GUEST COLUMN

Enabling Global Health: India's Rise in Biologics Accessibility

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Dr. Mahesh Bhalgat emphasizes about the India's role in enabling access of biologics to the world. He also spoke about the Research and Development (R&D) Initiatives and Investments in next-generation Biologics.

Biologics, a class of medical products derived from living organisms, has revolutionized the healthcare industry by providing innovative treatments for a wide range of diseases, including cancer, autoimmune disorders, and rare genetic conditions. However, despite their efficacy, biologics often come with exorbitant price tags, limiting access for many patients globally. In this context, India has emerged as a crucial player in democratizing access to biologics worldwide. Through its robust pharmaceutical industry, regulatory framework, and commitment to affordable healthcare, India has significantly contributed to making biologics more accessible to patients worldwide. Biologics represent a diverse array of therapeutic agents, including vaccines, monoclonal antibodies, recombinant proteins, and gene therapies. Unlike traditional small molecule drugs, biologics are complex molecules produced using living organisms such as bacteria, yeast, or mammalian cells. Their complexity often translates into higher manufacturing costs, making them expensive for patients and healthcare systems.

India's pharmaceutical industry is renowned globally for its expertise in manufacturing generic drugs and biosimilars, which are biologic products that are highly similar to already approved biologics.

The country's biopharmaceutical sector benefits from skilled workforce, cost-effective manufacturing processes, excellent demographic dividend coming from a young population, access to a large trial

Some examples, which are non-exhaustive include biosimilar versions of

- Insulin including insulin glargine and insuline aspart developed by Biocon.
- Trastuzumab, a monoclonal antibody used in the treatment of breast cancer and gastric cancer, developed by Dr. Reddy's Laboratories.
- Adalimumab, a tumor necrosis factor (TNF) inhibitor used in the treatment of autoimmune diseases such as rheumatoid arthritis and psoriasis, developed by Zydus Cadila.
- Pegfilgrastim, a granulocyte colony-stimulating factor (G-CSF) used to stimulate the production of white blood cells in cancer patients undergoing chemotherapy, developed by Intas Pharmaceuticals.
- Etanercept, a TNF inhibitor used in the treatment of autoimmune diseases such as rheumatoid arthritis and psoriasis, developed by Sun Pharmaceuticals

population and an evolving conducive regulatory environment. These factors have positioned India as a leading supplier of affordable medicines to both domestic and international markets. India launched the National Biopharma Mission in 2017 as part of its larger 'Make in India' initiative. This mission focuses on developing biopharmaceuticals, including vaccines, biosimilars, and biologics, to address healthcare challenges and enhance India's competitiveness in the global biotech market. Commendations from Dr. Kiran Mazumdar-Shaw and Dr. Cyrus S Poonawalla highlight constant CAGR of >50% for the last 5 years for the Biopharma sector and >24 WHO-approved vaccines for global supply. Association of Biotechnology Led Enterprises (ABLE) in India estimates the size of the broader economic impact for biologics to grow at a compounded annual growth rate (CAGR) of 22% to become USD 12bn by 2025. Contract research services in early discovery and clinical development for biologics and biosimilars in India are estimated to be USD 200Mn and growing at a CAGR of at upwards of 20% (source: Association of Biotechnology Led Enterprises: ABLE)

India is a major supplier of generics worldwide, meeting 50% of Africa's drug needs, 40% of the USA's, and approximately 25% of the UK's. While this "Pharmacy of the World" reputation comes from small molecule generics, there is a noticeable shift in India towards high-value drugs, beginning with value-added generics and now expanding into innovative medicines. India is also advancing in biologics, evident in its production of Covid vaccines, and biosimilars, recently highlighted through the approval of Ogivri (a Trastuzumab biosimilar) in multiple countries. Indian CDMOs enjoy higher operating margins (35% compared to 20% in the West), which encourages investment in biologics technologies. The biosimilars market is expected to grow six-fold in the next 6 years, with India having around 200 biosimilars in development. Biosimilar development in India takes 3-5 years on average, compared to 7 years in the West, at a cost that may be sometimes 10-times lower. Like the growth in generics, India's expertise in biologics is likely to fuel the expansion of CRO and CDMO services. Consequently, India is poised to lead in biologics growth globally in the next 5 years, with a burgeoning bio CDMO sector, similar to what is seen in the APAC region.

R&D Initiatives and Investments in Next-Generation Biologics

India's biopharmaceutical sector is characterized by a vibrant ecosystem of academic institutions, research organizations, and biotechnology companies engaged in innovative R&D activities. These efforts encompass a wide range of areas, including bioprocess optimization, cell line development, structure-function characterization, and novel drug delivery systems aimed at enhancing the efficiency, safety, and affordability of biologic therapies. Government support through initiatives such as the Department of Biotechnology's Biotechnology Industry Research Assistance Council (BIRAC) and various grant schemes encourages innovation and entrepreneurship in biotechnology.

These initiatives provide funding, infrastructure, and mentorship to researchers and startups, facilitating the translation of innovative ideas into commercially viable biologic products. The focus is on the development of next-generation biologics, including cell and gene therapies, RNA-based therapeutics, and therapeutic precision monoclonal antibodies targeting emerging diseases.

Emerging Biotechnology Hubs and Collaborations with Global Partners

India's biotechnology hubs, such as Hyderabad, Bengaluru, Ahmedabad, and Pune, serve as focal points for biopharmaceutical innovation and manufacturing. These regions host excellent research institutions, bio-parks, and industrial clusters, attracting domestic and international investments in biotechnology. The presence of state-of-the-art facilities for bioprocessing, analytics, and clinical research further accelerates the development and commercialization of biologics. Furthermore, India's participation in international consortia and research networks facilitates knowledge exchange and capacity building in biopharmaceutical innovation. Collaborations with organizations such as the Bill & Melinda Gates Foundation, the Wellcome Trust, and the Global Alliance for Vaccines and Immunization (IAVI/GAVI) contribute to addressing global health challenges and expanding access to biologic interventions in resource-limited settings.

India has taken several initiatives to make biologics more accessible and affordable globally, primarily through its robust generic pharmaceutical industry and policies favoring the production and distribution of affordable medicines. Some specific initiatives include:

Introduction of Biosimilar Guidelines: India's central drug regulatory authority CDSCO introduced guidelines for the development and approval of biosimilar products, allowing Indian pharmaceutical companies to produce cheaper versions of biologics after patent expiration.

Compulsory Licensing: India has provisions for issuing compulsory licenses, allowing domestic companies to produce generic versions of patented biologic drugs in the interest of public health. This has been utilized in cases where patented drugs are priced prohibitively high, enabling the production of more affordable alternatives.

Encouraging Export of Generic Medicines: India has actively encouraged the export of generic medicines, including biologics, to developing countries and regions facing health crises. This not only promotes accessibility but also strengthens India's position as the "pharmacy of the world."

Partnerships and Collaborations: Indian pharmaceutical companies often collaborate with international organizations, governments, and NGOs to expand access to biologics in low- and middle-income countries. These partnerships may involve technology transfer, capacity building, or joint ventures to manufacture and distribute affordable biologics.

Role of Chemistry, Manufacturing, and Controls (CMC)

CMC plays a crucial role in enabling access to biologics worldwide, and India's CMC capabilities contribute significantly to this process. Indian biotech companies and research institutions conduct research to engineer and optimize cell lines to produce biologic drugs. Efficient cell line development ensures high productivity, scalability, and consistency in biologics production. Indian biopharmaceutical companies focus on process development to optimize bioproduction processes and improve manufacturing efficiency. Process development involves optimizing cell culture conditions, fermentation parameters, downstream purification techniques, and formulation strategies to maximize yield, quality, and cost-effectiveness. India's expertise in process development enables the production of high-quality biologics at competitive costs, enhancing accessibility for patients worldwide.

Structural and functional characterization is essential for ensuring the safety, efficacy, and quality of biologic drugs. Indian researchers and analytical laboratories specialize in conducting comprehensive analytical studies to characterize the structure, post-translational modifications, and biological activity of biologic molecules. Advanced analytical techniques, such as mass spectrometry, chromatography, spectroscopy, and bioassays, are employed to assess the critical

quality attributes of biologics, ensuring consistency and comparability throughout the manufacturing process. Leveraging the talent base in India and looking at the growth of the biologics sector in India, companies such as Veeda, a traditional clinical research organization have also diversified into specialized analytical and process development CRO service providers. Such diversification, which is built on the foundation of strong biologics and analytical skills, has further strengthened the ecosystem in India.

Influence on Pricing, Challenges and Opportunities

The entry of Indian biosimilars into the global market has exerted downward pressure on the prices of biologic therapies. Competition from Indian manufacturers has compelled originator companies to reconsider their pricing strategies, leading to more competitive pricing and improved affordability for patients. Despite its significant contributions, India faces several challenges in its quest to enhance global access to biologics. Intellectual property rights issues, regulatory complexities, and the need for continuous innovation pose hurdles to the growth of India's biopharmaceutical sector. However, these challenges also present opportunities for collaboration, innovation, and policy reform to overcome barriers and further expand access to biologic therapies worldwide. The entry of smaller specialized biologics CMC service providers such as Veeda, maintains affordability, due to their smaller size and agility.

Clinical Research and Trials

India has a large and diverse patient population, offering access to a wide range of genetic backgrounds and disease profiles. This diversity is crucial for conducting clinical trials to assess the safety, efficacy, and pharmacokinetics of biologic drugs across different populations, thereby enhancing the generalizability of study results. Conducting clinical trials in India is more cost-effective compared to many Western countries due to lower operational costs, site expenses, and regulatory fees. Recruitment of patients across multiple therapeutic areas can be much faster as compared to many developed countries, especially through the use of real-world data based approaches. This cost advantage and the speed of recruitment attracts multinational pharmaceutical companies and contract research organizations (CROs) to conduct clinical trials in India, leading to increased access to biologics for patients worldwide. India has a pool of experienced investigators, clinicians, and research professionals who are proficient in conducting clinical trials according to international standards and guidelines.

Additionally, India has research infrastructure, including hospitals, clinics, and research centres, equipped to conduct various phases of clinical trials for biologics. India's improving regulatory approval process and efficient patient recruitment often result in shorter trial timelines compared to other countries. Accelerated trial timelines enable faster drug development and regulatory approval, expediting

the availability of biologics to patients worldwide. With an overall population of 1.4 billion, India offers access to patient populations with untreated or under-treated medical conditions, providing opportunities to evaluate the efficacy of biologic drugs in disease areas with significant unmet medical needs.

With the growing emphasis on decentralized clinical trials and inclusion of diverse populations, India is well equipped to contribute valuable data to support regulatory submissions and market approvals for biologics globally. Indian CROs and academic institutions collaborate with international partners to conduct multicenter clinical trials and share data. In some cases, Indian CROs, such as Veeda, have globalized their footprint not only through collaborations, but also by acquiring facilities in the West. This provides speed and consistency in global trial execution through a single reputed and established CRO. In addition, this facilitates the generation of robust clinical evidence, strengthens regulatory submissions, and accelerates the global acceptance and adoption of biologics. India specifically gains by getting access to biologic drugs earlier, which is a boon to patients, and doctors who now have more approaches for disease management. An additional factor that impacts access is, India's expertise in biosimilar development which allows manufacturing of high quality biologics at affordable prices. Clinical trials conducted in India play a crucial role in demonstrating the similarity, safety, and efficacy of biosimilars, expanding access to essential biologic therapies for patients worldwide.

Regulatory Framework

India's regulatory framework plays a pivotal role in enabling the development and commercialization of biosimilars, an important mechanism for improving access to biologics drugs. The Central Drugs Standard Control Organization (CDSCO) oversee the approval and regulation of biologic products, ensuring adherence to stringent quality and safety standards. The regulatory pathway for biosimilars in India follows established guidelines set forth by international regulatory bodies such as the World Health Organization (WHO) and the U.S. Food and Drug Administration (FDA), facilitating acceptance of Indian-manufactured biosimilars in global markets.

New Drugs and Clinical Trials Rules, 2019 and The Drugs and Cosmetics Act, 1940, along with its associated rules and regulations, provides the legal framework for regulating drugs, including biologics, in India. The Act governs various aspects of drug manufacturing, import, distribution, and sale, ensuring compliance with quality standards and safety requirements. Biopharmaceutical companies are required to obtain

approval from the CDSCO's Drug Controller General of India (DCGI) before initiating clinical trials in India. The approval process involves the submission of detailed clinical trial protocols, investigational product information, and documentation demonstrating compliance with ethical and regulatory standards. Before the global biologics are allowed to be tested on Indian clinical trial participants, the Indian regulatory authorities ensure that they meet the desired standards of safety, efficacy, and quality. The regulatory requirements for global biologics are well aligned with international standards, although there may be specific Indian regulatory considerations and requirements that companies need to address. Additionally, India is increasingly playing a role in the global regulatory landscape for biologics, particularly in biosimilars. Indian biopharmaceutical companies are developing biosimilar versions of global biologic drugs and seeking regulatory approval not only in India but also in other countries and regions around the world. This involves navigating the regulatory requirements of multiple jurisdictions to ensure compliance and market access for their biosimilar products.

Conclusion

India's role in enabling access to biologics for patients worldwide is undeniably critical. Through its thriving pharmaceutical industry, trained workforce, regulatory framework, and commitment to affordability, India has emerged as a key player in democratizing access to life-saving biologic therapies. By producing high-quality biosimilars, nurturing biologics CMC service providers, fostering global partnerships, and advocating for equitable healthcare, India continues to make significant strides in ensuring that patients worldwide can benefit from the transformative potential of biologic medicines India's expertise in biologics is poised to have a significant impact on the global biotech market over the next five years in several ways:

- Increased Access to Affordable Biologics
- Market Expansion in Emerging Economies (Asia, Africa and Latin America)
- Competition and Price Reductions
- Research and Innovation Collaboration
- Regulatory Harmonization and Standards Alignment

With access to a very large population, India is well suited to participate in global clinical trials, therefore opening the Indian market for manufacturers early. As the global demand for biologics continues to rise, India's contributions will remain indispensable in shaping a more accessible and inclusive healthcare landscape for all.

As the world continues to grapple with complex healthcare challenges, India's expertise, infrastructure, and commitment to equitable healthcare will remain instrumental in shaping a more inclusive and sustainable future for biologic medicines. India has made rapid progress in fostering innovation and promoting collaboration. The country is poised to make valuable contributions towards the advancement of biotechnology and the improvement of global health outcomes. ■