

# Personalized Medicines: Reforming Diagnostics and Therapeutics

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**Abstract:** Since the first use of the term 'Personalized Medicine' (PM) in 1990, many research and review articles have coined this term. Nevertheless, this topic has not been widely researched about till now. The PMs are the application of genomic and molecular data for developing therapies with unprecedentedly higher efficiencies, better safety, lower ADR's, and reduced costs of therapies. PMs are developed through molecular level knowledge of the drug targets and diseases, which leads to the promise of the right treatment for right patient at the right time. This paper gives a comprehensive view of PMs. For this purpose, this paper is divided into following sections: defining personalized medicines; the history and evolution of personalized medicines; the human genome project; drug discovery & development process; merits of personalized medicines; applications of personalized medicines; challenges on the road of personalized medicines; regulatory evolution in the generation of personalized medicines; role of US FDA in the era of personalized medicines and, conclusion.

**Keywords:** Pharmacogenetics, pharmacogenomics, biomarkers, precision medicines, targeted medicines.

## DEFINING PERSONALIZED MEDICINES

The fact that "the dream of personalized medicine was one of the driving forces behind the 13-year, \$3 billion Human Genome Project" [1] demonstrates the significance of Personalized Medicines (PMs). PMs are "the application of genomic and molecular data to better target the delivery of health care, facilitate the discovery and clinical testing of new products, and help determine a person's predisposition to a particular disease or condition" [2]. Personalized medicine is based upon targeted therapy and aims to deliver the right treatment for the right patient at the right time [3, 4]. Such an approach of being able to offer tailored therapeutics ensures greater safety and efficacy of the treatment [5]. Progress in the arena of molecular characterization of diseases has facilitated treatment using personalized medicines, which utilize molecular diagnostic procedures along with pathological diagnosis [6, 3]. Information regarding molecular basis of an ailment is vital as it leads to the recognition of novel targets, screening of toxicogenomic markers and development of molecular assays. Consequently, therapeutic decisions pertaining to selection of proper medication and dosage can be tailored to the individual's specific needs [3, 7, 4].

The development and approval of Herceptin® (trastuzumab) in 1998 marked the onset of the era of PMs. The successful completion of Human Genome Project further boosted the efforts to design novel diagnostics and therapeutics by enabling better comprehension of genetics behind health and disease.

Breakthroughs in the field of genomics, medical imaging and regenerative medicines, coupled with advanced computational and wireless technology have provided an impetus to the concept of personalized medicines. These medicines are rightly referred to as 'Precision Medicines', since these are designed to address individual disease patterns and promise greater patient benefits. The concept of PMs is based upon the principle of stratification, whereby patients suffering from a particular disease are divided into subgroups on the basis of some characteristics, exhibiting greater response to therapy with a particular drug. Alternatively, the patients comprising such a subgroup may be found to have lesser propensity of adverse effects associated with a particular therapy. From this viewpoint, these medicines are also termed as 'Stratified Medicines'[6]. In the beginning of 2015, the US President Barack Obama declared the National Precision Medicine Initiative worth US \$ 215 million. The fact that individual differences decide a patient's response to a specific treatment has been the driving force behind this initiative [8].

PMs deliver therapeutic benefits by use of two medical products, namely: a diagnostic device and a therapeutic product. A diagnostic device may be used to carry out *in vitro* measurements for genetic factors or *in vivo* diagnostic tests. With the advent of technology, it is also possible to improve patient outcomes by designing medical devices to suit an individual's needs and characteristics, i.e. patient anatomy, physiology and environment of use [6]. Some of the medical devices approved as personalized medicine are given in the following table (Table 1) [9]:

The concept of PMs has led to a paradigm shift in healthcare management by transferring the focus from

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**Table 1: Approved Personalized Medical Devices [6, 9]**

Personalized Medical Devices	Indications
Tinnitus Masker	The tinnitus treatment customizes the audio signals as per the individual patient's hearing requirement.
Pedicle Screw Spinal Systems	These are systems comprising of a rod/screw/hook connector kit. The surgeon assembles it to customize according to patient's unique anatomy/physiology with the help of MRI/CT imaging.
Software-based quantitative EEG analysis	The analysis predicts an individual's response to various psychotropic drugs and guides doctor in decision making.
The Zenith Fenestrated AAA Endovascular Graft	The Graft is approved for the endovascular treatment of patients with abdominal aortic or aortoiliac aneurysms with morphology suitable for endovascular repair. The fenestrated device enables treatment of patients with shorter proximal neck in comparison to those who can be treated using other endovascular grafts. Each device can be customized to the patient's individual aortic anatomy.
The Artificial Pancreas Device System	The device is under clinical investigation and is designed to automatically monitor patient's glucose levels and deliver patient-tailored insulin doses in diabetics. It's functioning is based on a computer-controlled algorithm and the device consists of a continuous glucose monitoring system and an insulin infusion pump.
Illumina MiSeqDx	A compact DNA sequencer that can scan the entire human genome in about 24 hours. It works by breaking down, rebuilding and recording the complete DNA sequence of a person in a parallel fashion.

treatment of disease to its prevention and, maintenance of health. The path for PMs, however, is not devoid of challenges. Responding to the scientific discoveries in the field of genomics and, translating them into PMs requires transcending considerable scientific, technical, economic and social challenges [10].

The present article provides an overview about PMs, including their history and evolution and, approved products. The paper also sheds light on the merits of PMs, followed by the challenges and the role of FDA with respect to the changing future of medicines.

## HISTORY AND EVOLUTION OF PERSONALIZED MEDICINES

As per the literature available in PubMed, the term 'Personalized Medicine' is said to have been used for the first time in 1990. The second use of the term is reported to have occurred only ten years hence. Since then, the field has attracted the attention of a number of scientists globally, which is evident from the fact that thousands of research and review articles have coined the term [11]. Yet, actual progress in the sphere of PMs has been made in the last decade only. Figure 1 depicts the advancements made in the arena of PMs.

The US FDA embraced the concept of Personalized Medicines in 2007 by granting approval to a genetic test called MammaPrint, used to forecast the reoccurrence of breast cancer [12]. The story of

Kalydeco™, a drug used to treat cystic fibrosis, also portends the forward thinking approach of US FDA in support of PMs. The drug (generic name- ivacaftor) was approved in January 2012, for the treatment of patients with G551D mutation. This specific genetic abnormality causes terrible impairment of lungs and digestive system owing to disturbed salt and water transport. The mutation is known to have a prevalence of 4% in the population of US. Kalydeco helps the patients by restoring the function of the protein that is made by the mutated gene. In other words, the drug targets the fundamental cause of the disease rather than the symptoms. The drug exemplifies the effective application of genomics to comprehend the underlying cause of a disease, to design and develop a medicine to target the cause and, further, to utilize a genetic test to guide prescribing decisions. The development of the drug entailed an investment of \$75 million and persistent efforts on the part of Cystic Fibrosis Foundation and Vertex Pharmaceuticals. The US FDA played its part by streamlining the drug approval process and allowing an expedited review. As a result, the drug was approved in less than three months time. The bygone years have witnessed many targeted therapies, especially for the treatment of cancer, such as tremetinib, dabrafenib, crizotinib, vemurafinib [6]. Table 2 [13] gives an account of selected medical products available for personalized treatment.

The most crucial role of the personalized medicines appears to be in the treatment of cancer, wherein patients with specific genetic characteristics are



Figure 1: Advancements in the field of personalized medicines.

Table 2: Selected Personalized Medicine Products [13]

Therapy	Biomarker/Test	Indication
Anti-retroviral drugs	TruGene <sup>®</sup> -HIV 1 Genotyping Kit	Guides selection of therapy based on genetic variations responsible for the resistance of HIV virus to certain anti-retroviral agents.
Camptosar <sup>®</sup> (irinotecan)	<sup>a</sup> UGT1A1	Colon cancer: Variations in the UGT1A1 gene can affect a patient's ability to breakdown irinotecan, leading to elevated blood levels of the drug and a greater risk of adverse events.
Drugs metabolized by cytochrome P450	Amplichip <sup>®</sup> <sup>b</sup> CYP2D6/ CYP2C19	FDA classification 21 CFR 862.3360: This device is used as an aid to determine the most appropriate treatment and to individualize treatment dose for therapeutics that are metabolized predominantly by the specific enzyme about which genotypic information is obtained from the system.
Gleevec <sup>®</sup> (imatinib mesylate)	<sup>c</sup> BCR-ABL	Chronic myelogenous leukemia (CML): Gleevec (imatinib mesylate) is approved for the use in patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after interferon-alpha therapy fails.
Gleevec <sup>®</sup> (imatinib mesylate)	<sup>d</sup> c-KIT	Gastrointestinal stromal tumor (GIST): Gleevec is also approved for the treating patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST).
Herceptin <sup>®</sup> (trastuzumab)	<sup>e</sup> HER-2/neu receptor	Breast cancer: The drug is indicated for the treatment of patients with metastatic breast cancer whose tumors over-express the HER2 protein and who have undergone one or more chemotherapy regimens for their metastatic disease.
Purinethol <sup>®</sup> (mercaptopurine)	<sup>f</sup> TPMT	Guides dosage adjustment in treatment of acute lymphoblastic leukemia: Patients with inherited little or no thiopurine S-methyltransferase (TPMT) activity are predisposed to severe Purinethol toxicity from conventional doses.
Tamoxifen	Estrogen receptor	Estrogen and progesterone values in breast cancer patients help to predict whether tamoxifen citrate therapy is likely to be beneficial.

<sup>a</sup>UGT1A1 = UDP-glucuronosyltransferase 1A1, <sup>b</sup>CYP = cytochrome P450 enzyme <sup>c</sup>BCR-ABL = breakpoint cluster region – Abelson, <sup>d</sup>c-KIT = tyrosine kinase receptor. <sup>e</sup>HER2 = human epidermal growth factor receptor 2, <sup>f</sup>TPMT = thiopurine S-methyltransferase.

identified by a diagnostic test and, thereafter, treated with the related therapeutic product [14, 15, 16]. The market for high-value diagnostics in the oncology segment is projected to attain \$3 billion by 2018. Along with other therapeutic segments the personalized medical diagnostic products and services is expected to cross \$6 billion mark globally [17]. Nevertheless, personalized approach is being increasingly investigated for treatment of various other disorders such as multiple sclerosis, scleroderma, cardiovascular disorders and cerebrovascular disease [18, 19, 20, 21]. Categorically, diagnostics based on biomarker has perceivable effect on both, therapeutic and diagnostic agents and, has given rise to the concept of theranostics [22].

The major developments in the field of PM can be attributed to the Human Genome Project (HGP) and Gene-mapping. The next section gives an overview of the HGP.

## THE HUMAN GENOME PROJECT

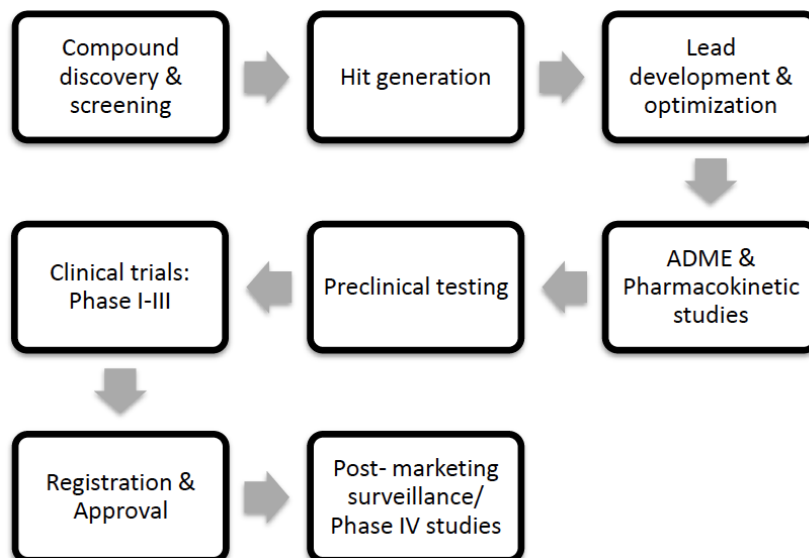
Human Genome Project can be called as the backbone of the drug discovery and development process for PM [23]. Launched in October 1990, on April 14<sup>th</sup> 2003, the International Human Genome Sequencing Consortium announced the completion of the HGP 2 years ahead of the scheduled date. This international effort to sequence 3 billion DNA letter is considered as one of the most important scientific undertakings of all the times, which was completed with the total spending of \$2.7 billion [24]. "The finished sequence produced by the Human Genome Project

covers about 99 percent of the human genome's gene-containing regions, and it has been sequenced to an accuracy of 99.99 percent" [24].

The entire sequence data generated by the Human Genome Project has been made freely accessible to researchers around the world, without restrictions on its use or redistribution, to enable maximal application of the outcomes of this project. Additionally, the Human Genome Project became the first large scientific undertaking to dedicate about 5% of its total budget for research to the ethical, legal and social implications (ELSI). For doing so, HGP studied how the exponential increase in knowledge about human genetic make-up may affect individuals, institutions and society [24].

Furthermore, National Human Genome Research Institute council, at its 59<sup>th</sup> meeting on 17-18 May 2010, gave clearance for the renewal of sequencing program during fiscal year 2011. Through this renewal, large-scale sequencing will evolve further. The program staff has recommended three new areas of research, including an effort to discover the majority of genes responsible for so-called Mendelian or single-gene diseases; clinical sequencing exploration projects; and efforts to produce software tools for sequence analysis that can be used by researchers inundated by data from the new sequencing platforms, especially as their use expands into medical sequencing projects beyond the large centers [25].

The HGP till now and with its upcoming developments indicates towards the brighter prospects in the field of personalized medicines. The next section



**Figure 2:** Traditional drug discovery and development process.

describes the Drug Discovery & Development (DD&D) for personalized medicines.

## THE PROCESS OF DRUG DISCOVERY & PRODUCT DEVELOPMENT

PM defies the traditional approach followed in the drug discovery and development process. Till recently, the drugs have been developed through a 'linear' approach (Figure 2) to produce all the drugs in a generalized way for all potential consumers.

On the other hand, the DD&D process of PM is an integrated feed-back process, which utilizes a 'knowledge management system' [4] by a heuristic approach (Figure 3). This newer approach has advantages such as reduced costs of target and lead discovery, reduced timelines and costs of clinical trials, better healthcare for patients, and emergence of new gene targets for drug discovery [4]. These advantages are discussed in detail in the later parts of this paper.

The development of new technologies and techniques has enhanced the ease and feasibility of the DD&D process of PM. The techniques such as positional cloning, expression arrays, proteomics, metabolomics, knock-out, animal models, disease models, robotics, microassays, chemi-informatics, structure based designs, ADME and scale-up chemistry have assisted in developing the 'knowledge management system' [26] due to which the dream of PMs can now be turned into reality.

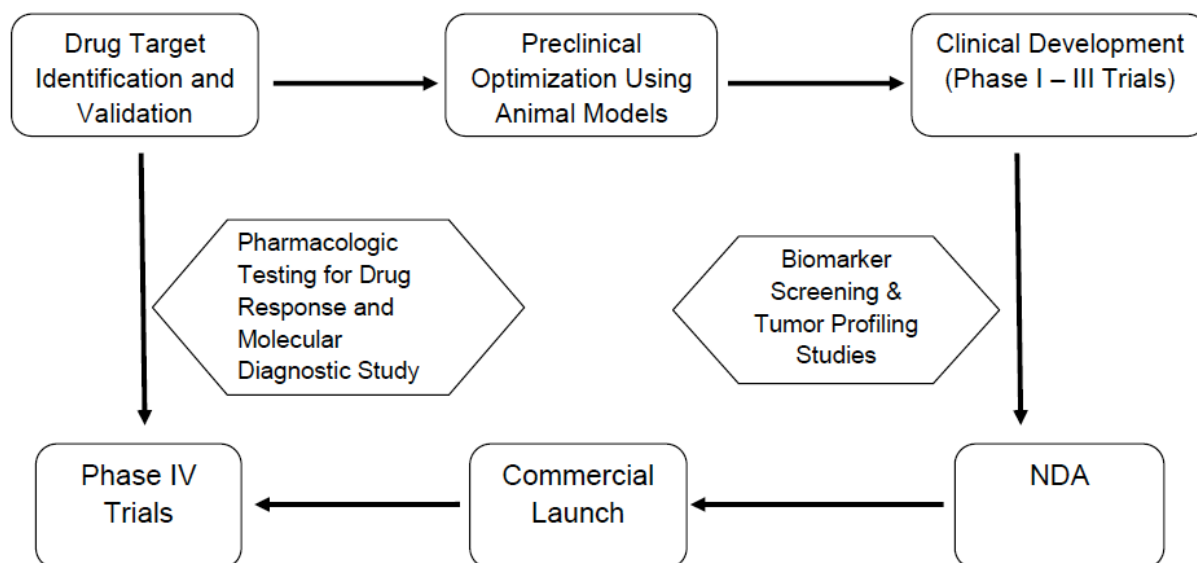
The data generated in this DD&D process can be stored, mined, and managed through this 'knowledge

management system'. This data, from the later part of the development process, can be fed-back into the earlier parts to make safer, highly efficient and more effective drugs. These drugs, when prepared in accordance to the molecular level profile of an individual, lead to the discovery and development of personalized medicines.

## MERITS OF PERSONALIZED MEDICINES

Personalized medicines have revolutionized the healthcare field and are set to change the standards for managing patient's health. PMs proffer hope of better treatment options and outcomes by virtue of several merits. They are listed as under: [4, 13, 22, 27, 28, 29, 30].

1. **Increased effectiveness** of drugs due to molecular level knowledge of health and disease, promoted by gene-centered research, which allows researchers to develop therapies specifically targeted to disease sites. It is noteworthy that the concept of PM is not only applicable to genetic disorders but may also be applied to optimize the treatment of several other diseases e.g. AIDS and epilepsy. Theranostics approach significantly decreases the false positive rates and also eliminates the probability of prescribing ineffective drugs.
2. **Better safety of drugs on first time** as doctors, on analysis of the genetic profile of an individual, can prescribe best available therapy for a disease. Conversely, the conventional trial-and-



**Figure 3:** Drug discovery and development process for PMs.

- error method of prescribing drugs involves guesswork.
3. **Ease in drug approval process** as trials target a group of individuals possessing a specific genetic profile. This enhances the chances of success of the clinical trials, thereby speeding up the drug approval process.
  4. **Reduced timelines for DD&D process** due to targeted approach, presence of the 'knowledge management system', ease in drug approval process, elimination of unwanted molecules at preclinical stage, high throughput screening and so on. All these factors together contribute towards time reduced timelines in DD&D process. This benefits the pharmaceutical companies as well as the end-users.
  5. **Reduced adverse drug reactions (ADR)** due to reduction in use of chemotherapeutic agent, elimination of guesswork and molecular level knowledge of the specific drug targets. Example includes testing of HIV Type I patients before beginning therapy with abacavir. This is to rule out hypersensitivity reaction to the drug, since 48-61 % of patients with human leukocyte antigen-B5701 allele are reported to develop life threatening symptoms.
  6. **Identification of new drug targets** during the molecular level genomic studies, which can lead to discovery and development of novel therapeutic agents as well.
  7. **Product differentiation for pharmaceutical companies** in the marketplace. This can be a win-win situation for both the drug companies and the end-consumers. Further, this can incentivize pharmaceutical companies to develop new drug molecules.
  8. **Shift in drug therapy from reaction to prevention** as analyzing the genetic profile of an individual can help in the estimation of that individual's predisposition towards particular disease(s). Thereafter, a treatment plan can be set up for that individual to prevent the development of the disease.
  9. **Reduction in overall cost of healthcare** due to reduced timelines of clinical studies, reduced incidence of ADRs, expedition of drug approval processes, shifting of drug therapies from

reaction to prevention and, reduced timelines of drug therapy in patients. The net effect is decrease in healthcare cost. Jakka and Rossbach suggest P4 medical approach, i.e. *predictive, preventive, personalized and participatory* medicine to provide better treatment through sophisticated diagnostics and targeted medicine, thus, enhancing the quality of healthcare and reducing treatment costs.

## APPLICATIONS OF PERSONALIZED MEDICINES

Personalized medicines are the most pertinent to the field of medical oncology as the target somatic tissue is easier to access. The next-generation sequencing approach further bolsters the hope for a bright future. The technique allows the sequencing of the genome of an entire tumor which can be compared with an individual's normal germline DNA. The purpose is to locate amplifications or deletions, mutations or copy number variations. The approach is still in its initial stages but is expected to become cheaper with the passage of time. However, there are concerns with respect to the analytical accuracy of these assays. Also, all the genetic abnormalities disclosed by these methods may not be clinically relevant. Dr. Daniel F Hayes of University of Michigan Comprehensive Cancer Center opines that the reporting criteria for tumor biomarker tests should be standardized, in order to ensure the reproducibility of these procedures [31, 32].

Recent studies in the area of stroke genetics have revealed interesting facts regarding the genetic background of different types of strokes i.e. atherosclerotic stroke and those caused by cardioembolism. Genome Wide Association Studies (GWAS) have also divulged new pathways leading to stroke. The discovery of histone deacetylase 9 (HDAC 9) is being viewed as potentially significant for understanding the pathogenesis of atherosclerotic stroke. But the advancement in the sphere of stroke genetics is rather slow because the genes responsible for stroke risk contribute only feebly towards increased risk, unlike cancer, where a specific genetic mutation highly increases the probability of developing a particular type of cancer. From a futuristic standpoint, pharmacogenomic information can be utilized to tailor the treatment and predict overall stroke risk in an individual [31].

The outlook for the management of diabetes by way of personalized approach augurs many benefits. While

in the past, pharmacotherapy focused on the reduction of blood glucose levels to impair the progression of complications, today the disease is being tackled by a multipronged approach. The treatment plan takes into account other factors such as hypertension, hyperlipidemia and exercise. Therefore, a patient-tailored approach is being adopted. In this context, discernment of the underlying pathophysiology and genetics can be employed to direct the treatment. Such an approach would allow the physician to strategize the treatment differentially for patients with impaired insulin secretion and those with insulin insensitivity, or for that matter, someone with mutated potassium channels of the beta cells. Further, PMs would enable to devise different therapy for the young and the geriatric patients, owing to varying risk and complication profile in each case [31].

### CHALLENGES ON THE ROAD OF PERSONALIZED MEDICINES

As the field of genetic medicine is advancing, the experts are beginning to see other facets of individualizing patient therapy using PMs. Personalizing treatment plans calls for the elucidation of the individual's clinical and family history along with genetic make-up and environmental risk factors. The information so obtained helps to individualize disease prevention or treatment. This approach is highly likely to be adopted in near future because the cost of whole genome sequencing has dropped to \$1000 in 2014 as opposed to \$300 million in 2001 [33]. Such procedures are already being practiced for treating leukaemia patients and for selecting the right dose of warfarin. Nonetheless, there are certain psychological, religious and ethical factors that pose significant barriers to the implementation of PM. The challenges associated with the implementation of PM are enumerated below: [4, 10, 28, 33, 34, 35, 36]

1. **Difficulty in locating genetic variations which affect drug response.** This is so because Single Nucleotide Polymorphisms (SNP), which occur after every 100-300 gene bases along the 3-billion human genome base pairs, must be identified and analyzed to determine their involvement in the drug response. Furthermore, the present level of knowledge of diagnosis based on genetic factors is constrained and also hampers prediction of drug response.
2. **Blockbuster model and one-drug-fits-all approach of pharmaceutical companies'**

success deters them from developing personalized medicines, which cater to a small group of population. Additionally, healthcare insurers have little incentives to include genetic testing in their services, in view of very high membership turnover rate. These tests cannot ensure long-term benefits for the companies.

3. **Limited present array of PMs** as currently very few approved PMs are available, if any, for each disease. This limited array does not cover patients of all the genetic make-up.
4. **Educating healthcare providers** as physicians need to carry out extra diagnostic procedures to find out which drug best suits the patient. This necessitates teaching genetics to all the physicians practicing personalized medicines.
5. **DD&D costs** of PMs, currently, are relatively higher than conventional medicines because of factors like limited research, developing technologies, data management costs, etc.
6. **Ethical issues** arise with respect to confidentiality, risk-benefit analysis, DNA banking, financial considerations and formulation of insurance policies.
7. **Certain psychological factors** are also responsible for the non-acceptance of PM by sections of the population. Genetic testing is not universally welcomed on account of stress associated with prediction of future disease.
8. **Many religious beliefs** also oppose personalized medicine owing to varying perspective about cause and meaning of sickness. Therefore, individuals may not accept PM if they find it conflicting with their religious doctrine or divinity of human life.
9. **Legal issues** related to the development of the PMs come up with regard to the approval of clinical trials, human testing, DNA banking, and genomic research.
10. **Proper data management** is another haphazard in PMs because of the current disjointed situation of the healthcare informatics system, which prevents scientists and physicians from making the most out of the personalized genomics research data. According to Dr. Frank Cockerill, Director of Laboratory Medicine, Mayo

Clinic, gathering genetic data is not as difficult as is the task of utilizing it and making it affordable.

11. **There is a need to develop patient-centered,** longitudinal and cross-institutional digital health database consisting of genetic information and results of genomic tests, while maintaining patient privacy. Such information will facilitate subgrouping of diseases, in view of high complexity of an individual's phenotypic and genotypic make-up [30].
12. **Heterogeneity** in the pathogenesis of different diseases is well understood. According to Genome Atlas published for different types of cancer, there are over fifty mutations within the same cancer type. But only few of them can be referred to as 'driver mutations' [17]. For example, studies in molecular biology of breast cancer have disclosed certain dominant driver mutations and epigenetic alterations which lead to tumor formation. Eventually, these mutations and alterations are reflected in the clinical behavior of a particular type of breast cancer [37]. Identifying these driver mutations is a challenging task.

The aforementioned factors not only implicate modifications in medical curriculum but also point towards the need to educate patients, and third-party payers. Besides, in such a complex scenario, genetic counselling of the patients assumes great importance [10].

## **REGULATORY EVOLUTION IN THE GENERATION OF PERSONALIZED MEDICINES**

Personalized medicines, as the next generation medicines, entail remodelling of the regulatory framework and advancement in regulatory science to illuminate the pathway for PM product approval [38]. In case of diagnostics, the companies developing approved tests do not have adequate IP protection under the present regulatory model and CLIA governance [17].

The Genomics and Personalized Medicine Act of 2010 postulates the functions of the Office of Personalized Healthcare in HHS (Health and Human Services). The Office has been set up with the objective of coordinating the activities between government agencies, creating translational research plan, providing for reimbursement to check the cost effectiveness and clinical merit of the genomic

technologies, streamlining the regulation of PM products, adverse event reporting, investigation of DTC genomic industry, verifying the analytical and clinical validity of the product and establishing a nationalized biobank for use in PM research [38].

## **ROLE OF US FDA IN THE ERA OF PERSONALIZED MEDICINES [6, 26]**

The future of clinical medicine, as envisioned in the era of PMs, demands substantial regulatory support from the US FDA. In fact, US FDA and National Institutes of Health (NIH) have joined hands in their endeavour to protect patients and promote innovation. Their efforts include investment in advanced translational research and regulatory science, defining the regulatory pathways for synchronized approval of co-developed diagnostic and therapeutic medical product, formulating risk-based strategies to evaluate diagnostics with regard to their validity and clinical worth and, lastly, to make such information easily accessible.

The US FDA has three centers, namely- Center for Devices and Radiological Health (CDRH), Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research- together with the Office of Special Medical Programs (OSMP). These centers are designated to set up regulatory mechanisms and policies for counteracting the challenges discussed above.

In the past decade, the US FDA has issued several guidance documents to address regulatory requirements, coordinate premarketing reviews, outline the roles and responsibilities of various centers and to achieve consistency and timeliness in the review of PM products. The challenges facing US FDA are as follows:

1. **Ensuring the availability of safe and effective diagnostics:** The evaluation includes analytical validity as well as clinical validity and utility of the test.
2. **Evaluating product interdependency:** The challenge is to time and align the development strategies of the two companion products and, designing the trial of the products.
3. **Product labeling:** The labeling of the diagnostic and the therapeutic product must be consistent. Also, the labels are required to provide information regarding genomic biomarkers and



pharmacogenomic information related to therapeutic indications, warnings and precautions.

- 4. Post-marketing surveillance:** Due to very small pre-market exposure of PMs, post-marketing surveillance of these products is of paramount importance. One of the challenges in this context is to trace, investigate and understand the adverse events for both the diagnostic and the therapeutic product.

In the year 2010, US FDA announced its 'Regulatory Science Initiative' with the view to upgrade regulatory science within the agency and all over the country. The aim of the program was to modernize the review and approval process of medical products, including PMs. Following are the major parts of the Initiative:

#### **Developing Regulatory Standards, Research Techniques and Tools**

Examples of the established programs include Biomarker Qualification Program, Genomic Reference Library for Evaluating Whole Genome Sequencing, Development of Molecular Tools to Facilitate Blood Group Typing.

#### **Conducting and Collaborating in Research Activities**

Some of the research projects undertaken are: Biomarker Identification and Development, Pharmacogenetics and Immunogenicity of Protein Therapeutics, Identification of Genetic Risk Factors for Vaccine Reactions.

#### **CONCLUSION**

Personalized medicines have truly arrived as 'the next generation medicines'. The dream of genetic medicine is materializing and it has raised the hopes of the physicians and the patients a great deal. The challenge now lies in balancing personalized medicine and personalized care, to meet patients' expectations. The need of the hour is to lay down a roadmap for the researchers with respect to drug discovery and development process, leading to clinical utility.

While in certain areas of medicine, patient-specific risk prediction and treatment are already being routinely practiced, in other fields, there is still a long way to go before scientific breakthroughs can be

translated into personalized medicines. Advancements in the arena of mobile health and availability of health apps have set the stage for even greater transformation in the way health is managed.

To conclude, the journey on the road to personalizing medicine has only begun. While there are challenges to be met and threats to be overcome, the genomic revolution does strengthen the hope for consequential improvements in management of diseases. The definitive prospects of the field will come to light in the years to come.

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