Journal of Primary Care & Community Health
Volume 13: 1–5

DOI: 10.1177/21501319211068638
journals.sagepub.com/home/jpc
SAGE

Industry 4.0 Technologies for the Manufacturing and Distribution of COVID-19 Vaccines

Azza Sarfraz[1,2], Zouina Sarfraz[1,3], Muzna Sarfraz[1,4], Aminah Abdul Razzack[1], Shehar Bano[3], Sarabjot Singh Makkar[1], Sindhu Thevuthasan[1], Trissa Paul[1], Muhammad Khawar Sana[1], Nishwa Azeem[5], Miguel Felix[6,7], and Ivan Cherrez-Ojeda[6,7]

Abstract

Background: The evolutionary stages of manufacturing have led us to conceptualize the use of Industry 4.0 for COVID-19 (coronavirus disease 2019), powered by Industry 4.0 technologies. Using applications of integrated process optimizations reliant on digitized data, we propose novel intelligent networks along the vaccine value chain. Vaccine 4.0 may enable maintenance processes, streamline logistics, and enable optimal production of COVID-19 vaccines. **Vaccine 4.0 Framework:** The challenge in applying Vaccine 4.0 includes the requirement of large-scale technologies for digitally transforming manufacturing, producing, rolling-out, and distributing vaccines. With our framework, Vaccine 4.0 analytics will target process performance, process development, process stability, compliance, quality assessment, and optimized maintenance. The benefits of digitization during and post the COVID-19 pandemic include first, the continual assurance of process control, and second, the efficacy of big-data analytics in streamlining set parameter limits. Digitization including big data-analytics may potentially improve the quality of large-scale vaccine production, profitability, and manufacturing processes. The path to Vaccine 4.0 will enhance vaccine quality, improve efficacy, and compliance with data-regulated requirements. **Discussion:** Fiscal and logistical barriers are prevalent across resource-limited countries worldwide. The Vaccine 4.0 framework accounts for expected barriers of manufacturing and equitably distributing COVID-19 vaccines. With amalgamating big data analytics and biometrics, we enable the identification of vulnerable populations who are at higher risk of disease transmission. Artificial intelligence powered sensors and robotics support thermostable vaccine distribution in limited capacity regions, globally. Biosensors isolate COVID-19 vaccinations with low or limited efficacy. Finally, Vaccine 4.0 blockchain systems address low- and middle-income countries with limited distribution capacities. **Conclusion:** Vaccine 4.0 is a viable framework to optimize manufacturing of vaccines during and post the COVID-19 pandemic.

Keywords

vaccination, global health, policy, community health, populations, COVID-19

Dates received: 11 October 2021; revised: 5 December 2021; accepted: 6 December 2021.

Introduction

There has been rapid progress and advancement in the development of vaccines during the coronavirus disease 2019 (COVID-19) pandemic.[1] Until 10th October, 2021, 106 vaccines are in clinical trials with another 75 in pre-clinical phases, and 6 vaccines in early or limited use; 37 have reached the final stages of testing.[1] We discuss the implementation of a novel framework to manufacture and distribute COVID-19 vaccines. We also highlight the utilization of Industry 4.0 technologies as scalable tools during global pandemics and epidemics.

[1]Larkin Community Hospital, South Miami, FL, USA
[2]The Aga Khan University, Karachi, Pakistan
[3]Fatima Jinnah Medical University, Lahore, Pakistan
[4]King Edward Medical University, Lahore, Pakistan
[5]Lahore General Hospital, Lahore, Pakistan
[6]Universidad Espiritu Santo, Samborondon, Ecuador
[7]Respiralab Research Group, Guayaquil, Ecuador

Corresponding Author:
Zouina Sarfraz, Division of Research & Academic Affairs, Larkin Community Hospital, 7031 SW 62nd Avenue, South Miami, FL 100181, USA.
Email: zouinasarfraz@gmail.com

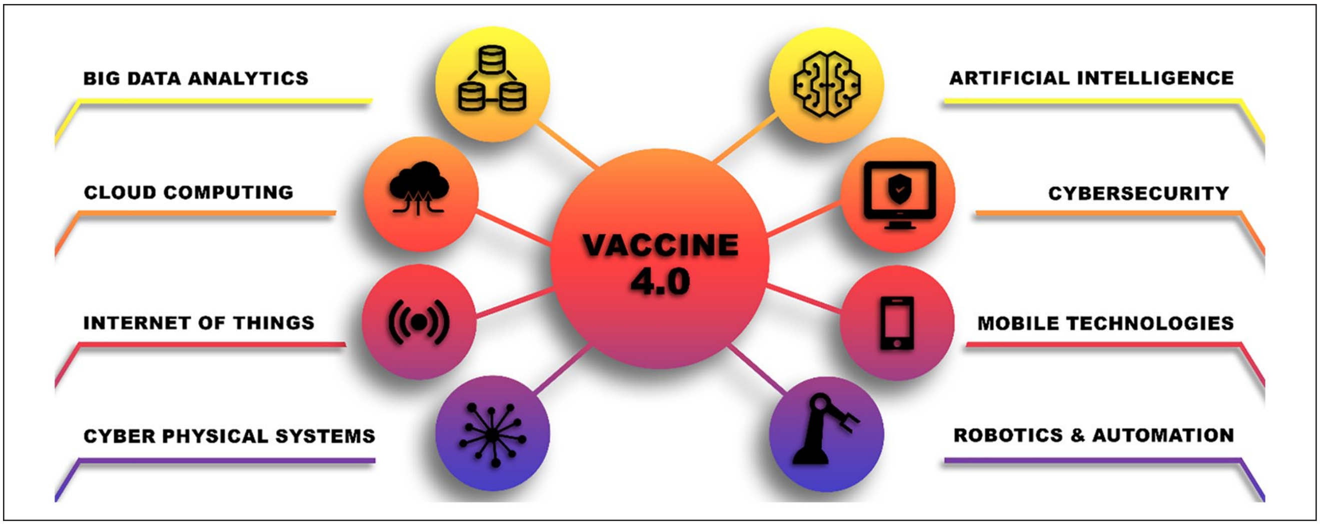

Figure 1. Driving forces of human and technology-led Vaccine 4.0 technologies.

Vaccine 4.0 Framework

The 4 evolutionary stages of manufacturing have led us to postulate Vaccine 4.0, a technology otherwise referred to as Industry 4.0. Using the basic principle of digitization and machines, we posit new intelligent networks along the vaccine value chain. These network help in predicting failures, enable maintenance processes autonomously, self-organize logistics, and react to changes in production. The potential for Vaccine 4.0 is wide and many pharmaceutical companies may adopt technologies such as cyber-physical systems, cloud computing, automation, and big data analytics to improve processes such as manufacturing and distribution (Figure 1).[2-4] A central challenge emerges before embarking on the path to Vaccine 4.0. Key technologies are required for digital transformation in the manufacturing, rolling-out, and distribution process. The economic benefits of wide-scale investment must be preemptively calculated by the chief financial officer or an accounting professional for every stage computing the expected return on investment (ROI). The barriers may persist consisting of internal validation of data and external data security issues, which may hinder the complete embracement to digitization in healthcare and pharmaceutical production processes.

Industry 4.0 technology is critical for machine-to-machine settings and is in sync with all regulations of the concerned health sector. Pharmaceutical companies are highly regulated, optimal for digitization, and may adopt continuous process verification (CPV) through vaccine manufacturing data validated and assessed against Food and Drug Administration (FDA) or region-specific guidelines. CPV consists of (1) statistical process control techniques, (2) quality ascribing to incoming materials, in process materials, and finished vaccines, (3) in-, on-, and at- line controls, and (4) risk-based real-time approaches to ensure the materials meet quality and control requirements. The CPV dashboard may be color coded (orange vs green) to provide status updates of the manufacturing process from incoming materials to outgoing vaccines. Big data analytics technology may be utilized to improve the quality of vaccines, profitability, and the entire manufacturing process. For example, if 1 pharmaceutical company produces a batch of vaccines with sub-standard raw materials detected upon completion, data analytics provides a single view of the manufacturing process.

Vaccine 4.0 analytics proposedly caters to (1) process performance, (2) process development, (3) process stability, (4) compliance, (5) quality assessment, and (6) optimized maintenance. The immediate benefits of digitization during the COVID-19 era are the continued assurance of process control, and the proposal of Big Data (BD) analytics to detect deviations from set parameter limits. The automatic monitoring may optimize the offerings by pharmaceutical companies of continuous data being validated against FDA or region-specific guidelines, and promoting compliance with the requirements in the concerned industry sector. The path to Vaccine 4.0 will enhance quality, improve efficacy, and improve compliance with the data-regulated regulatory requirements. The first step is to identify all problems in the manufacturing, storing, packaging, distributing, marketing, and usage of vaccines. The second step is to universalize the parameters of importance for similar health outbreaks in the future, and determine how information technology (IT) may aid in accessing data sources for worldwide application. The final step is to commence pilot projects of vaccine 4.0 in all continents across the globe with adequate budgeting, refined implementation, and ultimately speed rollout to other sites. Our proposed framework sets the path to Vaccine 4.0 by introducing a valuable era of manufacturing.

Equitable COVID-19 Vaccine Distribution

In striving for equitable access to vaccines, 1 potential way to reach low- and middle-income populations is through biometric digital IDs. In the past, biometric companies have partnered with telecom companies to develop biometric solutions for identifying vulnerable populations in rural settings.[5] This is a prime example of using digital tools to identify people who are lost to the system and provide them with digital identities, given that around 1.1 billion people worldwide lack formal identities.[6] Utilized in combination with surveillance systems, this may help ensure that digitally undocumented populations receive the COVID-19 vaccine. Biometrics are also being piloted in the United Kingdom (UK) for keeping track of those who have gained immunity or tested positive for antibodies.[7] Analyzing such data can subsequently determine pockets of the population that may be at higher risk of transmission. Vaccine tracing via biometrics and smartphone technology would be crucial in enabling necessary follow-ups in the case of required booster shots for the coronavirus vaccine. Rapid digital contact tracing that facilitates algorithmic, risk-stratified recommendations for quarantine or social distancing could significantly slow down the spread and allow some much-needed recuperation for many overburdened hospitals and healthcare workers.[8,9] To improve the current status quo of vaccinations in the elderly and to relieve the socio-economic encumbrance on our society, the role of inflammaging in vaccination response must be further explored and understood.[10] When analyzing the effect of age-related factors such as immunosenescence and inflammaging on immune response to vaccination in the elderly, we recommend systems biology approaches to identify biomarkers, stratify subpopulations, and incorporate databases to ethically configure vaccination methods customized for the elderly.[11]

Employing Biosensors Against the COVID-19 Pandemic

Biosensing refers to the detection of biomolecules using analytics devices (ie, biosensors) that combine the natural biological component (ie, a cell, protein, or nucleic acid) with a physiochemical detector.[12] The most notable model being used today is the glucose sensor which is used in clinical analysis and monitoring of the disease. Previously, several robust biosensors detecting antibodies have been constructed to control various infectious diseases like Malaria, Typhoid, HIV, and Adenovirus infection.[13] Two types of biosensors mainly chip-based and paper-based biosensors offer enormous potential for quick clinical determination. Material based, film-based or carbon-based biosensors have additionally been presented for possible extension of use for COVID-19.[14] Biosensors reliant on antibody-catalyzed water oxidation pathways can also be developed to identify antibodies of contagious diseases.[13]

Current trends in artificial intelligence include the usage of bio sensing gadgets for immune cell analysis.[15] Delicate recognition of COVID-19 antibodies by biosensors can become particularly significant for clinical recognition of humoral responses. Furthermore, the revolution of Industry 4.0 can be leveraged to develop artificial intelligence (AI)-enabled sensors for shipment of perishable vaccines that need to be stored at a certain temperature, pertinent in the COVID-19 pandemic. These sensors send signals when vaccines are defiled. Biosensor-based immunoassays can improve the identification of microbial antigens, improve accuracy of antibody tests (ie, false negatives and false positives), while multiplex location of host insusceptible reaction antibodies may improve the general particularity.

Implementing Blockchain Technology and Machine Learning to the COVID-19 Vaccine Supply Chain

Distribution of COVID-19 vaccines can be bolstered by artificial intelligence and machine learning applications for fabricating and assembling a block chain supply system, described in Figure 2. International health governing organizations will play an integral role in funding and providing financial aid to facilitate the building of an efficient block chain system. Distributing COVID-19 vaccine around the globe would require circulating 7 to 18 billion doses and block chain is fundamental to make it equitable. At least 60% to 70% of the population is required to have immunity in order to break the chain of transmission. Essentially, block chain will also help address issues like vaccine expiration and vaccine record hoaxes.[16] In the past, the Center for Disease Control and Prevention (CDC) highlighted the occurrence of various kinds of fraudulent activities like the illegal selling of federal government provided vaccines or ancillary supplies, consumer fraud, theft, and forged vaccines.[17]

The block chain system utilizes quick response (QR) codes such as barcodes and serial numbers printed at each level ensuring all stakeholders have complete openness from the producer to end-purchaser on a publicly available system. Block chain will also be fundamental for a fair COVID-19 vaccine dispersion. A worldwide consortium must be enforced to classify those in most need of COVID-19 vaccination. To accomplish this worldwide ideal, rather than a public or provincial ideal, immunization access will fundamentally rely upon a data framework with the most conceivable uprightness to avoid powers of personal stakes. BD analytics can therefore be leveraged to identify certain

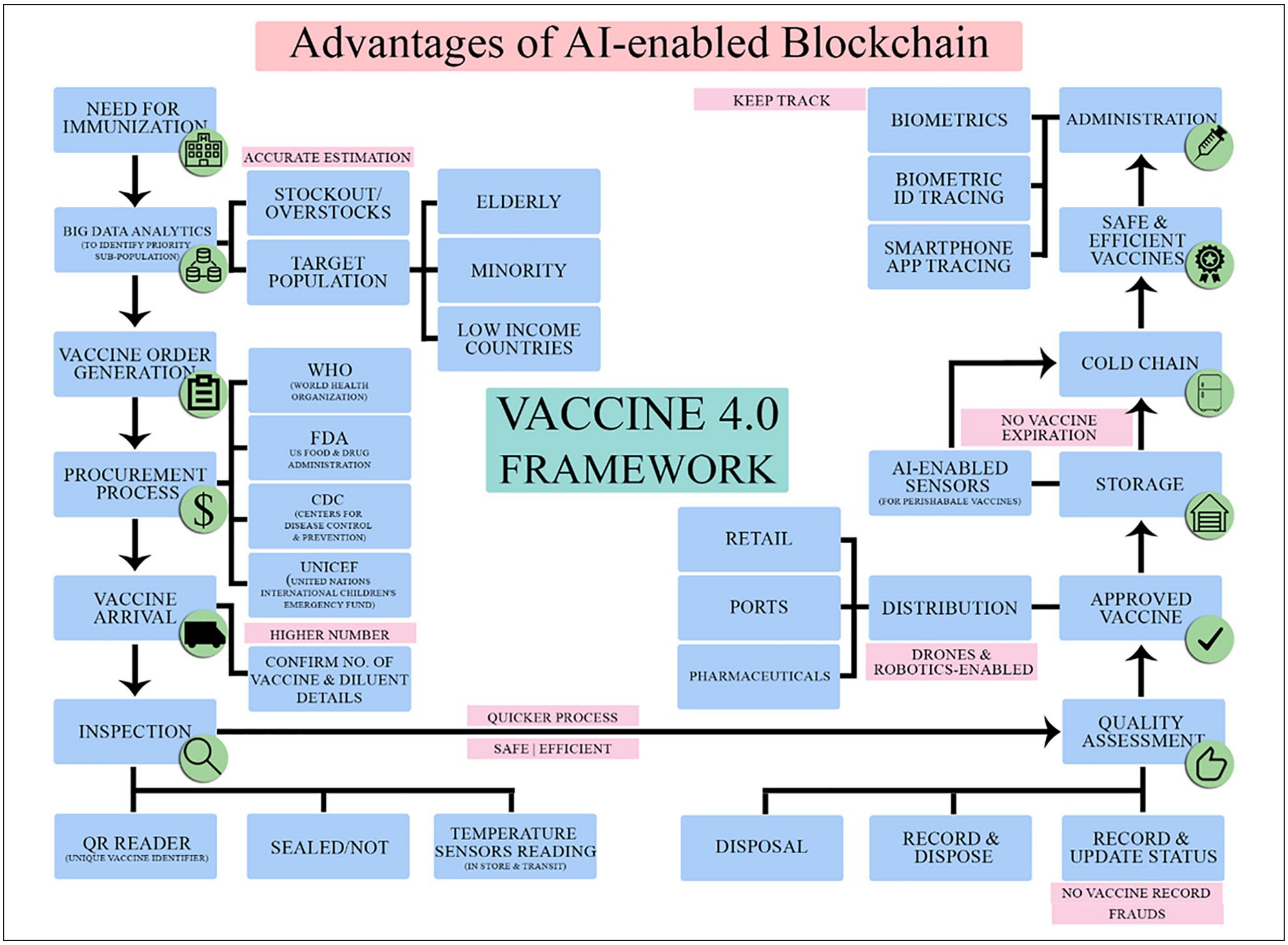

Figure 2. Implementation of blockchain technology in the era of Industry 4.0 for digital supply chain and its multiple benefits.

hotspots in low- and middle-income countries, and among vulnerable populations like the elderly and frontline healthcare workers.

The COVID-19 immunization supply chain data framework must be worked with continuous updates on variables like vaccine stockpiling levels, temperature control, stockouts, and amounts of auxiliary supplies. This is vital in figuring the most significant variables for vaccination campaigns, which include immunizing and protecting the population, halting the spread of COVID-19, and lastly, the wastage rates of vaccines.

Limitations and Barriers of Use in Developing Countries

First, due to the absence of working procedures and regulations in developing countries, impediments to the industry 4.0 technology are imminent. Second, there is a lack of proper legislative measures to grow cloud computing, cyber-security, artificial intelligence, and augmented reality in developing countries. Third, the lack of skilled workers to manage the complex industry 4.0 structures and lack of capital expenditure are present. Despite these barriers of use, the manufacturing of Industry 4.0 is primed by greater use of sensors, machines, and IT systems in lesser developed countries. With an active policy framework, it is possible to nurture new knowledge and capabilities that support Vaccine 4.0 in an effort to reduce inequalities in vaccine production and distribution.[18]

Conclusion

Vaccine 4.0 consists of digitizing the vaccine manufacturing process by continually monitoring development processes and optimizing maintenance. The framework is applicable to high income and low to middle incomes countries as it accounts for manufacturing and distributing barriers by incorporating big data analytics and biometrics.[19] The Vaccine 4.0 framework considers the potential Industry 4.0 technologies to ensure equitable global distribution and manufacturing of vaccines, which are necessary to eradicate pandemics, current and upcoming.

Acknowledgments

We would like to thank Dr Jack Michel (Larkin Health System, South Miami, USA), for his active support during the drafting of this paper.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Azza Sarfraz https://orcid.org/0000-0001-8206-5745
Zouina Sarfraz https://orcid.org/0000-0002-5132-7455
Shehar Bano https://orcid.org/0000-0002-6429-797X

References

1. Zimmer C, Corum J, Wee S-L. Coronavirus vaccine tracker. *NY Times*. 2020. Accessed October 11, 2021. https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html
2. Barenji RV, Akdag Y, Yet B, Oner L. Cyber-physical-based PAT (CPbPAT) framework for Pharma 4.0. *Int J Pharm*. 2019;567:118445. doi:10.1016/j.ijpharm.2019.06.036
3. Geiger K. Cloud computing in pharmaceutical R&D: business risks and mitigations. *Curr Opin Drug Discov Devel*. 2010;13:279-285.
4. Pesqueira A, Sousa MJ, Rocha Á. Big data skills sustainable development in healthcare and pharmaceuticals. *J Med Syst*. 2020;44:197. doi:10.1007/s10916-020-01665-9
5. World Bank. Identification for Development. https://id4d.worldbank.org/
6. The World Bank. 1.1 Billion 'Invisible' people without ID are priority for new high level advisory council on identification for development. *World Bank*. 2017. Accessed December 23, 2020. https://www.worldbank.org/en/news/press-release/2017/10/12/11-billion-invisible-people-without-id-are-priority-for-new-high-level-advisory-council-on-identification-for-development
7. Pitrelli MB. Why 'immunity passports' won't be the golden tickets to travel after all. *CNBC*. 2020. Accessed December 23, 2020. https://www.cnbc.com/2020/06/04/covid-19-update-will-immunity-passports-let-people-travel-again.html
8. Drew DA, Nguyen LH, Steves CJ, et al. Rapid implementation of mobile technology for real-time epidemiology of COVID-19. *Science*. 2020;368:1362-1367. doi:10.1126/science.abc0473
9. Ferretti L, Wymant C, Kendall M, et al. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. *Science*. 2020;368(6491):eabb6936. doi:10.1126/science.abb6936
10. Ciabattini A, Nardini C, Santoro F, Garagnani P, Franceschi C, Medaglini D. Vaccination in the elderly: the challenge of immune changes with aging. *Semin Immunol*. 2018;40:83-94. doi:10.1016/j.smim.2018.10.010
11. Wagner A, Weinberger B. Vaccines to prevent infectious diseases in the older population: immunological challenges and future perspectives. *Front Immunol*. 2020;11:717. doi:10.3389/fimmu.2020.00717
12. Ibn Sina AA, Koo KM, Ahmed M, Carrascosa LG, Trau M. Interfacial biosensing: direct biosensing of biomolecules at the bare metal interface. In: Wandelt K, ed. *Encyclopedia of Interfacial Chemistry: Surface Science and Electrochemistry*. Elsevier; 2018: 269-277. doi:10.1016/B978-0-12-409547-2.14188-5
13. Liu X, Jiang H. Construction and potential applications of biosensors for proteins in clinical laboratory diagnosis. *Sensors*. 2017;17:2805. doi:10.3390/s17122805
14. Choi JR. Development of point-of-care biosensors for COVID-19. *Front Chem*. 2020;8:517. doi:10.3389/fchem.2020.00517
15. Revzin A, Maverakis E, Chang HC. Biosensors for immune cell analysis-a perspective. *Biomicrofluidics*. 2012;6:21301-2130113. doi:10.1063/1.4706845
16. Yong B, Shen J, Liu X, Li F, Chen H, Zhou Q. An intelligent blockchain-based system for safe vaccine supply and supervision. *Int J Inf Manage*. 2020;52:102024. doi:10.1016/j.ijinfomgt.2019.10.009
17. Center for Disease Control and Prevention. Q and A: fraud and abuse related to 2009 H1N1 influenza vaccine. https://www.cdc.gov/h1n1flu/vaccination/h1n1_fraud_abuse.htm
18. Sarfraz A, Sarfraz Z, Sarfraz M. Survival of the wealthiest? Wait in line for COVID-19 vaccination. *Postgrad Med J*. Published online August 19, 2021. doi:10.1136/postgradmedj-2021-140970
19. Sarfraz Z, Sarfraz A, Iftikar HM, Akhund R. Is COVID-19 pushing us to the Fifth Industrial Revolution (Society 5.0)? *Pak J Med Sci*. 2021;37(2):591-594. doi:10.12669/pjms.37.2.3387