DBT- Centre for Biopharmaceutical Technology

BIOSIMILARS

BIOLOGICS

AFFORDABILITY

Conversations on **BIOSIMILARS**

Excerpts from **VAIBHAV** SUMMIT 2020

www.biotechcmz.com

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Foreword

Inventions and innovations are the key drivers that support scientific breakthroughs and revolutions. Vaishwik Bharatiya Vaigyanik (VAIBHAV) Summit functioned as a platform for discussion and collaboration amongst Indian luminaries in academic institutes and R&D Organisations across the world. The platform fostered deliberations on thought process, practices and R&D culture with a problem-solving approach for well-defined objectives.

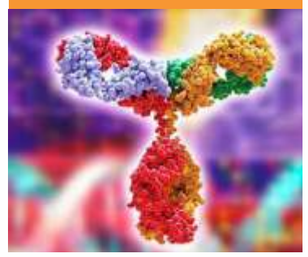
27 renowned scientists of Indian origin working in 5 countries participated in these deliberations. Discussions also related to the fulfilment of India's goal – **'AatmaNirbhar Bharat' and the possible contribution of policy initiatives like** Make in India and Start-up India.

As India's bio-manufacturing is moving towards complex products and alternative routes of administration, new regulatory challenges are highly likely. In addition, there is an issue of affordability associated with biosimilar/biotherapeutics development and production. Hence, it is pertinent to prepare a comprehensive regulatory roadmap for solving emerging challenges. Identification of unique challenges associated with the Indian landscape with respect to accessibility and affordability of these products is the need of the hour. Generating and maintaining common resources and solutions could ensure reduction in the turnaround time and thereby make this fledgling ecosystem sustainable. Academic involvement and collaboration with industry are critical in the development of new technologies for contributing to affordability issue associated with biotherapeutics.

Department of Biotechnology along with its PSU, BIRAC, are playing a pivotal role through a plethora of schemes and grants for promoting this sector. Several workshops, seminars, training are being organized from time to time for mentoring and capacity building. We are hopeful that this vibrant ecosystem provided to the innovators would enable them to provide globally recognized and sustainable solutions in the area of Biotechnology.

The summit, which was timely, has helped in identifying potential areas of collaboration amongst regulators, academicians and industry in the area of cost-effective manufacturing. VAIBHAV has led the way in establishing research capability as critical pathway towards effective international collaboration. I am confident that our collective efforts will help us realize the vision of an **'AtmaNirbhar Bharat'.**

(Renu Swarup)



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The वैश्विकभारतीयवैज्ञानिक (VAIBHAV) Summit was organized as a collaborative initiative amongst the various academic and science and technology organizations of India with a focus on verticals of national relevance to solve emergent challenges in India. The initiative was kicked off by the Hon'ble Prime Minister of India on the 2nd of October, 2020, followed by deliberations and panel discussions amongst the participating academicians and scientists from across the globe under the 18 identified verticals of national importance. The objective was to ideate on collaboration mechanisms and methods to strengthen the S&T base in India.

Biotherapeutics and Biosimilars was identified as one of the horizontals under the vertical Pharmaceutical and Biotechnology. Panel discussions pertaining to the horizontal were held under three themes namely; "Regulatory Perspectives on Biosimilars", "Biosimilars" and "Affordability of Biotherapeutic Products". The sessions were hosted virtually on 9th, 16th and 23rd of October, from 1900-2200 Hours IST by the DBT Centre for Biopharmaceutical Technology (**CBT**) at IIT-Delhi. Academicians and scientists from 27 institutes spread across 5 countries contributed as panelists towards these discussions and Q&A sessions. As an outcome, current and near-future challenges and potential areas of collaboration were identified and recommendations were made to the Government of India pertaining to the mechanisms of collaboration amongst regulators, academicians and industry, that key focus areas to bolster in-house, cost-effective manufacturing and policy renovations that would be needed to achieve these. Excerpts from these deliberations are presented herewith capturing key points of the discussions and the recommendations for the Government of India as an outcome of these discussions.

Biotherapeutics dominate the pipelines of pharmaceutical industry across the world today with products ranging from hormones, immune-modulators, monoclonal antibodies (mAbs), blood coagulation factors, enzymes and vaccines. However, they are considerably more expensive than generics and as a result there has been a rise in biosimilar developments and approvals, seen as an affordable alternative to the innovator product. In 2006, the European Medicines Agency (**EMA**) was the first regulatory agency to offer a regulatory framework for the development and approval of biosimilar products. Since then, other countries (USA, Canada, Europe, India, Australia, Japan, South Korea, South Africa, China, Brazil, Mexico, Argentina, Peru, Colombia, Venezuela, Chile, Cuba, Singapore, Malaysia, Thailand, Saudi Arabia, Egypt, Uganda, Turkey) have also introduced regulatory guidance for biosimilars.

Session 1:
Regulatory Perspectives on Biosimilars

What remains common in all guidance documents thus far is the need to establish an extensive analytical and clinical comparability with the corresponding innovator product. In some jurisdictions, demand for extensive clinical trials have been challenged as being too cautious and hindering biosimilar development. As more and more biosimilars hit the market, it has become necessary to harmonize the regulatory standards for biosimilars across the globe. Regulators play a key role in ensuring success of biosimilars, as well as the impact they have on improving affordability of biotherapeutics. While regulatory guidelines across the world are reasonably aligned, differences do exist with respect to expectations and data requirements and the success of biosimilars thus far has shown significant variation in different geographies.

Session Objective & Details

1: **VAIBHAV SUMMIT,** 2nd to 31st October, 2020

2: **18 VERTICALS,** V15. Pharmaceuticals & Biotechnology

3: **5 CHAMPION INSTITUTES, 4 HORIZONTALS**

V15H1: Biotherapeutics and Biosimilars
Hosted by
DBT Centre for Biopharmaceutical Technology,
IIT-Delhi

V15H1S1:
Regulatory Perspectives on Biosimilars
(9th October, 1900 to 2200 Hrs)

SESSION OPEN:
Introduction–1900-1910

SEGMENT 1:
Focused Q&A session–1910-2030

Break–2030-2035

SEGMENT 2:
Open discussion-2035-2140

SEGMENT 3:
Q&A from the audience to panelists–2140-2150

SESSION CLOSE:
Summary–2140-2200

Meet the **Panelists**

S. Eswara Reddy
(Session Chair)

Vinod P. Shah
(Co-Chair)

Narendra Chirmule
(Moderator)

Anurag S. Rathore

Mansoor A. Khan

Pallavi Trivedi

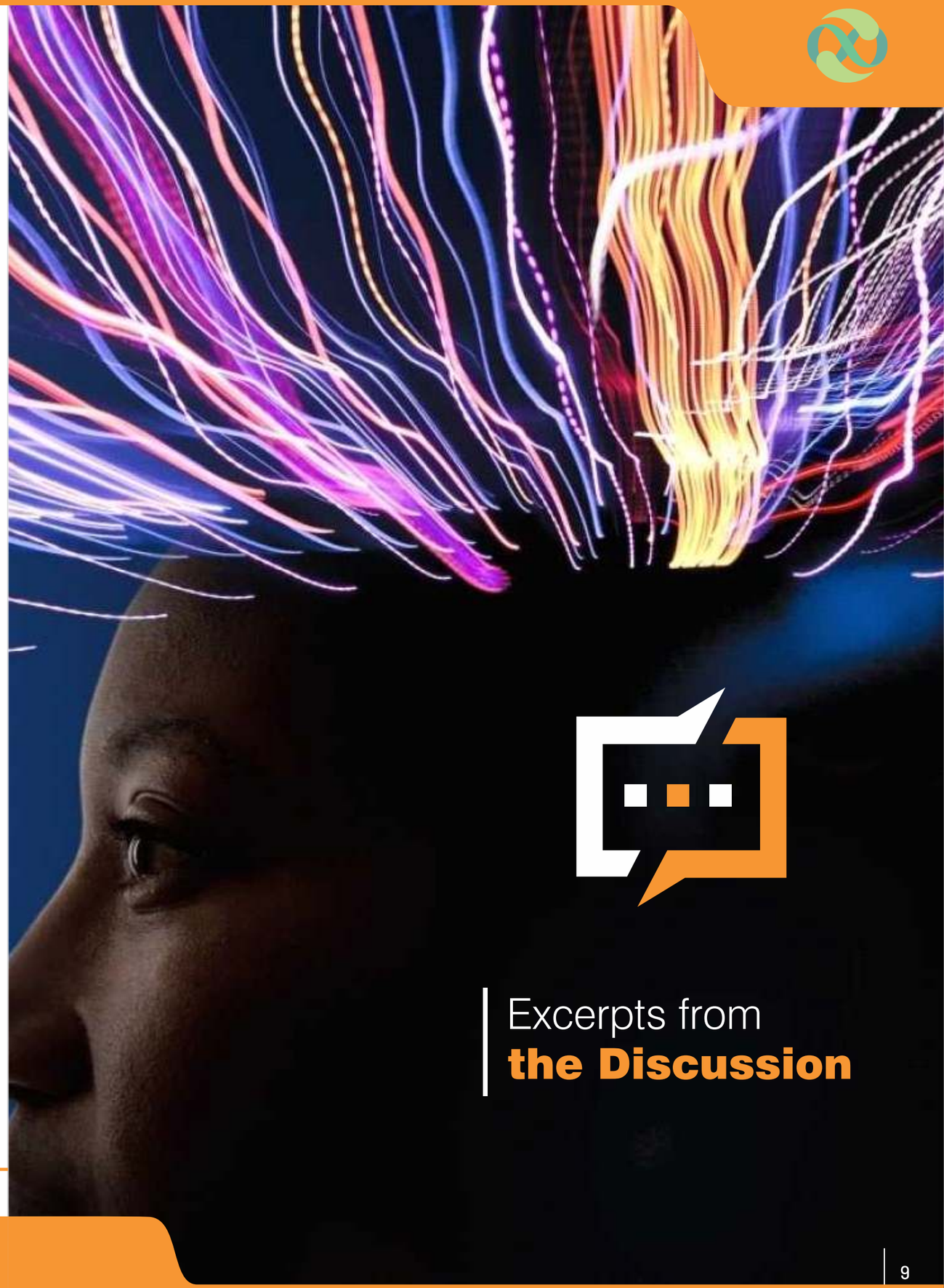
Janakiraman Subramanian

Kavita Singh

Arun Kumar B. Ramteke

Debendra K. Sahoo

Vishal K. Gupta



Excerpts from **the Discussion**

In the course of the discussion, panelists were asked to present their viewpoints on the following topics:

- Evolution of regulatory framework in India and recent advances made towards harmonizing guidelines with other established pathways such as from USFDA and EMA
- Ongoing efforts in streamlining of biosimilar regulatory pathways in India and its repercussions for future biosimilar developers/manufacturers.
- FDA and EMA perspectives on challenges associated with interchangeability and possible role of academia in this regard
- The spectrum of regulatory experience and associated challenges for industry with a focus on training and understanding of the guidelines.
- Framework for collaboration and networking amongst academia, industry and regulators.

Perspectives relating to current scenario, challenges and collaboration opportunities and recommendations from the panel are presented in this report.

Regulatory guidelines for similar biologics were first released in India in 2012 and a subsequent revision was issued in 2016. These guidelines address pre-market regulatory requirements, including comparability exercise for quality, preclinical and clinical studies and post-market regulatory requirements for similar biologics. The landscape of biosimilars is flourishing in India as evidenced by over 100 approvals granted successfully till date. As of now, approved biosimilars for 27 molecules are available in the Indian market. These products are becoming increasingly affordable and hence accessible. Further investment in technology and infrastructure is likely to bring significant reductions in the cost of these products.

There is also an increase in global acceptance of Indian manufactured biosimilars, especially in emerging markets as a result of increasing harmonization of India's regulatory framework with the international guidelines, where reliance on appropriate scientific data for verification of biosimilarity is emphasized to ensure continued safety and efficacy of the approved products. Indian biosimilars are exported to over 150 countries across the globe today. To recreate the success of small-molecule generics in biosimilars, especially in established markets such as US and Europe, convergence in thought process of all stakeholders (regulators, industry and academia) is needed. In this context, with respect to regulations, efforts are underway to restructure permissions and simplify approval process at The Central Drugs Standard Control Organization (**CDSCO**), which is the apex and national regulatory authority under the Government of India. Some of these changes include presence of **RCGM** subcommittee at **CDSCO** for rDNA products and demand approval system for Committee for the Purpose of Control and Supervision of Experiments on Animals (**CPCSEA**). Success of regulatory interventions in pushing the growth of biosimilars in India and abroad is highlighted by the following outcomes:

- More MoU's are being signed between **CDSCO** and other jurisdictions, including but not limited to **USFDA** and **MHRA**
- Maximum number of **USFDA** facilities outside of USA are in India
- An increasing number of multinational companies are starting their R&D facilities in India

While India is making efforts to strengthen its global footing in the field of biosimilars, certain challenges inherent to the field still remain, irrespective of geography. Potential market size for biosimilars is still a small fraction of the total market size for reference products. One reason for this is patient awareness about biosimilars, which has considerable scope for improvement. This is compounded by lack of clarity on interchangeability of these products. European Medicine Agency (**EMA**), which was the first to define political and license framework for biosimilars, currently has a "no centralized decision" stance on interchangeability. With the decision being left to the EU countries, currently most countries do not allow for switching / interchangeability from originator to biosimilar or amongst available biosimilars.

The regulatory hesitance in taking a decision on interchangeability exists because of current scientific lacuna regarding repercussions of multiple product switchings on product safety. Further, difficulties in tracking and tracing also remain. Currently, there is no consensus on a simplified mechanism to grant a blanket "interchangeable" status to a biosimilar, as it would call for parallel comparison studies of the putative product not only with the originator but also with existing biosimilars in the market.

Biosimilar development involves understanding and interpretation of regulatory guidelines and alignment with these guidelines from an early stage. From the regulator's perspective, challenges arise in quality assessment of biosimilars, not just with respect to comparability to the innovator molecule but also batch to batch variability.

The cost of these studies would be higher for late entrants of a given molecule as they would have to show comparability to all previously approved biosimilars for that given molecule.

Although some processes to establish a dialogue between the regulators and biosimilar manufacturers from nascent stages of biosimilar development do exist (new regulatory provisions for pre-submission meeting between the manufacturer and regulator), these alone are not enough and more effective engagements are required.

As both biosimilar development and the approval process are rooted in scientific understanding of the molecule, academicians as subject matter experts need to act as the guiding force, both for the manufacturers to ensure that processes are aligned to produce a consistent quality product each time, as well as with the regulators to ensure that the policies are scientifically aligned without being cumbersome and economically demotivating for the manufacturers.

This can be achieved by designing and providing suitable training to all stakeholders. Academicians can also play a role in increasing quality awareness of the products by publishing extensive quaity evaluations of post approval products in peer reviewed international journals. India also needs to cover significant grounds in terms of branding its products and showcasing its successes, to be able to match the brand awareness garnered by the US and European manufacturers. While enhanced publication and targeted dissemination of information pertaining to Indian biosimilar products would help in this regards, what is really needed is a larger presence and representation of Indian manufacturers/ regulators/ academicians in the forums of international dialogue to become a voice of influence. The recent inclusion of India as a member of **ICH** is an important step in that direction.

As biosimilar manufacturing moves towards more complex products and alternate cost-effective modes of administration, new regulatory challenges are likely to be on the horizon. In the coming years, the regulatory landscape needs to include frameworks for inclusion of emerging modalities and modes of administration, such as biosimilars developed for subcutaneous administration to be more cost effective.

Questions?

After the panelists presented their perspectives, they were requested to share their thoughts in response to a few directed questions.

What are some of the major regulatory challenges that regulators face in jurisdictions other than India when evaluating biosimilar applications? From a regulatory perspective, what recommendations can be given to Indian biosimilar producers who are aspiring to get approvals in other jurisdictions such as the US and Europe?

The **USFDA** perspective on the outcome of a similarity assessment is based on the totality of evidence presented. The challenge faced in this regard is with respect to demonstration of analytical similarity, product stability and consistency in product quality, optimally addressing residual uncertainty and batch to batch variability. Synergistic academic collaborations between Indian and US academicians and subsequent dissemination of training to the industry via academia, especially with respect to analytics ought to positively support the endeavors of Indian biosimilar manufacturers towards a favorable application outcome.

What is the role of government institutions outside the regulatory body in the arena of biosimilar development?

Not for profit organizations such as Biotechnology Industry Research Assistance Council (**BIRAC**), set up by the Department of Biotechnology, have taken to identifying gaps in the Indian biosimilar ecosystem and continual efforts are made to plug these gaps by means of funding mechanisms wherever applicable.

In addition, the Nation Biopharma Mission (**NBM**), a joint collaboration between **BIRAC** and the World Bank, has offered sustained infusion of funding. Addressing capacity in the biopharma sector has been a priority as a high capital expenditure (CAPEX) and operational expenditure (OPEX) capacity is required for biosimilar development. This priority also extends towards plugging in the missing capacity whether it is instrument intensive analytical laboratories, cell line repositories, process development laboratories for mammalian/microbial products or large scale GMP fill finish manufacturing plants and making these available to MSME or large sector. The results of investment in this high CAPEX structure should come to fruition in the next 2-5 years. In parallel, high risk projects have also been supported to give a stimulus to the Indian biosimilar industry. Funds have been allocated to support projects on development of in-house solutions for high cost consumables such as cell line media, small scale bioreactors which are required by start-ups and academic institutes and resins that are used in downstream processing. Currently, these high cost consumables are mostly imported.

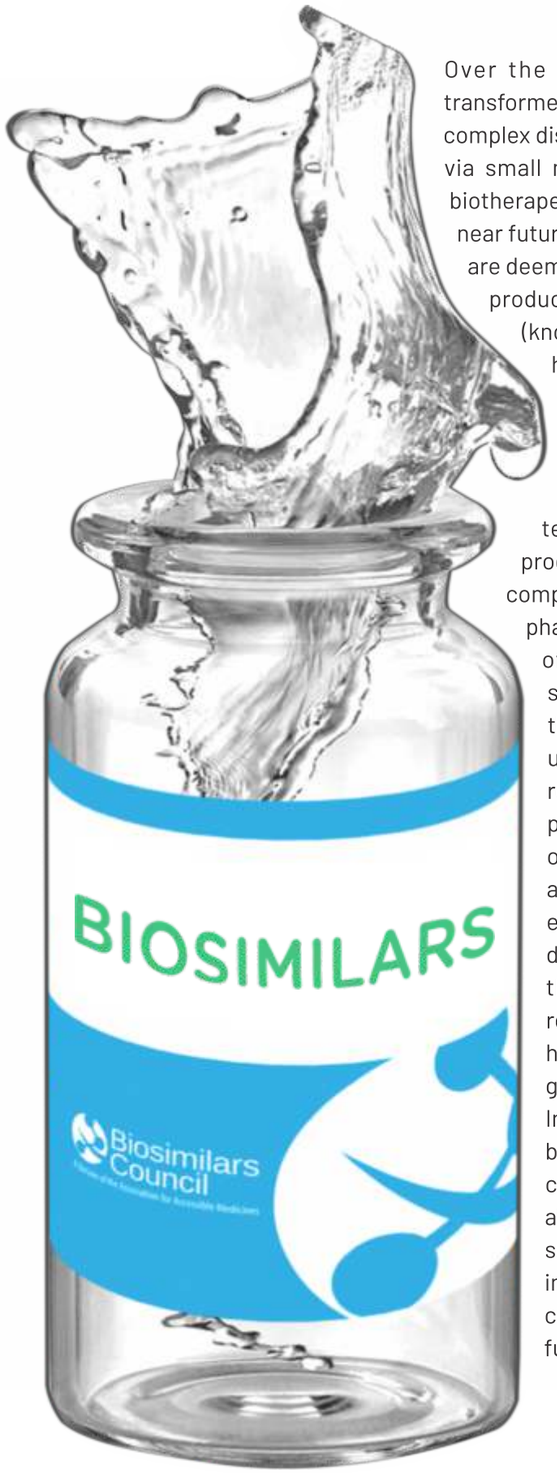
What can academia do and what are the gaps that exist which academia can step up and fulfill? What is it that the US or EU universities have that Indian universities need to gain?

There needs to be an increase in flow of sponsored research from industry to academia and academia should try to reach out to industry for such sponsored research projects. To do this, academia-industry relations need to be strengthened with an improved understanding of the strengths and weaknesses of each party. Another aspect is also increasing awareness with regards to the quality of Indian biosimilar products and for this institution such as the **DBT Centre for Biopharmaceutical Technology** (**CBT**) routinely publishes extensive similarity assessment studies of approved Indian biosimilars. Taking the example of the US, academicians have a liberal representation in the **FDA** and **NIH** and through that representation have a say in policy development. Representation of Indian academicians in policy making and development structure within India will help in giving them the visibility that is needed to gain confidence in securing investments from venture capitalists.

Another interesting perspective shared with regards to visibility of India and Indian products in the global arena is that of awareness. The running consumer perception of Indian products is a remanent of bygone days and does not correctly represent that progress made in terms of quality manufacturing as evidenced by the 45% market share that India currently holds for global exports in pharmaceuticals. In most cases, labelling on the drug vial indicates the name of the Marketing Authorization Holder (Europe) or the National Drug Code (**NDC**) and identity of different stakeholders involved from development till packaging is not disclosed. Therefore, even though for a major portion of these drugs might be manufactured in India (via contract manufacturing), the awareness amongst the consumers is limited in this regard. More can be done towards establishing "Brand India" as a brand associated with economical and high quality biotherapeutic products.

Session 2:
Biosimilars

Session 2: **Biosimilars**



Over the past three decades, biotherapeutics have transformed healthcare by offering effective treatments for complex diseases which were otherwise difficult to deal with via small molecule pharmaceuticals. Patents on several biotherapeutics have either expired or are due to expire in near future, and this has fueled growth in biosimilars, which are deemed to be similar to the already approved innovator products in terms of safety and efficacy. Biosimilars (known as Similar Biologics in India) are defined as highly similar to the reference product notwithstanding minor differences in clinically inactive components, such that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product". Production of biosimilars is a much more complex process compared to small-molecule generic pharmaceuticals due to inherent challenges in the use of rDNA technology based manufacturing. To streamline this with respect to market approval of these products, different jurisdictions have come up guidelines for approval of biosimilars. What remains common amongst these guidelines is presentation of evidence of similarity with the originator molecule based on a comprehensive analytical characterization. Although a costly exercise, it is on the basis of similarity demonstrated via analytical characterization that the regulatory agencies approve any in the requirement for further clinical data. So far, India has been quite successful in manufacturing of and gaining approval for over 20 biosimilar products in India via the Indian regulatory pathway and over 200 biosimilars are under development at over 52 companies. The local efforts in this domain have also translated into global success for companies such as Biocon that now have approved biosimilars in the EU and the US markets. This has given a lot of confidence to the Indian biotech industry and is further fueling interest in this area.

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V15H1: Biotherapeutics and Biosimilars
Hosted by
DBT Centre for Biopharmaceutical Technology,
IIT-Delhi

V15H1S2:
Biosimilars

(16th October,
1900-2200 Hrs)

SESSION OPEN:
Introduction–1900-1930

SEGMENT1:
Words from the panel – 1930-2025

Break - 2025-2030

SEGMENT2:
Q&A with the panel - 2030-2130

SEGMENT3:
Q&A from the audience to panelists – 2130-2150

SESSION CLOSE-
Summary from Chair- 2150-2200

Meet the **Panelists**

Mansoor A. Khan
(Session Chair)

Ramakrishna V. Hosur
(Co-Chair)

Anurag S. Rathore
(Moderator)

Dhinakar Kompala

Prashant Mhaskar

Balaji Somasundaram

Shishir P. S. Chundawat

Neel Sarovar Bhavesh

Krishna M. G. Mallela

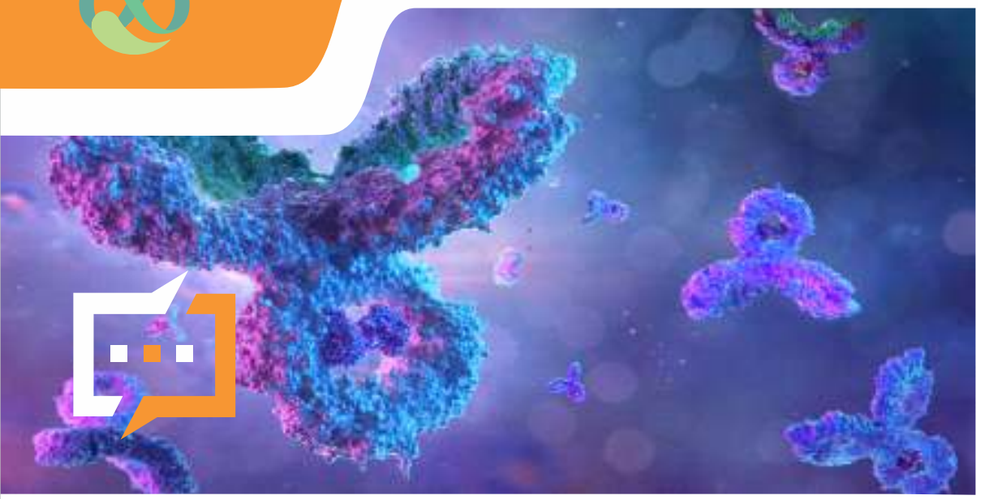
Srinivas Sistla

Mugdha Gadgil

G. R. Soni

Ravi P.N. Mishra

Excerpts from the **Discussion**



For this session, panelists were asked to present their viewpoints on the following topics:

- The potential of India to mimic its success in generic pharmaceutical manufacturing with biosimilars?
- Major hurdles or challenges that India is likely to face in this path towards becoming a preferred global destination for biosimilar manufacturing.
- What does it take for Indian companies to be at the cutting edge of best practices and technologies?
- The role that academia plays internationally and is likely to play in India in facilitation of this objective.

Although there has been recent successes in Indian biosimilar manufacturers getting regulatory approval from major regulatory agencies such as the **FDA** and the **EMA**, it is also evident that considerable hurdles remain for the industry to be able to duplicate the success that has been achieved in generic manufacturing. Complex nature of the bioprocesses, requirement of sophisticated infrastructure, trained expertise and development of manufacturing technologies that can make this class of product affordable are some of the major challenges. A topic that was addressed in this session as well as the other two sessions is that of getting adequate visibility and developing trust. In this regard, it is essential for the Indian biosimilar industry to understand key expectations of the global regulator bodies and then create and implement a plan that effectively allays these concerns. This is an ongoing process that requires continuous engagement with every evolving thought processes via interactions at conferences and other global events. For complex molecules such as monoclonal antibodies, developing the required analytical characterization package for demonstrating biosimilarity requires access to and use of sophisticated instrumentation which is currently limiting for not only smaller but also more established manufacturers in this domain

Efforts have been made in this direction by the national funding agencies such as **BIRAC** under **DBT** which in the last 6 years have provided the required financial support to kick start establishment of such facilities across India, **CBT** at IIT Delhi being one of them. In addition, Indian manufacturers with products approved in the US market should explore the possibility of availing funds through the channels such as Generic Drug User Fee Amendment **(GDUFA funds, FDA),** towards which they pay a licensing fees. Outside of financial support, panelists made suggestions to facilitate access to currently existing analytical capacities via creating a central website cataloging existing major instrumentation capacities across the country along with their points of contacts. This would also help in integration of skilled personnel into the biopharmaceutical ecosystem especially those returning to India. The associated facilities and people mentioned could serve as a point of contact for people returning or new people wishing to be a part of the ecosystem.

With respect to focus on scientific development at the cutting edge of research, two complementary schools of thought were presented. Pertaining to characterization of biosimilars, it was suggested that domains such as database research, mechanistic understanding of molecular interactions through systems biology, understanding of structure to function relationships should be focused on to build our fundamental understanding of therapeutic protein functioning at a molecular level. Investment in fundamental investigations will pave way for scalable technologies that may arise out of this work. The second and complimentary school of thought laid emphasis on choosing the right technologies to develop. It goes without saying that the current global pandemic has highlighted the need for development of indigenous technologies.

Within the biosimilar paradigm, what this means is that India must also focus on becoming self-reliant with respect to manufacturing technology. This is important as the present day manufacturing technologies to a large extent depend on consumables and equipment that are mostly imported. There is a need is to move towards continuous manufacturing for products, that have a high demand and consumption, globally. Continuous biomanufacturing and advanced real-time process analytical tools (**PAT**) can have a significant impact to reduce cost of biosimilars and biologics. The ongoing advancements in the areas of artificial intelligence (**AI**) and machine learning (**ML**) will further drive integration of real-time process analytics into process models to predict drug quality attributes as a function of input process parameters and material attributes.

Because of the complexity and nature of the process and the product in biotherapeutic manufacturing, academicians play a guiding role in both the commercial development as well as mapping a regulatory framework that serves as an efficient control point for release of efficacious drugs, without being detrimental to development of these drugs. The panelists suggested multiple modes where academic contribution would be valuable towards the development of the sector. Well furnished analytical labs should train and develop expertise and look towards extending operations as Contract Research Organizations (**CROs**) for biopharma companies. This would be especially beneficial for small to medium sized biosimilar manufacturers that currently struggle to get access to analytical instrumentation required throughout the biosimilar development process.

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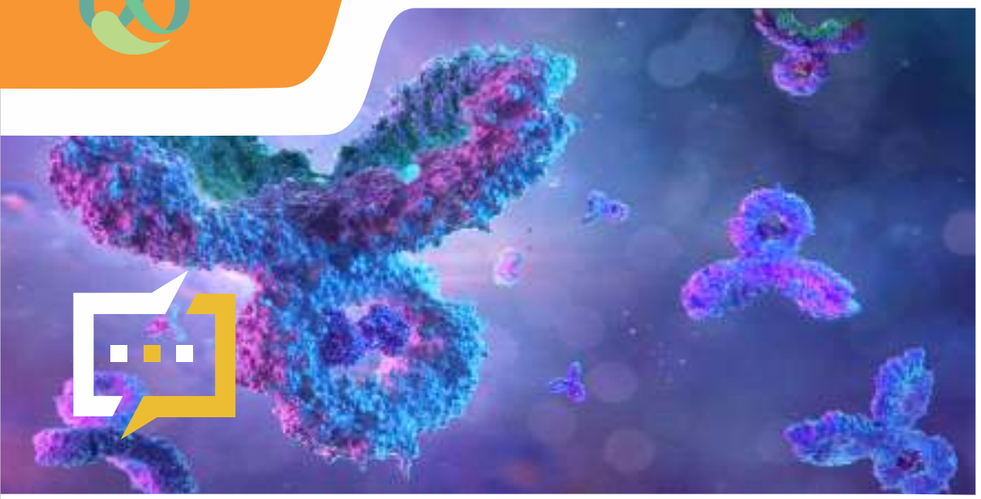


In addition, suitable collaborative industry-academic-regulatory virtual centers between India and other major players in the US and elsewhere can be established to maintain a platform via which ideas as well as resources can be shared. Similar initiatives have been taken up in the past such as in the area of bioenergy research commercialization through establishment of Indo-US based research centers (e.g., **IUSSTF**). A similar approach involving drug regulatory agencies and industry more closely with academia can be explored. Another example is the US-based **C-SOPS**/Engineering Research Center (https://www.csops.org) at Rutgers University that was established over a decade ago to advance methods for continuous manufacturing of small-molecule API based tablets and other non-biological drugs based pharmaceutical products. In fact, continuous manufacturing is likely one such area where Indian-origin faculty and scientists working in US universities and pharmaceutical companies can readily collaborate with faculty and scientists in India.

Questions?

For this session,
the following questions were posed to the panelists:

How are Indian biosimilar products with respect to quality?

In the past 5 years, **DBT Centre for Biopharmaceutical Technology** has published several extensive quality evaluation studies covering analytical as well as functional characterization of biosimilars (glycosylated as well as non glycosy-lated) marketed in India and have found them to by and large match the attribute profile of the originator. Similarly, other institutes such as **NIB** have also been conducting similarity assessment exercises from the perspective of quality evaluation. The consensus with respect to biosimilarity of the copy-biologics, is that the post-approval products currently in the market are highly similar to their respective originator. This is also reflective of the success of the regulatory process in maintaining a certain quality in the approved products

What role can technology play towards emergence of India as a global producer of biosimilars?

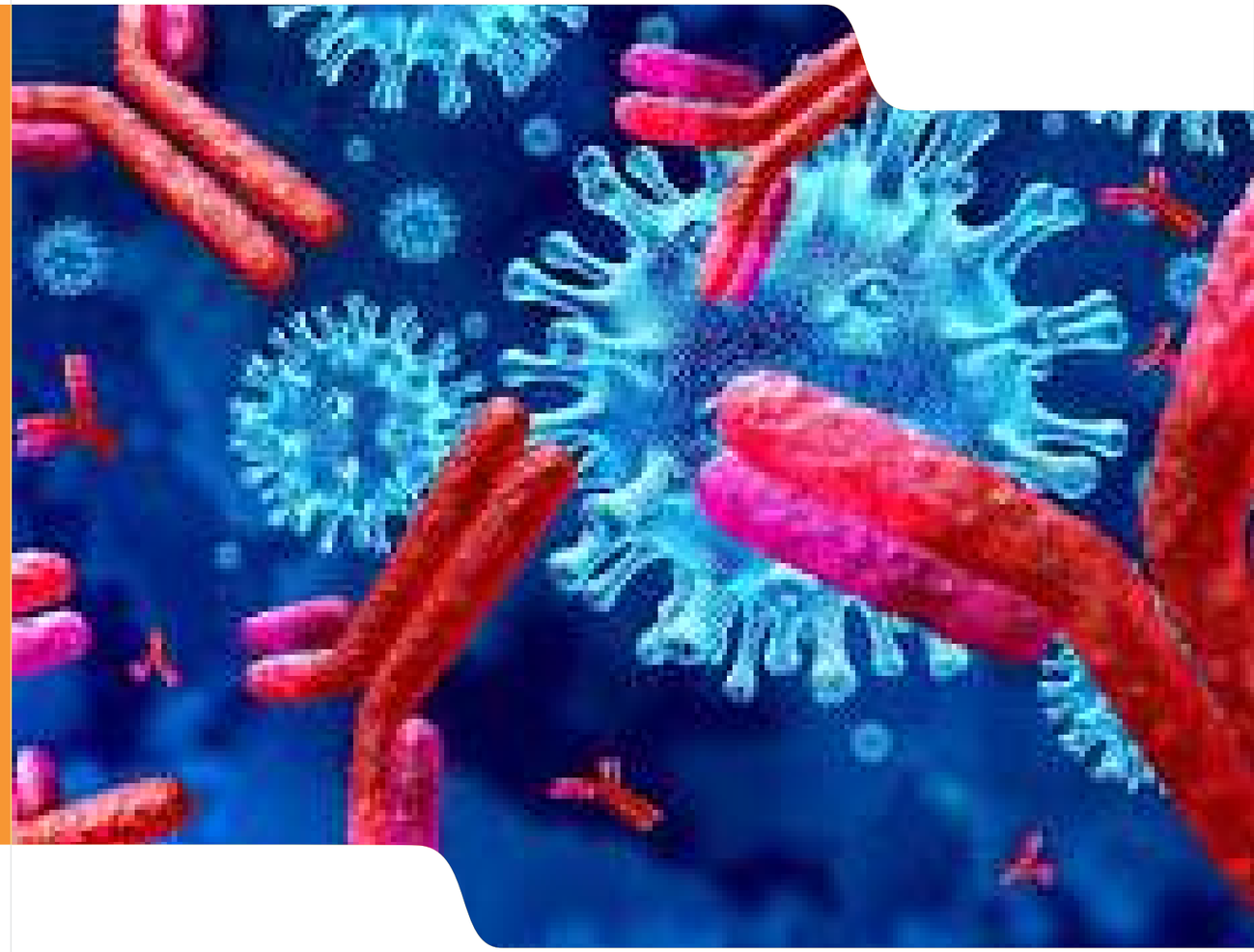
Making major technology investments with a long-term outlook is important for the Indian biopharma as this is likely to yield long term competitive advantage. One of the emerging areas that is likely to play a key role in the advancement of technology for In addition, advances in the area of real-time and integrated process analytics are critical. Continuous manufacturing is already being adopted for manufacturing of small molecule pharmaceuticals and is now being examined by biopharmaceutical manufacturers. R&D collaborations with credible academic institutions will play a key role in the industry's ability to achieve this.

What role can academia play to influence development of biosimilars? What can be done to enhance academia-industry collaborations?

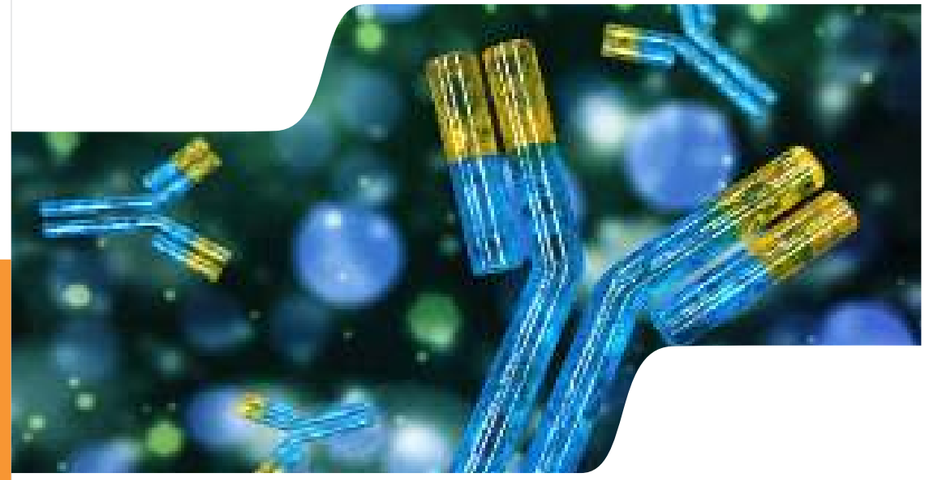
Academia has a big role to play in making the Indian biosimilar industry a success. Generating trained manpower is a key outcome. Undergraduate students, graduate students, and post-doctoral fellows if given adequate training, would serve the biopharmaceutical industry.

Academia can also play a key role in organizing training sessions for the industry. Such events are important for the industry to keep their workforce appropriately trained on the latest technological developments. In addition, academia also happens to be the creator of the recent technologies and is likely to be a significant partner in ensuring that manufacturing technologies stay at par with global best practices. Student internships as well as movement of personnel from academia to industry and vice versa can assist here and further strengthen academia-industry relations.

Session 3:
Affordability of Biosimilars



Biotherapeutic products constitutes one of the dominant products in the pharmaceutical industry as they contribute to more than 25% of the total pharmaceutical revenue today. In the 15th biopharma survey by Biospectrum (2018-19), it was highlighted that the industry had crossed Rs. 22,124 crores in revenue as compared to previous year's 18,290 crores. However, biotherapeutic products are 50-100 times more expensive than their generic counterparts and even though there has been a rise in the development of biosimilars, their affordability is a major issue in India as well as most of the world. Some of the factors that can make biosimilars affordable to the public include domestic capabilities, paying capacity, government policies and domestic demand. Lowering the prices of biosimilars can dramatically increase its demand. The opportunity of making it more affordable is not just limited to India, but also to most parts of the world.



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V15H1S3:
Affordability of Biotherapeutic Products
(16th October, 1900-2200 Hrs)

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SEGMENT3:
Q&A FROM THE AUDIENCE TO PANELISTS – 2130-2150

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Summary from Chair- 2150-2200

Meet the **Panelists**

Govind Rao
(Session Chair)

Ratnesh Jain
(Co-Chair)

Anurag S. Rathore
(Moderator)

Mahesh J. Kulkarni

Varun Ramamohan

Annu Uppal

Santosh Noronha

Sanjoy Bhattacharya

Raja Ghosh

Ajoy Velayudhan

Dhinakar S. Kompala

Excerpts from **the Discussion**

In the course of the discussion, panelists were asked to present their viewpoints on the following topics:

- Status on the affordability of biotherapeutic products around the world and in India.
- Unique challenges seen in India with respect to affordability of this class of products.
- Role of technology and academia in making biotherapeutic products more affordable.
- Framework for collaboration and networking amongst academia and industry that can help make biotherapeutics more affordable.

Perspectives relating to current scenario, challenges and collaboration opportunities and recommendations from the panel are presented in this report.

In a developed country like US, the cost of biotherapeutic products is significantly high. These products are affordable to the public primarily via government subsidies. Biosimilars are priced lower in India as compared to the developed nations. However, the purchasing power of an average Indian is significantly lower in comparison resulting on poor affordability and accessibility of these products. The cost of a given therapy is not always dependent on just the cost of the medicine but is influenced by other factors as well.

Major contributors to the overall cost of care in India include costs associated with the doctor's time and the nurse's time along with the cost of medication and treatment. Therefore, a sustainable mechanism for cost reduction is likely to involve strategies that call for a larger participation between the biopharma manufacturers as well as the hospitals. For example, 230 hospitals in Mumbai came together to standardize the treatment for cancer and order drugs together to bring the pricing down of the associated therapy. Hence, the hospital systems can do a lot-as a collective group of entity, on a larger scale.

Tackling the aspect of cost reduction via innovation in manufacturing practices has been discussed in the previous sections. Establishing infrastructure for developing technologies and analytics and developing in-house capabilities with respect to currently imported consumables and technologies are likely to boost the interest of small to medium enterprises in the affordable manufacturing space. Along with investing in new technologies at the R&D level, training and sensitizing companies towards adoption of these technologies is also of paramount importance. This requires structured and synergistic collaborations between academia where innovation typically originates and industry which has a critical role of maturing the innovation and ultimately implementing it. Assistance of government is required in facilitating percolation of this momentum to smaller towns via opening venture centers even outside of the major metropolitan hubs.

Affordability is also associated with regulatory challenges, corresponding policies, and intent of policymakers. Currently, there is a global lack in policy under any jurisdiction to create an ecosystem where affordable antibodies can be designed and manufactured. Although there have been efforts made in India, they are currently isolated. There is a need to create an ecosystem where utilization of locally available resources is efficiently maximized through research and development synergistic association between academic institutes. Concurrently the regulatory arm of the ecosystem should work towards smarter regulation of policies with better harmonization and suitable models to reduce the cost. Certain issues that can be addressed better along with way via policy

standardization include issues such as requirement of bridging studies for approval in multiple markets which eventually add to the cost of the biosimilar for that market.

The panelists also acknowledged that just like other ecosystems at a fledgling stage, there may be common manufacturing / analytics / infrastructure set-up issues faced by new members of the ecosystem. In such instances, generating and maintaining common resources and solutions to basic problems can cut short the progress time of the ecosystem as a whole. Instead of building walled gardens, some information must be made available in the public domain for the larger good of the community. currently does not take into account the complexities faced by the private player.

Another suggestion from the panelists towards utilizing effective costing strategies was to employ mathematical models that weigh in multiple factors to facilitate answering question such as, 'Is this drug worth paying for. Frameworks for such assessments do exist in the country currently, however they are limited by the input information which currently does not take in to account the complexities by the private player.

Questions?

The Q&A segment for this session included the following questions:

How affordable are biotherapeutics products in US and India?

Biotherapeutics cover a wide range of products and the affordability also varies in India. In general the products are cheaper compared to developed countries, however for biosimilars of complex modalities such as mAbs, the cost does not yet commensurate with the purchasing power of an average Indian . However, costs of some other modalities such as some small protein therapeutics (eg. Insulin) and of vaccines are relatively cheaper. Similarly in the US, outside of insurance, therapies relying on mAb based products, including biosimilars are quite costly and hence only affordable by a large section of the society.

What kind of unique challenges are seen in India with respect to this class of products?

The big contributors to the cost of care in India for cutting edge therapies including those using biosimilars are medication and other hospital and treatment related expenditures. In a country like India where the economic status of the population is diverse, it is difficult for these products to be affordable for all classes.

However, the challenge of affordability is not unique to India but rather is a global problem to be tackled. Challenges and areas of opportunities unique to India, currently, include development of in-house capabilities for all components that need to be imported and add to the cost of the final product.

There are also various policy and regulatory related challenges in India. For example, some enzymes can be manufactured in India, yet they are imported due to lack of investments in startups that can allow for their in-house manufacture. Moreover, collaboration efforts in biomanufacturing are isolated and hence the ecosystem needs to work synergistically. Along with biosimilars, some focus also needs to be shifted to creating novel biotherapeutics. Some other challenges are needed for building confidence in conducting clinical trials, strengthening availability of infrastructure to small and medium sized companies, focusing on translational and applied research, implementation of available technologies and utilization of **AI** and **ML**.

Is maintaining quality of this product a significant issue in making it more affordable?

India is already regarded as the global supplier of safe, efficacious and affordable generic products. The fact that Indian manufacturers supply more than 45% (a number that has been steadily increasing) of the pharmaceuticals sold in the US speaks volumes of the quality of products manufactured. The recent spate of approval of Indian manufactured biosimilars by **FDA** and **EMA** indicate that Indian manufacturers are capable of making quality biosimilars as well. However, the cost involved in achieving and consistently maintain product quality is high, an area of concern for the small and medium scale manufacturers.

What role can academia play in making this class of products more affordable? How can Indians in India and abroad interact to build partnerships that can help make biotherapeutics more affordable?

Academia can play a significant role in development of novel technologies, in particular, manufacturing technologies that can contribute to improving affordability of biosimilars. Major funding agencies (**DBT** and **DST**) already have grant schemes that can fund such co-development of novel technologies.

Recommendations

Collaborative relationships between Industry and Academia with respect to sponsored research, Industry and Regulators with respect to interpretation of guidelines, and between Regulators and Academia in form of increased academic representation in regulatory agencies and creating provisions for scientifically sound policy interventions and renovations.

Increased regulatory convergence via mutual recognition agreements with World Health Organization (**WHO**) and International Council for Harmonization (**ICH**) that serve as significant pillars shaping the regulatory landscape. Regulatory convergence offers the possibility to create transparency and eliminate duplication of work, thereby supporting affordability goals and increasing confidence in outcomes of assessment.

Simplified regulatory process and rationalizing regulatory requirements during the development process until the Go/ No Go decision is taken, building flexibility into the approval process.

Evaluating preparedness of regulatory pathways for complex biosimilars and addressing complex issues such as interchangeability.

Changing global public opinion on quality of Indian Biosimilars: Develop branding strategies around biosimilars, discussing them at major conferences discussion forums . Increasing visibility and representation of stakeholders in the global forums such as **ICH** and other such bodies.

Creating collaboration mechanisms encompassing the regulatory-academia-industry triad, with spaces for academic input from Indian-academic-diaspora:

A few examples of such collaborations include:

- Building a mission mode consortium of academic & industry partners
- Industry sponsored fellowship programs with a long-term outlook for cultivating expertise

Creation of virtual Centers of Excellence/Consortiums in collaboration with Industry and regulators for generation of commonly shared resources

Creating and maintaining a database of people with associated skill sets and resources.

Focusing on and incorporation of training in all aspects of biomanufacturing, including the regulatory aspects: In addition to the workshops held by **DBT** sponsored institutes, creating online courses for larger dissemination of training

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Creation of this document was done with the expectation that it may be used as the backbone for further discussions between academia, industry and regulatory agencies across the globe. This was made possible by the efforts of the **DBT Centre for Biopharmaceutical Technology** team with inputs from all the panelists and other stakeholders.

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