DRIVING SUSTAINABLE PHARMACEUTICAL MANUFACTURING

Through Pharma 4.0™ Technologies

By Amisha Patel

The pharmaceutical industry's embrace of digital technologies and sustainability is no longer a competitive advantage, but an operational necessity. As Pharma 4.0™ matures, its integration will be vital for achieving net-zero objectives and achieving pharmaceutical excellence.

INTRODUCTION

The pharmaceutical manufacturing industry is at a pivotal crossroads of responsibility and opportunity. The primary mandate of the industry has historically and traditionally been to keep patients safe while maintaining the highest quality products, which is enshrined in GMP and supported by stringent regulatory requirements. However, the landscape is rapidly changing. Pharmaceutical companies are increasingly called upon to not only maintain these standards but to also do so in sustainable working practices.

This shift is the result of global climate agreements that establish carbon reduction goals. Environmental, social, and governance criteria are now central to investment decisions and corporate reputation [1]. Regulators are providing clear indications that they are shifting to a more stringent approach to environmental enforcement, even as public scrutiny of pharmaceutical operations—including energy consumption, water stewardship, and waste management—continues to intensify.

In this scenario, the implementation of Pharma 4.0™ technologies presents a transformative opportunity. The Pharma 4.0™ framework, as championed by ISPE, adapts Industry 4.0 principles specifically to the unique needs of pharmaceutical manufacturing. Digitalization, automation, and advanced analytics are becoming essential enablers of sustainable, resilient, and compliant manufacturing. By deploying smart sensors, artificial intelligence (AI), digital twins, and blockchain across the value chain, manufacturers can improve product quality, meet regulatory requirements, and deliver step-change improvements in resource efficiency and environmental performance.

This article explores how the intersection of Pharma 4.0™ and sustainability is shaping the future of pharmaceutical manufacturing, outlining both opportunities and practical considerations for implementation.

DEFINING SUSTAINABILITY IN PHARMACEUTICAL MANUFACTURING

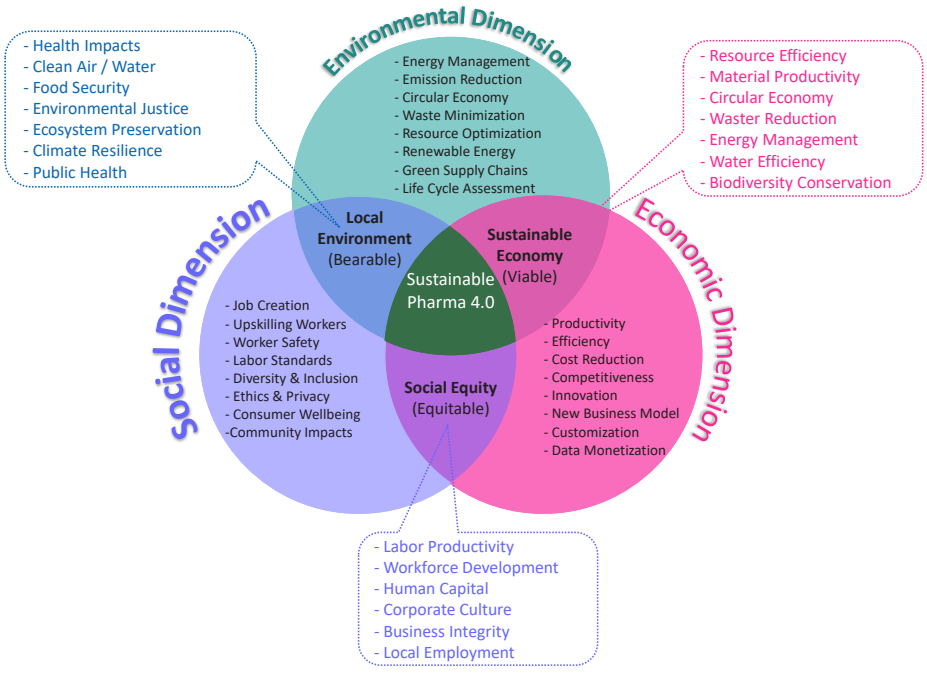
Sustainability represents a comprehensive commitment to meet present day needs while safeguarding the ability of future generations to do the same. Central to sustainable industrial processes is the 3Ps concept of sustainability—planet, profit, and people, often referred to as the triple bottom line [2]. As the industry faces increasing scrutiny from regulators, investors, and the broader society, a robust sustainability strategy is essential. Such a strategy not only ensures regulatory compliance, but also supports long-term business resilience, enhances stakeholder trust, and delivers value across environmental, social, and economic dimensions (see Figure 1).

Environmental Dimension

Pharmaceutical manufacturing is resource-intensive—consuming significant levels of energy, water, and raw materials—it may be responsible for generating hazardous waste. Addressing these challenges requires process efficiency, waste minimization, and emission control. The environmental impact of pharmaceutical manufacturing is commonly measured by greenhouse gas emission scopes 1–3 framework:

- Scope 1: Direct emissions from owned or controlled sources, such as on-site fuel combustion

Figure 1: Sustainable Pharma 4.0™: A triple bottom line approach [2].



- Scope 2: Indirect emissions from purchased energy, such as electricity
- Scope 3: All other indirect emissions from the value chain, including supplier activities, logistics and product disposal

A life cycle approach and supply chain collaboration are vital to achieving shared sustainability goals.

Social Dimension

Sustainability also encompasses social responsibility, which is central to industrial reputation and license to operate. Social sustainability is the unwavering commitment to product safety and quality, ensuring that medicines are manufactured to the standards in accordance with GMP requirements. It further entails fostering employee wellness, ongoing training, and career development. Companies play a part in empowering local societies, responsible sourcing, business ethics, and transparent communication that build trust across their value chain.

Economic Dimension

Sustainable economic success in pharmaceutical manufacturing requires an appropriate application of cost efficiency, technological innovation, and risk management. Organizations reduce operational costs by minimizing waste and by enhancing energy and resource efficiency. Adopting new technologies enabled by Pharma 4.0™ is essential for increasing productivity, manufacturing flexibility, and accelerating time to market. Proactive risk management is fundamental, as it allows companies to manage regulatory, environmental, and supply chain risk to maintain sustainable business continuity and competitiveness.

PHARMA 4.0™ PILLARS: THE DIGITAL TOOLKIT FOR SUSTAINABLE MANUFACTURING

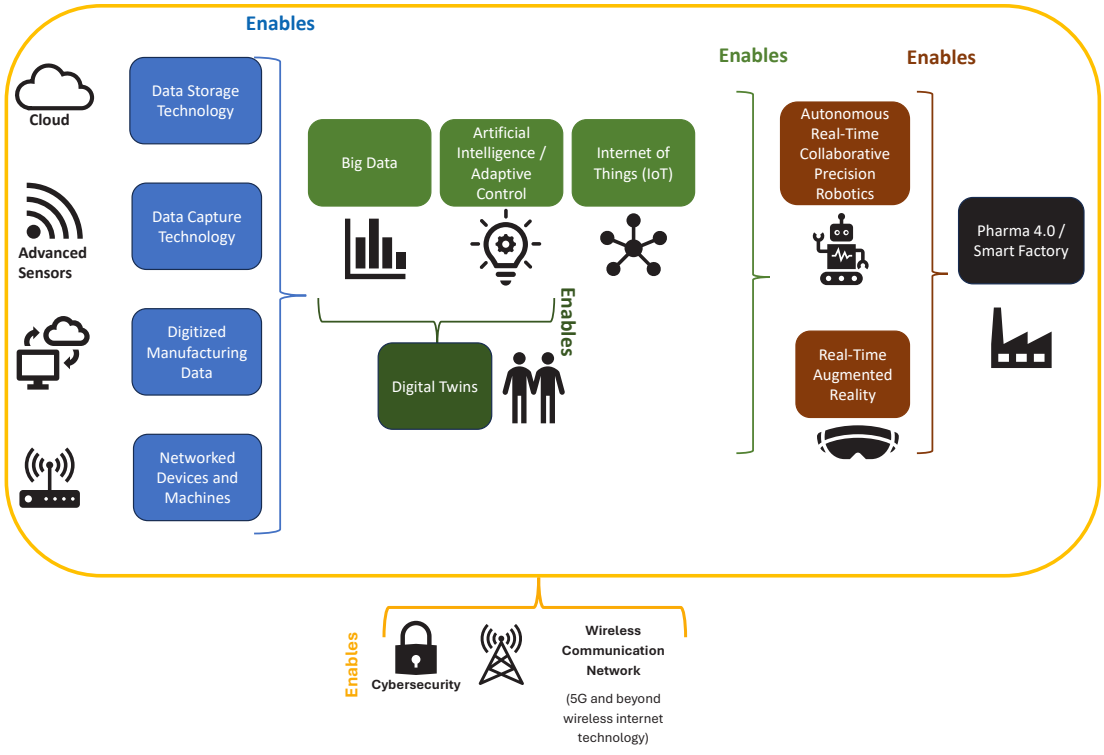
The harnessing of Pharma 4.0™ technologies (see Figure 2) is transforming pharmaceutical manufacturing and establishing a solid digital foundation for sustainability, resilience, and operational excellence. Leveraging real-time data, advanced analytics, and intelligent automation, pharmaceutical manufacturers can achieve significant gains in resource efficiency, reduce waste, and increase traceability throughout the value network, which are key outcomes that align with both sustainability goals and business performance.

Modern pharmaceutical facilities deploy advanced spectroscopic sensors, flow meters, noninvasive retrofits, and vibration or acoustic monitoring tools. By networking these smart sensors via the Industrial Internet of Things (IIoT), manufacturers are enabled with real-time data on their process parameters, machine condition, and ambient conditions. This data enables the rapid identification and correction of inefficiencies at the equipment or process level. Real-time resource usage monitoring enables instant corrective actions and strategic resource management. In addition, predictive maintenance algorithms, process vibration, and acoustic data from equipment are used to predict component failure before it occurs and to minimize downtime.

Smart Sensors and IIoT

Eli Lilly built a lean IIoT-based qualified building management

Figure 2: Pharma 4.0™: Technology enablers [7].



system (QBMS) that connects environmental sensors (temperature, pressure, humidity, CO_2, doors) through a Turck Excom remote input/output (I/O) into the AVEVA PI system, which standardizes tags, limits, alarms, and dashboards. Real-time alerts and clear visuals help teams catch excursions fast, stay audit-ready, and avoid heavy distributed control systems (DCS)/supervisory control and data acquisition (SCADA) complexity. This architecture cut project delivery costs by about 25% and reduced energy use by removing extra controllers and servers and by preventing energy-intensive recoveries after excursions [3].

AI and Machine Learning

AI and machine learning (ML) are changing pharmaceutical production through smarter process development, dynamic process control, and sustainable practices. Such technologies can quickly identify reaction conditions, media formulations, and scale-up parameters, saving experimental resources. On-the-fly adaptations of process parameters within the design space are used to achieve uniform quality and save energy, solvents, and materials. AI-powered analytics also aid in the choice of greener solvents, catalysts, and cell culture conditions, directly reducing the process mass intensity and hazardous waste generation. Through AI and ML technologies, pharmaceutical and biotechnology manufacturers increase the efficiency of their operations while minimizing environmental impact.

Pfizer used AI and ML learning to optimize the manufacturing of Paxlovid by analyzing supply chain data and dynamically adjusting process parameters, which reduced the cycle time of a critical production step by 67% and enabled 20,000 extra doses per batch. This initiative demonstrates how AI can drive smarter process development, real-time process control, and more sustainable use of resources in pharmaceutical production [4].

Digital Twins

Digital twins are real-time virtual models of physical assets, processes, or entire facilities. Integrating real-time sensor data, historical process information, and predictive analytics, a digital twin simulates and optimizes operations over the life cycle. This method leads to a first-time-right process design, reducing physical trial execution. Digital twins facilitate rapid process debottlenecking and adjustments to variability or demand fluctuations. Strong simulation capabilities enable rapid validation, support management of changes, and provide compelling evidence for regulatory submissions.

Sanofi used the VirtECS digital twin platform to rapidly analyze how to fit a new biologics product into an existing manufacturing facility, allowing them to simulate integration scenarios and accurately assess plant capacity and operational constraints. This digital twin approach reduced the time needed for facility fit analysis from weeks or months to just a few days, enabled precise planning for tech transfer, and minimized disruptions to ongoing operations. As a result, Sanofi accelerated time to market, avoided the expense of building a new facility, and maximized output from existing resources [5].

Advanced Analytics and Blockchain

Advanced analytics platforms deliver deeper insights into supply chain performance, life cycle greenhouse gas emissions, and logistics efficiency, enabling continuous improvement in sustainability. Blockchain technology provides immutable ledgers that authenticate green credentials, renewable energy certificates, and ethical sourcing claims. This transparency builds trust among stakeholders and regulators. In addition, smart contracts supported by blockchain automate vital functions of the supply chain, such as waste management, cold chain assurance, and logistics optimization. These technologies minimize manual intervention and incentivize sustainability, driving continuous improvements in supply chain sustainability and compliance.

Johnson & Johnson employs blockchain to create immutable, transparent ledgers across its supply chain, authenticating green credentials such as renewable energy certificates and documenting ethical sourcing claims. This approach boosts regulatory and partner trust by providing verifiable and tamper-proof sustainability records [6].

The vision of a sustainable pharmaceutical factory is becoming a reality, through the strategic integration of Pharma 4.0™ technologies, robust regulatory standards, and leading sustainability practices.

INTEGRATING PHARMA 4.0™, REGULATORY FRAMEWORKS, AND BEST PRACTICES

The vision of a sustainable pharmaceutical factory is becoming a reality, through the strategic integration of Pharma 4.0™ technologies, robust regulatory standards, and leading sustainability practices. Achieving this vision requires digital transformation and compliance pathways to be aligned, resources to be continually optimized, the adoption of circular economy approaches, and an empowered workforce [2] (see Figure 3).

Harmonizing Digital Transformation with Regulatory Compliance

Pharma 4.0™ solutions significantly enhance compliance by improving traceability, documentation, and process control. Continuous environmental monitoring supports effective deviation management and audits. Digital twins and advanced analytics further facilitate quality by design (QbD) by enabling comprehensive process understanding, robust risk assessment, and optimized control strategies, in line with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q8, Q10, and Q11 [8–10]. The integration of AI and ML within process analytical technology frameworks ensures real-time product quality assurance and reduces batch failures, aligning with U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidance [11, 12].

Regulatory Acceptance, Data Integrity, and Cybersecurity

Regulatory agencies are increasingly supportive of digital transformation, provided that data integrity, patient safety, and product quality are ensured. Initiatives such as the US FDA's Emerging Technology Program [13] and the EMA's Digital Transformation Plan [14] reflect this evolving landscape. Digital systems must adhere to ALCOA+ (attributable, legible, contemporaneous, original, and accurate) principles and regulatory requirements, such as 21 CFR Part 11 [15], with automated data collection and blockchain-based records to enhance data reliability. Robust validation, as outlined in *GAMP® 5 Guide 2nd Edition* [11], and strong cybersecurity controls are essential for maintaining trust and compliance. As manufacturing becomes more connected, the risk of cyber threats increases; therefore, a layered defense strategy, regular vulnerability assessments, and ongoing employee training are critical [11].

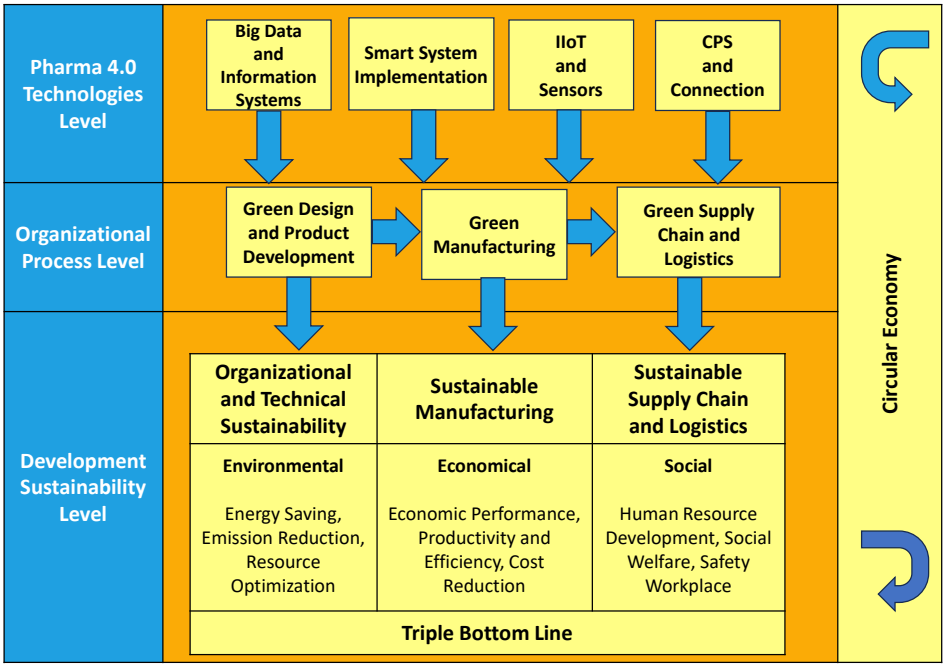
Integrated Approaches to Sustainable Manufacturing

Pharma 4.0™ technologies provide granular visibility into resource consumption, enabling targeted interventions such as dynamic equipment scheduling and process optimization to minimize energy and material use. Transitioning from batch to continuous manufacturing streamlines production, reduces downtime, and enhances resource efficiency by reducing waste associated with batch start-up and shutdown. The implementation of green chemistry principles, such as solvent recovery and the use of safer reagents, further reduces hazardous waste and environmental impact. Additionally, many facilities are investing in on-site renewable energy and purchasing renewable energy credits to support net-zero goals.

Circular Economy Initiatives

Digital platforms now track materials throughout their life cycle, supporting reuse, recycling, and take-back programs that are vital for addressing scope 3 emissions. Practices such as solvent recovery roles and by product repurposing are increasingly common. Advancements in smart packaging processes (for ease of tracking and recycling) can help cut down on landfill waste and support circular processes, further reinforces sustainability and compliance.

Figure 3: Integrating Pharma 4.0™ technologies with sustainable pharmaceutical manufacturing: A multilevel framework [7].



Workforce and Culture Transformation

A successful transition to sustainable and compliant manufacturing depends on workforce development and cultural transformation. Companies are investing in upskilling their staff in data analytics, process optimization, and sustainability best practices. Effective change management and cross-functional collaboration between the quality, engineering, sustainability, and operations teams foster innovation and accelerate the adoption of integrated solutions. Continuous improvement is embedded through regular audits, feedback loops, and innovation cycles, ensuring that green manufacturing practices evolve alongside regulatory and technological advancements.

CHALLENGES AND SOLUTIONS

Although Pharma 4.0™ offers significant potential for advancing sustainable pharmaceutical manufacturing, its successful implementation is often challenged by legacy infrastructure, data integration complexities, workforce skill gaps, and regulatory uncertainty. Overcoming these barriers requires a coordinated strategy that combines technological innovation, organizational development, and proactive regulatory engagement [16, 17].

Legacy Infrastructure

Many pharmaceutical plants still rely on legacy equipment and systems that were not originally designed for digital connectivity or data-driven optimization. Such assets hinder the adoption of smart sensors, advanced analytics, and integrated control systems. Addressing this challenge involves digital retrofitting, which entails deploying sensors, wireless transmitters, and edge computing devices to capture critical data from existing assets without major capital investment.

A phased transformation approach, prioritizing high-impact areas such as energy-intensive processes or critical utilities, allows organizations to demonstrate their value before scaling up. Hybrid architectures that integrate legacy systems with modern platforms using middleware and standardized protocols (such as the Open Platform Communications Unified Architecture) enable a gradual, manageable migration to a fully digital ecosystem.

Data Integration

The rapid proliferation of digital devices and platforms has resulted in data silos and increased cyber risk. Ensuring data integrity, confidentiality, and regulatory compliance (such as US FDA 21 CFR Part 11 [15] and EU Annex 11 [18]) is essential in this regard.

Solutions include adopting open data standards and robust integration frameworks to enable seamless data exchange across different systems. Cybersecurity must be embedded by design, with multilayered strategies such as network segmentation, encryption, real-time monitoring, and regular vulnerability assessments. Effective data governance—establishing clear policies for data ownership, access control, and audit trails—supports regulatory compliance and builds digital trust.

Workforce Skills Gap

A digital, sustainable manufacturing paradigm requires a mix of expertise in data analytics, AI, green chemistry, and circular

economy principles. The industry faces a shortage of talent with these combined skill sets. Addressing this gap requires targeted upskilling programs for existing staff, focusing on digital literacy, data-driven decision-making, and sustainability best practices. Collaborative learning initiatives with academic institutions, technology providers, and industry consortia can help co-develop relevant curricula and provide hands-on training. The strategic recruitment of new talent with expertise in digital transformation, environmental science, and process optimization is also critical. Notably, several leading firms have established "digital academies" and sustainability leadership programs to accelerate workforce transformation and foster a culture of continuous learning.

Regulatory Uncertainty

The pace of technological change can outstrip the evolution of regulatory frameworks, creating uncertainty regarding the acceptability of new digital tools, data sources, and sustainability claims. Proactive engagement with regulators through open communication about digitalization plans, pilot study results, and sustainability initiatives can help clarify expectations. Participation in regulatory pilot programs and innovation "sandboxes" offers opportunities to test new technologies in controlled and compliant environments. Industry collaboration is essential for advocating harmonized, forward-looking regulatory guidance that supports both digital and green innovation can be achieved with engagement in local ISPE Chapters.

CONCLUSION

The pharmaceutical sector transition toward net-zero emissions is accelerating, driven by ambitious corporate commitments, evolving regulatory frameworks, and rapid technological advances. Forward-looking manufacturers are moving beyond incremental improvements, adopting an integrated strategy that blends renewable energy, Pharma 4.0™ digitalization, and collaborative supply chain management to achieve sustainable outcomes.

Manufacturers are increasingly adopting renewable electricity at production sites, significantly reducing scopes 1 and 2 greenhouse gas emissions and setting new standards for decarbonization. At the same time, addressing scope 3 emissions has become a top priority. Companies are collaborating with suppliers to improve environmental performance, deploying digital tools for real-time emissions tracking, redesigning products and packaging for lower life cycle impact, and investing in green chemistry and alternative materials to reduce downstream emissions [19].

The adoption of Pharma 4.0™ technologies becomes central to this transformation. They enable the end-to-end supply chain visibility, demand forecasting, resource optimization, and waste

Our Innoweightion.
Your Progress.

New Scales Series MiNexx®

Discover the award-winning MiNexx® indicators: Combined with its weighing platforms or Minebea Intec load cells, MiNexx® covers almost any application imaginable. GMP compliance guarantees complete, traceable records. NSF certification ensures hygienic processes.

Boost efficiency and protect your brand reputation: Stay ahead in every step of your production.



NSF

reddot winner 2025
interface & user experience design

SCALE NOW

Minebea Intec GmbH
Meiendorfer Strasse 205 A
22145 Hamburg, Germany
info@minebea-intec.com
www.minebea-intec.com

Minebea intec
The true measure

minimization while supporting regulatory-compliant traceability and reporting. Regulatory agencies like the US FDA, EMA, and ICH are increasingly incorporating digitalization and sustainability considerations into guidance.

Realizing the full potential of sustainable pharmaceutical manufacturing in the Pharma 4.0™ era demands coordinated, deliberate action by industry stakeholders. The following priorities are recommended:

- Strategic investment in digital infrastructure: Implement advanced data acquisition, analytics, and automation platforms to enable real-time process control, regulatory-compliant traceability, and continuous improvement in resource efficiency.
- Integration of sustainability into governance and operations: Embed environmental and social performance objectives within corporate governance, quality systems, and operational decision-making frameworks to ensure alignment with both regulatory expectations and business performance targets.
- Proactive regulatory engagement: Collaborate with regulatory authorities through participation in innovation programs, pilot studies, and industry working groups to develop harmonized and forward-looking guidance for digital and green manufacturing practices.
- Cross-sector collaboration and knowledge sharing: Use industry platforms, such as ISPE Chapters and technical communities, to exchange best practices, standardize methodologies, and scale proven solutions across the value chain.

The convergence of digital technologies and sustainability principles is redefining pharmaceutical manufacturing, transforming it from a competitive advantage into an operational necessity. As Pharma 4.0™ matures, its integration will be vital to achieving net-zero objectives, improving patient outcomes, ensuring regulatory compliance, and strengthening environmental stewardship. Organizations that embrace this shift with urgency and strategic intent will set the benchmark for resilience, responsibility, and the next era of pharmaceutical excellence.

References

1. Saxena, A., R. Singh, A. Gehlot, S. Vaseem Akram, B. Twala, A. Singh, et al. "Technologies Empowered Environmental, Social, and Governance (ESG): An Industry 4.0 Landscape." *Sustainability* 15, no. 1 (2002): 309. doi:10.3390/su15010309
2. Khan, M., T. Yasmeen, M. Khan, N. Ul Hadi, M. Asif, M. Farooq, et al. "Integrating Industry 4.0 for Enhanced Sustainability: Pathways and Prospects." *Sustainable Production and Consumption* 54 (2005):149–89. doi:10.1016/j.spc.2024.12.012
3. Kishe, M. "Eli Lilly: Innovative Environmental Monitoring: Scalable Solutions with PI System and Remote I/O." Presentation at AVEVA World, San Francisco, CA, 26 April 2025. www.aveva.com/en/perspectives/presentations/2025/eli-lilly--innovative-environmental-monitoring--scalable-solutions-with-pi-system-and-remote-i-o/
4. Pfizer "2022 Annual Review Breakthroughs Changing More than 1.3 Billion Lives." 2022. www.pfizer.com/sites/default/files/investors/financial_reports/annual_reports/2022/files/Pfizer_Annual_Review.pdf
5. VirtECS. "Case Study: How a Biologics Company Uses a Digital Twin to Analyze Facility Fit." Accessed 10 August 2025. https://combination.com/case-study-how-a-biologics-company-uses-a-digital-twin-to-analyze-facility-fit/
6. Gaynor, M., K. Gillespie, A. Roe, E. Crannage, and J. E. Tuttle-Newhall. "Blockchain Applications in the Pharmaceutical Industry." *Blockchain in Healthcare Today* 7 (2024). doi:10.30953/bhty.v7.298. https://pmc.ncbi.nlm.nih.gov/articles/PMC11073477/
7. Arden, N. S., A. Fisher, K. Tyner, L. X. Yu, S. L. Lee, M. Kopcha. "Industry 4.0 for Pharmaceutical Manufacturing: Preparing for the Smart Factories of the Future." *International Journal of Pharmaceutics* 602 (2021):120554. doi:10.1016/j.ijpharm.2021.120554
8. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. "ICH Harmonised Tripartite Guideline Q8 (R2): Pharmaceutical Development." Published August 2009. https://database.ich.org/sites/default/files/Q8%28R2%29%20Guideline.pdf
9. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. "ICH Harmonised Tripartite Guideline Q10: Pharmaceutical Quality System." Published June 2008. https://database.ich.org/sites/default/files/Q10%20Guideline.pdf
10. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. "ICH Harmonised Tripartite Guideline Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities)." Published May 2012. https://database.ich.org/sites/default/files/Q11%20Guideline.pdf
11. International Society for Pharmaceutical Engineering (ISPE). *ISPE GAMP® 5: A Risk-Based Approach to Compliant GxP Computerized Systems (Second Edition).* July 2022. https://guidance-docs.ispe.org/doi/book/10.1002/9781946964571
12. International Society for Pharmaceutical Engineering (ISPE). *Baseline Guide Vol 8: Pharma 4.0™.* December 2023. https://ispe.org/publications/guidance-documents/baseline-guide-vol-8-pharma-40-1st-edition
13. US Food and Drug Administration. Emerging Technology Program (ETP). www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/emerging-technology-program-etp
14. European Medicines Agency. "EMA Strategy on Digitalisation." Presented by Z. Frias, P. Arlett, and H. Hamann, 6th Meeting of the Industry Stakeholder Platform on the Operation of the Centralised Procedure for Human Medicines. 2020. www.ema.europa.eu/en/documents/presentation/presentation-ema-strategy-digitalisation-z-frias-p-arlett-h-hamann_en.pdf
15. US Food and Drug Administration. "Guidance for Industry. Part 11, Electronic Records; Electronic Signatures—Scope and Application." August 2003. www.fda.gov/media/75414/download
16. Sharma, D., P. Patel, and M. Shah. "A Comprehensive Study on Industry 4.0 in the Pharmaceutical Industry for Sustainable Development." *Environmental Science and Pollution Research* 30 (2023):90088–98. doi:10.1007/s11356-023-26856-y
17. Mastrantonas, A., P. Kokkas, A. Chatzopoulos, M. Papoutsidakis, C. Stergiou, A. Vairis, et al. "Identifying the Effects of Industry 4.0 in the Pharmaceutical Sector: Achieving the Sustainable Development Goals." *Discover Sustainability* 5 (2024):460. doi:10.1007/s43621-024-00716-2
18. European Commission. "EudraLex, Volume 4: EU Guidelines for GMPs for Medicinal Products for Human and Veterinary Use. Annex 11: Computerised Systems." Published 2011. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/annex11_01-2011_en.pdf
19. Fernandez, M., and L. Pérez. "Accelerating the Transition to Net Zero in Life Sciences." McKinsey & Company. 11 August 2023. Accessed 8 July 2025. www.mckinsey.com/industries/life-sciences/our-insights/accelerating-the-transition-to-net-zero-in-life-sciences

About the author

Amisha Patel, MS, is an accomplished senior pharmaceutical validation engineer known for her notable technical contributions to the pharmaceutical, biopharmaceutical, and medical device industries. She specializes in sterile manufacturing compliance, process, and equipment and facility qualification. Her expertise combines technical rigor with collaborative leadership to advance best practices in pharmaceutical manufacturing, ensuring alignment with global regulatory standards. She holds an MS in pharmaceutical manufacturing engineering from Stevens Institute of Technology, including certifications in pharmaceutical manufacturing practices, validation, and regulatory affairs.