PROSPECTS AND ISSUES FOR DEVELOPING BIOTECHNOLOGY INDUSTRIES IN BANGLADESH: MEDICAL LABORATORY PERSPECTIVES.

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ABSTRACT

Bangladesh is one of the most densely populated countries in the world and has become a global partner in the pharmaceutical sector. However, it is still far behind in other biomedical industries such as biotechnology, medical devices and laboratory diagnostics. Like pharmaceuticals, all these segments are science driven and should be highly regulated. Among SEARC countries, India is well ahead in the laboratory diagnostic segment of biomedical industries.

Evidence-based patient management has become routine, thus small and medium scale laboratory diagnostic companies can play a crucial role both nationally and globally. Small and medium scale laboratory diagnostic companies in Bangladesh can grow in three stages: test development, commercialization and marketing. Test development is the most crucial part and should be based on trial and error methods. Funding for this phase should mostly come through the government sector. Commercialization and marketing can be channeled through venture capital or diversification funds (share market).

Biomedical graduates are underutilized in Bangladesh and they are highly capable in basic, applied, developmental and product-oriented research with proper research facilities. However, quality products and work environment could be a challenge initially but can be fixed if proper policy and planning are in place. A few examples on small and medium scale laboratory diagnostic companies, their prospects and challenges will be discussed.

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INTRODUCTION

Bangladesh is one of the most densely populated countries (1,021 people living per square km) in the world and has become a global partner in pharmaceuticals sectors. However, it remains far behind in other biomedical industries such as biotechnology, medical devices and Laboratory diagnostics. The enforcement of the National Drug Policy back in 1982 resulted in bringing the Bangladeshi pharmaceutical industry to this state. The sector has gone through a major transformation over the last three decades. Although multinational pharmaceutical companies used to dominate the sector earlier, they have lost their dominance at present. Bangladesh exports pharmaceutical products to 87 countries, including the US and a few European nations. The pharmaceutical sector has also earned the country over BDT.4.0 billion through export of medicines. The export potential has increased even more as the pharmaceutical companies are now working with many foreign partner companies. Currently there are 260 registered pharmaceutical companies, among which 191 are in operation. The manufactured products of these companies are meeting 97per cent of the domestic requirement. These 191 companies are marketing more than 1350 molecules with 23500 brands in the country.[(1)] Like pharmaceuticals, there is a crucial need for the national policy on industries related to medical devices and Laboratory diagnostics. Among SEARC countries, India is well ahead in biotechnology, especially in the laboratory diagnostics segment of biomedical industries.

The term "Biotechnology" was defined by a Hungarian engineer Karl Ereky in 1919, to describe methods and techniques which produce substances from raw materials with the aid of living organisms.[(2)] Another definition, derived from the Biological Diversity Convention in 1992 is "any technological application that uses biological system, living organism or derivatives thereof, to make or modify products and processes for specific use" and agreed upon by 168 member nations, FAO and WHO. According to this definition, medical biotechnology is applied living organisms to the diagnosis or treatment of diseases.[(3)] Since the early 80's after the first launch of recombinant Insulin, hundreds of biotechnology derived products such as pharmaceuticals, cancer biomarkers, autoimmune disease markers, diagnostic kits, and vaccines have been developed.[(4)] According to data available in 2006, therapeutic biotechnology products and vaccines that are marketed have an annual market of 98 billion US dollars, and are benefitting global populations.[(5)] Medical biotechnology can deliver another triumph for Bangladesh which would not only help to save foreign currency but will enhance employment generation and intellectual wealth generation, expand entrepreneurial opportunities, and promote industrial growth.

There are one medical University, 13 Govt. Medical Colleges, 39 Private Medical College Hospitals, eight private and one government dental colleges, two postgraduate Institutes, 3000 Hospitals and Clinics, and over 5,200 private registered Medical Laboratory Diagnostic Centers and Health centers in Bangladesh. The number of these medical college Hospitals, Diagnostic centers and Health centers is increasing rapidly.[(6)] Moreover, there are over 2900 private registered hospitals and clinics, 593 government hospitals under the Ministry of Health and Family Welfare,[6] of which 126 are at the secondary and tertiary levels.[(7)] In recent years, there have been dramatic changes in the medical laboratory diagnostic market. The range of test menus have greatly expanded and a few large diagnostic companies have been employing modern equipments. Another major notable change is the introduction of rapid point of care tests (RPOC). Quality controls of these diagnostic and health centers as well as RPOC are virtually nonexistent except in very few well-known laboratories such as ICDDRB. Clinical and

research laboratories, healthcare providers, and hospitals use medical diagnostic kits (MDKs) and devices in Bangladesh which consume over 5 million US dollars per year of in-vitro reagents, chemicals, and other consumables to evaluate individuals' overall health and diagnose, treat and monitor disease (personal communication). A 100% of those reagents, kits equipments and consumables are imported from other countries.

Biotechnology is a diverse area, and this article will specifically discuss clinical microbiology oriented companies related to disease. The discussion will be limited to one or two examples and products from small, medium and large-scale industries. For small industries, ready-to-use media and an advanced molecular testing laboratory, for medium scale industries, monoclonal antibodies production and POC, and for large-scale industries, vaccine production (Table 1) will be discussed.

Table 1: Proposed Biotech Industry Model

Scale of Industry	Type of Industry: Example	Approximate budget excluding Land and Infrastructure
Small	Ready to use Bacteriological Media Advanced Molecular Laboratory	BDT 10 to 50 million
Medium	Monoclonal Antibody Production	BDT 60 to 500 million
Large	Vaccine (Human and Animal)	BDT 600 Million to >3 billion

SMALL SCALE

READY TO USE BACTERIOLOGICAL MEDIA:

Bacteriological culture media are one of the key components for any diagnostic microbiology laboratory. There are hundreds of diagnostic laboratories using bacteriological culture media in their day-to-day operations to test samples, and physicians are relying on those test results to manage diseases or illness. Quality assured media is a key for the optimal growth of any pathogenic bacteria in the laboratory. Properly stored quality ingredients, pH, deionized water, supply of antibiotic free sheep blood, to name a few of those standards, should be maintained for preparing good quality bacteriological media. One small lab may be using 10-20 plates, and it is not be commercially feasible for them to make media adhering to all those standards. As it takes the same time and manpower to prepare 100 *vs* 1000 plates, it would not be

financially profitable for laboratories using 50-100 plates a day to make bacteriological media. It would be wastage of their valuable time as well.

With the collaboration with small or medium scale laboratories, a small number of ready to use media making industries can be started which eventually will look forward to producing other related products such as gels, buffers, special media, different stains and many more.

***ADVANCED MOLECULAR TESTING LABORATORY**:*

Molecular Microbiology techniques moved from the research lab to the clinical diagnostic labs in North America and European countries a long time ago and as a result, clinical diagnosis guidelines are changing rapidly. This format can be implemented by utilizing this knowledge for managing many life-threatening organisms.

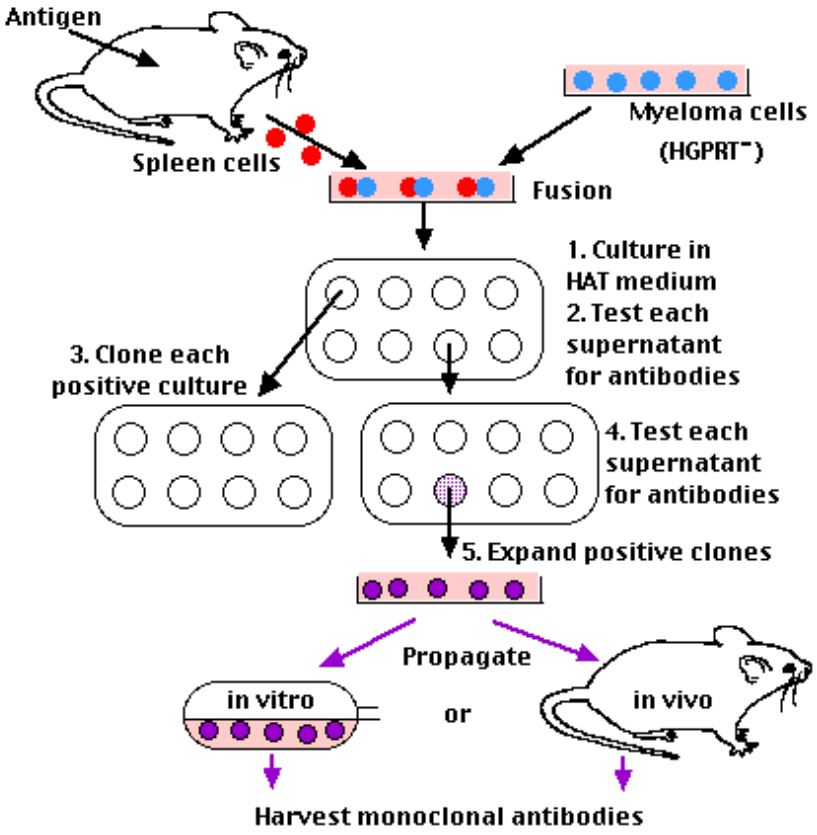
In Bangladesh there are 10 million carriers of the Hepatitis B virus. 25% of those cases could develop clinical jaundice and 1% will have liver failure (100,000 thousand patients).[8-9] It has been proved by many research works that determining viral load is a much better way to mange infection then measuring serum enzymes only. Molecular techniques would not only confirm active infection, but also establish viral load at base line, monitor viral load during therapy, determine duration of treatment and can assess drug no-responders. This kind of a laboratory could easily be established with existing manpower and can emerge as a specialized laboratory, which will not only provide stellar service but also foster advancing science in Bangladesh. This specialized laboratory can work together with large diagnostic laboratories as partners.

Most developing countries try to establish in-house tests to make testing cheaper, but, initially it would be better to stick to commercially available tests which will be quality assured so that quality of the tests will not be compromised.

MEDIUM SCALE

***MONOCLONAL ANTIBODIES**:*

Production of monoclonal antibodies involving human–mouse hybrid cells was described by Jerrold Schwaber in 1971.[10] Monoclonal antibodies are typically made by fusing myeloma cells with the spleen cells from a mouse that has been immunized with the desired antigen(Fig. 1).



Source: http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/M/Monoclonals.html

Figure 1: Schematic diagram of Monoclonal antibody production

Once a desired clone is achieved, Monoclonal antibodies can be grown in unlimited quantities. This technology is being used extensively in developing diagnostic kits, therapeutic treatment, cancer treatment, autoimmune disease treatment, etc. Monoclonal antibody production technology has been matured enough and is easy to implement. Since Bangladesh has an excellent scientific manpower pool as well as relatively low operational costs, opportunities may exist to work as a subcontractor with large diagnostic companies or bio-pharma industries.

RAPID POINT OF CARE TEST:

Rapid Point of care testing (RPOC) is defined as when testing can be done at or near the site of patient care at reasonably short times and in a simplistic manner.[11] In the early days, such testing developed

included diabetes (with blood glucose monitoring) and cardiac incidents.[12] RPOC related to infectious diseases started in early 80's and the market is rapidly increasing (Fig. 2).

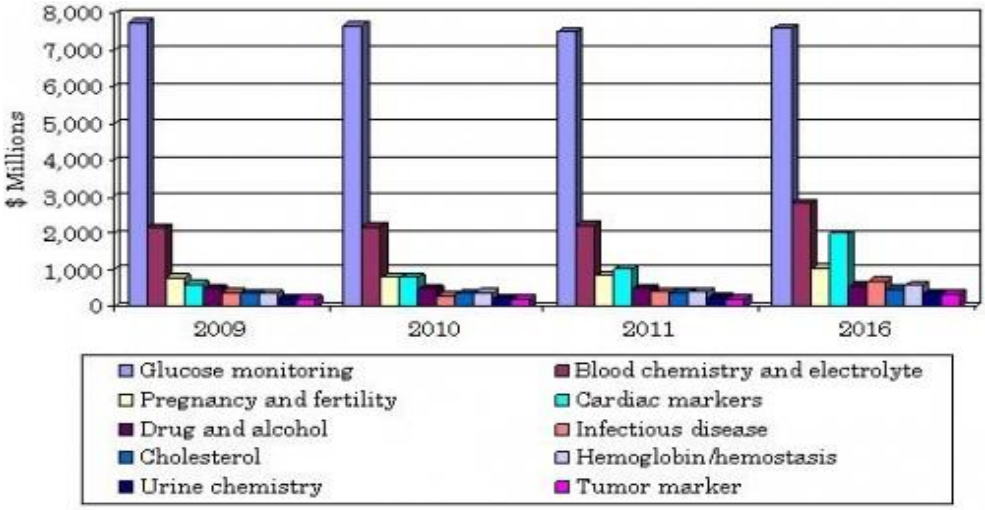


Figure 2. Global Rapid Point of Care Test Market Trend

Source: BCC Research. Code: HLC 043C. 2012. http://www.bccresearch.com/market-research/healthcare/point-of-care-diagnostics-market-hlc043c.html

Glucose monitoring seems saturated and no further growth is expected except technical and delivery systems; however, infectious disease related RPOC sale was about 2 billion in 2009 and is increasing a few hundred million dollars every year. In 2016, it will reach close to 3 billion dollars. Neighboring countries such as India and China are producing many Point of Care Test (POC)'s and earning millions of dollars revenue every year. Bangladesh has a huge potential in this field due to cases of Filaria, Toxoplasma, Anthrax, TB, syphilis, and dengue fever to name a few. Development of RPOC will not only allow earning foreign currency, it will also help provide services to the rural community through their practicing community health care workers including practicing physicians.

LARGE SCALE

VACCINE PRODUCTION:

Vaccines offer the most cost-effective approach to controlling infectious diseases in both humans and animals. Bangladesh's emerging economy has mainly depended on agriculture and agriculture-based products. Due to the huge population with a rising middle-class, poultry production in Bangladesh is

presently considered as one of the fastest growing industries. Like in other developing countries of the world, the main obstacle in flourishing this industry in Bangladesh is the outbreak of sudden common diseases, which causes mortality of almost 30% of poultry products annually and puts the farmers in an inhuman situation. A 10% reduction of mortality and morbidity of cattle and poultry animals can save billions of dollars in Bangladesh and in other developing countries in South-East Asia, Africa, and Latin America.

Currently, all vaccines for humans and most animal vaccines are imported in Bangladesh. Limited amount of conventional vaccines are produced in government facilities at Mohakhali, Dhaka. Current products produced in the government sector include vaccines for a) cattle - FMD, Anthrax, BQ, HS b) Goat- PPR c) poultry- RDV, BCRDV, Cholera, Pox, Salmonella, Gumburo, Marecks and Duck plague in a very limited scale. The bulk of the vaccines with the foreign currency of over 600 million US dollars are getting imported to fulfill the needs.

Although human vaccines have to go through rigorous regulatory process, this is not an impossible task. An example of Shantha Biotechnics will help to explain what is possible. Dr. V.K. Varaprasad attended an immunization conference in Geneva and pursued an idea to develop the Hepatitis B vaccine in India. He sold his inherited property and registered a company with the name of Shantha Biotechnics and he arranged for his staff to work at Osmania Univerity at Hyderabad. He exhausted his entire fund by 1995 and his company was at the verge of bankruptcy. Dr Varaprasad was lucky! The foreign minister of Oman agreed to give him $1.2 million US dollars to produce affordable vaccine for his people as well as ownership of 50% of Shantha Biotechnics. Shantha Biotechnics launched their first product, the Hepatitis B vaccine, with the name of Shanvac-B in 1997. In 1998 they sold 22million doses of Shanvac-B and the company never looked back. As Dr Varaprasad promised, the price of Hepatitis B vaccine dropped to $0.23 USD from $15 USD. In 2009, Shanta Biotechnics won a $340 million USD contract from UNICEF, and Sanofi-Aventis, the vaccine giant, acquired 80% of Shanta Biotechnics share valued at $780 USD.[13]

A sister branch of Incepta Pharmaceutical has already started a venture for producing human vaccines in Bangladesh but that is not even close to fulfill the county's needs. Home-grown companies in the developing countries such as Bangladesh could be the source of low cost vaccines for the global community.

FUNDING MODEL

In order to build up infrastructure and initial capital, a "Big Push" is needed by the government through the provision of substantial funding for seed money and venture capital funds to start-up firms or small industries. National and international research Institutes such as ICDDRB, BCSIR, AEC, Medical Institutions (BIRDEM, National and Private Medical Colleges), large medical diagnostic companies and academic institutions should partner together to implement their discoveries for mass scale production.

This would stimulate entrepreneurship among the scientists and recent enthusiastic graduates. To give an example, in India, the government-owned commercial banks have started their own venture capital funds and they have been quite successful in establishing many small scale bio-tech companies([14-15)

QUALITY CONTROL, QUALITY ASSURANCE AND MARKETING

We live in a global village. Information whether it is good or bad disseminate in a fraction of second to the world community. Therefore, whatever we target, the products should be excellent, should be regulated, and quality controlled well.

CONCLUSIONS

Medical biotechnology is rapidly expanding worldwide and many developing countries such as India, China, and North Korea are taking advantage of moving fast into this field. China, India and North Korea are pioneering globally in developing rapid point of care tests for most of the deadly infectious diseases. Bangladesh could easily enter into this profitable field, targeting both the local and international markets. Advancing into these areas will also create enormous opportunities for the academics, scientists, entrepreneurs and young and energetic graduates.

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