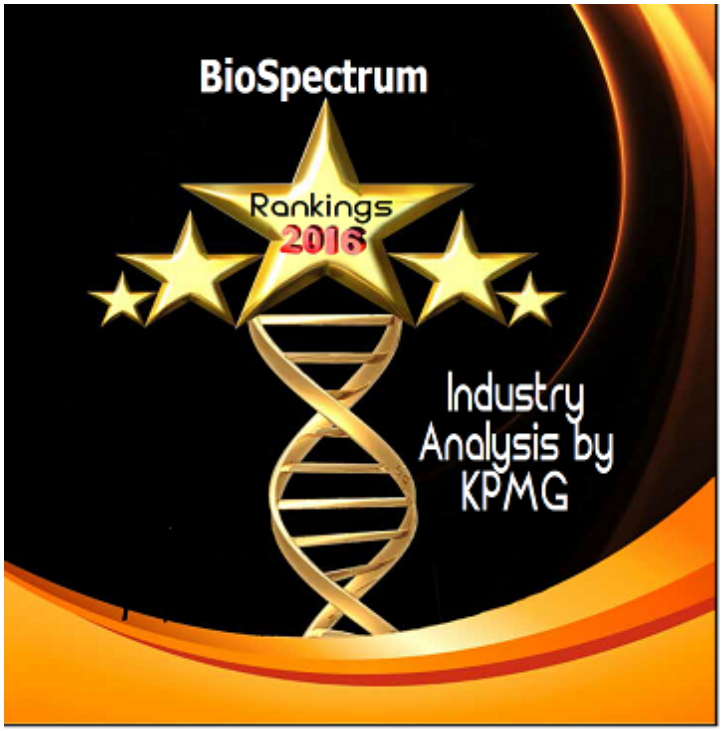
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BioSpectrum ranking Survey: KPMG Analysis



Global biotechnology market

Globally, the biotechnology industry, part of the life sciences sector has emerged as an attractive segment and is expected to grow by 37 percent at a Compound Annual Growth Rate (CAGR) of 8.2 percent over the four-year period 2015-19.

This growth, although single digit, is significantly higher than the more traditional segments in the life sciences sector, such as pharmaceuticals (expected to grow at a CAGR of approximately 4 percent during 2015-19).

The global sales contribution of biologic drugs in the total drug market is expected to increase from 23 percent in 2014 to 27 percent in 2020.

The Americas and Europe currently account for the largest share in the global biotechnology market; however, due to favourable government policies; a relatively low cost of conducting clinical trials and manufacturing products; and an improving healthcare ecosystem, higher growth is expected in the Asia Pacific (APAC) region.

Growth drivers of the global biotechnology market

Biotech-based products, including monoclonal antibodies and recombinant products are increasingly being used to effectively treat diseases such as cancer, rheumatoid arthritis, Hepatitis C and diabetes; the increasing prevalence of these diseases is likely to serve as a high-impact driver for this industry:

almost 14 million new cancer cases were diagnosed worldwide in 2012; by 2025, this number will be increase to 19 million new cases per annum

almost 400 million people had diabetes in 2015; the figure is expected to increase to 640 million by 2040

39 percent of the total drugs approved by the US FDA in 2015 were biologic drugs compared with 36 percent in 2014 and 22 percent in 2013; FDA approvals for biopharmaceutical products are expected to increase going forward.

Indian biotechnology market

India is the twelfth-largest biotechnology market in the world with a 2 percent share of the global market; it ranks third in APAC after Japan and China.

The Indian biotechnology sector was estimated at USD5.2 bn in 2015 with exports usually contributing to almost 50 percent of the total sales.

Increase in biotechnology applications providing effective and targeted treatment to patients; and about 400 biotechnology-based drugs and vaccines in clinical trial stage, targeting more than 200 diseases.

Market segmentation

India's biotech industry comprises biopharmaceuticals, bio-services, bio-agriculture, bioindustry and bioinformatics. Biopharmaceuticals is the largest segment of the Indian biotechnology market as it accounts for approximately 60 percent of

the total biotechnology sector 1 and is likely to remain so in the future as well. Biopharmaceuticals is dominated by vaccines, where India is the global leader by volume.

India's biopharmaceutical segment is one-third of the global vaccine market by volume.2 Further, India is the largest producer of Hepatitis B vaccines in the world.3
The Indian government has been keen to support the biotechnology industry's growth to counteract the threat of neglected tropical diseases. The 'Make in India' initiative along with other forms of input and assistance, is providing the necessary thrust to the indigenous production of biotech products.

Biopharmaceutical
Biopharmaceuticals comprise three main segments - vaccines, diagnostics and therapeutics.
There are as many as 100 players in the biopharmaceutical market in India, dominated naturally by vaccine makers.

Growth drivers
The sale of vaccines is expected to get a boost due to high demand from developing countries, and global efforts towards eradication of some diseases.
Therapeutics continue being the focus in Indian R&D, with human insulin being the most common area of research. Several opportunities in biosimilars are opening up for Indian companies with regulatory approval pathways in Europe and the U.S. becoming clearer.

Trend
Making a steady shift from traditional vaccines, Indian biopharmaceutical players are now stepping up their focus on biosimilars; several Indian pharmaceutical companies are also focussing on the biosimilar market.
With the FDA signalling changes in its stance on biosimilar medicines, Indian companies are now focussing on the U.S. market to tap this opportunity.
Additionally, Indian biopharmaceutical companies are making strong efforts to launch price-competitive bio-therapeutics and recombinant vaccines - both in India and in semi-regulated markets - likely to boost both revenue and margins.

Bio-services
The Bio-services segment mainly constitutes clinical research organisations that are involved in conducting clinical trials for domestic as well as international pharmaceutical companies.
India, which was once a lucrative clinical trial destination, has now less than 1.5 percent share in global clinical trials (by numbers) due to stringent regulatory laws.

Growth drivers
The Drugs Controller General of India has eased guidelines to conduct clinical trials in the country; these relaxations include removal in the restrictions on the number of clinical trials an investigator can undertake at a time, allowing clinical trials in less than 50-bedded hospitals etc.
With R&D cost increasing in developed markets, global pharmaceutical companies are outsourcing research services to enhance their drug pipeline. The average cost of conducting phase I studies in India is 50 percent lower that the U.S. and European nations.

Trends
Strategic alliances in the CRO industry has increased in the recent years. For example, a leading contract research and manufacturing organisation and a leading BioPharma company have been working together since 2007 to develop integrated capabilities in medicinal and process chemistry, biology, biotech, biomarkers, drug metabolism, pharmacokinetics and analytics.

Consolidation within the industry is another trend that one has observed in the recent years. For example, a leading Ahmedabad headquartered global lifesciences company acquired a Mumbai based CRO in 2014 to expand its services in clinical data management, pharmaceutical analytics and medical marketing.

Bio-agri
The Bio-agri segment mainly includes seed companies as well as technology development companies for seed producers
India has the fourth-largest area covered by genetically modified crops - largely BT cotton.
GM seeds follow a long drawn process of trials and approval. Due to the stringent regulations, only cotton is planted using GM seeds in India.

Growth Drivers
GM seeds could help improve yield of agriculture products, which can help address the rising food needs of the country

Trends
Increase in government interventions:
In March 2016, the government intervened to control cotton seed price in the country.

The government also launched GM Technology Agreement Guidelines, 2016, under which technology providers are required to compulsorily give licence to all applicants.2 However, these guidelines are yet to be implemented in the country.

Bio-industrial
The Bio-industrial segment primarily comprises enzyme-manufacturing and marketing companies.

India has a very low share in the global industrial enzyme market; however, we are in a sweet spot to leverage this opportunity with our low-cost manufacturing strength and R&D capabilities.

Lack of stringent government mandates have hurt the sector's potential. Interventions are required to promote usage of bio-enzymes.

Growth drivers
The Pharmaceutical sector is a prominent user of enzymes and therefore growth in pharmaceutical sector is expected to boost sale of enzymes as well
With stringent environmental laws and higher emphasis on energy conservation, demand for enzymes is expected to witness higher growth from various industries

Trends
Biotechnology companies in this space have started focusing on manufacturing cellulosic enzymes that aid the production of bio-fuels

Bioinformatics

The Bioinformatics segment is involved in the design and maintenance of extensive electronic databases for various biological systems.
Regulatory frameworks are required in the country to monitor and control genomic data.

Growth drivers
Availability of good infrastructure and skilled workers is likely to help the bioinformatics industry grow in India. The country possesses around 10 percent of the global professional and skilled bioinformaticians.3
There is thus a significant opportunity for India to utilise this talent pool in various areas, such as DNA sequencing, data mining, proteomics, functional genomics and molecule design simulation.

Trends
Increase in government funding and the opening of several bioinformatics institutes is expected to lead the future growth of the segment.

Increase in government support
Steps taken under the 'Make in India' initiative, such as new IP policy, setting up of biotech parks, entrepreneurship and skills development, can help position India as a leading hub for biotechnology products.

The Department of Biotechnology (DBT) has recently released the National Biotechnology Development Strategy 2015-20; implementation of which could help create and improve infrastructure for R&D and commercialisation; bring in investment capital, IP regime, technology transfer; help set up regulation standards, skills development etc

Emerging areas
With increased acceptance and demand for baiosimilars globally, India can potentially emerge as a key player in this segment. Many Indian companies have developed capabilities to manufacture biosimilars and have successfully launched them in the Indian market
The government has released draft guidelines in April 2016 to streamline the regulatory process for biosimilars and similar vaccines in India.
Domestic companies are also venturing into other emerging areas, such as cell therapies and regenerative medicine - which are still nascent in revenue terms but likely to grow rapidly in the near future.

Dominance of the biopharmaceuticals segment
The biopharmaceutical segment has been generating more than one-half of the Indian biotech industry's total revenues. The country is ranked as the world leader in the production of vaccines.
Pharmaceutical companies are also focussing on the biotech sector for future growth.

Greater collaboration
Global companies are collaborating with Indian biotech companies owing to India's cost advantage and availability of skilled manpower.
India has also signed pacts with foreign universities to promote research and innovation. For example, India has signed a pact with Cambridge University to develop a biotechnology-specific programme for early-career fellowships.

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Opportunities for Indian biotech players
Development cost for biosimilars is low: The global Biosimilar market stood at USD5 billion in 2015 and is expected to reach USD24 billion by 2020.2 This presents a good opportunity for growth due to low development costs in India as compared to the developed nations.

Domestic demand for vaccine is high: India's growing population and the fact that a large number of children are still not immunized keeps up the domestic demand for vaccines. Also, the government's impetus on eradication of a few diseases through vaccination present vast opportunities for vaccines manufacturers.

Global demand for vaccines: Sale of vaccines is also expected to get a boost from developing countries from global efforts towards eradication of diseases.
Other areas of growth
Opportunities in the agriculture biotech space: the success story of BT cotton in the agriculture biotech space has had a positive impact on rural lives in so many states and positioned India as a major producer of genetically engineered crops and vegetables globally

Availability of skilled workforce for the Bioinformatics industry: India's strong IT capabilities and availability of skilled manpower is expected to help the bioinformatics industry grow in the coming years. As the practice of using biological database for drug discovery grows, India's bioinformatics industry could well leverage this opportunity.

Growth in global industrial enzyme market: the global industrial enzyme market is likely to reach USD6.2 billion by 2020.1 Currently, India's share in this space is very low; however, strengths in low cost manufacturing and R&D could be growth drivers.

Advantage India

The following factors could potentially place India as a key biopharmaceuticals player:

Availability of low-cost inputs:
Compared with developed countries, India has lower cost of inputs to manufacture cost-competitive biotechnology-based products such as vaccines and insulin. These inputs include the initial land cost, electricity prices and low-cost skilled labour.
For instance, the compensation cost for labour in the manufacturing industry in India is much lower, compared to developed nations, such as the U.S., Germany and Italy.1
The labour cost is also lower in India as compared with other competing countries, such as China and the eastern European countries.
The price of electricity in developed nations, such as Germany, Spain, Japan, the U.K., France, among others, is more than twice the price prevalent in India.2 Moreover, many Indian states offer industrial power rates (ranging between INR4.2/KwH and INR6.4/KwH) that are equal to or even more competitive than the Chinese average of about INR6.4 /KwH.3

Presence of a large number of technical institutes:
Cost competitiveness also comes from the large pool of qualified personnel that come from the various nationally recognised technical institutes.
This can be further supported by the fact that the number of technical institutes providing pharmacy and engineering courses has consistently increased in the past five years.
Moreover, the enrolment percentages for science related streams have been encouraging and increasing over the years.

Large vaccine production base:
Indian companies have developed capabilities in producing large volume of vaccines. For example, a Pune-based vaccine manufacturer has an installed capacity of over one billion doses of different vaccines annually.5

Key Challenges faced by the biotechnology industry

Although significant opportunities exist in the biotechnology industry, India needs to immediately address the following challenges:

Multiple regulatory bodies:
There are multiple regulatory bodies, which directly, or indirectly, frame rules and guidelines for the biotechnology industry
This multiplicity has inadvertently led to inefficiencies in the drug approval process, often causing long delays
Moreover, the Biotechnology Regulatory Authority of India (BRAI), which was conceived in 2008 to bring biotechnology industry related regulatory processes under one umbrella, is yet to become operational.
Setting up single window clearance process could be a way forward for the industry.
Doing away with redundant processes and making use of online portals, wherever feasible, could also help in improving efficiency and transparency.

Sub-optimal alignment between the states and the central government:
When a biotechnology company needs to take a new drug approval from the central government, the manufacturing, sales and distribution licences for these new drugs are issued by the respective state government
This distributed responsibility sometimes creates divided agenda between the centre and states making the process tedious and time-consuming
Setting up a single Stakeholder Consultative Platform (SCP) with a fixed charter and representation from all stakeholders could help establish an efficient policy and drug approval process.
Complex clinical trial approval process:
Currently, clinical trial applications have to go through a three-tier approval system in India (passing through a subject committee of 10-12 members for specific therapeutic areas, then to a technical committee of 20 members and an apex committee for a go ahead).1 After getting due approvals, the application awaits a final approval from the Drug Controller General of India (DCGI).
Stringent guidelines laid down by the Supreme Court have also led to a sharp decline in clinical trials over the years.

Lack of stringent regulations for quality:
Lack of stringent regulations to oversee the quality of manufacturing; and low harmonisation on quality standards with various global regulators (USFDA and the Medicines and Healthcare Products Regulatory Agency - MHRA), hamper India's image as a high quality supplier in the international markets.

Proposed withdrawal of tax exemption on R&D:
The Central Board of Direct Taxes (CBDT) has recently proposed to reduce tax exemptions on investments made for scientific research from the current 200 per cent to 100 percent.2
The pharma and biotechnology industry has raised concerns over this development as they expect it to impact the innovation efforts of the industry.
Globally, many countries have introduced various steps to promote R&D initiatives in the form of R&D tax credit, R&D weighted tax deduction, patent box, etc; hence, the continuation of R&D weighted deduction is important for giving Indian companies a competitive advantage and also encourage innovation.

Low focus on cluster development and
collaboration:
A sector as technical as biotechnology requires quick access in the vicinity to low-cost raw materials, skilled manpower, R&D support and other allied support services; typically, a cluster-based approach would address these requirements.
In India, Bengaluru and Hyderabad are the only thriving clusters for the biotechnology industry; these, however require more collaboration amongst operating units with industry-academia linkage and technology transfer.
The government had also proposed to develop three Biotechnology Science Clusters in the 2014-15 Budget, which are yet to be made operational.

Lack of access to funding for early-stage companies:
Due to regulatory uncertainties and delay in product approvals, the sector has seen a drop in funding in the past few years.
Since biotechnology is a knowledge-driven sector, investors need to have a good grip on the dynamics involved so as to make informed decisions.
Further, PE and VC firms are also showing a keen interest in technology and e-commerce sectors, as they are perceived to

provide higher rate of returns with shorter gestation periods.

Lack of industry-academia partnership:
The current level of academia-industry collaboration is perceived to be inadequate, leading to gaps in the transfer of skills from academia to industry.

Unpredictable IP regime:
In the past, MNCs in India have often faced a crisis of confidence with respect to IP due to unclear and unpredictable regulations. Cases in point are a few cancer treatment drugs where patents have been successfully challenged in courts.
Section 3(d) of the Indian patent law does not support patents for inventions which are minor modifications of the current product. Though it is well accepted that authorities need to balance innovation and public health at large, bringing transparency in the IP regime could help remove ambiguity and enable biotech players plan business strategies around IP.
Steps undertaken by government to
remove challenges
Make in India programme
Initiatives under the 'Make in India' programme can potentially help the sector achieve its vision of being a global manufacturing hub
Regulatory
Strengthening and upgrading the drug regulatory system at the centre and state levels, with a budget of INR1750 crores, over the next three years.1
Will include setting up of new laboratories and training academies for regulatory and drug testing officials.
I**nfrastructure**
The Government is planning 50 research parks in the country and many of these will focus on biotechnology.2
The Government is planning to take steps such as establishment of national investment & manufacturing zones and industrial corridor to enable the sector
Sectoral policy
National Guidelines for Stem Cell Research and Guidelines on Similar Biologics-regulatory Requirements for Marketing Authorization in India.
FDI policy
100% FDI is permitted through the automatic route for greenfield projects.
IP Regime
India has recently released New National Intellectual Property Rights Policy which upon implementation could increase predictability, clarity and transparency with respect to IP.
Entrepreneurship and skill development
The Government is supporting entrepreneurship through BIRAC by providing funding and incubation support.
BIRAC has established nearly 15 incubators to provide high-tech equipment, mentor and hand-holding networks.
The country aims to have 1500-2000 biotech start-ups in the next two to three years from 500 start-ups currently.3
The Government has also launched the Skill India campaign to link entrepreneurship with skill development.

National Biotechnology Development (NBD) Strategy 2015-20
DBT has recently released the National Biotechnology Development Strategy 2015-20, which aims to propel India's biotechnology sector into a new phase of growth. Following are the key features of this strategy:

Capacity building
Establish specialised centers and technology platforms.
Skill development
Develop skills through trainings, new courses, faculty improvement programmes and fellowships.
Streamline regulatory system
Establish Biotechnology Regulatory Authority of India, a toxicology center for safety, and strengthen agencies such as Review Committee on Genetic Manipulation (RCGM), Drug Controller General of India (DCGI).
Enhance R&D and innovation
Enhance innovation through establishment of accelerators, rural technology support, application centers and new schemes to encourage commercialisation
Encourage start-ups and SMEs
Commercialise technology through establishment of technology incubators, technology transfer organisations and funding schemes.
Streamline clinical trials
DCGI has recently taken some positive steps to streamline clinical trial regulations in the country such as removal of the

requirement of no objection certificate (NOC) from DCGI for addition of new clinical trial sites, increase in number of clinical trials an investigator can undertake etc.
To increase transparency, the Central Drugs Standards Control Organization (CDSCO) had launched a new online submission sytem.
Global market overview
Over the past several years, biologics have gained prominence in the global pharmaceutical industry; global sales contribution of biologics is expected to increase from 23 per cent in 2014 to 27 per cent in 2020.1
The global biosimilar market is forecasted to grow to approximately USD24 billion in 2019 as compared with USD5 billion in 2015.2
The biosimilar market is dominated by the European Union followed by the Asia Pacific region.

Key growth drivers
Patent cliff
Biologic products with aggregate sales of approximately USD60 billion are expected to go off-patent in the U.S. alone by 2016.
Large biologics brands (such as Humira and Rituxan) are likely to open up biosimilar opportunities worth USD10 billion with expiration of their patents in 2016 alone. Moreover, by 2020, 25 per cent of biologics sales by value are expected to come from off-patent therapeutics.3

Evolving regulatory pathways
With regulatory approval pathways in Europe and the U.S. becoming more transparent and streamlined, significant opportunity is opening up in biosimilars.
In 2012, FDA issued first draft guidelines for biosimilars with several additional releases subsequently:
In March 2016, the USFDA released long-awaited biosimilar labeling guidelines.
In April 2015, the USFDA finalised three guideline documents related to biosimilar science and quality
In April 2016, the USFDA approved the second biosimilar for the US market.
Healthcare cost saving
With rising pressure to curtail growing healthcare cost, preference for generic versions is rising.
Biosimilars are expected to cost 10 to 30 per cent less than the biologic drug and therefore likely to save a lot in the healthcare bill.4
The Indian biosimilar market
The last few decades have seen generic versions of life-sciences' products emerge as a lucrative business option for the Indian pharmaceutical industry.
Taking advantage of India's low-labor costs and high technology skills, domestic companies have already established their presence in the global generic business of small molecules.
With more and more complex biological drugs going off-patent as compared to small molecules in near future, India has an opportunity to garner market share.
In India itself, the biosimilar market is witnessing strong growth due to launch of new products, growing acceptance of biosimilars and entry of many new players.

Key growth drivers
The key drivers of the Indian biosimilar market include:
Evolving regulations
India launched its first biosimilar guidelines in 2012; and the new guidance for biosimilars were released in March 2016 to further strengthen the regulatory regime.
In July 2016, the CDSCO among other things amended its guidelines on situations in which comparative studies of biosimilars and reference products are needed. The amendments are expected to provide clear guidelines for development and approval of biosimilars.
Increasing access to healthcare
The rise in the number and quality of tertiary care hospitals in the country has resulted in a greater usage of biologics.
Shift in diseases pattern
The increase in the number of patients inflicted by cancer, diabetes and cardiac ailments has created a demand for treatment options with biosimilars.
Global demand for low-priced biologics
Rising demand for low priced biologics globally is expected to provide export opportunities for Indian players.
Key trends
Increased collaboration to develop and launch biosimilars in developed countries
Many Indian companies are collaborating with foreign partners to launch their products in developed countries. For example,

in 2014, a Mumbai-based pharmaceutical company formed a joint venture with a Japanese pharmaceutical company for clinical development of certain biosimilars, including regulatory filings and obtaining marketing authorisation in Japan.
Similarly, a Hyderabad-based pharmaceutical company is also planning to launch a biosimilar product in Japan with a partner in 2018. The company had also previously partnered with a German pharmaceutical company to co-develop a portfolio of biosimilar compounds (such as, rituximab and pegfilgrastim) in the oncology space.
A Bengaluru-based biotechnology company has tied-up with a US-based pharmaceutical company to launch biosimilars in their market, starting fiscal 2017.

Growing number of pharmaceutical companies launching biosimilars in the domestic market
Many pharmaceutical companies in India are investing to increase their capacity and technology to launch biosimilar products in the domestic market. In the last one year itself many biosimilars were launched in India; this is likely to be the trend given the rising burden of NCDs and an increasing base of ageing population.
An Ahmedabad-based company, for example, has launched a biosimilar version of a US-based biopharmaceutical company's popular biologic, Humira (adalimumab), in India. Similarly, a Hyderabad-based pharmaceutical company has launched a biosimilar drug - Rituximab, used in the treatment of blood cancer.
Key challenges
High cost of development
Although biosimilar development cost is lower than developing a new biologic, it still requires significant investment not only in terms of time taken to bring a single drug to the market, but also in terms of the cost associated with R&D as compared with developing a conventional generic drug.
Further, innovator companies are likely to have the additional advantage of bringing their own follow-on biologics as compared to a company that is starting afresh. Setting up and running a manufacturing plant for biosimilars is costlier than that for small molecules.
Regulatory hurdle
Approvals from multiple government agencies are required to launch a biosimilar in the Indian market thus increasing the time taken to launch a product in the market.
Dearth of expertise in biologics
Capabilities in applied research in biology is limited as compared to chemical generics.
Talent development is required in molecular biology and process development for manufacturing biologics
Growing competition from other countries
Countries such as South Korea and China are likely to give stiff competition to India as they are actively supporting their biopharmaceuticals sectors.
In South Korea, regulatory pathways for biosimilars were introduced in 2009 and product-specific guidelines are also issued at regular intervals. The government is also providing funding support to the sector.
In China, the government announced final guidelines for biosimilars in 2015 to streamline the approval process.
Outlook
Strong technical skills, latest manufacturing technologies, ability to navigate through complex regulatory environments and a healthy balance sheet are prerequisites for companies that want to foray into the biologics universe.
With further strengthening of the IPR environment, global players are expected to open R&D centres in India; this move is expected to enhance technology skills of the industry. The country also needs to develop a research ecosystem in biology to gain strength in biosimilars.
"The vast opportunity offered by biosimilars would be challenged by regulatory hurdles and the cost associated with conducting clinical trials in various geographies. These costs are likely to mitigate the cost advantage that Indian companies have over other developed geographies"
Utkarsh Palnitkar, Partner, Head - Infrastructure, Government and Healthcare, and Life Sciences, KPMG in India

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