ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: https://ijrps.com

Challenges and Research Opportunities faced in Pharma Industries: 4.0

Om Prakash Goshain*, Satish Kumar Sharma

Department of Pharmaceutical Chemistry, Glocal School of Pharmacy, Glocal University, Mirzapur Pole, Saharanpur-247121, Uttar Pradesh, India

Article History:

Received on: 21 Oct 2020
Revised on: 21 Nov 2020
Accepted on: 23 Nov 2020

Keywords:

Industry 4.0,
Pharmaceutical Supply Chain,
Smart production framework,
Sustainability

ABSTRACT

The use of new technology from Pharma Industry 4.0 promotes sustainable production of value, makes pharmaceutical industry more flexible, clever and customized and thereby helps pharmaceutical companies to achieve economic benefit in long term. The present review discusses about the implications caused in enhancing pharmaceutical production and also investigate that how industry 4.0 aids in increasing the production. The review also discusses about the challenges faced by pharma industries 4.0 and addresses research opportunities faced in pharma industries 4.0. From the review it was observed that, main barriers which come in the way of increasing the production are high cost, time consuming design and framework development, seniors unsupportiveness, lack of good training skills, inadequate business inducement, lack of co-operation and communications. Further it was observed that, smart production system has led to the development of the increased production, but still difficulties and impediment to smart production should be considered in order to achieve expertize in supply chain managerial and sustainable practices.

*Corresponding Author

Name: Om Prakash Goshain
Phone: 9958166931
Email: omprakashgoshain@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v11i4.4028

Production and Hosted by

IJRPS | https://ijrps.com

INTRODUCTION

Industry 4.0 contemplate plants and production lines in which materials and machinery were linked to internet, wherein they communicate, share, collect and interpret data along with process alignment within distributed environment mode (Branke *et al.*, 2016). This unified data-driven framework would make the manufacturing process more reactive and make future plants more versatile. It stems from many influential emerging innovations: primarily, computer chips, sensors are getting increasingly smaller, fewer, and costly, enabling them to be incorporated within more equipment and products too. Secondly, wireless networking is all-embracing and enables virtual connection to the internet, fluttering the barrier among digital world and physical one, enabling direct and autonomous networking between devices and goods. The Industry 4.0 (I4.0) refers to fourth industrial revolution towards manufacturing of technical developments like digitization, robotics and other innovative production methods are being modified by artificial intelligence (Marr, 2002). I4.0 is often referred to as smart production, intelligent internet, or the "integrated market." I4.0 is also used as an integral feature of transition that is recently taking place in corporate sector is closely linked with different mega-trends, both historically and organizationally, like digitization, cloud computing and Internet of Things (Hofmann and Rüsch, 2017).

Together, such technologies enable development and sharing of decentralized, smart and customized

frameworks that gather and share information at an insane extent. Moreover, combination of other technical developments, like big data that allows even small businesses to scalable, large data processing that allows huge data to be managed and analyzed in real time, and quantum computing that enables devices to respond and adapt and enables one to have a powerful combination that transforms and contributes to a modern level of industrial processes (Douaioui *et al.*, 2018).

Industry 4.0 began as German effort, and given its title, after advent of steam engines, mass manufacturing, electronics, and IT sectors as its proponents saw it as fourth industrial revolution. Subject gathers traction worldwide and related ideas are recognized as 'Smart Factory,' 'Mordenized Manufacturers' or rather 'cyber-physical networks' and 'Internet of Things' not restricted to industrialized processes (Kagermann *et al.*, 2013).

Industry 4.0's features include self-organization wherein semi-finished products are contained within ground and evaluating it's processing efficiently with computers. Such scenario is really good for manufacturing since it intends to tailor mass cheaply and efficiently. Industries 4.0 possess some other beneficial features as well, some of which are discussed below (Rossit *et al.*, 2019).

Features of Industry 4.0

Industry 4.0 is able to regulate real time by generation of digitalized real time images of complete physical manufacturing becomes easy by aggregating the gathered data in a centralized manner. This subsequently leads to transparent production thereby offering immense opportunities to monitor, supervise and control current as well as farther locations.

It also maintain built in wherein, intelligent production lines continuously track and may alert relevant staff rapidly if problems are acknowledged or predicted or several problems are also resolved. Machines can predict optimal intervals of operation and replace autonomous parts. Self-organized systems of production that can make smart decisions are far more versatile and decentralized and respond to production systems operated centrally.

The pledges are much more suited for evolving demands or other unpredictable events as malfunctioning of the computer. Moreover, industry 4.0 is able to co-ordinate with the supply chain by carrying goods supply chain knowledge and a more integrated approach, and also connect and share end-to-end data and enable much better communication across the supply chain. Industry 4.0 implies that each goods give a single descriptor and can track all details about their manufacturing process. This will make it possible to make quality assurance more productive and help fast in identifying development process concerns.

This is significant, too for Quality by Design Phase (QbD) requirement. Products linked to Internet would not only coordinate to organize the development, but will also permit naive product functionality and new company for enhanced customer services templates. This involves the supply of "in-use" products information back to producer so that the commodity can be enhanced.

US, Japan and China have successively introduced their own Industrial Revolution proposals, since idea of Industry 4.0 was introduced within Germany around 2011 (de Campos *et al.*, 2017). The four main components of industry 4.0 include the "Internet of Things (IoT)", the "Internet of Services" (IoS) and "Cyber-physical Systems" (CPS). IoT is 'physical object network,' where most common techniques of recognition includes Radio-Frequency Recognition (RFID), Wireless Sensor networks (WSN) (Barreto *et al.*, 2017).

Centered on IoT technology and a near range of sensors, actuators as well as other instruments, both within and externally across whole of enterprise, CPS combines physical and cyber systems and thus offers smarter, more open and more effective knowledge sharing action (Barreto *et al.*, 2017). Such technologies help businesses create deeper, closer and versatile relations in development and therefore create value chains enhancement (Branke *et al.*, 2016).

It should be noted that enhancing medicines accessibility is a key factor. Pharmaceutical business liability since drugs are unique Goods — these goods directly affect patients ' life (Nematollahi *et al.*, 2018). Apart from available goods, conventional batch processing has more extreme environments effects on air pollutants, chemical contaminated matter, solid waste and polluted waste, with a contrast to more versatile and effective continuous manufacturing, which needs a lower usage of raw materials and also reduced risk solvency (Stegemann, 2016).

The "second highest" greenhouse gas emission source emerging energy costs, climatic changes impacts and stringent regulations had led the pharmaceutical industries concentrated more over usage and emissions decrease of pharmaceuticals over the whole life cycle (Nematollahi *et al.*, 2018). Other players throughout pharmaceuticals supply chain, particularly manufacturers, healthcare professionals, hospitals and alike, should develop its services

and innovations, including technology from smarter distribution and customized drug treatments, in order to fulfill the requirements of Pharma 4.0. This provides viable solution through suitable technologies like Auto-ID tags, intelligent cars, patient-centers sharing of knowledge, cloud computing, advanced analytics and alike (Campbell, 2017).

However, widening of pharmaceuticals industry conception to incorporate a range of other problems, like more human participation, end-to-end cooperation, sustainable concerns, stability and devastating effects, from manufacturers' alone, some errors may exist. This review highlights the challenges faced while implementing the industry 4.0 within Pharmaceutical supply chain (PSC) and also highlights what methods can be adopted to overcome the same. The review methodology involves sample selection, challenges faced by stakeholders while implementing Industry 4.0 and finally, the steps taken to overcome that. The main aim of the literature review involves integrating the historical and contemporary results of a certain domain by means of systematic and new interpretations.

Pharmaceutical supply chain (PSC) consists of primary producers, secondary manufacturers, insurers/wholesalers of logistical and medical facilities, as well as retail facilities (Savage *et al.*, 2006; Bals and Tate, 2016). In this segment, the agreements and arrangements of sustainability PSC is defined in four phases: manufacture, logistics, procurement and usage within healthcare sectors and domestic waste disposal, along with how industry 4.0 technology is implemented. In the present section, recent implementations of PSC is defined in four phases: manufacture, logistics, procurement and utilization in healthcare fields and domestic waste disposal, along with how smart manufacturing technology is implemented. As the pharmaceutical industry is becoming increasingly active in the procurement of pharmaceutical manufacturing and related facilities in developing countries (Schneider *et al.*, 2010; Zhang *et al.*, 2017).

Until manufacturing, pharmaceutical companies should choose the supplier and industrial base which value climate and social obligations of the most appropriate raw materials and pharmaceutical additives (Xie and Breen, 2014). Enyinda et al. and Low et al. also propose a system of analytic hierarchy (AHP) for choosing the most relevant suppliers and subcontracted producers in order to quantify environmental effects incurred by providers or production sites. It also allows everyone to select regulatory (Social Responsibility) and ecological (GHG-emissions) enforcement, besides the conventional requirements of cost, efficiency, service, financial reporting, etc (Enyinda and Tolliver, 2009). Environmentally effective, ISO 14000 certified suppliers can reduce environmental risks associated in purchasing of raw materials.

ISO14001 is not only criterion to determine whether business is nice to the world or not. Since certificate ISO14000 is Voluntary Standard, in developed countries, several drug companies chose to receive ISO14000 (Li and Hamblin, 2016). Except for the "green" element, through growing supplier investments production (direct or indirect) and supplier management to meet this requirement. This helps the pharmaceutical industry to boost social responsibility efficiency in its ethical business practices (Lee *et al.*, 2015; Rossetti *et al.*, 2011). First and foremost, focus company (manufacturer), which ensures that operations of suppliers are compliant with ethical and responsible practices, must have standard operating procedures (SOPs) as guideline and specifications.

Then audits were performed on an unscheduled and scheduled basis to examine possible hazards promptly and also to determine appropriate correctives. In addition, strategic cooperation allows suppliers to enhance their service and administration to meet corporate social responsibility (CSR) requirements of focal enterprises. But, in light of dominant role of focal system in the drug industry, this form of partnership is not much successful. In addition, training is too necessary in order to enhance transfer of information CSR output of suppliers, that can be done in combination with promotions or benefits to promote them (Zhang *et al.*, 2017). It is necessary to estimate burden within production processes after selection of suppliers and production plants. In particular, three primary pharmaceutical manufacturing phases are involved: development of active pharmaceutical ingredients (API), key component and secondary packaging.

As reported, the new industry-based technologies 4.0 make it possible for pharmaceutical producers to enhance from batch-centered mass manufacturing to agile manufacturing, smart, efficient and patient oriented, with near and online value control, where materials are constantly loaded into the framework while product is being continuously loaded (Lee *et al.*, 2015). This means that once a digitalized prescription has been obtained from hospital, or pharmacies, customized manufacturing processes may be applied through the development of combined drug schemes for particular populations or indeed "zero latency" real time development, for individual demands (Stegemann, 2016). The layout of entire

production process should also be transformed to take future developments into account.

The stringent regulations and immensely complicated implementation of naive drugs which will be introduced within the market, before they are licensed at regulatory level it is important to validate entire manufacturing procedure (i.e. processing methods, solvents, APIs, additives, paper products, quality assurances, etc.). In view of this, guideline of ICH Q8 (R2) cooperatively with other paper of FDA stresses that pharmaceutical manufacturers must reserve "design room" in which changes (for example, environmental sustainability) in response to production disruptions may be treated to ensure quality avoiding cost and labour intensive regulatory recertification after approval. As previously pointed out, the drug companies is still focused on an unknown batch method. Process Analytical Technologies (PAT) incorporation of Industry 4.0 offers a viable solution. In view of certain manual methods in conventional pharmaceutical industries, Industry 4.0 technology can boost productivity and quality in the manufacturing of drugs which may reduce human uncertainty errors and handle external factors quite effectively (e.g., sterility, particles etc.).

As previously pointed out, the drug companies is still focused on an unknown batch method. Process Analytical Technologies (PAT) incorporation of Industry 4.0 offers a viable solution. In view of certain manual methods in conventional pharmaceutical industries, Industry 4.0 technology can boost productivity and quality in manufacturing of drugs which may reduce human uncertainty errors and handle external factors quite effectively (e.g., sterility, particles etc.). When APIs or several other components do not meet quality requirements, they may be rejected before movement to downstream workstations with regards to conventional lot production (Lee *et al.*, 2015). Nevertheless, if same thing happens in continuous phase of output, the subsequent steps would be interrupted. The design room has somewhat broken the conventional position of oversight and is enabling pharmaceutical companies to develop quality control continuously.

The implementation of Pharma 4.0 is well beyond basic process control compared to traditional quality control approach focused on automatic process control (APC). Pharmacological logistics also faced many issues in terms of sustainable development some of which includes: The socially anxious members should guarantee that complete service levels for the prevention of future inventory outs (Nematollahi *et al.*, 2017; Borumand and Beheshtinia, 2018). Maintain high inventories for wholesalers and distributors and thus obstruct tight logistics. Thus, the SC administrators, governments or NGOs must have a payout which, while participating in social commitment — activities that will at least preserve the advantage of PSC members. Cross-border collective decision-taking increases drug access, rather than necessarily benefits (Nematollahi *et al.*, 2017).

DISCUSSION

Sustainable management of pharmaceutical supply chain remains a niche field for pharmaceutical academics and supply chain operators alike. The use of new pharmaceutical technology 4.0 allows sustainable value development and makes the pharmaceutical industry more flexible, seamless and customized. After conducting the survey of above cited papers it was observed that few of them have been published in business journals but no significant studies have been published in pharmaceutical journals. To date matter is still limited subject for pharmaceutical scientists, as topic has not yet been discussed by majority of supply chains and pharmaceuticals outlets despite their realistic relevance. Eighty per cent of the papers chosen in present research based on a case-study approach which depicts comprehensive understanding of complex dynamics and helps develop more hypotheses. This is still underexploration in emerging research.

Correlational information from the surveys or interviews is 20% of report. The three papers concentrate on conceptual context: holistic quality management in production process (Herwig *et al.*, 2017) logistics (Kumar *et al.*, 2008) and PSC green culture (Xie and Breen, 2012). In relation to modelling approach, eleven papers include qualitative or quantitative frameworks for successful PSCs. Explicitly, two researchers have utilized a casual-loop approach to understand links among price, quality, costs and reverse supply, but two research studies (Weraikat *et al.*, 2016) have developed coordinating frameworks to improve the effectiveness of the chosen suppliers and analysis methods for their suppliers (Enyinda and Tolliver, 2009). Nevertheless, only one of them performed a systematic research reversal of logistics, while others examined different ways without screening mechanisms of literature, studies as well as different secondary information.

In effort to stop counterfeit medicines and thus check the effectiveness of drugs, RFID is an identifiable technology utilized in the PSC, particularly when reminder and return are producers and dealers Drugs. There are two dimensions to the acces-

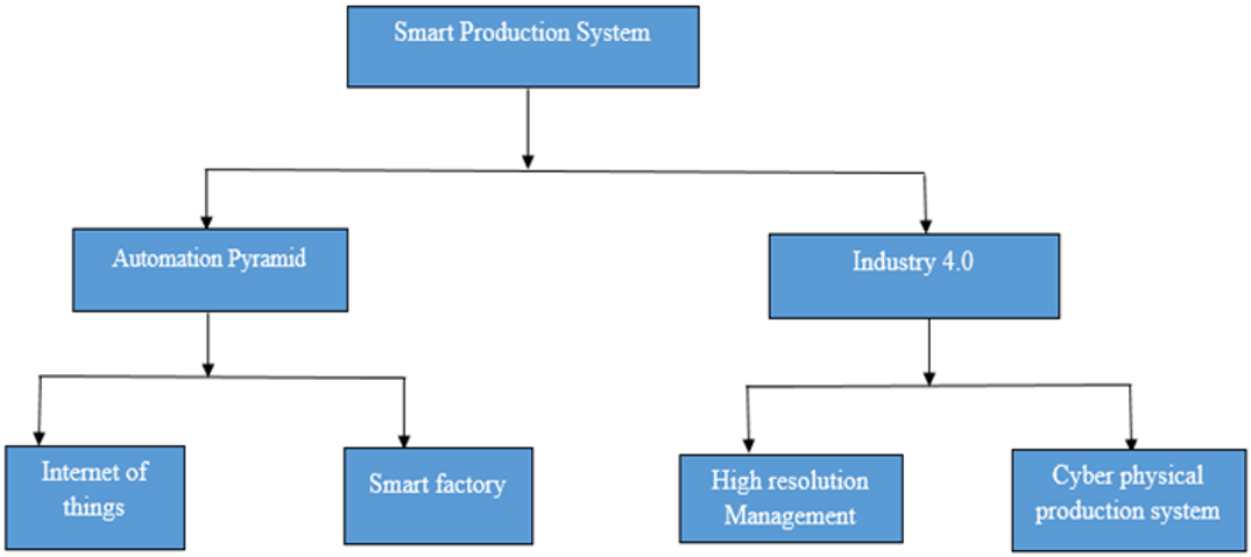

Figure 1: Methods under smart production system. The figure represents two methods (I) Automation pyramid, (II) Industry 4.0

sibility of medicines. Primary includes, subsidies, markets and donations may be circulated and reused by those unable to pay high prices for such expired medications during their shelf lives. Secondly, a sustainable procedure by correctly changing the dosage will significantly help minimize patients' costs.

In terms of usability, cooperation and innovative approaches across the supply chain may insure minimum needed drugs services without stock-out. Finally, the reasonable selection of medication dosage and personal tracking devices may reduce the number of intertwined adverse effects with regard to prescription drugs. At same period, proper waste management will avoid detection of bystanders without purpose. With the exception of certain four areas, new infrastructure, like crops or supplier centres, will provide more working prospects enhance regional developmental rate but some common social problems, like decent work and jobs, human rights, gender equalness and education, are also listed in other sectors. None of these articles addresses individual organizational relations, working conditions, social participation, housing, welfare, psychosocial health, etc.

The high material to waste levels in the pharmaceutical industry attracts considerable environmental safety and emissions, research interests and reduce and control waste. In order to minimize waste disposals and develop environmental protection framework, there exist a greater requirement to consider the emissions generated by the production process (Luthra *et al.*, 2017). New technology-equipped pharma companies will dramatically reduce GHG emissions, use of electricity, and waste water in continuous manufacturing. Improving the handling of raw materials and by-products. At about same time, manufacturers can monitor entire product life duration from root sources by evaluating suppliers which conform to environmental policies.

It is indeed worth noting that packaging of pharmaceutical products should also strive to raise consumer awareness, not only to concentrate on recycled, light-weight and sustainable content, but to reduce drug waste. Finally, release of APIs into the atmosphere, particularly release of APIs through pee or sweat glands, sewerage releases and drainage of waste from sites, is a big concern for customers' end-consumption. Those environmental issues are addressed by drug-take-back services and sustainable prescribing. It is clear that in light of regions, developed nations are placing much greater focus on ensuring in PSC than developing economies. In view of fact that enforcing PSC activities requires extremely costly expenditure and long-term retaliation, there still is a considerable distance for underdeveloped nations to go in prospective. While companies have considered sustainability, the shortage of rewards of government-focused tax reductions or reimbursements hinders pharmaceutical firms from participating in constructive sustainable development programmes.

Through carrying out various practices, PSC firms and other players are preventing the regulatory authorities from enforcing possible penalties on emissions, pharmaceutical issues, counterfeiting, inappropriate waste medicinal disposal, and so on.

Furthermore, producers benefit from selling unused medicines on subsidies markets. But they are far less than adequate. As visualized in green production processes like low-carbon emission machinery, waste water management, or process advancement, sustainability strategies are typically long-term. The shortage of monetary incentives, provided no payback period, decreases infrastructure investment, for example in combustion plants, identification centres, distribution centres and information systems, and also limits the scope of cooperation across the various sectors, particularly as regards medicinal reverse logistics.

In industries and organizations, competitive rewards are highlighted the fact that the above listed obstacles are not obliged or encouraged to participate entirely in viable PSC operations for final users and GPs, healthcare professionals or physicians. Finally general public, like general practitioners, retail agency staff, GPs and health professionals which were engaged directly in downstream distribution networks must become more informed of the value of sustainable growth. Last but not least, Pharmacies and consumers should, for example, concentrate more on eliminating emissions instead of minimizing pollution. GPs, doctors or pharmacists should also take part in the function of prescriptions and should educate patients about disposal of clinical remains properly as well as of encouraging them to remove expired medicines, as these are first level of PSC and first immediate point of touch for patients.

Backward knowledge through end-users, will strengthen relationship between retailers and consumers. In addition, environmental issues may be incorporated into medical experience to raise understanding of green procurement strategies. Complex processes at any hierarchical level, high product diversity and shorter product life cycles involve deep awareness and ongoing relationships with consumers, partners and stakeholders of all forms. Therefore, it is important to use capital efficiently from the perspective of globalization and increasing competitive pressures.

Industry 4.0 becomes a big data challenge in the processing of data through source abundance wherein the method of smart manufacture is integrated into production (Zuehlke, 2010). Viable countermeasures to resolve growth and output capacity of intelligent production framework therefore need to be introduced. Sustainable factors such as this should include technological, economical, environmental and social research using protective measures similar to those in EIA (Ott *et al.*, 2012). Therefore, e the following important considerations must be considered: helpful or harmful, reversible in nature or irreversible, repairable by management or irremediable, transient or constant, in shorter or longer term. Whilst EIA addresses the effect of project over social and environmental consequences over a span of between 6 to 20 years, where sustainability evaluation of smart production framework is required to analyze all main impacts over duration of one to 6 years as a result of expeditious field growth. Most importantly, such sustainable elements can possess greater influence on themselves, but in combination with different elements. For example, many researchers considers these impacts to be directly or indirectly linked and therefore devices are becoming shrewd and eventually take lower-tech work, a socially and technologically sustainable element which can be affected.

These employees could then be qualified to fill the jobs of aforementioned intelligent devices. The environment would not profit from production processes that manufacture goods that are exported internationally may be socially and economically viable feature. One technical and economic problem could be, cost of initial implementation and consequently risk is simply not economically useful for business. Another indirect impact, technological and environmental, may add stress to the natural resource and then sustain economic viability.

Requisite of an organization for using smarter production system

For smarter production system, following methodology should be adopted in order to enhance the production of the pharmaceutical products within the manufacturing units: Figure 1, represents the methods under smart production system.

Steenkamp defines procedure of implementation as an approach, where hardware architecture should first provide a strong base for software deployment (Dukalski *et al.*, 2017). The Machinery aspect involves Internet of Things to a degree in which shop floor consists of smart and intelligent machinery along with machine communication capability thereby providing the intelligent facility. Afterwards, a coordination and data collection process for such initiative must be developed in order to generate details at highest managerial levels including the managing manufacturing framework and enterprise resource planning systems.

Although smart production system is coherent in relation to increased production but still faces some barriers towards smart production. Many Subsequent software implementation might begin, which in combination with cyber-physical produc-

tion framework will involve a higher-resolution managerial framework forming basis of Industry 4.0. Therefore, at such stage the smarter system can be connected to smart service extent of performance and thus be turned into a smarter system of output (Dukalski *et al.*, 2017).

The lack of IT awareness amongst employees remains one of primary obstacles (Gnann and Plötz, 2011). Staff must possess solid IT skills throughout every area of intelligent factory. Workplace training is necessary to go all out to teach relevant abilities and appreciation of emerging technologies among workforce. Another challenge is that significant investments are often needed for the implementation of intelligent production frameworks. Investment volume can be greater than that produced through improvements in medium terms. Smarter technologies may especially be restricted to smaller and medium-sized enterprises (Wischmann *et al.*, 2015). IT protection is among the main concerns for the complexities of intelligent production frameworks. Organizations are utilized to maintain their confidential information as secure as possible and many of them feel serious about the idea of bringing the information into a cloud for output. In order to better secure sensitive data from surveillance, theft, malware, bugs or extremism, IT surveillance companies must build advanced technologies.

CONCLUSION

Smart Production framework strategy promises extensive changes at all business levels. Industry 4.0 evolution increases the pharmaceutical industry's competitiveness. During continuous output, material usage, energy use and GHG emissions can be minimized, resulting in increased commitments to security of the climate. Finally, IoT, CPS and Big Data analytics allow supply chain staff to take more independent decisions, particularly for people who serve in procurement without sufficient expertize in supply chain managerial and sustainable practices.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

REFERENCES

Bals, L., Tate, W. 2016. Implementing Triple Bottom Line Sustainability into Global Supply Chains. page 396. Routledge.

Barreto, L., *et al.* 2017. Industry 4.0 implications in logistics: an overview. *Procedia Manufacturing*, 13:1245–1252.

Borumand, A., Beheshtinia, M. A. 2018. A developed genetic algorithm for solving the multi-objective supply chain scheduling problem. *Kybernetes*, 47(7):1401–1419.

Branke, J., *et al.* 2016. Industry 4.0: a vision for personalized medicine supply chains? *Cell and Gene Therapy Insights*, 2(2):263–270.

Campbell, R. 2017. Pharma to table: 3-D printing and the regulatory future of home remedies. *Conn. L. Rev. Conntemplations*, 49:1.

de Campos, E. A. R., *et al.* 2017. Reverse logistics for the end-of-life and end-of-use products in the pharmaceutical industry: a systematic literature review. *Supply Chain Management: An International Journal*, 22(4):375–392.

Douaioui, K., *et al.* 2018. The interaction between industry 4.0 and smart logistics: concepts and perspectives. pages 128–132. International Colloquium on Logistics and Supply Chain Management.

Dukalski, R., *et al.* 2017. Portable Rapid Visual Workflow Simulation Tool for Human Robot Coproduction. *Procedia Manufacturing*, 11:185–197.

Enyinda, C. I., Tolliver, D. 2009. Taking Counterfeits out of the Pharmaceutical Supply Chain in Nigeria: Leveraging Multilayer Mitigation Approach. *Journal of African Business*, 10(2):218–234.

Gnann, T., Plötz, P. 2011. Status Quo und Perspektiven der Elektromobilität in Deutschland. *Working Paper Sustainability and Innovation*, pages 1–55.

Herwig, C., *et al.* 2017. A holistic approach to production control. *Pharmaceutical Engineering*, 37:44–49.

Hofmann, E., Rüsch, M. 2017. Industry 4.0 and the current status as well as future prospects on logistics. *Computers in Industry*, 89:23–34.

Kagermann, H., Wahlster, W., Helbig, J. 2013. Recommendations for implementing the strategic initiative Industrie 4.0: Final report of the Industrie 4.0 Working Group. pages 1–82. Forschungsunion: Berlin, Germany.

Kumar, S., *et al.* 2008. Rx for smart hospital purchasing decisions. *International Journal of Physical Distribution & Logistics Management*, 38(8):601–615.

Lee, S. L., *et al.* 2015. Modernizing Pharmaceutical Manufacturing: from Batch to Continuous Production. *Journal of Pharmaceutical Innovation*, 10(3):191–199.

Li, X., Hamblin, D. 2016. Factors impacting on cleaner production: case studies of Chinese pharmaceutical manufacturers in Tianjin, China. *Journal of Cleaner Production*, 131:121–132.

Luthra, S., *et al.* 2017. An integrated framework for sustainable supplier selection and evaluation in supply chains. *Journal of Cleaner Production*, 140(3):1686–1698.

Marr, B. 2002. What is industry 4.0. Here's A Super Easy Explanation for Anyone. Forbes.

Nematollahi, M., *et al.* 2017. Economic and social collaborative decision-making on visit interval and service level in a two-echelon pharmaceutical supply chain. *Journal of Cleaner Production*, 142(4):3956–3969.

Nematollahi, M., *et al.* 2018. Coordinating a socially responsible pharmaceutical supply chain under periodic review replenishment policies. *Journal of Cleaner Production*, 172:2876–2891.

Ott, K., *et al.* 2012. Environmental Impact Assessment: In Encyclopedia of Applied Ethics. pages 114–123. Elsevier.

Rossetti, C. L., *et al.* 2011. Forces, trends, and decisions in pharmaceutical supply chain management. *International Journal of Physical Distribution and Logistics Management*, 41(6):601–622.

Rossit, D. A., *et al.* 2019. Industry 4.0: Smart Scheduling. *International Journal of Production Research*, 57(12):3802–3813.

Savage, C. J., *et al.* 2006. A holistic analysis of pharmaceutical manufacturing and distribution: are conventional supply chain techniques appropriate. *Pharmaceutical Engineering*, 26(4):1–8.

Schneider, J. L., *et al.* 2010. Pharmaceutical companies and sustainability: an analysis of corporate reporting. *Benchmarking: An International Journal*, 17(3):421–434.

Stegemann, S. 2016. The future of pharmaceutical manufacturing in the context of the scientific, social, technological and economic evolution. *European Journal of Pharmaceutical Sciences*, 90:8–13.

Weraikat, D., *et al.* 2016. Coordinating a green reverse supply chain in pharmaceutical sector by negotiation. *Computers and Industrial Engineering*, 93:67–77.

Wischmann, S., *et al.* 2015. Industrie 4.0: Volks- und betriebswirtschaftliche Faktoren für den Standort Deutschland. *Bharat Fritz Werner*, pages 7–54.

Xie, Y., Breen, L. 2012. Greening community pharmaceutical supply chain in UK: a cross boundary approach. *Supply Chain Management: An International Journal*, 17(1):40–53.

Xie, Y., Breen, L. 2014. Who cares wins? A comparative analysis of household waste medicines and batteries reverse logistics systems. *Supply Chain Management: An International Journal*, 19(4):455–474.

Zhang, M., *et al.* 2017. Improving supply chain social responsibility through supplier development. *Production Planning and Control*, 28(6-8):500–511.

Zuehlke, D. 2010. SmartFactory—Towards a factory-of-things. *Annual Reviews in Control*, 34(1):129–138.