Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2025, Volume 13, Issue 12
ISSN: 2321–3647(online)

Digital Twins In Pharmaceutical Development and Manufacturing: A Paradigm Shift

Dommaraju R Arunakumari[1]*, Mediboyina Varshitha[1], V Renuka Devi[1], B Hemambika[1], S Pravallika[1], K M Haaris[1]

1. Seven Hills College of Pharmacy (Autonomous), Tirupati-517561, Andhra Pradesh, India.

ABSTRACT

The Digital Twin (DT), defined as a high-fidelity, real-time virtual representation of a physical system, is poised to revolutionize the pharmaceutical industry. DTs directly address critical challenges-including prolonged development timelines, substantial R&D expenditure, and the inherent limitations of resource-intensive physical experimentation-by enabling real-time simulation, prediction, and optimization across the entire drug lifecycle. DT functionality is predicated on the synergistic integration of advanced technologies, including the Internet of Things (IoT) for ubiquitous data acquisition, Artificial Intelligence (AI)/Machine Learning (ML) for complex predictive modeling, Big Data Analytics, and Cloud Computing for scalable computational power. This technological confluence facilitates predictive modeling and data-driven decision-making, resulting in demonstrable improvements in efficiency, accuracy, and cost-effectiveness. Key applications of DTs span the pharmaceutical workflow: from simulating drug-target interactions in drug discovery and optimizing Critical Process Parameters (CPPs) in formulation development, to enhancing process optimization and predictive maintenance in manufacturing and adherence to Quality by Design (QbD) principles. Despite the vast potential, significant barriers to widespread adoption include challenges related to data integration, the establishment of clear regulatory frameworks, and the computational complexity inherent in creating high-fidelity, multi-scale models. Nevertheless, the integration of DTs represents a cornerstone technology for the future of Pharmaceutical 4.0, promising to drive innovation, reduce time-to-market, and facilitate the development of more personalized and efficient therapeutic modalities.

Keywords: Digital Twins (DTs), Pharmaceutical development, Drug discovery, Artificial Intelligence (AI), Machine Learning (ML).

*Corresponding Author Email: arunavarma975@gmail.com
Received 10 November 2025, Accepted 15 December 2025

Please cite this article as: Arunakumari DR *et al*., Digital Twins In Pharmaceutical Development and Manufacturing: A Paradigm Shift. American Journal of Pharmacy & Health Research 2025.

INTRODUCTION

The pharmaceutical sector is confronted with persistent challenges such as protracted drug development timelines, escalating research and development (R&D) costs, complex regulatory frameworks, and the imperative for consistent product quality. [1]. Traditional pharmaceutical development and manufacturing processes largely depend on physical experimentation and retrospective quality assessments. Digital Twins represent a paradigm shift by creating real-time, synchronized virtual models of physical entities, which empower pharmaceutical scientists and engineers to simulate, predict, and optimize processes in real-time. [2,3]. Initially developed in the engineering field, DTs are now pivotal in advancing pharmaceutical sciences by supporting precision medicine, real-time quality assurance, and intelligent manufacturing.[4]. The evolution of DT architectures—from static digital models to fully integrated bi-directional digital twins—is summarized in Table 1 and Figure 1 , highlighting their increasing capability to support real-time monitoring, control, and self-optimizing pharmaceutical manufacturing systems.

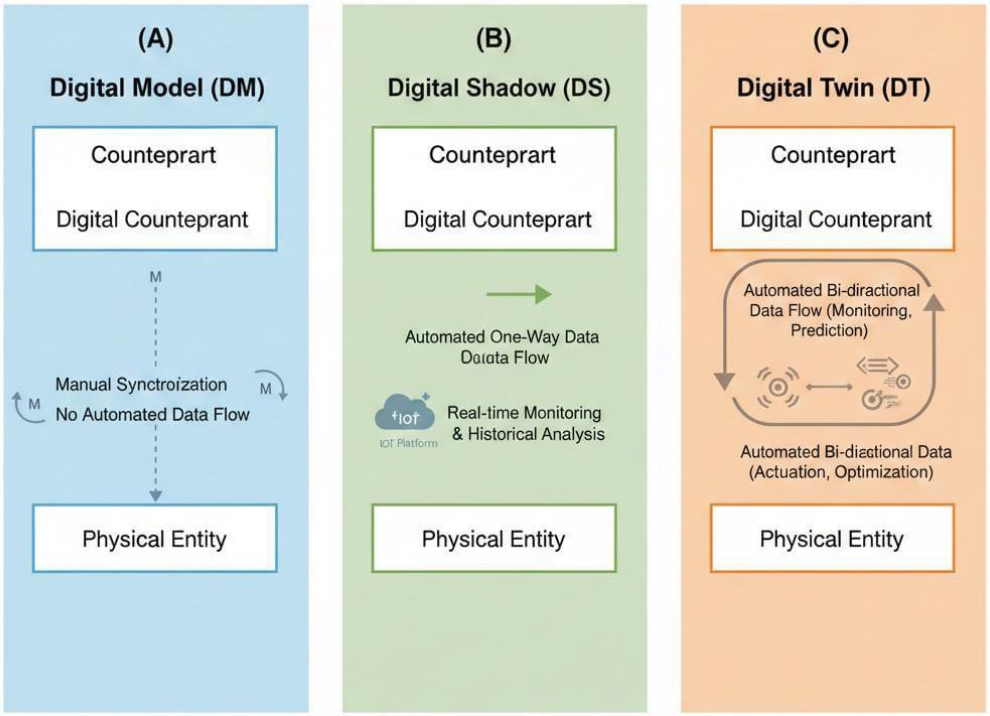

Figure 1: The Evolution and Integration Levels of Digital Representation

Table 1: Types of Digital Twin Architectures

Type	Data Flow	Description	Example in Pharma
Digital Model	None	Static virtual model	Offline process simulation
Digital Shadow	One-way	Physical → Digital data	Real-time temperature monitoring
Digital Twin	Two-way	Bi-directional real-time	Self-adjusting manufacturing system

Key Characteristics and Evolution of the Concept:

- **Real-time Connectivity**: A digital twin must continuously interact with the physical counterpart, compiling operational, maintenance, and sensor data in real-time.[5]
- **Predictive Capabilities**: A robust digital twin should be capable of predicting failures, forecasting behavior, and performing simulations.[6]
- **High Fidelity**: The virtual model must closely replicate the physical entity, maintaining a high degree of accuracy. [5,6]
- Tao & Zhang (2017) proposed a conceptual model comprising four critical components:
- **Physical Environment**: Real-world entities, including people.
- **Virtual Environment**: Multidimensional models incorporating geometric and behavioral data.
- **Data**: Information from both physical and virtual entities, analyzed collaboratively.
- **Services**: Commands derived from simulations and available information.[7]

ENABLING TECHNOLOGIES FOR PHARMACEUTICAL DIGITAL TWINS

Internet of Things (IoT)

- The IoT is vital for connecting machines, sensors, and software to provide real-time monitoring throughout the drug lifecycle, thereby enhancing process efficiency and ensuring compliance. [9].
- Key components such as sensors (for temperature and pressure), RFID tags (for inventory tracking), and connectivity (Wi-Fi, Ethernet) facilitate the continuous synchronization of the DTs with physical systems. [8].

Artificial Intelligence and Machine Learning

AI and Machine Learning (ML) technologies process vast datasets at high speeds, supporting enhanced decision-making and accelerated drug development. These systems act as the "brain" behind Digital Twins by providing predictive analytics, which forecast equipment failure and guide R&D efforts.[9]

Big Data Analytics & Cloud Computing

Big Data Analytics, underpinned by cloud computing and ML, are crucial for managing the substantial and ever-expanding datasets generated by the pharmaceutical industry [10]. Cloud computing facilitates scalable storage, computing power, and global collaboration, while analytics improve overall equipment effectiveness (OEE) across various stages such as drug discovery and personalized medicine. [11,12,13].

Cyber-Physical Systems (CPS)

Cyber-Physical Systems (CPS) integrate physical processes with computer-based algorithms through the internet, providing real-time control. Digital Twins extend the capabilities of traditional CPS by offering more sophisticated integration of emerging IT technologies for rapid product and process optimization. [14].

APPLICATIONS OF DIGITAL TWINS IN PHARMACEUTICAL DEVELOPMENT

Drug Discovery and Preclinical Research

DTs act as computational surrogates for biological systems, simulating drug–target interactions and predicting pharmacodynamics (PD), pharmacokinetics (PK), and ADMET profiles.

- Virtual Models: Creation of virtual mouse models and the use of deep learning (e.g., GANs) for realistic biological modeling reduce the need for live animal studies.
- Early Trials: DT-based virtual patient avatars enable early-phase virtual clinical trials to predict safety and efficacy, leading to rapid, ethical trial design [15,16]

Formulation Development

- DTs provide a virtual experimentation environment to predict stability and solubility and optimize critical process parameters (e.g., mixing, drying).
- Quality by Design (QbD): Real-time process modeling supports advanced QbD principles, linking process parameters to product quality and enabling Real-Time Release (RTR) testing.
- Efficiency: Virtual formulation and process optimization approaches help reduce material usage, experimental iterations, waste generation, and overall development costs. Representative applications of Digital Twins across key formulation stages, in

Manufacturing and Process Optimization

DTs enable continuous manufacturing optimization by creating up-to-date virtual replicas of production systems.

- Predictive Maintenance: Factory DTs drive predictive maintenance and real-time production scheduling, transforming operations from reactive to proactive [19]
- Quality and Consistency: They achieve "right-first-time" (RFT) manufacturing by identifying design flaws early and continuously monitoring production using real-time sensor data to prevent defects [19,20]

- Enhanced Control: DTs provide real-time monitoring and visualization, enabling in-depth process understanding and the testing of control strategies in the virtual environment before implementation [21]

Personalized and Precision Medicine (Health Digital Twins - HDTs)

Health Digital Twins (HDTs) are dynamic, data-driven virtual representations of individual humans, continuously updated from diverse health data (EHRs, wearables, genomics, imaging).

- Individualized Treatment: The "patient-in-silico" model allows clinicians to simulate different treatment outcomes *before* application.
- Personalized Dosing: DTs move beyond population averages to adjust dosages based on a patient's unique biological factors (e.g., renal function, receptor count).
- Hybrid Modeling: The fusion of AI and mechanistic (mathematical) models uses known biological understanding to augment real-world data and infer difficult-to-measure personalized biological parameters [22,23]

Clinical Trials and Post-Market Surveillance

DTs facilitate next-generation clinical trial designs by creating patient-specific avatars and simulating treatment responses.

- Trial Efficiency: They enable synthetic control arms in clinical trials, reducing time and cost, and support the efficient design and stratification of trials using virtual patient cohorts.
- Proactive Pharmacovigilance: DTs support proactive monitoring by predicting individual adverse events and continuously evaluating drug performance and safety in real-world settings [24]

Digital Twins in Pre-clinical Molecular Imaging:

This document highlights a pivotal application of Digital Twins (DT) within the pharmaceutical sector: pre-clinical molecular imaging, specifically leveraging rodent models.

The primary objective for integrating Digital Twins in this context is to address core ethical considerations related to animal usage—encompassing the principles of Reduce, Refine, and Replace (3Rs)—while concurrently driving enhanced efficiency in the development of novel drugs and radiopharmaceuticals.

As schematically represented in Figure 2, this methodology is structured across three interdependent phases:

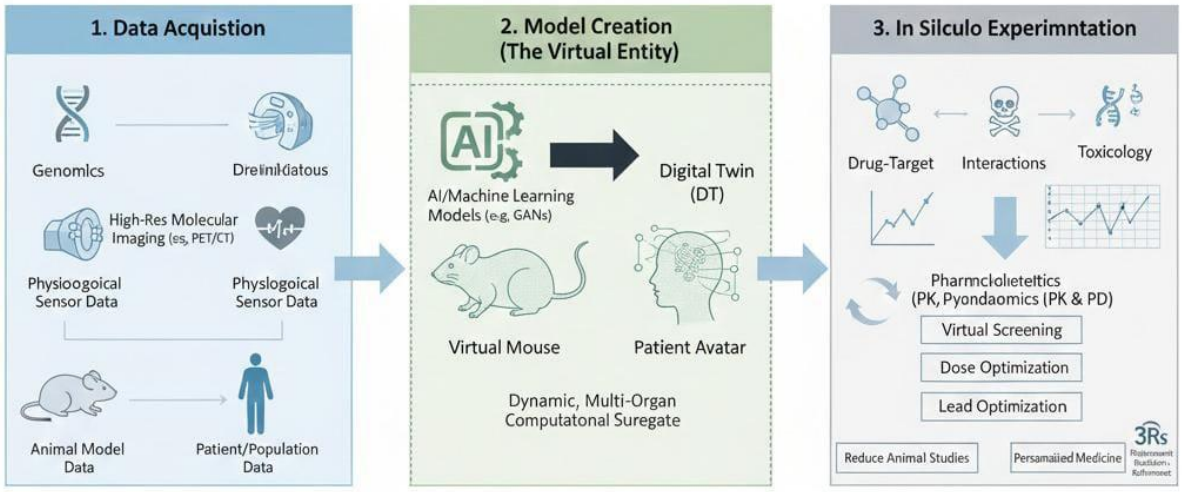

Figure 2: Digital Twin in Predeuanrial Research

1. Data Acquisition: Collection of diverse, high-resolution biological and physiological inputs.
2. Model Creation (The Virtual Entity): Development of the Dynamic, Multi-Organ Computational Surrogate (Virtual Mouse and Patient Avatar) using AI/Machine Learning Models.
3. In Silico Experimentation**:** Utilization of the Digital Twin for computational studies, including Virtual Screening, Dose Optimization, and Toxicology analysis, supporting Personalized Medicine.

The specific applications and related insights:

Creating Virtual Animal Models (Digital Twins of Mice):

- The core application is to "create a virtual model of mice" using digital twin technology. This means constructing highly accurate, dynamic digital replicas of mice used in pre-clinical studies.
- This directly supports the ethical imperative to "reduce, refine and replace animal imaging where possible" by providing a computational alternative to physical animal studies.

Enhancing Digital Twin Capabilities with Deep Learning (e.g., GANs):

- Suggests exploring the potential of "deep learning approaches the text to digital twin development" to enhance their capabilities.
- A Specifically, Generative Adversarial Networks (GANs) are mentioned as promising deep learning technique. GANs can "produce generated images that sufficiently resemble

reality," implying their use in creating highly realistic and detailed virtual representations (digital twins) of mice or their organs/systems.

- This can lead to more sophisticated and biologically accurate digital twins, improving their utility in simulations.

Targeting Specific, Homogenous Models for Enhanced Accuracy:

- The text notes that "Specific genetic mouse models have greater homogeneity," making them "more receptive to modelling and suitable specifically for digital twin simulation."
- This implies a targeted application where digital twins can be particularly effective for well-defined, consistent biological systems, potentially leading to more reliable and reproducible in-silico experiments.

Improved Outcomes and Efficiency in Drug/Radiopharmaceutical Development:

- Fewer Animal Studies: A direct benefit is the reduction in the number of live animal studies required, addressing ethical concerns and potentially accelerating research.
- Shorter Development Timelines: By leveraging simulations and virtual testing, the overall timeline for drug and radiopharmaceutical development can be significantly shortened.
- Lower Costs: Reducing reliance on physical animal experiments can lead to substantial cost savings in research and development.

These points provide concrete examples of how Digital Twins can be applied in the pre-clinical phase of pharmaceutical development, particularly in the realm of molecular imaging, to achieve both ethical and efficiency goals. [2,11,19]

Supply Chain and Logistics

DTs model inventory, demand forecasting, cold-chain performance, and warehouse operations, improving resilience and responsiveness.

CLINICAL TRIALS AND PATIENT-CENTRIC APPLICATIONS

Digital Twins enable virtual patient models for precision dosing and treatment simulations. Synthetic control arms reduce the number of patients required for placebo groups, improving ethical outcomes and reducing trial costs [25,26].

The broader role of Digital Twins across different stages of the pharmaceutical product lifecycle—from drug discovery to post-market surveillance—is presented in Table 3.

Table 2: Digital Twin Use in Formulation Development

Process Stage	Traditional Method	Digital Twin Advantage
Pre formulation	Trial-and-error	Virtual solubility prediction
Mixing	Fixed parameters	Real-time optimization
Granulation	Physical testing	Predictive quality modelling
Compression	Manual adjustment	Automated tuning

Table 3: Impact of Digital Twins Across the Product Lifecycle

Lifecycle Stage	Key DT Function	Benefits
Drug Discovery	Virtual screening	Faster lead identification
Preclinical	Virtual animal models	Reduced animal usage
Clinical Trials	Patient-specific twins	Personalized treatment
Manufacturing	Process twins	Quality consistency
Post-Market	Real-time monitoring	Rapid safety detection

BENEFITS OF DIGITAL TWINS IN PHARMACEUTICALS

1. Reduced Development Time: Simulation minimizes unnecessary physical trials.
2. Improved Product Quality: Continuous quality monitoring reduces defects.
3. Predictive Maintenance: Early detection of equipment failure.
4. Cost Efficiency: Reduced material wastage and batch rejection.
5. Regulatory Readiness**:** Real-time data logging supports audits and compliance [26,27,28].

A structured overview of the principal benefit categories of Digital Twins, along with their underlying mechanisms, is provided in Table 4.

Table 4: Benefits and mechanism of Digital Twins

Category	Key benefits	Mechanism
R&D Cost/Time	Reduced R&D costs and accelerated timelines (20% to 50% faster time to market)	Virtual prototyping reduces expensive physical prototypes and testing; Concurrent Engineering allows parallel development; Early defect identification avoids costly rework.
Quality & Consistency	Improved Product Quality and Right-First-Time (RFT) Manufacturing	Continuous quality monitoring with real-time sensor data; Predictive analytics anticipates and prevents defects before they occur; Virtual simulation identifies consistent process configurations.
Risk & Decision Making	Better Risk Management and Data-Driven Decisions	Continuous risk monitoring and forecasting potential future risks; Failure prognostics predict when a component is likely to fail; Virtual-to-Physical (V2P) closed loop enables control actions based on optimal requirements.
Supply chain	Optimized Inventory and Logistics	AI-powered DTs anticipate supply interruptions and optimize warehouse layouts; Predictive analytics improves demand forecasting and resource allocation.

CHALLENGES AND LIMITATIONS

Data Integration and Quality

Pharmaceutical systems often use legacy platforms leading to fragmented data silos. Inconsistent data quality can reduce model reliability.

Regulatory and Ethical Barriers

Lack of dedicated regulatory frameworks for DT-driven decision-making limits widespread adoption. Ethical considerations include data ownership, algorithmic bias, and patient consent [29].

Computational Complexity

High-fidelity biological models require significant computing resources, limiting real-time performance in some settings. Despite the transformative potential, significant challenges must be overcome for widespread DT adoption:

A. Data-Related Challenges

The performance of a DT is directly tied to the quality and management of its data.

- Integration and Standardization: There is a lack of standardization and interoperability across diverse, heterogeneous systems (e.g., R&D, manufacturing, legacy infrastructure). Data often remains in isolated silos and is fragmented across traditional, document-based methods.
- Quality, Volume, and Velocity: DTs require high-quality, noise-free, and continuous data streams. The rapid expansion of IoT generates massive data volumes, requiring high-speed networks and scalable cloud infrastructure for real-time synchronization.
- Multiscale and Multiphysics Complexity: Biological systems span vast spatial and temporal scales (nanometers to meters, microseconds to years),requiring the integration of multiple interacting physical processes (e.g., electrical, mechanical, fluid dynamics). This leads to models that are mathematically stiff and computationally intensive, demanding large computational resources [30,31]

B. Regulatory and Ethical Challenges

For medical DTs (HDTs), governance, privacy, and regulatory clarity are paramount.

- Privacy and Governance: HDTs hold vast sensitive data, requiring strict governance to prevent breaches and unauthorized access. Anonymized data risks re-identification, and secondary use raises ethical concerns. Transparency is vital for obtaining informed consent for continuous, multi-modal data collection from wearables.
- Bias and Inequality: Unequal data representation can bias AI models, leading to poorer outcomes for underrepresented groups, which risks widening healthcare disparities.

- Regulatory Uncertainty: There is a lack of a specific regulatory framework for Digital Twins in healthcare. Clear accountability frameworks are needed to define liability when DT-informed clinical decisions lead to errors or harm. Current pathways (e.g., FDA's DDT and IND) are resource-intensive for qualification [29,31]

FUTURE PERSPECTIVES

The future of Digital Twins in pharmaceuticals lies in fully autonomous, closed-loop manufacturing systems, AI-driven drug discovery, and personalized medical digital twins. Integration with blockchain for secure data governance and edge computing for faster analytics will further strengthen reliability and scalability. The future vision for the pharmaceutical sector is an end-to-end digital ecosystem powered by AI, digital twins, and cloud platforms for resilient, transparent, and individualized manufacturing and supply chains [32].

- Sustainability and Industry 4.0: DTs will support the Fourth Industrial Revolution (Industry 4.0) by enabling hyper automation, predictive maintenance, and closed-loop operational optimization to achieve key sustainability goals: reduced energy usage, minimized waste, and optimized supply chains.
- Expansion of Modalities: DTs are critical for accelerating the development of novel chemical and biological modalities, such as targeted protein degraders, PROTACs, antisense oligonucleotides, and RNA therapeutics, which address previously undruggable pathways.
- Standardization: Establishing standardized platforms and rigorous evaluation frameworks, such as the Best-Worst Method and Fuzzy Comprehensive Evaluation (BWM-FCE), is a top priority to ensure robust and nuanced platform appraisal.
- Ecosystem Integration: The integrated ecosystem will feature AI-enabled software platforms, IoT hardware, and development tools for real-time process monitoring, resource optimization, regulatory compliance, and personalized medicine [31,32]

CONCLUSION

Digital twins (DTs) are revolutionizing the pharmaceutical industry by offering a dynamic, virtual replica of physical systems that can be used throughout the drug lifecycle. They can be applied in pre-clinical stages to create virtual animal models, in drug development to optimize clinical trials, in manufacturing to improve quality control, and in post-market surveillance to identify safety signals. The successful implementation of this technology relies on a combination of IoT, AI, and cloud computing. Despite challenges such as data fragmentation and ethical

concerns, DTs have the potential to drive efficiency, improve patient outcomes, and create a more responsive pharmaceutical ecosystem.

REFERENCES

1. International Research Journal of Pharmacy and Medical Sciences (IRJPMS). Digital twinning in pharmaceuticals: A review. IRJPMS; 2023.
2. PharmOut. Digital twins: Transforming Pharma 4.0 manufacturing. PharmOut; 2022.
3. Grieves M. Digital twin: manufacturing excellence through virtual factory replication. White paper. Florida Institute of Technology; 2014.
4. Tao F, Zhang M. Digital twin shop-floor: a new shop-floor paradigm towards smart manufacturing. IEEE Access. 2017.
5. Tuegel EJ, Ingraffea AR, Eason TG, Spottswood SM. Reengineering aircraft structural life prediction using a digital twin. Int J Aerosp Eng. 2011.
6. Rasheed A, San O, Kvamsdal T. Digital twin: values, challenges and enablers from a modeling perspective. IEEE Access. 2020.
7. Barricelli BR, Casiraghi E, Fogli D. A survey on digital twin: definitions, characteristics, applications, and design implications. IEEE Access. 2019.
8. Macchi M, Roda I, Negri E, Fumagalli L. Exploring the role of digital twin for asset lifecycle management. IFIP Adv Inf Commun Technol. 2018.
9. Puri A, Kumar S, Moudgil M. Digital twins in pharmaceutical manufacturing and quality assurance: opportunities and challenges. J Pharm Innov. 2022.
10. Naga-Datta-Sasi-Mrudula K, Masa M, Sai Kumar MSSV, Vegesna S. Analytical integration of digital twins in pharmaceutical sciences. *Int J Pharm Pharm Res*. 2025
11. Nele L, Mattera G, Yap EW, Vozza M, Vespoli S. Towards the application of machine learning in digital twin technology: a multi-scale review. *Discov Appl Sci*. 2024
12. Wipro Technologies. The digital twin advantage: reimagining pharma's commercial edge. *Wipro Pharmaceutical & Life Sciences*. 2025
13. Ali S, Khan SS, Khan BF, Ali ASH. Digital twins and AI for end-to-end sustainable pharmaceutical supply chain management. *World J Biol Pharm Health Sci*. 2025
14. Shaikh AS, Shaikh Z. Digital twinning in pharmaceuticals: a review. *Int Res J Pharm Med Sci*. 2025
15. Mariam Z, Niazi SK, Magoola M. Unlocking the future of drug development: generative AI, digital twins, and beyond. *BioMedInformatics*. 2024

16. IEEE. Digital twins for cyber-physical healthcare systems: architecture and applications. *IEEE Access*. 2025
17. Badarinath AV, Morris KR. Predictive maintenance and digital twins in pharmaceutical manufacturing. J Pharm Innov. 2022
18. O'Leary R, McMahon G, Mulholland M. Digital twins for right-first-time pharmaceutical manufacturing. Comput Chem Eng. 2021.
19. Bruynseels K, Santoni de Sio F, van den Hoven J. Digital twins in health care: Ethical implications of an emerging engineering paradigm. Front Genet. 2018.
20. Viceconti M, Pappalardo F, Rodriguez B, Horner M, Bischoff J, Tshinanu FM. In silico trials: Verification, validation, and uncertainty quantification. Philos Trans A Math Phys Eng Sci. 2021
21. Polasek TM, Roberts JA. Personalized dosing and digital twins in clinical pharmacology. Clin Pharmacol Ther. 2022.
22. Enderling H, Chaplain MAJ. Mathematical modeling of cancer and its application to therapy design. Cancer Res. 2014.
23. Germain M, Knauf C, Menzel MI. Digital twins in preclinical imaging: Toward virtual mice. Eur J Nucl Med Mol Imaging. 2021.
24. Yi X, Walia E, Babyn P. Generative adversarial network in medical imaging: A review. Med Image Anal. 2019.
25. Thorlund K, Dron L, Park JJH, Mills EJ. Synthetic and external controls in clinical trials – A review. J Clin Epidemiol. 2020.
26. FDA. Use of real-world evidence to support regulatory decision-making for medical products. U.S. Food and Drug Administration; 2022.
27. Ivanov D, Dolgui A. Digital supply chain twins: Managing disruptions, resilience and recovery. Int J Prod Res. 2021.
28. Li L, Zhang H, Tao F, Cheng Y, Ren L. Digital twin-driven smart supply chain. J Manuf Syst. 2020.
29. Health Level Seven International (HL7). FHIR Release 4 (R4): Interoperability Standards. HL7; 2019.
30. ICH. ICH Q8(R2): Pharmaceutical Development. International Council for Harmonisation; 2009.
31. Mehrabi N, Morstatter F, Saxena N, Lerman K, Galstyan A. A survey on bias and fairness in machine learning. ACM Comput Surv. 2021.

32. Xu X, Lu Y, Vogel-Heuser B, Wang L. Industry 4.0 and industrial Internet of Things: A new wave of innovation. J Manuf Syst. 2018.