Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 14s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Comparative Analysis of Personalized Medicine Regulatory Frameworks and Challenges in the Usa and Europe

Katikala Tanvi[1], Sangita Mishra[2], M P Venkatesh[3]*

[1]Centre of Excellence in Regulatory Sciences, Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagar, Mysuru-570015, Karnataka, India.

Email ID: katikala2002@gmail.com

[2]Ph.D. Scholar, M. Pharm, Centre of Excellence in Regulatory Sciences, Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagar, Mysuru-570015, Karnataka, India

[3]Associate Professor, Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagar, Mysuru-570015, Karnataka, India,

Email ID: venkateshmpv@jssuni.edu.in

***Correspondence Author:**

"M P Venkatesh*

"Associate Professor, Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagar, Mysuru-570015, Karnataka, India, Guest Assistant Professor, Faculty of Pharmaceutical Sciences, UCSI University, Malaysia."

Email ID: venkateshmpv@jssuni.edu.in

Cite this paper as: Katikala Tanvi, Sangita Mishra, M P Venkatesh, (2025) Comparative Analysis of Personalized Medicine Regulatory Frameworks and Challenges in the Usa and Europe. *Journal of Neonatal Surgery*, 14 (14s), 318-330.

ABSTRACT

Objective: This study compares and contrasts the regulatory frameworks for personalized medicines (PM) in the EU and the USA, aiming to identify key differences, evaluate the current state of the field, and propose strategies for global harmonization.

Methods: A literature review was conducted to analyze regional regulatory policies, action plans, and initiatives related to personalized medicine. The study focuses on the regulatory bodies FDA and EMA and their impact on the development and approval of PMs.

Results: The review reveals that while the FDA in the USA supports faster PM development through conditional clearances and smaller clinical trials, the EMA's centralized approval process in the EU facilitates access across Member States. The global demand for PM, driven by the need to treat rare diseases and neurological, pulmonary, and infectious conditions, highlights regulatory challenges and the need for increased collaboration.

Conclusion: Global harmonization of regulatory frameworks is essential for accelerating PM development and ensuring equitable access. Continued collaboration between regulators, researchers, and stakeholders will be crucial to overcome existing roadblocks and foster innovation in personalized medicine.

Keywords: *Personalized Medicine (PM), Regulatory Frameworks, FDA (Food and Drug Administration), EMA (European Medicines Agency), Policy Harmonization, Precision Medicine, Rare Diseases.*.

1. INTRODUCTION

Personalized medicine (PM) is an emerging paradigm of medicine that aims at using knowledge of an individual genomic builds to create custom treatments, dosages, and interventions for the patient. The idea behind this approach is to overcome the shortcomings of classical treatments developed for an average patient, which are frequently not sufficient to meet the needs of a patient with a rare disease or an individual with particular characteristics of his/her illness. PM is used for enhancing healthcare by forecasting who is prone to a specific disease, creating diagnostics that fit a specific patient, and synthesizing medicines that have few consequences but are effective in the patient's body [1]. Modern redevelopment including systematic biology and predictive methods, have helped in differentiating between progression of diseases and other genetic parameters for enabling precise and perfect cure. However, PM has a number of obstacles, such as high costs for research and development, administrative constraints, restricted access to most innovative technologies, and the necessity

of international cooperation among all the parties involved [2]. The United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have critical responsibilities of approving as well as ensuring that PM therapies are available for various health conditions including; cancer, cardiovascular diseases, neurological disorders, inflammatory disorders, psychiatric disorders, pain management, infectious diseases [3]. These applications show that with PM's help it is possible to solve a wide range of medical problems, enhance patients' conditions, and reduce negative consequences [4]. The purpose of this research is twofold: the first goal of this study is to establish the findings about the current state of personalized medicine, the second is to recognize the existing opportunities and threats of further implementation of the given concept as well as the weakness and strengths of governmental regulation of the sphere. If these problems are solved, PM can dramatically change the healthcare industry and provide personalized services, which make patient treatment more effective and less costly in the long-term future [5].

2. METHODOLOGY

This paper is a review of existing literature on the basis of guidelines, regulations and documents, reports, newsletters, media updates, and journal articles that were collected mainly from the official websites of regulatory authorities including FDA and EMA. An initial search was done using keyword searches in such databases such as Scopus, ACM Digital Library, and PubMed in order to find relevant articles and research related to regulatory frameworks and PM development. Also websites of international organizations were used when searching for relevant information. The information obtained from these sources was then screened by relevance and suitability for inclusion in the present review, in order to unveil ethical, regulatory, and clinical integration issues in PMs. The following outcome of this review will aim at offering a comprehensive evaluation of the PM categories in healthcare domain, to analyze the new development in this area, and to respond to the key question which is concerned with how to incorporate PMs into practice and major concerns from regulatory and ethical perspective that needs to be addressed for wider implementation.

3. RESULTS

As for 2023 the overall distribution of newly approved drugs by the FDA raised an issue that almost half of them are orphan drugs that target rare diseases while many of them are PMs. There were also clear indications for sixteen authorized orphan PMs in 2023 as against six in 2022 [6]. Of these, applications in seven PMs were based on oncology while the rest of the three was for other therapeutic area. A portion of the approved PMs for 2023 is presented below in Table 1.

Table 1: Approved Personalized Medicines in 2023 in the USA and the EU [6, 7]

Sl. No.	Region	Active Ingredient	Brand Name	Indication/Treatment	Reference
1	USA	Exagamglogene autotemcel	Casgevy	Sickle Cell Disease (12+ years, vaso-occlusive crises)	[6]
2	USA	Iptacopan	Fabhalta	Paroxysmal Nocturnal Hemoglobinuria	[6]
3	USA	Velmanase alfa-tycv	Lamzede	Alpha-mannosidosis (non-CNS symptoms)	[6]
4	USA	Leniolisib	Joenja	Activated Phosphoinositide 3-Kinase Delta Syndrome	[6]
5	USA	Sparsentan	Filspari	Primary Immunoglobulin A Nephropathy (proteinuria)	[6]
6	USA	Pegunigalsidase alfa-iwxj	Elfabrio	Fabry Disease	[6]
7	USA	Lovotibeglogene autotemcel	Lyfgenia	Sickle Cell Disease (12+ years, vaso-occlusive events)	[6]
8	USA	Cipaglucosidase alfa-atga	Pombiliti	Pompe Disease	[6]
9	USA	Tofersen	Qalsody	Amyotrophic Lateral Sclerosis	[6]
10	USA	Beremagene geperpavec-svdt	Vyjuvek	Dystrophic Epidermolysis Bullosa (collagen VII mutation)	[6]

11	USA	Delandistrogene moxeparvovec	Elevidys	Duchenne Muscular Dystrophy (pediatric, with a mutation in the DMD gene)	[6]
12	USA	Nedosiran	Rivfloza	Elevated urinary oxalate levels	[6]
13	USA	Palovarotene	Sohonos	Fibrodysplasia Ossificans Progressiva (heterotopic ossification)	[6]
14	USA	Valoctocogene roxaparvovec-rvox	Roctavian	Severe Hemophilia A	[6]
15	USA	Pozelimab-bbfg	Veopoz	CHAPLE Disease	[6]
16	USA	Eplontersen	Wainua	Hereditary Transthyretin-Mediated Amyloidosis	[6]
17	EU	Nivolumab	Opdivo	Melanoma, non-small cell lung cancer	[7]
18	EU	Durvalumab	Imfinzi	Non-small cell lung cancer	[7]
19	EU	Elotuzumab	Empliciti	Multiple Myeloma	[7]
20	EU	“Pembrolizumab”	“Keytruda”	Melanoma: NSCLC: urothelial cancer: head neck cancer	[7]
21	EU	Necitumumab	Portrazza	Squamous non-small cell lung cancer	[7]

4. DISCUSSION

The application of technology plays a pivotal role in advancing personalized medicine (PM), bridging the gap between an individual's unique pharmacological response and tailored therapeutic modalities. Over the past decade, PM has steadily gained traction globally, driven by cutting-edge technological innovations, heightened public awareness, government initiatives, and advancements in genetic databases. The effective utilization of these therapies enhances therapeutic efficacy while reducing adverse effects, ultimately improving patient health outcomes. This shift is supported by increasing demand for customized treatments across various disease areas, including neurological, pulmonary, infectious, and psychiatric disorders. However, the rising costs of research and development (R&D), along with the potential for adverse effects, present ongoing challenges [8].

Growth in the Global Personalized Medicine Market

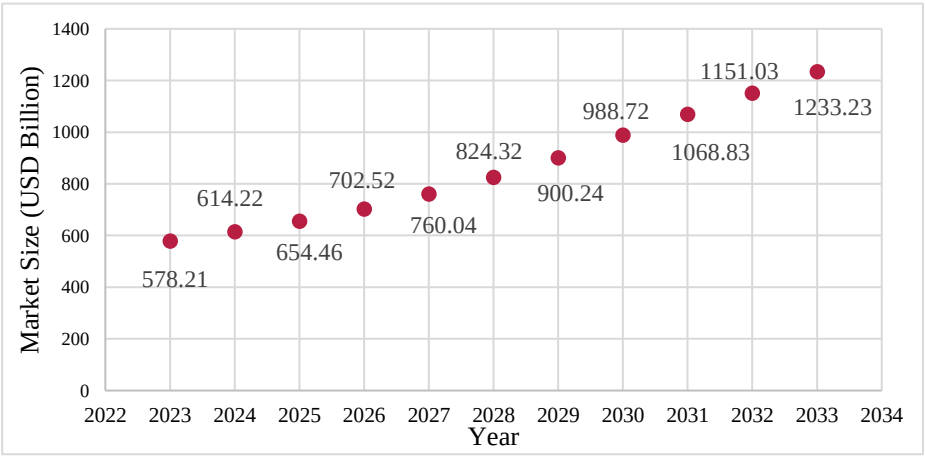

Fig.1: Global Market Size for Personalized Medicine (billion USD) [8]

The global PM market is experiencing remarkable growth, driven by rising demand for customized therapies and precision diagnostics. The market's current trajectory suggests significant expansion in the next decade, with North America leading the way as of 2023. This growth is attributed to the adoption of advanced healthcare IT systems, artificial intelligence (AI) for drug development and interaction modeling, and next-generation sequencing (NGS) technologies for personalized data generation. However, balancing the high costs of infrastructure with the quality and efficacy of PMs remains a critical concern. Research institutions are playing an increasing role in addressing these challenges, particularly through the integration of pharmacogenomics, which is expected to further drive innovation in R&D for PM. Illustrated in **fig. 1**, the global market size for PM is projected to grow exponentially over the next decade.

Transformational Impact of PM in Oncology

PM has revolutionized oncology, offering transformative advancements in treatment approaches that enhance patients' quality of life. With a deeper understanding of host-related factors, PM ensures long-term survival, reduced toxicity, and improved effectiveness in cancer treatments. For instance, the FDA and the National Comprehensive Cancer Network (NCCN) have established protocols combining chemotherapy with immunotherapies (e.g., ipilimumab and nivolumab) for treating non-small cell lung cancer (NSCLC), achieving high success rates. These innovations are supported by breakthroughs in identifying driver mutations, resistance mutations, and the interplay between cancer and the immune system. However, the implementation of such therapies is often hindered by high costs, requiring innovative solutions to make PM more accessible [9].

Regulatory Landscape for Personalized Medicines

USA: The U.S. FDA plays a central role in regulating PMs by ensuring they are based on scientifically validated results from NGS tests. Advances in genome sequencing since 2003, along with initiatives like the *Precision Medicine Initiative* launched in 2015, have provided a foundation for precision diagnostics. Key FDA initiatives include:

NGS Testing Recommendations: In 2018, the FDA issued guidance documents to support the submission and evaluation of NGS-based assay data, facilitating clinical validation and ensuring accuracy. Public databases like ClinGen, recognized by the FDA, allow developers to validate tests using reliable data sources [10].

Analytical Validation Guidance: The FDA provides recommendations for developing and validating NGS assays while encouraging community engagement in establishing performance standards [11, 12].

PrecisionFDA Platform: This secure, cloud-based platform promotes global collaboration in NGS analysis and bioinformatics, enabling clinicians to leverage genetic profiles for disease prevention, diagnosis, and treatment [13]. The FDA has also issued numerous guidance documents to accelerate PM development, as summarized in **Table 2**, spanning topics such as pharmacogenomics, drug-device co-development, and biomarkers.

Table 2: FDA issued guidance documents on PM [14-24]

Title	Year
"IND Submissions for Individualized Antisense Oligonucleotide Drug Products: Administrative and Procedural Recommendations Guidance for Sponsor-Investigators"	2021
"Enrichment Strategies for Clinical Trials to Support Determination of Effectiveness of Human Drugs and Biological Products"	2019
"Principles for Co-development of an In Vitro Companion Diagnostic Device with a Therapeutic Product"	2016
"Clinical Pharmacogenomics: Premarketing Evaluation in Early Phase Clinical Studies and Recommendations for Labelling"	2012
"E16 Guidance on Biomarkers Related to Drug or Biotechnology Products Development: Context, Structure, and Format of Qualification Submissions"	2011
"In vitro Companion Diagnostic Devices"	2011
"Qualification Process for Drug Development Tools Guidance for Industry and FDA Staff"	2010
"E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories"	2008
"Pharmacogenomic Tests and Genetic Tests for Heritable Markers"	2007

"Pharmacogenomic Data Submissions Concept Paper on Drug-Diagnostic Co-Development"	2005

European Union (EU)

The EU supports PM innovation through regulatory frameworks, beginning with the establishment of the *European Research Network for PM (ERA-PerMed)* in 2017. This network facilitates collaborative efforts to advance PM development across member states.

Notable EU regulations include:

In Vitro Diagnostics (IVD) and Medical Device Legislation: Regulations (EU 2017/746 and EU 2017/745) improve the companion diagnostics consultation process and harmonize laws with scientific advancements [25-26].

Clinical Trials Regulation (EU-No.536/2014): Aims to accelerate clinical trials for PM development by unifying authorization procedures and ensuring the availability of trial data for researchers [27].

Personalized Medicine Policies (2008-2020): Supported by programs like *Horizon 2020* and *Horizon Europe*, these policies emphasize research funding, data standardization, and digital health infrastructure.

However, disparities among national regulatory agencies regarding financing and policy enactment need to be addressed to achieve EU-wide harmonization. **Table 3** highlights major EU policies on PM, focusing on cross-border healthcare, digital health transformation, and data standardization.

Table 3: Personalized Medicine policies in the EU from 2008 to 2020 [29-47].

Document Title & Reference	Issuing Body	Year	Main Focus Area	Reference
"Shaping Europe's Digital Future (2020/C202 I/01)"	"Commission of the European Communities (EC)"	2020	Enhancing healthcare workflows, surveillance systems, and ensuring long-term health system sustainability.	European Commission, 2020
Cybersecurity Framework for Healthcare (EU 2019/881)	European Parliament & Council of the EU	2019	Addressing cybersecurity risks in healthcare ICT systems through a certification framework.	European Parliament, 2019
European EHR Exchange Format (EU 2019/243)	Council(EU)	2019	Facilitating the exchange and availability of electronic health records across EU Member States.	Council of the EU, 2019
"Joint Report on Health and Long-Term Care in the EU"	Council (EU)	2019	Promoting integrated care solutions as part of the EU's long-term health care strategy.	Council of the EU, 2019
"Digital Transformation in Health (COM/2018/233 final)"	European Parliament & Council of the EU	2018	Standardizing EHR interoperability and promoting citizen empowerment within the digital healthcare space.	European Commission, 2018
"Data-Driven Healthcare Innovation (2017/C 440/05)"	Council(EU)	2017	Exploring big data, analytics, and citizen empowerment for improved healthcare sustainability.	Council of the EU, 2017
"European Interoperability Framework Strategy (COM/2017/0134 final)"	European Parliament & Council of the EU	2017	Advancing interoperability of EHRs and adopting digital health technologies across the EU.	European Commission, 2017
"Digital Single Market Strategy (COM/2017/0228 final)"	European Parliament & Council of the EU	2017	Improving data infrastructure, disease prevention, and personalized healthcare services through digital tools.	European Commission, 2017
General Data Protection Regulation (GDPR) (EU 2016/679)"	European Parliament & Council(EU)	2016	Protecting health data and enhancing privacy rights within the EU.	European Parliament, 2016

Conclusions on Personalized Medicine (2015/C 421/03)	Council(EU)	2015	Focus on patient-centric strategies, education, and collaboration in personalized medicine.	Council of the EU, 2015
"Efficient, Accessible, and Resilient Health Systems (COM/2014/0215)"	Council(EU)	2014	Enhancing the effectiveness, accessibility, and resilience of healthcare systems within the EU.	European Commission, 2014
Conclusions on Therapeutic Innovation (2014/C 438/06)	European Parliament & Council(EU)	2014	Promoting research and development of innovative healthcare products and services.	European Parliament, 2014
Clinical Trials Regulation (EU No 536/2014)	Commission of the European Communities (EC)	2014	Creating a unified EU portal to standardize clinical trial authorization procedures.	European Commission, 2014
Reflection on Healthcare Modernization (Reflection Process on Healthcare Modernization)	Council(EU)	2013	Enhancing sustainability, accessibility, and integration of healthcare systems within the EU.	Council of the EU, 2013
Conclusions on Healthcare Modernization for Sustainability (2011/C 202/04)	Council(EU)	2011	Making EU healthcare systems more responsive to emergencies and diseases while ensuring financial sustainability.	Council of the EU, 2011
Conclusions on Innovation in Medical Devices (2011/C 202/03)	Council of the EU & European Parliament	2011	Promoting patient-centered innovation and strengthening research infrastructure for medical devices.	Council of the EU, 2011
Rights of Patients in Cross-Border Healthcare (Directive 2011/24/EU)	Council(EU)	2011	Improving cross-border healthcare and access across EU Member States.	European Commission, 2011
Action Plan for Rare Diseases (2009/C 151/02)	Council(EU)	2009	Collaborative efforts in rare disease research and development of therapeutic innovations.	Council of the EU, 2009
Recommendation on Cross-border Interoperability of Electronic Health Record Systems (EHS)	Commission of the European Communities (EC)	2008	Focus on standardizing and facilitating the shared use of EHS, ensuring accessibility across the EU.	European Commission, 2008
Treaty of the European Union (Article 168)	Commission of the European Communities (EC)	2008	Responsibilities of Member States to provide equitable healthcare across the EU.	European Union, 2008

Challenges and Opportunities

Despite significant advancements, personalized medicine (PM) continues to face several challenges. The high costs associated with research and development, infrastructure investments, and sequencing technologies often limit accessibility. Regulatory asymmetry, with variations in policy adoption across different regions, poses another barrier to global implementation. Additionally, the use of genomic data requires robust regulatory frameworks to ensure patient privacy and data security. However, the opportunities for growth in PM are substantial. Advances in artificial intelligence (AI) and next-generation sequencing (NGS) technologies are revolutionizing diagnostic and therapeutic development. Collaborative frameworks, including public-private partnerships, are emerging to mitigate costs and drive innovation. Furthermore, increasing global awareness and strong support from governments and research initiatives are fostering the expansion and adoption of PM, paving the way for more personalized and effective healthcare solutions.

Legislative Policies in the US and EU

Initiatives like the Critical Path Initiative in the US promote business partnerships to tackle the issues in drug development and accelerate the pace of personalized medicine advancement. As a regulatory agency, the FDA could expedite the development process by endorsing conditional approvals and permitting more affordable and smaller clinical trials for customized medications. Clinical Outcomes of patients and compliance can be tracked via personal Digital Health Technologies (DHTs), ensuring the quality and safety of the treatment [48].

The European Union's governing body, the European Medicines Agency (EMA), is in charge of advancing public health and safety and overseeing and approving innovative treatments and diagnostics. The Centralized approval process of EMA expedites access to PMs across all Member States [49]. Providing patients access to safe and effective medications is one of the EMA's main goals. An "EMA/CHMP think-tank group on innovative drug development" was established to achieve this goal. This specialist group seeks to discover scientific roadblocks in the R&D of the pharmaceutical sector as well as in academic settings that impede the development of novel medications. A comparative analysis of regulations and guidance documents related to personalized medicine in the US and EU is shown in **Table 4.**

Table 4: Regulatory Aspects of Personalized Medicines in the US and EU [14, 50]

Aspect	**USA**	**Europe**
Regulatory Body	US Food and Drug Administration (FDA)	European Medicines Agency (EMA)
Preferred Term	Precision Medicine	Personalized Medicine
Key Documents	*-Public Human Genetic Variant Databases -Design and Validation of NGS-Based IVDs for Germline Disease Diagnosis*	*- Regulation (EU) 2017/746 (IVDR) - Regulation (EU) 2016/679 (GDPR) - Regulation (EU) No 536/2014 (Clinical Trials)*
Initial Milestone	Precision Medicine Initiative launched by the US President on December 18, 2015.	European Commission Conference held in 2011 to explore PM perspectives.
Policy Development	Critical Path Initiative	EMA/CHMP Think-Tank Initiative to foster innovative therapies.
Support Structures	Human Genome Project	ERA-PerMed (European Research Area Network for Personalized Medicine)

As a next step, cooperation between regulatory bodies, healthcare providers, patient advocacy organizations, and industry players is necessary to develop a legislative framework that promotes innovation, safeguards patient confidentiality, and guarantees the efficient and secure provision of customized medical care. Furthermore, to address the significant disparities in therapeutic accessibility, there is an urgent need for global harmonization across regulatory bodies. To improve accessibility and generalisability, novel therapies should be subjected to Global Clinical Trials (GCTs). Since it is not always practical to design Randomized Controlled Trials (RCTs) involving patients from different countries and ethnicities, it is important to adopt innovative trial designs and complex trials for PMs for rare diseases and other critical disorders.

Challenges in Personalized Medicine Development

Design and Conduct of Clinical Trials [1, 9, 51-57]

Randomised Controlled Trials (RCTs): Although PM faces difficulties with RCTs, they are the gold standard for regulatory approval. Conventional trials look at vast populations; PM looks at smaller, more specialized groups. This propels for the fast and cost-effective development of therapies, guaranteeing safety and efficacy.

Cost and Lead Time: Clinical studies are expensive ($2.87 billion) and take ten to fifteen years. Due to rising costs and problems with payment, these exorbitant expenses, when paired with the smaller patient populations in PM, can financially deter clinical studies and impede treatment access.

Biomarkers: Biomarkers are important because they can be used to predict how a patient will react to treatment. Finding and confirming biomarkers, however, is difficult and expensive. The evidence needed for validation may be hard to come by and the regulatory requirements are vague. This affects the trial design and may cause therapeutic approval to be delayed or denied.

Clinical Trial Design: The smaller and targeted groups of PMs may not always meet the regulatory standards of clinical

studies. Smaller studies may overlook rare adverse outcomes and can result in statistical or sampling bias. The inability to use retrospective analysis to resume unsuccessful trials further complicates trial designs.

Uncertainty in the Approval Process: PM developers must deal with uncertainty in the regulatory approval process because of different requirements for trial design and evidence across geographies and varied research incentives. Investment in studies for individualized treatments is thereby impacted in resource-constrained economies. Small patient samples in PM trials make risk-benefit assessments difficult.

Recommendations [9]

Defining and Guidance: Innovative assessment methodologies should be adopted and instructions on submission and usage of biomarker data during the approval procedure should be revised.

Postmarket Study and Surveillance (PMR): To expedite the approval of certain medications requiring phase IV PMR, PMR conditions should be strengthened, phase IV trials should be supported, continuing data collection techniques should be developed, and limited or conditional approval provisions should be implemented. A centralized Adverse Event reporting database should be implemented to promote timely data collection and reporting.

Innovative clinical trial designs: PM markers should be further explored to develop new clinical trial methods, like adaptive group sequential designs for sensitive subgroups and adaptive trials that enroll "likely responders" based on biomarkers. Data generated from smaller trial populations can be accepted by the regulatory bodies supported with Real-world Evidence (RWE). RWE can be further used to identify relevant biomarkers and clinically relevant endpoints.

Single Subject Research Design (SSRD): To identify target patients who respond quickly to treatments and to further customize the drug action, using 'N of 1' or SSRD investigations, should be encouraged.

Uncertain Regulations on Evidentiary Standards [1, 9, 53-61]

Unreasonable or Unclear requirements: PM developers encounter difficulties getting clearance and reimbursement due to the ambiguity in regulatory evidentiary requirements.

Regulatory Compliance: Companies frequently fall short of regulatory obligations because of their inability to execute phase IV studies and unclear data expectations.

Cost and Delay: PM development is hampered by high expenses and protracted deadlines to satisfy regulatory data requirements.

Inadequate Data: There is not enough information available or generated by clinical research to extend applications to more indications.

Clinical Utility: Payers' decision-making is complicated by the lack of clarity in the standards of clinical outcomes. This causes a lack of evidence to support a reimbursement model for PM treatments.

Implications

Uncertainty in Data Requirements: PM developers face difficulties due to inconsistent requirements between payers and regulators.

Phase IV Studies: Limited data on novel drug uses results in delayed identification of Serious Adverse Events (SAE). This is caused due to low compliance with post-market study obligations (PMS).

Cost and Practicality: PMSs are expensive, time-consuming, and challenging to do, which affects the availability of continuing data and clinical efficacy evaluations.

Recommendations [9]

Higher Quality Evidence: Manufacturers must offer high-quality data as evidence to satisfy payer, provider, and regulatory requirements and to demonstrate the PM's cost-effectiveness.

Adaptable Strategies: Regulators must embrace adaptable and creative strategies for PM clinical trials and approvals, incorporating various types of evidence-generation techniques such as statistical models, exploratory analysis, and comparative data from similar or comparable applications.

Clear Technical direction: Regulators must offer precise technical direction on genomic data generation, clinical evidence generation, and the application of biomarkers in pharmacogenetic and drug development research.

Cost-Effective Data Generation: To confirm biomarkers, reduce expenses, and speed up the production of evidence, public-private partnerships and cross-institutional investigations should be promoted.

Handle Non-Compliance: Through regulatory programs like the Sentinel Initiative, which tracks medical product

performance and identifies serious adverse events (SAE) using a variety of data sources, the FDA should continue to reduce the backlog of postmarket study commitments (PMR) and ensure more compliance.

Information Systems and Privacy [1, 9, 56-61]

Three primary subthemes are highlighted by the regulation of information systems for PM, which addresses the conflicts between patient privacy and the data demands of PM developers:

Data Privacy Concerns: Although genetic data from biospecimens and personal health information (PHI) are essential for PM R&D, they also present serious privacy concerns. Informed consent is crucial as genetic information can disclose personal and family health information. PHI usage in the USA is governed by the Health Insurance Portability and Accountability Act (HIPAA). However, regulatory gaps exist particularly in organizations like data brokers and research agencies not covered by HIPAA. It is debatable if broader consent for future research is appropriate because it might violate patient privacy and long-term consent for using health information.

Sample Collection and Storage: Human tissue samples are frequently connected to medical records to aid PM research. This presents issues with patient consent and privacy related to health data. Rules and regulations differ across geographies and data processing purposes, and getting repeated consent for different research goals is not feasible. Personal health data protection regulations are beneficial to protect patient privacy but also hinder PM research and development.

Heterogeneous Regulations: PM development is hampered by different national and international laws on the sharing, storing, and using of biospecimens. Inconsistent standards lead to ambiguity and hinder the exchange of research materials and data. The US has different federal and state restrictions, which makes using tissue samples and related data more difficult. Privacy and discrimination concerns are aggravated since not all organizations handling PHI are covered by HIPAA laws.

Recommendations [9]

Information exchange: Standardise procedures and policies to facilitate improved researcher information exchange, including using an encrypted PHI.

Biospecimen Collection and Storage: Gather and sequence samples with enough lead time to guarantee data availability to support trials and enrich the representation of genetic variations in clinical trial submissions.

Create robust procedures for collecting and storing samples for future usage to identify biomarkers and perform safety and efficacy assessments.

Consent and Privacy Protections: Expand the scope of consents to enable the use of biospecimens and PHI in research in the future.

Tighten federal laws to safeguard personal health data and combat genetic discrimination outside the purview of the Genetic Information Nondiscrimination Act (GINA).

Enact clear privacy laws backed by the law to safeguard people's rights to personal health information.

Federal Funding and Initiatives: Improve the FDA portal to promote genetic data sharing and innovation. Expand federal support to biobanks in order to standardize security and data management procedures,

Frameworks for Privacy and Data Security: Support precise legislation on privacy and stabilization of vigorous rules for the data protection proposed by the National Institute for Standards and Technology and the White House. Popularize EHR as data can be safely exchanged and archived in electronic documents comparing to paper ones.

Regulatory Incentives and Intellectual Property (IP) Barriers [1, 9, 55-61]

There are two basic ways that intellectual property (IP) rights, especially patents, impede the advancement and innovation of PM: **Inadequate, Predictable Patent Protection**: Since specialty cures yield lower profits and drug development is more expensive, PM developers seek more incentives. It has been observed that the patent protections provided to novel drugs stifle PM investment and innovation and **Patents Impeding Originality**: Stakeholders such as patients, patient groups, and smaller developers contend that robust patent rights impede innovation, produce patent tangles, and limit access to medications and medical equipment. Barriers may arise from broad or overlapping patents because subsequent inventors may fear infringement.

Issues

Evergreening: Repackaging medications for a narrower patient base without providing scientific support to prolong patent protection.

Uncertainty Regarding Medical Device Patents: The extent and enforcement of patents covering PM devices and diagnostics are ambiguous due to evolving patent laws.

Recommendations [9]

Recommendations for advancing precision medicine (PM) highlight several strategic initiatives aimed at fostering innovation and accessibility. **Improved patent incentives** include extending patent durations or market exclusivity for medications sold as companion diagnostics (CDx) and innovative manufacturing techniques, alongside clearer patent rules and mechanisms like patent pools and gene-patent clearinghouses. Measures such as mandatory licensing, fair royalties, and march-in rights address patent challenges in genetic test development, while research exclusions under the Patent Act shield doctors and researchers from patent infringement claims. The **Orphan Drug Act (ODA) model** proposes granting PM medicines market exclusivity and developing a sui generis framework akin to the ODA for PM products. Additionally, the **Humanitarian Device Exemption** allows PM device manufacturers market exclusivity, while the **Priority Review Voucher Program** advocates expanding its scope to include PM devices beyond rare disorders. The **21st Century Cures Act** emphasizes expediting FDA approvals for novel PM technologies targeting severe illnesses and enhancing the Humanitarian Device Exemption to cover devices for conditions affecting up to 8,000 individuals. Predictable financing and tax incentives include funding studies for underrepresented populations, reducing FDA user fees for collaborative drug and device development, and offering financial incentives for diagnostic firms generating pharmacogenomics data for smaller patient groups. These measures collectively aim to overcome regulatory, financial, and operational barriers in PM innovation and deployment.

5. CONCLUSION

A comparative analysis of laws about personalized pharmaceuticals highlights the need for harmonization across regions. This review compares various regulations on PMs in the USA and Europe. The harmonization method should resonate with the larger scientific community considering regional variations and nuances. This approach should be balanced against data privacy and consent. This necessitates controlled access to the study data and any individual-level derivatives thereof. PM treatments are tailored to the genetic and physiological needs of individual patients. As a result, regulatory agencies such as the U.S. FDA and the EMA have had to adapt and develop new guidelines to accommodate this paradigm shift. Current regulatory obstacles can be addressed using innovative approaches to regulatory decision-making and bringing a new era of personalized healthcare with creativity, commitment, and strategic competence. Engaging stakeholders such as researchers, policymakers, regulators, healthcare providers, and patients in policy-making, data management, and research can create patient-focused health services and provide much-needed impetus to PM research and development.

REFERENCES

[1] Goetz LH, Schork NJ. Personalized medicine: motivation, challenges and progress. Fertil Steril. 2018 Jun;109(6):952-963. doi: 10.1016/j.fertnstert.2018.05.006.

[2] Krzyszczyk P, Acevedo A, Davidoff EJ, Timmins LM, Marrero-Berrios I, Patel M, White C, Lowe C, Sherba JJ, Hartmanshenn C, O'Neill KM, Balter ML, Fritz ZR, Androulakis IP, Schloss RS, Yarmush ML. The growing role of precision and personalized medicine for cancer treatment. Technol (Singap World Sci). 2018;6(3-4):79–100. doi: 10.1142/S2339547818300020.

[3] Malone ER, Oliva M, Sabatini PB, Stockley TL, Siu LL. Molecular profiling for precision cancer therapies. Genome Med. 2020;12:8. doi: 10.1186/s13073-019-0703-1.

[4] What is Personalized medicine. Available online: https://www.jax.org/personalized-medicine/precision-medicine-and-you/what-is-precision-medicine (accessed on 25 July 2024).

[5] Focus Area: Individualized Therapeutics and Precision Medicine. Available online: https://www.fda.gov/science-research/focus-areas-regulatory-science-report/focus-area-individualized-therapeutics-and-precision-medicine (accessed on 25 July 2024).

[6] Novel Drug Approvals for 2023. Available online: https://www.fda.gov/drugs/novel-drug-approvals-fda/novel-drug-approvals-2023 (accessed on 25 July 2024).

[7] Nimmesgern E, Benediktsson I, Norstedt I. Personalized medicine in Europe. Clin Transl Sci. 2017;10(2):61-63. doi: 10.1111/cts.12446.

[8] Personalized Medicine Market Size, Share, and Trends 2024 to 2034. Available online: https://www.precedenceresearch.com/personalized-medicine-market (accessed on 26 July 2024).

[9] Knowles L, Luth W, Bubela T. Paving the road to personalized medicine: recommendations on regulatory, intellectual property and reimbursement challenges. J Law Biosci. 2017;4(3):453-506. doi: 10.1093/jlb/lsx030.

[10] FDA finalizes guidances to accelerate the development of reliable, beneficial next generation sequencing-based tests. Available online: https://www.fda.gov/news-events/press-announcements/fda-finalizes-guidances-accelerate-development-reliable-beneficial-next-generation-sequencing-based (accessed on 28 July 2024).

[11] FDA Recognition of Public Human Genetic Variant Databases. Available online: https://www.fda.gov/medical-devices/precision-medicine/fda-recognition-public-human-genetic-variant-databases (accessed on 2 August 2024).

[12] Jennings LJ, Arcila ME, Corless C, Kamel-Reid S, Lubin IM, Pfeifer J, Temple-Smolkin RL, Voelkerding KV, Nikiforova MN. Guidelines for validation of next-generation sequencing–based oncology panels. J Mol Diagn. 2017;19(3):341-365. doi: 10.1016/j.jmoldx.2017.01.011.

[13] About precisionFDA. Available online: https://precision.fda.gov/about (accessed on 2 August 2024).

[14] Hemburg MA. Paving the Way for Personalized Medicine. FDA's Role in a New Era of Medical Product Development. October 2013.

[15] Guidance for Industry Pharmacogenomic Data Submissions. Available online: https://www.fda.gov/media/122944/download (accessed on 2 August 2024).

[16] Pharmacogenomic Tests and Genetic Tests for Heritable Markers. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pharmacogenetic-tests-and-genetic-tests-heritable-markers (accessed on 2 August 2024).

[17] E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories. Available online: https://www.fda.gov/media/71389/download (accessed on 2 August 2024).

[18] Qualification Process for Drug Development Tools Guidance for Industry and FDA Staff. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/qualification-process-drug-development-tools-guidance-industry-and-fda-staff (accessed on 2 August 2024).

[19] E16 Guidance on Biomarkers Related to Drug or Biotechnology Products Development: Context, Structure, and Format of Qualification Submissions. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e16-biomarkers-related-drug-or-biotechnology-product-development-context-structure-and-format (accessed on 2 August 2024).

[20] In vitro Companion Diagnostic Devices. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/in-vitro-companion-diagnostic-devices (accessed on 2 August 2024).

[21] Clinical Pharmacogenomics: Premarketing Evaluation in Early Phase Clinical Studies and Recommendations for Labelling. Available online: https://www.fda.gov/files/drugs/published/Clinical-Pharmacogenomics--Premarket-Evaluation-in-Early-Phase-Clinical-Studies-and-Recommendations-for-Labeling.pdf (accessed on 2 August 2024).

[22] Principles for Co-development of an In Vitro Companion Diagnostic Device with a Therapeutic Product. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/principles-codevelopment-in-vitro-companion-diagnostic-device-therapeutic-product (accessed on 2 August 2024).

[23] Enrichment Strategies for Clinical Trials to Support Determination of Effectiveness of Human Drugs and Biological Products. Available online: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enrichment-strategies-clinical-trials-support-approval-human-drugs-and-biological-products (accessed on 2 August 2024).

[24] IND Submissions for Individualized Antisense Oligonucleotide Drug Products: Administrative and Procedural Recommendations Guidance for Sponsor-Investigators. Available online: https://www.fda.gov/media/144872/download (accessed on 2 August 2024).

[25] Regulation (EU) 2017/745 of The European Parliament and of The Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. Available online: https://eur-lex.europa.eu/eli/reg/2017/745/2023-03-20 (accessed on 02 August 2024).

[26] Regulation (EU) 2017/746 of The European Parliament and of The Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. Available online: https://eur-lex.europa.eu/eli/reg/2017/746/2017-05-05 (accessed on 02 August 2024).

[27] Regulation (EU) 536/2014 of The European Parliament and of The Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. Available online: https://eur-lex.europa.eu/eli/reg/2014/536/2022-12-05 (accessed on 02 August 2024).

[28] Beccia F, Hoxhaj I, Castagna C, Stroha¨ ker T, Cadeddu C, Ricciardi W, Boccia S. An overview of Personalized Medicine landscape and policies in the European Union. Eur J Public Health. 2022;32(6):844-851. doi:

10.1093/eurpub/ckac103.

[29] Consolidated version of the Treaty on the Functioning of the European Union - Part Three: Union Policies and Internal Actions - Title XIV: Public Health - Article 168 (ex Article 152 TEC). Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX%3A12008E168 (accessed on 03 August 2024).

[30] Commission Recommendation of 2 July 2008 on cross-border interoperability of electronic health record systems (2008/594/EC). Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32008H0594 (accessed on 03 August 2024).

[31] Commission Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02). Available online: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF (accessed on 03 August 2024).

[32] Directive 2011/24/EU of The European Parliament and of The Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. Available online: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:en:PDF#:~:text=This%20Directive%20aims%20to%20establish,States%2C%20whilst%20fully%20respecting%20the (accessed on 03 August 2024).

[33] Council conclusions on innovation in the medical device sector (2011/C 202/03). Availableonline:https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2011:202:0007:0009:EN:PDF (accessed on 03 August 2024).

[34] Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on the European Strategy for the Digitalisation of Health and Care. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52020DC0076 (accessed on 03 August 2024).

[35] Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on a European Health Data Space. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52021PC0227 (accessed on 03 August 2024).

[36] Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31995L0046 (accessed on 03 August 2024).

[37] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data, and on the free movement of such data (General Data Protection Regulation). Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32016R0679 (accessed on 03 August 2024).

[38] Regulation (EU) 2019/953 of the European Parliament and of the Council of 5 June 2019 on the European Health Data Space. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52019PC0216 (accessed on 03 August 2024).

[39] Council Recommendation 2019/C 273/01 on a European framework for the digital transformation of health and care. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52019XC0906%2803%29 (accessed on 03 August 2024).

[40] Data protection impact assessment (DPIA). Available online: https://ec.europa.eu/info/law/law-topic/data-protection/data-protection-eu/what-data-protection-impact-assessment-dpia_en (accessed on 03 August 2024).

[41] European Data Protection Supervisor. Opinion 4/2016 on the General Data Protection Regulation and its impact on cross-border health data processing. Available online: https://edps.europa.eu/sites/edp/files/publication/16-11-04_opinion_health_data_en.pdf (accessed on 03 August 2024).

[42] European Commission. European Commission - Digital Health. Available online: https://ec.europa.eu/health/ehealth/policy_en (accessed on 03 August 2024).

[43] WHO. Personal Health Records: A Policy Framework. Available online: https://www.who.int/health-topics/personal-health-records (accessed on 03 August 2024).

[44] National Institutes of Health (NIH). National Strategy for Personalized Medicine. Available online: https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-strategy-personalized-medicine (accessed on 03 August 2024).

[45] European Commission. Digital Single Market for Health. Available online: https://ec.europa.eu/digital-strategy/our-policies/european-health-data-space_en (accessed on 03 August 2024).

[46] European Medicines Agency. Personalized Medicine and the EMA. Available online: https://www.ema.europa.eu/en/human-regulatory/research-development/personalised-medicine (accessed on 03 August 2024).

[47] Medical Devices and In Vitro Diagnostic Devices. Available online: https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices (accessed on 03 August 2024).

[48] European Union. The EU Health Strategy. Available online: https://europa.eu/european-union/policies/health_en (accessed on 03 August 2024).

[49] Commission Implementing Decision (EU) 2020/1277 of 29 September 2020 on the adoption of a framework for the interoperability of electronic health records. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32020D1277 (accessed on 03 August 2024).

[50] Directive 2005/36/EC of the European Parliament and of the Council of 7 September 2005 on the recognition of professional qualifications. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32005L0036 (accessed on 03 August 2024).

[51] Council Directive 93/42/EEC of 14 June 1993 concerning medical devices. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31993L0042 (accessed on 03 August 2024).

[52] European Parliament. The EU and Precision Medicine: A Policy Overview. Available online: https://www.europarl.europa.eu/thinktank/en/document.html?reference=EPRS_BRI(2020)654548 (accessed on 03 August 2024).

[53] European Commission. Digital Health and Care: Action Plan 2021-2027. Available online: https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/home (accessed on 03 August 2024).

[54] European Parliament. Cross-border Healthcare: European Union Legislation. Available online: https://www.europarl.europa.eu/factsheets/en/sheet/47/cross-border-healthcare (accessed on 03 August 2024).

[55] Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A31998L0079 (accessed on 03 August 2024).

[56] Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on the setting standards of quality and safety for human tissues and cells. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32004L0023 (accessed on 03 August 2024).

[57] Council of the European Union. Council Conclusions on Digital Health. Available online: https://www.consilium.europa.eu/en/press/press-releases/2018/12/13/council-conclusions-on-digital-health/ (accessed on 03 August 2024).

[58] E-Health Network: Interoperability and the Cross-Border Exchange of Health Information. Available online: https://ec.europa.eu/health/ehealth/policy_en (accessed on 03 August 2024).

[59] Regulation (EU) 2015/842 of the European Parliament and of the Council of 21 May 2015 on the European Health Insurance Card. Available online: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32015R0842 (accessed on 03 August 2024).

[60] Commission Communication on the European Health Union. Available online: https://ec.europa.eu/health/system/files/2021-11/eu-health-union-communication_en_0.pdf (accessed on 03 August 2024).

[61] Resolution on eHealth: An Action Plan for Europe. Available online: https://www.europarl.europa.eu/doceo/document/TA-6-2018-0083_EN.html (accessed on 03.