

Understanding Drug Development Failures: Scientific, Financial, and Regulatory Drivers

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Abstract

The development of new drugs is expensive and time-consuming, with later-stage clinical trials leading to high expenses. Herein, we examine the cases of recent late-stage drug failures to determine which drugs failed due to a lack of scientific innovation as well as those we feel might have avoided failure had different strategies been pursued. From this analysis, the important considerations for effective drug development become clear. These include an understanding of the pathophysiologic mechanism of the disease in question, its molecular targets, and their pharmacological activity in terms of safety and efficacy, as well as its pharmacokinetics and optimal dosage. Early stage studies should be planned to provide answers to important questions, but with an emphasis on knowledge gathering during the earlier stages of development rather than Phase 3 being used for validation purposes.

Keywords: drug discovery and development, attrition, clinical trials, regulatory approval, target validation, financial risk, and precision medicine

I. Introduction

1.1 Background and Importance of Drug Development

Drug development is the process of developing a new drug molecule for clinical use. In its broadest sense this includes all steps from the basic research process of identifying an appropriate molecular target to supporting the commercial launch of the drug. Only the clinical parts of this process are called development in a narrower sense, discovery is the term used for the nonclinical research parts. Drug discovery is very significant in advancing health care because it provides novel treatment options for diseases where there is no existing or effective treatment method. This will

result in better patient survival rate and improved quality of life. A critical component of drug discovery is the thorough evaluation of toxicity using animal and cellular models. This is important because it determines whether drugs are safe enough to be used in humans. Drug discovery also provides the scientific basis for safety, quality, and efficacy, which form the grounds for the approval of any drug by authorities like the FDA.[2]

1.2 High Attrition Rates in Drug Development

Drug attrition is the term used to describe the high failure rate encountered by drug candidates undergoing clinical testing, usually due to safety reasons, poor efficacy, or excessive toxicity. More than half of all drugs in clinical trials are terminated because of safety problems. Apart from the enormous costs incurred in the process of developing new drugs, drug attrition has delayed the introduction of life-saving medicines into the market. In an effort to minimize attrition rates in clinical trials, clinical pharmacologists have employed various quantitative methods such as PK/PD models.[3]

1.3 Objectives and Scope of the Review

This review aims to provide a clear and evidence-based overview of the major reasons for the failure of drug development for pharmaceutical science professionals and students in pharmacy schools. The scope of this article ranges from preclinical to post-clinical drug development and considers problems that relate to manufacturing, science, finances, regulation, and the external market. This analysis also outlines innovations in technologies and methods that can be useful in reducing the attrition rate in the future.

II. Overview of the Drug Development Process

2.1 Drug Discovery and Preclinical Research

Preclinical studies are conducted using a design that mimics conditions that will prevail during the clinical trial. It entails using an appropriate model as well as performing statistics to determine whether the findings of a study are valid. Designing a study also entails choosing an appropriate sample size, study duration and end-points that reflect the safety and efficacy of a particular drug. Toxicity studies examine reactions to higher doses of a drug and activity or pharmacology studies examine the effect of it on treating a disease.[4]

2.2 Clinical Development Phases (Phase I-III)

The clinical trial procedure is the way through which scientific advancement is attained when it comes to drug treatments in humans. The major principle involved in the clinical trial process involves ensuring the safety of subjects within clinical trials. Each phase of the clinical trial procedure is concerned with testing the safety of the subjects alongside specific objectives. Pharmaceutical companies sponsor clinical trials of medical drugs, while at the same time making application for the approval by FDA after completion of Phase 3 trials. In Phase 4, investigations are carried out regarding infrequent adverse effects and effectiveness of drugs. Clinical trial process takes between 10 to 15 years from start until drug registration.[5]

2.3 Regulatory Approval and Post-Marketing (Phase IV)

Phase IV is not synonymous with post-marketing surveillance (PMS), although all post-marketing surveillance studies are phase IV studies. Phase IV studies also play an important role in drug development. Specifically, in the context of real-world drug effectiveness, the phase IV study design represents a complement to the clinical efficacy data obtained from pre-market randomized controlled trial (RCT). The safety profile of any drug can only be known for sure from a post-marketing surveillance program involving spontaneous adverse event reporting and analysis as well as non-interventional phase IV studies.[6]

2.4 Timeline, Cost, and Success Rates

It is well established that the costs associated with drug R&D, as well as the time required for developing a new drug, have risen

during the last few decades. In turn, this resulted in the continuous decline in R&D efficiency, which is determined by the amount of money spent per one drug project. Given that innovation is the key factor for growth in the pharmaceutical sector, information regarding R&D efficiency and solutions to existing problems become of great importance.[7]

III. Epidemiology of Drug Development Failures

3.1 Attrition Rates Across Phases

Many firms decided to invest in developing departments for the identification of drug metabolism and pharmacokinetics, where weaknesses of compounds could be overcome during lead optimization. The primary reason for attrition continued to be lack of efficacy. It is believed that currently attrition rate in Phase II represents the largest attrition rates in all phases, with some statistics suggesting as many as 66% of candidates being abandoned. Similar to other biological sciences that have to deal with population studies, drug discovery and development in the clinical phase face the issue of signal versus noise.[8]

3.2 Therapeutic Area Variability

There is considerable variability in success rates and time frames based on the therapeutic areas involved. According to Kaitin, neuropharmacological drugs take 10.8 years and have a 14% success rate while oncology drugs take 9.3 years and have just 8% success rate. In Cummings et al., there is a reported remarkably low success rate of 0.4% (failure rate of 99.6%) in Alzheimer's disease drug development over the period of 2002-2012.[9]

3.3 Historical Trends and Recent Data

There have been a number of major milestones in drug design science that helped establish this method as the primary one in the contemporary and upcoming practice of drug discovery. In its turn, this hypothesis has been repeatedly verified by X-ray crystallography and molecular docking approaches, and nowadays it is evident that ligands do indeed take up specific conformations when binding.[10] In 2019, the pharma industry invested a sum of \$83 billion in research and development. These expenditures ranged from the search and examination of new pharmaceutical products to the further development of existing ones in a form of product extensions, as well as their clinical trials performed for safety

assessment or marketing purposes. This sum is about ten times larger compared to annual expenditures in the 1980s when adjusted for inflation.[11]

IV. Scientific Drivers of Drug Development Failures

4.1 Lack of Efficacy

With the consideration that about 40-50% of clinical failures of drug discovery programs are attributed to lack of clinical efficacy, great emphasis has been placed on improving efficacy of the drugs in both preclinical and clinical studies. The real differences make the development of a first-in-class drug difficult. During drug screening, both computational screening and HTS of chemicals have been done to choose the right scaffolds to prevent any nonspecific binding to the targets.[12]

4.2 Safety and Toxicity Issues

Identifying the mechanisms involved in the toxicity of drugs is one of the key steps towards enhancing drug safety testing by providing a foundation for mechanism-based risk assessment. However, although there have been decades of studies into mechanisms of drug-induced toxicity and the use of different technologies in preclinical safety evaluation, the overall effect on preclinical drug testing remains minimal. The assessment of risk associated with human exposure to novel drugs is still dependent on preclinical testing in animal models, which in many instances, but not all, correlate well with results obtained from humans. Targets for the implementation of innovative technologies such as *in silico* screening, biomarkers, surrogate tests and 'omic technologies are discussed. Improvement of drug safety testing will involve enhancement of the implementation of mechanism-based risk assessment as well as improvement in collaborative efforts between public and private institutions so that research into mechanisms of drug toxicity focuses on the most significant areas.[13]

4.3 Poor Target Validation

Target validation is the process by which suitable targets are identified and validated for developing drugs for treatment. The most useful role of high content screening in target validation is in the initial steps where genetic techniques (such as RNAi), are used on numerous possible targets. In this stage, both efficiency and thoroughness are necessary. It is described here with various examples in the field of oncology target validation. The Akt signal transduction pathway is employed to show

the most efficient method of selecting HCS-compatible reagents for the development of assays. RNAi transfection techniques are examined. An HCS assay is described which quantifies the two nodes in the Akt pathway, namely Akt substrate phosphorylation and RPS6 phosphorylation. There is another example of an HCS assay that measures proliferation (DNA synthesis) and apoptosis (Histone H2B phosphorylation) concurrently.[14]

4.4 Inadequate Biomarkers and Endpoints

Many considerations exist in favor of using biomarkers in drug development. These include having the potential to serve as the rationale for choosing lead candidates, in determining or establishing mechanism of action or pathophysiology, and in working toward the qualification and use of a biomarker as a surrogate endpoint. Examples of biomarkers vary greatly in terms of how they are measured clinically or in the laboratory. An example of an important biomarker that served as a surrogate endpoint and is clinically significant is total cholesterol level. Most biomarkers need to be validated before being used in a study setting. Biomarker assay validation is crucial in generating high quality data in support of biomarker research. Qualification of a biomarker is essential for its use as a surrogate endpoint. Putative biomarkers are identified owing to their relevance to specific steps in the pathophysiology cascade.[15]

4.5 Translational Gaps from Preclinical to Clinical Studies

Drug discovery and development is indeed a tedious and costly process taking almost 10-15 years and an approximate cost of \$1-\$2 billion to develop new compounds for clinical trials. Non-clinical tests are basically done under basic science experiments which mainly focus on evaluating the safety and tolerability of drugs. During the process of choosing a non-clinical model, it is indeed essential to formulate clear objectives and also ensure that the model chosen will suit our purposes. Even after spending billions on developing novel compounds for use, the rate at which they succeed in the clinical stage is rather low. In fact, nine out of ten candidate drugs will definitely fail in phase I, II, and III clinical trials. The rate of failure could indeed be minimized through the application of stringent parameters before proceeding to the clinical stage of drug development. "Bench to bedside" translational research is certainly very important in linking basic research with clinical trials. Early recognition of the drugs likely to fail

will certainly result in minimizing costs incurred during the development of such drugs.[16]

4.6 Patient Heterogeneity and Disease Complexity

In this view, there is an opportunity for using individualized networks as a new tool for studying diseases by means of patients' stratification and thus contributing to precision medicine. We would like to draw attention to the significance of patient-to-patient heterogeneity due to both genetic and environmental sources and illustrate how individualized networks help us advance drug discovery and diagnostics. With the advent of systems biology, which implies incorporating multifactorial information into analyses, the point has been reached where biological network modeling becomes feasible at an individual resolution. With individualized networks available, there are numerous options for applying them to personalized medicine, including the identification of malfunctions and the choice of personalized therapies. In brief, precise individualized networks may speed up medical research since they allow one to study inter-individual heterogeneity and select personalized pharmacological targets for therapy. Thus, there is a need to develop varied inexpensive approaches to constructing such networks.[17]

V. Clinical Trial Design and Operational Challenges

5.1 Study Design Flaws

Clinical trials come in different forms. The most basic way of conducting a trial is by giving an individual some medication, whereby the response to the medication will be measured. Some measures of the response include blood pressure, electrocardiography data, as well as the titer of any bacterial or viral pathogens, before and after the administration of the drug.

The aim of phase I clinical trials, conducted using a limited number of subjects, is usually focused on evaluating the safety of a drug, drug pharmacokinetics, food influence on drug PK, the dosage leading to maximum efficacy, and the best way of administering the medication. The routes of administration include per os, intramuscularly, intravenously, subcutaneously, rectally, as well as inhalational administration. [18]

5.2 Patient Recruitment and Retention Issues

The recruitment of the desired number of subjects within the stipulated period is the major challenge in clinical trials in the process of new drug

development. It results in missed deadlines in clinical trials, cost escalation, and time consumption, which are greater than in other clinical trial areas. Recruitment processes take 30% of development time and around 1.2 billion dollars are expended on the process. The challenges faced during patient recruitment often cause a delay of between one and six months in a large number of clinical trials. The rest take an even longer time to complete the task, hence the loss of between 600,000 dollars and 8 million dollars per day by the pharmaceutical companies. Given that 11% of clinical sites cannot recruit any patient while 37% have fewer patients, the patient recruitment process should be given consideration beforehand and throughout the trial.[19]

5.3 Endpoint Selection and Statistical Limitations

End Points in clinical trials refer to the specific quantitative variables suggested or implied by the goals of the clinical trial itself. An end point should be a clear and definable event that is a key aspect of the disease process, is not subject to personal opinion, and can be both objectively quantifiable and realistically measurable. Dichotomous end points could include death, disease progression, or remission, while continuous end points are those whose alteration by the treatment effect represents the main objective of treatment.[20] The drug development process refers to the identification and development of therapeutically useful drugs into effective medicine and obtaining reliable data concerning proper drug dosages and dosage intervals. In light of increasing demands from regulatory agencies in regards to such endeavors, statistics plays an indispensable part in the drug development process. [21]

5.4 Protocol Deviations and Data Quality

The protocol deviations could negatively affect the quality and integrity of the data collected, the rights, safety, and well-being of participants, and the validity and reliability of the study data scientifically. Protocol deviations are the primary reasons for Food and Drug Administration (FDA) inspections' warning letters. Warning letters are sent out for violations that are likely to result in further action if not fixed immediately. Warning letters are issued to secure voluntary compliance and seek a response to their request for corrections. The FDA will begin proceedings to remove the clinical investigator of any authority to receive an investigational drug/biologic, if such investigator was found repeatedly or purposely in violation of

the regulatory requirements or provided intentionally or repeatedly false information to the sponsor/FDA in the required reports. During the inspection, the regulators will verify the documentation and reporting of any protocol deviation.[22]

5.5 Role of Adaptive Trial Designs

Development of new drugs in clinic is a lengthy and expensive process, and there is a necessity for developing solutions that could make this process shorter and more efficient. With its application of flexibility in design of clinical trials, adaptive design helps to achieve this goal by allowing drug development decisions to be reached in a more rapid manner. In spite of any possible difficulties that arise, the perspective of such an innovative approach to drug development should not be overlooked. Risk control of type I error and other possible operational risks inherent in this strategy becomes critical when talking about later phases of drug development. Nevertheless, owing to some new developments in methodology, this problem can be effectively solved, and the future belongs to the adaptive design of drug trials. [23]

VI. Financial Drivers of Drug Development Failures

6.1 High R&D Costs and Budget Constraints

There is an unmet need for novel pharmaceuticals in many countries particularly in the treatment of cancers, immunologic diseases, and orphan diseases. There are increasing difficulties in financing new pharmaceuticals due to escalating drug prices and increased pharmaceutical volumes due to increasing diseases that include infectious diseases and non-communicable diseases in many countries. The above situation has brought about innovation in new models that could effectively manage the introduction of new drugs, finance new drugs using new financial models, as well as prescribe drugs more efficiently. More is needed however. Thus, the main purpose of this research is to investigate possible approaches that would lead to optimal use of novel drugs considering rising costs amidst budgetary constraints.[24]

6.2 Investment Risks and Return on Investment (ROI)

ROI calculation is one of the many methods employed in analyzing the return of a particular product by pharma or biotech firms. In other words, ROI helps a firm decide whether to continue developing a project or product or

terminate such activities before the company starts incurring any loss. ROI measures how profitable a particular product will be compared to the amount invested in its research and development. Risk elements are considered during ROI calculations through considering different aspects of profitability, competitor products, and the need in the market among others. In other words, an ROI calculation allows the company to determine a metric for assessing the project at hand. This is more effective than relying on profit alone because ROI calculation provides information about profitability, but not limited to that. The use of ROI in conjunction with SWOT analysis and other financial tools can offer invaluable insight to the value of projects and potential products under assessment.[25]

6.3 Funding Gaps for Small and Mid-Sized Companies

The resource limitations faced by SMEs are quite harsh. Drug development typically costs more than one billion USD for biological products (DiMasi et al., 2016), but European SMEs receive significantly fewer investment funds compared to American ones at late stages of development (McKinsey, 2019). As a result, companies are forced to cut corners, whether through sequencing clinical trials, concentrating on a single product candidate, deferring registrations in developing nations, or concentrating on outlicensing. The theory of transaction cost economics suggests that SMEs will benefit from outsourcing costly and complex functions such as Good Manufacturing Practice, regulatory submissions, and pharmacovigilance (Williamson, 1991). Nevertheless, this strategy is risky due to coordination problems and lack of strategic flexibility.[26]

6.4 Market Competition and Commercial Viability

By using the lowest price estimates of APIs reported by WHO, and by making use of published data of production costs per dose for ARVs, our estimated baseline results indicated that generic Indian firms would have been profitable on selling only one out of thirteen types of ARVs in both years (2010 and 2012). Likewise, our public firms could have been profitable selling five out of 13 formulations in 2010, and three out of 13 formulations in 2012. In order to obtain profits for public and Indian firms for selling the majority of their products, we needed to assume a reduction in API cost by 20% and 40%, respectively. Over the two year period (2010 to 2012), we found that - within the portfolio of ARVs - there was a decline of

about 6% to 7% in the gross margin, relative to sales price. Generic firms argued that the current prices were not sustainable. They identified important changes in tenders procedures, simpler procedures for regulatory approval, and simplifying the ARV guidelines, among other things.[27]

6.5 Pricing and Reimbursement Challenges

In cases where there are sufficient treatments, accessing such treatments could be difficult due to high medication prices that are not affordable either by individuals or by their communities. Making affordable, appropriate, and effective medications accessible to all is a challenging process. In order to avoid the financial difficulties that may result from seeking treatment services, including medications, and to enhance access to medicine, the World Health Organization (WHO) has been advocating for Universal Health Coverage (UHC). During the past few years, several countries have sought UHC. [28]

VII. Regulatory Drivers of Drug Development Failures

7.1 Evolving Regulatory Requirements

There are several regulatory requirements in place in drug development, which have brought about a drastic change in the way new drugs are evaluated and approved, with patient safety being one of the focal points. Some of the terms introduced by the regulatory agencies include adaptive pathways, real-world evidence, and expedited reviews, among others. The regulatory requirements have also been influenced by digitization and global harmonization. Pharmacovigilance has ensured the safety of the drugs is handled properly. This necessitates that pharmaceutical organizations adopt a flexible approach and integrate regulatory requirements into their development process.[29]

7.2 Stringent Approval Standards

The drug approval and regulation procedure serves as an important aspect within the pharmaceutical industry that attempts to ensure the safety, effectiveness, and quality of the drug under market scrutiny. It also aims to compare regulation processes and identify existing attempts towards harmonization in this sphere. This research paper will attempt to analyze different aspects of drug regulation, and determine challenges posed by them in the process. The ultimate purpose of this research paper is to provide an understanding of the intricacies and dynamics associated with the drug

approval process on a global scale. As far as the challenges facing drug approval and regulation are concerned, regulating this process is necessary for the sake of ensuring that the new drug is safe for consumption because the introduction of any new drug poses several challenges other than safety and effectiveness.[30]

7.3 Delays in Regulatory Review

There are certain similarities in the regulatory decisions regarding NASs from the regulatory agencies. Perhaps this could be attributed to the rise in the worldwide development of medicines in addition to the harmonization of regulations worldwide through the coordinated efforts of regulatory agencies, industries, and academia in recent years. However, regardless of whether or not it is common, there could be certain differences in the regulatory decisions between the regulatory authorities.

The average approval time for new drugs has already become comparable across different regulatory agencies such as PMDA, FDA, and EMA despite the differences in the average approval time between the three authorities. Nevertheless, there could be certain drugs that require more time in the review process due to their questionable effectiveness and safety. The reason for the delay and difference in the review process of new drug applications, which could reflect the decision-making process between regulatory agencies, is one of the issues in regulatory science.[31]

7.4 Compliance Issues and Deficiencies

The process of therapy is based on the idea that what the clinician writes as a prescription is what will be provided to the patient. Both industry and governmental bodies have established processes and regulations to ensure that there is quality in CMC for medicines, covering factors that can be detrimental to the well-being of patients. This encompasses material acceptance, manufacture, packaging, labeling, quality control, release, storage, and distribution, which are collectively referred to as Current Good Manufacturing Practices. Unique controls for ocular products involve particulate foreign matter control, preservation efficacy studies, sterility, and chemical migration from containers into the drug substance.[32]

7.5 Role of Agencies such as US Food and Drug Administration and European Medicines Agency

In America, the beginning of the regulations regarding the production of medical

devices was in 1906 when the Food and Drug Act came into place. Through the Food and Drug Act and its amendments, the authorities could stop the circulation of medicines that were unsafe to use and had false claims of effectiveness.[33]The European Medicines Agency (EMA) originated in 1995 in London. Its jurisdiction covers an approximate of 450 million people within the EU region. The role of the EMA is to ensure that both humans and animals in the EU and the EEA regions are safe.[34]

VIII. Manufacturing and Quality-Related Failures

8.1 Scale-Up Challenges

The scaling up of manufacturing processes in the pharmaceutical industry is an important step in moving new drugs from their early-stage development stages to full-scale production. The importance of this process cannot be overlooked since many lives depend on it, but it comes with its own set of difficulties. It is necessary to overcome these difficulties using a structured approach, and this is what our article is all about.[35]

8.2 Process Validation Issues

Process validation is an essential component of guaranteeing the quality and safety of products across several industries such as pharmaceuticals, medical devices, and biotech. It is the systematic collection of proof demonstrating that a process delivers a product with specifications that satisfy predetermined criteria. The definition of process validation may be simple; however, putting it into practice can be difficult. With increasingly high expectations in the industry, increased demands from regulators, and technological advancements, traditional process validation practices are becoming more difficult to conduct. Digitalization of process validation holds the key to overcoming many of these difficulties.[36]

8.3 Good Manufacturing Practice (GMP) Compliance

The quality and safety of cell therapy products (CTPs) need to be ensured in their entire life cycle of production and quality control (QC), which will allow their use for the purpose of patients' treatment. According to the ICH Q2 guidelines and EU pharmacopeia, the QC process requires validation of the analytical procedure used for testing purposes. The results of such a procedure can serve as evidence of the accuracy, reliability, and precision of analytical data.[37]

8.4 Supply Chain and Stability Problems

The idea of chemical supply chains has been gaining more interest in the community of process systems engineers in recent years. One of the basic problems involved in the management of a pharmaceutical company is that of finding the best possible way of distributing the limited resources among the unlimited number of potential investments. In this paper, we focus on the analysis and optimization of three critical stages of the life cycle of a new pharmaceutical product, which are the management of the product development pipeline, capacity planning, and supply chain management.[38]

IX. Data Integrity and Decision-Making Failures

9.1 Poor Data Quality and Management

Data management is vital for the effective and efficient process of developing drugs. This study focuses on the significance of implementing a sound data management strategy in all phases of drug development, from pre-clinical stages to post market surveillance. It explores the issues surrounding the large amounts of data being managed in today's drug development process. The literature review focused on the existing data related to drug discovery and development, data management, and targets, among others. [39]

9.2 Bias and Misinterpretation of Results

However, underreporting of adverse drug reactions is one of the limitations that cannot be avoided when interpreting research conducted in pharmacovigilance databases. The objective of pharmacovigilance cannot be the exhaustiveness of adverse reactions; only their significance in terms of a risk must be taken into account. In France, the percentage of serious adverse drug reactions reported would not exceed 5%.[40]

9.3 Lack of Transparency and Reproducibility

However, pharmaceutical firms are not the only ones that have had challenges replicating their published findings. For instance, an editorial in the journal GigaScience published in 2015 showed that reproducing findings in a computational biology paper involved no less than 280 hours of effort despite using the same data sets (Kenall et al., 2015). Moreover, a 2015 editorial in the Journal of Cell Biology emphasized a study that evaluated consistency in over 200 articles on a critical research question of determining the cellular origin of matrix-degrading proteases in four types of

human cancers. The findings demonstrated significant inconsistencies among the findings of the 200 articles, even for those that used proper controls (Madsen and Bugge, 2015)[41].

9.4 Impact of Digital Systems and Big Data

In addition, there have been many changes in the pharmaceutical industry over time, adapting itself to the different advancements made during the past few years of the 21st century. Two of these developments include AI and big data technologies that have brought about revolutionary changes to the field of drug discovery. Considering the current research trends, we will take a look at the power of such algorithms based on AI technology and their ability to collect, analyze, and derive information from large amounts of big data. It is clear that the future of drug discovery holds great promise in this regard. [42]

10. External and Market-Driven Factors

10.1 Competitive Landscape

There are currently many changes taking place within the generics industry. After a time of unprecedented patent expirations, which began in the late part of the last decade, the industry will experience a slowdown in its growth after 2006. The main drivers of change in the competitive environment in the generics industry include the entry of many new firms from India, brand defense measures, vertical integration, and consolidation of firms to create industry giants without their like. In response to such threats, generics manufacturers have engaged in merger and acquisition activities. There are several strategies being employed in this regard, such as scaling up, niche formulations, vertical integration, and brand business development. [43]

10.2 Changes in Clinical Practice

The draft version E6(R3) of the Good Clinical Practice Guideline has been issued by the International Council for Harmonisation for public discussion. The aim of the revised guideline is to ensure that the new guidelines can be implemented in various kinds of trials and remain valid in case of further developments in methodology and technology. Version E6(R3) of the guidelines represents radical changes regarding the content and structure of the previous version E6(R2) which will influence all phases of the clinical trials process. The aspects such as principle-based, technology-driven, ethical, and quality-driven approach of the revised guidelines will bring additional burdens for

ethics committees, the investigator, and the sponsor.[44]

10.3 Public Health Emergencies and Global Crises

Clinical studies within existing regulatory frameworks may be impossible during a public health crisis. The regulatory authority is supposed to try and achieve a balance between ensuring as much access to treatment through new medications as possible while simultaneously collecting evidence about their safety and efficacy. In order to discuss contemporary policies, I analyze once again the underlying ethical reasoning behind limiting new medications to clinical trials, at any phase and involving any group of patients (based on the precautionary principle), and prove that its purpose to safeguard public health either now or in the future might soon become impossible to fulfill during a pandemic. Offering greater access to therapy and coordinating natural experiments, such as cluster (or wedged cluster) trials, might constitute an adequate balance in this situation. Nevertheless, several issues of justice have to be addressed first.[45]

10.4 Patient and Physician Acceptance

Patient Focused Drug Development (PFDD) is a recent initiative launched by the Food and Drug Administration (FDA) aiming at incorporating patient voices in an earlier phase of product development. The hope is that patients would be able to put patient context for assessing the benefit-risk balance and contribute to review groups while also helping in developing innovative methods of assessment, study endpoints, and risk communication. The aim of this paper is to summarize information available until date on FDA's PFDD Initiative and discuss its implications for patients, researchers, payers, and the biopharmaceutical sector. This paper would also outline a strategy which stakeholders can follow to define their roles in PFDD and expand its reach beyond the 20 conditions being considered by FDA currently.[46]

11. Case Studies of Drug Development Failures

11.1 Scientific Failure Case

The drug development process is plagued with a very high rate of success at only 10%. This failure can be attributed mainly to inefficacy (40-50%), toxic effects (30%) and poor pharmacokinetics. Some notable failures in 2024 include Sage Therapeutics' Dalzanemdor which

failed Phase II trials in three different types of neurodegenerative disorders.[47]

11.2 Regulatory Rejection Case

The rejection of a drug by the regulating agencies is one of the major challenges during its developmental stages and may emanate due to insufficient efficacy, safety concerns, production issues, labeling errors, or non-conformity with regulatory requirements. The and other regulatory agencies carry out detailed analyses of the risk-benefit balance before approving the marketing of any drug. The majority of drugs undergoing clinical trials fail during the later stages owing to their inability to prove sufficient efficacy and safety within acceptable dosages. Strategic planning and adherence to stringent standards play a crucial role in preventing rejection and ensuring greater chances of approval.[47]

11.3 Financial Collapse Case

Financial bankruptcy in drug development is one of the major problems faced by the pharmaceutical and biotechnology sectors globally. In order to develop a drug, an organization needs considerable investments, prolonged periods of research and high costs for clinical trials without any certainty about their success. As these smaller firms require further funding in order to pursue their research initiatives, they have to rely on the funds provided by venture capital firms and others to continue their research process. The failure to conduct their clinical trial successfully and being rejected by the regulatory authorities and failing in the market can lead to insolvency.[48]

11.4 Lessons Learned from High-Profile Failures

Regardless of this, there remains an issue of inefficiency in terms of drug discovery and development processes in the form of high cost and time consumption. While initial successes and setbacks in clinical drug development may serve as cautionary tales that AI is not the magic bullet for addressing the productivity issue in new medicines, there has yet to be an FDA-approved drug developed through AI.[49]

12. Strategies to Mitigate Drug Development Failures

12.1 Improved Target Validation Techniques

Computationally derived approaches for target prediction through molecular similarity-based and network-based approaches, docking and others have emerged as useful and powerful means to

facilitate the difficult process of identifying the mode of action of biologically active small molecules like drugs and drug-like chemicals. An important step to understanding the strength and weakness of any method used for predicting targets is its evaluation procedure. Ideally, large-scale experimental studies are performed to examine the effectiveness of the model; unfortunately, due to high costs and time required, this may not be a feasible option. For this reason, statistical validation methods using retrospectives knowledge are often adopted to evaluate a method's predictive strength. There exist various forms of statistical validation methodologies that differ in sophistication. In this review, we consider some validation approaches adopted, illustrating the advantages and disadvantages of the validation schemes and metrics involved in assessing the performance.[50]

12.2 Use of Biomarkers and Precision Medicine

The potential importance of biomarkers in the evolution of precision medicine constitutes a critical window through which technology can be developed to promote health in human beings and also decrease costs associated with health care delivery. The idea behind precision medicine entails tuning of therapy for individuals or groups of patients by using the disease-specific biomarkers. Indeed, much debate surrounds the general effectiveness of this personalized approach in finding out molecular targets that would allow pinpointing therapies. However, there is no denying that technology is not lacking and several techniques are available for use such as molecular imaging, genomics, proteomics, metabolomics, and next-generation sequencing. The application of these and other methods has led to the development of more than a dozen biomarkers and therapies of cancers, which have been approved by FDA. It is too early to come to a conclusion although the hunt for desirable biomarkers in support of precision medicine has never been greater before. Also, apart from cancer diagnosis and treatment, there are several applications of disease-specific biomarkers.[51]

12.3 Innovative Clinical Trial Designs

Clinical trials form the benchmark test used to establish whether the tested drugs are effective and safe before being approved for marketing. However, there have been a few problems encountered in traditional clinical trials including long periods taken for their conduct and rising costs among other difficulties. In order to make the process of conducting clinical research more

efficient, several accelerated methods of conducting clinical trials have been formulated and employed in the modern day clinical drug development processes. These innovative designs of human clinical studies have been established by successfully getting approvals of important drugs and their use in the clinical setting as well as introducing many blockbuster drugs into the market. They seek to motivate clinicians and developers not only to engage with regulatory authorities on time, but also interpret scientific breakthroughs into innovations.[52]

12.4 Strengthening Regulatory Strategy

The current regulatory system within the region is further complicated by national requirements which hinder the development of new health products in the region. In order to help overcome such obstacles, the Centre for Regulatory Excellence of Duke-National University of Singapore (Duke-NUS) CoRE was established in 2014 with the specific aims of enhancing regional regulatory bodies through capacity building, regulatory harmonization, work sharing, and network development.[53]

12.5 Risk-Based Decision Making

Decision-making under uncertainty plays a crucial role in the initial phase of the development of the chemical process. Multiple goals including SHE and economic considerations are taken into account under an information-poor condition. The screening of possible synthesis pathways is conducted in a teamwork setting involving subject matter experts from various backgrounds like chemists and chemical engineers. Ranking approaches are employed, but they seldom explain the reasons for decision-making.[54]

13. Role of Emerging Technologies

13.1 Artificial Intelligence in Drug Discovery

Artificial Intelligence has found its successful implementation in areas such as computer science, voice recognition, natural language processing; however, it is now entering into fields that require lots of knowledge like biology, physics, and chemistry to increase the success ratio and decrease the cost involved in discovering medicines. Another area where the pharmaceutical companies are using the power of AI is for unifying the various sources of data which used to be silos until now, recruiting data scientists, and building infrastructure. The use of AI in drug

discovery can be divided into novel discovery and target identification, hypothesis generation, virtual screening, compound generation, chemical properties prediction, ADME/Toxicology, prediction of outcomes of clinical trials, and actuarial pharmacology based on real-world evidence.[55]

13.2 Machine Learning for Clinical Trials

With the tremendous amounts of biological and medical data present in addition to machine learning models that have been extensively studied, one is able to develop completely automated processes in the area of drug creation. Such a process could lead to faster drug discovery or even facilitate the discovery of more details about various diseases and biological processes. Preclinical and possibly even clinical testing could be facilitated through such a process. This automation could solve the problem of the low productivity rate of pharmaceutical firms.[56]

13.3 Real-World Evidence (RWE)

The global health care systems will become unsustainable, and this trend will persist without policy measures and regulations grounded in scientific and technical data. In order to solve this problem, the Italian Society of Pharmacology (Società Italiana di Farmacologia, SIF) has organized a first working group that will work out a tentative map and consider the applicability of real-world evidence (RWE). The proposals put forward by the working group will be assessed by a larger group of stakeholders, including payers, patients, academicians, and regulators, through pilot studies and publications in scientific papers and presentations at conferences.[57]

13.4 Digital Twins and Predictive Modeling

In silico testing is currently being considered as an approach to evaluate the efficacy and safety of new pharmaceuticals and medical devices. Models of diseases created using the profiling data of patients are being developed to create the interactome of genes and proteins for inference of causation within the physiopathology, thereby allowing the modeling of the effect of the drug on the target. Patients can be created using medical records and digital twins to model organs and their reactions to certain medications to assess the efficiency of treatment at the individual level. With the increasing acceptance of digital evidence by regulators, predictive AI models will help develop confirmatory clinical trials in humans and

facilitate efficient drug discovery and medical device development.[58]

14. Collaborative and Policy Approaches

14.1 Industry-Academia Partnerships

Academia-industry collaboration has been highlighted as a subject of many governmental studies and actions during the last 15 years and it is seen as a good approach to benefit from world-class research capacity in the UK. Nevertheless, more research should be conducted on the impact of these collaborations within the area of translational medicine since this area involves an extensive process that includes long-term, costly, and high-risk clinical trials.[59]

14.2 Public-Private Collaborations

In line with a popular perception held by some academics, practitioners, and policymakers alike, we propose that cooperation between the two sectors helps achieve success. The effect of within- and cross-sector cooperation is then investigated using the data on success in clinical trials. Unlike the above popular perception, we find no evidence in favor of the positive impact of such cooperation. Instead, we observe that clinical trials carried out by single firms have four times higher success rates compared with those performed cooperatively with public entities. This implies that, rather than sharing technologies or ideas with each other, companies seek public cooperation to avoid development risk.[60]

14.3 Global Regulatory Harmonization

The variation of pharmaceutical regulatory requirements results in a very complicated and expensive process of marketing new pharmaceutical products and causes a significant delay in introducing innovative and important drugs on the market. As a result of the above-mentioned globalization phenomenon, there was a strong demand for a new strategy in pharmaceutical regulations, which included increased collaboration and harmonization. The globalization of pharmaceutical regulations became necessary and desirable for many groups of neighboring countries in several parts of the world due to the need for rationalizing unnecessary and redundant requirements and saving time and money on drug regulation. Regional pharmaceutical regulation is associated with a range of initiatives which are primarily motivated by economical and social factors and are conducted with the help of various

global organizations, such as WHO and ICH. There is an increasing difference in terms of development between the countries participating in regional harmonization processes.[61]

14.4 Role of Organizations like International Council for Harmonisation

The ICH has developed numerous guidelines that sponsors can apply to different areas of pharmaceutical development research and documentation. The guidelines are usually adopted by regulatory authorities upon their issuance. These guidelines are categorized into four classes: quality, safety, efficacy, and multidisciplinary. The development, issuance, and regular updating of two such guidelines, namely ICH S7B and ICH E14, are explained in this editorial as an example of regulatory science.[62]

15. Future Perspectives in Drug Development

15.1 Personalized and Precision Medicine

Precision medicine (PM) has been described as an approach using information about someone's genetic makeup, environmental exposures, and lifestyle to guide decisions on how to best manage and treat diseases. It is true that PM has been used successfully in the treatment of some types of epilepsy. The field of precision medicine has seen significant advancements through breakthroughs in genetics of epilepsy.[63]

15.2 Decentralized Clinical Trials

The coronavirus outbreak resulted in a shift in clinical trial strategy to ensure clinical research is still conducted, with regulatory modifications facilitating more implementation and development of a decentralized trial strategy. The feasibility and efficacy of the trial strategy can only be shown through the observations done on phase 2 and 3 clinical trials, which would be much easier considering that safety issues in earlier phases have already been addressed. The early stages of drug development are a lengthy and costly process where accrual and safety considerations become crucial elements of success. Using a decentralized trial approach to phase 1 trials can help with patient accrual by eliminating geographical limitations, increasing patient heterogeneity, supporting rare tumor evidence, and lessening burden on patients. However, issues related to safety, data quality, shipping, and administration of the investigational product are potential barriers.[64]

15.3 Sustainable and Cost-Effective Models

In the case of developing drugs sustainably and economically, the best methods will be to utilize the technologies that will ensure the least amount of waste, cost, and time required throughout the process. This includes artificial intelligence in the development of the drug formula, simulation technology to reduce toxic effects, and high-throughput screening technology on a low-scale level.[1]

Conclusion

Drug development failure is a complex, multi-faceted problem, influenced by various factors such as operation issues, financial constraints, regulatory issues, uncertainty in science, and pressure from the market environment. The high rate of drug development failures seen across the entire process of developing drugs amounts to tremendous wastage of resources, and, above all, causes a great delay in providing much-needed drugs to the patients.

Knowledge about these failure factors is basic knowledge for MFAM students and early-stage pharmaceutical researchers which will form the foundation of everything that they do professionally. There are several opportunities available through artificial intelligence, precision medicine, decentralized trials, and regulatory harmonization to reduce failure rates and improve efficiency in the development pipeline of this rapidly evolving sector.

There is no such thing as a zero-risk program for drug development. Nevertheless, the pharmaceutical industry could certainly ensure success of new drugs by employing a combination of good science, sound financial management, effective regulation, and innovative operation practices. Drug research may not become easier in the future, but there is a possibility that it may become much smarter.

References

- [1]. 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):80-93.
- [2]. ScienceDirect Topics. Drug development [Internet]. Amsterdam: Elsevier; [cited 2026 May 7]. Available from: [ScienceDirect Drug Development Topic](#)
- [3]. Prashant Sharma. Significance of quantitative tools and techniques in reducing drug attrition. *Excelra*; 2023 Jun 22 [cited 2026 May 6]. Available from: [Excelra blog article](#)
- [4]. PPD (Pharmaceutical Product Development). Preclinical studies in drug development [Internet]. Wilmington (NC): PPD; [cited 2026 May 6]. Available from: [Preclinical studies in drug development](#)
- [5]. Ogbaudu E, Ohaya TC, Smith JF, Elahi MA. Phases of clinical trials. In *Translational orthopedics 2024* Jan 1 (pp. 295-299). Academic Press.
- [6]. Suvarna V. Phase IV of drug development. *Perspectives in clinical research*. 2010 Apr 1;1(2):57-60.
- [7]. Schuhmacher A, Gassmann O, Hinder M. A review of the pharmaceutical R&D efficiency: costs, timelines, and probabilities. *Value creation in the pharmaceutical industry: the critical path to innovation*. 2016 Feb 16:60-79.
- [8]. Boyer S, Brealey C, Davis AM. Attrition in drug discovery and development. *Attrition in the Pharmaceutical Industry: Reasons, Implications, and Pathways Forward*. 2015 Dec 15:5-45.
- [9]. Moretta GL. Pharmaceutical drug lifecycle: a comprehensive scientific review of research and development phases, attrition rates, and global disparities. *Preprints.org* [Preprint]. 2026 Feb 12.
- [10]. Doytchinova I. Drug design—past, present, future. *Molecules*. 2022;27(5):1496. doi:10.3390/molecules27051496.
- [11]. Congressional Budget Office. Research and development in the pharmaceutical industry [Internet]. Washington (DC): Congressional Budget Office; 2021 Apr 8
- [12]. Sun D, Gao W, Hu H, Zhou S. Why 90% of clinical drug development fails and how to improve it?. *Acta Pharmaceutica Sinica B*. 2022 Jul 1;12(7):3049-62.
- [13]. Stevens JL. Future of toxicology mechanisms of toxicity and drug safety: where do we go from here?. *Chemical research in toxicology*. 2006 Nov 20;19(11):1393-401.
- [14]. Blake RA. Target validation in drug discovery. In *High Content Screening: A Powerful Approach to Systems Cell Biology and Drug Discovery 2007* Jan 1 (pp. 367-377). Totowa, NJ: Humana Press.

- [15]. Wagner JA. Overview of biomarkers and surrogate endpoints in drug development. *Disease markers*. 2002;18(2):41-6.
- [16]. Mahalmani V, Sinha S, Prakash A, Medhi B. Translational research: Bridging the gap between preclinical and clinical research. *Indian journal of pharmacology*. 2022 Nov 1;54(6):393-6.
- [17]. Latapiat V, Saez M, Pedroso I, Martin AJ. Unraveling patient heterogeneity in complex diseases through individualized co-expression networks: a perspective. *Frontiers in Genetics*. 2023 Aug 10;14:1209416.
- [18]. Brody T. Clinical trials: study design, endpoints and biomarkers, drug safety, and FDA and ICH guidelines. Academic press; 2016 Feb 19.
- [19]. Chaudhari N, Ravi R, Gogtay NJ, Thatte UM. Recruitment and retention of the participants in clinical trials: challenges and solutions. *Perspectives in clinical research*. 2020 Apr 1;11(2):64-9.
- [20]. Fransen J. Are better endpoints and better design of clinical trials needed?. *Best Practice & Research Clinical Rheumatology*. 2004 Feb 1;18(1):97-109.
- [21]. Senn S, Barnett V. *Statistical issues in drug development*. Chichester: John Wiley; 1997 Oct 20.
- [22]. Chodankar D. Impact of protocol deviations on the clinical study. *Perspectives in clinical research*. 2023 Apr 1;14(2):47-8.
- [23]. Curtin F, Heritier S. The role of adaptive trial designs in drug development. *Expert review of clinical pharmacology*. 2017 Jul 3;10(7):727-36.
- [24]. Godman B, Bucsics A, Vella Bonanno P, Oortwijn W, Rothe CC, Ferrario A, Bosselli S, Hill A, Martin AP, Simoens S, Kurdi A. Barriers for access to new medicines: searching for the balance between rising costs and limited budgets. *Frontiers in Public Health*. 2018 Dec 5;6:328.
- [25]. Schoukroun-Barnes LR, Duchars P, Bartolowits M, Sarno K. What does return on investment (ROI) mean to the pharmaceutical/biotechnology industry?. *Theoretical Issues in Ergonomics Science*. 2019 Jan 2;20(1):39-50.
- [26]. Epskamp CR. *Built to Exit?: Exploring Acquisition Dynamics and Market Strategy in European Pharmaceutical SMEs* (Doctoral dissertation, ResearchSpace@ Auckland).
- [27]. Nakakeeto ON, Elliott BV. Antiretrovirals for low income countries: an analysis of the commercial viability of a highly competitive market. *Globalization and health*. 2013 Feb 15;9(1):6.
- [28]. Vogler S, Zimmermann N, Ferrario A, Wirtz VJ, Babar ZU. Challenges and opportunities for pharmaceutical pricing and reimbursement policies. *Journal of Pharmaceutical Policy and Practice*. 2015 Dec 31;8(sup1):E1.
- [29]. Eichler HG, Oye K, Baird LG, Abadie E, Brown J, Drum CL, et al. Adaptive licensing: taking the next step in the evolution of drug approval. *Clin Pharmacol Ther*. 2012;91(3):426–37.
- [30]. Gomase VS, Sharma R, Dhamane SP. Global Analysis of Regulatory Frameworks and Drug Safety Standards in the Drug Approval Process. *Current Drug Safety*. 2025.
- [31]. Tanaka M, Idei M, Sakaguchi H, Kato R, Sato D, Sawanobori K, Kawarasaki S, Hata T, Yoshizaki A, Nakamura M, Ikuma M. Rationales of delay and difference in regulatory review by Japan, the USA and Europe among new drugs first approved in Japan. *British Journal of Clinical Pharmacology*. 2021 Aug;87(8):3279-91.
- [32]. Kaufman B, Novack GD. Compliance issues in manufacturing of drugs. *The ocular surface*. 2003 Apr 1;1(2):80-5.
- [33]. Diehl DL, Tierney WM, Adler DG, Conway JD, Farraye FA, Kantsevov SV, Kaul V, Kethu SR, Kwon RS, Mamula P, Pedrosa MC. The role of the US Food and Drug Administration in device evaluation and monitoring. *Gastrointestinal Endoscopy*. 2010 Jul 1;72(1):5-10.
- [34]. Kagan J. European Medicines Agency (EMA): Role, Functions and Significance. *Investopedia*. Updated December 8, 2025. Available from: <https://www.investopedia.com/terms/e/european-medicines-agency-ema.asp>
- [35]. Chauhan S. Overcoming challenges in scale-up production. *World Pharma Today*. [Internet]. Available from: [Overcoming Challenges in Scale-Up Production](#)
- [36]. Wright L. Navigating the challenges of process validation: 10 strategies for success [Internet]. Kneat Solutions; 2023 Dec 7 [cited 2026 May 6]. Available from: <https://kneat.com/article/process-validation-challenges-and-solutions/>

- [37]. Rustichelli D, Castiglia S, Gunetti M, Mareschi K, Signorino E, Muraro M, Castello L, Sanavio F, Leone M, Ferrero I, Fagioli F. Validation of analytical methods in compliance with good manufacturing practice: a practical approach. *Journal of Translational Medicine*. 2013 Aug 27;11(1):197.
- [38]. Azzaro-Pantel C. New product development and supply chains in the pharmaceutical industry. In *Computer Aided Chemical Engineering 2018 Jan 1 (Vol. 41, pp. 1-26)*. Elsevier.
- [39]. ravindra Babu S. The Importance of Data Management in Drug Development. *Bulletin of Engineering Science and Technology*;1(2):1-27.
- [40]. Faillie JL. Case–non-case studies: principle, methods, bias and interpretation. *Therapies*. 2019 Apr 1;74(2):225-32.
- [41]. Gannot G, Cutting MA, Fischer DJ, Hsu LJ. Reproducibility and transparency in biomedical sciences. *Oral Dis*. 2017 Oct 1;23(7):813-6.
- [42]. Ashiwaju BI, Orikpete OF, Uzougbo CG. The intersection of artificial intelligence and big data in drug discovery: a review of current trends and future implications. *Matrix Science Pharma*. 2023 Apr 1;7(2):36-42.
- [43]. Karwal V. The changing competitive landscape in the global generics market: Threat or opportunity?. *Journal of Generic Medicines*. 2006 Jul;3(4):269-79.
- [44]. Bhatt A. The revamped Good Clinical Practice E6(R3) guideline: Profound changes in principles and practice! *Perspectives in Clinical Research* 2023;14(4):167-171. doi:10.4103/picr.picr_184_23.
- [45]. Edwards SJ. Ethics of clinical science in a public health emergency: drug discovery at the bedside. *The American journal of bioethics*. 2013 Sep 1;13(9):3-14.
- [46]. Perfetto EM, Burke L, Oehrlein EM, Epstein RS. Patient-focused drug development: a new direction for collaboration. *Medical care*. 2015 Jan 1;53(1):9-17.
- [47]. Sun D, Gao W, Hu H, Zhou S. Why 90% of clinical drug development fails and how to improve it? *Acta Pharmaceutica Sinica B*. 2022;12(7):3049-3062. doi:10.1016/j.apsb.2022.02.002.
- [48]. Hughes B. Biotech's perfect storm. *Cell*. 2009;138(3):413-5.
- [49]. Braddock M, Jeziorski K. Learning from the successes and failures of early artificial intelligence (AI) adoption for drug discovery in Big BioPharma. *Expert Opinion on Drug Discovery*. 2026 Feb 1:1-8.
- [50]. Mathai N, Chen Y, Kirchmair J. Validation strategies for target prediction methods. *Briefings in bioinformatics*. 2020 May;21(3):791-802.
- [51]. Slikker Jr W. Biomarkers and their impact on precision medicine. *Experimental Biology and Medicine*. 2017 Sep 19;243(3):211.
- [52]. Chen D, Qi EY. Innovative highlights of clinical drug trial design. *Translational Research*. 2020 Oct 1;224:71-7.
- [53]. Lim JC. Strengthening health products regulatory systems to enhance access to quality health products in the Asia-Pacific. *Therapeutic Innovation & Regulatory Science*. 2018 Nov;52(6):751-4.
- [54]. Manipura A, Martin EB, Montague GA, Sharratt PN, Houson I. Risk-based decision making in early chemical process development of pharmaceutical and fine chemical industries. *Computers & chemical engineering*. 2013 Aug 8;55:71-82.
- [55]. Chakraborty C. *Role of AI in the Advancement of Drug Discovery and Development*. Jenny Stanford Publishing; 2022 May 25.
- [56]. Réda C, Kaufmann E, Delahaye-Duriez A. Machine learning applications in drug development. *Computational and structural biotechnology journal*. 2020 Jan 1;18:241-52.
- [57]. Martini N, Trifirò G, Capuano A, Corrao G, Pierini A, Racagni G, Pani L. Expert opinion on Real-World Evidence (RWE) in drug development and usage. *Pharmadvances*. 2020 Jul;2(2):41-50.
- [58]. Moingeon P, Chenel M, Rousseau C, Voisin E, Guedj M. Virtual patients, digital twins and causal disease models: Paving the ground for in silico clinical trials. *Drug discovery today*. 2023 Jul 1;28(7):103605.
- [59]. Davie N. *Academia-industry collaboration in translational medicine* (Doctoral dissertation, University of Oxford).
- [60]. Crispeels T, Willems J, Scheerlinck I. Public–private collaborations in drug development: Boosting innovation or alleviating risk?. *Public Management Review*. 2018 Feb 1;20(2):273-92.
- [61]. Lakkis MM. Global and regional drug regulatory harmonization initiatives. *Drug*



- information journal: DIJ/Drug Information Association. 2010 May;44(3):289-97.
- [62]. Turner JR. The International Council for Harmonisation and a case study in regulatory science. *Therapeutic innovation & regulatory science*. 2019 Sep;53(5):561-3.
- [63]. Sisodiya SM. Precision medicine and therapies of the future. *Epilepsia*. 2021 Mar;62:S90-105.
- [64]. Silva DJ, Nelson BE, Rodon J. Decentralized clinical trials in early drug development—a framework proposal. *Journal of Immunotherapy and Precision Oncology*. 2024 Aug 1;7(3):190-200.