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Editorial Introduction

Krishna Ravi Srinivas*

Welcome to the joint second and third issue of Volume 26 of the Asian Biotechnology Development Review! We express our sincere gratitude to all the contributors and all members of the International Editorial Advisory Board. The response to the last issue was excellent.

The current issue features two articles, an event report and two book reviews. One of the articles featured in this issue pertain to study of socially responsible model of innovation in healthcare, while the second one is on harmonizing regulatory policies for genome-edited crops.

In the first article, Kirti Tyagi and Yennapu Madhavi discuss the case study of Shri Brij Seva Samiti TB Sanatorium, Vrindavan (TBSV) in TB management, presented as a socially responsible innovation model got healthcare, by utilising qualitative research methods and developing a novel analytical framework for socially responsible innovation by adapting the theoretical principles of responsible and social innovation. Social determinants of health play a significant role in managing tuberculosis (TB). Controlling tuberculosis, therefore, requires an inclusive health policy and a model of socially responsible innovation. This paper explores the relevance of a sanatoria model in the current context where modern biology and biotechnology applications are predominant. TBSV combines faith, its core cultural beliefs, and its close linkage with the National TB Elimination Programme (NTEP). The article also discusses the role of TB sanatoriums in the success of National TB Elimination Programme (NTEP) from a public health perspective as well as the innovations in biotechnology and their adaptation in combination with a sanitorium-based care model that can lead to NTEP nearing its goal of TB elimination as per the goals set in the National Strategic Plan 2017-25 (NSP).

In the second article, Mansi Mishra argues for the need for harmonization of the regulatory framework for genome-edited crops for advancing scientific and technological cooperation in the agriculture sector. The need

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for sustainable agricultural practices and climate resilient crop varieties hs being felt due to the rising global population and climate change. Moving ahead with modern biotechnologies beyond GM technologies such as CRISPR/Cas9 have emerged as a groundbreaking tool for precise and efficient genome editing of crop plants enabling enhanced crop productivity, quality, and resilience to abiotic and biotic stresses. Moreover, such CRISPR genome-edited crops are not bound by stringent regulations like GM crops. However, effective scientific and technological cooperation needs a well-defined policy framework to enable the efficient use and sharing of such technologies across countries. In light of this, author's argument for the harmonization of the regularity practices sounds interesting.

A paradigm shift in the pharmaceutical sector has been witnessed with the generics coming into play in a big way. Since the last decade, with the increasing thrust towards shifting away from chemically-synthesized pharmaceuticals to biopharmaceuticals, another paradigm shift can very well be envisaged in the pharmaceuticals sector. As key elements of biopharmaceuticals, both biologics and biosimilars, are gaining huge traction in the R&D as well as policy discourses across the world including India. Against this background, RIS, in collaboration with the Third World Network, organised a Roundtable on Biosimilars with the aim to discuss the emerging trends in technology and recent developments in the regulatory environment and its implementation within the Indian Biosimilar Regulatory Framework which will help to facilitate affordability and access of biotherapeutic products to patients in need of such treatments. The salient points emerged during the Roundtable is captured in the event report.

Book reviews by Sneha Sinha and Anupama Vijayakumar of the volumes related to CRISPR and Synthetic Biology respectively adds significant value to this issue.

Your comments, responses and ideas are welcomed.

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Tuberculosis Sanatoriums: A Socially Responsible Model of Innovation in Healthcare

Kirti Tyagi* and Yennapu Madhavi**

Abstract: Social determinants of health play a significant role in managing tuberculosis (TB). Controlling tuberculosis, therefore, requires an inclusive health policy and a model of socially responsible innovation. TB is a social disease eliminating which may require a mix of biomedical and social interventions. The pre-antibiotic era utilised TB sanatoriums for disease management. This paper explores the relevance of a sanatoria model in the current context where modern biology and biotechnology applications are predominant. A case study of Shri Brij Seva Samiti TB Sanatorium, Vrindavan (TBSV) in TB management is presented as a socially responsible innovation model by utilising qualitative research methods and developing a novel analytical framework for socially responsible innovation by adapting the theoretical principles of responsible and social innovation. TBSV combines faith, its core cultural beliefs, and its close linkage with the National TB Elimination Programme (NTEP). TBSV provides patients with quality care, nutrition and clean open-air area to recover. Patients are diagnosed timely using latest diagnostics, are enrolled in Ni-kshay to receive anti-tubercular treatment (ATT) and other social incentives which help TBSV to emerge as a powerful actor in TB control in the district. It also discusses the role of TB sanatoriums in the success of NTEP from a public health perspective as well as the innovations in biotechnology and their adaptation in combination with a sanitorium-based care model that can lead to NTEP nearing its goal of TB elimination as per the goals set in the National Strategic Plan 2017-25 (NSP).
Keywords: Tuberculosis, socially responsible innovation, social reengineering, health policy, biotechnology R&D, public health,

Introduction

Tuberculosis (TB) is a communicable disease, the management of which is directly influenced by social determinants, wherein poverty and health inequality play a direct role, thereby putting the marginalised section of the population at higher risk of illness (Ferreira *et al*., 2023). It is considered a disease of people with low incomes in middle and lower-middle-income countries (Pescarini *et al*., 2017). India has the highest TB burden in the world. The estimated point prevalence at the national level of

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microbiologically confirmed pulmonary TB among persons over 15 years is 316 (290–342) per lakh population. As per the National TB Prevalence Survey report, the prevalence of all forms of TB is 312 per lakh population (Rade *et al*., 2022). The overall country age distribution for TB is 15 to 30 years. Over 90 per cent of the economic burden is due to mortality by the disease. As per the Global TB Report (2023), the estimated incidence of all TB in India for 2022 was 199 per 100,000 (169–231 per 100,000 population). TB is a treatable and social disease that may require a mix of biomedical and social interventions to eliminate. India has been sparing no effort over the last seven decades to bring down the TB disease burden through various policy changes and strategic approaches from time to time (India TB Report 2023).

In the late nineteenth and early twentieth centuries, to stop TB spread among communities, patients were treated in isolation in a sanatorium model of care (providing good rest, good nutrition, and a refreshing environment) until technocentric approaches became prominent. The first description of TB sanatorium care is seen in the published works of Hermann Brehmerin (Barberis *et al*., 2017; Daniel, 2011). Being a TB patient himself, Brehmerin travelled to the Himalayas and reported his cure, after which he established the first-ever sanatorium in a mountain town in Germany (Sachdeva *et al*., 2020). The same model of care was then replicated across various parts of the world to provide care for and a chance to cure TB patients (Bisen *et al*., 2013). This paper explores the role and relevance of sanatoriums in treating TB, even in current times, through the socially responsible innovation model as a case study.

TB sanatoriums in India

The first open-air sanatorium for TB treatment, including isolation of patients, was established in 1906 in Lithuania, near Ajmer, in India. The next one followed in Almora in 1908. The third sanatorium, which was non-missionary, was founded in 1909 near Shimla. It was followed by the establishment of the United Mission Tuberculosis Sanatorium (UMTS) in 1912 in Madanapalle, Andhra Pradesh (Central TB Division 2012). Another set of sanatoriums is still functional in Uttarakhand state (India), such as the TB sanatorium Bhowali, established in 1912 (Debnath *et al*., 2022). Although TB sanatoriums became a popular method of providing TB care, the literature exploring all of the TB sanatoriums established in the country — both the remaining sanatoriums and those that no longer exist — remains sparse. In the early to middle 20th century, no treatment was available; diagnosis relied mainly on clinical examination, and the main line of treatment was nutritious food, open air, a dry climate, and rest (Sandhu,

2011). The sanatorium style of care, especially for TB, took precedence. The sanatoriums were also set up in that era to isolate the patients and prevent the spread of the disease (Sood *et al*., 2021).

After antibiotics were discovered to treat TB, sanatoriums also played a role in conducting clinical studies on the role of antibiotics and isolation in the spread of TB to household contacts of patients (Kamat *et al*., 1966). This study showed that with the advent of antibiotics, TB care could be provided equally well at home, which led to a decline in the TB sanatorium model of care. Another study in South India looked at a comparative analysis of home and sanatorium treatments of pulmonary TB (TCC 1959). With time, most TB sanatoriums are not functional in their original form and have been repurposed to incorporate management of various other diseases. However, one such sanatorium still providing TB care is the Shri Brij Seva Samiti TB Sanatorium, Vrindavan (TBSV) in Uttar Pradesh (UP), India; it is the main focus of this article as an exemplary case of socially responsible innovation in delivering affordable healthcare to TB patients.

This sanatorium (TBSV) is based in the religious town of UP, where the beliefs of social well-being and service to society are deeply rooted in people's day-to-day lives. The sanatorium has a rich history of support from eminent national figures, such as the then Prime Minister of India, Pandit Jawahar Lal Nehru, who generously donated the sum of Rs. 1950, which was the cost of treating a patient for a year at that time (TBSV Annual Report 2000). The following sections explain the functioning of the sanatorium in detail, including the admission patterns and duration of stay, and how, with minimal facilities and partly through a social philanthropy model, it stands out as a unique healthcare delivery model. Some argue that the sanatorium model of care still needs to be recovered as we approach the post-antibiotic era (Venkat, 2019). India has the highest burden of drug-resistant TB, and cases of extensive drug-resistant TB (XDR TB) have surfaced over the years. However, there is no conclusive evidence to chart a number reflecting the magnitude of the problem (Prasad, 2012). In his review, Venkat, therefore, argues that it would be worthwhile to explore the sanatorium care model from the pre-antibiotic era with the advantage of the right factors, such as fresh air, rest, and proper nutrition, that play a role in improved treatment outcomes (Venkat, 2019).

Even though TB sanatoriums are a concept of the early twentieth century, they remain a valuable factor within the TB ecosystem. What makes TBSV different from other TB care-providing institutions in the country is the involvement of various actors of society at large, both at individual and organisational levels. The paper's discussion section dives deep into how

various elements of socially responsible innovation are integrated within the functioning of the sanatorium. The case study reveals the intricate web of actors, each working towards a common goal of TB management in the area. The mix of age-old concepts of the sanatorium model, such as good ventilation and nutrition along with ample rest, with modern technological advancements in diagnostics, availability of antibiotics, patient support mechanisms, and patient's belief in the system, have made TBSV a solid aid to the National TB Elimination Programme (NTEP) in the district as it integrates its institutional mechanisms with the program, thereby producing excellent treatment outcomes. Thus, TBSV has emerged as an example of socially responsible innovation.

Since TB is a social disease, the social determinants of health play a significant role in its control. It is, therefore, important to discuss the concepts of responsible innovation and the role of society as a predominant determinant, thereby making TBSV a socially responsible model of innovation in delivering health services. The paper, therefore, tries to emphasise that even though TB sanatoriums have lost their popularity as the preferred choice of TB treatment and management, it is worth re-discovering this decades-old model of healthcare service delivery in TB from the pre-antibiotic era because of a unique arrangement it offers, i.e., rehabilitation with nutritious food, clean air and rest along with advanced diagnostics and treatment options. The paper will also connect the role of the sanatorium in the success of NTEP through its adoption of newer technological advancements. Along with this, we also briefly discuss the innovations in biotechnology that can lead to NTEP nearing its goal of TB control and elimination as per the goals set in the National Strategic Plan 2017-25 (NSP).

Theoretical Framework

Innovation is the need of the hour in healthcare to improve patients' overall wellbeing. However, when we speak about innovation in the case of TB, we are not just restricting ourselves to product innovation in a research laboratory or institution. Since TB is a social disease, the inclusion of society in managing the disease becomes very important. TB demands close monitoring of patients who have started treatment and providing support at various points during treatment, as well as post-treatment monitoring. This kind of engagement at a social level ensures that patients' demands are being met and that the institution is evolving and strengthening its institutional mechanisms in a socially responsible way. Socially responsible innovation, therefore, can be visualised as a mix of social responsibility and responsible

innovation. It is worthwhile to look at the four dimensions of responsible innovation as given by von Schomberg (2021), along with the definition of Responsible Research and Innovation, as follows:

A transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability and societal desirability of the innovation process and its marketable products (in order to allow a proper embedding of scientific and technological advances in our society).

Socially responsible innovation is a phenomenon in which multilevel innovation involves multi-disciplinary actors and is deeply embedded into the local social values, thereby working at a ground level to achieve a common goal (Batayeh *et al*., 2018).

The current work attempts to explore Shri Brij Seva Samiti TB Sanatorium through the lens of a socially responsible innovation framework. We aim to see how the sanatorium model of care is relevant to the current era, its alignment with the NTEP, and the factors that help it emerge as a successful actor in TB management. The following section talks about responsible innovation in a social context. The methodology section presents an analytical framework for analysing TBSV as a case study. The paper discusses the relevance of this model of TB care through its functionality and institutional mechanisms that have fostered the social ecosystem of innovation.

With the above background, the present case study was designed to evaluate the effectiveness of TB sanatoriums in the twenty-first century, focusing on TBSV, especially for achieving a high treatment success rate, with the following objectives:

- To look at the institutional mechanisms – establishment, facilities, functioning, and decision-making of the sanatorium
- To study the local and national network of stakeholders involved
- To identify bottlenecks and barriers in TB management services

Methodology

Four officials were interviewed for this work, including the manager of TBSV, the senior treatment supervisor (STS) appointed by the CTD, the TBSV pharmacist, and the TBSV lab technician. Convenience and purposive sampling techniques were used for this study, as these participants were

readily available for an interview. The participants were also included based on their characteristics, such as current job profile at TBSV, knowledge, involvement in the functioning of TBSV, experience in the field, and its relevance to the objectives of the current research. Any official not directly related to the TBSV or does not have the characteristics mentioned above was excluded from the study.

Secondary data was also analysed for this study. The case study included reviewing the available literature on the history of TB sanatoriums in India. We looked at the annual report to understand the institute's funding mechanisms. This was followed by conducting in-person semi-structured qualitative interviews with the management and staff of TBSV, lasting 30 minutes to an hour. The main themes covered in the interview were the functioning of TBSV, facilities provided to the patients, funding mechanisms, administrative decision-making, linkage with the NTEP, procurement of drugs, the role of society in TBSV's functioning, their strengths, and any challenges faced by them.

Real-world data was collected through the interviews and analyed simultaneously. The recordings of the interviews were converted to verbatim transcripts. The transcripts were analyed by keeping the principles of a responsible innovation framework in mind. The role of society was the central theme that emerged from iterative data analysis and, thereby, the motivation to combine responsible innovation with social innovation to develop the framework of socially responsible innovation.

Analytical Framework

The framework for responsible innovation that we have described includes responsibility, works through four dimensions, couples anticipation, reflection, and deliberation, along with agency and action, and explicitly states the need to connect with the cultures and practices of governance.

This paper uses this theory to create an analytical framework contextualised for TB management in India. TBSV works around similar dimensions; however, we add the element of societal responsibility in a much more pronounced way. As observed through the case study, we explore the role of social actors who have come forward to strengthen TBSV in a socially responsible way. The framework is adapted by (Owen *et al*., 2013; Stilgoe *et al*., 2020). They also describe responsible innovation in a broader term as '[r]esponsible innovation means taking care of the future through collective stewardship of science and innovation in the present.'

Combining the two approaches, we aim to analyse TBSV's acceptability, sustainability, and societal desirability of innovation. The way these dimensions have been incorporated into the framework, all the actors are working together to achieve the common goal of eliminating TB.

The case of Shri Brij Seva Samiti TB Sanatorium, Vrindavan UP

History, features, structure, funding and facilities

TBSV is a unit of the Shri Brij Seva Samiti TB Sanatorium Trust that was registered in February 1950 under the Societies Registration Act 1860 and is managed by a board of trustees consisting of a president, vice president, secretary, deputy Secretary, treasurer, and other members. Shri Brij Seva Samiti TB Sanatorium was established in 1951 in Vrindavan, a town in Uttar Pradesh in India. Its main aim has been to propagate, protect, and preserve public health by providing medical relief to the general public with limited resources.

From the beginning, TBSV has dedicated itself to the service of TB patients – in 1951, the sanatorium founder Lala Hargulal Ji Beriwala, along with his close associates, set up a 32-bed TB sanatorium in Braj (Vrindavan). A portion of the land was generously donated by Sh. Ladli Kishore Ji Goswami was a prominent social figure in Vrindavan then. Saint Shri Karpatriji founded the stone and the inauguration. Since then, TBSV has been managed by the Trust, which is comprised of well-known and reputed members of society. The administration of TBSV was given to retired officials from the Indian Defence Services. Dr. Batra was the first medical superintendent, and Dr. Samuel Johans was the first surgeon appointed at TBSV. Both of them were renowned TB specialists at the time.

Facilities of sanatorium

The outpatient department (OPD) for TB is up to 400 patients daily. Since 2012, the sanatorium has provided TB OPD consultation, testing, and treatment to senior citizens free of cost. Patients from across the country come to TBSV to receive treatment. Since its inception, the sanatorium has treated 9.3 million cases of TB. The sanatorium is currently spread across an area of 40 acres and has a capacity of 100 beds (TBSV 68th Annual Report 2018–19, unpublished). The sanatorium has its treatment provision and a referral system in place, in which all multidrug-resistant TB (MDR-TB) patients are referred to the district TB hospital for treatment.

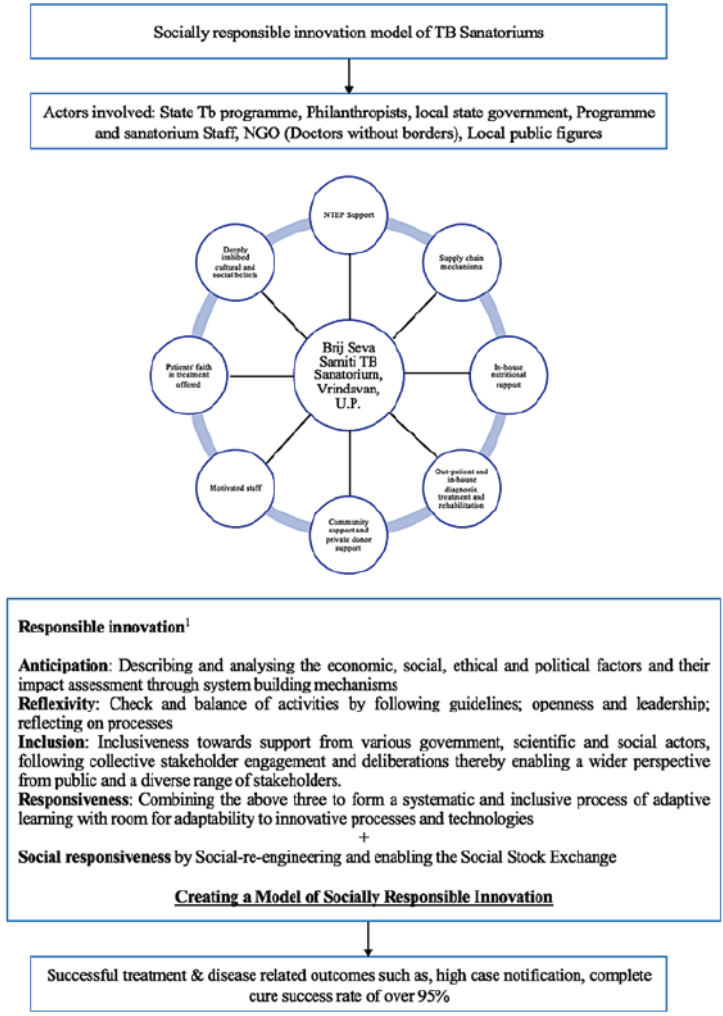
The X-ray department has three X-ray machines and two X-ray film developer systems. The sanatorium also has a liquid culture and sensitivity testing facility for first- and second-line TB drugs. Under the District TB program, the sanatorium is also equipped with a CBNAAT machine. The sanatorium claims to have achieved a complete cure success rate of over 95 per cent, significantly higher than the national average of 85 per cent. The sanatorium is believed to provide a clean, pollution-free, and lush green forest surrounding to ensure the speedy recovery of TB patients, along with nutritious vegetarian food.

The main features of this sanatorium are the following:

1 The organisation is a registered society and is private in its functioning.
2 Patients from poor socioeconomic backgrounds are treated.
3 Private donors majorly support the funding.
4 The patient registration fee is minimal (Rs. 50) and includes the cost of testing and medicine.
5 The two-mode functioning of the organisation is i) in private mode and ii) in coordination with the Central TB Division.
6 The board of trustees makes administrative and financial decisions.
7 Use of advanced biotechnology-based TB diagnostics that are sensitive and less time taking, such as GeneXpert and the latest therapies/treatment regimens, such as the use of FDCs, DR-TB and TPT regimens, as prescribed by NTEP guidelines.

The strong religious belief that the registered society of Brij Seva Samiti Sanatorium should serve humanity, that patients believe they will be cured in the spiritual town of Vrindavan, and that the dedicated team of professionals are what set the sanatorium apart. The sanatorium's acceptance by the TB patient community is well reflected by the number of cases treated, high case notification rates, and high treatment success rates. Experts have suggested that TB care requires the element of human touch by healthcare providers, especially those who are at the frontline of the TB care cascade (Berger *et al*., 2020), which is very well shown in the case of TBSV, where the NTEP and sanatorium staff have been helping patients feel heard, holding their hands throughout the treatment process, and helping with patient support-related issues. This is why the staff claims, ' Here patients come not only from Mathura but also from other districts for treatment.'

Figure 1: Framework of Socially Responsible Innovation



Source: Authors own adaptation 1Owen *et al*., 2013 and Stilgoe *et al*., 2018

TBSV has a strong base of private generational donors who believe in the cause of TB management and social welfare at large and are driven by the religious beliefs of the town of Vrindavan. In an interview, a TB programme official appreciated the work done by the sanatorium in providing TB care and being one of the district's most significant sources

of new TB notifications. With this impeccable support from society, the TB programme as well as the staff, for decades, patients have developed faith that they will receive quality care, support, and a cure at TBSV.

The following analytical framework (figure 1) depicts TBSV as a socially responsible innovation model and a successful example of providing economical TB treatment to patients.

Discussion

As discussed above, the TBSV case study outcome brings it forward as an example of socially responsible innovation. The TB programme works very closely with TBSV, where case notification is done through Ni-kshay integration. The presence of a senior treatment supervisor (STS) from NTEP on the ground also helps with the day-to-day treatment needs of the patients. TBSV was analysed through the lens of responsible innovation, using its four dimensions: anticipation, reflexivity, inclusion, and responsiveness. The TBSV analysis through responsible innovation is also directly influenced by the definition of responsible innovation given by Von Schomberg (2021).

In the case of TBSV, these dimensions have been deeply embedded in the institutional mechanisms of the sanatorium rather than just theoretical ideologies. The added societal component in the form of solid community engagement throughout the cascade of TB care makes TBSV unique. TBSV is supported by social responsiveness, wherein an individual or organisation is deeply motivated to work towards the betterment of society to achieve a common goal. In the case of TBSV, this has been done by a group of generational philanthropists and through social reengineering and resource mobilisation via new donors, including individuals, NGOs, cooperative societies, faith-based organizations, and corporate organisations.

TBSV has thereby emerged as an example of advocacy, communication, and social mobilisation (ACSM) by the WHO (2006), which is a significant component of the TB control strategy of the NTEP (Deane *et al*., 2006). We therefore propose the analytical framework that showcases TBSV as a unique example of socially responsible innovation. Through ACSM, TBSV has been tackling the challenge of improving the case-detection rate for the district of Mathura and improving treatment adherence through the involvement of a dedicated STS and their team. TBSV also empowers TB patients by enabling community engagement to provide them with nutritional support.

Anticipation

The sanatorium also leverages the government's strong political will and active involvement in monitoring the TB programme. TBSV has an institutional mechanism in place in which funding sources are drawn from philanthropists in society, and the NTEP provides incentives. TBSV has utilised societal support in its favour to contribute towards TB management and control. TBSV has also analysed the economic, social, ethical, and political factors and their impact on its functioning and has addressed the challenges through system-building mechanisms. Additionally, TBSV exemplifies social innovation by creating, capturing, and distributing social value (Bokoko, 2020a). Through the initial efforts of early philanthropists, new donors have been motivated to participate in the social cause of TB management for the marginalised population of the country. Additionally, with the help of government schemes, such as the National Multi-sectoral Action Framework for TB-free India (Central TB Division 2019) and community engagement efforts, such as 'TB Mukt panchayat' (or TB free village council) under the Pradhan Mantri TB Mukt Bharat Abhiyaan (PMTBMBA) of NTEP (Central TB Division 2022), various individuals and religious and non-governmental organisations have come forward to support the sanatorium.

Reflexivity

TBSV maintains a delicate balance of activities by following guidelines, promoting openness and leadership, and reflecting on processes. TBSV, in its close functioning with the NTEP, makes sure that all contextually relevant guidelines and policies are followed. Its leadership is open to change regarding the adoption of newer technologies, changing guidelines, or inclusion of social determinants, such as nutritional support by the programme. It follows the NTEP guidelines and fortifies them by incentivising the patients who have completed treatment. TBSV is also open to the inclusion of various actors into the process of the TB care cascade.

Inclusion

TBSV shows inclusiveness towards support from various government, scientific, and social actors, following collective stakeholder engagement and deliberations and enabling a broader perspective from the public and a diverse range of stakeholders. Through the study, various actors emerged as part of the ecosystem supporting the sanatorium. The significant actors identified as part of the case study are the state TB programme, philanthropists, state government, programme and sanatorium staff, NGOs (Doctors Without Borders, Mundona Rural Development Foundation,

Jagadguru Kripalu Parishat), local public and religious figures, and private donor support as well as community support in the form of Ni-kshay Mitra, for treatment and nutrition. This case study also highlights how different segments of society, i.e., public (NTEP), private (TBSV), and voluntary groups (individual donors and organisations), add value to the social aspects and enhance the existing systems of the TB ecosystem.

Responsiveness

TBSV, therefore, combines the above three to form a systematic and inclusive process of adaptive learning with room for biotechnological innovative processes and technologies responding to the societal challenge of TB (Bokoko, 2020a). According to TB officials in the district, TBSV does not present its unique set of challenges. However, the larger societal and health system challenges are being addressed by TBSV by the process of responsible innovation and its four dimensions, coupled with the society emerging as the most significant support system. The sanatorium serves not just as a hospital for treating TB patients but as a social ecosystem, separate from the rest of the outside world, where nutritious food, clean air, living spaces, and medical care such as diagnostics, drugs, and rehabilitation are provided. It would not be wrong to call the TB sanatorium a community. During the interviews, we observed that the patient footfall in the sanatorium is not limited to the district of Mathura but also reaches far outside the district or state of Uttar Pradesh. This is because of the involvement of the staff both at the programme end and at TBSV to provide quality care to the very sick and marginalised patients with TB.

TBSV has been receiving support at all levels of the healthcare delivery cascade from NTEP. Due to this, the sanatorium has kept itself updated on new developments in TB elimination. With antibiotic resistance as a threat to TB, the programme may replicate more sanatorium-based models to encourage multi-sectoral participation from society and individuals. The programme cannot fight TB alone. Societal engagement has emerged as the main element in achieving high treatment adherence and cure rates, along with high case notifications by the TBSV. Therefore, the governments not only in India (such as, Ni-kshay Mitra, increase corporate social responsibility and investments in TB and TB mukt panchayats) but also across the globe may speed up their efforts of implementing various policies for more robust community engagement at the ground level to provide further socioeconomic support to the patient. This will enable the global TB ecosystem to achieve the target of zero catastrophic costs and promote equitable access to health care. An example of CSR can be seen in an initiative by Fujifilm supporting the NTEP with its hand-held

x-ray facility for screening high-risk populations in Gujarat, India, for TB (Fujifilm India 2023).

There remains a gap in the literature regarding utilising a responsible innovation framework or its adaptation, as presented here, by coupling the four dimensions with the theory of social innovation, both in healthcare and TB. The framework of responsible innovation has been utilised in assessing digital health innovators in the UK and Norway (Naughton *et al*., 2023). Another study assesses how collaborative processes in healthcare can be managed and promoted to create more sustainable health systems (Lehoux *et al*., 2022). Both of these theoretically push towards a more socially inclined approach to a problem. In the case of TB, this becomes a major highlight because the disease is governed by social determinants of health as much as the clinical aspects. The current case study is an experiment to see the feasibility of utilising two separate frameworks that have a commonality regarding society as the demand generator and the supplier of TB care. It is the first time these two frameworks have been adapted to create another framework of socially responsible innovation and its application in analysing an institution supporting the NTEP in India.

TB sanatoriums and NTEP

TB sanatoriums' contribution to the NTEP's success in India can further be explained through the lens of TB control from the public health paradigm and understanding the history, changes in trends, and its effects on present-day TB programmes. TB sanatoriums as a primary mode of treating TB had a significant role in forming the basis of the early strategies of TB control that, in turn, helped in the evolution of and success of NTEP. The primary objective of sanatoriums was to reduce TB contagion, which was a significant public health issue in the pre-antibiotic era, thereby playing an important role in preventing TB outbreaks. (Raviglione & Pio, 2002).

Sanatoriums offered residents short-term convalescent care, which stabilised the patients and prevented further disease development in most cases. These practices formed the basis of what was to evolve into more systematic and data-driven approaches to the treatment plan of TB, which may be seen as part of the NTEP today (Daniel, 2006). TB sanatoriums were also instrumental in training physicians and other healthcare practitioners on diagnosing and managing TB patients. This created a pool of human capital that could be useful later when developing other, more robust TB control programmes, such as the NTEP. (Rao & Ananthakrishnan, 2016). Some other functions of sanatoriums were to inform the patients and society about tuberculosis, its mode of spread, and prevention (Narain, 2002).

Sanatoriums' role in the current TB care cascade has changed significantly. The learnings from TB sanatoriums are now incorporated into overall public health policies rather than remaining a more central aspect of the TB control process. Even though their direct involvement has diminished, the concepts and procedures established in sanatoriums have influenced current TB control initiatives. This is especially true in patient management, public health sensitisation, and the creation of community-based models of care.

Role of Biotechnology for the Elimination of TB in India

Tuberculosis continues to be a significant public health problem in India as it contributes to a significant tuberculosis burden in the world (Daad *et al*., 2018). A key area of focus in achieving the NTEP objectives is based on the application of biotechnology R&D in diagnosis, treatment, and vaccines. Biotechnology has been instrumental in the advancement of the tuberculosis innovation pipeline. Technological developments in molecular biology, genomics, proteomics, and bioinformatics are some of the areas that biotechnology has supported and continues to support in advancing the TB innovation pipeline.

The early diagnosis of MTb and its treatment resistance profile has been improved with the development of quick and precise diagnostic technologies like GeneXpert MTB/RIF, line probe assay, Lipoarabinomannan (LAM) and TrueNat. These molecular diagnostics paired with portable point-of-care devices are critical in resource-constrained environments where traditional laboratory infrastructure can be inadequate (Pai *et al*., 2016).

Till now more than twenty anti-TB drugs have been developed. Isoniazid (INH) and Rifampicin (RIF) were effective as first-line drugs for DS- TB. With the emergence of drug resistance, the second-line drugs such as Bedaquiline (BDQ) and Delamanid (DMD) have become essential (Zumla *et al*., 2015). Newer drugs including Pretomanid and Linezolid are also being developed to deal with increasing resistant strains of MDR-TB and XDR-TB with some success. However, because of the constant emergence of drug resistance, there is a need to focus on the discovery of new targets for drugs and mechanisms of resistance (Khan *et al*., 2023). The identification of viable TB drug candidates is being sped up by the incorporation of artificial intelligence (AI) into drug discovery, making the process more effective than conventional approaches (Lee & Oh, 2020). Additionally, biotechnology plays a role in genomic monitoring by enabling accurate tracking of drug resistance and TB strains, which can be critical for personalised medicine methods in treating tuberculosis (TB) (Walker *et al*., 2018).

Biotechnology is contributing to the development of next-generation vaccines, such as M72/AS01E, which provide higher protection than the conventional Bacillus Calmette-Guérin (BCG) vaccination. Furthermore, advancements in adjuvant systems and delivery platforms augment vaccine efficacy by generating more robust and long-lasting immune responses (Schrager *et al*., 2020). The current diagnostic methods, such as culture DST and smear microscopy lack sensitivity and ease of access, especially in resource-constraint settings. Newer diagnostic technologies are being explored to enhance accuracy and simplify sample collection and processing (Hu *et al*., 2024).

Future Implications of Biotechnology in Furthering the TB Innovation

Therapeutics

Innovations in biotechnology, such as, genome editing (CRISPR/Cas9), nanomedicine for drug delivery and antibody-drug conjugates (ADCs) are the drivers of modern medical treatments. These cutting-edge technologies have been seen to transform drug discovery offering targeted and personalised therapy for chronic diseases, like cancer (Ravichandran and Verma, 2021). The above-mentioned technological innovations have the potential to revolutionise personalised medicine and drug delivery in TB, especially in the case of MDR-TB. Cell-based therapies, such as, stem cell treatments and regenerative medicine could be helpful in the restoration of damaged lung tissue in TB. In addition, to shorten treatment time and minimise adverse effects, host-directed treatments (HDTs) are being investigated to modify the host's immune response.

Diagnostics

The discovery of novel biomarkers which can be easily converted for point of care testing can address the problems of cost, accessibility, and precision, especially in the vulnerable population (Leo *et al*., 2024). At present, both pathogen and host based biomarkers are also being researched upon (Nogueira *et al*., 2022). Biotechnology has also intensified the molecular diagnostics in TB through methods such as the next generation sequencing, transcriptomics, and microarrays through increasing the efficiency in the diagnosis of TB and its treatment. One major area that should receive emphasis should be translational research (Khan *et al*., 2023). Translational barriers that have been identified in the development of new TB treatments and vaccines are regulatory challenges, high attrition rates in clinical trials, lack of synergy between academic institutions and industry, which is critical

for improving patient outcomes of early diagnosis and preventing the spread of TB (Ravichandran & Verma, 2021).

Vaccines

There is a need for better vaccines than the BCG, developed in 1921. Some of the key issues that are yet to be addressed include; the definition of immune CoP that would predict vaccine effectiveness and development and the identification of immunodominant antigens (Yang *et al*., 2024). In the innovation pipeline of TB vaccines 21 TB vaccine candidates including, live whole cell vaccines, inactivated whole cell vaccines as well as the subunit vaccines of which M72/AS01E are there. Some of the other types of vaccines, which are still under consideration and research due to their ability to elicit broader immune responses include viral-vectored vaccines and mRNA vaccines. Newer discoveries such as the RhCMV/TB and intravenous BCG vaccination in NHP models have shown the potential of attaining sterilising immunity which has placed high expectations in highly effective TB vaccines (Lai *et al*., 2023).

Therapeutic vaccine[1] is a novel concept for achieving increasing therapeutic efficacy and minimise relapse among TB patients, especially with increasing drug resistance. Currently, there are different types of candidate vaccines undergoing clinical trials, including, killed whole-cell, live attenuated and viral vectored vaccines. Furthermore, monoclonal antibodies against mycobacterial antigens are in the pre-clinical stages of development. There still exist barriers, such as the requirement of multiple doses, huge costs as well as immunopathology, and warrant further pre-clinical and clinical testing (Bouzeyen & Javid, 2022).

Conclusion

TB sanatoriums provided a solid base for the first control activities of TB and were oriented on isolation, chronic treatment, and prevention. The principles and practices learned in the sanatorium movement particularly impacted the NTEP in the formal and rigorous treatment programmes and the drive towards early detection and public enlightenment. Despite a modification of their functions by the discovery of antibiotics and institution-based care, their influence is still reflected in the current strategies for controlling TB in India.

The Brij Seva Samiti TB Sanatorium has emerged as a model of socially responsible innovation. The sanatorium is highly dependent on private donors for its functioning. The sanatorium is located in a religious town of Uttar Pradesh, which points to faith and other cultural factors, along with

cooperation from the staff, who go beyond their duty to help and support the patients, playing a role in a patient's choice to be treated at the sanatorium.

In conclusion, there is a combination of diagnostics, treatment, nutritional support, and in-house residence for the treatment period. Overall, the sanatorium works well with the objectives of the NTEP. TBSV functions as a place where patients receive quality care, proper nutrition, and a clean, open-air place to stay and recover. They are diagnosed on time and enrolled in the programme to receive quality antituberculosis treatment and guidance, as well as other supports like direct benefit transfers, ration packets, and other incentives that encourage them to complete treatment and recover, thereby making TBSV an influential actor in TB control in the area and enabling them to achieve high case notifications as well as treatment success outcomes.

The study shows the relevance of the sanatorium model of TB care in the modern age. The integration with the NTEP and a solid social support infrastructure makes TBSV a success story in TB control. The programme may replicate More models to strengthen the country's TB ecosystem. The sanatorium combines care in both social and clinical aspects, thus providing a complete solution to managing the TB issue in a microenvironment. This case study and analysis enable policymakers to include social determinants of health as one of the main components of the TB care model. Also, as TB is a social disease, it is of the utmost importance that society participates in TB elimination efforts in India. TBSV is a successful model of socially responsible innovation that highlights the importance and relevance of society as one of the country's prominent actors in TB management.

Endnote

[1] While preventative vaccines are those which are used to protect an individual against a given disease agent, therapeutic vaccines are those that are employed to either alter the reaction of an organism during active disease or prevent reactivation of a disease agent.

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Harmonizing Regulatory Policies for Genome-Edited Crops

Manasi Mishra*

Abstract: The growing global population and manifold implications of climate change have created the need for sustainable agricultural practices and climate-resilient crop varieties. In the past decades, development of transgenic crop varieties has augmented the output of the agriculture sector. However, owing to the transgenic crops biosafety concerns, limited dissemination of information and awareness about the GM crops in public purview, and constraints of regulatory policies country-wise, several useful crop varieties have been pending approvals for commercial release to market. Second-generation gene-editing technologies like CRISPR/Cas9 have emerged as a groundbreaking tool for precise and efficient genome editing of crop plants enabling enhanced crop productivity, quality, and resilience to abiotic and biotic stresses. Moreover, such CRISPR genome-edited crops are not bound by stringent regulations like GM crops. Therefore, effective scientific and technological cooperation needs a well-defined policy framework to enable the efficient use and sharing of such technologies across countries. The flow of technology and knowledge can take place without any political and regulatory hindrances thereby generating positive public perception about these technologies and saving time, resources, and manpower across countries. Finally, the proposed article stresses the harmonization of the regulatory framework for advancing scientific and technological cooperation in the agriculture sector.
Keywords: Genetic modification, Genome-editing, Genome edited crops, CRISPR/Cas9, Regulatory policies, Food security.

Introduction

Agriculture plays a significant role in ensuring food and nutrition security and transforming economies to achieve sustainable development goals. Sustainable and inclusive agricultural development is critical in achieving the second UN Sustainable Development Goal (SDG) of zero hunger (SDG2) by 2030 and feed the projected world population of 9.7 billion by 2050 (Department of Economic and Social Affairs, United Nations 2017). In developing countries, agriculture continues to be the main source of livelihoods, employment, and income for about 70% of the population and thus remains crucial to economic growth (Economic Survey 2019-20, Kwa 2001). Though a significant sector, in India the share of agriculture in total Gross Value Added (GVA) of economy has declined from 35% in 1990-91

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to 15% in 2022-23 (The Economic Times 2023). Due to heavy population pressure and its rapid increase in developing countries, the demand for food supply is increasing at a faster rate. In past years, agricultural investments, reforms, and technological innovations have boosted the productivity and growth of yields across the world. Continuous growth in food grains, cereals, pulses, and oilseeds has provided for the nutritional requirements of the increasing population. Since the 70s, the adoption of industrial agricultural methods (high chemical input) and green revolution 'miracle' seeds have been actively promoted with a focus on increasing yields (Kwa 2001). However, the dependence on imported inputs has not been economically sustainable for developing countries especially for small farmers in developing countries for ensuring their livelihoods. It has also depleted the earth's soil, and its biodiversity and contributed to climate change. Therefore, there has been a need for alternate food production systems which are development-friendly and economically sustainable.

Traditionally, selective breeding had been used as a technique to develop desirable traits in crop plants. Though effective, conventional breeding techniques are time-consuming because they would give improved varieties over successive generations and rely on naturally occurring genetic variation. In the last two decades, advancements in genetics, plant biotechnology, and genetic engineering have proven to be 'game changers' by introducing ways to integrate desired traits directly into a plant's DNA and significantly increase the productivity of cereal crops (viz., rice, cotton, wheat, maize, sugarcane, and pulses), thereby addressing the issue of food security to a larger extent (India Brand Equity Foundation 2022, Mishra 2023). Since then, initiatives have mostly focused on nutritional security and 'biofortification' to produce improved food crops with high nutritional value. However, the agriculture sector at the global level is facing multiple challenges such as climate change, depleting water resources, loss of biodiversity, degradation of natural resources, and crop losses due to pests and pathogens, which can cause losses to food production, agriculture growth, and welfare of farmers. The Food and Agriculture Organisation of the United Nations (FAO) estimates annual losses of up to 40 percent in global crop production to pests and pathogens, accounting for almost US$220 billion of the global economy (Food and Agriculture Organisation of the United Nations 2021). Abiotic stresses like drought, water logging, extreme weather events like heatwaves, wildfires, salinity, and mineral toxicity have a substantial negative impact on the growth, quality, and yield of crops (Gull 2019). These losses are bound to escalate due to the risks posed by global climate change (Deutsch 2019). Rising temperatures and irregular weather patterns such as increased frequency of droughts or floods can make the conditions worse for growing crops in different regions. Temperature and precipitation changes can also very likely expand the

occurrence and range of insects, weeds, and diseases (Velasquez 2018). Therefore, there is a need to adopt to a sustainable approach of climate-smart agriculture which helps transform agri-food systems towards green and climate-resilient practices. Technologies that can bring new avenues for crop productivity and crop resilience to changing climatic conditions need to be emphasized for scientific cooperation and knowledge sharing by intergovernmental panels.

Genetically modified (GM) crops in 'modern agriculture': Applications and Controversies

Genetic modification (GM) is a technology in which an organism's genome is altered with DNA. Plant cells are injected with fresh DNA to create a genetically modified plant. The cells are typically produced in tissue culture from which they sprout into plants. These plants will develop seeds, and those seeds will carry modified DNA. The first genetically modified crop plants, antibiotic-resistant tobacco and petunia were developed in 1982 (Fraley 1983). This was followed by field trials of genetically engineered herbicide-resistant tobacco plants in France and the US in 1986 (James and Krattiger 1996). By 2010, several countries had conducted field trials of transgenic crops and planted commercialized biotech crops subject to regulatory approvals. Most of the trials were conducted in the USA, Canada, France, the United Kingdom, and the Netherlands, followed by Belgium, Argentina, Italy, China, Germany, Australia, Chile and Mexico. The advancement of genome sequencing technologies (short-read next-generation sequencing (NGS) has improved the production of highly contiguous genome assemblies and there has been effective utilization of this enormous sequence data for genetic engineering in crop plants to increase crop yields, enhance nutrient composition and food quality, development of resistance to pests and diseases and develop abiotic stress tolerance (Abdul Aziz 2022). According to International Service for the Acquisition of Agri-biotech Applications (ISAAA) reports, globally a total of 29 countries had planted biotech crops in 2019. In terms of area, the most common GM crops cultivated were soybean, corn, cotton, and canola as of 2019 (Statista 2024). The most widely targeted traits included herbicide tolerance, insect resistance, disease resistance, abiotic stress tolerance, and altered growth/yield (ISAAA, Inc. GM Approval Database). The top five countries with the widest area of biotech crops were the USA, Brazil, Argentina, Canada, and India. High biotech adoption rates in countries have impacted 1.95 billion people globally in terms of food security and nutrition security (ISAAA Brief 55-2019). However, several beneficial crop varieties are still awaiting approvals for commercial release to the market due to biosafety concerns surrounding transgenic crops, insufficient public education about the advantages of GM crops, and national regulatory policy limitations.

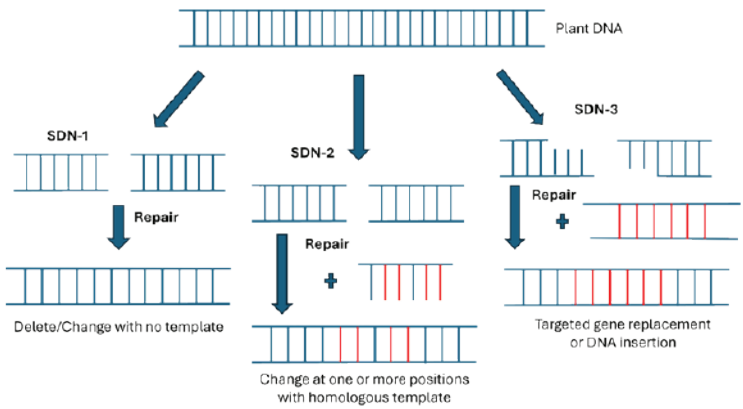
Genetically modified organisms and products thereof including GM crops are regulated products in India under the Environment Protection Act, 1986 (Ministry of Environment, Forest and Climate change, Government of India 2015). In addition to the regulatory constraints, there are several risks and controversies surrounding the use of GM crops. Though the genes being transferred occur naturally in other species, there are assumptions of unknown consequences of altering the natural state of an organism through foreign gene expression. There are speculations that foreign gene expression can alter the organism's metabolism, growth rate, response to environmental factors leading to altered interaction with other species and ecosystems. Secondly, the possibilities of horizontal gene transfer and vertical gene transfer between GM crops and other organisms or wild-type counterparts cannot be completely negated (Begna and Mohammed 2021). For example, the risk of transfer of antibiotic-resistance genes from microorganisms to humans has been raised. Farmers have expressed concern about the development of BT resistance in insects and pests that feed on BT crops (Turnbull 2021). These speculations have sparked health and environmental controversies leading to reluctance towards growing and consuming such crops across the world. Moreover, creating GM crops is an expensive and complex process which is mostly taken up by multinational companies ideating that private firms may claim ownership of the crops they generate and refuse to make them available to the public/small farm holders at a reasonable cost. Therefore, it is argued that GM crops may ultimately hurt the economy and environment because monoculture practices by large-scale farm production centres will dominate over the diversity contributed by small farmers who can't afford the technology (Phillips 2008). In the last two decades, the products of plant gene technologies have been adopted at different pace across different regions of the world. Public acceptance to GM crops has shown mixed trends across US, Europe and Asia depending on the country and public debate at the time of survey (Hoban 2004). The perception towards biotechnology, precisely genetic engineering and GM crops depends upon people's level of education and their interpretation of specific terminologies.

Second-generation Genome Editing technologies: Methods and applications in crop improvement

Second-generation genome editing technologies involving nucleases has transformed biotechnology by providing an easy, efficient and versatile platform for genome modifications. This is emerging as a highly active area of research. Genome-editing technologies also represent a groundbreaking advancement in agriculture, with significant potential for improving crops worldwide and ensuring food security. Clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated protein 9 (Cas9),

transcription activator-like effector nucleases (TALENs), and zinc-finger nucleases (ZFNs) are three foundational technologies which have facilitated a genome-editing revolution. Particularly, CRISPR-Cas9 has driven the revolution in genome editing for diverse applications because of its ability to efficiently induce targeted DNA double-strand breaks (DSBs). These DNA breaks then drive the activation of cellular DNA repair pathways and facilitate the introduction of site-specific genomic modifications enabling precise mutagenesis (Chen 2019, Samanta 2016). There are three types of genome-editing that can be done involving CRISPR nucleases: site-directed nuclease type 1, 2 and 3 (SDN1, SDN2 and SDN3) edited varieties (Friedrichs 2019, Ricroch 2019) (Figure 1). SDN1 produces a double-stranded DNA break that undergoes unguided repair via nonhomologous end joining, which randomly deletes or adds nucleotides, often causing a frameshift mutation. This type of mutation may cause gene-silencing, gene knock-out or change in the activity of gene. In SDN2, the double-stranded break is repaired by homologous recombination, which uses a sequence donor-synthetic DNA template (short single-stranded DNA) to add, delete or replace specific nucleotides. By contrast, SDN3 introduces a gene segment, or whole gene(s) at a specific site in the genome using homologous recombination resulting in a transgenic product. This method involves a template guided repair of the double-stranded break using a sequence donor which is a double-stranded DNA containing an entire gene. SDN1 is a highly efficient method while efficiency of SDN2 and SDN3 are lower than SDN1 and varies depending upon the species, donor design and time and method of delivery. Therefore, CRISPR applications are not limited to just knocking out plant genes or inserting new genes but also introducing site-specific nucleotide changes without permanently inserting any transgenes into the host genome (Samanta 2016).

Figure 1: Schematic Diagram of SDN1, SDN2 and SDN3 Techniques used for Gene Editing (Author creation)



Source: Authors' Compilation.

Consortium of International Agricultural Research Centers (CGIAR) and its partners have focused on SDN1 and SDN2 edits to address issues such as climate resilience in rice; disease resistance in banana, maize, potato, rice, wheat, and yam; and nutrition improvement and consumer and environmental safety traits in cassava (Pixley 2022). Therefore, SDN1 and SDN2 systems have accelerated the development of improved crop varieties without the involvement of transgenes. CRISPR/Cas9 technique is being used most extensively to edit model plant genomes (Arabidopsis, Rice, Tobacco). It has been adopted in several crop species as well for yield improvement, biotic and abiotic stress management (Ricroch 2017). Biotic stress on crops by pathogenic microorganisms' accounts for more than 42 per cent yield loss and around 15 per cent global decline in food production (Oerke 2005). CRISPR/Cas9-based knocking out of specific genes has been utilized to increase crop disease resistance in rice, wheat, maize, tomato, soybean, citrus, cotton, potato, grapes, alfalfa, and legumes as reported in published scientific articles as 'proof-of concept' studies (Endo 2016, Liu 2017, Shan 2013, Shan 2014). CRISPR has been used for triggering resistance to pathogens either by editing the pathogen's viral genes that are critical for viral pathogenesis or by editing the host defense genes. Genome editing can play an important role, especially for those traits where genetic variation is not available in the natural genetic pool and traits cannot be developed using a conventional breeding approach. It has become a very popular tool for crop improvement due to its simplicity, versatility, and cost-effectiveness. Being cost-effective, it can be potentially available to small actors in developing countries and not just remain limited to multinational companies based in developed countries. The business model for commercialization of GE crop varieties has not yet fully evolved yet various models are being implemented to also cater to the needs of smallholder farmers. For example, CGIAR implements various models to promote and ensure access to genome edited new varieties through national agricultural research programs and local and global seed companies that serve smallholder farmers. However, to accelerate gene-edited crop commercialization the regulatory policy framework and the technical limitations should be addressed as a priority.

Genome edited crops for improved food security and sustainable growth: Potential concerns

Genome-editing technologies are widely accessible and are being used for improvement and diversification of several major and minor crops, including those that are essential for food security in low- and middle-income countries. Genome editing is being applied to almost 40 crops across various countries mostly for addressing food quality, abiotic and biotic stress tolerance (Menz

2020, Pixley 2022). Transgene free CRISPR-edited crops produced using SDN1 and SDN2 systems, can be significantly transformative in the context of global climate change and food security challenges. This technology can help farmers and scientists meet the challenge of good quality food for everyone at affordable prices. One of the main advantages of genome editing is its capacity to hasten the dissemination of improved cultivars to smallholder farmers. It is no longer necessary to backcross, a process used in conventional plant breeding to introgress a feature from a non-elite or wild relative known as a "trait donor," because genes can be tweaked directly in elite breeding lines or commercial varieties. This reduces the time needed to generate an improved variety by nearly two-thirds and lowers linkage drag caused by non-elite residual genes from the donor parent, which are impossible to eradicate through traditional backcross breeding. Thus, multiplex genome editing and multiple alleles stacking at a particular locus can expedite the genetic improvement of plants for desirable traits (Pixley 2022). At present, this is not attainable using traditional genetic engineering or conventional breeding. Moreover, CRISPR-edited crops pose minimal risk to ecosystems, human health, and the environment as compared to GM crops (Ahmad 2021). However, to date only six genome-edited crop traits- in soybean, canola, rice, maize, mushroom, and camelina have been approved for commercialization. This is because of the uncertainty about growing and regulatory guidelines for genome-edited crop varieties. Several scientific, political, and social considerations are impacting these decisions to a larger extent. The scientific community yet remains concerned about the off-target effects and potential environmental impacts of releasing CRISPR-edited crops (Cribbs 2017, Mueller 2019, Omodamilola 2018). The international debate on likely impacts associated with CRISPR-edited crops and how they are biologically and legally different from GMOs has emerged. This is accompanied by legal, ethical, and policy issues associated with these crops.

CRISPR crops are emerging at the global level with the potential to boost food security, but the world is divided over their regulatory oversight. Different countries have different regulatory frameworks and, in most cases, the policies and regulations of gene-edited crops are controversial. For most countries, the development and commercialization of genome-edited crops are mainly subject to GMO regulatory frameworks. Many countries are still uncertain about how to grow and regulate genome-edited crop varieties. Many countries have excluded SDN1 and SDN2-generated crops from regulatory frameworks as they do not contain transgenes. A section of the scientific community believes that CRISPR-edited varieties should not be subject to existing GM regulations because they are similar to conventional breeding. The world community remains divided about the safety and regulation of CRISPR-edited crops. Transgene-free CRISPR-

edited crops generated using SDN1 and SDN2 systems can prove to be very significant in the context of global climate change and upcoming food security challenges. However, if CRISPR-edited crops are classified as GM crops and regulated like GMOs, their future cultivation, commercialization, and public acceptance will be disputable (Zhang 2020). Without a universal and specialized regulatory system, CRISPR-edited crops may face a similar future to GMOs. The success and future potential of CRISPR-edited crops in agriculture can be economically transformative, especially for low- and middle-income countries.

An overview of the regulations of Genome-edited crop plants in different regions

Many countries have legally categorized genome-editing approaches using the SDN 1/2/3 systems but only a few have released regulatory guidelines specifically for genome-editing and related technologies. Some have made amendments to their current regulations as per the development of new technologies while the majority of countries are stuck in the debate on how to regulate the genome-editing technologies and products developed using such genome alteration processes (Menz 2020). The initial appeal of genome-editing technologies stemmed from the expectation that they would not be subject to regulatory oversight, in contrast to transgenic or "GMO" techniques. However, it was an offset when in 2018, the Court of Justice of the European Union (CJEU) ruled that GE crops would be regulated like transgenics in the EU (European Commission 2019). This judgment was at odds with the emerging consensus that GE crops with only single-point mutations (SDN1) are not justified to be regulated like transgenics. In the past, the EU stance on transgenics had discouraged developing countries from adopting such varieties due to differential market requirements and high costs (Alston 2014). Therefore, the benefits of transgenics could not reach low and middle-income countries and their farmers with small land holdings. A similar path could be predicted for GE crops.

Later in 2018, a coalition of nine countries led by the United States, Canada, Argentina, and Australia signed a statement within the World Trade Organisation (WTO) to proclaim that cultivars derived from genome-editing should be regulated in the same way as conventional cultivars (Holman 2019). Concerns were expressed by the US, Argentina, and Paraguay regarding the CJEU's position, arguing that it would not only impose unfair trade restrictions on genetically engineered crops but also impede agricultural innovation and research at a critical juncture (Menz 2020). The United Kingdom after its exit from the EU has gradually distanced itself from the CJEU ruling on GE crops. Japan has indicated its intent to not

classify most of the GE crops as transgenics. China's stance on regulation of GE crops could also prove decisive for global harmonization because it is one of the largest economies and secondly, it is investing heavily in genome editing research. Most of the countries in Latin America, including Brazil, Colombia, Honduras, Uruguay and Chile are only imposing regulations for the GE crops with permanent insertion of foreign DNA (Gatica-Arias 2020, Schmidt 2020).

There are no restrictions on genetically engineered crops in the USA, Brazil, Argentina, Paraguay, Ecuador, Colombia, Israel, and Chile. In these nations, the use of gene editing to modify genomes by adding or deleting base pairs, such as SDN1 and SDN2, is accepted as being similar to traditional breeding (Bullion and Malhotra 2023). Targeted mutagenesis and cisgenesis are being considered non-GM in countries including Canada, Nigeria, the Russian Federation, Japan, Australia, India, Pakistan, the Philippines, and Indonesia, which have established explicit policies and procedures for the case-by-case assessment of gene-edited products. On the other hand, China, the UK, and the European Union are creating new regulations for plants that are created by gene editing.

Within Asia Pacific, Australia and Japan have a well-defined regulatory system for GM products and clear guidelines on gene-edited products. SDN1 products are not considered GMOs, SDN2 products are evaluated case-by-case basis while SDN3 products, which have transgenes are considered GMOs. The Philippines also states that the absence of a new combination of genetic material in the final product makes it non-GMO. China has also released guidelines for the safety evaluation of gene-edited plants in agriculture. The guidelines cover all the products which do not have exogenous genes (i.e. all except SDN3 approaches). India released its new guidelines for gene-edited plants in March, 2022 stating that SDN1 and SDN2 products without exogenous DNA are comparable to naturally occurring events and should be deregulated while SDN3 products should be regulated as GMOs and need to undergo the pre-market safety assessment (DBT, GoI 2022). Other countries in South-East Asia like Bangladesh, Vietnam, and Taiwan are still in debate on their regulatory policies (USDA 2021b; USDA 2021c). The two countries with the highest population worldwide, China and India have clarified their policies on genome editing and cultivation of GE crops opening the avenues for their use in commercial agriculture. Many of the top agricultural producer countries (China, The United States, India, and Brazil) have eased up on the deregulation of GE crops. Even now, genome editing is a contentious issue, particularly for the European Union and its allies, who are major trading partners for many nations in the agriculture sector (Sprink 2022). However, gradually

many countries are opening up including Africa, EU members (Hungary) and associated countries (Switzerland, The United Kingdom, Norway) and discussing regulatory options for gene editing. Now, the European Union is actively reassessing its stance.

Regulatory regimes for GE products/crops have been evolving rapidly over the past two years (since 2022) to enable the use of genome editing in agricultural products. Technological developments in the field of genome editing are also evolving at a very fast pace making it possible that released regulations become outdated soon and some techniques or products may eventually be not captured under the regulations. As a result, developing globally harmonized regulatory regimes that are flexible enough to keep up with technology improvements and guarantee legal certainty for all products, producers, traders, and consumers will be a difficult undertaking in the years to come.

Harmonizing the Regulatory landscape of GE crops

To feed the continuously growing world population, world food production needs to increase by 25% to 70% (Hunter 2017). The biggest challenge in agriculture is now to mitigate the negative impact of climate change together with feeding the growing population. To address the issues of climate change and biodiversity, as well as to guarantee food and nutritional security, agriculture must be intensified sustainably. The role of GE and GM crops can be very significant in ensuring food security and nutritional security thereby economically benefiting the countries especially low-and middle-income countries. Genome-editing can reduce breeding costs and accelerate the delivery of novel varieties to smallholder farmers. However, the future of genome-edited crops will be defined by the national and international regulatory landscape of policies and the socioeconomic scenario. Despite several benefits, the real potential of GE crops may not be realized if the technology is poorly regulated across countries. Harmonization of GE regulatory policies in major agriculture-focused countries remains the biggest challenge for the adoption and successful commercialization of GE crops.

The primary goal of genome-editing in agriculture is to develop crops, which are resistant to abiotic stress, emerging pests, and pathogens and that can have higher nutritional values. At present, the potential risks of genome-edited crop varieties are being considered along with their benefits in the context of agricultural applications. Scientifically, one of the most cited risks of genome editing is that it could lead to non-target mutations.

However, continuous improvement in bioinformatics tools and approaches used to design the genome-edits are mitigating and significantly reducing the likelihood of occurrence of non-target edits in crop plants. This has ensured the safety of the technique by producing sophisticated CRISPR systems with more fidelity and fewer non-target alterations (Ahmad 2021).

Scientific, political, and societal factors influence policies related to the regulation of genetically engineered crops. These factors can be exacerbated by the inconsistent usage of terminology related to genome editing and by a lack of knowledge about the technology. For example, genome-editing events may or may not include the introduction of foreign gene/transgene, may or may not generate product significantly different than the one produced through conventional breeding. Therefore, precise use of accurate terminology is essential to fairly communicate the process, products, benefits and risks to the public domain for building trust in genome-editing technologies. The "social license," or the readiness of consumers, users, and society at large to adopt the technology, is influenced by a number of variables, including public perceptions of the benefits and risks, local regulatory frameworks, international regulatory harmonization, trade and product-labeling requirements, and governmental policies. Lack of transparency may lead to lack of trust in product developers, regulators, producers and genome-edited products. A freely accessible register where developers can declare the exact techniques utilized for the development of GE crops and disclose the usage of GE technologies is one of the tools proposed for ensuring transparency (Pixley 2022). These registries might continue to exist independently of regulatory risk assessment and patent systems. A voluntary framework developed by The Center for Food Integrity through their coalition for Responsible Gene Editing in Agriculture, is intended to increase transparency and stakeholder engagement to build trust in the products developed through gene editing (Coalition for responsible gene editing in agriculture 2024). The framework is developed by representatives from academic institutions, farmer organisations, non-governmental organisations, GE technology developers and food companies. Academic institutions play a role in developing regulatory guidelines for genome edited crops in several ways, including providing scientific guidance, issuing guidelines and certifying crops. For example, in India, Institutional Biosafety Committee (IBSC) and the Department of Biotechnology (DBT) play a role in issuing guidelines for the safety assessment of genome-edited plants and certifying gene-edited crops before they can be released commercially (IBKP, DBT, GoI 2024). IBSC is constituted of scientists from DBT and research institutions that develop gene-edited crops. The issued guidelines determine the regulatory requirements for different types of experiments and provide scientific guidance on data requirements.

Specialized projects, strategic alliances and explicit biotechnology and bioeconomy policies can help overcome the challenges which limit the widespread use of GE crop varieties. For example, African Orphan Crops Consortium (africanorphancrops.org) and the African Agricultural Technology Foundation (www.aatf-africa.org) aim to facilitate the technology access and deployment of innovative Agri technologies to smallholder farmers in Sub-Saharan Africa. Specific genome editing projects for improvement of plants are being undertaken in East African countries on crops like Sorghum, maize, banana, mustard, cassava, wheat (Karembu 2021). Public sector institutions are already actively engaged in genome-editing research to develop crop varieties which are more suited to modern agriculture. Now, pertinent policy, government and trade community support is required for developing necessary institutional capabilities. The G20 Meeting of Agricultural Chief Scientists 2021 (G20 MACS) held a special session on genome-editing technologies and discussed the application of genome editing in agriculture, its potential benefits and risks, its potential use for sustainable development, as well as the public perception, and the status of regulatory policies (G20 Italy 2021). The discussions deliberated on encouraging international exchanges to reinforce science-based understanding and knowledge of genome-editing and its application in agriculture to support food system resilience and security.

It is recommended that policies should be made to support the use of genome-editing technologies and GE crops. More effort is required from all stakeholders (researchers, scientists, students, journalists and farmers) to improve and prioritize the science-based information exchange about genome-editing to create a market for the technology's beneficial products. Global cooperation on these issues across regions is crucial to avoid regulatory-related bottlenecks in production of GE crops and their global trade in agriculture. There is an urgency of enabling policies, bilateral cooperation and trust especially in Asia Pacific owing to their population pressure and need for sustainable agriculture. This will not only grant 'social license' to the technology but also significantly help in improving the livelihoods of small holder farmers and populations of low-and middle-income countries by boosting agricultural productivity.

Conclusions

The debate over genome-edited crops is multifaceted and involves weighing potential benefits against possible risks. Supporters emphasize the technology's potential to enhance food security and sustainability, while critics highlight concerns about environmental, health, and ethical

issues. As technology continues to advance, ongoing research, transparent regulation, and open dialogue will be crucial in addressing these concerns and harnessing the benefits of genome editing in agriculture. Therefore, harmonizing regulatory policies for genome-edited crops is crucial for several reasons.

1. Different countries have varying levels of scientific expertise and resources. Effective harmonization requires collaboration between governments, scientific communities, industry stakeholders, and the public. This will facilitate international technology exchange and ensure commercialization of genome-edited crops without excessive delays and additional costs.
2. Consumer concerns should be addressed to win the support of people for genetically modified crops before their commercialization. Governments should support efficient communication between developers and the public while establishing clear and unbiased regulatory policies on genetically modified agricultural products.
3. By raising public knowledge of CRISPR-based crops, fostering confidence in safety guidelines and their creators, and providing transparent analysis of benefits and risks, it may be possible to gradually increase public acceptance of transgene-free crops.
4. Harmonization should also address ethical and societal concerns related to genome-edited crops. This includes considerations around transparency, public participation in decision-making, and addressing potential impacts on rural communities and smallholder farmers.
5. Harmonization must be balanced with rigorous safety assessments. Policies should ensure that genome-edited crops are thoroughly evaluated for potential risks to human health, the environment, and biodiversity. A consistent approach to safety can help maintain public trust and support for agricultural biotechnology.
6. Genome editing technology is rapidly advancing, and regulatory frameworks must be adaptable to keep pace with scientific progress. Harmonized policies should include mechanisms for periodic review and updates to address new developments and emerging knowledge.

An appropriate regulatory framework with a uniform approach would not only increase the public acceptance of GE crops but also ensure that regulations are science-based, globally accepted and benefit both developers and consumers.

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Event Report

Roundtable on R&D Trends and Regulation for Biosimilars: The Way Forward

The advent of generics has ushered in a paradigm shift within the pharmaceutical sector. This has led to an increasing thrust towards orchestrating a shift from chemically synthesised pharmaceuticals to biopharmaceuticals. In this context, biologics and biosimilars are gaining huge traction in the R&D as well as policy discourses across the world including India. However, the lack of access to biotherapeutic presents a major challenge in many developing countries including India. This can be attributed to prevailing patent regimes leading to low generic/non-originator competition in this segment. This is aggravated by prohibitive costs, primarily due to the rigid entry barriers relating to their manufacturing, intellectual property and regulatory approvals.

Recent developments in the biosimilar regulatory environment have the potential to enable equitable access to low cost, safe and efficacious biosimilars globally. The recently issued WHO Guidelines on Evaluation of Biosimilars (Guidelines), which replace the earlier Guidelines on the Evaluation of Similar Biotherapeutic Products (SBP Guidelines), 2010 focus significantly on removing some of these regulatory barriers affecting the cost of production of biosimilars prominent being the waiver for comparative efficacy trials. Similar regulatory changes have also been introduced by the UK and considered by the European Union. These efforts have focused on the need to re-evaluate current requirements to improve clinical efficacy, while streamlining development and evaluation processes to maintain highest standards of safety and efficacy. This will not only help to ensure the development of safe and efficacious biosimilars but will also help in fuelling access to biosimilars by patients.

In this context, RIS, in collaboration with the Third World Network (TWN), organised a Roundtable on Biosimilars on 24 October 2024 at New Delhi, to guage emerging trends in technology and gather experts' perspective on the Indian Biosimilar Regulatory Framework and changes to the regulatory environment. The roundtable further sought to bring together regulators, policymakers, biopharmaceutical developers, scientist and academic researchers in order to discuss a roadmap for lowering regulatory barriers for the marketing approval of biosimilars without compromising

the quality, safe and efficacy and the key changes that can be brought to the Indian Biosimilar Guidelines of 2016.

Specifically, it sought to achieve the following objectives:

- To understand the implications of emerging trends in technology for biosimilar regulation
- To bring together policy makers, scientists , industry and CSOs to discuss the concern of affordable access to biosimilars Biotherapeutics
- Summarizes the current changing Biosimilar Regulatory landscape globally
- Describe stakeholders' experience with the current biosimilar regulatory process
- To identify efforts to bring changes in the Indian Similar Biosimilar Guidelines of 2016
- To explore the possibility of a road map for lowering the regulatory barriers for the marketing approval of biosimilars without compromising access, quality, safety and efficacy.

Inaugural Session

The event commenced with an inaugural address from Professor Sachin Chaturvedi, Director General, RIS. Providing a brief background on the issues that the roundtable is seeking to address, Professor Chaturvedi noted that the discussion focuses on ensuring access, equity and inclusion in medicine through biosimilars. Brinign into context the barriers posed by intellectual property regimes, Professor Chaturvedi also highlighted evolving trends in global regulation and particularly on how the World Health Organization is taking measures to facilitate faster uptake of biosimilars. He also discussed India's contribution to ensuring global access to affordable medicines at the WTO. He further acknowledged collaborations with regulatory agencies, entities, and partnerships, as well as the significant contributions of individuals like Dr. Renu Swaroop in making technology governance more people-centric.

Dr. Renu Swarup, Former Secretary, Department of Biotechnology, Government of India, delivered the inaugural address which referred to various dimensions of biosimilar regulation including stakeholder collaboration, public private partnerships and global harmonization of regulatory standards. Dr. Swarup emphasized the need for agreed-upon frameworks for technology licensing and IP management to facilitate swift access to medicines in emergencies and also suggested creating a regional framework for the Global South to enhance access and technology sharing.

namely capacity building (infrastructure and human resources), leveraging cutting-edge technologies, fostering collaboration between public and private sector (including with startups) and instituting and implementing robust governance and regulatory frameworks.

Dr. Swarup emphasized the long-standing partnership between India's government and the private sector, especially in the biopharma industry, as being crucial in advancing biosimilars and other pharmaceutical innovations. She highlighted four pillars as essential to facilitating advances in biosimilars namely:

- **Capacity Building** through strengthening infrastructure and human resources.
- **Cutting edge technologies**, the advances in which are necessary for the development of new therapeutics, biosimilars, and biomanufacturing processes.
- **Collaboration** between industry, academia, and startups must collaborate to develop new products and technologies.
- **Governance, regulation and harmonization** through a strong regulatory framework and harmonized standards, including efficient intellectual property management, is crucial for robust growth.

Citing the loopholes and gaps which became evident during the pandemic, Dr. Swarup highlighted the need for harmonized regulatory processes globally to ensure better access to medicines. Particularly to address emergency situations, she proposed for the institution of agreed upon templates for facilitating compulsory licensing and intellectual property management to enable access to medicines. She referred to ambitious targets outlined under the India's Biopharma Vision to reach 150 billion dollars by 2025 and stressed the country's strength in biopharma manufacturing, innovation and collaboration. She further underlined the priorities for the Global South including its significance in global policy and advocated for regional frameworks to address needs and challenges in the biopharma sector.

Delivering his presentation on behalf of the Drug Controller General of India (DCGI), Sh. Arvind Kukrety, Deputy Drug Controller, CDSCO, discussed the progress as well as challenges faced by Indian regulators. Noting how India received a maturity level 3 rating in WHO assessment of biological regulation, he mentioned how India is approaching efforts to achieve global harmonization of biosimilar regulations. He drew attention to measures taken to make Indian regulatory system more transparent and predictable while providing clear guidelines and timelines for approval. The

discussion also delved into policy interventions including the 2019 New Drug Testing Rules and the 2016 Biosimilar Guidelines which have helped meet the need for access to safe and effective medicines.

He further highlighted India's successes in the biotherapeutics sector with 29 manufacturers in the biosimilar space and over 150 recombinant DNA origin products approved, including 42 biosimilars — the highest number globally. This success reflects both advancements in technology and the industry's commitment to quality. He pointed to how India's biosimilar regulation is facilitating a strong environment for new molecules, having approved 122 clinical trials over the past three years. This also allows India looking to leverage new technologies like mRNA vaccines. He characterized India's regulatory approach as collaborative with channels of communication remaining open between the regulators and manufacturers. To help startups, pre-submission meetings have been organized with regulatory officials to clarify the technical aspects. On a concluding note, he emphasized upon how India's regulatory landscape is forward looking to ensure safety, speed and scale through streamlining approvals for the benefit of India as well as the global community.

The presentation delivered by Professor Sarfraz K. Niazi, Adj. Professor of Pharmaceutical Sciences, College of Pharmacy, University of Illinois, Chicago, USA, offered a critical examination on the current biosimilar regulatory landscape, particularly those relating to animal testing, clinical efficacy testing and guidelines in general for biosimilars. Professor Niazi argued that animal testing cannot be employed in biosimilar testing due to the relevant receptors being lacking in animals. Newer testing methods which are more sensitive and affordable in nature should be introduced instead, he stated.

Continuing with the discussion on the various inefficiencies of employing traditional clinical trials for biosimilars, particularly for efficacy testing. He further terms large trials performed at the scale of one million patients as unnecessary, while highlighting the mathematical and logistical infeasibility of such trials. Drawing from his own experiences of having engaged with the US Food and Drug Administration, he noted that alternative methods such as MAT (Monocyte Activation Test) and recombinant factor C tests to be used for pyrogen and endotoxin testing. The presentation also brought to the fore existing inconsistencies running through global biosimilar regulation, which makes it difficult to ensure that biosimilar products originating from different regions may comply with the same standards. Recommending agencies including the CDSCO (Central Drugs Standard Control Organization) to modernise their guidelines, he

urged for focus to be laid on rigorous analytical testing and post-market safety monitoring. He also suggested that biosimilars should be treated the same as other biologics, including antibody-drug conjugates that third-party audits could improve the regulatory process.

In her presentation, Dr. Shefali Misra, Group Vice-President of Public Policy & Government Affairs, Biocon, mentioned various efforts made towards supporting R&D in biosimilars including the setting up of the National Research Foundation (NRF). Noting biosimilars as a critical sector from the point of view of investment, she pointed to Biocon's success in global markets as having set an important precedent and referred to India's potential to evolve as a leader in biosimilars and play a significant role in reduction of global healthcare costs. She called for harmonization of standards. mentioned the need for India to consider adopting international best practices like interchangeability, which would allow pharmacists to substitute biosimilars without specific doctor approval. She also emphasized the importance of post-market surveillance and regulatory flexibility in facilitating innovation.

The keynote address was delivered by Dr Carlos María Correa, ED, South Centre, Geneva. Dr. Correa started his presentation by referring to cost effectiveness as the primary advantage offered by biosimilars. While biosimilars are not identical to the original, they are similar. In this regard he argues that similarity should be the guiding principle. "The classification of treatment is one advantage that biosimilars are bringing in terms of oncology, diabetes you mentioned in many other, many other diseases", he noted. Referring to the tremendous market potential that India holds with respect to biosimilars (estimated at 20-25% annually), he alluded to India having a crucial role to play in manufacturing vaccines for domestic and global consumption, particularly in the Global South. Flagging evergreening practices followed by multinational companies, particularly in the area of biologics and monoclonal antibodies and as a major concern, Correa underlined the need to look very carefully at what the situation is in terms of freedom to operate in India's case.

He further noted that patent policies need to be aligned with the goal of making healthcare and medicines accessible. Delving into the obstacles faced by developing countries such as India and Argentina, he observed "that economies of scale are important and therefore opening export markets are a significant step for biosimilar production". He also referred to the importance of business models that companies involved in the development, production and marketing of biosimilars are involved in. Herein he suggested startups and companies to strategise as per costs and available infrastructure. For

instance, some companies engage in development and production, but not marketing which requires investment in infrastructure. Forming joint ventures with foreign companies was suggested as another way forward.

"There is a great expectation in the developing and developing world about the role that India can can play as it has played in, in relation with the, the products of, of chemical synthesis", he noted. He further pointed to the need to focus on global harmonization of regulatory frameworks while cautioning against avoiding multinational interests dominating the process. Meanwhile, the voices of the Global South may be amplified in global discussions through strengthening South-South cooperation.

Session 1: Recent Developments in R&D in Biosimilars and Global and National Regulatory Landscape

This session was moderated by Mr KM Gopakumar, Sr. Researcher, Third World Network. The keynote presentation delivered by Professor Hubbs Schellekens, Utrecht University/Erasmus Medical Center, The Netherlands, focused on the regulatory pathways for biologics and biosimilars. Professor Schellekens pointed to a lack of proper scientific definition for biosimilars while classifying it as a regulatory construct. This is a "key issue" in all discussions concerning biosimilars and biologics. Drawing from his extensive experience in the field of medicine and clinical trials, he pointed to evidence and existing research indicating "there is no scientific basis anymore for for a separate biological or biosimilar", particularly from the point of view of regulation. What matters in this context is are the effects that minor clinical differences could have on efficacy and safety.

He criticised the existing mode of regulating the original and the biosimilar separately and pointed to several contradictions. Indicating that clinical trials are insufficient to characterise the effects, he noted that the clinical effects in several cases have been small. Herein he drew attention to advances since 1980s which have helped minimise safety risks and also mentioned how widespread standardisation of manufacturing practices makes the products broadly similar. Even problems such as immunogenicity which result out of the presence of impurities or protein aggregates can be reduced through quality control. Pointing to a lack of scientific basis for separation, Professor Schellekens concluded by suggesting that biosimilars should be regulated under the same pathways as generics. He proposed that if clinical data is needed, well-designed pharmacokinetic (PK) and pharmacodynamic (PD) studies would suffice, rather than the extensive trials currently required for biosimilars.

The points presented by Dr. Amit Parikh, Scientist-F, Department of Biotechnology, Government of India, focused on institutional and policy interventions with respect to mainstreaming biosimilars. Highlighting the role of the Review Committee on Genetic Manipulation (RCGM) which was set up in 1998, Dr. Parikh spoke on the progress made by the body in regulating Genetically Modified Organisms and biosimilars. He also spoke of the empowerment of Institutional Biosafety Committees (IBSCs) to take on some responsibilities that were previously handled by RCGM. He further highlighted regulatory efforts made towards streamlining the application process which has resulted in processing time reducing from 200 days to 30 days, while increasing meeting frequency to every two weeks. Regulators are also focusing on improving transparency and procedures related to biosimilars for which the first guidelines were introduced in 2012. Referring to regulatory measures in the pipeline he mentioned that the Ministry of Environment and Forest and the CDSCO (Central Drugs Standard Control Organization) are exploring ways to streamline approvals further and possibly introduce exemptions for certain scenarios, particularly for established technologies like monoclonal antibodies.

Dr. Samir Sangitrao, Vice President and Head Regulatory Affairs and R&D QA, Biologics, Zydus Group, drew from his rich experience in the field of biotherapeutics to highlight how biosimilar development and uptake could be boosted through regulatory and procedural interventions that seek to save both cost and time. He pointed to measures adopted in the Indian regulatory scenario that have helped save time and resources such as digitisation. Having online meetings as well as opening applications online have helped enhance efficiency and communication to the end of ensuring faster approvals. Pointing to a lack of scientific basis for toxicity studies, Dr.Sangitrao noted that these can be done away with to achieve faster processing of application. Health Canada and the MHRA do not require toxicity studies. Drawing attention to the amount of time taken to apply for marketing authorisation,, he noted that a lot of time can be saved if manufacturing can be done parallelly as the regulatory process is ongoing. Such systems are in place in the USA and Europe.

He further pointed to suggested that India could benefit from more flexibility in extrapolating indications. Dr. Samir Sangitrao further advocated for doing away with phase- 4 trials, particularly in a country like India where robust pharmacovigilance systems have been put in place. Moreover, at least ₹72 crores can be saved each month and development time could be reduced by about 27 months without requirement for animal studies and phase three trials. He additionally noted that the regulatory pathways for generics and biosimilars would likely merge in the future significantly

helping streamline the process. A key insight that came up during the discussion following Dr. Sangitrao's presentation had to do with the need to sensitise judiciary on matters related to patents and public health, particularly against evergreening.

Mr. Syed Ahmed, Head of TechInvention and Member of EBPMN, offered insights from a startup point of view, while also delving into the biosimilar approval procedures laid down by the World Health Organization (WHO) and urgent areas of priority intervention in India. Discussing the WHO's Pilot Prequalification Procedure for biosimilars instituted in 2017 as presenting major opportunities for Indian companies. Prequalification could help Indian vaccine manufacturers capture over 50 per cent of the global market. He also pointed out that the prequalification procedure waives fees, making it an attractive option for companies. He further criticized India's limited involvement in the WHO's mRNA hub which was created in 2021 "to build capacity in low- and middle-income countries to produce mRNA vaccines through a centre of excellence and training". He warned that India might fall behind in this space if it does not focus on the sector. Mr. Ahmed further introduced the innovative One Health Concept which links both human and animal health. He urged regulators to consider facilities that could manufacture products for both humans and animals, facilitating broader production and sustainability.

Dr Harish Shandilya, Vice President and Head of Global Portfolio Strategy and Compliance, Enzene Biosciences, highlighted the need for proactive and rational regulatory approaches geared toward encouraging innovation and reducing costs to improve affordability. He advocated for existing procedures, especially around protocol approvals and biosimilarity studies to be simplified to be reduced. He also spoke on the importance of harmonizing regulatory standards at the global level. Urging Indian innovators to consider simplifying procedures, he termed the requirements mandating animal immunogenicity studies and extensive biological and analytical assays during early phases of developments as unnecessary. Even for clinical protocol trial approvals, the time taken is lengthier compared to global standards. Such delays may be reduced through protocol approvals, particularly for drugs like monoclonal antibodies. Inefficiency also flows from the requirement for securing multiple approvals through stages of R&D to commercial manufacturing. The scenario is further complicated by variability in recommendations from different Scientific Evaluation Committees (SEC). He further urged for regulatory support for innovative technologies such as continuous manufacturing and gene therapy which can reduce production costs.

Dr Raja Sekhar Vanga, Vice President, Biocon Biologics Limited, discussed the global shift in regulatory frameworks particularly in the USA and Europe. These frameworks are continuously reviewing and adjusting their respective approaches based on data and experiences from handling approval processes. These shifts have translated into measures includes eliminating patient studies and waiving animal studies, which could also benefit from India's extensive data due to its large patient pool and two decades of experience. He also mentioned the need to leverage global clinical data for product approval in India, instead of conducting redundant local studies, especially when there are no ethnic differences in product performance. Additionally, he called for high-level guidance based on therapeutic areas to simplify the process for obtaining regulatory approval, particularly for cancer drugs, and for better use of reliance procedures for products already approved by stringent regulatory authorities.

The discussion which ensued during the question and answer session served to showcase various perspectives on the key points raised by the speakers. To help form effective regulatory interventions, attention was drawn to the need for industry to be more proactive in terms of providing position papers and increasing engagement. Deliberations revolved around WHO prequalification programme on which the perspectives were varied. s. While some questioned its commercial value, particularly without procurement from UN health agencies, others argued that it plays a crucial role in building trust regarding product quality, especially in low and middle-income countries. One speaker emphasized that the program fosters credibility and quality control, which can help in market expansion.

Session 2: Access to Biosimilars-based Therapeutics: Opportunities and Challenges

Deliberations during this session brought to the fore the activities being undertaken under the National Biopharma Mission to improve access to biosimilars. It was chaired by Dr K Ravi Srinivas, Consultant, RIS.

The keynote speech delivered by Dr. S.R. Rao, Founder & CEO, Genentech Regulatory Solutions LLP, Former Sr Advisor, DBT, Co-Founder, APAR & Former Vice President, Sri Balaji Vidyapeeth University, Pondicherry, highlighted various issues surrounding affordability, accessibility Emphasising on approaching questions related to accessibility and affordability from a patient's perspective, Dr. Rao also pointed to the state of education and skills in biopharmaceuticals. He pointed to drawbacks in existing medical and pharmacy courses who do often disregard biosimilars

and biotherapeutics. Speaking on trends with respect to the uptake of biologic therapies including biosimilars across different countries, Dr. Rao highlighted the differences in biosimilar consumption patterns, while also discussing the unique challenges faced by emerging biologics markets in Asian countries. He highlighted that while the consumption of biologics is much higher in the U.S. (200 per 1000 population) compared to India (0.2 per 1000), other countries like those in Europe have better uptake, especially of monoclonal antibodies. High prices of medications and the lack of harmonization in regulations negatively impact the biosimilar segment of the biopharma markets in Asian countries and affordability also remains a major challenge.

Delving into the affordability aspect further, Dr. Rao further mentioned the nuances that add to the affordability problem leading to lowered prices not resulting in improved access. Herein, he suggested for regulators to promote policies that encourage market competition to realise favourable dynamics and accessible pricing. Emphasis also needs to be laid on increasing awareness on the benefits of biosimilars among healthcare professionals in India and other countries in Asia. In conclusion, Dr. Rao raised several key points for discussion, including improving regulatory policies, reducing research and development costs, addressing supply chain issues, and fostering collaboration between government, pharmaceutical companies, and biotech sectors. He stressed the need for innovative pricing strategies to address inequalities in access to biologics.

Dr. Madhvi Rao, Chief Manager, National Biopharma Mission, BIRAC, discussed trends and challenges in India's biopharma sector, focusing on biosimilars. She highlighted the increasing efforts by large and small companies to develop biosimilars not only for the Indian market but also for global markets, starting from early stages of clone development and understanding regulatory compliance. Key trends include the shift towards continuous manufacturing, the integration of process analytical tools, and the adoption of AI/ML to reduce development cycles.

Co-funded by the DBT and the World Bank, the Mission aids biosimilar development to render treatments accessible through making them affordable. The Mission aims for a 30-40 per cent reduction in drug prices compared to innovators. In addition, it offers support to startups and academia through providing cutting-edge facilities and equipment including bioreactors and laboratory information management systems. Such support is provided free of cost. The mission is also supporting establishment has supported establishment of clinical trial networks across. Policy focus is now being laid on improving the access of small companies to these research

facilities. the country Dr. Madhvi Rao elaborated upon success story of the liraglutide biosimilar for diabetes and obesity. The drug was launched with a cost 60-70 per cent below that of the original drug.

The presentation from Professor Ashwani Mahajan, National Co-Convenor, Swadeshi Jagran Manch and Professor, Delhi University, drew attention the interventions made by non-governmental organisations such as the Swadeshi Jagran Manch in lobbying against unequitable practices propounded by the WTO TRIPS Regime. Speaking of how such efforts would translate into provisions on affordable access to medicines in the Patents (Amendment) Act, 1970, Professor Mahajan pointed to the importance of prioritising public health over corporate interests. Professor Mahajan further stressed on how biosimilars could help more cancer patients access medical care. He concluded by calling for government action and support for affordable treatments, asserting that India has the capacity to lead in providing accessible healthcare solutions on a global scale.

Delving deeper into the nitty-gritties of the affordability and accessibility question surrounding biosimilars, Dr. Chetali Rao, Senior researcher, TWN, delineated the "stark reality" surrounding it. A bulk of the population is unable to access life-saving drugs due to high costs. This is particularly so in the case of cancer patients. She discussed the case of Keytruda, a cancer drug which is used in treating melanoma, cervical cancer and non-squamous lung cancer. The drug costs nearly four lakh rupees a month for a treatment cycle, requiring an individual to spend as much as 96 lakh rupees over two years. Oncologist India report that only 1% of the people are able to afford this drug, she noted. To make the medicine more accessible, efforts are being made to reduce the dosages of Keytruda and combining it with nivolumab, a biosimilar which can be manufactured by about a hundred Indian companies.

She further drew attention to the challenges flowing from existing patenting practices in the industry and intellectual property regimes which hinder affordability and accessibility. She pointed to evergreening strategies " where you either change the formulations, you change the route of administration, and if more so, the new therapy new thing has come where you combine the drugs" being followed by companies in Europe as resulting in increased costs. She noted that the regulatory burden, especially the cost of clinical and animal trials, further hinders the development of affordable biosimilars, despite the potential for many biologic drugs to have biosimilar options. She further underlined the importance of not compromising on safety and security while making drugs affordable.

Ms Leena Menghaney, South Asia Director, Access to Medicines Campaign, Médecins Sans Frontières (MSF), drew attention to the misalignment between government interventions aggravating the biosimilars accessibility problem. While government entities including BIRAC are actively allocating taxpayers dollars to further R&D and improve supply, the patent office "is handing out patents to bigpharma like candy", thereby undermining the former efforts. She further called on all stakeholders, including NGOs and patient advocacy groups to to raise the evergreening problem before the patent office.

She further highlighted the MSF's willingness to consult with the government on decentralized models which can build a pipeline of products that reach the market and the patient. She termed the pooled procurement of generics by both state and central governments as absolutely imperative to lowering prices and benefiting from generics that are being produced in the country. She further vouched for the strategizing around the pipeline of biosimilar products to look beyond cancer into other infectious diseases. Herein, she pointed to a need to pay attention to R&D in anti-venoms, which currently remain neglected.

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Book Reviews

Ethical Concerns of CRISPR Use in Humans: An Anticipatory Approach

Title: Anticipatory Ethics and The Use of CRISPR in Humans
Author : Michael W. Nestor and Richard L. Wilson
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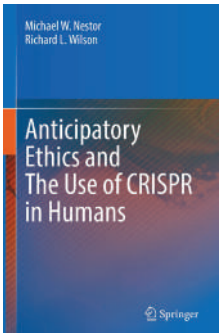

Emerging technologies like artificial intelligence (AI), gene editing, synthetic biology, quantum computing are rapidly developing, and often outpace the establishment of regulatory and governance frameworks posing a significant challenge. The disruptive and transformative potential of these emerging technologies entwined with uncertainties and unpredictabilities of their long-term impacts make forecasting difficult, further complicating their regulatory and governance frameworks. The book under review *Anticipatory Ethics and The Use of CRISPR in Humans* illustrates interdisciplinary collaboration between Michael W. Nestor, a neuroscientist and Richard L. Wilson, a philosopher specialising in ethics. It provides a bridge and dialogue between the two, making the necessary interdisciplinary efforts in addressing the challenges posed by technologies like CRISPR.

In October 2020, two scientists, Emmanuelle Charpentier and Jennifer Doudna were awarded the Nobel Prize for the development of a gene manipulating method. The revolutionary 'Clustered, Regularly Interspaced, Short Palindromic Repeats' in association with the Cas9 DNA-cutting enzyme (CRISPR/Cas9 genetic scissors) is 'one of gene technology's sharpest tools for rewriting the code of life' (The Royal Academy of Sciences, 2020). Though its benefits are immense, CRISPR is seen as a 'double-edged sword' (Yang *et al*., 2020; Zhu *et al*., 2020). It is increasingly criticized for its limitations and potential risks. Scientists have raised numerous scientific, ethical, societal and governance issues associated with CRISPR (Shwartz, 2018; Davies, 2019; NAP, 2020; Ayanoğlu *et al*. 2020;

Wiley *et al*. 2024). The COVID-19 pandemic highlighted the critical need for rapid and effective medical interventions, demanding the transformative potential of technologies such as CRISPR in combating emerging infectious diseases. Research has demonstrated CRISPR's utility in developing diagnostics, antiviral therapies, and vaccine platforms with unprecedented precision and speed (Jena *et al*., 2021). Beyond healthcare, CRISPR-based genome editing has shown abundant possibilities in agriculture by enabling the development of genetically modified crops with enhanced resilience to environmental stressors, thereby addressing food security concerns amidst a changing climate (Zhang *et al*., 2021).

The pandemic has also emphasized the importance of ethical foresight in integrating technologies like CRISPR into public health and agriculture. Studies pointed out the embedding principles of responsible innovation to ensure these technologies are deployed equitably, transparently, and with societal benefits at the forefront. By learning from the global responses to COVID-19, stakeholders can use the potential of CRISPR, not only to address current challenges but also to build robust frameworks that align scientific progress with sustainable and inclusive solutions for future global health and agricultural security. The book focuses on anticipatory ethics framework and advocates proactive governance and ethical analysis of gene editing technologies like CRISPR. This framework incorporates the use of scenario planning and foresight for understanding the potential ethical implications of the technology, emphasising on the significance of proactive ethical analysis to keep pace with rapid advancements in genomic and molecular biology.

The book consists of ten chapters, addressing different dimensions of CRISPR technology and its ethical considerations. The first chapter provides a brief introduction to CRISPR Cas9. The chapter traces the historical development of CRISPR/Cas9, bringing forth the rapidly changing nature of the technology, its mechanism, current animal/human models for treating diseases as well as its existing clinical applications in humans. It also highlights the transformative role of CRISPR in treating the development of pharmaceuticals, genetic diseases and medicines. Additionally, the chapter discusses the present and future challenges in utilisation of CRISPR/Cas9 including off-target effects, safety, delivery methods, etc. The next chapter introduces the concepts of anticipatory ethics which recently has emerged as an important new orientation in analysing emerging technologies. It is an approach towards ethical decision-making which focuses on identifying and addressing potential ethical issues, challenges and short-term and long-term consequences of emerging technologies before they occur. It also aims to

proactively take into account implications and societal impact of innovation for shaping the future in a responsible and just way. Recognising the dynamic and rapidly changing nature of science and importance of forecasting potential outcomes, the chapter advocates proactively anticipating and considering ethical challenges. The chapter seeks to develop a framework for anticipatory analysis of the use of CRISPR by focusing on three sets of stakeholders i.e. scientific researchers, clinicians and patients.

In the third chapter, authors explore the concepts of phenomenology and postphenomenology to analyse the ethical implications of CRISPR technology on human lived experience. It also uses intersubjectivity and post-phenology to understand the social and ethical dimensions of gene editing, and tries to connect the lived experiences of the identified stakeholders to the anticipatory ethical framework. The next chapter delves into the ethical and philosophical considerations surrounding the use of CRISPR technology to modify genes that influence human cognition and perception. The authors examine the impact of such genetic interventions on an individual's sense of self, identity, and personhood.

Apart from the transformative and disruptive potential of emerging technologies, another critical aspect of these are the issues of access, equity and inclusion of their benefits and understanding of their potential risks. The fifth chapter rightly acknowledges this aspect of CRISPR use and its access for socially disadvantaged and marginalised communities. The issues of access and equity in deploying CRISPR technology is the central theme of the chapter. It also raises issues of social justice and inclusion of disadvantaged groups in decision-making and examines ethical dilemmas associated with its deployment and use. The next two chapters focus on the future of CRISPR with chapter six discussing the gene drives and chapter seven focusing on kill switches. Gene drives are technologies designed to override traditional Mendelian inheritance through CRISPR-based systems. Their deployment raises ethical concerns, and the book emphasises on the importance of anticipatory ethics to evaluate these questions before implementation of gene drive technologies. Therefore, highlighting the need for proactive ethical deliberation to guide its responsible development and application. Similarly, the following chapter focuses on 'kill switches' which are engineered mechanisms designed to control and potentially deactivate the activity of CRISPR systems, thereby enhancing safety and preventing unintended consequences. Since they ensure CRISPR-based modifications do not continue uncontrollably, the chapter focuses on the need for addressing ethical and safety concerns associated with them. These chapters highlight the need for maintaining a balance between innovation

and responsible precaution, together with underlining their ethical and governance challenges, and preventing misuse of such technologies.

As the regulatory framework for applications of CRISPR is still evolving, the eighth chapter of the book aptly reviews the domestic and international regulatory frameworks for CRISPR, comparing the policies in the United States, United Kingdom, China and France. In their discussion on current governance frameworks for CRISPR technology, they highlight the positions of prominent organisations such as the World Health Organization (WHO), the National Academy of Sciences, National Academy of Medicine, and the British Royal Society. These institutions acknowledge that CRISPR technology is quite new, and its applications in clinical treatments is still in its early stages. Thus, advocating for a cautious approach, recommending that any clinical use of CRISPR be evaluated on a case-by-case basis to thoroughly assess potential risks. There is a need for cohesive global governance for CRISPR with an inclusive multi-stakeholder participation. It is necessary to review these guidelines with rapid developments and international cooperation is essential for sharing comprehensive guidelines.

The ninth chapter of the book provides policy recommendations/ frameworks for the use of CRISPR germline editing in humans. The authors provide policy guidelines for limiting CRISPR use in humans, discuss analogies to AI governance and also propose creation of a CRISPR Cognition Gene Databases to monitor sensitive genetic targets. The concluding chapter summarizes the interdisciplinary dialogue among scientists, ethicists and policy makers and stresses on the significance of anticipatory governance to mitigate risks of CRISPR technology and maximise its outreach and benefits, moving towards more responsible and inclusive innovation. Thus, providing a template for tackling ethical and governance challenges that are posed by rapidly developing emerging technologies at present.

There are scientific, ethical, societal and governance challenges linked to CRISPR technology which include unintended genetic modifications, access, informed consent. In this regard, the present book stresses the need for ethical foresight of the technology. Thus, addressing the gap in the literature by addressing the ethical complexities of CRISPR from an anticipatory lens. The book gives a balanced interdisciplinary conversation on CRISPR technology by combining the perspectives from the scientific community and that of a philosopher, bridging the gap between rapid growing scientific developments and societal and ethical concerns. The fulcrum of the book is the anticipatory ethical framework which will encourage researchers and policy makers to assess the long-term impacts of not just the CRISPR

technology, but other emerging and disruptive technologies as well. The book is very timely and coincides not just with the advancements in the CRISPR technology but also greater sense of responsibility in the usage and governance of biomedical technology in the light of the COVID-19 pandemic. The book rightly brings forth the social, ethical aspects and issues of access, equity and inclusion concerning CRISPR technology, which are inherently central to other emerging technologies as well. Such discussions on the practical implementation of the policy recommendations enumerated in the book would be useful together with an analysis of the barriers and challenges in fostering international cooperation and developing global governance frameworks.

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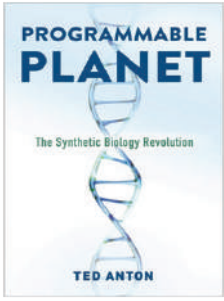
Book Review

Engineering Life: The Promises and Perils of Synthetic Biology

Title : Programmable Planet: The Synthetic Biology Revolution.
Author : Ted Anton
Publisher : Columbia University Press
Year : 2023
Pages : 411 pp.
ISBN- 9780231205108 (hardback)
ISBN-9780231555845 (ebook)
Price: USD 35.28



What if humanity could turn to biology to solve all looming existential crises? Ted Anton's book titled "Programmable planet: The synthetic biology revolution" illuminates the optimism surrounding such a prospect. The book tells the story of how the field of synthetic biology grew rapidly in the post-1980s era, driven by the persistent efforts of proficient scientists who sought to use science to solve problems, ranging from cancer to climate change. It would eventually be the endeavours of these men and women that would rise the occasion to help humanity combat one of the biggest and unforeseen challenges in the 21st Century: the coronavirus pandemic. The post-Covid era has witnessed such prospects of synthetic biology becoming more evident. The looming threat of environmental collapse in particular is driving a widespread transformation in how manufacturing processes and their remediation is being thought of.

The book effectively illustrates the utilization of creative non-fiction as an effective tool for science communication. The author approaches the evolution of the field of synthetic biology itself as stories featuring scientists as the central characters. Their academic or formative environments are presented as settings and breakthrough inventions or events as objects (Merkle, 2019). In this way, the evolution of the field is portrayed as a sequence of events which elucidate upon how key breakthroughs in laboratories moved into broad spectrum applications and commercialization. The author's employment of lucid and simple language in explaining complex and technical subject matter is notable. It further represents an earnest effort to engage the audience on important developments that directly pertain to the society and day-to-day life.

Keeping jargon away as much as possible, Anton simply defines synthetic biology as "the science of engineering life at the level of a cell" (p.2). The end-goal of such endeavours is to engineer life forms to fulfill certain applications or purposes. Key breakthroughs in the field such as CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) and messenger RNA manipulation for therapeutic purposes have also been elaborated upon. Anton's narrative herein works to ensure that the readers who recently experienced the pandemic grasp the magnanimous impact these inventions had on returning the world back to status quo ante. Meanwhile, ample attention is also paid to grand quixotic projects conceptualized to recreate the woolly mammoth and potentially dinosaurs.

As captured in the title, the book views the developments in synthetic biology as ushering in a novel "bioindustrial revolution", the conceptual discourse on which is very nascent in the academic sphere in science and technology studies and related fields of social sciences. Anton places the diffusion of synthetic biology tools as akin to the assembly line and semiconductors which brought forth the second and third industrial revolutions respectively. The book, however, stops short of contextualizing the same within technologies and techniques that are realizing the fourth industrial revolution. Elaborating on whether the bioindustrial revolution in itself is enabling the fourth industrial revolution, or whether the former is a subset of the latter could have added substantial value to the conceptual narrative that the author is attempting to pitch. In any case, the author's elaboration on the bioindustrial revolution in itself may have given ample food for thought for academics to embark upon relevant conceptual work.

In this regard, the author alludes to a potential convergence between the digital and biological realms and their ability to feed into each other to enable advances. The potential for DNA to be used as a means of digital storage, much like a silicon chip has been highlighted. Meanwhile, innovations such as the San Francsisco-based Twist Biosciences' use of semiconductors to print "oligos" (DNA snippets) on silicon chips to enable automated production of DNA have also been mentioned. However, a discussion on the Nano-Bio-Info-Cogno (NBIC) convergence, its implications for the society and for facilitating the evolution of artificial intelligence to higher levels of efficiency, would have constituted an interesting and relevant dimension to explore.

The section titled "Race to the vaccine" is perhaps the highlight of the book. Anton appeals to the world's collective memory of the pandemic in recounting how humanity employed the tools of synthetic biology to go after the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Synthetic biology tools, utilized at various stages of the world's fight against the pandemic including in developing at-home test kits and antibodies, drug cocktails and vaccinations have all been captured. The fight against Covid-19 has been aptly used as a case in point to illustrate an important lesson, " if one invested billions of dollars, one may realise the immediate, sweeping benefits from pure research such as what had been happening in synthetic biology" (p.209). Side-by-side, the various theories on the origins of the SARS-CoV-2 have been rationally dissected. Anton thereby draws attention to the uncomfortable reality that synthetic biology may have been used to create a lethal virus that globally claimed millions of lives.

Alongside illustrating the speed, scale and power that the field of synthetic biology is propelling forward, the author has also discussed associated ethical debates. Particularly, around the use of tools such as CRISPR to create new life forms or edit embryos, the ongoing debates are heavily polarized. Whether the scientific community's pursuit of synthetic biology is primarily driven by optimism or with core ethical concerns at their heart is something that the reader might be forced to think over. Moreover, little is said about the military applications of synthetic biology, although the role of the Defense Advanced Research Projects Agency (DARPA) in funding non-weapon projects is mentioned.

Overall, the book is optimistic on synthetic biology and its potential to save humanity and the planet, and significantly aid humanity's quest to inhabit outer space in a more permanent manner. The optimism primarily draws from the immense potential the field of synthetic biology holds. However, its translation to reality is hindered by several factors including the geopolitical trends, rate of advances in the technology and entry barriers to access the same. The growing role of commercial actors for instance may decide the extent to which synthetic biology can solve the world's problems, especially in the Global South. Anton's work captures the promise of synthetic biology and all that it can achieve for the planet and the future generations in a commendable manner. However, the promises ought to be measured against the potential perils and cost-benefit analyses while envisioning the kind of future elaborated upon in the book.

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Reference

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Guidelines for Contributors

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3. Use 's' in '-ise' '-isation' words; e.g., 'civilise', 'organisation'. Use British spellings rather than American spellings. Thus, 'labour' not 'labor'.
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All references should be embedded in the text in the anthropological style–for example '(Hirschman 1961)' or '(Lakshman 1989:125)' (Note: Page numbers in the text are necessary only if the cited portion is a direct quote).

Citation should be first alphabetical and then chronological–for example 'Rao 1999a, 1999b'.

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(b) Edited volumes:

Shand, Ric (ed.). 1999. *Economic Liberalisation in South Asia.* Delhi: Macmillan.

(c) Articles from edited volumes:

Lakshman, W. D. 1989. "Lineages of Dependent Development: From State Control to the Open Economy in Sri Lanka" in Ponna Wignaraja and Akmal Hussain (eds) *The Challenge in South Asia: Development, Democracy and Regional Cooperation*, pp. 105-63. New Delhi: Sage.

(d) Articles from Journals:

Rao, M.G., K. P. Kalirajan and R. T. Shand. 1999. "Convergence of Income across Indian States: A Divergent View". *Economic and Political Weekly,* 34(13): pp. 769-78.

(e) Unpublished Work:

Sandee, H. 1995. "Innovations in Production". Unpublished Ph.D thesis. Amsterdam: Free University.

(f) Online Reference:

World Health Organisation. 2000. "Development of National Policy on Traditional Medicine". Retrieved on March 31, 2011 from http://www.wpro.who.int/sites/trm/documents/Development+of+National+Policy+on+Traditional+Medicine.htm

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In this issue, there are two articles, one event report and two book reviews. The first article discusses a socially responsible model of healthcare The second article, on the other hand, argues for the harmonisation of regulatory practice for genome-edited crops. The event report captures the salient points emerged during RIS's Roundtable on Biosimilars. The book reviews of volumes on CRISPR and Synthetic Biology adds value to this issue.

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