures and inoculants has increased rapidly in the past decade due to improved biotechnological production schemes. Nitrogen fixing biofertilizers were the most widely used biofertilizers accounting for over 78% of the global demand in 2012, followed by phosphate solubilizing biofertilizers, with 14.6% of the market share.

The biofertilizers market in 2015 was valued at USD 946.6 million and it is expected to grow at a CAGR of 14.08% from 2016 to 2022. With the increasing pressure on global food production, the demand for fertilizers is expected to increase, which in turn would enhance the growth of the biofertilizers market [7].

The rapid progress made in molecular genetics, bioinformatics and molecular biology has broadened the panel of tools available for making high quality conventional breeding and in addition has allowed the development of new genetically engineered crop varieties with agronomic traits that are important for the farmer, the consumer and the environment.

Since 1996, nine GM crops have been grown commercially worldwide including soybean, maize, cotton and canola which support several industries including food, feed, textile and health. The direct global benefit from GM crops is estimated at USD 18.8 billion [8] and socioeconomic studies have revealed that it is also beneficial for small hold farmers from developing countries which is translated into improvements in health, education, debt repayment, maternal care services and food security [9].

However, today the potentialities of genetic engineering are exponentially growing. Indeed the first generation of genetically modified plants were primarily beneficial for the farmer with traits such as herbicide tolerance or insect resistance. The actual technologies are bringing also new products that have the potential to help malnutrition by engineering metabolic pathways to have enrichment in micronutrients that are missing in the usual diet of some of the poorest populations. For instance, the pro-vitamin enriched rice (golden rice) or a folate enriched rice that could both be very helpful in preventing some diseases [10,11].

In addition, biotechnology also brings solutions to improve the post-harvest processing and thus optimize the bioeconomy sector in its whole. For instance, in the forestry sector, biotechnology proposes solutions to reduce lignin content of trees or crops reducing the highly polluting processing of the wood in the paper or biofuel industry.

In conclusion, biotechnologies should be used today not only to perform commodity research to increase food production but should serve to provide nutritive food that can be produced in ways that can be sustained environmentally, economically and culturally [12]. Therefore it's important that public research adjusts its focus from major crops to more orphan crops. Indeed, making available tools and genomic data for nutritive orphan crops will allow help the sustainability and allow diversifying future diets. An example of an initiative in this sense is the African Orphan Crop Consortium (http://africanorphancrops.org/).

Industrial biotechnology

Fermentation is one of the oldest forms of biotechnology and a key component of many industrial applications involving the processing of biological material. Since the advent of microbial citric acid production commercially in the 1930s, fermentation-based industry is currently worth over USD 127 billion, [13]. Recombinant DNA technology and protein engineering have allowed the development of more efficient microbes and thus contributed to further increases in microbial production.

The value of the fermentation industry to production of consumer goods and services cannot be overemphasized from the direct application in processing (such as in foods and beverages) to the production of fermentation derived fine chemicals such as amino acids, vitamins, alcohols, polysaccharides, and antibiotics mostly by the food and pharmaceutical industry.

Enzyme biocatalysis is another major biotechnology with wide industrial application. Industrial enzymes are divided into four major categories on the basis of application: detergent enzymes, technical enzymes, food enzymes and feed enzymes. Food enzymes derived from gene technology have been on the markets since the 1990s. Within the group of food enzymes, those for milk and dairy dominate the market.

The technical enzymes segment is further divided into textile enzymes, leather enzymes, pulp and paper enzymes, fine chemicals enzymes, fuel ethanol enzymes and others [14]. In 2013, the global market for industrial enzymes was valued at just over USD 4 billion and expected to reach around USD 7.1 billion by 2018 at a compound annual growth rate (CAGR) of 8.2% [15].

While the bulk of consumption of industrial enzymes lies in industrialized countries, developing countries, nevertheless, are expected to become important consumers of enzymes for the food and feed segments, as the increase in per capita income in these regions will drive more demand for meat and dairy [16].

Feed enzymes are incorporated in animal feed to increase the digestibility of nutrients and to degrade components of the feed that can be harmful or of little or no value. This leads to greater efficiency in feed utilization [16]. In addition, their use has a positive impact on the environment by reducing faecal nutrient level applied to land, controlling pollution.

The global value of feed enzymes is expected to reach a value of USD 1284.6 million by 2020 at a CAGR of 7% [17]. Europe is the highest consumer of feed enzymes, especially in the poultry industry. Among developing countries, Asia-Pacific is the fastest growing region. This is mainly due to the increased awareness among the farmers about the benefits of enzymes and simultaneous growth in adoption.

Industrial biotechnology and health

The medical and healthcare industry is one of the most vital sectors of the world's economy. In fact, growth of the biotech industry is mainly due to the applications in the healthcare industry, which have facilitated the development of health care products, diagnostic services, biopharmaceuticals and related products. Most traditional biotech products have relatively modest market values compared to biotech products generated by recombinant DNA technology. Recombinant-based technology that allows the modification of large complex molecules, has been applied in the pharmaceutical industry since the 1970s, resulting in the development of a whole new range of treatments. These include human insulin with different rates of action, antibody-based novel cancer therapies, interferons for the treatment of viral infections and a range of therapies for non-communicable diseases such as multiple sclerosis and rheumatoid arthritis.

Biopharmaceuticals generated by modern molecular biology are by far the fastest-growing part of the whole pharma industry. The number of biotechnological drugs has increased exponentially in the last three decades. In the USA alone, the FDA has approved 34 monoclonal antibodies, 26 enzymes or enzyme modulators (e.g. dornase alfa, alteplase, reteplase) and 31 modulators of receptor function (e.g. insulin, interferon alpha-2a, erythropoietin) [18].

At the end of 2014, 260 new products were approved covering over 230 indications [19]. In 2013, the total cumulative sales reached the value of USD 140 billion. This value surpasses the gross domestic product (GDP) of three-quarters of the 214 economies ranked by the World Bank [20]. According to Standard & Poor's industry data, biotechnology products are expected to account for 48% of the top 100 drugs of 2016.

The contribution of biotechnology to the health industry is not limited to the production of biotherapeutics. Genetic manipulation and recombinant protein production is essential for the generation of diagnostic systems for viral infection and genetic disorders. The latter field has substantially benefitted from the information generated by the genome sequencing projects.

The global In Vitro Diagnostic (IVD) market is forecast to reach USD 75 billion by 2020 [21]. In addition, genomics and synthetic biology now permit the generation of microbial factories that produce large and cost-effective compounds used by the chemical industry as drug precursors. For example, production of semi-synthetic artemisinin (an antimalarial compound) from artemisinic acid produced by microbial factories, is an early success story that combines metabolic engineering and synthetic biology [22].

As far as the monoclonal antibody market is specifically concerned, this is estimated to be worth no less than USD 75 billion, thus representing almost half of the total sales of all biopharmaceutical products. For a comparison, the worldwide annual revenues for all pharmaceuticals are now estimated at over USD 650 billion [23].

Biotechnology is also enabling new diseases to be vaccinated against, such as Human Papilloma Virus that is the cause of cervical cancer, and it enables improved vaccines for other diseases such as pneumonia and meningitis. Vaccines are indeed one of the most cost-effective public health tools to prevent infectious diseases. There is already a Developing Country Vaccine Manufacturers Network, however, more can and is being done to develop vaccine production facilities in the developing world to improve access and security of supply for these critical health products.

The health bioeconomy in the developing countries

Biosimilars are new follow-on biological medicines such as monoclonal antibodies, that exhibit a high degree of similarity to a reference product already been authorised for use, as supported by appropriate analytic testing and clinical trials. The first-generation biotechnology based medicines are now off-patent and the biosimilars are significantly reducing the cost of these products. In 2013, the first generic version of the infliximab monoclonal antibody against TNF-alpha was the world's first biosimilar monoclonal antibody to be approved by the European Medicines Agency. In principle, generic manufacturers do not have to bear the cost of drug discovery and thus generic medicines can be offered at a significantly lower price than the original drugs.

However, there are critical issues in the production of biological drugs that set them apart from small molecule drugs, which can be produced as generics in a much simpler manner. Proteins not only need to assume proper structure for activity, they also often require post-translational modifications, are generated in complex biological systems (microbial or vertebrate cell lines), are intrinsically unstable and show remarkable micro-heterogeneity [24]. In addition, their production, purification and validation are complex processes that require adequate skills. A challenge for developing countries is to properly develop these human skills to ensure proper domestic production. The issue of capacity building in the field of biotechnology, therefore, becomes an essential prerequisite for the development of an internal generics pharmaceutical industry.

In recent times, large biopharma corporations are seeking a partnership with the local biopharmaceutical industry in emerging economies to perform manufacturing in these countries, with local contract manufacturing organisations (CMOs). This strategy is likely to facilitate the emergence of a biosimilar industry as well as drug development services in these countries.

Similar considerations also apply to the development of diagnostic kits for infectious and genetic diseases. These can certainly be produced domestically by developing countries at costs that are significantly lower than those of imported products, with comparable sensitivity and specificity. This is well exemplified by the large industry of diagnostic kits in India, where the in vitro diagnostic market is estimated to be worth approximately USD 150 million per annum for reagent kits and laboratory equipment and is growing at 20% per annum on a compounded basis [25]. This success, however, is strictly linked to the huge investment that has been made by both the Indian government and the private sector in the field of biotechnology over the last couple of decades, which has significantly improved university education in both biomedicine and entrepreneurship.

Current and future challenges of biotechnology in the health industry

With respect to the healthcare industry, biotechnology is also expected to face a formidable challenge in the coming years, essentially as a consequence of the progressive aging of the human population and the impelling demand to develop novel therapeutics against degenerative disorders. According to a 2015 United Nations report on world population aging, the number of people aged 60 and older is projected to more than double in the next 35 years, reaching almost 2.1 billion individuals [26]. While most of those who are 80 years old or more live in the industrialized world, the younger and faster growing segment of 60 years or more mostly resides in developing countries. The problem, however, is that the maximum human life span is intrinsically set at a maximum of 120 years [27]. This will imply a progressively growing problem of degenerative conditions.

The novel applications of biotechnology, such as stem cells and nucleic acid-based therapeutics for degenerative conditions, offer unique possibilities for innovative drug development and thus unprecedented options for economical exploitation. Interestingly, their business development follows a trajectory that is significantly different from that of standard small molecule drugs, because they are no longer driven by the large pharmaceutical companies. Instead it is carried out by small biotech companies, initially with limited economic support, but possessing knowledge-intense capacity. These are usually initiated as spin-offs of universities or research centres, and endowed with specific intellectual property strictly related to the application under development.

While this represents a conceptual revolution over the common practice of large pharmaceutical industries in the developed countries, it also offers an unprecedented opportunity for developing countries: constituting a new class of biotech companies that are small and focused, so that they can rely on relatively limited economic support to achieve competitive success. However, this essentially relies on the creation of capacity building that extends beyond laboratory skills to include knowledge on intellectual property protection, fostering innovative applications and nurturing entrepreneurship skills. Creating proper conditions for the growth of this small and dynamic biotech industry remains a challenge for the immediate future.

Cleaner production and resource efficiency

Biotechnological processes are inherently cleaner than petrochemical or thermochemical processes. They are performed in a contained environment, and have the potential to produce high yields of specific products with low energy use and minimal waste generation. The positive impact of industrial biotechnology on climate change by creating savings in non-renewable energy consumption and lowering of CO_2 emissions has been reviewed elsewhere [28].

One of the oldest applications of industrial enzymes is in the leather industry. They play a key role in the various stages of leather processes for soaking, dehairing, bating, dyeing, degreasing, as well as in effluent and solid waste treatment. It is estimated that using enzymes in biopreparation of hides and skins can potentially save up to 8 million GJ of energy and 0.7 million tons of CO_2 per year [29].

Conclusion

The value of industrial biotechnology in monetary terms had a total revenue of USD 323.1 billion in 2014, representing a compound annual growth rate (CAGR) of 7.2% between 2010 and 2014 [30]. The role of the biotechnology, however, goes beyond industrial growth, as it provides opportunities for progress towards many of the UN sustainable development goals (SDGs). In the energy and chemical sector, biotech innovation is reducing dependence on petroleum and fossil fuels, and has consequently a positive impact on the environment. In the health care sector, biotech drugs, vaccines and diagnostics are contributing to improved health and quality of life. In the agricultural field, biotech innovations are simultaneously increasing food supplies, reducing damage to the environment, conserving natural resources of land, water and nutrients and increasing farm income in economies worldwide.

Although the uptake of these technologies is routine in industrialized countries, many developing countries however, are lagging behind in adopting some of these modern biotechnologies for the sustainable growth of industry. Furthermore, not all countries are faced with identical challenges and priorities, and each country is at a distinct stage of development, with a wide difference in technological capabilities.

The benefits of biofertilizers, for instance, have not been widely adopted by farmers especially in developing countries, mainly due to the poor-quality inoculants and inappropriate application methods in assuring viability of the inoculum [31]. As such, more effort is needed in promoting these technologies in order to ensure the potential of industrial biotechnology, and this through collaboration and partnerships between technology providers, the private sector and policy makers. N2AFRICA, a science-based "research-in-development" is working with small and medium scale enterprises (SMEs) to enable African smallholder farmers to benefit from the use of inoculants in legume productions [32]. There is also the need to support such SMEs to improve their production capacities more efficiently.

Building capacities for biosafety in developing countries also is crucial to enable them to explore the range of biotechnologies and their derived products to sustainably boost production in agriculture and other bio-industries. Recently, the UNIDO biosafety manual for practitioners was published [33].

A large proportion of the agricultural produce in developing countries does not reach the consumers, due to poor logistic systems and limited local capacity for processing. This generates huge post-harvest losses and food waste that may reach up to 60% of the produce. As such, to foster sustainable food security, there is the need to increase the ability of the agriculture and food industries to respond to the multiple global challenges, and this in the form of volatile food prices, climate change, environmental degradation and growing demand for food. This requires the increased application of existing as well as new and innovative agriculture and management practices and technologies to reduce postharvest losses, the adaptation to climate change, and the increase of resource efficiency.

The development of robust food systems is frequently the first step in an economy's transition from agriculture to industry. Appropriate technology transfer, under adequate in-country conditions, enables capacity building, which in turn contributes to increased competitiveness in domestic and international markets.

This includes for instance the deployment of improved fermentation technologies to improve the quality of processed products, from small-scale traditional to industrial scale. Although not widely used, the deployment of lacto peroxidase in milk collection is recommended for use in a situation where inadequate power supply will affect the cold chain for storage and transportation of milk from the farms to the processing site [34].

Some of the much debated issues concerning biotechnology and biotech products include the issue of ethics, intellectual property rights and the implications of patents on the cost of technology in developing countries. These topics are discussed in this Special Issue (Krauss and Kuttenkeuler - *Intellectually property rights derived from academic research and their role in the modern Bioeconomy*. Nevertheless, for the large majority of industrial uses of biotechnology and biotech products, it is well established that patents promote greater innovation and product development [35], enabling investment companies and researchers to derive the benefits of their inventions and further contribute to the availability of new products on the market.

Public acceptance of biotechnology is also crucial for the advancement of its application in industry. The development biotechnologies into products and resources for human use need to be researched alongside the ethical, environmental, economic, legal and social implications in order to avoid, for example, the negative publicity that characterized the GM crops. Discussions on the potential risk and benefits of these technologies should include plans to support research in this area.

Middle and low-income countries' activities in the medical/healthcare biotechnology sector are basically relying on existing technologies. While some emerging economies like Brazil, China and India are performing relatively well on the vaccines and diagnostics, they have a difficult entry point to biologic drugs.

As the patents on biologics are expiring and a market for follow-on products opens, there are other challenges that need to be met by developing countries so they can develop biosimilars. These challenges include the cost of the technologies, infrastructure requirements, skills and the enabling regulatory requirements.

Establishing public-private partnerships (PPPs) between government agencies, multilateral development agencies, national and global pharmaceutical companies is likely to facilitate the emergence of a biosimilar industry, as well as drug development services in these countries. Since 2006, UNIDO has supported the production of essential generic medicines in developing and least developed countries.

As with the biopharma industry, patents on GM crop products and traits are expiring and thus opening the prospect of developing agbiogenerics, as well as bringing a new competitive landscape of GM crops.

In conclusion, the innovation of biotechnology offers solutions to many development challenges our world faces today, from feeding and fuelling a growing population to addressing a worldwide epidemic of chronic diseases. Through public private partnership in the delivering of technical cooperation programmes, the potential of industrial biotechnology can be harnessed for the inclusive and sustainable industrial development of developing countries. Furthermore, biotechnology for inclusive and sustainable industrial development can contribute to our responsibilities towards the achievements of the Sustainable Development Goals (SDGs) particularly, Goal 2: to end hunger and achieve food security; Goal 3: to ensure healthy lives and promote well-being for all at all ages; Goal 9: to promote inclusive and sustainable industrialization and foster innovation and Goal 12: to ensure sustainable consumption and production patterns.

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