Journal of Pharmaceutical Research International

33(43B): 438-450, 2021; Article no.JPRI.73382
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Health in Digital World: A Regulatory Overview in United States

Ashutosh Mishra[1], M. P. Gowrav[1*], V. Balamuralidhara[1] and Kolli Suhas Reddy[1]

[1]Department of Pharmaceutics, Pharmaceutical Regulatory Affairs Group, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara, Mysuru – 570015, Karnataka, India.

Authors' contributions

This review article was written in collaboration with all four authors. Author AM wrote the first draft of this review article. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i43B32573
Editor(s):
(1) Dr. Prem K. Ramasamy, Brandeis University, USA.
(2) Dr. Y.C. Tripathi, Forest Research Institute University, India.
Reviewers:
(1) Damtew Solomon Shiferaw, Ethiopia.
(2) Gabriela Olagnero, Maimónides University, Argentina.
(3) Darlan Tavares dos Santos, Federal University of the State of Rio de Janeiro (UNIRIO), Brazil.
Complete Peer review History: https://www.sdiarticle4.com/review-history/73382

Review Article

Received 05 August 2021
Accepted 10 September 2021
Published 15 September 2021

ABSTRACT

Adaptation towards digitalization in pharmaceuticals leads to the utilization and development of Artificial Intelligence (AI). Significantly it is reducing human workload with the help of an algorithm. Already AI is acting as a key in clinical trial, health care, quality management, manufacturing, product development, and management. Top pharmaceutical companies have adopted AI in different applications within the pharma sector. Different AI models like Machine learning, Artificial Neural Network, Deep Learning, robotics, and Natural Language Processing are being used in pharmaceuticals and healthcare systems. The Worldwide AI market is growing remarkably with a compound annual growth rate of 49.6% and is expected to reach $18,119 million by 2025. So, for better regulation, concerning safety, privacy regulatory strategy is heading towards a better framework. Different regulatory authorities like China, Europe, and United States (US) have adopted AI for economic and policy aspects. Emerging countries are using these tools for administrative work. US has begun implementing frameworks for AI adaptation, research, and development. The AI policy strategy started in 2016 with a series of workshops conducted under the Obama administration. Federal Food and Drug Administration (FDA) has also published draft

**Corresponding author: E-mail: gowrav@jssuni.edu.in;*

guidance for regulatory oversight of AI and Machine Learning. In 2021 FDA published a draft regulation for software as a medical device. This review article provides a snapshot of AI implementation in pharmaceuticals and health care with the regulatory approach in the US.

Keywords: Artificial intelligence; pharmaceuticals; health care; regulation; United States.

1. INTRODUCTION

Due to digitalization, Artificial Intelligence (AI) is presently exceptionally famous in various sectors mainly in pharmaceuticals [1]. Because of the same, the challenge for collecting and applying information to manage complicated clinical problems is inherent. Enormous data processing through automation empowers the utilization of AI and also diminishes Human Intelligence without influencing manpower [1]. AI is increasing potentially for achieving social, economic and political benefits. In recent years AI patent application is expanded in quantity in nation like US, Europe, South Korea etc [2]. In 2017, the worldwide AI in pharmaceuticals market was worth $719 million, and it is expected to grow to $18,119 million by 2025 with a 49.6% Compound Annual Growth Rate. Welltok, Intel, Nvidia, Google, Microsoft, and InSilico Medicine are the market leading operators [3]. Considering broad use of AI, the US has begun crafting regulations in terms of safety, efficiency, liabilities, data protection and security [4]. The main objective of the study is to exhibit the distinctive utilization of AI in both the pharmaceutical and health care sectors by discussing the under fostering regulation identified with AI in the US. In first section we will discuss the broad application of AI in pharmaceuticals and Healthcare and in second section we will give an insight of regulation in USA.

Coming to the classification, AI is divided as pointed in Fig. 1. Machine Learning (ML), as a component of AI, performs tasks with the help of an algorithm [5]. Also, Natural Language Processing (NLP) and ROBOTICS are additionally mainstream in the healthcare framework [1]. Supervised and Unsupervised ML fall into the general categorization of ML algorithm, and some cases a hybrid technique among Supervised and Unsupervised generally refers [6]. Linear Regression, LightBGM, Support Vector Machines (SVMs), Random Forests (RF), and ANNs (Artificial Neural Networks) are instances of Supervised ML models [7]. Hidden Markov model, Gaussian Mixture, and K- nearest neighbour (KNN) are few examples of Unsupervised methodologies [7,8]. ANN, KNN, SVM, Decision Tree (DT), Random Forest (RF), Linear Regression LightBGM are common ML methodology in pharmaceuticals. ANNs is the most widely recognized model used in numerous applications such as drug research, design, development, Etc and also it consists of processing elements and coefficients. Deep Learning (DL), a recent advance, is becoming another popular method of ML [7].

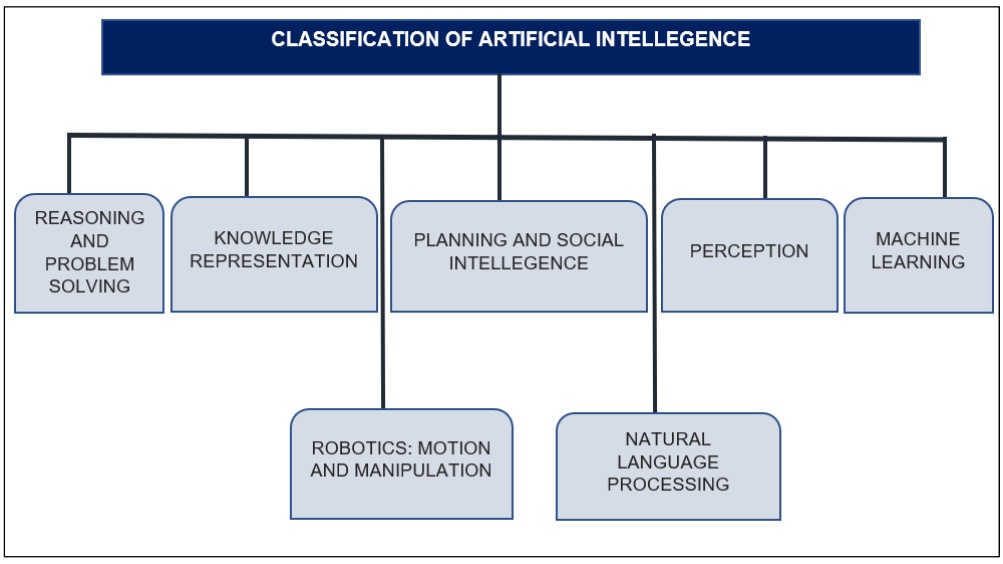

Fig. 1. Classification of artificial intelligence [17]

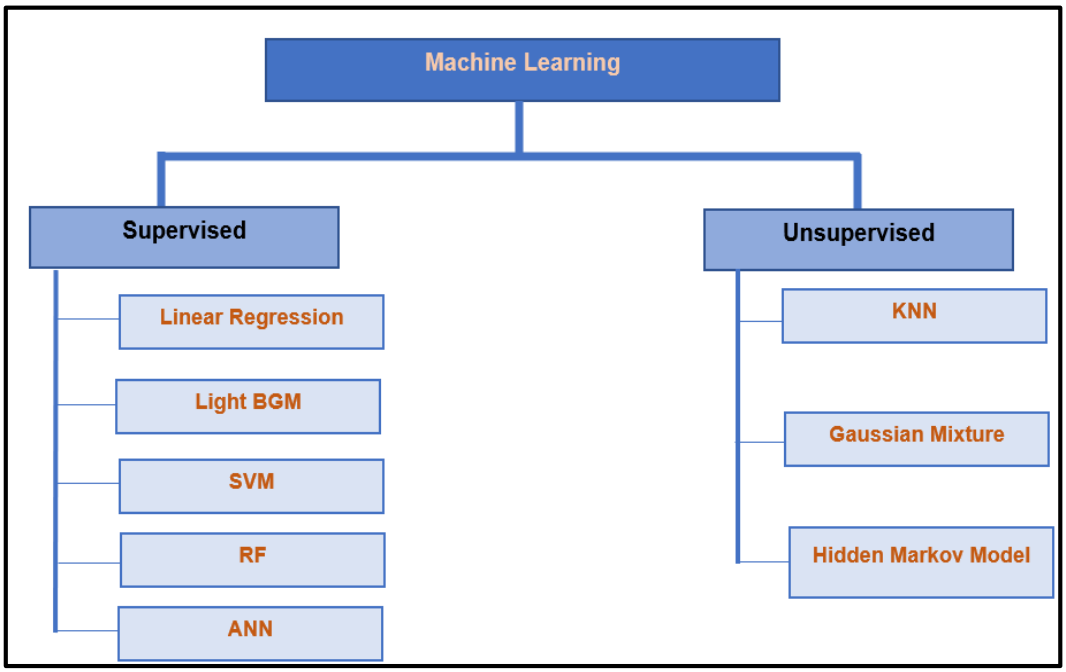

Fig. 2. Classification of machine learning algorithm

1.1 Application of AI in Various Area of Pharmaceuticals and Healthcare

AI is to be a focal part in the progression of pharmaceuticals and healthcare in the future since it could assist in drug discovery, drug development, reasonable treatment choices for patients including modified treatments, taking care of clinical information, maintaining quality, marketization of product and in clinical research [1].

1.1.1 Regulatory affairs

Recently, regulatory agencies have begun to receive and accept silicon evidence on safety and efficacy to grant product marketing authorization. The FDA Center for Devices and Radiological Health (CDRH) issued the first advice on "Reporting of Computational Modelling Studies in Medical Device Submissions" in 2016, followed by the release of technical standard "Assessing Credibility of Computational Modelling through Verification and Validation: Application to Medical Devices" in 2018 by “The American Society of Mechanical Engineers (ASME)” [9]. Official articulations from the United States (USA), the European Union (EU), and China highlight AI and advanced mechanics as strategies for economical and policy perspectives [10]. New technologies such as NLPs are being utilized for data extraction for Summary of product characteristics and Chemistry Manufacturing and Control documentation review. Robotic process automation and machine learning simplify administrative tasks such as review processes [11]. HURRA (The Human Use Regulatory affairs Advisor) is an information base intended to redo the learning source and information correspondence [12]. Pharma and Biotechnology firms are progressively utilizing ML for pharmacovigilance (PV), including the reporting of adverse events. Some organizations, such as Eli Lilly, Merck and Co, Pfizer, Gentech, and Johnson & Johnson, have adopted AI in regulatory operations and drug supervision [13]. FDA OEIO (Office of Enforcement and Import operations) is utilizing AI for risk management and trade flow optimization [14]. Emerging national regulatory agencies are using Facilitated Regulatory Pathways (FRP) to accelerate the administrative method and setting up connections between innovators and National Regulatory Authorities (NRAs) [15].

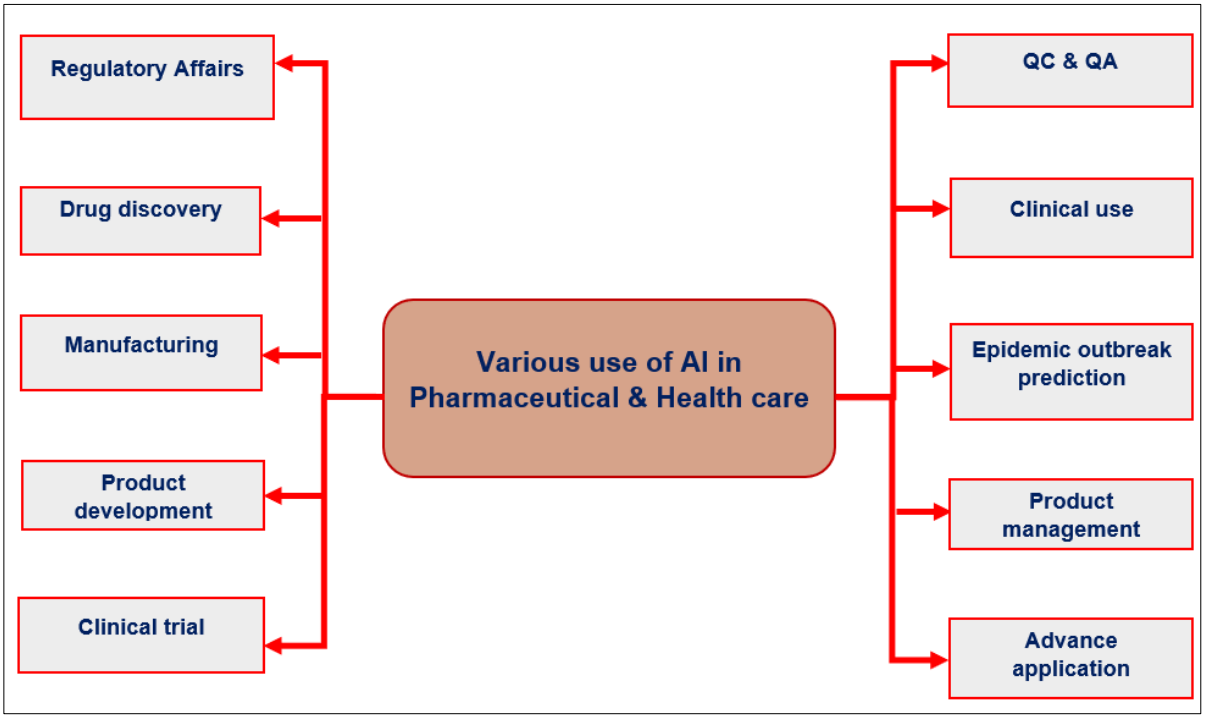

Fig. 3. Various use of AI in Pharmaceutical industry and Healthcare

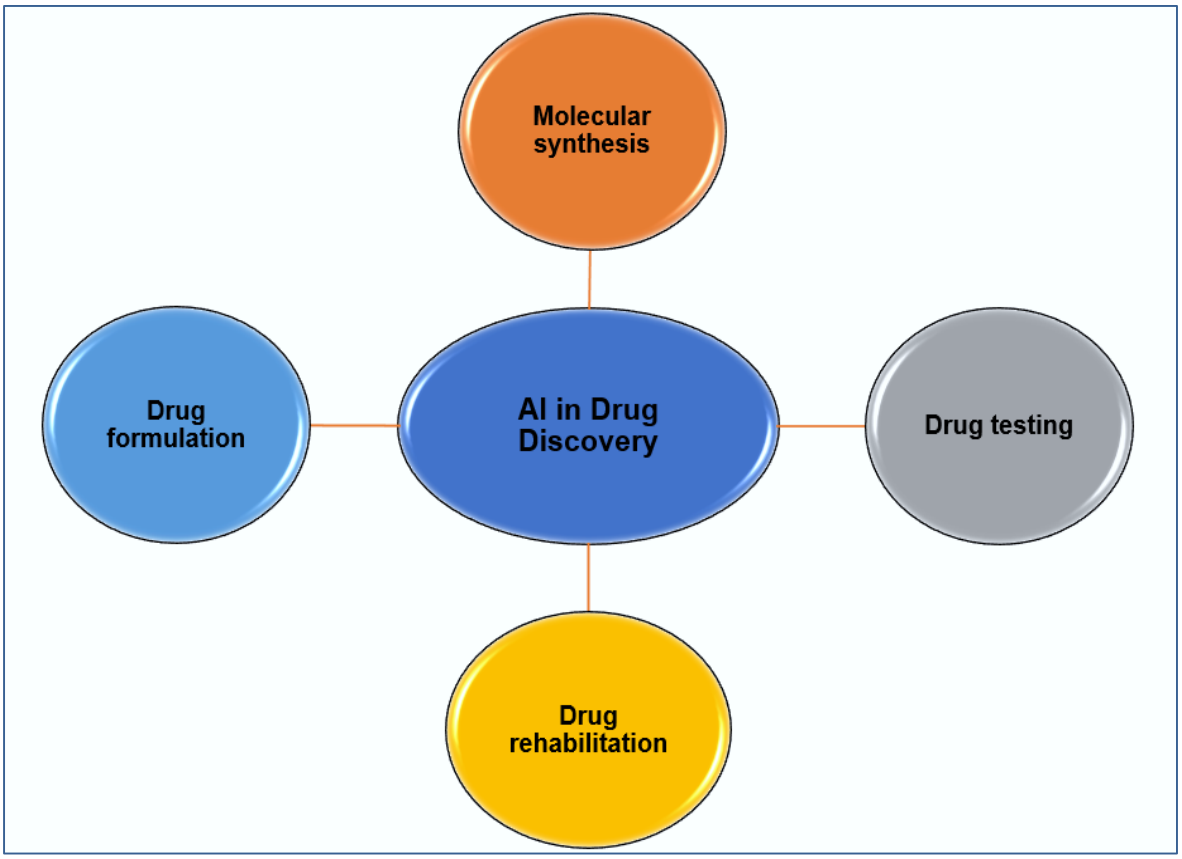

Fig. 4. Use of AI in Drug Discovery

1.1.2 Drug discovery

AI is utilized in drug discovery to further develop drug formulation, molecular synthesis, drug testing, and drug rehabilitation (Fig. 4) [1]. Since it is a big challenge for full automation in chemistry [16], computer-assisted drug formulation coupled with AI may take out challenge associated with traditional drug availability such as inefficiency, inaccurate delivery of targets, etc [17]. Algorithms like ANN, Deep Neural Network (DNN), and SVM are often employed in pharmaceutical development and formulation. ANN, DNN, SVM have commonly implemented the algorithm in drug Formulation & Development. AI can be used for chemical detection and validation, peptide synthesis, and physical examination. AI system predicts on & off-target and *in-vivo* safety profile reduces drug development time [18]. Technology and neural network software are being employed. Numerous silico methods are being used for the selection of molecular profiles. Toxicity prediction is getting easier by DeepTOX, PROCTOR. RASAR (Read-across structure–activity relationships) is now being used for cytotoxicity prediction. In advancing natural drug discovery, "SPIDER" is playing as an alternative for chemoproteonics. MICROARRAY, RNA seq. and the HTC (Heat transfer coefficient) process tend to analyse big data that takes up a new era of drug discovery. Treatment terms observed could be done by Genome Wide Association Study (GWAS) database [17]. Chemspider, ChEMBL, PubChem, zinc are important database compounds for compounding and drug testing and design [19]. 'De novo molecular design', Quantitative Structure Activity Relationship and Quantitative Structure property Relationship is used to predict the synthesis of new molecule generators and biological and pharmacodynamics activity respectively [20]. KronRLS, SimBoost, DeepDTA, and PADME(Protein And Drug Molecule interaction prediction) are the ML and DL methods used to determine the binding activity and degree of resemblance of drugs with protein [1].

1.1.3 Product development

In production including development stages AI is currently being used in various activities to give technological help and developing product as required [21]. Product development time is becoming shorter due to rising usage of AI tools. These trends and new tools are data-dependent and modify existing product development methods irrevocably [22]. AI integrated in 3D printing is now a key player in product development [23]. The traditional trial and error methodology can be superseded with AI such as Introducing a hybrid method for direct-filling hard piroxycardium gelatin capsules according to the dissolving profile settings, Guo et al merged expert systems (ES) and ANN. The Model Expert System (MES) generates judgments and suggestions based on the input parameters for formulation development [1]. Several mathematical approaches like CFDs (computational Fluid Dynamics), discrete element models, and Finite Elements have been used to analyse the impact flowing property of powder. CFD may also be used to study the shape of tablets in the dissolving profile. Faster manufacturing of pharmaceutical products could be done by AI coupling with mathematical models [1]. COMOS, ANSYS, Solidworks, CREO, Onshape tools are commonly being used in the design and analysis process of product development [24]. BatchPlus for recipe development and mass/energy balance calculations, Batches for dynamic simulation of batch processes, and PHASuite for process safety analysis in pilot plant operation is often used in process/product development [25]. Also researcher could use software tool named M3DISEEN designed to accelerate the formulation development process using AI/ML [23].

1.1.4 Manufacturing

The effective formulation of products can be enhanced by artificial intelligence-based method therefore, leads to boost uniformity, and quality [1]. The multidimensional relationships of input variables may be stressed by artificial neural networks (ANN) and linked closely with the design space to produce products within acceptable limits [26]. New advancements in AI, particularly ML, have demonstrated an impressive ability to modify the manufacturing field through state-of-the-art analytical tools to analyse large quantities of production data [27]. In 2008 the International Society of Pharmaceutical Engineering (ISPE) developed the Good Automated Manufacturing Practice (GAMP) guideline to promote automatic control systems deployment in the pharmaceutical sector. It gives robust assistance from the industry to identify and manage the risks associated with computer algorithms in GxP settings and ensures detection, analysis, assessment, and risk management [28].

Manufacturing Execution Systems (MES) advantages in improved compliance with Good Manufacturing Practices, production planning, and cost control. The production planning could be enhanced by AI which helps in monitoring and integrating real production process data with the expected marketing strategy [29]. In-process wear prediction systems using ANNs have been developed for efficient milling process. In predicting the average width of flank wear and the maximum depth of crater wear, Chungchoo and Saini designed an FNN (False neural network) [30]. Granulation is enhanced by integrating AI technologies in granulators. Major parameters can be correlated to their response using technology and neuro-fuzzy logic. They created multiple equations to estimate both geometrically identical and unequal granulators for the percent of the granulation fluid to be added, required speed, and diameter of the impeller [1]. Response Surface Method (RSM) and ANNs being used in Quality by Design to enhance product quality [31].

1.1.5 Clinical trial

Despite high expenditure and more time investment, companies are making investments in research of new drugs for the regulatory approvals, but only a few drugs get approval [32]. So, the use of AI accelerate and facilitate the development of new drugs, leading to a cheaper, more efficient process led to the successful conduct of clinical trials [33]. A study showed statistical improvement in decision-making, the quality of the overall decision-making level, patient satisfaction, and functional outcome in an AI-based randomized clinical trial [34]. Individual Case safety report (ICSR) is a document of a particular format to print a specific FDA guidance on the use, bring the NPP (Named Patient Program) information and product-related issues, and consumer reports. AI is used for ICSR data extraction in accordance with the required legislation and also for the decision-making process to separate the variables in adverse event reports (ADRs), classifying and correlating drugs, etc [35]. ML, DL, and NLP could be used to relate the large and diverse data sets, such as the Electronic Health Record (EHR), medical literature, and the testing of databases, to improve the selection of patients before the study, and the automatic and continuous follow-up of patients in the study, thereby enabling better engagement in control and detection of endpoints [32]. In phase 2 of the clinical trials, the study participants activities could be reviewed and externalized to better understand and predict efficiency through AI [36]. IBM Watson is an example of an AI-based system used in healthcare for various use also in clinical trials [37]. As phase IV clinical trial is very beneficial for safety, effectiveness, and post approval assessments also Known as Post-marketing surveillance (PMS) [36] AI can improve patient safety including ADR monitoring [38]. VigiRank, VigiMatch are examples of AI-based databases for PV [35].

1.1.6 Clinical use

In the era of big data and AI, every health institution has established its own database, which is generally supported by computation. The swift adaptation of AI has beneficial in healthcare data mining to produce advanced systems, that automatically diagnose and make a more accurate treatment model [39]. Artificial intelligence (AI) is a technique that lets people forecast health concerns by monitoring their health data via the application and smart devices. Researchers developed LIME by Recurrent Neural Networks (RNNs) to find the numerous health complications, including renal failure, anaemia, and diabetes, heart failure prediction. XAI model-diagnosis tools such as Anchors and Shapley values have been designed and employed in Medicare [40]. AI could be essential to supporting diagnostic, therapeutic, and surgical intervention [41]. It is used to highlight how typical clinical problems could be resolved and describe progression in different categories of tumors (lung, brain, breast, and prostate). It also vows to make great steps in the subjective translation by clinician specialists on malignancy imaging, including time-long volumetric tumour outline, clinical result forecast, and the effect of illness and therapy on the nearby organ [42]. Primarily ML and NLP, can assist doctors by providing up-to-date health information from journals, textbooks, and clinical practices, ensuring proper treatment and reducing diagnostic and therapeutic errors, as well as collecting useful information from a large patient population to aid in making real-time conclusions for health risk warnings [6]. In almost every medical care framework in the USA, EHRs were executed. The EHR is generally evolved to aid in administrative management, as well as in fundamental clinical treatment [43]. The AI algorithms are being used to interpret chest X-ray images, detect breast cancer screening, analyse CT scans (Computed tomography) of photographs, detect brain tumours, and predict

Alzheimer's disease using positron radiation. AI is valuable in the recognition of a polyp during a colonoscopy, improvement of hereditary conditions, and foetus evaluation in development for baby conception [44].

1.1.7 Quality control and quality assurance

The employment of AI approaches, advanced modelling, and simulation can provide quality control solutions [45]. AI-enabled automation must also be bolstered with efficient quality control programs, consisting of many critical components to match the performance of quality control systems. Progress in AI is capable of enhancing several elements of digital diagnostics [46]. AI-based STCEQ (Sistema Tutorial Inteligente para Controle Estatı´stico da Qualidade) is a Smart Tutoring System for Statistical Quality Control (SQC) that may give a suitable atmosphere for upskilling in Quality Control [47]. According to a study, Convolutional Neural Network (CNN) could be used for quality control of Esophagogastroduodenoscopy (EGD) [48]. It is well acknowledged that Quality Management is unachievable when developing and producing complex systems without utilization of a system approach and automation of all tasks including data gathering. So, for creating quality management system application of AI should be expanded [49]. Information processing and various literature sourcing techniques in the Total Quality Management expert system could be utilized in critical decisions and the emergence of novel technologies for the smart quality control system [1]. Fuzzy logic, ML ,Big data analysis, Game theory and multi-agent systems, Simulation (Digital modelling), Evolutionary/bionic algorithms, Expert systems, and DSS (decision-support systems) tools can be applied to develop quality management in each step like Design and development, Verification and validation and management process, etc. CALS-technologies link directly to Quality System development (continuous information support for the supply and life cycle of products) [49]. The FDA also updated the Current Good Manufacturing Practices (cGMP) with incorporating a quality by design method intend to product quality [1].

1.1.8 Epidemic outbreak

Since covid 19 is created a crucial situation, AI may be used around the world for treatment, diagnosis, and prediction of an epidemic outbreak [50]. For public health management, a replacement to the epidemiological models of Covid-19 spread in China, AI-inspired techniques are proposed for real-time forecasting the outbreak [51]. The hybrid ANN with updated algorithms improve data transformation methods combines forecast models and enhances the knowledge and generalization of ANN in the outbreak prediction [52]. For infection forecasting, Illustrious models like text analysis and machine learning are employed to assist physicians and also to prevent infection spread worldwide in one region [53]. According to an investigation, ML models like MLP (Multilayer perceptron) and ANFIS (adaptive network-based fuzzy inference system) reported a high generalization ability for long-term prediction in determining covid 19 outbreak [54]. AI provides fresh optimism that dangers of infectious diseases can be prevented and managed successfully, also that health-seeking behaviours and public emotional feelings will be understood via epidemics. Also, it is successfully implemented in outbreaks such as Chikungunya, Ebola, and Dengue [55]. Tableau is a visualization tool that could be connected to any database and visualization to estimate the worldwide breakthrough spread. TF-IDF (Term Frequency - Inverse Document Frequency) and Naive Bayes is an excellent way to forecast epidemic problems [56].

1.1.9 Product management

Product lifecycle management (PLM) covers the complete life cycle of a product through many types of technical, operations, and management activities from the beginning of an imaginary conception to the reprocessing of a final product [57]. AI may be adapted in the management of pharmaceuticals such as in marketing strategy, assessment of the business, and estimating product cost [1]. Novel products and commercial designs including leapfrogging, pyramid-free solutions, access to credit, and automation of fundamental business operations help in cost reduction can be quite possible by AI [58]. In market research, this can collect the data, analyse the market and consumer insight. At the stage of the marketing strategy, ML may be used for the segmentation (recognition and recommendation). At the promotion stage, ML may be used for standardization, personalization, and AI for rationalization at the marketing activity [59]. With the advent of the computer and the digitization of data, new approaches to the inventory management have become apparent that the use of the computer's intelligence.

Together with this, the smart technology can provide an effective combination, stock control and management, which is highly effective in the prevention of mismanagement [60]. For many years, the world has been moving towards digitization, and industry 4.0 is considered to be a forward-looking basis. AI is one of the most important techniques that helps in solving problem and directs new marketing strategy [1]. kanban system within a multi-echelon pharmaceutical supply chain (MEPSC) could be implemented to enhance visibility and inventory control in the supply chain [61]. Wise Athens, Navetti Price Point, which allows the user to set the product prices provided the pharmaceutical companies to assist in the product price calculation [1]. Visualization model can be incorporated to PLM process for better results in management [62]. The swarm particles enhancement together with ANN offers a better understanding of the market and help to decide product advertising according to consumer expectation. Eularis' E-VAI is a dynamic and observational AI model that gives plans and methodologies dependent on rivals, provides insights to acquire market benefits and also helps to wipe out lacked performance [1].

1.1.10 Advance application in artificial intelligence

3D printing (3DP) has paved the way for the production of fully customizable medicines. The use of AI integrated into the 3DP frame eliminates the need for human practices and is giving a step towards achieving streamline and automation [63]. The 4D printing technology that has been developed recently could be used in surgery, treatment, and rehabilitation [64]. Advanced recycling programmable computer or robot with integrated AI could be used for accurate detection of the waste components in the field of waste management and assist with an effective strategy for the constantly growing waste in the matrix [65]. Nanorobots, future advances in targeted drug delivery systems might be developed by integrating AI [1]. AI in the Malignant Research development is beneficial to detect and classify cancer, and the molecular characteristics of the tumour, and its microenvironment, to identify and control the drugs to predict the treatment [66]. Optimization technique by AI could be used in development of combination drug formulations. The use of AI is on the rise for nanotechnology research for nanomaterial quantification, Nano system design, and stimulation and nano-computing [67].

1.2 Regulation in United States

In 2016, a series of workshops and a subcommittee was initiated at the White House under the Obama administration on AI/ML. The US AI policy was generously bloomed. Those endeavours brought about three papers being issued: “The National Artificial Intelligence Research and Development Strategic Plan”; “Artificial Intelligence, Automation, and the Economy”; and “Preparing for the Future of AI”. The "AI, Automation and the Economy" study was published in order to provide an overview of AI's impact on US economy and labour force [4]. Those studies showed a path for the National AI Research and Development Strategic Plan. Then US government took steps forward in promotion of AI Research and development. It highlighted the federal government's responsibility in promoting research, development, and teaching programs through coordination and collaboration amongst stakeholders [68]. A White House Executive Board Team of the President, including staff of the Council of Economic Advisors, the National Economic Policy Council, the Management and Budget Bureau, and the Office of Science and Technology Policies, published the report entitled "Artificial intelligence, automation and economics" in December 2016 [69].

In May 2018, the Trump Administration hosted the Artificial Intelligence Summit for American Industry and issued a complementary report which enlightened the assistance of Federation to public sector for AI technology development [68]. In July 2018, the President's Executive Office pronounced that US leadership in AI is an important budget goal for 2020 for the administration of Research and Development [70]. In August 2018 the Congress established an independent bipartisan Committee of the National Security Commission on Artificial Intelligence (NSCAI) to "review tools and materials to advances AI/ML and related technologies [68]. US President Donald Trump signed a Management Order in February 2019 to establish the US AI Initiative, which intends to deal with the improvement of AI in the USA [71].

In January 2020 USA released Draft provisions for the regulatory oversight of AI. Government comprises of concepts to be followed by organizations as public trust in AI, public participation, scientific integrity, and quality information, risk assessment and management,

benefits and costs, flexibility, fairness and non-discrimination, disclosure and transparency, safety and security, and interagency coordination. A yearly report on the American AI Initiative was also issued by the White House in February 2020 summing up the progression achieved such an underline the OECD (Organization for Economic Co-operation and Development) policies. The White House has also introduced a new website ("AI.gov") focusing on AI that providing a forum for the public to study AI and its prospects. In the USA, AIs are already in clinical usage mostly in diagnostic and imaging fields. A total of 40 AI-based medical devices have previously been approved by the FDA [70]. To discuss emerging AI application in radiologic imaging, including AI/ML devices for automatic diagnostic FDA facilitated workshop on the Evolving Role of AI in Radiological Imaging in February 2020. The first cardiovascular ultrasonography device to exhort users using AI was announced on 7 February 2020 by the FDA which is endorsed by the De Novo route [72].

AI/ML program of the FDA CDRH conducts regulatory research, ensuring patients access to safe, efficient medical equipment through AI/ML collaboration with the Office of Science and Engineering Laboratories of CDRH [73].

The International Medical Device Regulators Forum has characterized AI-based innovation comprise the concept "software as a medical device" (SaMD), and the FDA has placed a healthcare digital transformation strategy by consolidating AI innovation which format the idea to SaMD [74]. In Jan 2021 FDA has issued the first Medical Device Action Plan for AI/ML from the agency with addition to previously published “Proposed Regulatory Framework for Modifications to AI/ML-Based Software as a Medical Device (SaMD) - Discussion Paper and Request for Feedback” where Good Machine Learning Practices was the main focus for implementation [72]. The FDA announces the software precertification pilot program as a self-administrative approach that consolidates a legal framework ideally equipped for the evaluation of software innovations [75].

The first FDA-approved autonomous AI system was IDx-DR, and has implemented for diabetes monitoring in patients. Arteries is the first DL-based clinical platform authorized by the FDA [74]. To identify and emphasize type of fracture, FDA-approved OsteoDetect employs ML approaches to analyse two-dimensional X-ray pictures [70,74]. The GI Genius device, a first AI/ML technology used medical device in the colon to help physicians in real-time in colonoscopy, has already approved by FDA [76].

2. CONCLUSION

AI has been adopted mostly in pharmaceuticals from regulatory decision making to research, marketing, patient care, production and many more. ML, NLP, DL, ANN are vastly used technique in pharmaceutical and healthcare sectors. In drug discovery to drug development and each phase of clinical trial AI may lead to a proficient tool for completing task and solving problem in an efficient manner. In clinical management these tools are expanding its application expectedly. For affirming of product quality to evaluating patient safety these tools are working enormously. In pandemic it is being used as a forecasting tool. AI is being used in advancing the pharma sector like in field of nano research, waste management and etc. It is expected to be a market player in near future. Still there are some challenges that barriers to AI implementation [1]. This should be well structured in the wider pharma sector. So, The USA is coming forward in a direction for a better regulatory framework and strategies for AI development. Artificial Intelligence is expanding significantly in FDA planning and implementation. At the same time FDA is considering safety and efficacy by regulatory oversight and prequalification program. So, The U.S. Government has begun to draught rules for the use of AI in grounds of safety efficiency, liability, data protection, and security. They enlighten the better approach towards innovation. Still regulation need to be improved in a better compliance to government and public which could elevate AI to a best segment in this digital world.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

The authors wish to express their profound gratitude the Regulatory Affairs Group of JSS College of pharmacy, Mysuru, Karnataka for support during data collection.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade R. Artificial intelligence in drug discovery and development. Drug Discov Today. 2021;26(1):80–93.
2. Economic impacts of artificial intelligence (AI) [Internet]. EPRS | European Parliamentary Research Service. 2019;1–8.
[Cited 2021 Aug 2].
Available:https://www.europarl.europa.eu/RegData/etudes/BRIE/2019/637967/EPRS_BRI(2019)637967_EN.pdf
3. Kunsel T, Chandra G. Artificial intelligence in medicine market size and industry analysis 2025 [Internet]; 2018.
[Cited 2021 Aug 2].
Available:https://www.alliedmarketresearch.com/artificial-intelligence-in-medicine-market
4. Gerke S, Minssen T, Cohen G. Ethical and legal challenges of artificial intelligence-driven healthcare. Artificial Intelligence in Healthcare. Elsevier. 2020;295–336.
5. Bratko I. Machine learning in artificial intelligence. Artif Intell Eng. 1993;8(3):159–64.
6. Park Y, Jackson GP, Foreman MA, Gruen D, Hu J, Das AK. Evaluating artificial intelligence in medicine: Phases of clinical research, JAMIA Open. BMJ Specialist Journals. 2020;3:326–31.
7. Damiati SA. Digital Pharmaceutical Sciences. AAPS PharmSciTech 2020 216. 2020;21(6):1–12.
8. Dash SS, Nayak SK, Mishra D. A review on machine learning algorithms. In: Smart Innovation, Systems and Technologies. 2021;495–507.
9. Viceconti M, Pappalardo F, Rodriguez B, Horner M, Bischoff J, Musuamba Tshinanu F. In silico trials: Verification, validation and uncertainty quantification of predictive models used in the regulatory evaluation of biomedical products. Methods. 2021;185:120–7.
10. Wachter S, Mittelstadt B, Floridi L. Transparent, explainable, and accountable AI for robotics. Sci Robot. 2017;2(6).
11. Van Belkum S, Brun N, Cleve S, McGovern P, Lumpkin M, Schaeffer PE, et al. Artificial intelligence in clinical development and regulatory affairs – Preparing for the future. Regul Rapp. 2018;15(10):17–21.
12. Hu X, Graesser AC. Human use regulatory affairs advisor (HURAA): Learning about research ethics with intelligent learning modules. Behav Res Methods, Instruments, Comput. 2004;36(2):241–9.
13. Lamberti MJ, Wilkinson M, Donzanti BA, Wohlhieter GE, Parikh S, Wilkins RG, et al. A Study on the Application and Use of Artificial Intelligence to Support Drug Development. Clin Ther. 2019;41(8):1414–26.
14. Solis, Dan. Office of regulatory affairs Dan R. Solis Assistant Commissioner for Import Operations [Internet].
[Cited 2021 Aug 2].
Available:www.fda.gov
15. Liberti L, Breckenridge A, Hoekman J, Leufkens H, Lumpkin M, McAuslane N, et al. Accelerating access to new medicines: Current status of facilitated regulatory pathways used by emerging regulatory authorities. J Public Health Policy. 2016;37(3):315–33.
16. Tarsellia MA, Potier Y, Fletcher AE. Automating automation how close are we to Artificial Intelligence impact ? Drug Discov World. 2019;16–21.
17. Gupta R, Srivastava D, Sahu M, Tiwari S, Ambasta RK, Kumar P. Artificial intelligence to deep learning: machine intelligence approach for drug discovery. Mol Divers 2021. 2021;1:1–46.
18. Mak KK, Pichika MR. Artificial intelligence in drug development: Present status and future prospects, Drug Discovery Today.2019;24:773–80.

19. Brown N, Ertl P, Lewis R, Luksch T, Reker D, Schneider N. Artificial intelligence in chemistry and drug design. Journal of Computer-Aided Molecular Design. Springer. 2020;34:709–15.
20. Jiménez-Luna J, Grisoni F, Weskamp N, Schneider G. Artificial intelligence in drug discovery: recent advances and future perspectives. Expert Opin Drug Discov. 2021;1-11.
21. Nozaki N, Konno E, Sato M, Sakairi M, Shibuya T, Kanazawa Y, et al. Application of artificial intelligence technology in product design. Fujitsu Sci Tech J. 2017;53(4):43–51.
22. Bickel S, Spruegel TC, Schleich B, Wartzack S. How do digital engineering and included AI based assistance tools change the product development process and the involved engineers. In: Proceedings of the International Conference on Engineering Design, ICED [Internet]. 2019;2567–76. [Cited 2021 Aug 2]. Available:https://www.designsociety.org/publication/42037/How+do+Digital+Engineering+and+included+AI+based+assistance+tools+change+the+product+development+process+and+the+involved+engineers
23. Elbadawi M, Muñiz Castro B, Gavins FKH, Ong JJ, Gaisford S, Pérez G, et al. M3DISEEN: A novel machine learning approach for predicting the 3D printability of medicines. Int J Pharm. 2020;590.
24. Marion TJ, Fixson SK. The Transformation of the Innovation Process: How Digital Tools are Changing Work, Collaboration, and Organizations in New Product Development*. J Prod Innov Manag. 2021;38(1):192–215.
25. Venkatasubramanian V, Zhao C, Joglekar G, Jain A, Hailemariam L, Suresh P, et al. Ontological informatics infrastructure for pharmaceutical product development and manufacturing. Comput Chem Eng. 2006;30(10–12):1482–96.
26. Aksu B, Paradkar A, De Matas M, Özer Ö, Güneri T, York P. Quality by design approach: Application of artificial intelligence techniques of tablets manufactured by direct compression. AAPS PharmSciTech. 2012;13(4):1138–46.
27. Arinez JF, Chang Q, Gao RX, Xu C, Zhang J. Artificial intelligence in advanced manufacturing: Current status and future outlook. J Manuf Sci Eng Trans ASME. 2020;142(11).
28. Martin KC, Perez A. GAMP 5 quality risk management approach. Pharmaceutical Engineering. 2008;28:24–34.
29. Adler DJ, Herkamp J, Henricks D, Moss R. Does a manufacturing execution system reduce the cost of production for bulk pharmaceuticals? ISA Trans. 1995;34(4):343–7.
30. Wu D, Jennings C, Terpenny J, Gao RX, Kumara S. A comparative study on machine learning algorithms for smart manufacturing: Tool wear prediction using random forests. J Manuf Sci Eng Trans ASME. 2017;139(7).
31. Aksu B, Paradkar A, De Matas M, Özer Ö, Güneri T, York P. A quality by design approach using artificial intelligence techniques to control the critical quality attributes of ramipril tablets manufactured by wet granulation. Pharm Dev Technol. 2013;18(1):236–45.
32. Harrer S, Shah P, Antony B, Hu J. Artificial intelligence for clinical trial design, trends pharmacol sci. 2019;40:577–91.
33. Rashid MBMA. Artificial intelligence effecting a paradigm shift in drug development, SLAS Technology. SLAS Technol. 2021;26:3–15.
34. Jayakumar P, Moore MG, Furlough KA, Uhler LM, Andrawis JP, Koenig KM, et al. Comparison of an artificial intelligence-enabled patient decision aid vs educational material on decision quality, shared decision-making, patient experience, and functional outcomes in adults with knee osteoarthritis: A randomized clinical trial. JAMA Netw Open. 2021;4(2):e2037107–e2037107.
35. Murali K, Kaur S, Prakash A, Medhi B. Artificial intelligence in pharmacovigilance: Practical utility. Indian J Pharmacol. 2019;51(6):373–6.
36. Park Y, Jackson GP, Foreman MA, Gruen D, Hu J, Das AK. Evaluating artificial intelligence in medicine: Phases of clinical research. JAMIA Open. 2020;3(3):326–31.
37. Strickland E. IBM Watson, Heal Thyself. IEEE Spectr [Internet]. 2019;24–31. Available:SPECTRUM.IEEE.ORG
38. Bates DW, Levine D, Syrowatka A, Kuznetsova M, Craig KJT, Rui A, et al. The potential of artificial intelligence to improve patient safety: A scoping review. NPJ Digit Med. 2021;4.

39. Panch T, Mattie H, Celi LA. The “inconvenient truth” about AI in healthcare. npj Digit Med. 2019;2(1):1–3.
40. Pawar U, O’Shea D, Rea S, O’Reilly R. Explainable AI in healthcare. In: 2020 International Conference on Cyber Situational Awareness, Data Analytics and Assessment, Cyber SA 2020. Institute of Electrical and Electronics Engineers Inc.; 2020.
41. Han C, Rundo L, Murao K, Nemoto T, Nakayama H. Bridging the gap between AI and healthcare sides: Towards developing clinically relevant AI-powered diagnosis systems. In: IFIP Advances in Information and Communication Technology. Springer. 2020;320–33.
42. Bi WL, Hosny A, Schabath MB, Giger ML, Birkbak NJ, Mehrtash A, et al. Artificial intelligence in cancer imaging: Clinical challenges and applications. CA Cancer J Clin. 2019;69(2).
43. Kim E, Rubinstein SM, Nead KT, Wojcieszynski AP, Gabriel PE, Warner JL. The evolving use of electronic health records (EHR) for research. Semin Radiat Oncol. 2019;29(4):354–61.
44. Kelly CJ, Karthikesalingam A, Suleyman M, Corrado G, King D. Key challenges for delivering clinical impact with artificial intelligence. BMC Med 2019 171. 2019;17(1):1–9.
45. Kovács GL, Mezgár I, Kopácsi S, Gavalcová D, Nacsa J. Application of artificial intelligence to problems in advanced manufacturing systems. Comput Integr Manuf Syst. 1994;7(3):153–60.
46. Larson DB, Boland GW. Imaging quality control in the era of artificial intelligence. J Am Coll Radiol. 2019;16(9):1259–66.
47. Reis MM, Paladini EP, Khator S, Sommer WA. Artificial intelligence approach to support statistical quality control teaching. Comput Educ. 2006;47(4):448–64.
48. Choi SJ, Khan MA, Choi HS, Choo J, Lee JM, Kwon S, et al. Development of artificial intelligence system for quality control of photo documentation in esophagogastroduodenoscopy. Surg Endosc; 2021.
49. Chesalin AN, Grodzenskiy SY, Nilov MY, Pham VT. Intelligent quality management tools for digital production and knowledge management system for their application. In: IOP Conference Series: Materials Science and Engineering [Internet]. IOP Publishing. 2020;042032.
50. Jamshidi M, Lalbakhsh A, Talla J, Peroutka Z, Hadjilooei F, Lalbakhsh P, et al. Artificial Intelligence and COVID-19: Deep Learning Approaches for Diagnosis and Treatment. IEEE Access. 2020;8:109581–95.
51. Hu Z, Ge Q, Li S, Xiong M. Artificial intelligence forecasting of COVID-19 in China. Int J Educ Excell. 2020;6(1):71–94.
52. Manliura Datilo P, Ismail Z, Dare J. A review of epidemic forecasting using artificial neural networks. Int J Epidemiol Res. 2019;6(3):132–43.
53. Joe J. Epidemic Outbreak Prediction Using Artificial Intelligence; 2018.
54. Ardabili SF, Mosavi A, Ghamisi P, Ferdinand F, Varkonyi-Koczy AR, Reuter U, et al. COVID-19 outbreak prediction with machine learning. Algorithms. 2020;13(10):2020.04.17.20070094.
55. Ganasegeran K, Abdulrahman SA. Artificial intelligence applications in tracking health behaviors during disease epidemics. Hum Behav Anal Using Intell Syst. 2020;6:141.
56. Adhikari NC Das, Alka A, Kurva VK, S S, Nayak H, Rishav K, et al. Epidemic outbreak prediction using artificial intelligence. Int J Comput Sci Inf Technol. 2018;10(4):49–64.
57. Wang L, Liu Z, Liu A, Tao F. Artificial intelligence in product lifecycle management. Int J Adv Manuf Technol. 2021;114(3–4):771–96.
58. Strusani D, Houngbonon GV. The role of artificial intelligence in supporting development in emerging markets. Role Artif Intell Support Dev Emerg Mark; 2019.
59. Huang MH, Rust RT. A strategic framework for artificial intelligence in marketing. J Acad Mark Sci. 2021;49(1):30–50.
60. Singh K. Smart inventory management using electronic sensor based computational intelligence. In: Studies in Computational Intelligence. Springer, Cham. 2019;3–25.
61. Mouaky M, Berrado A, Benabbou L. Using a kanban system for multi-echelon inventory management: the case of pharmaceutical supply chains. Int J Logist Syst Manag. 2019;32(3/4):496–519.
62. Sauza Bedolla J, Ricci F, Martinez Gomez J, Chiabert P. Fostering PLM implementation in SMEs: Modelling and managing verification processes. In: IFAC

Proceedings Volumes (IFAC-PapersOnline). Elsevier; 2013;1762–7.
63. Elbadawi M, McCoubrey LE, Gavins FKH, Ong JJ, Goyanes A, Gaisford S, et al. Harnessing artificial intelligence for the next generation of 3D printed medicines. Adv Drug Deliv Rev. 2021;175.
64. 4D printing soft robots guided by machine learning » 3dpbm [Internet]. [Cited 2021 Aug 2]. Available:https://www.3dprintingmedia.network/4d-printing-soft-robots-guided-by-machine-learning-and-finite-element-models/
65. Das S, Lee SH, Kumar P, Kim KH, Lee SS, Bhattacharya SS. Solid waste management: Scope and the challenge of sustainability. Journal of cleaner production. 2019;228:658-78.
66. Bhinder B, Gilvary C, Madhukar NS, Elemento O. Artifi cial intelligence in cancer research and precision medicine. Cancer Discov. 2021;11(4):900–15.
67. Sacha GM, Varona P. Artificial intelligence in nanotechnology, Nanotechnology. IOP Publishing; 2013;24:452002.
68. Shackelford SJ, Nti Asare I, Dockery R, Raymond A, Sergueeva A. Should we trust a black box to safeguard human rights? a Comparative Analysis of Ai Governance. SSRN Electron J [Internet]; 2021. [Cited 2021 Aug 2]; Available:https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3773198
69. Cath C, Wachter S, Mittelstadt B. MT-S and engineering, 2018 undefined. Artificial intelligence and the “good society”: the US, EU, and UK approach. Springer. 2018;24(2):505–28.
70. Gerke S, Minssen T, Cohen IG. Ethical and legal challenges of artificial intelligence-driven health care. SSRN Electron J; 2020.
71. Including Insights from the Comptroller General’s Forum on the Oversight of Artificial Intelligence An Accountability Framework for Federal Agencies and Other Entities; 2021.
72. Kumar A, Finley B, Braud T, Tarkoma S, Access PH-I, 2021 undefined. Sketching an AI Marketplace: Tech, Economic, and Regulatory Aspects. ieeexplore.ieee.org [Internet]. [cited 2021 Aug 2]; Available:https://ieeexplore.ieee.org/abstract/document/9319656/
73. Artificial Intelligence and Machine Learning Program: Research on AI/ML-Based Medical Devices | FDA [Internet]. [Cited 2021 Aug 2]. Available:https://www.fda.gov/medical-devices/medical-device-regulatory-science-research-programs-conducted-osel/artificial-intelligence-and-machine-learning-program-research-aiml-based-medical-devices
74. He J, Baxter SL, Xu J, Xu J, Zhou X, Zhang K. The practical implementation of artificial intelligence technologies in medicine. Nature Medicine. 2019;25:30–6
75. Digital Health Software Precertification (Pre-Cert) Program | FDA [Internet]; 2019. [Cited 2021 Aug 3]. Available:https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-software-precertification-pre-cert-program
76. The Food and Drug Administration. FDA authorizes marketing of first device that uses artificial intelligence to help detect potential signs of colon cancer [Internet]. [Cited 2021 Aug 2]. Available:https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-first-device-uses-artificial-intelligence-help-detect-potential-signs-colon

Peer-review history:
The peer review history for this paper can be accessed here: