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RESEARCH ARTICLE

BIOSIMILARS: PRESENT STATUS, CHALLENGES AND FUTURE PROSPECTS

Mithun Rudrapal¹, Shubham J. Khairnar¹, Nazim Hussain², and Khomendra Kumar Sarwa^{3*}

¹Sandip Institute of Pharmaceutical Sciences, Sandip Foundation, Nashik, Maharashtra, India

²Kingston Imperial Institute of Technology and Science, Dunga, Dehradun, India

³Department of Pharmacy, Govt. Girls Polytechnic, Raipur, Chhattisgarh, India

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ABSTRACT

New guidelines for “similar biologics” launched August 15 will help address local patient access to expensive drugs while serving to attract international manufacturers to India. The Department of Biotechnology and Central Drugs Standard Control Organisation developed the regulatory framework with input from industry and academia. Under the new guidelines, manufacturers must prove similarity to a reference biologic already approved in India or licensed and sold for at least four years in a regulated market. The biosimilar should be comparable to the innovator drug in safety, efficacy and quality as demonstrated by analytical and clinical trials and the preclinical and clinical studies should also be comparative in nature. Approval “without involved clinical trials” is possible if manufacturers prove close similarity to its reference product, and show consistency in production process. Present article cover the all the aspects of Biosimilar on Indian prospect: How they grow and impact on society.

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INTRODUCTION

Biopharmaceutical drugs have become an essential part of modern pharmacotherapy. These comprise proteins derived from recombinant DNA technology and hybridoma technique. Examples include biological proteins (cytokines, hormones, and clotting factors), monoclonal antibodies, vaccines, cell and tissue based therapies. Living organisms such as plant and animal cells, bacteria, viruses and yeast are employed for the production of biopharmaceuticals. Owing to affordability and easy accessibility, biosimilars have established a good reputation among healthcare professionals. Though biosimilars are gaining popularity in national and international markets, it is important to remember that the biosimilars are not biological generics. These are rather unique molecules which are supported by only limited clinical data at the time of approval. [Nowicki] Therefore, there are concerns regarding their efficacy, long-term safety and immunogenicity. In India because its acceptance is great depends upon the need of society, affordability, and applicability and various health resources and finally economy of consumer and country.

Chemical as therapeutic molecules: A long history of chemical in Indian pharmaceuticals products are accepted, the first Indian pharmaceutical company “Bangol Chemical, Kolkata” is one of chemical industry which produced chemical

approved as Drug. Till date Indian pharmaceutical industry is governed by central ministry of chemical and fertilizer. Before biological product, the entire drug is chemical, but due to development of economical and education status and India are enjoying the all the field of science and Indian are hold the position in Multinational and International company and research institutions.

Development in biotechnology and Microbiology: Seed of biosimilar: From the last two decades Indian microbiology and biotechnology are well developed and engaged in development of the product which is accepted by human being, not only as medicine but as daily product. Now Indian government has set a no of Biotechnology Park, act as catalyst for the Indian biological/biosimilar. Specially with the help of recombinant DNA technology, control gene expression or antibody technology, recombinant hormones, growth factor, blood product, monoclonal anti-body based product, recombinant vaccines, gene and cell therapy biological products, thrombolytic agents, interferon, interleukins. (Sekhon), this kind of product is very important and helpful of treatment to the life threatening and rare illnesses such as cancer, diabetes, anemia, rheumatoid arthritis and multiple sclerosis and growth regulator hormones (Leader) monoclonal antibodies and recombinant protein products. Biologics are some of the best treatment options for serious medical conditions such as cancer, autoimmune diseases, and Alzheimer's. Unlike traditional chemical drugs, biologics are made from living organisms and are significantly more complex.

*Corresponding author: Khomendra Kumar Sarwa,
Department of Pharmacy, Govt. Girls Polytechnic, Raipur, Chhattisgarh,
India

How bear the pressure from health sector: India is a developing country and expends the lot of budget for growth of health sector, so Indian pharmaceuticals sector most of the feel the pressure for development of low cost product with similar potency and therapeutic potential (Roger, /SEKHON). This pressure is expected to well bear by biotechnology sector and similar product with generic version of original innovator product (Roger, Avidor, IMS, Hincal) called Biosimilars. There are about 100 biopharmaceutical companies actively involved in research and development, manufacturing and marketing of biologics in India and the country has witnessed drastic increase in the number of branded biosimilars in the last few years.

Concept of Biosimilars: For complex molecular drug an innovator puts a drug in market after proper approval for regulatory authorities: obviously it has a brand name it is protected under patent rights its structure may be correctly known or not known. Another manufacturer may discover complex molecule using different source of cloning or process with structure known or not known. The complex molecule has similar action as that of 1st innovator.

Its biosimilar

How hot is biosimilars?

Biosimilars was slated as the hot segment for investment by Indian companies. Yet it has not taken off the way it was predicted two years ago. "Indian companies are yet to grapple with the fact that biosimilars is a different ball game than small molecules. There is no room for short cuts in biosimilars research. The research is complex and investments in time and money are huge. Also, marketing them in markets such as the EU and the US require strict adherence to quality standards," says an industry expert who did not want to be named.

Terminology: Biosimilars term are reported in European magazines, similar other term "follow on pharmaceuticals" in United States and Japan, subsequently enter biological in Canada, Biocomparables in Mexico (Sekhon).

Biogeneric and biopharmaceutical are also reported: In General terms biosimilar are large molecule protein base complex compound having a three dimensional conformational structure. They are well differ from generic product. Biosimilar are produced by host cell line higher weight molecular compound. These terms are not accepted as similarity in between biological product some time generic (chemical) version with their biotechnology product having same/ similar therapeutic potential but differ in identical from innovator biopharmaceuticals (JAY). Most of the interesting fact that biosimilars are identical copy to an innovator but similar not the same, twin but not the clone. (SEKHON). This biosimilar term has come in focus from 2 and 3 years because the loss of patent protection by many first generation innovator products in the last few year and expectation that a few more will suffer the same fate in the next years. Definition "A biological product/ drug produced by genetic engineering techniques and claimed to be "similar" in terms of safety, efficacy and quality to a reference biologic, which has been granted a marketing authorization in India by DCGI on the basis of a complete dossier, and with a history of safe use in India." Indian Guidelines at 22.

Deference between Biological and generics: Biosimilars differ from generic drugs because their active ingredients are huge molecules with intricate structures. Such molecules are nearly impossible to replicate in every detail — even in the hands of the original manufacturer, minute variations in production yield slight differences. Unlike the relatively simple construction of a small-molecule drug, making a biosimilar is more like placing a complicated family recipe in the hands of a new chef. The overall result may be roughly the same, but it is not exactly how mother used to make it — and it may not precisely match the safety and therapeutic effects of the original.

What is a catalyst for Biosimilar: Secondary think, treatment of some chronic disease like cancer, paralysis, brain heamrage and diabetes rising cost of treatment with innovator. Beside the consumer factor, industrial factor also responsible for growth biosimilar like under TRIPS agreement, pre 1995 product patents were exempt thus granting some biological, the right to continue manufacturing. Some time at present biotechnology drugs are free from the drug price control order 1995, allowing independence in price setting

Development Problem: One of the biggest challenges in developing and manufacturing antibodies is proving the equivalence or similarity to the reference product. Antibodies are highly complex molecules with secondary and tertiary structures subject to post-translational modifications such as glycosylation. Many times they may be heterogeneous and contain a small population of antibody variants (microheterogeneity). Small alterations in process development can lead to unacceptable changes in safety and efficacy. It is also quite possible that the subtle differences encountered in a biosimilar antibody in terms of molecular structure cannot be detected by current methods. It could be a challenge to demonstrate that such differences have no impact on clinical efficacy and safety. This complexity is reflected in the amount of documentation required to be submitted for the marketing authorisation application,

Is it economical?

Development of biosimilar is very expensive, due to the difference in chemical process especially process, process instrument and training process, how Indian company bear this cost without enhancing price of product is big issue over Indian manufacturer including the cost or R&D necessary expenses which make identical copy of original innovator product or generic product. Biosynthesis is very specific in nature and govern by no of process variable and strongly affect the product characteristic. If Indian company merge and omit the difference between pharmaceutical and biotechnology they can easy attend the all necessary manpower and technology energy.

Is Indian Company are ready to bear the initial expenses ?

In Indian pharmaceutical industry basically two types of manufacturer one having a big capital (big manufacture/multinational) and having an intermediate capital (small manufacturer), for the both manage of initial expense is bother condition especially on small industry based on loan licenses and totally depends on other for technology: can they able to compete in market\$, whats the future of their loan\$, how long they exist if biosimilar has replace the generic

version totally or partially\$. Most of attention giving point is a large no of employee are work in this small scale pharmaceutical sector, and greatly affect the Indian economics, so before taking a many major decision about existing of biosimilar in Indian prospect a close and depth study of what the long term effect of biosimilar in foreign country will examined. At present initial the cost of setup of production and R&D, will be bear by cost of production and finally provided by consumer pockets can we ready for that\$.

Is it safe for society?

The two biosimilar have different origin-
The two biosimilars may have same therapeutic effect-
But may have different side effect and toxicology-
Hence require thorough testing-

Great example is polymer industry, there are no doubt about applicability of polymer on all part of human live and it totally change the life style of human being, but it strongly effects the other metal industry and small scale industry, beside their environmental effect is now a serious problem for any government. Imitation is enhanced the critical situation for any government not only the developing country but also for developed country. So before making an any regulation in Indian prospect government should aware about all aspect which ultimately determined the growth of biosimilar product in India and there export value and finally related with Indian economic. Genetic engineering is a school whether biosimilars are tailored and packed in pharmaceutical institution and applied on human being, where each patients have an identical genetic structure and a common phenomenon is extrusion of foreign material by body. Specified word immunogenicity is of particular concern for protein since the immune system is recognizing as toxin so performance of the product may differ from patient to patient, in this prospect clinical data are necessary before give an approval to each biosimilar and considered as safe for human and animal being and what their limit completely considered as equivalent to generic chemical product.

What the current status of Biosimilar: When you go through the status of biotechnology product in India was around US\$ 200 million in year 2008; it was reaches to US\$580million by 2012 and expected to worth more than US\$ 167 billion by 2015 (Global Biopharmaceutical Market Report (2010–2015) IMARC October 29, 2010:234 Pages. Pub ID: IMRC2849563.). If they will achieve no doubt around five of the top ten position in the pharmaceutical industry (<http://www.icis.com/Articles/2010/02/15/9333235/followw-on-biologicspresent-opportunity-to-big-pharma.html>).

Is it acceptable in Indian circumstance?

In Indian health care system, rural and urban cover more part compare to city and town are, where how biosimilar and protein based drugs are handled is a big question over Indian for acceptance\$ How and whether, they stored, one of the example Polio Vaccine, need a refrigeration temperature 2-8C, how they maintained it up to the whole life of product, Biotechnologist/microbiologist/pharmacist have technical skill about of drug product including storage and handle but number of non-trained non educated health worker engaged on drug dispensing. Now a day National Rural Health Program in

one of the example whether a health worker, nurses, maintain including NGO have important position on running of this program and unofficially dispense the medicines. So the safety and applicability of biosimilar expected to affected by this system/how government have monitor the use of biological is controversial. Similarly a number of frauds registered medical practitioner are work in rural and urban area, this is a big issue for discussion over Indian drug regulation\$ before approving new biosimilar product.

India is living in villages, around 80% of the population are living in a rural and urban area, in an survey 70% population are living in BPL (below than poverty line) and, approximate 85% of the population have no health insurance, In this condition how biosimilar are biological product manufacturer insure the safety is big issue same time above than 1.1 cr population is itself as power, which can able to turn of the any flow if used in a great direction, but how government can monitor the each product for microbial or viral contamination; endotoxin, exotoxins, pyrogens; No nucleic acids (which were thought capable of delivering oncogenes and transforming the DNA of a potential patient.

How Indian drug regulation Authority make Guidelines?

A number of acts and rules govern the genetically modified drug and rDNA product including new regulation

1. Environmental (Protection)Act, 1986 and Rules, 1999
2. Industrial (Development and Regulation) Act, 1951; New Industrial Policy and Procedure, Exim Policy
3. Drug and Cosmetic Act, 1940 and Rules 1945
4. Pharmaceutical Policy, 2002
5. Seeds Act 1966 and Seeds Rules, 1968
6. Seeds (Control) order, 1983
7. PVP and Farmer Right Act, 2001
8. Food Safety and Standard Act, 2006

So preparation of biological and biosimilars with the help of genetic modification drug and recombinant technology with the following the following act along with new biosimilar guidelines release on august 2012 is not easy for any manufacturer. Each coin has two side, one is merit and another is demerits. Beside the applicability of biosimilar in India, how indian FDA has handle the approval process of biosimilar. Each similar products are different in structure even addition of new process, new formulation and even new containers and closure affect the protein structure (B1). So Indian regulation authority assay the each product, when they make standards and what are criteria over biosimilar are matched. Although I believe that many parts of the Affordable Care are bad and will weaken care the FDA's ability to approve biosimilars will foster investment, ensure patient safety, expand patient access to biotech medicines. Most importantly, the FDA will continue its work to develop a regulatory pathway for safe and effective use of biosimilars. One challenge for regulators remains patient safety. Because biologics are made from living organisms, biosimilars can only be similar to their innovator product, never identical. Consequently, these copycat drugs can present safety challenges above and beyond traditional chemical drugs. Any small difference in the structure or makeup of a biosimilar may cause serious side effects, if not properly regulated. Therefore, the FDA cannot take shortcuts. The FDA should include robust clinical testing for biosimilars,

unique product names, labels and codes, as well as a means to track and trace these advanced medicines. Additionally, requiring a tracing system will make it easier to identify and remove a faulty product from the pharmacy shelves and medicine cabinets. Updated on 16 August 2012 The biotechnology industry in India says while the guidelines will raise the bar for domestic manufacturers, the industry still needs a single agency like that in the US and Europe for clearances.

Expectation of manufacturer of biological: India's biotechnology industry believes more needs to be done to streamline the existing regulatory framework for biologics and vaccines. In the last few years, India has seen a robust growth in its biosimilars portfolio. The growing biosimilars market offers huge potential for companies involved in research and development and manufacturing. Biosimilars can also go a long way in meeting India's need for affordable healthcare for its huge 1.2 billion population. The guidelines have taken into consideration exceptions in the generally outlined product development pathway. "For example, the innovator product may have been developed in a particular host, but if the current expression systems are better in terms of quality of the product and yield, the guidelines have provisions for approval of products developed in a different host on a case-to-case basis. Similarly, approval of new formulation of an existing drug can be sought based on sound scientific data," points out Mr Subramaniam. "However, some areas such as critical indications (clinical trials involving infants) or where very long-term end points are measured could have been further clarified leading to faster approval of the drugs." Dr Ella also raised concerns over some points in the draft. "It is too complex due to the involvement of multiple departments from different ministries. The Indian biotech industry requires a single window regulatory authority that is strict and transparent. The current system has companies applying to multiple regulatory authorities under different ministries to obtain permissions for biologic material import, product development, preclinical testing, clinical trials, marketing authorizations. Central Drugs Laboratory (CDL), Kolkata, has to take responsibility for the availability of authorized reference standards and their identities, which currently is under ambiguity. CDL Kolkata also could be developed along the lines of CDL, Kasauli, which receives batch samples for vaccines for testing and product release.

How traditional health care system handle biosimilar: The key question is selling of biological and biosimilar in India, is Indian health workers (engaged in dispensing of medicine) preferred substitute to an innovator biological and chemical generic. Up to the 2012 Indian drug regulation does not have any clear guidelines for acceptance of biological, how the differentiate the original innovator, because biosimilar are proteins, more complex than small molecules, it is not possible to demonstrate the identical nature of two biological product arising from different manufacturer source and need additional non clinical and clinical data to demonstrate that they have an equivalent safety and efficacy profile to the original product (B1/page 1). Biologics are so complex that minor manufacturing changes often change the properties of the drug.

Why Biosimilar are not as simple chemical moiety: At present chemical moiety is well accepted as medicine they are

simple well characterized but biologicals are not simple, because they are cells or living organism or as protein (14/SEKHON), probably 100 to 1000 time larger having a amino acid as monomer unit with different sequence by peptide bonds to form polypeptide (15/SEKHON).

Why approval is problematic: Chemical moiety are organized so wide range of novel techniques for characterization is possible and make a quality standard, but biosimilar is complex and in practice differentiated by amino acid with inherent complexity, so how differentiate the each biosimilar product which are similar in therapeutic action, now a day pharmacodynamics and pharmacokinetic parameter is not universal standard for comparison of two generic product but characterization of physicochemical parameter and pharmaceutical properties are universal parameter for comparison. In the view of biological product change in sequence of single amino acid in complex proteins structure may affect the physicochemical and pharmaceutical factor with or without changing/ alteration in therapeutic action but this alteration in basic amino acid sequence for development of biosimilar from innovator. In the another turns each biological and biosimilar product obviously differ in chemical and physiological properties, which affect the pharmaceutical parameter. If authority will set pharmacodynamics and pharmacokinetic parameter as stander for individual product is not practical possible. All this fact preparation of standard or quality control parameter is well complex compared to generic molecules. No doubt about technical skill of Indian but how much time taken by scientist for development\$ can we wait. According to this new pathway, biological products will be approved on demonstrating that they are biosimilar to, or interchangeable with, a biological product that is already approved by the FDA. When it comes to getting new biosimilars products to the market, the FDA has taken an innovative approach to support their development at every step of the process.

Need of clinical data: Europe's framework for approving biosimilars was established in 2004, and copies of three drugs have already hit the European market. Some observers expect the FDA guidelines to be broadly similar to the European ones, which generally require clinical tests of biosimilars, but the extent and nature of the tests depends on the class of drugs being copied. A relatively simple and familiar molecule such as insulin, for example, may require less testing than a complex protein carrying several chemical modifications. All biosimilars will probably require some clinical trials in the United States, says Mark McCamish, head of global biopharmaceutical development at Sandoz, a generics company based in Holzkirchen, Germany, but the FDA should expect a lively debate about how extensive those clinical trials must be.

"The requirement for comparative clinical trials will certainly have an impact on the company's budget allocation,"

Relationship between Indian regulation and others: These Guidelines will be implemented on August 15. India is an important jurisdiction in the world of biosimilars ("similar biologics" in Indian parlance); not only does it have a burgeoning market for biologics, it has a vibrant pharmaceutical industry which is leading the way in biosimilar

development. Thus the Indian Guidelines may well have an impact on the global biosimilar marketplace. Comparison between the Indian Guidelines and the U.S. and European regimes demonstrates an overall similarity and philosophy and approach, but some important differences that may differentiate the Indian biologics market. The similarity of the requirements plus the lack of market exclusivity for first-approved products may make India a logical jumping-off point for a global approval strategy. Unlike in the U.S., the Indian authorities have been approving Indian-produced "generic" biologics with reference products that have been approved in the U.S. or Europe under an *ad hoc* abbreviated approval pathway for many years.

Who get profit Manufacturer of Consumer or country:

Some companies see biosimilars as a low-risk way to bolster dwindling drug pipelines. Biological drugs are expensive, and even with a 20–30% reduction in the original price, biosimilars can still pull in a huge profit. "Not a day goes by when you don't read a press release saying some company is getting into biosimilars," says Michael Malecki, head of the biosimilars group at Decision Resources, a market-research firm based in Burlington, Massachusetts. But if regulators require extensive testing, biosimilars could falter. For example, in 2006, the Croatian drug maker Pliva decided to abandon its copy of the best-selling anaemia drug erythropoietin after learning that the EMA would require more clinical trials than the company had anticipated.

Opinion of Manufacturers on current biosimilar drug regulation:

In pharmerging countries, the emergence of biosimilars is being seen as a key macroeconomic factor for generating revenues by attracting foreign direct investment in starting manufacturing units. He adds that the guidelines state that all biosimilars should be compared to the reference or innovator product through all phases of development. "There is clarity on the quality and quantity of data expected, for example, the number of batches, bioassays and analysis of products for post translational modifications. Animal studies have also been rationalized by allowing short-term studies in relevant animal species. When such models are not available, it is recommended to follow Schedule Y of the Drugs and Cosmetics Act. Some redundant studies have been eliminated reflecting the current scientific understanding. Guidelines laid out for clinical evaluation, pre clinical evaluation, manufacturing process validations, product characterization, etc. are welcome and these guidelines should be enforced strictly across the industry.

Compulsory Licensing on Biologicals: Most of the manufacturer does not feel the need of compulsory licensing of innovative products or technology generally is an effective means of promoting access or affordability of healthcare. Moreover, it undermines incentives for companies and individuals to innovate in India, since it creates uncertainty about receiving economic returns for their innovations, the participants revealed. Indiscriminate use of compulsory licenses would thus jeopardize India's goal of developing a research oriented biotechnology industry, and is unsound policy, according to participants. All participants agreed that the issuance of India's Guidelines on Similar Biologics is a step in the right direction. "The guidelines recognize the scientific and regulatory complexities presented by the development and manufacture of biologic medicines.

Collaboration of Indian and globe companies: A milestone for Biosimilar Market: There are mixed opinions over whether this would impact Biocon's prospective partnerships with global drug giants in the future and whether it has affected the global community's confidence in Indian companies. "Definitely, there will be some dent in the trust factor. But Biocon as a brand is strong enough to tide over this scenario. They already have many regional partners and will continue to do their business,"

Recent deals between Mumbai-based Emcure Pharma and Basel-based Roche and between Merck Serono and Dr. Reddy's Laboratories in Hyderabad are a testament to India's growing attractiveness as a biosimilars manufacturing hub. While pointing out that every partnership deal goes through extensive scientific, commercial and market due diligence with milestones clearly articulated. "Hence, if any deal goes through or fails, it is dependent on its merits and achievement of milestones and not on the overall corporate performance. Biocon's future partnerships with MNCs will be based on the diligence of the research milestones and future potential of the product. Current termination will not have any impact on the future partnerships," he remarks. Regardless of the consequences of this deal annulment, MNCs are here to stay in India. "At the end of the day, India is a big market for MNCs and they will never think of restricting themselves from striking collaborations with Indian companies and investing in the country," adds Mr Sudarshan Padmanabhan of Prabhudas Lilladher. The question remains as to who could be Biocon's next prospective commercialization partner who could give the former the same bandwidth as Pfizer. "Globally today, Novo-Nordisk, Eli-Lilly and Sanofi Aventis are the leading names in the insulin market. Biocon can look at these partners.

Indian Players for global Biosimilar Market

- India is exposed to vast opportunities in biosimilars
- Competent houses are already making great headway
- Govt has to develop the pathways for safe arrival of biosimilars in indian market
- Pharmacovigellence is going to play very prominent role in the advent of biosimilars
- Lot of cautions precautions and warnings will be encountered

A responsible role is required to be played by all and every one. Every one has to rise above all motives to provide safe biosimilars.

Challenge for Indian Manufacturer in Global: These regulatory guidelines will also help indian biosimilars developers to enter the globe market. So far, the biggest challenge for Asian players that have high dominance in generics drugs in Asia, is the absence of clearly defined regulations in different countries to develop biosimilars. They have limited close interactions with regulatory agencies, which is very critical for a successful biosimilar application. With the clarity coming from the US, the Asian players will now get a chance to develop generic drugs for the vast market of the US, supplying cheaper versions of highly crucial drugs. Asia already has many companies such as Cipla, Dr Reddy's Laboratories, Biocon, Wockhardt, Samsung, LG Life Sciences, Celltrion, SK Chemicals, Simcere and ScinoPharm that have proved their capabilities and competitiveness in

developing and commercializing biosimilars for the Asia market. Reacting to the developments, "There is no defined guidelines and requirements for all biosimilars products and in cases where they exist, there is no guarantee that they will not change."

This can be looked at from three angles: One is that many Indian players have experimented on different business models. Some have succeeded, some have partially succeeded, and others have failed. We have not analyzed the reasons for the failures or partial successes and learnt from them. Secondly, pharma companies in emerging markets need leaders to address issues in the region. There is a leadership failure in getting the direction right. Lastly, in terms of regulations, we are just not attractive enough as compared to the emerging markets of China and Korea,"

What the next for Biologicals: What follows next is industry collaboration in the implementation of these guidelines in a manner that continues to protect patient safety and ensure continued R&D of new cures and treatments," said Mr Alan Eisenberg. However, he pointed out that India needs to recognize scientific differences between small molecule therapeutics and biologics. It was a path-breaking deal that had many eye balls rolling. Industry soothsayers predicted it to be the beginning of an exponential growth for the biotech industry in India. The landmark \$350-million deal inked between global pharmaceutical player Pfizer and India's top biotechnology company Biocon, signed on October 2010, was viewed as a catalyst bolstering confidence of multinational firms in Indian companies, which could spur more such R&D collaborations in the future. According to the strategic deal, Pfizer had to pay \$200 million for exclusive rights to globally commercialize several of Biocon's insulin products -- Recombinant Human Insulin, Glargine, and Lispro. Biocon was to receive an additional payment of \$150 million from Pfizer towards further development of drugs and to meet regulatory milestones. Biocon was also to receive payment linked with Pfizer's sale of the insulin products. Indeed a win-win situation for both parties, bringing together Pfizer's strong marketing and commercialization capabilities, especially in the highly regulated developed markets of the world, and Biocon's expertise in biotech R&D. The insulin products were slated to roll out in the emerging markets by 2011, followed by Europe and the US in 2012 and 2015, respectively. The industry was in for a shock when this much-talked about deal was amicably shelved in less than 18 months. While the reasons for calling off of the deal is yet to be revealed in a press statement, both companies mentioned that their individual priorities for their respective biosimilars businesses propelled them to move forward independently. As of March 12, 2012, all rights licensed to Pfizer will revert to Biocon, and all insulin distributed under the brand names Univia and Glarvia will be commercially available from Biocon only, and will be exclusively manufactured, supplied, marketed and supported by Biocon. Also, Biocon would retain the upfront payment of \$100 million and also the \$100 million that Pfizer paid as an escrow account for Biocon to develop insulin products. It will, however, have to forgo the \$150 million that it would have received from Pfizer for further developments and meeting regulatory milestones. Reacting to the developments, Ms Kiran Mazumdar-Shaw, chairman and managing director, Biocon, said, "We remain committed to delivering our biosimilars insulins portfolio to global markets in our

endeavor to make a difference to diabetic patients across emerging and developed economies. We will continue to work with our existing partners in several markets and will pursue a commercial strategy on our own and through new alliances in other markets." "Cost of development coupled with huge marketing costs has restricted biosimilars drugs to very few niche areas, such as diabetes, oncology and rheumatology. The highest selling segment in India is still the anti-infectives and cough and cold therapies that were launched almost 20 years ago. Biosimilars need to go beyond the current areas it is serving to make a real dent in the market,"

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