Leveraging Bionanotechnology for Sustainable and Inclusive Growth

Prospects for Indo-German Collaboration in Ensuring Affordable Healthcare

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Leveraging Bionanotechnology for Sustainable and Inclusive Growth: Prospects for Indo-German Collaboration in Ensuring Affordable Healthcare

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जं इच्छसि अप्पणतो, जं च न इच्छसि अप्पणतो ।
तं इच्छ परस्स वि या, एत्तियगं जिणसासणं ।।

"The teaching of Jina (Tirthankaras*) is that you should desire for others, what you desire for yourself; and what you do not desire for yourself, you should also not desire for others."

[Jin Sutra]

**As per Encyclopædia Britannica, a Tirthankara, also called Jina ("Victor"), refers to a savior in Jainism who has made a path for others to follow.)*

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TABLE OF CONTENTS

TABLE OF CONTENTS III

LIST OF FIGURES V

LIST OF TABLES V

LIST OF BOXES V

KEY ABBREVIATIONS & SYMBOLS VI

TECHNICAL NOTES VII

FOREWORD BY THE CONSUL GENERAL IX

PREFACE BY THE AUTHORS X

EXECUTIVE SUMMARY XI

1 Introduction 13

1.1 Study background 13

1.2 Structure 15

2 The field of Bionanotechnology 16

2.1 Sectoral scope and potential applications 16

2.2 Global market & developments 18

2.3 Challenges, emerging trends & opportunities 21

3 Nanobiotechnology in India's Healthcare Sector 24

3.1 Country's brief socioeconomic profile 24

3.2 Key trends in healthcare 24

3.3 India's innovation system in brief 25

3.4 Nanobiotechnology/Nanomedicine research & ecosystem in India 26

3.5 International partnerships 29

4 Nanobiotechnology in Germany's Healthcare Sector 33

4.1 Brief socioeconomic profile 33

4.2 Sectoral overview & growth prospects 34

5 Scope for Indo-German Cooperation 39

6 Concluding summary 43

APPENDIX A: EXAMPLES OF GERMAN UNIVERSITIES WITH ACADEMIC/RESEARCH PROGRAMS ON NANOBIOTECHNOLOGY 44

APPENDIX B: EXAMPLES OF INDIAN UNIVERSITIES WITH ACADEMIC/RESEARCH PROGRAMS ON BIONANOTECHNOLOGY 48

Appendix C: Examples of Indian Universities with Academic/Research Programs on Bionanotechnology 50

Appendix D: Select Examples of Funded Bionanotechnology Projects in India 53

References 57

Useful Contacts 61

About the Authors 62

List of Figures

Figure 1: Global nanotechnology market, 2010-2020 (billion USD) 18

Figure 2: Diagrammatic representation of nanobiotechnology market segmentation........... 20

Figure 3: Challenges, emerging trends & opportunities of bionanotechnology...................... 22

Figure 4: Thrust areas of the High-Tech Strategy 2025 33

Figure 5: No. of institutions/organizations in different technology fields of nanobiotechnology in Germany 35

Figure 6: Expanding role of biopharmaceuticals in Germany (2010-2020) 37

Figure 7: A framework for bilateral cooperation in the field of bionanotechnology 41

List of Tables

Table 1: A landscape of nanomedicine in India 26

Table 2: International partnerships forged by the DBT 30

List of Boxes

Table 1: A landscape of nanomedicine in India 26

Table 2: International partnerships forged by the DBT 30

KEY ABBREVIATIONS & SYMBOLS

$	United States Dollar (USD)
€	Euro
AI	Artificial Intelligence
BfR	German Federal Institute for Risk Assessment (*Bundesinstitut für Risikobewertung*)
BIRAC	Biotechnology Industry Research Assistance Council
BMBF	German Federal Ministry for Education and Research (*Bundesministerium für Bildung und Forschung*)
BMWi	German Federal Ministry of Economic Affairs and Energy (*Bundesministerium für Wirtschaft und Energie*)
CAGR	Compound Annual Growth Rate
CRO	Contract Research Organizations
CRAMO	Contract Research and Manufacturing Organizations
cf.	Confer
DBT	Department of Biotechnology, Govt. of India
DST	Department of Science & Technology, Govt. of India
EU	European Union
FY	Fiscal Years
FDI	Foreign Direct Investments
GDP	Gross Domestic Product
INR	Indian National Rupees
IT	Information Technologies (IT)
KET	Key Enabling Technologies
MoU	Memorandum of Understanding
mRNA	Messenger Ribonucleic Acid
R&D	Research and (experimental) Development
SDGs	Sustainable Development Goals

TECHNICAL NOTES

- The present study works with the following definitions proposed by Ramsden (2016):
  - The term *biotechnology* refers to "the directed use of organisms to make useful products, typically achieved by genetically modifying organisms".
  - *Nanotechnology* is "concerned with observable *objects*, namely, materials and devices [...] with engineered structure in the nanoscale, and with processes capable of manipulating individual atoms or nanoscale blocks with ultraprecision".
  - *Bionanotechnology* can be "defined as the application of biology to nanotechnology" [...], the use of biological molecules in nanomaterials, nanoscale devices or nanoscale production systems".
  - Ramsden (2016) suggests that if bionanotechnology is applied to human health then it may also be called nanomedicine, nanobiotechnology, or even bionanobiotechnology. However, for the sake of simplicity, the present study does not further differentiate between these terms and uses them interchangeably, as marking of disciplinary boundaries lies beyond its scope.
- One nanometer (1 nm) refers to the one billionth part of a meter and correspondingly to the one millionth part of a millimeter (1 nm = 0.000 000 001 m = 10^{-9} m)
- The term "Nanomaterial", as recommended the European Commission (2011/696/EU) denotes "a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm."
- Official fiscal years (FY) in India pertain to the period from April of a given calendar year to March of the following year. For instance, "FY 2020-21" refers to the period from April 2020 to March 2021. This pattern has been followed in the report regarding all official data for India, unless specified otherwise.
- All monetary values that were originally only available in Indian rupees (INR) have been converted to Euro or US Dollars based on average exchange rates for a given fiscal year as published by the Reserve Bank of India (RBI), unless specified otherwise.
- Monetary figures available in Indian denominations (such as "lakhs" and "crores") have been converted to international units (10 lakhs = 1 million; 1 crore = 10 million; 100 crores = 1 billion) for the sake of better understanding for international readers.
- Where appropriate, figures have been rounded off to ensure a smooth flow in reading. This may at some places cause a minimal discrepancy in data.
- All figures in Dollar ($) refer to US Dollars, unless specified otherwise.
- Limitations of the secondary data cited in this report have not been thermalized for reasons of space and for ensuring a better flow while reading. Readers are advised to refer to original sources if requiring precision about the data and its limitations.

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भारत का प्रधान कौंसलावास
हैम्बर्ग

CONSULATE GENERAL OF INDIA
HAMBURG

FOREWORD BY THE CONSUL GENERAL

The Government of India has identified biosciences for human health as a crucial area of research. The government puts tremendous emphasis on ensuring an affordable access to high-quality healthcare with the help of technological advancement and has over the years engaged in concerted efforts to support research and development in this field. Digital transformation of the society, e.g. in the form of telemedicine, is playing an important role in this strategy.

Another important role that the digital transformation plays in achieving the objective of "affordable excellence" in healthcare is through advancements in the confluence zone of nanotechnology and biotechnology. The prefix "nano" in nanotechnology is reported to be derived from the Greek word "nanos", which means dwarf. Small devices for early diagnosis or target-specific treatment of potentially serious diseases can lead to faster recovery, less unwarranted side-effects and efficient use of natural resources, while enhancing affordability. In a world beset with an increasing share of lifestyle-related diseases, depleting natural resources and growing population, nanomedicine holds an immense promise – not just for India, but for the entire humankind. And, this is where – I believe – Germany and India could and should join hands.

Therefore, it is with immense pleasure that I present this report on "Leveraging Bionanotechnology for Sustainable and Inclusive Growth: Prospects for Indo-German Collaboration in Ensuring Affordable Healthcare". The study has been authored by Dr. Sadhana Tiwari and Prof. Dr. Rajnish Tiwari from the Center for Frugal Innovation (CFI) at Hamburg University of Technology (TUHH). The report intends to provide insights into recent developments and market opportunities for the benefit of Indian and German companies looking to expand or enhance their business with each other; as well as for other relevant stakeholders, e.g. industry associations, institutional bodies and policy makers from both sides.

I would like to thank the authors, CFI-TUHH and the other affiliated institutions, viz. University of Hamburg and Hochschule Fresenius for this fruitful collaboration in producing a highly informative study. My team and I look forward to many more productive collaborations in future. The publication of this report was made possible under the Market Expansion Activities Programme of the Economic Diplomacy Division of the Ministry of External Affairs.

John H. Ruolngul
Consul General of India, Hamburg

March 2022

PREFACE BY THE AUTHORS

The interplay of nanotechnology with biotechnology has given rise to new opportunities, especially in, but not limited to, the field of Life Sciences. It is increasingly possible to engage in early diagnosis of potentially critical ailments and to initiate highly-specific treatments. These applications can possibly revolutionize the healthcare, with great effectiveness, less side-effects and high resource efficiency. The principles of frugal innovation, as expressed in the term "affordable excellence" could act as guiding principles in this endeavor.

This field holds great promise: for India, for Germany, and for the global community. It makes sense for both countries to collaborate in multiple domains: on the level of governments, on the level of firms/enterprises, and on the level of academic and research institutions, to name but a few. The bilateral collaboration in the spirit of frugal innovation can help us achieve affordable, high-quality healthcare for all, as envisioned by the Sustainable Development Goals of the United Nations.

We hope, readers – especially stakeholders from the field of nanobiotechnology and Life Sciences – would find our study useful. We would like to take this opportunity to thank Mr. John H. Ruolngul, Hon'ble Consul General of India in Hamburg, and Mr. Gulshan Dhingra, Vice Consul, for initiating the idea of this study and enabling us to, yet again, present our research to firms as well as to policy and decision makers in India, Germany and beyond.

We look forward to continued cooperation and collaboration with the Consulate General of India, Hamburg and other entrepreneurial and institutional actors. For, we are convinced that this collaboration contributes to the deepening of the bilateral relations in all spheres and is in mutual interest of both nations while supporting the greater good.

Dr. Sadhana Tiwari

Hamburg, March 2022 — Prof. Dr. habil. Rajnish Tiwari

EXECUTIVE SUMMARY

The field of bionanotechnology, sometime also referred to as nanobiotechnology, has emerged from the intersection of nanotechnology and biotechnology. Today, it constitutes one of the fastest growing research fields due to its enormous potential. A particularly promising area of application for bionanotechnology is Life Sciences or Healthcare, where nanomedicine can help with advance diagnostics and targeted, patient-specific treatment in an effective and speedy manner while reducing the use of resources. Thus, bionanotechnology shows high compatibility with principles of “affordable excellence” that lie at the roots of the modern concept of frugal innovation.

India and Germany both have made substantial progress in this field and many research institutions, universities, startups and established enterprises are active stakeholders of this industry, along with government bodies. Biomaterials, biosensors, functional systems, drug transport/targeting and implants are the five most active technology fields in Germany’s nanobiotechnology sector, while a strong focus can be observed in the application areas of diagnostics, medical devices, therapeutics and regenerative medicine within the Health/Pharma sector. These areas coincide with India’s thrust areas of research that is, however, still largely concentrated in research institutions. A bilateral cooperation between India and Germany can be highly rewarding as it can use complementary strengths of the respective ecosystems and help each other in overcoming their weaknesses, e.g. in ensuring translational research, developing common regulatory/safety standards, better utilization of resources & infrastructure, and creation of cutting-edge knowledge through joint research and exchange programs for researchers, scientists, students and entrepreneurs to intensify interaction.

The study suggests a three-pronged approach for a bilateral cooperation: (a) identify promising avenues of cooperation, (b) pool resources, and (c) develop frugal solutions that have high chances of diffusion across the globe. The potential market-size and the lead market function of India in the field of frugal innovations can help the solutions that are developed in bilateral (or eventually multilateral) cooperation achieve faster commercial success while raising standards of living for all potential beneficiaries of the scientific progress, across the globe. This would make a very valuable contribution to the achievement of the Sustainable Development Goal (SDG) #3 related to “Good Health and Well-being”.

Keywords:

India; Germany; Indo-German Partnership; Nanobiotechnology; Bionanotechnology; Nanotechnology; Biotechnology; Biosensors; Nanomedicine; Life Sciences; Healthcare; Frugal Innovation; Affordable Excellence; Affordable Green Excellence.

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1 Introduction

1.1 Study background

> "As the world looks for quick solutions to meet the huge healthcare challenges exposed by the COVID-19 pandemic, our effort is to ensure that our innovations continue to focus on scalability, sustainability and replicability. The integration of new and emerging technologies, linking biological science with data science, clinical research and engineering sciences, is the way forward to prepare to meet our ambitious target of achieving a US$150 billion bioeconomy by 2025 and to India becoming a US$100 billion biomanufacturing hub." (Swarup, 2020)

The quote above from an article written by Dr. Renu Swarup, then-Secretary, Department of Biotechnology, Government of India & Chairperson, Biotechnology Industry Research Assistance Council (BIRAC) indicates the importance that India attaches to biotechnology and related disciplines. Furthermore, it also points towards ambitious goals that India has set itself in this sphere. India's new *Science, Technology, and Innovation Policy* (STIP) proposed in December 2020 sees biosciences for human health as a crucial area of research (GOI-DST, 2020b). It is not difficult to understand, why India is keen on this research area: "Precisely engineered nanobiomaterials, nanobiodevices and nanobiosystems are anticipated to emerge as next-generation platforms for bioelectronics, biosensors, biocatalysts, molecular imaging modalities, biological actuators, and biomedical applications" (Nagamune, 2017).

And, therefore, not surprisingly, India is not alone in this endeavor. A report prepared on behalf of the European Commission identifies biological transformation that brings together biotechnology, IT and engineering ("a bio-intelligent economy") as being crucial for "prosperity and healthy and sustainable (qualitative rather than quantitative) growth" (Müller and Potters, 2019). In addition, advanced materials, life-science technologies and micro/nano-electronics and photonics have been identified among six key enabling technologies (KET) by the European Commission.[1] These developments are not surprising, as a survey of R&D managers in 2018 identified bioengineering/biology, nanotechnology and bionanotechnology[2] as belonging to the likely most important technologies by 2021, in addition to technologies, such as information technologies (IT), artificial intelligence (AI), big data, robotics/ automation etc. (R&D Magazine, 2019).

The broad societal relevance of these technologies is evident from the global sustainable development goals (SDGs) of the United Nations. One of the major threats to peace and security is non-availability or unaffordability of healthcare. A good healthcare system plays a major role in strengthening socio-economic structure of a nation. Therefore, "Good Health

[1] See, https://ec.europa.eu/info/research-and-innovation/research-area/industrial-research-and-innovation/key-enabling-technologies_en, last retrieved: 12 Mar. 2022.

[2] For the purpose of this report no further distinction is made between the terms "bionanotechnology" and "nanobiotechnology". How these two terms differ in relation to their focal areas is briefly explained in chapter 2.

and Well-Being" has acquired a top position in the priority right next to the goals of "No Poverty" and "Zero Hunger", among seventeen SDGs set by the UN. The objective of this goal is to "ensure healthy lives and promote well-being to all at all ages". One of the targets set under this objective relates to supporting the research and development (R&D) work on "vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines [...]".[3]

The objective to provide affordable and accessible healthcare is challenging enough in the face of existing societal inequalities, technological divide and infrastructural shortcomings. The challenge has been further intensified by the climate change and the ongoing Corona pandemic. Gita Gopinath, then-Economic Counsellor and Director of Research at the International Monetary Fund (IMF), in her foreword to the October 2021 edition of the World Economic Outlook report, writes: "While reducing the likelihood of a prolonged pandemic is a key immediate global priority, another urgent priority is the need to slow the rise in global temperatures and contain the growing adverse health and economic effects of climate change" (IMF, 2021: xiii-xiv). The target of providing high quality healthcare in an affordable manner is even more important due to the shrinking of fiscal space in many economies in the face of the pandemic. The IMF (2021) cautions that healthcare spending need to remain on a high priority and should become more targeted.

It is in this backdrop that experts expect bionanotechnology to make a very valuable contribution. Bionanotechnology, which broadly speaking, concerns the "incorporation of biological molecules into nanoartifacts" (R&D Magazine, 2019), can For example enable clinicians to "diagnose diseases at faster rates with improved sensitivity and specificity" (Chan, 2006: 90). According to VFA Bio, an industry association of biotechnology firms in Germany, bionanotechnology offers a wide range of possible applications: in drug development, in the development of new drug dosage forms, in diagnostics, in the field of imaging procedures such as computer tomography or magnetic resonance imaging, and in the therapy of diseases. Therefore, it holds great potential for research and development, scientific and medical progress, for patients and for nations as a research and business location (VFA Bio, 2007).

According to Hurst (2011: V), nanomaterials, owing to their unique size-dependent properties, "have the potential to revolutionize the detection, diagnosis, and treatment of disease by offering superior capabilities compared to conventionally-used materials". Furthermore, nanomaterials can enable real-time disease detection and therapy with the help of to advance point-of-care (POC) systems. POC hand-held devices based on bionanotechnology can often detect very low concentrations of some specific protein biomarker in a blood or biofluid sample enabling early detection and treatment on the one hand, and substantially reduce

[3] See, https://sdgs.un.org/goals, last retrieved: 12 Feb. 2022.

costs of diagnosis and medication on the other (Tiwari, S., Vinchurkar*, et al*, 2017).[4] Studies also show that such novel solutions do not have to be expensive. For example, low-cost, paper-based platforms are gaining increasing relevance in modern diagnostics and biosensing. Targeting of cost-effective yet high-quality solutions in healthcare devices with the help of bionanotechnology may contribute to the development of substantially affordable and very effective healthcare solutions for the benefit of the society (Tiwari, S., Garnier*, et al*, 2017).

A primary scope and objective of this report is to conduct a desk research-based study that would showcase the potential of bionanotechnology in India and investigate the scope of bilateral Indo-German cooperation.

1.2 Structure

This study is structured along the following lines: after a brief introduction to the study background and the objectives in chapter 1, the next chapter (2) defines the scope of the field of bionanotechnology and identifies some relevant global developments. Chapter 3 contains a brief socio-economic profile of India, and an overview of key features of the bionanotechnology sector in the country. An analysis of the German bionanotechnology sector is undertaken in chapter 4. The scope of a mutually beneficial bilateral partnership between India and Germany is investigated in chapter 5. A summarizing discussion in section 6 concludes the report.

[4] For a good and recent overview of potential innovative solutions using nanotechnologies in medicine, see the special issue of *Accounts of Chemical Research* (vol. 52, issue 9; 2019) on the theme of "Nanomedicine and Beyond": https://pubs.acs.org/page/achre4/nanomedicine-beyond, last retrieved: 5 Dec. 2021.

2 The field of Bionanotechnology

2.1 Sectoral scope and potential applications

Bionanotechnology can be regarded as the bio-branch of nanotechnology and constitutes one of the fastest emerging research fields (Gaikwad *et al*, 2020). The nanoscience domain is typically concerned with dimensions that range between 1 nm and 100 nm.[5] According to the German Federal Institute for Risk Assessment (*Bundesinstitut für Risikobewertung*; BfR), "Nanotechnologies offer the possibility to develop structures, techniques and systems in which materials show completely new properties and functions. It is expected that this potential will provide beneficial applications, for example in robotics, sensor technology, process technology, biotechnology and medicine, as well as in further development in food, consumer goods and cosmetic products. Nanotechnology is considered therefore as an important key technology worldwide" (BfR, 2021). It has emerged as key research field with promising implications for both diagnostics and therapeutics, and "is expected to accelerate fundamental biomedical research via the creation of novel state-of-the-art tools" (Chan, 2006: 87). Nanotechnology has "emerged as a novel and powerful tool to manipulate matters at a 'nano-scale'" and enables the intersection with many other disciplines, such as biotechnology, medicine, agriculture, environment protection, information technology etc. (Lee and Moon, 2020).

Nanoparticles play an important role in a range of diagnostic devices and test methods to increase performance, e.g. sensitivity and/or speed, or to enable a detection method that would not be possible without nanotechnology. For example, plasmonic nanoparticles being "extremely strong absorbers and scatterers of light [.] are used in lateral flow diagnostics, surface-enhanced spectroscopy, cell labelling and color-changing sensors. Nanoparticles with electrochemical, magnetic or fluorescent properties are also used in many diagnostic applications" (BIOZOL, 2021). As a result, there exist numerous nanobiotechnological applications: for instance, nanoparticles are used to imitate the self-cleaning ability of lotus leaves; such biomimetic surfaces can be found in façade paints, on the glass of toll system cameras and in outdoor jackets that should not get dirty. In the healthcare sector nanobiosensors can be used, for example, to diagnose Alzheimer's disease in an early stage and thus treat it better; a nanofilter can selectively fish toxins out of the blood (Open Science, 2013). The biological and medical research communities, according to Chan (2006), "have exploited the unique properties of nanomaterials for various applications (eg, contrast agents for cell and animal imaging and therapeutics for treating cancer), and, because of these demonstrations, new avenues and promises have been created for nanotechnology research.

[5] One nanometre (1 nm) is one billionth of a meter and correspondingly one millionth of a millimetre. To illustrate it with an example, if all distances of our macroscopic world could be shrunk by one billion, one meter would become 1 nm: "In this case the distance between the earth and the moon (≈ 360,000 km) would become 36 cm and the distance between the earth and the sun (≈ 150,000,000 km) would become 150 m" (Ngô and Natowitz, 2017: 15)

Terms such biomedical nanotechnology, bionanotechnology, and nanomedicine are used to describe this hybrid field" (Chan, 2006).

According to Sawitowski (2004: 10), "Progress in medical device technology is clearly linked to progress in materials science technology [...]. Nanotechnology can, in certain very well-defined areas, improve the biocompatibility of implants either passively by the use of thin films, or actively by releasing therapeutic agents from implant surfaces. As thin-film technology is a well-established technology, it can be claimed that active devices are the main area of nanotechnology". He argues that nanomedicine can help avoid undesirable side effects while allowing for a more efficient use of cost-intensive drugs, "thereby reducing both patient burden and the economics of the healthcare system". As a major area of potential application for such modern devices Sawitowski (2004: 11) cites the examples of stents in cardiology: "Rather than perform bypass surgery, a minimally invasive intervention can ultimately lead to the same outcome for the patient, but with less surgical trauma and a reduced time in hospital. Among the many concepts currently proceeding through scientific development phases, it seems inevitable that nanotechnology will ultimately become medical routine." The following examples of nanobiotechnology research projects provide a glimpse of the possibilities in the field of nanomedicine:[6]

- Biochips for tests that can be used to detect diseases such as Alzheimer's, cancer, multiple sclerosis or rheumatoid arthritis very quickly and at an early stage.
- Nanoparticle-based contrast agents that bind specifically to diseased cells and can enable much faster and better diagnostics with imaging methods.
- Nanoscale polymer capsules with which chemotherapeutic agents are brought directly to the tumor and released there by means of a laser pulse, sparing the surrounding healthy body tissue.
- Nanoparticles that can cross the blood-brain barrier, for example, to enable the targeted treatment of brain tumors.
- Nano cancer-therapy, in which tiny iron particles are injected into the tumor tissue or directed there with a magnet and then stimulated to vibrate with the help of an alternating magnetic field; the resulting heat kills the tumor cells.

When we talk about the applications of nanotechnology in healthcare sector, it is evident that there should be some interaction with biological materials or biological phenomenon. Here emerges a new subarea of nanotechnology termed as "nanobiotechnology" or "bionanotechnology". The exact boundaries of *nanobiotechnology* vs. *bionanotechnology* have not been delineated very clearly. The key difference between these two closely related fields is seen in "the primary direction for the transfer of knowledge and innovations": while nanobiotechnology "aims to exploit advances in nanotechnology for improving biotechnology", the latter "takes advantage of natural or biomimetic systems and designs to

[6] See, https://www.vfa-bio.de/vb-de/aktuelle-themen/forschung/nanobio.html, last retrieved: 7 Mar. 2022.

produce unique nanoscale structures".[7] Although there is no formal distinction in the definition of both these terms, there is one fundamental difference between the two. Nanobiotechnology can be seen as "a discipline in which tools from nanotechnology are developed and applied to study biological phenomena. For example, nanoparticles can serve as probes, sensors or vehicles for biomolecule delivery in cellular systems."[8] On the other hand, "bionanotechnology" is defined as the incorporation of biological molecules into nanoartifacts.[9] Bionanotechnology takes advantages and inspirations from biological systems to create nanodevices for various applications most importantly for healthcare sector (Ramsden, 2016). In both cases, this new discipline leads to merger of biological research with nanotechnology. Therefore, both terms are often used interchangeably.[10]

2.2 Global market & developments

It is difficult to find reliable data on the global or even national/regional volume of bionanotechnology owing to unclear statistical definitions and due to the interwoven relation of bionanotechnology to multiple application fields. Therefore, it seems useful to estimate the market size with the help of heuristic methods, looking at different indicators. One such useful indicator could be to look at the estimated size of the global nanotechnology market. As Figure 1 shows, the global nanotechnology market, in general, has grown with a CAGR of over 17% between years 2010 and 2020. The markets-size has increased nearly five-folds from about $16 billion to approximately $76 billion in this period (Casaleggio Associati, 2019).

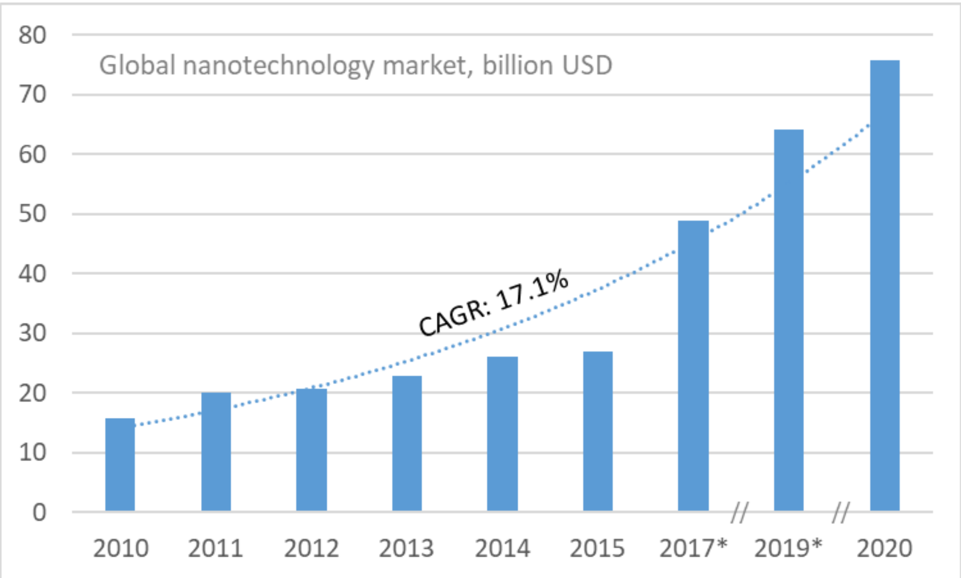

Figure 1: Global nanotechnology market, 2010-2020 (billion USD)[11]

[7] See, https://biointerface.org/bi/nanobio/, last retrieved: 11 Dec. 2021-
[8] See, https://www.nature.com/subjects/nanobiotechnology, last retrieved: 8 Mar. 2022.
[9] See, https://www.sciencedirect.com/topics/engineering/bionanotechnology, last retrieved: 8 Mar. 2022.
[10] The present study too does not differentiate further between these two terms treating them as synonyms since marking of disciplinary boundaries lies beyond the scope of this work.
[11] Source: own illustration based on data from Casaleggio Associati (2019), * break in data series.

Nanoenigneered surfaces that are of especial relevance for nanomedicine have also been on a growth trajectory. Statistical data compiled by Statista suggest that the global market value of nanoengineered surfaces that are used in a variety of fields, e.g. in biomedical applications, solar energy, and electronics, is expanding rapidly. The market volume, which reportedly stood at around $403 million in 2017, was projected to grow more than four-folds to $1.7 billion by 2022, within a short span of five years.[12]

Looking at the specific data for nanobiotechnology, the picture is similar, even if the data is more scarce and/or less reliable. According to a recent report from BCC Publishing, the global market for nanobiotechnology stood at $38.5 billion in 2021 and was expected to reach $68.4 billion in the next five years, implying a CAGR of 12.2% in the period of 2021-2026.[13] Another report from the same institution forecasts that the global market for nanoparticles in biotechnology, drug development and drug delivery will grow from $83.4 billion in 2020 to $123.6 billion by 2025, at a CAGR of 8.2%.[14]

Yet another report by Global Industry Analysts, Inc. puts the estimated volume of the global market for nanobiotechnology at $62.3 billion in 2020, and presumes a CAGR of 7.1% till 2027, so that the market is expected to reach the volume of over $100 billion by 2027. The largest market for nanobiotechnology is reported to be the USA ($18.4 billion in 2020), closely followed by China, that is expected to command a market worth $17.6 billion by 2027. Other important geographic markets are Japan (expected CAGR 6.7%) Canada and Germany (expected CAGR for both 5.7%).[15]

Despite this multitude of data, it becomes quite obvious that the global market for nanotechnology and nanobiotechnology is on a growth path and can be reasonably expected to grow even further due to the promising application areas in both communicable and non-communicable diseases. The recent Corona crisis has also given a new impetus for this research. The nanobiotechnology market can be categorized along several dimensions, such as based on application areas, technologies, geographies or diseases (see, Figure 2).

Nanotechnology offers prospects to create new rapid, efficient and simple solutions for disease prevention, detection as well as treatment. Hence it provides a big scope to the healthcare market. As per a report of Mordor intelligence the healthcare nanotechnology market has been estimated at about $220 billion in 2020, and it is anticipated to cross $461 billion by 2026, with a CAGR of approximately 11.9% during the forecast period of 2021-

[12] See: https://www.statista.com/statistics/1076943/global-market-value-nanoengineered-surfaces/, retrieved last: 5 Dec. 2021.

[13] See, https://www.bccresearch.com/market-research/nanotechnology/nanobiotechnology-market.html, last retrieved: 8 Mar. 2022.

[14] See, https://www.bccresearch.com/market-research/biotechnology/nanoparticles-biotechnology-drug-development-drug-delivery-report.html, last retrieved: 8 Mar. 2022.

[15] See, https://www.researchandmarkets.com/reports/344092/nanobiotechnology_global_market_trajectory_and#rela1-5315044, last retrieved: 8 Mar. 2022.

2026.[16] After the success story of nanoparticles based vaccines for Covid-19, nanomedicine market is experiencing many new entries globally. Some of them are completely new i.e. Start-Ups and some are existing pharma giants, chemical industry or biotechnology companies. The key players in this sectors are; Sanofi SA, Pfizer Inc., Merck & co., Abbott Laboratories, Sigma Aldrich Company, Dendritic Nanotechnologies Inc., Celgene Corporation, Luminex Corporation, Fresinuns Kabi AG and Taiwan Liposome Company Ltd. Global nanobiotechnology based healthcare market is broadly segmented in four categories on the basis of applications, technology used, geography and diseases.

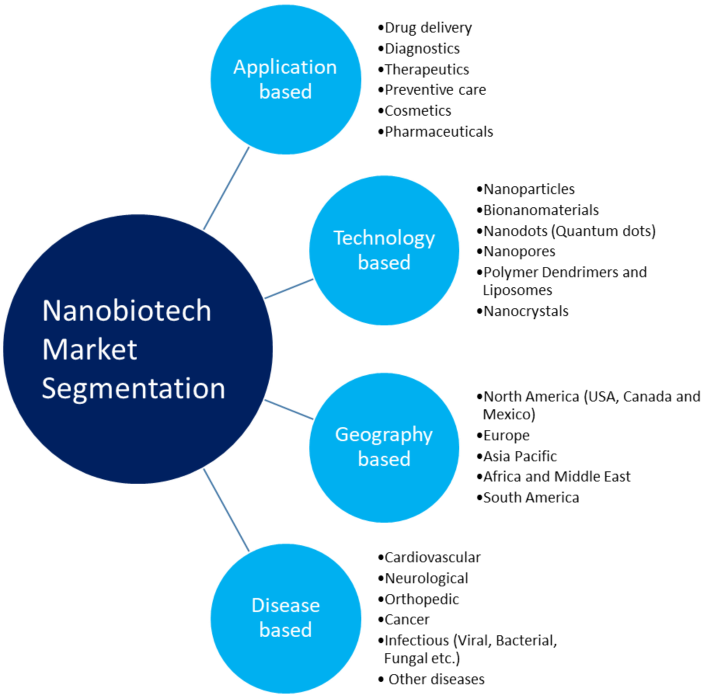

Figure 2: Diagrammatic representation of nanobiotechnology market segmentation[17]

The key market trends emerge out through the nanobiotech market segmentation, as shown in Figure 2, indicates that among application based segments, drug delivery has been observed as the largest segment with a recorded 55% of total market share, in the base year 2020. It can be interpreted that among the other industries pharma and biotech industries are predicted to be remain as the principal end-users of bionanotechnlogy. In addition to this nanoparticle assisted drug delivery is also the most focused area of research and development in these industries. In the second category i.e. Technology based segmentation, the most popular technology is polymer dendrimers and liposome with a market share of near about 50%, as this technology is widely used in most of the therapeutic healthcare applications like; cancer treatment, drug delivery, vaccine development etc. Among the geography based segments North America was and forecasted to occupy the largest market share of global nanobiotech sector, followed by Europe, Asia pacific, South America and the lowest share is

[16] See, https://www.mordorintelligence.com/industry-reports/healthcare-nanotechnology-nanomedicine-market#, last retrieved: 7 Mar. 2022.
[17] Source: own illustration, partly based on PR Newswire (2021)

taken by Africa and Mid-East. The nanomedicine market summary also stated Asia pacific region as the fastest growing for the nanobiotechnology based healthcare throughout the forecast period 2021-2029. There are many factors which play a crucial role in this market growth in Asia Pacific region, like; more investment in developing healthcare services, research and development and healthcare infrastructure. Beside this public awareness related to life risking diseases and acceptance of new technologies for diagnosis and treatment, is also very vital which provided a big push to bionanotech based healthcare market.

Nanobiotechnology is benefiting the modern medical field in both diagnostics and therapeutics in various forms. For example, nanobiosensors, nanoneedles, nanotweezers, nanozyems, nanoparticles mediated drug delivery, imaging technology and many more. The most recent and successful example of application of nanoparticles in healthcare is the mRNA technology based Covid-19 vaccines developed by Pfizer/BioNTech and Moderna, where mRNA (containing blueprints for specific protein production) is encapsulated inside lipid-nanoparticles. This lipid-nanoparticles envelop protects mRNA facilitate the journey of mRNA to the site through blood, where the protein production takes place. “The global market for mRNA therapeutics should grow from $46.7 billion in 2021 to $101.3 billion by 2026, at a CAGR of 16.8% for the period of 2021-2026.”[18]

2.3 Challenges, emerging trends & opportunities

Figure 3 summarizes the (societal) challenges, which lead to the emergence of certain trends and the opportunities that arise out of them. As discussed in the previous sections, the global society is confronted with some grand challenges, such as ensuring affordable and accessible long-term healthcare for all, as envisaged by the UN in its SDGs. This goal becomes especially important in ageing societies with increasing average life expectancy. Maintaining social interaction and providing support is a challenge in a digital world. We also live in a world with finite and depleting natural resources on the one hand and a growing population on the other.

The efforts to address these challenges is leading to emergence of trends such as self-care, person-centric healthcare as opposed to mass-care that is based on average values, and finally there is a need for “affordable excellence” so that technological advancement can be ensured at an affordable cost. In this context it is important to understand that affordability cannot and should not be measured merely in terms of financial aspects. It has been proposed that affordability needs to be seen as a multidimensional construct, which include affordability of an innovation to the society-at-large as well as to the ecological environment (Herstatt and Tiwari, 2020). The emerging trends create opportunities, for example, to create frugal innovations as enablers of affordable excellence in fields as diverse as health communication, prototyping, co-design, product development etc.

[18] See, https://www.bccresearch.com/market-research/biotechnology/mrna-vaccines-and-therapeutics-market.html, last retrieved: 8 Mar. 2022.

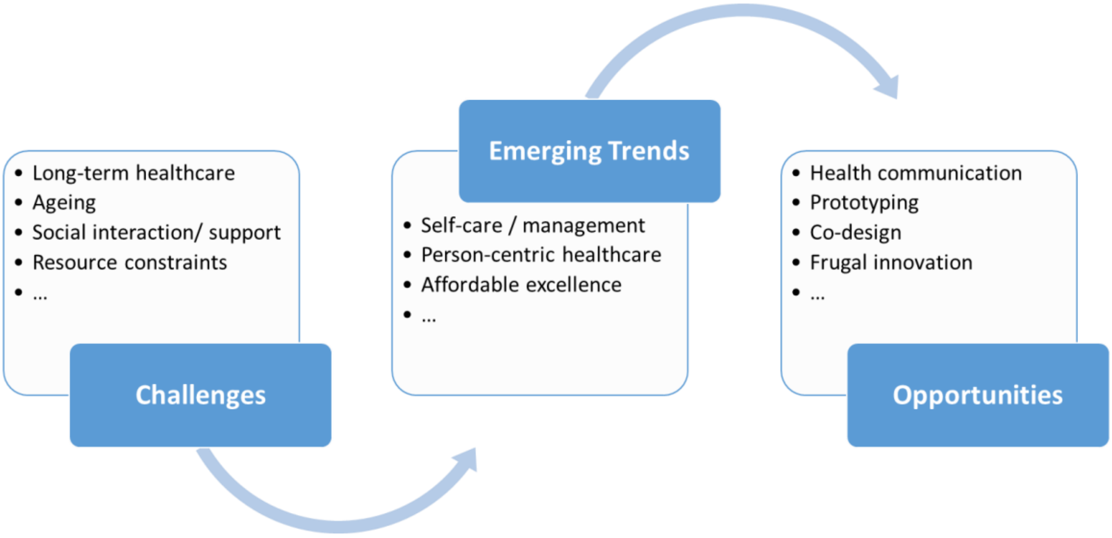

Figure 3: Challenges, emerging trends & opportunities of bionanotechnology[19]

As many game-changing nanotech innovations move from the research lab to commercialization, marketing issues are likely to become increasingly important (Tomczyk, 2011). In addition, there is the crucial issue of risk identification, assessment and mitigation. As of today, there seem to be quite a few unanswered questions about the potential health-related hazards of nanomaterials. According to BfR, "There is no general answer to whether nanomaterials or products that contain them may pose health risks for consumers" and the possibility of "[...] an elevated and possibly new type of health burden on the general population" cannot be ruled out because in comparison to conventional materials, "nanomaterials demonstrate altered, and in some cases even new, properties and/or functions" (BfR, n.d.). The BfR identifies the following potential risks (see, Box 1):

Box 1: Potential health risks from nanomaterials[20]

"**Toxicokinetics**: Due to their small size, nanomaterials can pass through some barriers in the body more easily and are therefore distributed differently in the body than corresponding non-nanoscale materials.

Biopersistence: Some nanomaterials could remain in specific organs for a very long period of time, so that significant amounts can accumulate over time and may lead to chronic health issues

Reactivity: Nanomaterials have a large specific surface area (surface to volume ratio), which is often associated with greater reactivity. This increases the risk of persisting inflammatory responses, which can lead to organ damage."

A government report by Germany's BMBF (2016: 13) says: "Since nanotechnology applications are increasingly advancing into different areas of people's lives, alongside health and

[19] Source: own illustration, adapted from on Tsekleves and Cooper (2017: 391)
[20] Source: BfR (n.d.)

ecological also ethical, legal and socio-economic issues must be better taken into account at all stages of the innovation chain – over the entire life cycle of nanoproducts. The principle of responsible research and innovation is also becoming ever more important in the context of nanotechnology and is shaping current scientific policy debates."

Similar concerns in terms of ethical, legal, social and environmental issues have also been identified and articulated in the Indian context by Patra *et al* (2009). According to Karpagam (2014), especially developing countries would need to resolve issues pertaining to research, technology development, skills requirement, risk management, dynamic & adequate regulatory and governance structure, transparency in policy making and stakeholder engagement, to fully exploit the potential of nanobiotechnology. It has also been pointed out that *in vitro* (under controlled laboratory conditions) and *in vivo* (in human body) applications can be very different and the complexities involved in *in vivo* studies make the translational research involving nanoparticles much more difficult (Cheon *et al*, 2019).

Therefore, addressing global health challenges goes much beyond mere identification of technical problems and creation of technological solutions to overcome them. Salamanca-Buentello and Daar (2021) warn that "the excitement over novel technologies can hinder serious examination of the social and cultural contexts in which healthcare is delivered", which, in their opinion, is "a crucial component of the success of any health intervention". That such concerns do not relate only to the developing nations can be seen in this quote from the European Commission:

> "Nanobiotechnology has the power to drastically transform society, yet all too often the dialogue regarding this science has been dominated by fear", necessitating an urgent public debate on its merits (European Commission, 2008).

3 Nanobiotechnology in India's Healthcare Sector

3.1 Country's brief socioeconomic profile

Since starting on the path of economic liberalization in 1991,[21] India has witnessed rapid economic growth. The International Monetary Fund (IMF) data shows that India's gross domestic product (GDP) in current prices has grown significantly despite some severe disruptions due to exogenous shocks such as the financial crisis of 2008/2009 and the currently ongoing COVID pandemic. India's GDP increased more than ten-fold from $275 billion to reach the mark of $2.95 trillion in 2021, and is forecasted to grow by a cumulative 50% within the next five years, reaching $4.4 trillion by 2026 (IMF, 2021). Since 1991 the country's population has also grown from 891 million to an estimated 1.4 billion in 2021. Population growth in the post-Independence period can be largely attributed to an increased average life expectancy resulting from better standards of living, hygiene conditions and availability of medical facilities.

GDP per capita in current prices has grown, in the face of growing population, from about $308 per annum in 1991 to $2116 per annum in 2021, and is forecasted to cross the mark of $3000 in 2026. In terms of purchasing power parity (PPP), GDP per capita is estimated to have grown from about $1100 in 1991 to more than $7300 in 2021, and is expected to be touching $11,000 by 2026. Even though poverty and inequality remain a major concern for India, data suggest that the recent economic growth has helped to curb abject poverty. The share of people living below poverty line in India halved from over 45% in FY 1993-94 to less than 22% in FY 2011-12. Noteworthy is that urban poverty has decreased more rapidly (~14%) in comparison to rural poverty (~26%) in this period (GOI-MOSPI, 2018).

3.2 Key trends in healthcare

The increasing average life expectancy and the better standards of living have led to increasing expenditure on healthcare. India's healthcare sector is expected to grow almost three-folds between 2016 and 2022: to reach $372 billion in 2022 from $110 billion in 2016 (CAGR of 22%), as per a report of IBEF (2021).

Per capita expenditure on health in terms of purchasing power parity (PPP) has increased from PPP$ 18 in year 2000 to PPP$ 64 in year 2019, as per World Bank data.[22] Government expenditure on health has increased in terms of its share in GDP from 1.15% in FY 2013-14 to 1.35% in FY 2017-18.[23] The government plans to increase this expenditure to 2.5% of GDP by 2025 as per goals set in the National Health Policy of 2017. In absolute terms, the budget allocation for the Department of Health & Family Welfare has increased substantially in the past few years from INR 371 billion in FY 2016-17 to INR 671 billion in FY 2020-21. Budget

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[21] For a discussion on the causes, process and impact of economic liberalisation in India, see, e.g., Ahluwalia (2002), Kumar, N. (1996), and Tiwari, R. *et al* (2011).

[22] See, https://data.worldbank.org/indicator/SH.XPD.PVTD.PP.CD?locations=IN, last retrieved: 15 Mar. 2022.

[23] The latest available National Health Account estimates pertaining to FY 2017-18 were released in Nov. 2021.

allocation for health research in FY 2020-21 was hiked by 7.7% in comparison to the previous year. In addition, there are substantial relevant R&D activities that take place in other ministries, such as Department of Science & Technology (DST), Department of Scientific & Industrial Research (DSIR), Department of Biotechnology (DBT).[24]

Under National Health Mission the central government provides financial and technical support to states and union territories (UTs) "for accessible, affordable and quality healthcare in rural and urban areas. All States/UTs are supported for providing free services in maternal health, child health, adolescent health, universal immunization, family planning, communicable diseases such as Tuberculosis, HIV/ AIDS, vector borne diseases like Malaria, Dengue and Kala Azar, Leprosy etc. and non-communicable diseases, provision of free drugs & diagnostics in public health facilities [...]".[25]

3.3 India's innovation system in brief

As of 2019, India's R&D expenditure in PPP terms, was estimated at $96 billion, which accounts for a 4% share in global R&D spending and places it 5th globally on the list of countries with the highest gross expenditure on R&D (GERD). This is well behind the US (25%) and China (23%) as well as also behind Japan (8%) and Germany (5%), but it still puts India ahead of countries such as Korea, France, Russia or the UK. Even though India's R&D intensity as a share of GDP remains at a low level of < 1%, it should be noted that the sustained economic growth of the last decade has led to a significant increase in R&D efforts in absolute terms. Measured in market prices, India has seen a remarkable increase in its investment in R&D since the turn of the millennium. In market prices, India's GERD was estimated in FY 1999-00 at about INR 144 billion (about €3.2 billion in then exchange rates). By FY 2018-19, India's R&D expenditure is estimated to reach INR 1.2 trillion. (about €15.3 billion). The growth in GERD has been primarily driven by the private sector and by universities (GOI-DST, 2020a; Kroll *et al*, 2021).

For a long time, the government has been providing fiscal incentives for domestic R&D, e.g. through tax incentives: R&D expenditures may be deducted from taxes with a weightage of 150%. In addition, the central government has launched a number of "missions" (e.g. "Start-up India", "Digital India", "Make in India", or "National Smart Cities Mission") to enable a societal transformation of the country and to boost the innovation potential in the country. Examples of newly launched and ambitious funding programs are (Kroll *et al*, 2021):

- AIM ("Atal Innovation Mission") under the jurisdiction of NITI Aayog,
- IMPRINT - Round 2 ("IMPacting Research, Innovation and Technology") under joint responsibility of the Ministry of Education and DST,
- INSPIRE ("Innovation in Science Pursuit for Inspired Research") under the responsibility of the DST,

[24] For a recent and detailed analysis of India's national innovation system co-authored by one of the authors of the present report, see: Kroll *et al* (2021). The report is in German.
[25] See, https://pib.gov.in/Pressreleaseshare.aspx?PRID=1580410, dated 26 Jul. 2019, retrieved: 12 Mar. 2022.

- "Biotechnology Programme for Societal Development", under the responsibility of the DBT; and
- PRISM ("Promoting Innovations in Individuals, Start-ups and MSMEs" under the responsibility of the DSIR.

3.4 Nanobiotechnology/Nanomedicine research & ecosystem in India

A mapping of nanomedicine landscape in India published by scholars from the Foundation for Innovation and Technology Transfer, Indian Institute of Technology Delhi and Baylor College of Medicine, Houston (USA) in 2018 revealed the following picture (see, Table 1):

Table 1: A landscape of nanomedicine in India[26]

Institutions/organizations in the domain of nanomedicine	Nos.	Output	Nos.
Universities & institutes	87	Products in the market	17
Special centers	33	Products undergoing clinical trials	19
Business enterprises (established firms)	31	Patent applications	615
Business enterprises (startups & entrepreneurs)	23	Publications	615
Governmental supporting agencies	5		
Venture capitalists	7		
Contract Research Organizations (CROs) & Contract Research and Manufacturing Organizations (CRAMOs)	8		

The mapping in Table 1 shows that India has an active and considerably large ecosystem for nanobiotechnology, especially with a focus on healthcare applications (viz. nanomedicine). A fairly large number of universities and business enterprises (both established firms and startups) are active in this domain and have succeeded in commercializing some of their inventions. The products belong to Analgesics and pain management, Antimicrobials and anitinfectives, Cancer treatment, Biomaterials and implants, as well as Ayurvedic

[26] Source: Own illustration based on Bhatia *et al* (2018)

nanoformulations (Bhatia *et al*, 2018). In the field of biotechnology publications between 1999 and 2018, India has seen strong growth and accounted for 7.7% of global scholarly output in the period (Collins *et al*, 2021). A key weakness of the ecosystem might be seen in the rather small numbers of both CROs and CRAMOs, who "are crucial stakeholders in the development of therapeutics [and] also act as the interface between knowledge source and industry participants" (Bhatia *et al*, 2018: 144). CROs and CRAMOs are very important parts of the innovation ecosystem as they can provide access to R&D infrastructure and related and test facilities that a startup, an individual entrepreneur or academic institutions may lack. Availability and accessibility of CROs and CRAMOs is crucial for reducing "the time for transition of product from laboratory to market. However, the number of CROs and CRAMS involved with nanomedicine in India are limited even though they are required to bridge the gap in translational research" (Bhatia *et al*, 2018: 144). It has been also pointed that universally accepted or recognized quality and safety standards for value chain activities, such as material manufacturing, product development, and clinical testing for enhanced compatibility and interoperability were still under development as of 2018 (Bhatia *et al*, 2018).

A key player in this field is the Department of Biotechnology (DBT), which was established in 1986 and is the nodal ministry for 16 autonomous research institutions and 3 public sector undertakings (PSUs).[27] The DBT has initiated funding R&D in this area in 2007. So far, it has supported over 5,000 extramural R&D projects. According to its then-Chairperson, Renu Swarup (2020):

> "Over the last three decades, DBT has created a very strong research and translation ecosystem across the country and has built strong foundations, leveraging the strength of national and international partnerships. With more than 15,000 scientists and 800 institutes and laboratories supported, DBT supports nearly 10,000 biotechnology research fellows and students annually. World class state of the art infrastructure has been created, which through the DBT's SAHAJ scheme has now been made accessible to all researchers and startups to take research and innovation across the country. Skill Vigyan life science and biotechnology centers have helped build an employable skilled human resource base."

While initially exploratory projects were funded, the approach has now shifted to fund "application/translation oriented projects". A primary objective of this program is to address socially relevant issues in health, energy, agriculture and environment by advancing research and promoting innovation through applications of nanobiotechnology. As per DBT, major thrust areas include development of new therapeutics and targeted drug delivery vehicles, efficacy enhancement for existing drugs, diagnostics for early disease detection and imaging; design and development of smart-nanomaterial for medical applications, development of nanosensors for detection of chemicals and pathogens in food and crops etc.

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[27] Information for this section is drawn from the DBT's webpage on Nanobiotechnology (https://dbtindia.gov.in/schemes-programmes/research-development/nanobiotechnology), unless specified otherwise. The site was last updated on 17 Feb. 2022.

At present, the DBT is widening the scope of the program "by envisaging new programs on applications of nanobiotechnology [...] to uplift the agrarian economy, development of novel nanomaterials & small molecules based nanoprobes for Brain, Lungs, Liver, Ovarian, and other cutting edge technologies. Unmet needs for a larger societal perspective & Multidisciplinary regulatory science based program along with technology Demonstration programs would be undertaken. Department is committed to use the bed to bench side approach as a powerful tool in supporting the nanobiotechnology research and development projects".

Especially in the field of healthcare DBT sees the nanotechnology intervention having a promising role and potential to innovate new generation of diagnostic and therapeutic modalities for important diseases. Support is being provided to the nanobiotechnology research in the area of infectious & non-infectious diseases. The DBT has now also focused on oral health and dentistry and has invited project proposals on "Nanotechnology interventions in Dentistry and Bone diseases". The intention is to support innovative solutions related to dental diagnostics, prosthodontics, endodontics, conservative and aesthetic dentistry, periodontics in the field of dentistry as well as in infective, metabolic and neoplastic involvement of bone and bone tissue engineering in the field of orthopedics/bone disease.

Key institutions with affiliation to the DBT that are engaged in R&D in bionanotechnology in India are (Kumar, A. and Desai, 2013):[28]

- National Institute of Immunology, New Delhi
- National Centre for Cell Science, Pune (NCCS)
- Institute of Life Sciences, Bhubaneswar
- Rajiv Gandhi Centre for Biotechnology, Thiruvanthapuram
- Translational Health Science and Technology Institute, Gurugram

According to the DBT, 30 patents have been filed and 6 technologies for commercialization have been generated. Some other significant achievements of this program are as follows (also see, Appendix D):

- Generation of leads "in development of protein nanomedicine which is a Transferrin–conjugated Albumin Sorafenib Nano Particles (T-AbSorf) for treatment of CML, Liver & Renal tumor"
- Research on "self-fluorescent cell permeable glucose derived carbon Nanospheres as a brain targeting vehicle having implications in drug delivery and imaging for Alzheimer's disease, Multimodal contrast agent based on bio-mineral nanoparticles & Magnetic nanopropellers for cancer specific applications."

[28] Some more examples of institutions that conduct R&D in bionanotechnology without having a formal affiliation to the DBT can be found in Appendix C. A comprehensive list of selected examples of organizations & individuals that have been funded by the DBT in the space of bionanotechnology can be found in Appendix D. For an excellent overview of the nanomedicine landscape in India, including key players, relevant regulations and an overview of the output generated in the past, see Bhatia *et al* (2018).

- "A startup emerged from InStem Bangluru, which primarily focuses on the development of on-demand, bio-responsive deliverables to reduce pathologies associated with chronic inflammation. The product under development minimizes exposure to toxic pesticides through skin contact and inhalation, during the spraying of pesticides. This is of relevance to the farming community."
- "Release of the 'Guidelines for evaluation of Nanopharmaceuticals in India' jointly formulated by Department of Biotechnology, ICMR and CDSCO and 'Guidelines for evaluation of Nanobased Agri and Food Products in India' to push innovation and product development" (GOI-DBT, 2021: 16).

Furthermore, in 2012, the DBT established the Biotechnology Industry Research Assistance Council (BIRAC), which works as a non-profit PSU. It acts as an intermediary to promote industry-academia collaboration to enable biotech companies, especially start-ups and SMEs, to engage in strategic research and innovation and meet national needs. BIRAC is mandated to provide access to venture capital through targeted funding, technology transfer, IP management and handholding schemes that help biotech companies achieve innovative excellence and make them globally competitive.[29]

As of 2021, India had about 5000 biotech startups, whose number is expected to double by 2025. The ecosystem is, however, also faced with certain challenges. As per BIRAC (2021):

"While the infrastructure (both human resources and facilities) and the overall environment that facilitates entrepreneurship and innovation has improved significantly in the recent past, there still exists a gap between engagement of industry and academia for translating gains of academic research into products and processes for societal benefit."

India needs scaling up of the biotech innovation ecosystem to harness its full potential. Moreover, innovation pathway in this field involve long gestation period, which creates substantial pressure on start-ups. There is a general lack of private equity, especially in the funding space of INR 10-50 million, that is approx. €120,000 to €600,000 (BIRAC, 2021).

3.5 International partnerships

India also actively engages in international cooperation with several countries in this field. As Table 2 shows, the DBT has established cooperation mechanisms with a number of reputed institutions worldwide. The collaborations agreements cover both advanced and emerging economies. Thrust areas of cooperation is affordable healthcare, e.g. in cancer related research.

Table 2: International partnerships forged by the DBT[30]

[29] See, https://birac.nic.in/desc_new.php?id=89, last retrieved: 15 Mar. 2022.
[30] Source: Own compilation based on https://dbtindia.gov.in/scientificdecisionunits/international-cooperation-1, last retrieved: 15 Mar. 2022.

Country	Cooperation details
Australia	"The Department is collaborating with Australia's Department of Innovation, Industry, Science and Research (DIISR) since 2006. The Indo-Australian Biotechnology Fund supports Indian and Australian scientists, from both the public and private sectors, to collaborate on leading edge science and technology in order to contribute to the economic, social and environmental wellbeing of both countries. Under this collaboration joint call once a year is announced in the priority areas after mutual consent between the two departments. DIIS funds the Australian investigators and DBT funds the Indian Investigators of the project."
Brazil	"The objectives of the MoU are to broaden and deepen cooperation in Science & Technology in the field of Biotechnology."
Canada	"Department collaborates with the Indian Canada Centre for Innovative Multidisciplinary Partnerships to Accelerate Transformation and Sustainability (IC-IMPACTS), Canada International Science and Technology Partnerships, Canada (ISTP, Canada), Grand Challenges, Canada and NRC: PBI, Canada in all areas of Biotechnology."
Cuba	"The MoU is focused to (a) transparently broaden and deepen cooperation in Science & Technology in the field of Biotechnology and b) encourage industrial and basic R&D, related investment flows, bilaterally and/or regionally in the field of Biotechnology."
Denmark	"The goal of this Programme [2018-2020] is to encourage and facilitate cooperative activities between research institutions, universities, companies and other stakeholders in the respective national sciences and innovation systems of both countries."
European Union	"The Department collaborated with the European Union in all areas of biotechnology, and till date 33 projects have been funded."
Finland	An "MoU with Innovaatiorahoituskeskus Business Finland (Business Finland) to cooperate based on mutual interest with BIRAC, for funding and implementing ambitious industry-led innovative and transnational projects within the broad scope of research and innovation in Mission Innovation, Bio-future platforms, Environmental and energy applications of biotechnology, Business development of start-up and growth companies, Education technologies in life sciences."
Germany	"Department is partnering with German Federal Ministry of Education, Science Research and Technology (BMBF) and German Research Foundation (DFG) in areas of biotechnology."
Netherlands	"The Department is partnering with The Directorate General for Enterprises and Innovation, Ministry of Economic Affairs, Agriculture and Innovation, Government of Netherlands in the mutually agreed area of cooperation of Plant Sciences and related Biotechnology, Food & Nutrition, Medical Biotechnology."
Russia	"Department is collaborating with Russia under the four priority areas of 'Genomic & Proteomics Instrumentation' Nano-Devices; 'Bioenergy-Photosynthesis based only' and Bioreagents."
South Korea	"MoU signed between the Government of India and the Government of the Republic of Korea in the field of Biotechnology, Bio-economy, Science and Technology with the objective to expand and develop bilateral/ multilateral relations and cooperation in the field of Science and Technology and in the area of Biotechnology"
Spain	"Department collaborates with Centre for the Development of Industrial Technology (CDTI), Government of Spain to promote and fund market driven research and technology development as well as to encourage partnerships and business led R&D&I collaborative projects in the field of biotechnology."

Sweden	Agreement with the Swedish Governmental Agency for Innovation Systems (Vinnova). “The broad subject areas of cooperation under the Protocol shall be, but not limited to: Circular and bio-based economy, including biomaterials, Health and life sciences including biomedical devices and Start-ups, incubators, testbeds and bioclusters”.
United Kingdom	A “5-year bilateral collaborative research initiative with Cancer Research UK (CRUK) that will focus on affordability of cancer prevention and care, and the potential to make significant progress against cancer consequences. Both CRUK and the DBT will invest £5m (~47 Crores INR) each in this initiative. This initiative will bring together leading Indian and UK experts to identify a core set of research challenges under the theme ‘affordable approaches to cancer’” “Department also partners with Department for International Development (DFID); INNOVATE; British Council; Academy of Medical sciences (AMS); Cambridge University. It also collaborates with Biotechnology and Biological Sciences Research Council (BBSRC), Medical Research Council (MRC), Natural Environment Research Council (NERC), Economic and Social Research Council (ESRC) through Research Councils U.K. (RCUK) in all major areas of Biotechnology.”
United States of America	The DBT “has been implementing collaborative programmes with the National Institute of Health (NIH), since its inception. Major efforts have been implemented through the NIAID (National Institute of Allergy and Infectious Disease) and also through NEI (national Institute of Eye) and NCI (National Cancer Institute)-NIH.” “The Indo-US Vaccine Action Programme (VAP) is a bilateral programme between Department and National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), USA; which supports a broad spectrum of activities relating to new and improved vaccines. The programme is under implementation since 1987 and is recognized internationally and considered as a model bilateral programme in biomedical research.” “The Department has signed a Statement of Intent on Indo-US Collaboration on Expansion of Vision Research with the Department of Health & Human Services, Government of the United States of America, with the objective of translating research outcomes to develop potential interventions to reduce eye disease burden in India and the USA. The mandate of this collaboration is to strengthen research focusing on Diabetic Retinopathy, Genetics of Ophthalmic Diseases and Ocular Inflammation.” “The Department is collaborating with National Cancer Institute of AIIMS [India], and National Cancer Institute of NIH for cooperation on Cancer Research, Prevention, Control and Management The main aim of the collaboration is to promote and conduct high quality cancer research in order to strengthen the evidence base necessary for cancer prevention, treatment and management. As one of the action points emerging out of various discussions with the NCI, it is proposed to establish an International Collaborative Research Center (ICRC) at National Cancer Institute, AIIMS, New Delhi. The aim of this centre will be: Translational research in prevention and cure of India centric cancers like tobacco related cancers, carcinoma gall bladder and carcinoma cervix. Besides these cancers, the centre would also focus on common cancers like breast cancer, carcinoma lung and evolving trends in cancer diagnostics and treatment.”

Box 2 illustrates a particularly successful example of collaboration with Australia. The IITB-Monash Research Academy is though not exclusively focused on the area of biotechnology, but it regularly carries out such products through Ph.D. grants.

Box 2: Example of Indo-Australian cooperation: IITB-Monash Research Academy[31]

IITB-Monash Research Academy
The IITB-Monash Research Academy is an Australian-Indian research collaboration established in 2008 between the Indian Institute of Technology Bombay (IITB) and Monash University in Melbourne. The academy is focused on training doctoral students and takes "a solution-oriented approach to address major societal challenges". The academy offers up to 50 scholarship-funded PhD positions each year with a minimum one-year research stay in Australia. PhD students are supervised by both IITB and Monash University, with the involvement of industry partners on externally funded projects where appropriate. The program has so far conducted over 400 research projects in seven key research areas: Advanced Computational Engineering, Simulation and Manufacturing, Infrastructure Engineering, Clean Energy, Water, Nanotechnology, Biotechnology and Stem Cell Research, and Humanities and Social Sciences.
For example, in a project on "Nanoparticles for ophthalmic drug delivery", researchers at IIT Bombay have developed a formulation of biodegradable protein nanoparticles for a non-steroidal, anti-inflammatory drug. It is used to treat inflammatory and vasculopathic disorders of the posterior chamber of the eye, [and] the nanoparticles allow a sustained release of the drug over a prolonged period, [whereas] only 1-2% of conventional eye drops reach the deeper tissue of the eye. In another project, one of the co-authors of the present study worked on the development of a low-cost affinity biosensor for cardiac applications. The aim was to develop a low cost, robust, sensitive and instantaneous cardiac marker sensor based on affinity measurement with the piezo-resistive polymer cantilever platform (Tiwari, S., 2018).

4 Nanobiotechnology in Germany's Healthcare Sector

4.1 Brief socioeconomic profile

With an estimated GDP of $4.2 trillion in market prices in 2021, Germany is the fourth largest economy in the world after the USA, China and Japan. With a population of a little over 82.5 million at the end of 2016, Germany constitutes the largest economy in the European Union (EU) as well as in the Euro Area (EU-19) that currently encompasses 19 out the 28 member

[31] Source: Compiled from https://www.iitbmonash.org/, last retrieved: 15 Mar. 2022.

states of the EU. While accounting for a little over 16% of the EU population, Germany contributed more than 21% to the EU's GDP.

Germany is a highly innovative country, consistently ranking among the top-10 in the Global Innovation Index. Cumulatively, German enterprises and research institutions invest 3.13% of GDP in R&D activities, which translates to over €72 billion for in-house R&D activities. The overall annual expenditure on developing and launching new products, services and processes is estimated at €173 billion. Nearly 33,700 companies in Germany engage in R&D while close to 181,400 companies regularly launch new products and services in the market.[32]

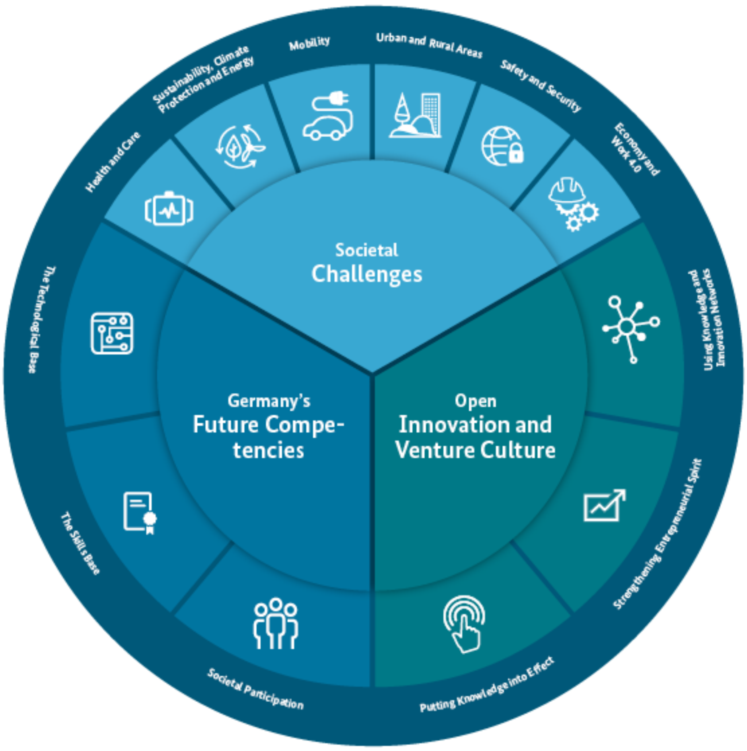

Figure 4: Thrust areas of the High-Tech Strategy 2025[33]

The country currently pursues a "High-Tech Strategy 2025", which [...] "encompasses a broad spectrum, including technological innovations, new business models and social innovations" and seeks to tackle the grand challenges, such as "Health and Care", "Sustainability, Climate Protection and Energy", "Mobility", "Urban and Rural Areas", "Safety and Security" and "Economy and work 4.0" (BMBF, 2021); see, Figure 4.

Furthermore, the German federal government has developed a National Research Strategy BioEconomy 2030, which aims at driving bio-based sustainable development within ecologically-permissible boundaries. The strategy states that "Germany will strengthen its role as a forerunner in the sustainable, circular bioeconomy, as well as in designing sustainable

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[32] See, https://www.bmwi.de/Redaktion/EN/Dossier/innovation-policy.html, last retrieved: 15 Mar. 2022.
[33] Source: https://www.hightech-strategie.de/hightech/en/home/home_node.html, last retrieved: 14 Mar. 2022.

technologies and developing the jobs of tomorrow. This is because biological knowledge and sustainable technologies are the pillars of a sustainable economic system. And by sustainably producing a raw material base within ecological limits, the Federal Government is contributing in particular to climate protection" (BMBF, 2021). The key objectives can be summarized as follows:[34]

1) "Develop bioeconomy solutions for the sustainability agenda
2) Recognize and harness the potential of the bioeconomy within ecological boundaries
3) Enhance and apply biological knowledge
4) Provide a sustainable raw material base for industry
5) Promote Germany as the leading location for innovation in the bioeconomy
6) Involve society in the bioeconomy and intensify national and international collaboration"

The objective of Health & Care is especially interesting, since Germany – apart from its pursuit of new technology frontiers and innovation leadership, is also confronted with a demographic challenge: the increasing average life expectancy has led to a growing share of the elderly in the population resulting in a growing expenditure for healthcare. According to the World Bank, per capita health expenditure in PPP terms has increased from about PPP$ 2700 in year 2000 to more than PPP$ 6700 in year 2019. Share of health expenditure in GDP has increased from 9.9% to 11.7% in these 20 years.[35] Nanobiotechnology with its potential benefits discussed in chapter 0 therefore seems to have an added benefit to the country.

4.2 Sectoral overview & growth prospects

Germany, as a leading industrialized nation with strong scientific base, became active in the field of nanotechnology and nanobiotechnology. A report of the federal government, published in 2013, showed that around 2300 institutions/enterprises were already active in the field of nanotechnology. While the largest engagement was in the field of nanomaterials (515 research organizations and 475 business enterprises), the field of nanobiotechnology was the fourth largest with 270 research organizations and 169 business enterprises. Health/Pharma sector was also the fourth largest application area having attracted 216 research institutions and 202 business enterprises. Only Chemicals, Mechanical Engineering and Service sectors were ahead of Health/Pharma, and fields such as Energy, Information and Communication Technology (ICT) or Optics (BMBF, 2014).

[34] See, https://www.bmbf.de/bmbf/en/research/energy-and-economy/bioeconomy/bioeconomy_node.html, last retrieved: 14 March 2022.
[35] See, https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?locations=DE, last retrieved: 14 Mar. 2022.

About eight years later, the landscape has apparently become more consolidated.[36] As of March 2022, the BMBF data shows that there are 1419 organizations and institutions active in the field of nanotechnology. In Health/Pharma sector, the largest application areas are Diagnostics and Medical Devices with engagement of 135 organizations each, followed by Therapeutics (93), Regenerative Medicine (56) and other (100).

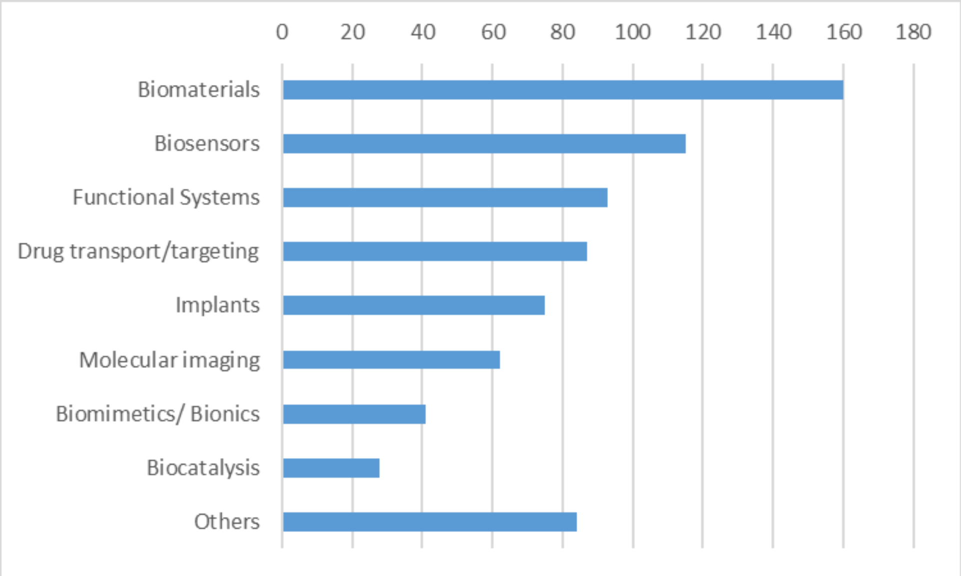

Figure 5: No. of institutions/organizations in different technology fields of nanobiotechnology in Germany[37]

As Figure 5 shows, biomaterials, biosensors, functional systems, drug transport/targeting and implants are the five most active technology fields in Germany's nanobiotechnology sector, which are followed by molecular imaging, biomimetics/bionics and biocatalysis.

Data from StatNano, which is not as comprehensive as that of the BMBF, but has more details, shows that around 277 companies in Germany are active in the field of nanotechnology and have commercialized 798 products by year-end 2021. Nanomedicine plays an important role in this domain, as 112 products of 35 companies belong to it. Only Construction (148 products from 61 companies) and Automotive (123 products from 46 companies) were ahead of Medicine in terms of the use of nanotechnologies.[38] Box 3 showcases the example of nandatec GmbH which is active in the space of bionanotechnology.

Box 3: Example of a bionanotechnology firm in North Germany[39]

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[36] All data related to the landscape of nano- and related technologies in 2022 is taken from the following website of the BMBF: https://www.werkstofftechnologien.de/service/kompetenzkarten/nanokarte-forschung-und-innovation-nano-map, last retrieved: 21 Mar. 2022.
[37] Source: Own illustration based on BMBF (2022) data.
[38] See, https://statnano.com/country/germany, last retrieved: 15 Mar. 2022. See Appendix B for a list of these companies and their products.
[39] Based on information on company webpage and Hamburg News (2020)

nandatec GmbH[40] "is a Nanobiotechnology company focusing on biochemical engineering, synthesis and surface modification of biocompatible nanoparticles for applications in the field of Life Science, particularly in Regenerative Medicine, Medical Technology, Biosensing and Clean Tech". It uses biocompatible nanoparticles to develop more environment friendly applications for the life science sector, among others. Company's products are stated to be biocompatible and biodegradable and are tested in animal-replacement models.

The company's employees use laboratories in Lübeck, Kiel, Flensburg and Hamburg, among other places, to conduct their research on state-of-the-art equipment. Its founder Dagmar Schneider has co-also founded a cooperation network, the Nano-FunDuS, to create and exploit synergies, which received a project funding from the Federal Ministry for Economic Affairs & Energy (BMWi).[41] The company is a member of various industry-specific networks, e.g. Life Science Nord, NanoMedNorth, NANOfutures Europe and Biopeople Denmark.

Fields of application of its nano-products include the life science sector, where the technology is used to develop sensors for rapid medical tests, or in the food industry. The product is reported to be theoretically even edible in lower concentrations, so it offers new application possibilities in food packaging.

Customers for the products are found in the chemical as well as the pharmaceutical industry, but also, for example, among sports boat sailors. The goal, according to Schneider, is to convince people to switch from toxic agents to a biocompatible product.

The strong role of nanotechnologies in the field of medicine corresponds to another study in the field of biotechnology. According to a recent annual report prepared by Boston Consulting Group (BCG) on behalf of VFA Bio, biosimilars tend to grow quickly in Germany after their market launch; reaching a substantial market share of up to 60% within the first year of their launch (Lücke *et al*, 2021). As per the same report, 25 newly approved biopharmaceuticals accounted for 45% of all new approvals in Germany. The report says that "Germany as a production site for biopharmaceuticals is characterized by both light and shadow": Germany is second only to the USA in terms of active biopharmaceutical substances with EU approval. However, Germany is only on fifth place in terms of production. The authors say that this is partly due to the prevailing tax framework (Lücke *et al*, 2021: 5). Furthermore, the report calls for utilizing the Corona pandemic "as an opportunity to reduce bureaucracy and specifically strengthen promising and innovative industries and technologies such as drug research, development and production, including medical biotechnology, in Germany".

[40] See, https://www.nandatec.com/, last retrieved: 8 Mar. 2022.
[41] See, https://tu-dresden.de/ing/maschinenwesen/int/forschung/bioverfahrenstechnik/bt_projekte/NanoFunDus?set_language=en, last retrieved: 8 Mar. 2022.

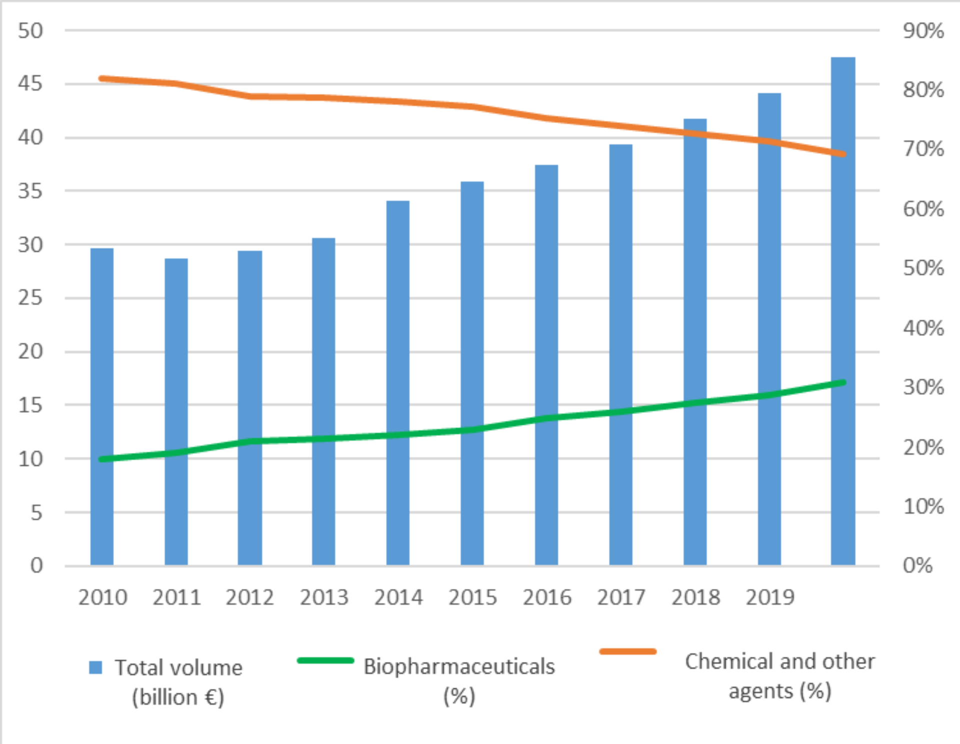

Figure 6: Expanding role of biopharmaceuticals in Germany (2010-2020)[42]

As Figure 6 shows the pharmaceuticals market has grown in the previous decade between 2010 and 2020 quite substantially. The total volume of the market grew with a compounded annual growth rate (CAGR) of 4.8% fro, €29.6 billion to €47.5 billion. The growth has, however, been propelled primarily by biopharmaceuticals. Their contribution to the total volume grew almost three-times, reaching in absolute terms the mark of €14.6 billion in 2020, staring from a base of €5.3 billion in 2010. In relative terms the share of biopharmaceuticals grew from 18% to nearly 31% in this period. The CAGR for biopharmaceuticals in this period stood at 10.6% as opposed to 3.1% for chemical & other agents.

The role of nanomedicine and nanobiotechnology can be expected to enhance further in future as is discussed in the following: Major diseases of the advanced economies are non-communicable diseases and generally concern cardiovascular ailments or cancer. For example, in 1998, "[...] circulatory diseases (including myocardial infarction) caused more than 500 000 deaths, or 58% of all deaths [and] more than 210 000 people died from cancer, representing 25% of all deaths in Germany" (Sawitowski, 2004). About 2 decades later, the situation has improved in terms of circulatory diseases as far as their relative share in all reported deaths is concerned. As per data of the Federal Statistical Office, circulatory diseases accounted for over 36% of all deaths in Germany (nearly 1 million) in 2020, while cancer accounted for close to 26% of all deaths.[43] There is clearly a continued need for early detection

[42] Source: own illustration based on various reports of VFA Bio, available at https://www.vfa-bio.de/vb-de/vb-presse/vb-publikationen, last retrieved: 8 Mar. 2022.

[43] See, https://www-genesis.destatis.de/genesis/online?operation=previous&levelindex=1&step=1&titel=Ergebnis&levelid=1647413801674, published: 16 March 2022, last retrieved: 16 March 2022.

and improved treatment of these and other diseases. Sawitowski (2004) pleads for a "local rather than systemic treatment". Local treatment is the basis of every implant used. For example, when treating diseased vessels with stents the implant is inserted very precisely into the stenotic area; the same holds true for seeds used to treat prostate cancer."

Turning to academic and research institutions it may be noted that several German universities have introduced courses in the field of nanobiotechnology and are engaged in R&D work. For example, an interdisciplinary research group "Nano-Opto-Fluidics Lab" at the Institute for Nanostructure and Solid State Physics (INF) of the University of Hamburg is "working on state of the art nanofabrication techniques, micro and nanofluidics, nano-optics, biosensing and plasmonics". The objective "is to develop a portable, integrated (a lab-on-a-chip) to study single (bio)molecules" with a strong focus on (bio)applications.[44] The Fraunhofer Center for Applied Nanotechnology (CAN) in Hamburg develops inorganic nanoparticle systems to create "solution strategies for new or improved products, especially in the fields of functional materials (displays, LED and lighting, solar and fuel cells), life science (diagnostic tools, biomarkers) and home and personal care (additives for cosmetic products, detergents and specialty polymers as formulation aids)".[45] In North Germany, universities in Kiel and Bremen too have research related to nanosciences. The BfR has been conducting nano safety research and risk communication for several decades.[46] The strength of the country lies in its technological expertise, advanced infrastructure, global networks and favourable market conditions. On the negative side, Germany also faces certain challenges, such as shortage of skilled professionals, high operational costs, and to some extent the negligence of opportunities in the field of nanobiotechnology/nanomedicine probably due to its industrial composition.

Overall speaking, the nanobiotechnology scene in Germany is advanced and continues to evolve dynamically, especially since the Corona crisis, which has been an eye opener for many; but there are also certain hurdles to overcome to fully exploit the potential of nanobiotechnology.

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[44] See, https://www.physik.uni-hamburg.de/en/inf/jg-fernandez-cuesta.html, last retrieved: 16 Mar. 2022.

[45] See, https://www.iap.fraunhofer.de/en/research/CAN.html, last retrieved: 16 Mar. 2022.

[46] Detailed information about the BfR's work on risk assessment of nanomaterials can be accessed here: https://www.bfr.bund.de/en/nanomaterials_research-10431.html, last retrieved: 5 Dec. 2021.

5 Scope for Indo-German Cooperation

The chapters above have shown that nanobiotechnology/bionanotechnology have a promising and still-largely-untapped potential, especially (but certainly not exclusively) in the healthcare sector. Nanomedicine could change the healthcare in future in very fundamental ways. As shown in chapter 2.3, the application of bionanotechnology offers many opportunities that are rooted in the global societal challenges and the resultant emerging trends.

India and Germany, both, have set ambitious programs to exploit the potential of bionanotechnology in Life Sciences and Healthcare, and it seems that are many potential areas of mutually beneficial collaboration by identifying synergies and complementarities. As discussed in the previous sections, application of bionanotechnology still faces challenges related to translational research, market acceptance, risk assessment etc. And as Singhal and Rogers (1989: 171) observed over three decades ago, “India has many ingredients for developing high-tech industry: political will, relatively low cost brainpower, low labor costs, good quality universities, R&D investment, and a large domestic market”.

Since then India has made many strides and is endowed with a well-performing national innovation system. As a recent study conducted on behalf of the BMBF concluded: “In recent years, India has become increasingly visible as a science nation and is now - at least quantitatively - on par with Germany. Particularly with regard to digital technologies and software, but also in the fields of chemistry, pharmaceuticals and biotechnology, India has developed into a relevant academic partner for Germany and Europe. If the development of recent years continues, India in the medium term could become the second most important scientific nation in Asia after China [...] its absolute technological outputs have meanwhile reached the level of medium-sized western economies such as Canada.” (Kroll *et al*, 2021: 17)

While Germany has proven technological capabilities, both countries have set up mechanisms of cooperation and India’s DBT has an established cooperation with the BMBF and German Research Foundation (DFG) in areas of biotechnology. The Indo-German Science and Technology Centre (IGSTC) has been active in promoting bilateral cooperation (see, Box 4) and can be mandated to further intensify the cooperation in the field of bionanotechnology. A possible orientation could be, for instance, the German-Israel partnership program, which is designed “to promote the interlinking of research, technology and business in both countries in order to create new business and exploitation models. It is primarily tailored to small and medium-sized enterprises and start-ups. It is also intended to supplement the existing funding programs for German-Israeli cooperation with the component of application-oriented research and utilization”. [47] Taking this program as a template, India and Germany could try to learn from each other, especially through the means interdisciplinary projects targeted at

[47] See, https://www.bmbf.de/bmbf/shareddocs/kurzmeldungen/de/deutsch-israelische-regierungs-narbeit-in-der-nanotechnologie.html, published: 16 Feb. 2016, last retrieved: 12 Mar. 2022.

development of new materials, processes, and standards for personalized medicine and other applications of nanomedicine, and in other areas of nanobiotechnology.

Box 4: IGSTC as a promoter of Indo-German cooperation

Indo-German Science and Technology Centre (IGSTC) was established in 2006 through an intergovernmental initiative of the German Federal Ministry of Education and Research (BMBF) and the India's DST. It aims to "strengthen Indo-German R&D networking through substantive interactions between government, academia/research systems and industry to promote innovation for the economic and social development of both countries". In 2015, the cooperation was extended "to 2022 and beyond" and the annual funding volume was doubled to €8 million.

The flagship of the IGSTC is the 2+2 program, which involves one academic and one industrial partner each from both countries. It supports various areas of national priority for India and Germany. Funding is provided in the form of grants of up to INR 23 million per project from the Indian side and up to €450,000 from the German side, for a period of up to three years. While industrial partners are expected to contribute 50% of the eligible costs, academic and research institutions receive 100% of the eligible costs as a non-refundable grant.

In FY 2018-19, IGSTC had 22 ongoing projects with a funding of €15 million in this mode in various areas of common interest, e.g. sustainable energy, advanced manufacturing, biomedical devices and biotechnology, nanotechnology and water and wastewater technologies. IGSTC, thus, enables substantial interaction between the two countries. The ongoing projects in FY 2018-19 involved 88 academic and industrial organizations, and 500 scientists, researchers and engineers from both countries. In addition, the IGSTC-CONNECT Plus program was launched in collaboration with the Humboldt Foundation to support short-term research stays in India and Germany.

A future cooperation could be built around three core components, as depicted in Figure 7 and elaborated in the following:

1. Identify avenues of collaboration

Both countries should identify promising areas of cooperation that build on the strengths of their respective innovation ecosystems in the field of bionanotechnology and that can provide complementary strengths to compensate their weaknesses. For example, as discussed in section 3.4, the bionanotechnology sector in India is strong in university research, there is a lot of government support and public funding for people-centric innovations. A key thrust of the Indian government is create high-quality, affordable solutions for advances in Life Sciences. There is a strong match in this regard with the innovation strategy (as formulated by the High-Tech Strategy 2025) of the German government, who is very much interested in social inclusion and SDGs. This is a possible field of cooperation.

Another potential area of cooperation could be in collaborating in the development of common standards so that technologies developed in one country can be used seamlessly in the other due to interface compatibility, interoperability and regulatory compliance. For this, risk assessment and mitigation also seems to be a promising area of collaboration.

Exchange of students, researchers and university faculty, development of joint courses and initiating of common research projects would be one more possible avenue of collaboration. As Table 2 shows, India has forged some very promising and specific partnerships with international partners. It would make sense, if Germany and India can also set up some specific and ambitious mechanisms of cooperation in this field.

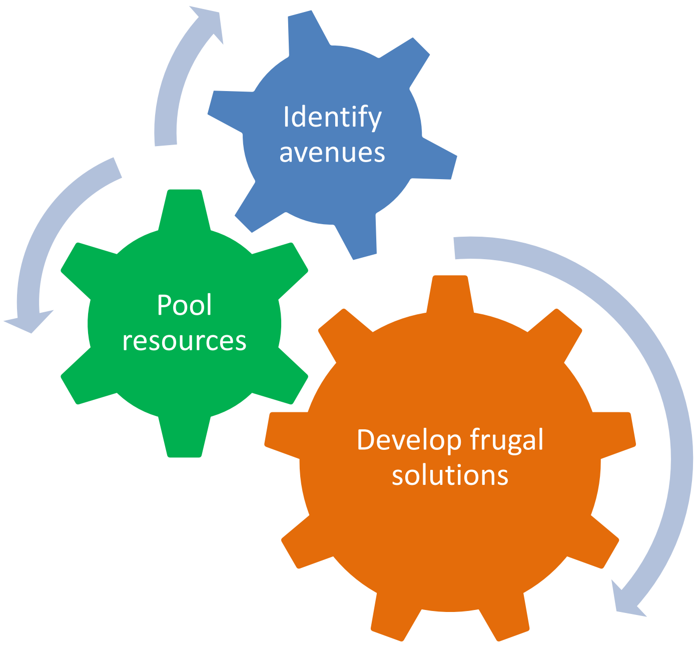

Figure 7: A framework for bilateral cooperation in the field of bionanotechnology

2. Pool resources

The two countries should explore options to create a pool of shared scientific, infrastructural and knowledge resources. This would not only reduce R&D costs, which is not only an imperative for developing affordable solutions, but which also intensifies interaction and knowledge exchange, and inter alia results in creation of new knowledge.

India still have less CRO and CRAMO facilities that are crucial for agile and cost-effective projects. It should be explored if German companies or other research institutions can offer these services either from within Germany, where feasible, or open their own subsidiaries in India. Vice versa, Indian companies can look at offshore models of setting up research facilities in Germany and/or offer services from within India to reduce R&D costs in general. India has also emerged as a leading center for startup activity in the recent years and engagement with startups, for example through venture capital, R&D collaboration or distribution partnership etc. could enable mutual advantage for both countries.

Develop frugal solutions

Indo-German collaboration can benefit by targeting creation of solutions based on the principles of frugal innovation, where frugal innovations “refer to those innovative products, services, processes, technologies or business models that aim at to high affordability, high target-specificity and the most effective resource utilization. Modular architecture of the solution allows product differentiation to maximize the fit to individual customer aspirations while minimizing the use of material and financial resources in the entire value chain. While complying with all relevant regulatory norms in the target market, frugal innovations may disrupt prevailing industry standards” (Tiwari, R., 2021: 272).

Studies suggest that frugal solutions are increasingly required – globally – and match with the stated objectives of both governments for achieving high affordability of nanobiotechnology products. India is widely considered as a “lead market” for frugal innovation and German firms can benefit from developing market-specific solutions taking into consideration the given geographic and socio-economic factors. Collaborative efforts to develop frugal solutions can lead to highly promising products that can be utilized globally.

6 Concluding summary

This study set out with the objective of exploring and identifying the large-scale and yet-untapped opportunities for Indo-German bilateral collaboration in the area of bionanotechnology with a special focus on healthcare. The investigation has shown a strong potential for a fruitful and promising cooperation, which can serve both nations and the world at large, profitably.

India and Germany both have made substantial technological advancement in this field and are endowed with a thriving research and innovation ecosystem. Germany has a specialization in biomaterials, biosensors, functional systems, drug transport/targeting and implants and a strong focus can be observed in the application areas of diagnostics, medical devices, therapeutics and regenerative medicine. These areas have a large overlap with India's thrust areas of research, which, however, also faces the challenge of insufficient academic/industry collaboration. A bilateral cooperation between India and Germany can be highly beneficial as the complementary strengths of the respective ecosystems can be leveraged for ensuring translational research, developing common regulatory/safety standards to mitigate risks and enhance public acceptance, better utilization of resources & infrastructure, and creation of cutting-edge knowledge through joint research and exchange programs for researchers, scientists, students, startups and other entrepreneurs to intensify targeted interaction.

The key to this cooperation lies in a framework that builds upon a paradigm of identifying cooperation avenues, pooling resources and developing frugal solutions based on the principles of "affordable excellence", where affordability is not merely a monetary consideration but also includes societal and environmental aspects. Technological advances that are possible with bionanotechnology (or with nanobiotechnology) in the field of Life Sciences hold an unmatched potential for a better, efficient and affordable healthcare. They, therefore, are critically important for the long-term societal welfare. The relevant stakeholders in both countries need to leverage their complementary strengths to engage in productive, translational research, develop common regulatory and safety standards and foster knowledge exchange.

This partnership is promising not only for both countries but also for the humanity at large.

APPENDIX A: EXAMPLES OF GERMAN UNIVERSITIES WITH ACADEMIC/RESEARCH PROGRAMS ON NANOBIOTECHNOLOGY

(Source: own compilation)

Institution	Example of activities pursued in this field
University of Hamburg	B. Sc. And M. Sc. Degree program in Nanoscience of Science and Collaborative Research “Nanosciences form one of the largest research foci at the University of Hamburg and are also among the most important research centers in an international comparison. Nanosciences deal with the production, investigation and application of functional structures and dimensions below about 100 nanometers (one nanometer corresponds to one millionth of a millimeter). In these size ranges, the properties of nanomaterials lead to innovative applications, e.g. in the fields of health, mobility and energy. The interdisciplinary bachelor's program is jointly organized by the departments of chemistry, computer science and physics.”
Fraunhofer Center for Applied Nanotechnology (CAN), Hamburg	“At the Fraunhofer Center for Applied Nanotechnology CAN in Hamburg, inorganic nanoparticle systems are being developed. We transfer research results into solution strategies for new or improved products, especially in the fields of functional materials (displays, LED and lighting, solar and fuel cells), life science (diagnostic tools, biomarkers) and home and personal care (additives for cosmetic products, detergents and specialty polymers as formulation aids).”
Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute, Jena	Collaborative Research “In numerous individual projects and coordinated collaborative projects, we are gaining new insights into the biosynthesis and function of natural products. We use this knowledge to develop innovative active ingredients for the diagnosis and therapy of diseases, including new anti-infectives. By integrating the research results and the models derived from them, we contribute to the development of a systems

	biology of infection. All units of Leibniz-HKI work together towards these goals.”
Center for Nanoscience at Ludwig-Maximilians-University Munich	Collaborative Research “The Center for NanoScience (CeNS) was founded in 1998 at the Ludwig-Maximilians-University (LMU) Munich. The mission of CeNS is to promote and coordinate interdisciplinary research in the field of nanoscience in the Munich area. CeNS is an association of junior and senior scientists from basic research and industry and is conceived as a network, joining people from various institutions (LMU, TU Munich, University of Augsburg and others)”
Brandenburg University of Technology, Cottbus - Senftenberg	“The working group has various commercial and self-made measuring devices at its disposal for effective development of biosensors and characterization of sensor surfaces.”
Johannes Guttenberg University, Mainz	“The research focuses on noble metal nanoparticles as molecular sensors for single bio-molecules, plasmonic particles for biomedical diagnostics, and metal-semiconductor hybrid nanoparticles for photocatalysis.”
University Bielefeld	M. Sc. Nanotechnology “The concentration of research in the field of nanosciences has already been taken into account in teaching in the bachelor's phase. The range of courses is to be supplemented by an in-depth offer in an independent master's program in nanosciences, research-oriented but with a strong application focus.”
Chemnitz University of Technology	“The University offers a 4-semester international master's programme in Micro and Nano Systems. The programme provides world-class, future-oriented education in design, manufacturing, characterization and integration of miniaturized components into engineering systems.”
Leibniz University Hannover	M. Sc. Nanotechnology “The interdisciplinary master degree courses provide extensive training in the field of nanotechnology. The Faculties of Electrical Engineering and Computer Science, Mechanical Engineering, Mathematics and

	Physics, and Natural Sciences have combined forces to offer this joint programme.”
Munich University of Applied Sciences	M. Sc. Micro- and Nanotechnology “This internationally recognized Master of Science (M. Sc.) course of study offers students of the natural sciences an advanced degree coupled with practical experience. The Course of Study may be completed in three semesters of full-time study or over a longer period of time for students whose professions only permit part-time study.”
Saarland University	M. Sc. Microtechnology and Nanostructures “The interdisciplinary course of study in microtechnology and nanostructures combines the fundamentals of physics with engineering sciences with a thematic focus on miniaturization. Special importance is attached to the interdisciplinary system idea.”
Technical University Ilmenau	Master in Micro- and Nanotechnologies “The aim of the program is to provide the scientific and technological basis for the creation of micro- and nanostructures and to enable students within the field of study to drive future developments in micro- and nanotechnologies and nanotechnical systems.”
Technical University of Dresden	M. Sc. Nanobiophysics “The 2-year master program aims to teach students the fundamentals in biophysics and bio-nanotechnology with a twofold aim: to use nanotechnological approaches to better characterize and understand complex molecular machines such as biomolecules, but also to harness these molecules in technological systems or use them as templates or model systems for a bottom-up nanotechnology.”
University Duisburg Essen	M. Sc. NanoEngineering “The Master's program consists of two specializations, nanoprocess technology and nano(opto)electronics. Both directions have some courses in common, in which mainly extended basics are worked out.”

University Erlangen-Nürnberg	M. Sc. Nanotechnology “This new course of study adds an important field to the existing opportunities for students in the natural sciences and engineering. Nanoscience & Technology is a course of study that lies between the natural sciences and engineering, i.e. a good basic education in natural science subjects is necessary in order to be able to develop new technological applications.”
University of Kassel	“In the Center for Interdisciplinary Nanostructure Science and Technology (CINSaT) a main focus is the research interdisciplinarity of nanotechnology. Due to the extension of departments beyond biology, chemistry and physics the scientific center of the Kassel university requests and promotes the cooperation of miscellaneous working groups. Due to the contribution of the special expertises of the groups specific novel project ideas are developed to fabricate, analyze and characterize nanostructures and are implemented into new applications.” CINSaT also offers the interdisciplinary Bachelor & Master study program nanostructure sciences.
University of Würzburg	M.Sc. hon. Nanostructure Technology “As a research-oriented and time-compressed study program of the Faculty of Physics and Astronomy of the Julius-Maximilians-University of Würzburg, the study program FOKUS Physics Nanostructure Technology is offered within the framework of the Elite Network Bavaria (ENB) with the degree Master of Science with Honors. The Master of Science degree program prepares students for scientific activities in research and development in the field of nanoscience.”
	M. Sc. Nanostructure Technology “The Master of Science program prepares students for scientific activities in the field of nanostructure technology. It also prepares students for a doctorate (Dr. rer. nat. or Dr.-Ing.). The aim of the training is to provide students with in-depth knowledge of scientific work in research and application of nanosciences and its content-related fundamentals”

Appendix B: Examples of Indian Universities with Academic/Research Programs on Bionanotechnology

(Source: own compilation based on https://statnano.com/country/germany, last retrieved: 15 March 2022)

S. No.	Name of Company	Product	Application (Properties)
1.	CTC Nanotechnology GmbH	NANOIDENT® PERMADIS GEL	Hand Sanitizer(Anti-bacterial Activity, Disinfection, Anti-Germ)
2.	ApaCare	Liquid antibacterial tooth and mouth balm	Dentistry (Bacteria removal, Teeth Protection, Teeth remineralization)
		Apacare Remineralising Toothpaste	
		Apacare Polish	
3.	Particular GmbH	Gold Nanoparticles	Biomedical (Optical absorption)
4.	Proidee	Uvex Variomatic sunglasses	Eye Protection (UV Protection, Anti-fog, Lightweight, Easy-to-clean)
5.	Nano-Care Deutschland AG	Liquid Guard	Coronavirus (Self-sterilizing, Anti-microbial activity, Anti-fungal Activity, Water resistance, Antiodor, Mold Resistant, Antiviral)
6.	Vileda	Nano Tech micro	Wipes (Anti-bacterial Activity, Germs removal)
7.	Hobutec GmbH	Eyeglasses fit	Eyeglass (Anti-fog, Anti-static, Biodegradability, Dirt resistance)
8.	ARTOSS GmbH	NanoBone SBX Putty	Surgery, Formation of strong bones, Osseous defects, Defects resulting from traumatic injury to bone (Biodegradable, Porous)
		NanoBone QD	Formation of strong bones (Hydrophilic, Porous)
9.	MagForce AG	NanoTherm®	Cancer therapies,Tumors (Anticancer Drug)

10.	Percenta Nanotechnology	Antibacterial Nano Coating for Plastic	Plastics (Anti-bacterial Activity, Self-cleaning, UV Protection, Hydrophobic, Dirt resistance, Transparent, Anti-dust)
11.	Forschungszentrum Jülich	Nano-Gold at the Bio-Interface	Biomedical (Gold nanoparticles solution)
12.	B. Braun Melsungen AG	Contiplex® S Ultra	Nerve stimulation, Ultrasound stimulation (Microneedles)
13.	aap Implantate AG	LOQTEQ® Anatomical Plating System	Locking screw fixation, Fracture treatment, Anatomical fit (Corrosion resistance, Antibacterial, Biocompatibility, Anatomical reduction, Permanent retention, Fractures stabilization)
14.	Aeterna Zentaris	Apifiny®	Medicine, Prostate cancer blood test
15.	NanoFocus AG	µsurf implant	Prosthesis and Orthopedy
16.	Panasonic Healthcare Co., Ltd	NANOZR milling blank	Dentistry (Mechanical Resistance, Thermal stability, Toughness, Bio-compatibility)
17.	Beiersdorf AG	Antibacterial Waterproof Plaster	Wound dressing (Silver Nanoparticles)
18.	TEXAMED® GmbH	PADYCARE® textiles	Atopic Eczema Textile (Nanosilver-coated textiles was developed especially for Neurodermatitis)
19.	Fresenius Kabi	DIPRIVAN®	Anesthetic
20.	Bayer HealthCare Pharmaceuticals Inc.	Feridex I.V.®	Contrast Agent

APPENDIX C: EXAMPLES OF INDIAN UNIVERSITIES WITH ACADEMIC/RESEARCH PROGRAMS ON BIONANOTECHNOLOGY

(Source: own compilation)

S. No.	Name of Institution	Overview
1.	Centre for Nano Science and Engineering (CeNSE), Indian Institute of Science Bangalore, Karnataka	Master and Ph. D. Program The Centre for Nano Science and Engineering was established in 2010 to pursue interdisciplinary research across several disciplines with a focus on nanoscale systems. Current research topics include, but are not limited to nanoelectronics, MEMS/NEMS, nanomaterials and devices, photonics, nano-biotechnology, solar cells and computational nano-engineering.
2.	Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR) Bangalore, Karnataka	Master and Ph. D. Program Jawaharlal Nehru Centre for Advanced Scientific Research is a multidisciplinary research institute. Our mandate is to pursue and promote world-class research and training at the frontiers of Science and Engineering covering broad areas ranging from Materials to Genetics. The Centre is an autonomous institution under Department of Science and Technology, Govt. of India and a deemed to be university.
3.	Institute of Nano Science and Technology (INST) Mohali, Punjab	Ph. D. Program Institute of Nano Science and Technology, an autonomous institution of the Department of Science and Technology (DST), Government of India, has been established under the umbrella of NANO MISSION, initiated by DST to boost research and development in the field of Nanoscience and Nanotechnology in India.
4.	Centre for Research in Nanotechnology & Science (CRNTS), Indian Institute of Technology Bombay Mumbai, Maharashtra	Ph.D. Program Centre for Research in Nanotechnology & Science (CRNTS) has been established by the support from Department of Science & Technology (DST), Govt. of India. At IIT Bombay, over 45 faculty members from 9 different departments/schools are working together in the broad areas of Nanotechnology, with support from various government agencies are private industries.

5.	Centre for Nanotechnology Indian Institute of Technology Guwahati Guwahati, Assam	Ph. D. Program "Established in the year 2004 Centre for Nanotechnology, IITG possesses a vision to foster the development of research and education in the multi-disciplinary area of Nanotechnology at IIT Guwahati, to develop human resources gifted with leading-edge competitive advantages in the multi-disciplinary area of Nanotechnology required for meeting the future challenges, to augment academic partnerships with industry in the area of Nanotechnology."
6.	Centre for Nanotechnology Research (CNR), Vellore Institute of Technology Vellore, Tamilnadu	Master and Research Program “The Centre for Nanotechnology Research (CNR) at VIT, Vellore was established in June 2008 to support Academic and Research Programs in Nanotechnology. The major focus of the centre is on printed and flexible devices towards research areas of national priorities such as energy, sensors and healthcare. The centre is equipped with the state of the art research equipment in nanomaterials synthesis, characterization and simulation tools. CNR undertakes consultancy on nanomaterials characterization and provides a requisite technical support to Academic Institutes and Industry.”
7.	Amity Institute of Nanotechnology Noida, Uttar Pradesh	Bachelor and Master level Program “The programme at the Amity Institute of Nanotechnology comprises of conceptual knowledge of nanoscience and nanotechnology, including preparation of nanomaterials, their characterization and applications.”
8	Centre for Nanoscience and Nanotechnology, Jamia Millia Islamia University New Delhi	Master and Research Program “The mission of this Centre is to promote forefront basic and applied research in the fields of Nanoscience and Nanotechnology, with potential applications towards fulfilling national strategic needs. The main research focus of the Centre includes Nano-fabrication & Nano-device, Nano-materials & Nano-structures, Nano-biotechnology & Nano-medicine, Nano-structure characterization & measurements.”

9	SRM University Chennai, Tamilnadu	Bachelor and Master level Program The program imparts several courses in Material Science, Thermodynamics, Mathematical physics, Quantum Physics, Nanochemistry initially. These fields cover a spectrum ranging from medicine (drug delivery) and catalysis to surface/bulk chemistry and controlling even at the atomic/molecular scale to quantum computing.

APPENDIX D: SELECT EXAMPLES OF FUNDED BIONANOTECHNOLOGY PROJECTS IN INDIA

(Organizations/Individuals supported by BIRAC in healthcare sector under different programs)

(Source: own compilation based on https://birac.nic.in/desc_new.php?id=145, last retrieved: 15 March 2022)

S. No.	Entity/Place	Project
1	Actorius Innovations and Research (Pune)	Detection of Circulating Tumor Cells by Multifunctional Highly Dispersible Polymeric-Magneto-Antibody Nanosystem
2	AIIMS - All India Institute of Medical Sciences (New Delhi)	Minimally invasive nano enabled targeted technology for Sentinel Lymph Node SLN detection
3	Aodh Lifesciences (Hyderabad)	Intravascular Oxygen filled Nanobubbles for attenuation of Critical Care Hypoxia.
4	Biopraxis Private Limited (Aurangabad)	To demonstrate POC for a novel, Nano-conjugate based dialysis cartridge system that reduces blood urea which can be appended to existing dialysis machines resulting in reduction of patient dialysis duration from 4 hours to 1 hour.
5	Bioroot Exploration India (Thiruvanathapuram)	Nano-lipid emulsion for diagnostic imaging
6	CSIR - Institute of Microbial Technology (Chandigarh)	Development of potential anti-cancer biotherapeutic bi-specific nanobody
7	Dr. Vandita Kakkar (Chandigarh)	Proof of Concept Studies on Combinatorial Novel Nanolipid Hybrid of White Curcumin and Tacrolimus for Dermatitis
8	Dr. Rupesh Chaturvedi (New Delhi)	Bio-engineered mesoporous dialysis nano-beads for the specific removal of excess body toxins, water and ions from kidney failure patients
9	Exocan Healthcare Technologies (Pune)	A nano formulation of cisplatin as advanced drug delivery system
10	Hitech Formulations (Chandigarh)	Lipidic nanocarriers as an innovative technology for topical fungal infections, resistance and recurrence
11	Imgenex India (Bhubaneswar)	Nanotechnology based delivery of peptide inhibitors for the treatment of Osteoporosis.

12	IISER - Indian Institute of Science Education and Research (Pune)	Electro spun Nanofibre based Multi-stimuli Responsive Transdermal B12 Delivery Patch
13	ICGEB - International Center of Genetic Engineering and Biotechnology (New Delhi)	Development of dipeptide based targeted nanoformulation for breast cancer.
14	ITrace Nanotech (Secunderabad)	Advanced Active Transdermal Drug Delivery for Migraine Management
15	Jupiter Bioscience (Bidar)	Development, optimization and characterization of ligand RGD peptides targeted nano constructs encapsulating anticancer chemotherapeutic agents for effective treatment of lung cancer Gemcitabine and stabilization of lypophilized or spray dried formulation for direct local delivery or by injection through systemic circulation.
16	Lifecare Innovations (Gurugram)	Production of poly (lactide-co-glycolide) nanoparticles (PLG-NP) and poly (lactide-co-glycolide) nanoparticles encapsulating antitubercular drugs (rifampicin, isoniazid and pyrazinamide- PLG-NP-ATDs) in GMP facilities
17	Losjovenes Clinilogic (Bhubaneswar)	Matricaria chamomilla L. Chamomile nanospheres in the treatment of Skin Hyperpigmentation- a novel approach with stem cell extracts
18	Luxmatrainnovations (Ernakulam)	Engineered nano-immuno platform for Cancer Immunotherpay Nano-Biomineral Theranostic Agent for Image Guided RF Hyperthermia of Liver Tumor
19	Module Innovations (Pune)	A simple platform based novel,rapid and color changing one-time and reusable nanofiber strips for selective detection of Enterohaemorrhagic Escherichia coli (EHEC)O157:H7
20	Nanoclean Global (New Delhi)	Nano-Respiratory Nasal Filter
21	NanoSniff Technologies (Mumbai)	Development of a prototype instrument (sensor & detection electronics) to detect Heart Fatty Acid Binding Protein (hFAbP) Rapid Detection of Acute Myocardial Infarction by sensing Cardiac Markers using Micro Cantilever Technology

22	Nurture Earth Research and Development (Aurangabad)	Testing the feasibility of Nano magnetic disc based ablation of Cancer cells in vitro
23	Oniosome healthcare, (Mohali)	Bleomycin sulphate bearing nanostructured lipid particles for targeting brain cancer. Development and validation of Nanofibrous Ocular Patch Pre-clinical studies of Bleomycin Sulphate bearing Nanostructured Lipid Particles for Targeting Brain Cancer
24	Partima Solanki (New Delhi)	Towards nanomaterials-based biosensor device for measuring of 25-hydroxy Vitamin D
25	Piscium Health Sciences (Navi Mumbai)	Nano Engineered Dental Burs for superior finesse, cavosurface integrity, efficiency and longer life Nano-engineered dental burs with better durability, efficiency, heat conduction, and reduced vibrations
26	Primary Healthtech (New Delhi)	Nanotechnology based affordable, portable and easy to use multi diagnostic point-of-care device for Kidney, Liver, Pancreas, and Thyroid disorders
27	Purius Nanosystems (Chennai)	Development Of A Biosensor Based Point-Of-Care Nucleic Acid Testing System
28	Rasayani Biologics (Pune)	Evaluation of Platinum Nano Particles for the Treatment of Hormone Refractory Prostate Cancer.
29	Relisys Medical Devices (Hyderadad)	Manufacture and clinical evaluation of Non polymeric Nanocarbon porous matrix Drug Eluting Stent DES.
30	Robust Herbals (Bangalore)	Development of Long Circulating Biodegradable Nanoparticle MRI Contrast Agents Based on Hydroxypropyl-beta-Cyclodextrin
31	Saveer Biotech (New Delhi)	Commercial Scale Production of Nanopesticides and Nanofungicides for Indian Agro-industry
32	SIAMAF Healthcare (Bangalore)	Pulse Induction Magnetic Nanoparticle Detector for Lymph Node Mapping
33	Sita Logics (Hyderabad)	Biomimetic Bone Substitutes: A proof of concept prototype for synthetic bone substitute consisting of a nano composite of Demineralised matrix and hydroxyapatite.
34	Tata Chemicals (Pune)	Inorganic and polymer nano-composites for micronutrient & pesticide delivery: Boosting crop health and yield.

35	V.B. Medicare (Hosur)	Development and characterization of lipid carrier based nanogel formulation for 5Fluorouracil
36	Vegrandis Therpautics (Hyderabad)	Delivery and retention of Irinotecan loaded magnetic nanoparticles for treatment of brain tumors.
37	VNIR Biotechnologies (Bangalore)	Development and validation of nanoparticle based high fidelity cell-free-DNA extraction kits for cancer to prenatal diagnostics
38	Weinnovate Biosolutions (Nagpur)	A novel organic and inorganic nano-formulation for rapid wound healing and control of infection
39	Windlas Biotech (Dehradun)	Enhancement of oral bioavailability of poorly water soluble drugs using NanoCrySP* technology. *A patented nanocrystalline solid dispersion (NSD) technology platform developed at NIPER, S.A.S. Nagar. Clinical evaluation of formulations based on NanoCrySP technology Programme -BIPP

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Federal Ministry for Economic Affairs and Energy (BMWi) www.bmwi.de	**Department of Science & Technology (DST)** New Delhi, India https://dst.gov.in/
VFA BIO https://www.vfa-bio.de/	**Council of Scientific & Industrial Research (CSIR)** New Delhi, India https://www.csir.res.in/
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