Supporting long duration R&D programs to avoid time compression diseconomies

By Rishikesha T. Krishnan & N. Dayasindhu| May 27, 2021

The first Covid-19 vaccine came in record time but it's easy to forget the decades of research into mRNA, which underpins the Pfizer-BioNTech vaccine

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The Covid-19 pandemic has brought the importance of R&D to the forefront in India. Our R&D teams have worked hard to develop test kits, vaccines and ventilators to help us manage the pandemic. Many of these were developed in very short timeframes. But, complex technologies today often involve “R&D to product lifecycles” that work on a decadal timescale. Often this decadal timescale cannot be shortened and any attempts may lead to ineffective and inefficient results resulting is what researchers in strategy call “time compression diseconomies” of R&D.

This implies that India has to strengthen its capabilities to effectively manage long-duration R&D programs. This involves increasing the collaboration among diverse R&D teams across organizations, modernizing the infrastructure required for commercially translating R&D, and developing models of funding that support R&D across various phases in the lifecycle.

RSS**How does the R&D to product lifecycle play out in the context of complex technologies?**

On March 17, 2020, Pfizer and BioNTech agreed to co-develop a messenger RNA (mRNA) based coronavirus vaccine aimed at preventing Covid-19 infection. mRNA is a molecule that carries genetic code from DNA in a cell's nucleus to ribosomes where the cell makes proteins. Proteins would never get made without mRNA. BioNTech contributed mRNA vaccine candidates while Pfizer's contribution was its leading global vaccine clinical research and development, regulatory, manufacturing, and distribution infrastructure capabilities.

On November 9, 2020, Pfizer and BioNTech announced that the first set of results from the Phase 3 trial provided the initial evidence of their vaccine's ability to prevent Covid-19. On December 2, 2020, UK's Medicines & Healthcare Products Regulatory Agency (MHRA) granted a temporary authorisation for emergency use for the vaccine. On December 11, 2020, the US Food and Drug Administration (FDA) followed suit.

While it might appear that it took just nine months for the development of this vaccine, what is overlooked is the decades of arduous research and development (R&D) that has gone into making this vaccine available in such quick time once Covid-19 hit us. For starters, the foundation of this collaboration was built on an R&D collaboration that Pfizer and BioNTech entered in 2018 to develop mRNA-based vaccines for prevention of influenza—caused by a virus similar to the SARS-CoV-2.

The backstory of mRNA vaccines goes back even further. It was in the 1960s that Sydney Brenner at the University of Cambridge identified mRNA. In the early experiments where lab synthesized mRNA molecules were introduced in the human cells, our immune system often destroyed them. It was only in 2005 that Katalin Kariko and Drew Weissman at the University of Pennsylvania, showed how to introduce a mRNA molecule into human cells without being destroyed by our immune system. Kariko and Weissman licensed their technology to BioNTech, where Kariko is a Senior Vice President since 2013. BioNTech was founded by the husband-and-wife team of clinicians and cancer researchers Ugur Sahin and Ozlem Tureci.

BioNTech's objective from its founding in 2008 was to develop innovative therapies that will stimulate the immune system to fight cancerous cells. It soon became a leader leveraging mRNA technologies. Clearly, the start of the R&D for an mRNA vaccine goes back to 2005 at least—fifteen years before the Pfizer BioNTech COVID-19 vaccine was approved. If we want to be more conservative, it has taken five decades since the identification of mRNA to productize a mRNA vaccine.

The important lesson for us is that it often takes decades for a technology to mature from R&D to a product. We often make the error of considering only the last mile effort of translation from lab prototype to a popular product, and tend to ignore the effort of the entire "R&D to product lifecycle" that often spans multiple research teams and organisations. This former interpretation leads us to an inference that we can compress R&D effort especially in times of a crisis. However, research from economics and business strategy has shown us that "time compression diseconomies" in R&D are for real. What this implies is that maintaining a rate of R&D effort and spending over an extended time interval produces a larger increment to the level of R&D know-how than say compressing it by carrying out twice this rate of R&D effort and spending over half the time interval. Economists since the 1960s have shown that rapid burst R&D programs, are generally less effective than R&D programs where expenditures are lower but spread out over a longer period of time.

There is a common perception that this phenomenon of decadal R&D lifecycles is only true for domains like the life sciences, and that R&D in information technology and other emerging domains has shorter lifecycles. While shorter lifecycles may be true in some cases, this is not a generalised rule.

For example, in 1979 Dieter Seitzer's team develops the first digital signal processor capable of audio compression in Erlangen-Nuremberg University in Germany. His student Karlheinz Brandenburg, started employing psychoacoustic principles in the audio coding schemes and achieved continuous improvement of their coding algorithms. His doctoral thesis was on an algorithm that encapsulates his theoretical work. A variant of this algorithm was chosen as a standard for digital audio coding by the Moving Picture Experts Group, a part of the International Standards Organization, in 1991. Finally in 1995, after sixteen years since the first audio compression in a digital signal processor was demonstrated, the .mp3 file format was first licensed. By this time, the R&D had moved to a team in the Fraunhofer Institute for Integrated Circuits.

How does the fact that many complex technologies have decadal "R&D to product lifecycles" impact Indian R&D?

First, the decadal lifecycles require collaboration among diverse R&D teams across organisations and multiple hand-offs. India has a good track-record of managing this kind of collaboration if the R&D teams are in organisations under one umbrella organisation like ISRO or the Department of Atomic Energy. We need to do better when R&D teams are dispersed across government labs, academia and industry. What will help India to succeed in this context are flexible processes, sophisticated program management, and inter-organisational coordination where R&D output and personnel can move seamlessly between teams in different organisations.

Remember that when BioNTech realised that mRNA technology was critical, they brought Karliko on board. The coupling of various R&D teams and organisations and transfer of tacit knowledge takes time to nurture. In the Indian context, the collaboration between National Institute of Virology that isolated the SARS-CoV-2 strain used by Bharat Biotech in their Covid-19 vaccine development is a case in point. Bharat Biotech had the tacit and explicit knowledge of being a part of successful public-private partnerships in the past as they had worked with AIIMS as the R&D partner to develop the Rotavac vaccine.

Second, as complex technologies evolve over decades, it is imperative to ensure that the infrastructure required for their commercial translation is also modernised over time to keep abreast of the latest products in the R&D pipeline. For example, India could have been better prepared to produce more numbers of Covid-19 vaccines if manufacturing infrastructure of public sector organisations like Pasteur Institute of India and Haffkine Bio-Pharmaceutical Corporation Ltd. had been regularly upgraded to manufacture the latest types of vaccines.

Third, India needs to develop models of funding that support R&D across decadal programs and for various phases in the lifecycle. Biotechnology Industry Research Assistance Council (BIRAC), an organisation under the Department of Biotechnology, is an Indian pioneer in this aspect. BIRAC operates the Grand challenges India program and Biotechnology Ignition Grant in the research stage of R&D. It has programs like the Small Business Innovation Research Initiative for the development stage. BIRAC has the Contract Research Scheme and Accelerating Entrepreneurs Fund for the commercialisation stage. A similar scaled-up bouquet of funding programs may be needed to support India's ambitious and important national R&D programs like the National Mission on Interdisciplinary Cyber-Physical Systems of the Department of Science and Technology.

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