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Indiaâ??s National Chemical Laboratory (NCL), one of the most well-established labs in the wider Council of Scientific and Industrial Research (CSIR) network, has made some major contributions to improving the countryâ??s manufacturing processes for pharmaceutical intermediates and APIs. Director Dr Ashish Lele outlines the approaches the lab is pursuing, such as continuous flow chemistry, to tackle Indiaâ??s over-dependency on Chinese APIs and discusses the governmentâ??s Production Linked Incentives (PLI) scheme to encourage Indian industries to produce materials through organic chemistry.

Could you start by introducing yourself and the laboratory, and by explaining your current focus, and top priorities?

I am the current director of the National Chemical Laboratory (NCL) and a trained chemical engineer. I completed my bachelorâ??s in chemical engineering at Mumbai University and my PhD at the University of Delaware in the US. I joined the National Chemical Laboratory as a scientist in 1993.

The National Chemical Laboratory is a vital component of the Council of Scientific and Industrial Research (CSIR). We operate under the Ministry of Science and Technology as a central government laboratory falling under the domain of science and technology. CSIR encompasses 37 laboratories throughout India, spanning diverse fields such as aeronautics, the chemical industry, biotechnology, advanced materials, and agriculture. Out of these 37 labs, the National Chemical Laboratory is one of the first, having been established in 1942 and predating Indiaâ??s independence in 1947. The lab has been actively contributing to scientific advancements since it opened in 1950. With a focus on the chemical and allied industries, the laboratory interfaces with chemistry, biology and chemical engineering.

The mission of the laboratory is to support the Indian chemical industry in achieving global competitiveness and the use of world-class technologies. The laboratory engages in the complete research and development life cycle, including demonstration and deployment. We also collaborate closely with industry stakeholders to bring innovations from the lab to the market. As the laboratory approaches its Platinum Jubilee after 75 years of dedicated service, it remains committed to ensuring that the highest quality research translates into tangible advancements within the chemical industry and beyond.

What are the most significant opportunities and challenges facing the field of chemical research in India, and how is the CSIR-National Chemical Laboratory addressing them?

The laboratoryâ??s roadmap spans seven decades, marked by notable contributions, such as playing a pivotal role in Indiaâ??s emergence as a global leader in generic drug manufacturing. In the 1970s, a significant policy change regarding product patents for pharmaceuticals was put in place. This was a necessary step because income levels were low and healthcare was becoming unattainable. This change catalysed the laboratoryâ??s development of new processes, positioning India as a major contributor to the global pharmaceutical supply chain. For this reason, India has become the pharmacy of the world, with 25 percent of North American and European generic drugs coming from India.

The lab has made major contributions to producing the best processes with more than 140 technologies being developed for manufacturing pharmaceutical intermediates and APIs in the country. Eminent figures from within the industry such as Yousef Hamid, the founder of Cipla, publicly expressed that if it was not for the NCL, the Indian market would have not grown so quickly.

In the 1990s, a pivotal policy shift opened Indiaâ??s markets. It allowed big industry players to come to India and sell their products across categories such as chemicals, materials, polymers and more. The opening of markets in India presented both challenges and opportunities for laboratories like ours. The challenge emerged as a shift in funding dynamics, transitioning from government dependency to self-sustainability. While the government continued partial funding, the laboratories were urged to manage themselves independently. However, this challenge brought with it an opportunityâ??the ability to offer R&D services globally rather than just in India. With the markets now open to the world, laboratories, including ours, were able to extend their services to major multinational companies. This led to the filing of the first US patents in the early 90s, marking the beginning of substantial collaborations with prominent global entities, particularly in the pharmaceutical sector.

Simultaneously, the second challenge arose as Indian companies faced increased competition, particularly in the local market. Responding to this, they began substantial investments in R&D. Our laboratory played a crucial role by providing strategic guidance, manpower through our students, and technological support to these companies.

As we move into the current decade, climate change and regulatory pressures for decarbonization are the biggest challenges. The focus lies on addressing pollution, achieving decarbonization, and navigating the complexities of sustainability aligning with the global push for environmental responsibility. Our laboratory recognizes its responsibility to contribute meaningfully to addressing these critical challenges defining this decade.

What are some of the current research initiatives and challenges that the laboratory is actively working on?

One of the prominent challenges the country is facing is the over-dependency on China for APIs. As a country we want to avoid this dependency and rely on our own manufacturing abilities and to be self-sufficient. In that sense, our laboratory has outlined a roadmap with seven focal themes, particularly emphasizing clean energy and decarbonization-related chemistry. The themes include process chemistry, finance, and specialty chemicals, especially in the pharmaceutical sector. One notable concept we are exploring is continuous flow chemistry, a departure from traditional batch processes. To illustrate this, batch processes are like cooking in a pot, yielding a mixture of desired and undesired chemicals. 20 percent of energy goes into downstream purification to extract the desired chemicals. Continuous flow chemistry, conducted in a pipe, offers clarity in the resulting mixture, with significantly reduced downstream costs and enhances safety.

This shift to continuous manufacturing is particularly pertinent for various industries dealing with complex reactions involving toxic materials and exothermic processes. If not done right it can lead to explosions and the risk of spreading harmful chemicals. By running such reactions in a continuous loop, we achieve efficiency, safety, and economic advantages.

The driving force behind the implementation of this change is decarbonization. For example, batch plants entail distillation. Distillation relies on steam, and the traditional methods of generating steam involve burning coal or gas contributing to carbon emissions. The imperative to decarbonize compels companies to seek alternatives. By transitioning from batch to continuous processes, they can significantly reduce distillation and their carbon footprint. This shift represents a strategic move to align with environmental sustainability goals and decrease emissions, both gaseous and liquid.

Large pharmaceutical companies are embracing this approach and heavily investing in research and development of continuous flow chemistry. However, the challenge in achieving this transformation relates to current assets. There are current assets, such as batch plants with depreciated values that still generate profits. Company management faces the dilemma of investing in a new plant that utilizes continuous flow chemistry, or depending on old processes.

China is already ahead in implementing this change to continuous flow chemistry whereas India is still in the transitional phase, navigating this shift. Chinaâ??s government is taking a decisive stance to only permit new pharmaceutical plants if they adhere to continuous batch processes.

The NCL is collaborating with numerous companies, including prominent players in the pharmaceutical industry showing them how the adoption of continuous processes can be implemented and that it can be advantageous. Companies are accustomed to traditional methodologies and are often sceptical about executing a continuous flow system. To address this scepticism, we have established a â??living labâ?• featuring various platform chemistries such as continuous flow setups for hydrogenation, sulfonation, ozonolysis, and chlorination. We invite industry players to witness first-hand how these processes can be seamlessly integrated. This shift demands a change in mindset, and our role is to catalyse this transformation.

Notably, we have engaged in a substantial partnership with a UK laboratory, the CPI (Centre for Process Innovation), which is part of the renowned catapult network. This collaboration aims to establish a cutting-edge living lab, and their dedicated team has visited us recently to interact with major pharmaceutical companies in Hyderabad and Bangalore.

Can you share more about how biology is advancing in India and the contributions of the lab to this advancement?

The implementation of biology is a relatively new field for India. During the COVID-19 pandemic, India confronted its heavy reliance on China for imports, particularly strategic materials known as Key Starting Materials (KSM). Recognizing the urgency to incentivize domestic manufacturing of these critical components, the government introduced the Production Linked Incentives (PLI) scheme. This initiative, spanning PLI one, PLI two, and now extending into PLI three, is focused on encouraging Indian industries to produce materials through organic chemistry. In the initial phase, PLI one concentrated on identifying 53 key strategic materials, that are 100 percent imported from China, urging companies to manufacture them domestically. Within this, 26 molecules were allocated to be manufactured through conventional organic chemistry production. The remaining 27 molecules ventured into the realm of bio-based production. This shift brought forward the realization that India lacked essential competencies in large-scale fermentation, a critical aspect of bio-based manufacturing.

With respect to biotechnology, India is emerging but faces challenges in scaling up from lab-level fermentations to industrial-scale operations. Smaller companies lack the financial means to independently acquire cutting-edge biotech solutions. While larger enterprises may seek technology licenses globally, smaller players face constraints. The government is actively acknowledging and supporting the need to bridge these gaps, fostering an ecosystem for large-scale fermentation, downstream purification, and other essential components of bioprocessing. Despite the hurdles, some companies demonstrated resilience and invested in perfecting these technologies, paving the way for pre-clinical and clinical trials.

Within the Ministry of Science and Technology, specifically the Department of Biotechnology, there is a concerted effort to propel advancements in biotechnology. The Secretary of this department, Mr Rajesh Gokhale has initiated a ground-breaking policy known as the Bio-entry Policy. This policy is a significant stride toward utilizing biology to manufacture materials, chemicals, and various products traditionally not associated with biological processes. Its primary objective is to catalyse research and innovation in the field of biotechnology within India.

In line with this vision, we are discussing plans to establish specialized centres dedicated to translational research. These centres will be equipped to handle volumes ranging from 1,000 to 10,000 litres, providing an open facility accessible to all. The idea is to foster a beneficial environment for start-up companies with limited resources. The proposed centres aim to limit constraints by offering rental services for larger fermenters. The start-up can rent the necessary facilities for a week, conduct their trials, generate sufficient material, and return to their laboratory. This innovative approach fosters a collaborative ecosystem, facilitating the growth and success of emerging companies on the biotechnology landscape.

What are some contributions the lab has made to the field of biosimilars?

Our laboratory is actively assisting various companies, both major players and others entering the field. Two noteworthy examples highlight our contributions in this area. Firstly, we have licensed technology for a biosimilar designed to address diabetic retinopathy. Given the absence of competition in small molecules for treating highly diabetic retinal disorders, biosimilars become the sole viable route. The appeal lies in the fact that larger companies with no alternative, are eager to tap into this lucrative market.

The second contribution pertains to snakebite-related fatalities. This is a significant issue in rural India, causing between 60,000 to 70,000 deaths annually. With regulatory pressures intensifying with respect to the purity of anti-snake venom treatments, traditional production methods faced challenges. We guided companies on transitioning to newer technologies, ensuring compliance with stringent regulatory standards.

By demonstrating how to navigate regulatory pressures we facilitate the adoption of advanced technologies. This approach is particularly relevant for biomolecules with practical significance for India. As we embark on this journey, we acknowledge the importance of building confidence gradually. Initiatives involve identifying suitable candidates, launching investments, and then expanding operations.

How does the laboratory support the professional development of its researchers and scientists, and what opportunities are available for students and early-career researchers?

The laboratory engages in extensive training programmes. Although we are not an established university, we provide training through the CSIRâ??s Virtual University which encompasses virtual campuses across all CSIR labs. This initiative involves mentoring 400 PhD students, acting as catalysts for innovation. Additionally, postdoctoral fellows, with varying experience levels, contribute to the laboratoryâ??s endeavours.

The focus lies not only on high-quality scientific research but also on preparing students for industrial roles, emphasizing the translation of scientific knowledge into practical applications. The laboratory operates on three key fronts: research, services, and developing skilled human resources. Our approach involves combining curiosity-driven science with focused, application-oriented programmes. This strategic alignment enables the creation of intellectual property based on fundamental science.

Do you have any final message to share with PharmaBoardroomâ??s international audience?

Bio manufacturing is key for India, urging a timely implementation of transformative measures. The transition has gained momentum with the support of the policies in place by the Department of Biotechnology. The strategic alignment with these policies allows us to catalyse bio manufacturing and continuous flow synthesis both of which are pivotal areas of focus.

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