World Health Organization

Benefits and risks of using artificial intelligence for pharmaceutical development and delivery

World Health Organization

Benefits and risks of using artificial intelligence for pharmaceutical development and delivery

Benefits and risks of using artificial intelligence for pharmaceutical development and delivery

ISBN 978-92-4-008810-8 (electronic version)
ISBN 978-92-4-008811-5 (print version)

Suggested citation. Benefits and risks of using artificial intelligence for pharmaceutical development and delivery. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at https://iris.who.int/.

Sales, rights and licensing. To purchase WHO publications, see https://www.who.int/publications/book-orders. To submit requests for commercial use and queries on rights and licensing, see https://www.who.int/copyright.

Layout: Imprimerie Centrale (Luxembourg)

Contents

Acknowledgements

This discussion paper was developed by Andreas Reis (co-lead, Health Ethics and Governance Unit, Department of Research for Health) and Sameer Pujari (Technical Officer, Department of Digital Health and Innovation) with direction from Deirdre Dimancesco (Technical Officer, Department of Health Products Policy and Standards) and the overall guidance of John Reeder (Director, Research for Health), Alain Labrique (Director, Digital Health and Innovation) and Jeremy Farrar (Chief Scientist).

Rohit Malpani (consultant, France) was the lead writer. The co-chairs of the expert group on ethics and governance of AI for health, Effy Vayena (ETH Zurich, Switzerland) and Partha Majumder (Indian Statistical Institute and National Institute of Biomedical Genomics, India), provided overall guidance on drafting of the report and leadership of the expert group.

WHO is grateful to the following individuals who contributed to development of the guidance.

WHO expert group on ethics and governance of AI for health

Najeeb Al Shorbaji, eHealth Development Association, Amman, Jordan; Maria Paz Canales, Global Partners Digital, Santiago de Chile, Chile; Arisa Ema, University of Tokyo, Tokyo, Japan; Amel Ghouila, Bill & Melinda Gates Foundation, Seattle (WA), USA; Jennifer Gibson, WHO Collaborating Centre for Bioethics, University of Toronto, Toronto, Canada; Kenneth Goodman, Institute of Bioethics and Health Policy, University of Miami Miller School of Medicines, Miami (FL), USA; Malavika Jayaram, Digital Asia Hub, Singapore; Daudi Jjingo, Makerere University, Kampala, Uganda; Tze Yun Leong, National University of Singapore, Singapore; Alex John London, Carnegie Mellon University, Pittsburgh (PA), USA; Partha Majumder, Indian Statistical Institute and National Institute of Biomedical Genomics, Kolkata, India; Thilidzi Marwala, University of Johannesburg, Johannesburg, South Africa; Roli Mathur, Indian Council of Medical Research, Bangalore, India; Timo Minssen, Centre for Advanced Studies in Biomedical Innovation Law, Faculty of Law, University of Copenhagen, Copenhagen, Denmark; Andrew Morris, Health Data Research UK, London, United Kingdom; Daniela Paolotti, ISI Foundation, Turin, Italy; Jerome Singh, University of Kwa-Zulu Natal, Durban, South Africa; Jeroen van den Hoven, University of Delft, Delft, Netherlands (Kingdom of the); Effy Vayena, ETH Zurich, Zurich, Switzerland; Robyn Whittaker, University of Auckland, Auckland, New Zealand; and Yi Zeng, Chinese Academy of Sciences, Beijing, China.

Observers

David Gruson, Luminess, Paris, France; Lee Hibbard, Council of Europe, Strasbourg, France.

External reviewers

Yara Aboelwaffa (Dubai, United Arab Emirates); Andreas Bender (Cambridge University, Cambridge, United Kingdom); Michelle Childs (Drugs for Neglected Diseases Initiative, Geneva, Switzerland); Alexandrine Pirlot de Corbion (Privacy International, London, United Kingdom); Rieke van der Graaf (Julius Centre, University Medical Centre, Utrecht, Netherlands (Kingdom of the)); Tim Hubbard (King's College, London, United Kingdom); Karen Jongsma (Julius Centre, University Medical Centre Utrecht, Utrecht, Netherlands (Kingdom of the)); Charles Mowbray (Drugs for Neglected Diseases Initiative, Geneva, Switzerland); Janneke van Oirschot (Health Action International, Amsterdam, Netherlands (Kingdom of the)); Laura Piddock (Global Antibiotic Research and Development Partnership, Birmingham, United Kingdom); Mario Ravic (Ericsson Nikola Tesla, Zagreb, Croatia); Tim Reed (Health Action International, Amsterdam, Netherlands (Kingdom of the)); Sarah Simms (Privacy International, London, United Kingdom); and Tom West (Privacy International, London, United Kingdom).

All experts, observers and external reviewers declared their interests in line with WHO policies. None of the interests declared were assessed to be significant.

WHO

Craig Burgess (Development Cooperation Specialist, Division of Data, Analytics and Delivery for Impact); Steve Estevao Cordeiro (Technical Officer, Health Products Policy and Standards); Jeremy Farrar (Chief Scientist); Christine Guillard (Knowledge Management Adviser, Regulation and Prequalification); Luther Gwaza (Team Lead, Health Products Policy and Standards); Mattias Helble (Scientist, Research for Health); and Vasee Sathiyamoorthy (Coordinator, Research for Health).

Abbreviations

AI	artificial intelligence
COVID-19	coronavirus disease 2019
IP	intellectual property
R&D	research and development
TRE	trusted research environment
USA	United States of America

Executive summary

WHO recognizes that artificial intelligence (AI) holds great promise for pharmaceutical development and delivery. However, AI also presents risks and ethical challenges that must be addressed if societies, health systems and individuals are to fully reap its benefits.

This discussion paper examines the expanding application of AI to each step of development and deployment of medicines and vaccines. AI is already used in most steps of pharmaceutical development, and, in the future, it is likely that nearly all pharmaceutical products that come to market will have been "touched" by AI at some point in their development, approval or marketing. Although these uses of AI may have a commercial benefit, it is imperative that use of AI also has public health benefit and appropriate governance.

This discussion paper also addresses the opportunities and ethical challenges of using AI for pharmaceutical R&D and in certain marketing registration and post-approval activities. This includes long-standing ethical challenges and risks associated with pharmaceutical development that pre-date the emergence of AI, but which AI has the potential to exacerbate. The paper also examines other risks with the use of AI, many of which were previously discussed in WHO guidance published in June 2021 on the *Ethics and governance of artificial intelligence for health*.

WHO is issuing this paper to inform a broad range of stakeholders, in particular policymakers, researchers and civil society, on the scope of use of AI in pharmaceutical development and delivery. More research and analysis and future guidance are required to keep pace with this fast-moving field and to study use cases and the benefits and risks of such uses.

1 Introduction

Artificial Intelligence (AI) reffers to the ability of algorithms encoded in technology to learn from data so that they can perform automated tasks without explicit programming of every step by a human *(1)*. WHO recognizes that AI holds great promise for the advancement of human health and for attainment of universal health coverage; however, AI also presents risks and ethical challenges that must be addressed if societies, health systems and individuals are to fully reap its benefits. The development and adoption of appropriate principles, rules and regulations have become more urgent with the speed of technological advances in use of AI and its rapid adoption and uptake for diverse and occasionally unforeseeable uses.

A fast-growing use of AI has been in the lifecycle of discovery, clinical development and delivery of pharmaceutical products (medicines and vaccines). This discussion paper provides a brief overview of the ever-expanding application of AI to each step of development and deployment. Although the document does not address the growing use of AI for medical devices, including diagnostic technologies, many of the principles and challenges discussed are relevant to that use. WHO has published guidance on training, validation and evaluation of AI for cervical cancer screening *(2)*.

Present-day use of AI in the pharmaceutical sector is not the first use of computational approaches for this purpose. Computing has played a critical role for decades: computer-aided drug design dates to the 1970s *(3)*, and, in the early 1980s, the "next industrial revolution" was proclaimed, with pharmaceuticals designed solely by computers *(4)*. Computational approaches are also routinely used, for example, for screening compound libraries *(5)*.

Table 1. Use of AI in the pharmaceutical sector

Category (date)	Quantity or amount	Reference no.
Scientific papers describing use of AI in biology and medicine (in 2022)	46 339	*6*
AI-based pharmaceutical discovery programmes (February 2022)	158	*7*
AI-derived compounds in clinical development (February 2022)	73	*8*
Digital end-points (September 2021)	225	*9*
Cumulative investment in AI for pharmaceutical development (2012–2022)	US$ 115.84 billion	*10*
Total number of AI-based biotechnology and pharmaceutical companies	600	*10*

The past decade has witnessed a dramatic increase in use of AI in pharmaceutical research and development (R&D), beyond previous uses. In 2021, the US Food and Drug Administration received more than 100 submissions for registration of medicines, including biological therapeutics, with AI components *(6)*. Table 1 provides a quantitative overview of the current breadth of AI outputs for pharmaceutical development.

Although the figures in Table 1 indicate accelerated interest in, investment in and outputs from use of AI in pharmaceutical development, there is concern that the increasing hope in the potential of AI is yet another example of the AI "hype" cycle. While at least 73 AI-derived compounds are in development, all but two are in phase I or phase II trials *(8)*, and no novel compound fully designed or identified with AI has been approved for use in humans (although AI has played a role in the development of novel medicines and vaccines that have been approved for human use).

As described in the next section, AI is already used in most steps of pharmaceutical development, and, in the future, it is likely that nearly all products that come to market will have been "touched" by AI at some point in their development, approval or marketing *(11)*. Although these uses of AI may have a commercial benefit, it is imperative that use of AI also has public health benefit. This discussion paper also describes the few initiatives in which AI has been used to advance public health or to address unmet medical needs. In comparison with the size of the investment and the scale of commercial use of AI for pharmaceutical R&D, it is apparent that use will focus overwhelmingly on generating commercial benefits. This will only widen existing inequity in pharmaceutical R&D unless there is a collective effort to identify public interest-oriented principles and appropriate governance.

This discussion paper addresses the opportunities and ethical challenges of using AI for pharmaceutical R&D and in certain marketing registration and post-approval activities. WHO recognizes that the uses of AI in the development and delivery of new medicines and vaccines vary and that certain applications do not pose significant ethical risks. WHO also recognizes that certain long-standing ethical challenges and risks associated with pharmaceutical development and delivery pre-date the emergence of AI. Nevertheless, AI has the potential to exacerbate these long-standing risks and challenges.

WHO is issuing this paper to inform a broad range of stakeholders, in particular policy-makers, researchers and civil society, on the scope of use of AI in pharmaceutical R&D. More research and analysis are required to keep pace with this fast-moving field and to study use cases and the benefits and risks of such uses.

2 Uses of AI in pharmaceutical development and delivery

Pharmaceutical R&D consists of the discovery and testing of medicines or vaccines with the aim of obtaining regulatory approval for their clinical use. Improvements in AI have gradually extended the tasks that AI can execute on behalf of pharmaceutical scientists and companies. It is now used in every stage of the pharmaceutical development cycle and for marketing registration and delivery of medicines. The current or anticipated uses of AI in the pharmaceutical development cycle are described below.

2.1 Basic scientific research

Pharmaceutical discovery usually relies on basic scientific research or comprehensive understanding of human disease at the molecular level *(12)*. AI now supports various types of scientific research, including for formulating and evaluating scientific hypotheses *(13)*. AI is also used in research for pharmaceutical discovery. A particular breakthrough was use of AI to solve the "protein folding problem", the question of how a protein's amino acid sequence dictates its three-dimensional atomic structure *(14)*. In December 2020, DeepMind, an AI company, announced that its AlphaFold2 system had solved the protein folding problem by developing a system that can reliably predict the three-dimensional shape of a protein *(15)*. This discovery, which will eventually provide researchers with the shape of every known protein, may be a critical contribution to structural biology and to scientific research on the underlying causes of diseases *(16)*. AlphaFold2 has already been used for screening and designing new ligands, as it provides accurate predictions of protein structures that would be targeted by a compound. DeepMind collaborated with the European Bioinformatics Institute of the European Molecular Biology Laboratory to create a public database with 200 million such predictions *(17)*. AI is also used to select, design and plan experiments and improve measurement and observation, such as by converting low-resolution images of mitochondria into high-resolution, low-noise images *(18)*.

2.2 Pharmaceutical discovery and design

AI has various uses in pharmaceutical discovery and design (referred to as bioinformatics), many of which have been applied for decades. AI can be used to identify potential new targets for pharmaceuticals by analysing large amounts of biological data, thereby identifying specific biomarkers or mutations related to a disease *(18)*, thus improving understanding of disease mechanisms, which can be used in the discovery of pharmaceuticals *(19)*. Companies are using existing data sets, acquiring data sets developed by third parties and developing their own data sets to train machine learning models that can be used to identify pharmaceutical

targets or new compounds *(3)*. Companies are also using synthetic data, or "artificially-generated data that mimic real-world patterns and characteristics" *(20)*, to identify disease targets for which there are few experimental data (such as for rare diseases) to train AI models to identify targets that might otherwise be overlooked or to validate predictions made by AI algorithms *(20)*. The quantity, quality and translational relevance of all types of data to identify appropriate treatments remain, however, a major challenge; synthetic data in particular have significant limitations *(20)*.

One example of such data use for pharmaceutical discovery is that of a genetic testing company that collected genetic data on about 10 million people (as of 2020) and secured permission from customers to use anonymized data for pharmaceutical research. The company used the data to identify a candidate medicine (and conduct animal studies) that was licensed to a pharmaceutical company, which is now completing clinical development *(21)*. The genetic testing company has also shared the genetic data with pharmaceutical companies, including one multinational pharmaceutical company, which purchased exclusive rights to use of the data for pharmaceutical development and acquired a US$ 300 million stake in the company *(22)*. There are, however, ethical concerns about the company's collection of consumer health data, including inadequate regulatory oversight *(23)*, their secondary use for commercial purposes, and potential violations of customers' right to privacy because of difficulty in full anonymization of the data and the possibility of cybersecurity breaches or leaks *(24)*. Concern about secondary use of consumer data in the development of medicines is discussed below.

As has been the case for several decades *(25)*, AI is also used to screen compounds, providing researchers with a much larger chemical space than traditional processes (large-scale, high-throughput screening), and facilitating identification of molecules with relevant biological properties *(3)*, including those for addressing diseases for which few or no treatments exist. This use of AI could allow researchers to "fail faster" and therefore assess more candidates before conducting additional research *(8)*.

Recently, researchers at McMaster University, Canada, and the Massachusetts Institute of Technology, USA, trained an AI algorithm with an estimated 7500 compounds to predict whether structurally new molecules were active against the bacterium *Acinetobacter baumanii (26)*. Once trained, the algorithm was used to screen 6680 molecules selected by the research team, leading to identification of a novel investigational compound, abaucin, which can now be tested for its effectiveness against *A. baumanii (27)*. Using AI, the researchers at MIT, collaborating with other institutes, identified a new class of compounds that could kill methicillin-resistant Staphylococcus aureus (MRSA) grown in a lab dish and in two mouse models, while showing low toxicity against human cells *(28)*.

AI is also now used in the design of novel medicines and vaccines *(29)*. For example, in the development of therapeutic mRNA vaccines against cancer, AI is used to identify which mutations on a tumour drive its growth and are likely to generate an immune response so that an mRNA molecule can be synthesized and then translated into protein fragments identical to those on the tumour cell to generate an immune response *(30)*. AI could also be used to

design the RNA sequence used in mRNA vaccines by both choosing a sequence that encodes a desired protein and optimizes its stability, so that it persists long enough to express sufficient protein before degradation *(31)*. One large pharmaceutical company formed a partnership with an AI-focused drug-discovery firm to accelerate formulation of an antiviral combination (nirmatrelvir plus ritonavir), which was used widely during the coronavirus disease 2019 (COVID-19) pandemic *(32)*.

AI has been used for de-novo drug design *(33)*. Current approaches rely on generative AI, the AI method used in large multi-modal models such as ChatGPT, to develop compounds with specific properties *(34)*. Researchers have now developed a large multi-modal model, ESMFold, a protein language model, that can predict a full atomic-level protein structure from a single sequence and is faster than DeepMind's AlphaFold2, which requires multiple sequence alignments *(35)*. ESMFold can generate a database of more than 600 million structures of metagenomic proteins, including more than 225 million proteins that are predicted with high confidence *(36)*. However, in a competition hosted by the Critical Assessment of Techniques for Protein Structure Prediction in 2022 *(37)*, ESMFold performed "significantly worse" than the DeepMind AlphaFold with respect to protein structure prediction. The large technology company that developed and maintains ESMFold may now abandon or deprioritize it (see below).

AI can also be used to repurpose existing medicines (repurposing is a strategy to identify new indications or uses of an approved medicine). For example, during the COVID-19 pandemic, one AI-based company added a few clues about how SARS-CoV2 acts into its algorithm, which then searched over 50 million medical journal articles to identify the biological pathways that should be targeted to find an approved pharmaceutical that could be repurposed *(38)*. The company identified baricitinib in only 4 days, and the medicine was subsequently recommended by WHO to treat patients with severe or critical COVID-19.

2.3 Preclinical studies and pharmaceutical development

Researchers are also training machine learning models for use in preclinical studies to predict the properties of a given molecule, such as its binding affinity to a target protein or its toxicity *(34)*. Until now, preclinical studies have been conducted with animal models to replicate aspects of human disease, which, however, cannot include all aspects of the disease. It may become possible to use machine learning models with data from heterogeneous biological systems that are sufficiently relevant (such as organoids or organs-on-a-chip) to gradually replace animal models, with comparable or better performance *(39)*. The US Food and Drug Administration Modernization Act 2.0, enacted in late 2022, includes a provision that eliminates the requirement that investigational compounds undergo animal testing before human trials begin *(8)*. The European Union is also examining alternative approaches, which may include AI, to identify and introduce alternatives to animal testing *(40)*.

AI could be applied in pharmaceutical development (chemistry, manufacturing and controls), in procedures used to assess the physical and chemical characteristics of pharmaceutical

products, and to ensure their quality and consistency during manufacture. This would include use in process design to reduce waste and development time, quality control, process monitoring and fault detection *(41)*. Machine learning could also be used, for example, for single-step and multi-step retrosynthesis *(42,43)*, although such uses of AI are considered to be "far from a mature state" *(44)*.

2.4 Clinical trials and regulatory approval

Once developers or researchers are ready to enter a medicine or vaccine into clinical development, AI is used to support or automate various aspects of clinical development – design, recruitment, conduct and analysis *(45)*. AI has also been used in filing for regulatory approval.

First, AI is used by pharmaceutical development professionals and clinical trialists to assist with design of clinical trials *(46)*, including decentralized trials with "real-world" data, electronic health records and medical claims *(47)* for predicting trial outcomes *(48)*, to assist in site selection *(47)*, to optimize the selection of doses or dosing regimen for a study *(47)*, for selecting clinical end-points *(49)* and to improve adherence to medication in order to reduce attrition and increase accuracy. One data analysis company has developed software for identifying a person and their prescribed treatment and confirming whether it has been taken *(46)*. If such software is used involuntarily, however, questions may be raised about privacy and potential intrusive surveillance, as discussed below. Prediction of patient outcomes, and particularly serious adverse events, can be used to stratify patients into groups and to monitor or exclude them "depending on the predicted severity of the adverse event" *(47)*.

Secondly, AI is used increasingly to streamline and accelerate patient recruitment by identifying or selecting candidates according to their medical history, demographics and other data, such as social media content *(50)*. This use also raises concern about mining of individual data, including sensitive health data, for commercial purposes or notifying individuals to participate in trials that may violate their privacy and autonomy. AI has also been used to identify biomarkers for use in selecting patients *(51)*, and clinical trials in which biomarkers were used for selecting patients were more likely to succeed than trials in which biomarkers were not used *(52)*. AI tools have been developed to assist individuals in searching for trials, which gives individuals more opportunities to seek appropriate trials and treatment that are difficult to identify and access through other channels *(46)*.

Thirdly, AI is used in clinical trials for collecting, managing and analysing the data that accumulate in various digital health technologies during a specific trial *(47)*. AI can also be applied to the assessment of clinical end-points, such as safety signals (including in real time during a trial) and outcomes, from sources of data that could not otherwise be analysed *(47)*. AI researchers are discussing the prospect of replacing clinical trials with virtual trials *(46)*; however, there are many unanswered questions about the feasibility of this proposal, and discussion between AI researchers and regulators remains at an early stage.

Fourthly, AI could be used for analysing results, providing more informative insights for drug developers, for automating inclusion of data into statistical analytical tools and for producing the documents, tables, reports and labels required during clinical development of a compound. One challenge for use of AI for analysis is that the algorithms require additional development and validation *(45)*. AI is used in preparing the reports required for regulatory approval *(47)*. It could also be used in registration by generating the standard language used in package information, including summaries of product characteristics and other information *(53)*. If AI is used in producing any documentation during drug development, there must be human oversight, review and quality assurance to avoid generation of false information and "hallucinations".

2.5 Post-approval activities

Once a pharmaceutical product has been approved, AI may be used to a limited extent in pharmacovigilance, including automation of reporting of individual case study reports to a drug regulatory authority, such as is done for the US Food and Drug Administration *(47)*. AI has also been used in this way by the medical products agency in Sweden *(54)*. Other potential applications of AI in pharmacovigilance are discussed below. Pharmaceutical companies have increasingly used AI in various aspects of pharmaceutical manufacture, including process design (to reduce waste and development time), advanced process control, process monitoring and fault detection (including use of computer vision to identify packaging irregularities) *(55)* and trend monitoring, including consumer complaints and reports of manufacturing-related deviations *(56)*.

Pharmaceutical companies are increasingly using AI to manage the supply and distribution of medicines *(57)*, including monitoring the cold chain for transport of vaccines *(58)*. AI can also be used in forecasting demand, monitoring and identifying corruption in the supply chain, and anticipating or detecting shortages and stock-outs *(59)*.

AI is also used by pharmaceutical companies to design marketing strategies *(60)*, to set prices *(34)* and to predict where the company can maximize sales of a new medicine *(34)*. AI-based analysis of demographic data, medical data, prescriptions and information from physicians is used to adjust marketing strategies, specifically to trigger use of mass e-mails, paid advertisements and social media to maximize contact with health-care professionals *(60)*. Generative AI (such as large language models) can be used for patient education and to increase adherence to medication and could be integrated into patient support systems or digital therapeutics applications *(61,62)*. Such uses of AI, which may increase the revenues of pharmaceutical companies, could raise numerous concerns about improper influence on medical professionals and could fuel inappropriate use of medicines, distort markets or lead to other commercial practices that raise ethical concerns, including about patient privacy.

3 Are commercial uses of AI beneficial for public health?

Pharmaceutical and technology companies are investing in AI for drug development primarily to increase their profits. However, such uses of AI may not generate benefits for broader public health or for individual patients. Such uses may also give rise to ethical risks and lead to outcomes that undermine fundamental rights.

3.1 Precision medicine and personalized medicine: More specific but more exclusionary?

A common expectation of AI is that it will allow the pharmaceutical industry to move drug development towards precision medicine and personalized medicine. While most medical treatments are designed for the "average patient", in precision medicine, treatments (and vaccines) are tailored to different genetic profiles, environments and lifestyles *(63)*. Personalized medicine is an "extreme" form of precision medicine in that a treatment is tailored to the genetic characteristics of a single individual. For example, companies that developed mRNA COVID-19 vaccines, even before the COVID-19 pandemic, were developing therapeutic cancer vaccines to direct an individual's immune system to attack his or her disease by using the data on that person's tumour to choose appropriate targets *(48)*. One company is working to find an appropriate antidepressant and its dosage for an individual by using AI to analyse the patient's medical history and genetic data and exposing brain cells from the patient to several antidepressants to identify biomarkers *(38)*. While such uses of AI could provide better outcomes for individual patients, the benefits could be available and accessible to only a select few, thus accentuating health inequality or disparity, for at least three reasons.

First, researchers and pharmaceutical companies might develop treatments only in therapeutic areas or only on behalf of individuals and population subgroups for which there are already adequate data. The areas in which significant scientific research and progress have been made are likely to be those that are already of commercial interest to pharmaceutical companies. A recent Wellcome Trust review of scientific publications on the use of AI in drug development indicates such a trend, noting that they focus on "therapeutic areas that are both data-rich and commercially attractive", such as oncology and COVID-19 *(8)*. While infectious diseases are also well represented in the scientific literature, most articles address diseases for which there are "significant commercial incentives" or philanthropic funding, such as HIV/AIDS, tuberculosis and malaria. Less than 1% of scientific publications address all other infectious diseases, including neglected tropical diseases *(8)*. This situation could result in

skewed investment in the long-term, whereby R&D that results in new data or insights in one area encourages companies to focus on that specific therapeutic area or population.

Secondly, tailoring of therapies to individuals could accentuate inequality (and the tendency of pharmaceutical R&D to focus on profitable populations) by directing resources for drug development to ever smaller, privileged cohorts of patients, ignoring a significant number of unmet needs, such as medicines for infectious diseases that can affect children and babies in low- and middle-income countries. Thirdly, while such uses of AI may result in better outcomes for individual patients, the high prices of personalized therapy may only be affordable for a privileged few. *(65)*.

3.2 Improving drug discovery rates and clinical trial success: reducing overall costs, but for whom?

Another expectation of the use of AI is that it could dramatically improve the speed of drug development, from the slow, anaemic rate today to significantly shorter timelines and success rates of 20–50% *(19)*, mainly because scientists will be able to predict how investigational compounds will behave in the human body and abandon those that might not be successful *(16)*. The better success rate is expected to save pharmaceutical companies billions of US dollars in drug development costs *(19)*. Use of AI to direct resources more efficiently could, however, result in loss of serendipity, which has been a key factor in drug discovery *(66)*.

Clinical trials could be improved and perhaps conducted more quickly and accurately, at least for identifying patients or sub-populations that are particularly suited to an investigational compound *(67)*, improving adherence to medication and reducing attrition during clinical trials *(48)*. This could reduce costs significantly and improve the overall efficacy of a medicine. As discussed above, however, such selection could accentuate and reinforce disparities and biases in R&D, as developers might focus on populations and diseases for which companies already have good-quality data. AI could nevertheless significantly accelerate drug development *(39)*.

Any savings made by use of AI could allow pharmaceutical companies to reduce the prices of medicines and vaccines, as the high cost of R&D and the high rate of failure are the main reasons given by companies for charging high prices for medicines *(68)*. Studies have demonstrated, however, that the prices that pharmaceutical companies charge for medicines, whether on or off patent, are not related to the amount of money invested by those companies into R&D *(68)*. Insofar as companies can reduce R&D costs, any savings on a medicine that is under patent are unlikely to be passed on to health systems and individuals.

Another concern is that the use of AI to accelerate the development of medicines may increase a medicine's effective patent life (effective patent life is the period of patent protection remaining for a drug at the time of regulatory approval), and therefore the total time a

company can charge high prices and maximize revenues. This could accentuate the tendency of companies to get to the market as quickly and as inexpensively as possible by addressing the most profitable indications or subpopulations and ignoring indications or populations, such as children or babies (due to the requirement for additional clinical development after approval for use in adults), that may produce an overall greater public health benefit. Furthermore, speed might be prioritized over the quality of R&D, including the reproducibility of results *(69)*. However, it has been noted that the quality of R&D decisions, including which compounds to take forward and the conduct of clinical trials, can reduce the failure rate, and therefore "has by far the most significant impact on project value overall, multiple times that of a reduction of the cost of a particular phase or a decrease in the amount of time a particular phase" *(4)*.

3.3 Improving clinical trial recruitment, adherence and marketing: support or surveillance?

As noted above, AI is used to refine and improve recruitment and adherence to the protocol in clinical trials and to improve targeting of marketing and sales of new medicines to specific patient groups with unmet needs. This gives pharmaceutical executives and scientists tremendous power to refine the decisions that are made throughout drug development and commercialization to focus on individuals identified by algorithms as best suited to maximize both clinical trial results and commercial returns.

Use of AI, for example, to improve patient adherence or to identify patients who could benefit from a product, either during clinical trials or once a medicine has been approved, could have a public health benefit. These uses of AI could also serve pharmaceutical companies to: shorten the time for enrolment and recruitment into clinical trials, improve outcomes by ensuring better adherence, and increase sales. These goals, which are commercially profitable, could lead companies to collect and use data in ways that undermine patient privacy and informed consent, either for use of data or informing patients, otherwise unaware, that they could benefit from a therapy. It could also increase the use of surveillance for commercial returns. Targeted marketing, even for public health, also raises concern about micro-targeting, manipulative marketing and amplification of biases, especially in ways that negatively affect minority populations *(1)*.

4 Identifying and maximizing the public health benefits of AI for development and delivery of pharmaceutical products

AI could provide broader benefits for public health and global health. This would require intentional use of AI to address unmet needs or to strengthen aspects of drug development or access that are neglected in the current pharmaceutical system. It would also require supportive investments, policies and practices through proactive action by the public sector, philanthropies and not-for-profit organizations. A few potential uses are described below.

4.1 Medicines and vaccines to address unmet needs

AI could be used to develop medicines and vaccines that are not developed in the current system of pharmaceutical R&D. Three areas in which investment has already been made are antimicrobial resistance *(39)*, neglected tropical diseases *(70)* and vaccines against pandemic threats *(71)*.

The Drugs for Neglected Diseases Initiative, a not-for-profit partnership for the development of new medicines against neglected tropical diseases and other infectious diseases (such as hepatitis C and COVID-19), has formed a partnership with DeepMind, wherein the team in charge of AlphaFold2 (see above) can predict protein structures for a target disease. An initial focus of the partnership has been a protein on *Trypanosoma cruzi*, the parasite that causes Chagas disease, to determine whether an investigational compound being developed by DNDi can bind to the protein and eliminate the parasite. This could also indicate other compounds that could bind to the protein *(72)*. The Global Antibiotic Research and Development Partnership, another not-for-profit partnership that develops new treatments for drug-resistant infections, has also formed a partnership with DeepMind to investigate unrealized targets for antibacterial drug discovery.

The Coalition for Epidemic Preparedness Innovations, a global partnership to accelerate the development of vaccines against epidemic and pandemic threats, has issued two grants for application of AI in the development of novel vaccines. For example, the partnership has provided funding to a vaccine research consortium to use AI in developing broadly protective beta coronavirus mRNA vaccines *(71)*.

While these are promising examples of application of AI in the development of new treatments for drug-resistant infections, they will not come to fruition unless pharmaceutical companies are willing to share or themselves apply AI technologies for such therapies. They will also require "push funding" for not-for-profit organizations or pharmaceutical companies (whereby governments provide direct funding for specific stages of R&D projects in the form of grants, investments, tax credits or low-interest loans for which governments bear the development risk) or "pull incentives" (whereby governments encourage private sector engagement by rewarding successful development through creating viable market demand or ensuring future revenue) to encourage companies to use AI-based technologies to meet these needs.

4.2 Making clinical trials more inclusive

A study conducted in 2014 found that 86% of clinical trial participants were White, and a study conducted in 2019 found that 79% of genomic data were from people of European descent. Bias in relation to sex and gender is found throughout R&D, such as exclusion of people of child-bearing age and pregnant and lactating women from clinical trials *(73)*. Improvement of diversity in clinical trials in general will require various measures, including legal requirements, incentives and partnerships with not-for-profit organizations and other entities. There has been recent progress, for example, the USA enacted legislation in 2022 that requires "diversity action plans" for clinical trials that are used by the US Food and Drug Administration in determining whether a medicine is safe and effective *(74)*. In 2022, WHO Member States approved a resolution to strengthen clinical trials *(75)*, in which the Director-General is requested to provide

> guidance on best practices for non-State actors in the design and conduct of clinical trials and in strengthening the global clinical trial ecosystem to meet the needs of major population groups that the intervention is intended to benefit, with a particular focus on under-represented populations, developed in consultation with Member States and relevant non-State actors.

Use of AI for recruitment into clinical trials introduces both risks and opportunities for improving or undermining inclusivity. Use of AI could, for example, either accentuate or mitigate racial bias or bias in relation to differences in sex and gender. AI-powered patient matching algorithms could improve the diversity of trial cohorts if they are used to increase outreach to identify a more diverse patient cohort *(46)*. To do so, other investments will be required, including measures to address the digital divide (uneven distribution of access to, use of or effect of information and communication technologies in distinct groups) and appropriate safeguards to respect patient privacy. Such investments, when accompanied by other measures, can help to overcome entrenched barriers to equitable participation in clinical trials, including injustice to racial and ethnic minorities in the name of science, lack of access to care due to physical distance and unaffordable health care.

4.3 Strengthening pharmacovigilance

AI could be used to improve detection of safety signals (information about a potential adverse event due to a pharmaceutical product) both during a clinical trial and after approval of a medicine. With increasing reports of adverse reactions, AI could be used to detect safety signals that are difficult to identify with current methods, including drug–drug interactions, drug–disease interactions, medication errors, secondary malignancies, changes in the frequency and severity of known events, patterns of use of medications, and misuse *(76)*. AI could be used in identifying adverse events for case reports, such as to assess whether the report is valid and meets minimum reporting requirements *(47)*. WHO has developed an open-source monitoring tool, the Peek Platform, in which AI is used to detect, identify and classify adverse events associated with COVID-19 vaccines reported in online discussions *(77)*.

There is, however, broader concern that such use of AI, whether by pharmaceutical companies, governments or international agencies, could undermine the right to privacy if the data are not collected within a robust national and international regulatory environment. In response, the Council for International Organizations of Medical Sciences formed a working group in February 2022 to promote principles and guidance for use of AI in the field of pharmacovigilance *(78)*.

Even if AI could simplify pharmacovigilance and the conduct of post-marketing studies, pharmaceutical companies might not choose to conduct such studies if there is no legal requirement, incentive or both. If developers wish to use AI-based systems to simplify pharmacovigilance, such use might require additional approval by a regulatory authority *(79)*. These applications could eventually be superseded by using AI to examine electronic health records to assess how a population responds to a new treatment or vaccine.

4.4 Monitoring the procurement, supply and distribution of medicines in low- and middle-income countries

The inter-related challenges in supplying and distributing medicines and vaccines, especially in low- and middle-income countries, include lack of transparency in the supply chain and shortages and stock-outs of medicines. These undermine work to achieve universal health coverage. Although pharmaceutical companies are increasingly using AI to manage the supply and distribution of medicines *(57)*, including monitoring the cold chain for transport of vaccines *(58)*, introduction of such uses of AI by low- and middle-income countries will require significant investment to overcome the digital divide to ensure that appropriate data are collected. Those parts of a country's health system most susceptible to shortages and stock-outs may also be less likely to have the appropriate connectivity to collect data.

5 Risks and challenges

AI technologies not only provide benefits for public health and drug development but also pose challenges and risks. WHO guidance on the ethics and governance of AI for health *(1)* identifies 10 specific concerns with use of AI for health. These challenges are relevant to use of AI in drug development, as discussed below.

5.1 Bias

As noted above, development of medicines and vaccines is already affected by bias. Clinical testing of investigational compounds often does not represent all potential patient populations according to race, ethnicity, gender, age and other characteristics *(46)*. This can undermine achievement of universal health coverage. For example, the average delay in access to paediatric versions of adult medicines for infectious diseases such as HIV/AIDS and for antibiotics is 10 years *(80)*.

Biases and discrimination are often replicated by AI technologies used in health care. The three most common forms of bias are in the data sets used to train AI technologies, those related to who develops AI technologies, and those in deployment of the technology (contextual bias) *(1)*.

Thus, data sets used to train algorithms for use in drug development may contain certain biases, including under-sampling of people with irregular or limited access to health care. These include ethnic minorities, women and socially disadvantaged groups and can be expressed in electronic health records, genomic databases and biobanks *(81)*. Training or validating algorithms with these data can encode the biases in algorithms, making them unrepresentative, such that the models are not sufficiently generalizable, resulting in suboptimal outcomes or harm for disadvantaged groups *(81)*. For example, if a researcher uses machine learning with a biased dataset and finds a biomarker for predicting the response to a therapy, there is no guarantee that the biomarker will be appropriate for a more diverse population than that represented in the training data. If the biomarker is used to define the approved indication for a medicine, the medicine could have different effects in different racial groups *(82)*.

Another form of bias is that electronic health records and other forms of health data encode disparities in healthcare access and quality, as well as human biases and discriminatory biases in clinical care. The discriminatory patterns in such data will infiltrate AI models trained with them *(81)*. Biases may also be introduced according to who funds and designs an AI technology, as AI-based technologies have tended to be developed by people of one gender in one demographic group. This can increase the likelihood of certain biases in the design *(1)*.

5.2 Safety

Patient safety can be endangered if the algorithms used in drug development are not tested for potential errors or for whether they provide, for example, false-positive or false-negative recommendations. It has been shown that an algorithm can not only identify or design new, medically beneficial compounds but could also be used to discover 40 000 toxic chemical compounds that could be used as biological weapons in less than 6 h. Thus, in the words of a researcher, "let loose on the world of biology, AI could be dangerous" *(38)*. While humans could conduct such research without AI, the diffusion of such technology with the speed and accuracy of AI heightens such concerns. WHO has identified dual use research as a major area of bio-risk and has released guidance to govern such research *(83)*. To prevent these types of risks, governments will have to introduce laws and regulations.

5.3 Explainability and transparency

As for all uses of AI in health care and medicine, researchers, regulators and health-care providers may find ethical difficulty in relying on use of AI for the development of medicines when decisions are made based on "black-box" algorithms. The widely held convention is that many algorithms, such as those based on artificial neural networks and other complex models, are "black boxes" that make inferences and decisions that are not understood, even by their developers *(1)*. There is a possible trade-off between full "explainability" of an algorithm (at the cost of accuracy and effectiveness) and accuracy and effectiveness (at the cost of explainability). WHO recommends that all algorithms be tested rigorously in the settings in which the technology will be used to ensure that they meet standards of safety and efficacy. The testing should include the assumptions, operational protocols, data properties and output decisions of the AI technology *(1)*. Certain black box algorithms could be used if the developer can demonstrate to a relevant regulatory authority that interpretable models show "unsatisfactory performance or robustness" *(79)*.

Another concern is the degree to which developers are transparent, including sharing the data used to train an algorithm, the source code and the performance of the AI. Ultimately, regulators must determine whether use of AI technologies in the design, discovery, development and post-marketing monitoring of new medicines can be trusted, and the information that is required to validate use of specific AI technologies in drug development or use of new medicines *(76)*.

5.4 Responsibility and accountability

Responsibility ensures that individuals and entities are held accountable for any adverse effects of their actions. Responsibility is also necessary to maintain trust and to protect human rights. It can include preventing any harm or damage in the first place *(84)*.

Certain characteristics of AI technologies affect notions of responsibility (and accountability), including their opacity, reliance on human input, interaction, discretion, scalability, capacity to reveal insights and the complexity of the software. One challenge in assigning responsibility is the "control problem", whereby developers and designers of AI may not be held responsible because AI-guided systems function independently of their developers and may evolve in ways that the developers can claim were not foreseeable. This creates a gap in responsibility. Use of AI that does not function as it was intended to at any point in drug development could place an undue burden on the victim of any harm. Developers or designers may not be deemed responsible, as they have no control, but they may still be responsible, as they are the only people who can bear responsibility.

A second challenge is the problem of "many hands" or the "'traceability" of harm, which bedevils health-care decision-making systems and could bedevil a complex system for development of a new medicine. Development of both AI and medicines involves many different entities, which can make it difficult, both legally and morally, to assign responsibility, as it is diffused among all the contributors. Furthermore, some entities involved in the development or use of AI may not yet be within the scope of relevant legal or regulatory mechanisms.

The participation of a machine in making decisions may discourage assignment of responsibility to the humans involved in the design, selection and use of the technology. Diffusion of responsibility may mean that an individual is not compensated for the harm he or she suffers; the harm itself and its cause are not fully detected or traced back to the source (including the lifecycle of the data); the harm is not addressed; and societal trust in such technologies may be diminished if it appears that none of the developers or users can be held responsible.

5.5 Privacy and informed consent

The collection, analysis and use of health and other data are critical at each step in the use of AI in drug discovery, development and post-marketing commercialization. Therefore, both pharmaceutical and technology companies that invest in AI for drug development use data that they already have, such as the large stores of data that pharmaceutical companies have from clinical trials. Companies also collect data on patients from other sources, such as hospital systems, including cellular data and genetic information, and from social media *(85)*.

The potential benefits of health data and biomedical "big data" can be ethically important, as they can be used to identify new drug targets, improve the accuracy and speed of clinical trials and reduce the rate of attrition. There is, however, concern about use of health data in AI-guided drug development, particularly for safeguarding everyone's right to privacy. The collection, use, analysis and sharing of health data have consistently raised broad concern about individual privacy, because lack of privacy may either harm an individual (such as discrimination, manipulation or exploitation of individuals or their families on the basis of

health status) or cause a wrong, such as affecting a person's dignity, autonomy or safety if sensitive health data are shared or broadcast. Sharing or transferring data can make people vulnerable to cyber-theft, accidental disclosure, government exploitation, discriminatory health insurance terms or exploitative marketing practices *(1)*.

Use of health data in AI-based drug development presents unique concerns. For example, in clinical trials, patients who are recruited through AI (by mining health records and other information, such as social media) must give informed consent that is meaningful for such uses of their data. They might have to be contacted proactively and additional measures used to ensure that their informed consent is meaningful. Use of publicly available data (such as from social media) or combining health-care and non-health-care datasets is inherently risky unless high standards of protection for privacy and human rights are followed.

Another concern is that the investigators in clinical trials in which AI is used might request third parties to make sense of the data or to apply proprietary algorithms. The participation of third parties raises concern about the handling of sensitive health data, the commitment of any third party to the business and professional standards of health-care companies, subsequent uses of the data and to whom access is provided *(50)*.

Pharmaceutical companies are working with health systems and hospitals to prepare and use data sets that could provide unique insights for drug discovery and clinical development. For example, the Mount Sinai Health System in the USA is building a vast database of genetic information on patients that can be used by researchers. One large pharmaceutical company, which is assuming the cost of sequencing many DNA samples, will in return have access to the genetic sequences and anonymized medical records of each participant, comprising diagnoses, laboratory reports and vital signs. The genetic datasets can be used to identify mutations that are either associated with a disease or protect against it *(86)*. While such collaboration may provide ethically important medical benefits, including knowledge of mutations and their association with illnesses, there is strong concern that if such datasets are leaked, sold or stolen, individuals and their families could be discriminated against. Furthermore, once such data have been used, they may not be carefully protected, which could result in unauthorized access and disclosure *(86)*.

A further issue is that entry of technology companies, including the world's largest, into the field of AI for drug development could introduce data practices that raise concern. Large technology companies, many of which are now in partnership with the pharmaceutical industry, operate in a sector in which data-sharing and protection of privacy are less constrained than in the biomedical domain. Thus, large technology companies may not observe many of the practices of companies that have provided health-care products and services for decades, and technology companies may not be subject to relevant regulations or laws, as they are not yet characterized as "health providers". Given broader concern about how technology companies use data, including exploitation, their business practices might have implications for how they use medical and health data in AI to develop medicines *(87)*.

6 Challenges in governance

Introduction and use of AI in the pharmaceutical value chain will pose new challenges to governance of the pharmaceutical sector. Furthermore, although drug development is regulated both individually and collectively by governments, the introduction of AI will require revision of existing regulatory approaches and new standards to ensure quality, safety and efficacy. Some challenges in governance that should be addressed collectively by the international community and governments to keep up with this fast-changing sector are discussed below.

6.1 Governance of data

Data are critical to the discovery and development of medicines and vaccines with AI. The use and sharing of data raise considerations of privacy. In some situations, it will be illegal or unethical to share data that were collected only for purposes to which the user specifically consented. Datasets that were collected legally and ethically for use in drug development might not be available or permitted for use to improve the development of new medicines and vaccines *(29)*. This might be the case, for example, when generation of data was either supported financially or done by a company, when the data sets would be considered a commercial benefit that is proprietary and, in some jurisdictions, protected by intellectual property (IP) rights. At present, several types of IP rights, including trade secrets, copyright and database rights (in a few jurisdictions), may apply to data. Conferring IP and related rights to health data could discourage open sharing of the data, especially if companies that exercise IP rights do not make the data sets available to third parties or on commercially reasonable terms *(1)*.

Currently, pharmaceutical companies are collaborating to develop systems for combining data to strengthen their work on drug discovery *(88)*. While such data-sharing platforms may be rich and can benefit the pharmaceutical industry *(8)*, they may not be available to other entities, including not-for-profit developers and smaller pharmaceutical firms that usually target unmet needs that will generate public health benefits *(29)*.

One means for wider distribution of the benefits of AI is to ensure open data or to make datasets that are legally collected and used for or generated by R&D open and freely available, at least for non-commercial use. This concept was supported by over 80 governments that adopted the “Open Data Charter”, which commits signatory countries to develop policies for making data accessible and freely available, while protecting the individual rights of people and communities *(29)*. A concern related to open data approaches is that the data sets lack adequate “depth, dimensionality and scale” for application of AI to drug R&D *(8)*. Some governments have taken steps to improve the availability of open data for biomedical

research by supporting cohorts of volunteers who have consented to use of their data in research. One of the largest is the UK Biobank in the United Kingdom, with 500 000 participants, which allows distribution of de-identified data to approved researchers who are investigating common and life-threatening diseases *(89)*. Its Ethics and Governance Council applies a framework to govern ethical use of the data that are collected and shared *(90)*.

Population-wide data, such as from an entire health-care system, would be preferable for research, rather than smaller, potentially biased cohorts. Citizens' concern about the privacy of sensitive health data, even after anonymization, has led to development of models in which data are not distributed, and can be accessed only by researchers in secure environments. The United Kingdom, through Health Data Research UK, has been advocating for adoption of "trusted research environments" (TREs), which are single locations from which researchers can access datasets, encourage collaboration and assure those who contribute data that such data are accessed securely and their privacy is protected *(91)*. The TRE approach has been adopted as policy by the English National Health Service, which is establishing a number of regional "secure data environments" to support research. The approach creates specific challenges for AI and for other intensive data analysis, as any software required by researchers should be moved into a TRE, which must have access to sufficient computer resources to run it.

At a multinational level, the European Union is developing a European Health Data Space *(92)*, a

> health-specific data sharing framework establishing clear rules, common standards and practices, infrastructures and a governance framework of electronic health data by patients and for research, innovation, policy making, patient safety, statistics or regulatory purposes.

Currently, it is envisaged that individual data will remain within national boundaries in TRE-like infrastructure. This will require use of "data federation" technology to analyse data from several countries, which will pose challenges for training AI models while preserving privacy. Introduction of broader standards that can be applied worldwide could improve data-sharing and governance but would require strong cooperation among databanks, academic institutions, funders and governments *(8)*.

6.2 Ownership and intellectual property

There is debate about assigning ownership for inventions that rely on AI, including whether an entity or an individual that uses AI can claim "inventorship". This raises the issue of whether new medicines developed with use of AI can be patented *(93)*.

The impact of IP on the development of and access to medicines is a long-standing, critical issue. While IP rights provide pharmaceutical companies with a limited right to recuperate

investments in R&D through the exclusive right to register and market a new medicine or vaccine, such monopoly rights can lead to unaffordable prices and other practices, such as distortion of markets and inadequate supplies, which limit access *(94)*. Furthermore, IP rights do not encourage companies to invest in R&D for commercially unattractive areas, such as neglected tropical diseases, paediatric health, drug-resistant infections and pandemic threats *(95)*. Use of AI in drug development introduces new considerations for policy-makers, such as finding and using alternative models to pay for development of and access to AI to be used in the public interest.

First, mining of data can help to identify promising new compounds and vaccines. If the data are collected from individuals for other purposes, however, it is questionable whether they can be used for commercial purposes if the medicines developed from such data are not available to those who provided the data and more broadly if the compounds and vaccines are not available in the public interest, such as by setting affordable prices *(96)*.

Another concern is the increased patenting of algorithms used in drug development and the use of trade secrets to prevent use of algorithms except by their IP owner, which could lead to IP "lock-up" *(8)*. IP restrictions on algorithms will exclude most entities from using them to improve drug development, especially academic researchers, not-for-profit organizations and entities in low- and middle-income countries *(8)*, all of whom are more likely to focus on unmet needs ignored by the pharmaceutical industry *(97)*. Exclusive control of algorithms also impedes advancement of science and limits the potential broader social benefits of AI. Exercise of IP rights encourages secrecy, as companies will not disclose source code or other information about their proprietary algorithms. While companies may have a commercial rationale for lack of transparency, this can undermine public trust and prevent regulators from ascertaining whether medicines developed with AI meet regulatory standards. Patenting also often involves protection of AI algorithms that were originally developed with public funding or by publicly funded research *(97)*.

Companies that develop AI algorithms may not themselves develop medicines and vaccines but may issue licenses to the highest bidder, thereby limiting use of the technologies to the world's largest pharmaceutical and technology firms or for use in certain geographical locations. Such licensing practices are ending, however, as companies that develop AI-based platforms and technologies are developing new medicines rather than out-licensing their software *(8)*. Pharmaceutical companies are also spending significant sums of money to acquire compounds developed by smaller companies that use AI for drug development *(98)*, thereby increasing the incentive for those companies to protect their proprietary algorithms and to focus on diseases that generate profits from the pharmaceutical industry.

6.3 Governance of the private sector

The ownership of data sets and IP protection of algorithms contribute to potential concentration of decision-making and power in a small group of companies that use AI in drug

development. There is concern about the emergence of "walled gardens" in the private sector with respect to use of AI *(98)*. Companies already exert significant control over data, including through industry-owned pre-competitive platforms. Furthermore, there is a growing number of partnerships between large technology companies and large pharmaceutical companies, which could consolidate power in the hands of a few. Such companies are likely to have not only significant financial resources but also data, computing power, technology and most AI programmers. The size of a company's platform, including for drug development, may create a monopoly. As AI, such as generative AI to design new medicines, becomes increasingly sophisticated and requires more resources, few companies will be able to use it. Monopoly power can concentrate decision-making in the hands of a few individuals and companies, which can result in higher prices for goods and services, less consumer protection and less innovation, and the choices, priorities and outputs of AI will be limited by the decisions made by a few companies *(99)*. These could include decisions to deprioritize or abandon products and services that may be of significant public health importance and instead prioritize services that can generate revenue. In 2023, one major technology company "axed" the team that had developed the protein-folding model ESMFold (see above), and there is concern about whether the company will "absorb the costs to keep the database running, as well as another service that allows scientists to run the ESM algorithm on new protein sequences" *(29)*.

Competition and anti-trust laws, depending on the degree of concentration and exclusion, may be necessary to sustain or promote equitable access to critical AI technologies, a healthy innovation eco-system and affordable prices for end products, while avoiding ethical risks such as discrimination and bias.

Companies often refer to use of their own ethics codes to guide use of AI, and pharmaceutical companies are increasingly developing their own ethical standards for use of AI *(100)*. While consideration of ethics by a company is welcome, it can raise concern that the companies are engaging in "ethics-washing" and that the measures are intended to forestall regulation instead of adapting to oversight *(88)*. Such codes are not an alternative to or a substitute for legal rules and obligations set by governments. One means for governments to ensure that companies select and use AI appropriately is impact assessments, which can address ethics, human rights, safety and data protection throughout the life cycle of an AI system.

In addition to regulatory standards written and enforced by governments, open science machine learning can be promoted to improve access to AI technologies in drug development. Examples include the Therapeutic Data Commons *(1)*, the Open-Source Molecular Foundation and the Human Immunome Project *(101)*.

6.4 Regulatory oversight and approval of AI-developed medicines and vaccines

As AI increasingly automates or replaces some functions usually carried out by humans in the development and delivery of medicines, regulatory authorities could act to preserve "human-led governance" *(8)* of AI-based pharmaceutical R&D, particularly to uphold core ethical principles, human rights obligations and legal and safety requirements. New approaches will be needed to ensure that independent oversight and review of pharmaceuticals developed with AI technology do not impede use of such technologies but also do not ignore risks. This should be done individually and collectively, such as the on-going efforts of the International Coalition of Medicine Regulatory Agencies to reflect on the challenges of AI and to identify a common response *(47)*.

Regulators will have to address many challenges to assess both AI technologies that companies wish to use in development and delivery of medicines and the medicines and vaccines in which AI technologies have been used. First, as for all AI technologies, regulators will have to overcome the lack of explainability of how algorithms arrive at decisions that may guide pharmaceutical discovery and development, especially in highly complex models *(76)*. Secondly, there may be concern about the quality of the data used to train AI, including bias *(47)*. Thirdly, regulators will need to coordinate with other relevant government agencies, such as data protection agencies, to ensure that data were collected lawfully, according to national or international principles and standards for data protection. Fourthly, they must overcome the reticence of companies to be fully transparent about the source code or data sets used in AI technologies, which undermines the ability of regulators to assess the uses of AI *(102)*. Fifthly, different regulatory standards may emerge around the world, which could pose a challenge to both regulators who assess AI technologies and developers who use AI *(76)*.

Irrespective of such risks and challenges for regulatory authorities, it is the responsibility of developers who choose to use AI technologies to ensure that the tools and methods are "fit-for-purpose" and adhere to all ethical, technical, scientific and regulatory standards designated and enforced by regulatory agencies *(76)*.

7 Next steps

The promise of AI requires the international community and governments to ensure that use of the technology in pharmaceutical and vaccine development and delivery does not exacerbate inequity but contributes to addressing the needs of neglected populations (such as children and infants) and countries, and to find new vaccines and medicines for unmet needs. To do so, governments must establish an effective approach to governance, including defining standards, rules, regulations and legal frameworks that prioritize public health and the public interest. WHO will continue to examine and monitor how AI is affecting the development and delivery of medicines and vaccines and identify ways in which WHO, Member States, pharmaceutical companies, civil society and global health-oriented product development partnerships and researchers can harness AI to improve pharmaceutical development and access to address unmet health needs. WHO may also develop new ethics guidance and address issues of governance for management of data, regulatory considerations and legislation to address the many benefits and challenges associated with use of AI in the development and delivery of medicines and vaccines.

References

1. Ethics and governance of artificial intelligence for health. Geneva: World Health Organization; 2021 (https://www.who.int/publications/i/item/9789240029200, accessed 13 April 2023).

2. Generating evidence for artificial intelligence-based medical devices: a framework for training, validation and evaluation. Geneva: World Health Organization; 2021 (https://iris.who.int/bitstream/handle/10665/349093/9789240038462-eng.pdf?sequence=1).

3. Savage N. News feature. Tapping into the drug discovery potential of AI. Nature, 27 May 2021 (https://www.nature.com/articles/d43747-021-00045-7, accessed 13 April 2023).

4. Bender A, Cortes-Ciriano I. Artificial intelligence in drug discovery: what is realistic, what are illusions? Part 2: a discussion of chemical and biological data. Drug Discov Today; 2021;26(4):1040–52. doi:10.1016/j.drudis.2020.11.037.

5. Artificial intelligence and machine learning for drug development. Silver Spring (MD): Food and Drug Administration; 2023. (https://www.fda.gov/science-research/science-and-research-special-topics/artificial-intelligence-and-machine-learning-aiml-drug-development, accessed 26 June 2023).

6. National Library of Medicine, National Center for Biotechnology Information (https://pubmed.ncbi.nlm.nih.gov/?term=(((%22deep%20learning%22%5BTitle%2FAbstract%5D)%20OR%20(%22machine%20learning%22%5BTitle%2FAbstract%5D))%20OR%20(%22artificial%20intelligence%22%5BTitle%2FAbstract%5D))%20OR%20(%22computer%20vision%22%5BTitle%2FAbstract%5D)%20OR%20(%22natural%20language%20processing%22%5BTitle%2FAbstract%5D)%20OR%20(%22reinforcement%20learning%22%5BTitle%2FAbstract%5D)&timeline=expanded, accessed 14 April 2023).

7. Madura KPJ, Xie W, Ruder L, Schulze U, Meier C. AI in small-molecule drug discovery: a coming wave? Nat Rev Drug Discov. 2022;21(3):175–6. doi:10.1038/d41573-022-00025-1.

8. Unlocking the potential of AI in drug discovery. London: Wellcome Trust; 2023 (https://wellcome.org/reports/unlocking-potential-ai-drug-discovery, accessed 4 August 2023).

9. Miseta E. DiMe reports significant growth in digital endpoints. Clinical Leader, 9 December 2021 (https://www.clinicalleader.com/doc/dime-reports-significant-growth-in-digital-endpoints-0001, accessed 14 April 2023).

10. Artificial intelligence for drug discovery. Landscape overview Q3 2022. London: Deep Pharma Intelligence; 2022 (https://www.deep-pharma.tech/ai-in-dd-q3-2022-subscribe, accessed 13 April 2023).

11. Furlong A. Regulating the machine: Europe's race to get to grips with AI drugs. Politico, 7 April 2023. (https://www.politico.eu/article/regulate-europe-race-artificial-intelligence-ai-drugs-medicines/, accessed 25 April 2023).

12. Mohs RC, Greig NH. Drug discovery and development: Role of basic biological research. Alzheimers Dement (N Y). 2017;3(4). doi:10.1016/j.trci.2017.10.005.

13. Wang H, Fu T, Du Y, Gao W, Huang K, Liu Z et al. Scientific discovery in the age of artificial intelligence. Nature. 2023;620(7972):47–60. doi:10.1038/s41586-023-06221-2.

14. Dill KA, Ozkan SB, Shell MS, Weikl TR. The protein folding problem. Annu Rev Biophys. 2008;37:289–316. doi:10.1146/annurev.biophys.37.092707.153558.

15. Metz C. London AI lab claims breakthrough that could accelerate drug discovery. The New York Times, 30 November 2020 (https://www.nytimes.com/2020/11/30/technology/deepmind-ai-protein-folding.html, accessed 23 April 2023).

16. Heaven WD. AI for protein folding. MIT Technology Review, 23 February 2022 (https://www.technologyreview.com/2022/02/23/1044957/ai-protein-folding-deepmind/#:~:text=That%20changed%20with%20DeepMind's%20AlphaFold2,techniques%20used%20in%20the%20lab., accessed 23 April 2022).

17. AlphaFold protein structure database. Hinxton: EMBL-EBI; 2023 (https://alphafold.ebi.ac.uk/about, accessed 20 September 2023).

18. Nolan A. Artificial intelligence and the future of science. Paris: Organisation for Economic Co-operation and Development; 2021 (https://oecd.ai/en/wonk/ai-future-of-science, accessed 22 April 2023).

19. Kollewe, Julia, Drug companies look to end "hit and miss" research. The Guardian, 20 February 2021 (https://www.theguardian.com/business/2021/feb/20/drug-companies-look-to-ai-to-end-hit-and-miss-research, accessed 22 April 2023).

20. Pun FW, Ozerov IV, Zhavoronkov A. AI-powered therapeutic target discovery. Trends Pharmacol Sci. 202344(9):561–72. doi:10.1016//j.tips.2023.06.010.

21. Wetsman N. 23andMe sold the rights to a drug it developed from its genetic database. The Verge, 10 January 2020 (https://www.theverge.com/2020/1/10/21060456/23andme-licensed-drug-developed-genetic-database-autoimmune-psoriasis-almirall, accessed 22 April 2023).

22. GSK and 23andMe sign agreement to leverage genetic insights for the development of novel medicines. London: GlaxoSmithKline; 2018 (https://www.gsk.com/en-gb/media/press-releases/gsk-and-23andme-sign-agreement-to-leverage-genetic-insights-for-the-development-of-novel-medicines/, accessed 22 April 2023).

23. Seife C. 23andMe is terrifying, but not for reasons the FDA thinks. Scientific American, 27 November 2013 (https://www.scientificamerican.com/article/23andme-is-terrifying-but-not-for-the-reasons-the-fda-thinks/#, accessed 5 August 2023).

24. Paul K. Fears over DNA privacy and 23andMe plans to go public in deal with Richard Branson. The Guardian, 9 February 2021 (https://www.theguardian.com/technology/2021/feb/09/23andme-dna-privacy-richard-branson-genetics, accessed 5 August 2023).

25. Schneider G, Böhm HJ. Virtual screening and fast automated docking methods. Drug Discovery Today, 1 January 2002 (https://pubmed.ncbi.nlm.nih.gov/11790605/, accessed 5 August 2023).

26. Liu G, Catacutan D, Rathod K, Swanson K, Jin W, Mohammed J et al. Deep learning-guided discovery of an antibiotic targeting Acinetobacter baumannii. Nature Chem Biol. 2023. doi:10.1038/s41589-023-01349-8.

27. Yang M. Scientists use AI to discover new antibiotic to treaty deadly superbug. The Guardian, 25 May 2023 (https://www.theguardian.com/technology/2023/may/25/artificial-intelligence-antibiotic-deadly-superbug-hospital, accessed 23 June 2023).

28. Using AI, MIT researchers identify a new class of antibiotic candidates. Eurkalert. Massachusetts Institute of Technology; 2023 (https://www.eurekalert.org/news-releases/1029354, accessed 3 January 2024).

29. Artificial intelligence for public good drug discovery: recommendations for policy development. Paris: Global Partnership on Artificial Intelligence; 2021 (https://gpai.ai/projects/ai-and-pandemic-response/public-domain-drug-discovery/ai-for-public-domain-drug-discovery.pdf, accessed 22 April 2023).

30. Geddes L. A silver lining: How Covid ushered in a vaccines golden era. The Guardian, 7 April 2023 (https://www.theguardian.com/science/2023/apr/07/covid-vaccines-golden-era-pandemic-techology-diseases, accessed 22 April 2023).

31. Blakney AK. A tool for optimizing messenger RNA sequence. Nature. 2023;621(7978):262–4. doi:10.1038/d41586-023-01745-z.

32. Matsuyama K. AI drug discovery is a $50 billion opportunity for Big Pharma. Bloomberg Businessweek, 12 May 2023 (https://www.bloomberg.com/news/articles/2023-05-09/pharmaceutical-companies-embrace-ai-to-develop-new-drugs, accessed 11 May 2023).

33. Schneider G. De novo molecular design. Hoboken (NJ): Wiley; 2013 (https://wiley.com/en-us/De+novo+Molecular+Design-p-9783527677030).).

34. Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade RK. Artificial intelligence in drug discovery and development. Drug Discov Today. 2021;26(1):89–93. doi:10.1016/j.drudis.2020.10.010.

35. Sphere L. How huge protein language models could disrupt structural biology. Towards Data Science, 22 November 2022. (https://towardsdatascience.com/how-huge-protein-language-models-could-disrupt-structural-biology-6b98193f880b, accessed 2 June 2023).

36. Lin Z, Akin H, Rao R, Hie B, Zhu Z, Lu W et al. Evolutionary-scale prediction of atomic-level protein structure with a language model. Science. 2023;379(6637):1123–30. doi:10.1126/science.ade2574.

37. Elofsson A. Progress at protein structure prediction, as seen in CASP15. Curr Opin Structural Biol. 2023;80:102594. doi:10.1016/sbi.2023.102594.

38. Kuchler H. Will AI turbocharge the hunt for new drugs? Financial Times, 20 March 2022 (https://www.ft.com/content/3e57ad6c-493d-4874-a663-0cb200d3cdb5, accessed 23 April 2023).

39. Artificial intelligence in healthcare: Benefits and challenges of machine learning in drug development. Washington DC: Government Accountability Office; 2019 (https://www.gao.gov/assets/gao-20-215sp.pdf, accessed 27 April 2023).

40. Commission acts to accelerate phasing out of animal testing in response to a European Citizens' Initiative. Brussels: European Commission; 2023 (https://ec.europa.eu/commission/presscorner/detail/en/ip_23_3993, accessed 20 September 2023).

41. Craven J. AI in drug manufacturing: Stakeholders call for harmonization, further guidance. Regulatory Focus, 9 May 2023 (https://www.raps.org/News-and-Articles/News-Articles/2023/5/AI-in-drug-manufacturing-Stakeholders-call-for-har, accessed 20 September 2023).

42. Jiang Y, Yu Y, Kong M, Mei Y, Yuan L, Huang Z et al. Artificial intelligence for retrosynthesis prediction. Engineering. 2023; 25(6). doi:10.1016/j.end.2022.04.021.

43. Lowe D. The machines rise a bit more. Science, 20 October 2020 (www.science.org/content/blog-post/machines-rise-bit-more, accessed 5 August 2023).

44. Zhong Z, Song J, Feng Z, Liu T, Jia L, Yao S et al. Recent advances of artificial intelligence for retrosynthesis. arXiv:2302.05864v1. doi:10.48550/arXiv.2301.05864.

45. Askin S, Burkhalter D, Calado G, El Dakrouni S. Artificial intelligence applied to clinical trials: opportunities and challenges. Health Technol (Berl). 2023;13(2):201–13. doi:10.1007/s12553-023-00738-2.

46. Woo M. Trial by artificial intelligence. Nature. 2019;573:2100–2. (https://media.nature.com/original/magazine-assets/d41586-019-02871-3/d41586-019-02871-3.pdf, accessed 23 April 2023).

47. Using artificial intelligence & machine learning in the development of drug & biological products. Silver Spring (MD): Food and Drug Administration; 2023 (https://www.fda.gov/media/167973/download, accessed 26 June 2023).

48. Zhavoronkov A, Vanhaelen Q, Oprea TI. Will artificial intelligence for drug discovery impact clinical pharmacology? Clin Pharmacol Ther. 2020;107(4):780–5. doi:10.1002/cpt.1795.

49. Reed J. How AI-based technologies improve clinical trial design, site selection and competitive intelligence. Drug Discovery and Development, 21 July 2022 (https://www.drugdiscoverytrends.com/how-ai-based-technologies-improve-clinical-trial-design-site-selection-and-competitive-intelligence/, accessed 5 August 2023).

50. Fultinaviciute U. AI benefits in patient identification and clinical trial recruitment has challenges in sight. Clinical Trials Arena, 20 April 2022 (https://www.clinicaltrialsarena.com/features/ai-clinical-trial-recruitment/, accessed 23 April 2023).

51. Tanaka I, Furukawa T, Morise M. The current issues and future perspective of artificial intelligence for developing new treatment strategy in non-small cell lung cancer: harmonization of molecular cancer biology and artificial intelligence. Cancer Cell Int. 2021;21:454. doi:10.1186/s12935-021-02165-7.

52. Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters. Biostatistics. 2019;20(2):273–86. doi:10.1093/biostatistics/kxx069.

53. Bergman E, Sherwood K, Forslund M, Arlett P, Westman G. A natural language processing approach towards harmonisation of European medicinal product information. PLoS One. 2022;17(10):e0275386. doi:10.1371/journal.pone.0275386.

54. Consultation on good practices for health products manufacture and inspection: industry consultation. Geneva: World Health Organization; 2023 (https://www.who.int/publications/m/item/consultation-on-good-practices-for-health-products-manufacture-and-inspection--industry-consultation, accessed 5 October 2023).

55. Galata DL, Mészáros LA, Kállai-Szabó N, Szabó E, Pataki H, Marosi G et al. Applications of machine vision in pharmaceutical technology: a review. Eur J Pharmaceutic Sci. 2021;159:105717. doi:10.1016/j.ejps.2021.105717.

56. Artificial intelligence in drug manufacturing. Silver Spring (MD): Center for Drug Evaluation and Research, Food and Drug Administration; 2023 (https://www.fda.gov/media/165743/download, accessed 26 June 2023).

57. Keeping an eye and ear on patients' needs: Where AI meets supply chains. Darmstadt: Merck Group; undated (https://www.merckgroup.com/en/research/science-space/envisioning-tomorrow/precision-medicine/ai-in-supply-chain.html, accessed 25 April 2023)

58. Gao Y, Gao H, Xiao H, Yao F. Vaccine supply chain coordination using blockchain and artificial intelligence technologies. Comput Industr Eng. 2023;175:108885. doi:1016/j.cie.2022.108885.

59. Role of AI in pharmaceutical supply chain management. Bellevue (WA): Xenore; 2023 (https://www.xenore.com/role-of-ai-in-pharmaceutical-supply-chain-management/, accessed 16 May 2023).

60. Khanna V, Ahuja R, Popli H. Role of artificial intelligence in pharmaceutical marketing: a comprehensive review. J Adv Sci Res. 2020;11(3):54–61. (https://sciensage.info/index.php/JASR/article/view/506/226, accessed 23 April 2023).

61. The future of patient support. Cairo: NAOS Solutions; 2023 (https://naos-solutions.com/the-future-of-patient-support/, accessed 5 August 2023).

62. Bhalodia P, Edwards K. How pharma companies can enhance patient support programs with generative AI. Chicago (IL): West Monroe; 2023 (https://www.westmonroe.com/perspectives/in-brief/how-pharma-companies-can-enhance-patient-support-programs-generative-ai, accessed 5 August 2023).

63. Precision medicine. Silver Spring (MD): Food and Drug Administration; 2018 (https://www.fda.gov/medical-devices/in-vitro-diagnostics/precision-medicine#:~:text=Precision%20medicine%2C%20sometimes%20known%20as,genes%2C%20environments%2C%20and%20lifestyles., accessed 24 April 2023).

64. Lisbona N. How artificial intelligence is matching drugs to patients BBC News, 17 April 2023 (https://www.bbc.com/news/business-65260592, accessed 11 May 2023).

65. The promises and perils of personalized medicines. Pittsburgh (PA): Knowledge at Wharton, University of Pennsylvania; 2012 (https://knowledge.wharton.upenn.edu/article/the-promise-and-perils-of-personalized-medicine/, accessed 23 April 2023).

66. Ban TA. The role of serendipity in drug discovery. Dialogues Clin Neurosci. 2006;8(3):335–44. doi:10.31887/DCNS.2006.8.3/tban..

67. Artificial intelligence in healthcare: Applications, risks and ethical and societal impacts. Strasbourg: European Parliament, Panel for the Future of Science and Technology; 2022 (https://www.europarl.europa.eu/RegData/etudes/STUD/2022/729512/EPRS_STU(2022)729512_EN.pdf, accessed 24 April 2023).

68. Angelis, A, Polyakov R, Wouters OJ, Torreele E, McKee M. High drug prices are not justified by industry's spending on research and development BMJ. 2023;380:e071710. doi:10.1136/bmj-2022-071710.

69. Sohn E. The reproducibility issues that haunt health-care AI. Nature. 2023;613(7943):402–3. doi:10.1038/d41586-023-00023-2.

70. Harnessing AI and new technologies for pharmaceutical R&D. Geneva: Drugs for Neglected Diseases Initiative; undated (https://dndi.org/advocacy/ai-and-new-technologies-for-pharmaceutical-rd/, accessed 24 April 2023).

71. CEPI partners with Japan's NEC Group to develop artificial intelligence-designed broadly protective betacoronavirus vaccine. London: Coalition for Epidemic Preparedness Innovations; 2022 (https://cepi.net/news_cepi/cepi-partners-with-japans-nec-group-to-develop-artificial-intelligence-designed-broadly-protective-betacoronavirus-vaccine/, accessed 24 April 2023).

72. Cox D. DeepMind wants to use its AI to cure neglected diseases Wired, 23 June 2021 (https://www.wired.co.uk/article/deepmind-alphafold-protein-diseases, accessed 24 April 2023).

73. Gender equity in drug development. Geneva: Drugs for Neglected Diseases Initiative; undated (https://dndi.org/advocacy/gender-equity-in-drug-development/, accessed 6 August 2023).

74. Baumann J. Diversity in clinical trials at FDA gets a boost from new law. Bloomberg Law, 19 January 2023 (https://news.bloomberglaw.com/pharma-and-life-sciences/diversity-in-clinical-trials-at-fda-gets-a-boost-from-new-law, accessed 6 August 2023).

75. Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination (WHA 75.8), 27 May 2022. Geneva: World Health Organization; 2022 (https://apps.who.int/gb/ebwha/pdf_files/WHA75/A75_R8-en.pdf, accessed 6 August 2023).

76. Horizon scanning intelligence report. International Coalition of Medicines Regulatory Authorities; 2021 (https://www.icmra.info/drupal/sites/default/files/2021-08/horizon_scanning_report_artificial_intelligence.pdf, accessed 25 April 2021).

77. Unmaking safety signals during a pandemic. Technical meeting report. Geneva: World Health Organization; 2021 (https://cdn.who.int/media/docs/default-source/medicines/pharmacovigilance/unmasking-safety-signals-in-an-infodemic_technical-report.pdf?sfvrsn=5890874b_1&download=true, accessed 6 August 2023).

78. Artificial intelligence in pharmacovigilance: Proposal to form a CIOMS expert working group. Geneva: Council for International organizations of medical Sciences; 2022 (https://cioms.ch/wp-content/uploads/2022/05/CIOMS-Concept-Note-on-AI-in-PV_final-02.02.2022.pdf#:~:text=An%20Expert%20Working%20Group%20managed%20by%20the%20Council,or%20intelligence%20augmentation%20in%20the%20field%20of%20pharmacovigilance, accessed 6 August 2023).

79. Reflection paper on the use of artificial intelligence in the medicinal product lifecycle. Copenhagen: European Medicines Agency; 2023 (https://www.ema.europa.eu/en/documents/scientific-guideline/draft-reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf, accessed 10 August 2023).

80. Pennezato M, Lewis L, Watkins M, Prabhu V, Pascual F, Auton M et al. Shortening the decade-long gap between adult and paediatric drug formulations: a new framework based on the HIV experience in low- and middle-income countries. J Int AIDS Soc. 2018;21(12):e25049. doi:10.1002/jia2.25049.

81. Leslie D, Mazumder A, Peppin A, Wolters MK, Hagerty A. Does “AI” stand for augmenting inequality in the era of covid-19 healthcare? BMJ. 2021;372:n304. doi:10.1136/bmj.n304.

82. Fisher CK. The FDA needs to set standards for using artificial intelligence in drug development. STAT, 7 November 2019 (https://www.statnews.com/2019/11/07/artificial-intelligence-drug-development-fda-standards-needed/, accessed 25 April 2023).

83. Global guidance framework for the responsible use of the life sciences: Mitigating bio-risks and governing dual-use research. Geneva: World Health Organization; 2022 (https://www.who.int/publications-detail-redirect/9789240056107, accessed 10 May 2023).

84. Sand M, Durán JM, Jongsma KR. Responsibility beyond design: Physicians’ requirements for ethical medical AI. Bioethics. 2022;36(2):162–9. doi:10.1111/bioe.12887.

85. Neville S. Drug companies hooked on data. Financial Times, 27 January 2020 (https://www.ft.com/content/8f5de4e2-6847-11ea-a6ac-9122541af204, accessed 26 April 2023).

86. Goldstein J. Hospital and drugmaker move to build vast database of New Yorkers’ DNA. The New York Times, 12 August 2022 (https://www.nytimes.com/2022/08/12/nyregion/database-new-yorkers-dna.html, accessed 26 April 2023).

87. Schuhmacher A, Haefner N, Honsberg K, Goldhahn J, Gassmann O. The dominant logic of Big Tech in healthcare and pharma. Drug Discov Today. 2023;28(2):103457. doi:10.1016/j.drudis.2022.103457.

88. Our commitment to ethical and responsible AI. Basel: Novartis AG; 2023 (https://www.novartis.com/about/strategy/data-and-digital/artificial-intelligence/our-commitment-ethical-and-responsible-use-ai, accessed 26 April 2023

89. About us. Background. Stockport: Biobank; 2023 (https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/about-us, accessed 10 August 2023).

90. Ethics Advisory Committee. Stockport: Biobank; 2023 (https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/governance/ethics-advisory-committee, accessed 10 August 2023).

91. Trusted research environments. London: Health Data Research UK; 2023 (https://www.hdruk.ac.uk/access-to-health-data/trusted-research-environments/, accessed 11 August 2023).

92. Questions and answers – EU health: European Health Data Space (EHDS). Brussels: European Commission; 2022 (https://ec.europa.eu/commission/presscorner/detail/en/qanda_22_2712, accessed 10 August 2023).

93. George A, Walsh T. Artificial intelligence is breaking patent law. Nature. 2022;605(7911):616–8. doi:10.1038/d41586-022-01391-x.

94. Public health, innovation and intellectual property rights: Report of the Commission on Intellectual Property, Innovation, and Public Health. Geneva: World Health Organization; 2006 (https://www.who.int/publications/i/item/9241563230, accessed 27 April 2023).

95. Research and development to meet health needs in developing countries: strengthening global financing and coordination. Geneva: World Health Organization; 2012 (https://www.who.int/publications/i/item/9789241503457, accessed 27 April 2023).

96. Hamzelou J. 23andMe sold the rights to develop a drug based on its users' DNA New Scientist, 10 January 2020 (https://www.newscientist.com/article/2229828-23andme-has-sold-the-rights-to-develop-a-drug-based-on-its-users-dna/, accessed 27 April 2023).

97. The Guardian's view on DeepMind's brain: the shape of things to come. The Guardian, 6 December 2020 (https://www.theguardian.com/commentisfree/2020/dec/06/the-guardian-view-on-deepminds-brain-the-shape-of-things-to-come, accessed 27 April 2023).

98. Taylor NP. Lilly inks US$425 million biobuck drug discovery pact with Schrodinger. Fierce BioTech, 6 October 2022 (https://www.fiercebiotech.com/biotech/lilly-inks-425m-biobuck-drug-discovery-pact-schrodinger, accessed 27 April 2023).

99. Veale M. Privacy is not the problem with the Apple-Google contact tracing toolkit. The Guardian, 1 July 2020 (https://www.theguardian.com/commentisfree/2020/jul/01/apple-google-contact-tracing-app-tech-giant-digital-rights, accessed 27 April 2023).

100. Criddle C, Murphy H. Meta disbands protein-folding team in shift towards commercial AI. Financial Times, 7 August 2023 https://www.ft.com/content/919c05d2-b894-4812-aa1a-dd2ab6de794a, accessed 18 September 2023).

101. Huang K, Fu T, Gao W, Zhao Y, Roohani Y, Leskovec J et al. Artificial intelligence foundation for therapeutic science. Nat Chem Biol. 2022;18(10):1033–6. doi:1038/s41589-022-01131-2.

102. You Y, Lai X, Pan Y, Zheng H, Vera J, Liu S et al. Artificial intelligence in cancer target identification and drug discovery. Signal Transduct Target Ther. 2022;7(1):156. doi: 10.1038/s41392-022-00994-0.

World Health Organization
20 Avenue Appia
CH-1211 Geneva 27
Switzerland
Website: https://www.who.int