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Review Article

Biomarkers: tracing their evolution, development, market trends, patentability, and current regulatory landscape

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ABSTRACT

Biomarkers are crucial tools in clinical research, precision medicine, and drug development. Throughout the drug development process, they play an important role in disease diagnosis, patient stratification, safety monitoring, therapeutic response assessment, and clinical decision-making. This review provides a comprehensive overview of biomarker definitions, classification, and development, with a major focus on biomarker validation and qualification. The article also examines current market trends, key industry developments, and patentable biomarker technologies used in the diagnosis and management of various diseases. In addition, the commercialization process of biomarker-based diagnostic technologies and the evolving regulatory frameworks governing biomarker qualification are discussed, with particular emphasis on the pathways established by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Furthermore, the review highlights the challenges, opportunities, and future prospects associated with biomarker development and implementation. This review provides valuable insights into the growing role of biomarkers in advancing medical research, drug development, and personalized healthcare.

Keywords:
Biomarkers
Biomarker development
Regulatory landscape
Patentability
Market trends

Introduction

Biomarkers are measurable characteristics that provide information about biological processes, pathological conditions, or responses to therapeutic interventions. In clinical practice, biomarkers serve as objective indicators of normal biological processes, disease states, and pharmacological responses to treatment [Atkinson et al., 2001; Aronson, 2005]. Over the past several decades, the concept and definition of biomarkers have evolved alongside advances in biomedical research and clinical medicine. Historical descriptions have included the terms "biochemical markers," "biological markers," and later "biomarkers," with the latter becoming the most widely accepted terminology in both research and clini-

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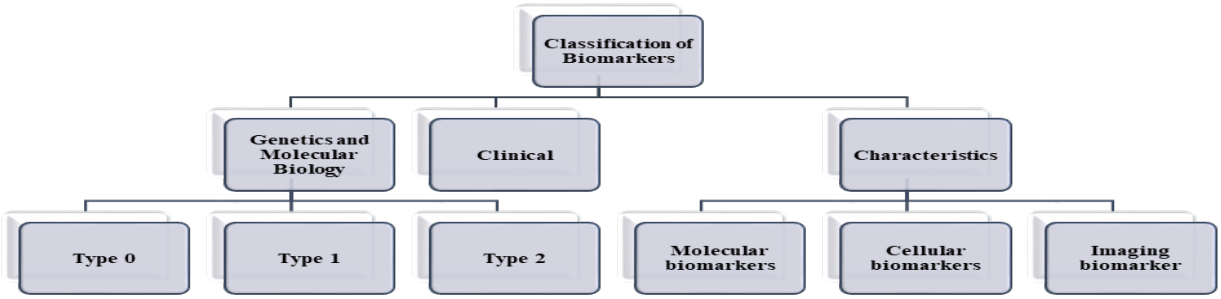

FIGURE 1. Classification of Biomarkers

cal practice [Mundkur, 1949; Porter, 1957; García-Gutiérrez et al., 2020].

The definition proposed by the National Institutes of Health Biomarkers Definitions Working Group in 2000 has been broadly adopted and describes biomarkers as characteristics that are objectively measured and evaluated as indicators of normal biological processes, pathogenic processes, or pharmacologic responses to therapeutic interventions [Atkinson et al., 2001]. Biomarkers that are strongly associated with clinical outcomes may also function as surrogate endpoints in clinical research and drug development [Aronson, 2005].

Recent technological advances have significantly accelerated biomarker discovery and validation. Next-generation sequencing (NGS) has facilitated the identification of disease-associated genetic variations and mutations, while liquid biopsy approaches based on circulating tumour DNA (ctDNA) have enabled non-invasive disease detection and monitoring [Weintraub et al., 2015]. Furthermore, biomarkers such as programmed death-ligand 1 (PD-L1) expression and microsatellite instability (MSI) have become important tools for predicting responses to immunotherapy. The COVID-19 pandemic further highlighted the importance of biomarkers in assessing disease severity, immune responses, and inflammatory processes. Future advances are expected through the integration of multi-omics technologies, including genomics, proteomics, and metabolomics, with modern bioinformatics approaches, thereby improving biomarker discovery, qualification, and clinical implementation [Ali et al., 2023; Macnamara et al., 2015; Gil, 2001; Califf, 2018].

Biomarker Categorization and Development

Biomarkers can be classified according to their biological characteristics, clinical applications, and molecular or genetic mechanisms [Wishart et al., 2021; Mondello et al., 2015; Pospelova et al., 2022; Eggener et al., 2020; Dhama et al., 2019; Aizpurua-Olaizola et al., 2018; Nadkarni et al., 2019; MacKay et al., 2019; Anderson et al., 2018; Verber et al., 2019]. Figures 1 and 2 summarize the classification and major clinical types of biomarkers.

Biomarker development is a multidisciplinary and iterative process that begins with the identification of candidate biomarkers in healthy and diseased populations. Advances in computational biology, analytical technologies, and measurement techniques have substantially accelerated biomarker discovery and evaluation. The development pathway generally includes biomarker discovery, analytical validation, clinical validation, regulatory qualification, and assessment of clinical utility. Figure 3 illustrates the overall biomarker development process from discovery to validation.

During the pre-analytical stage, factors such as sample collection, processing, handling, and storage are standardized to ensure data quality. Analytical validation evaluates assay performance, including reliability, reproducibility, sensitivity, and specificity. Clinical qualification establishes the relationship between a biomarker and relevant biological or clinical outcomes. Despite significant progress, biomarker development remains challenging because of difficulties in reproducing findings, risks of misinterpretation, lengthy validation requirements, and the substantial resources required for qualification and regulatory acceptance [Gupta, 2019].

Research Methodology

A literature search was conducted up to August 2023 using PubMed, Embase, Web of Science, Scopus, and the Cochrane Library. The search strategy included the

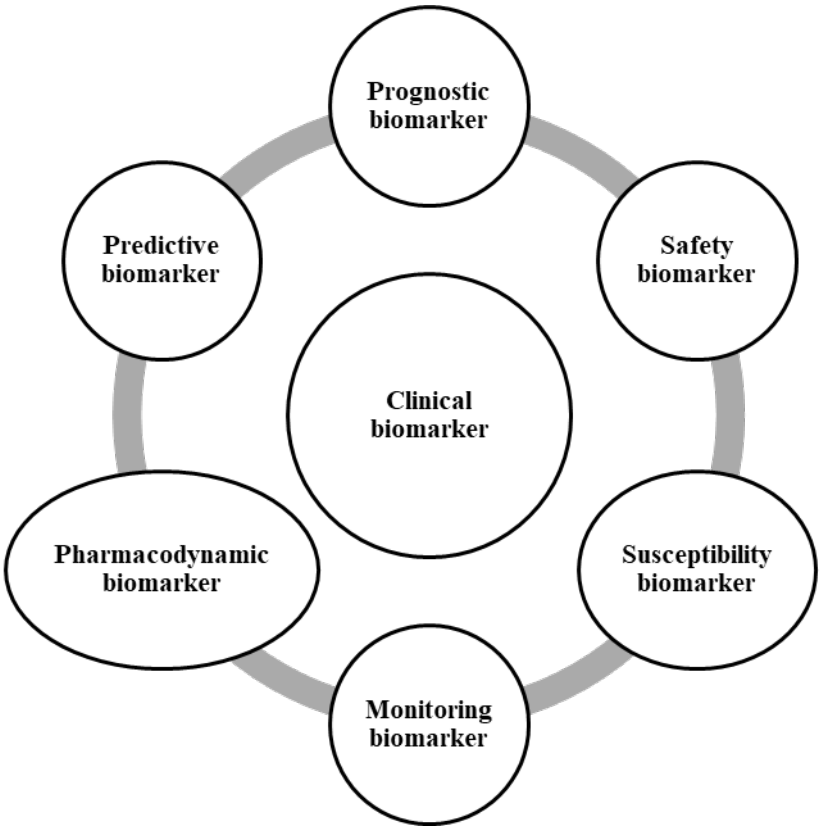

FIGURE 2. Classification of Clinical Biomarker

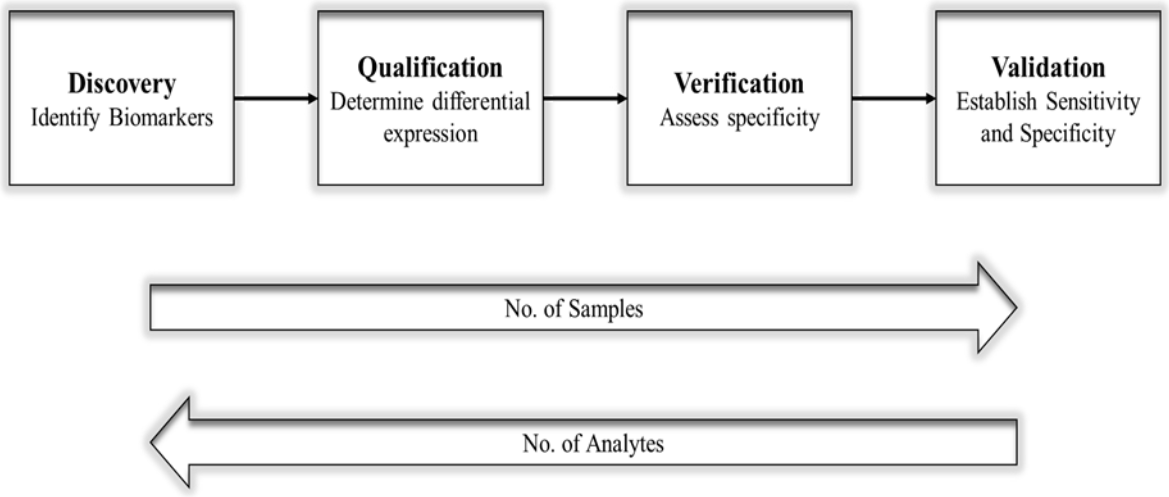

FIGURE 3. Development Process of Biomarkers

terms "biomarkers," "biomarker development," "regulatory aspects of biomarkers," and "biomarker patents." Retrieved records were screened after duplicate removal, and titles and abstracts were evaluated for relevance. A total of 91 publications were included in the review, comprising 25 articles from Scopus, 18 from Web of Science, 16 from the Open Biomarkers Journal, and 32 from Advances in Biomarker Science and Technology.

Market Trends of Biomarkers

According to market estimates, the global biomarkers

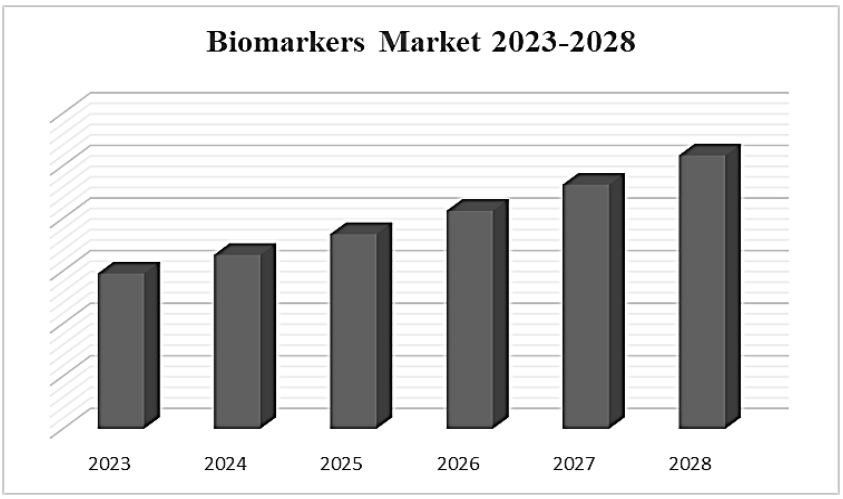

FIGURE 4. Biomarkers Market share from 2023 to 2028

TABLE 1: Report Metrics of Biomarkers

Metrics Report	Details
Revenue of the Market in 2023	Billion $59.1
Projected Revenue by 2028	Billion $104
Revenue Rate	Poised to grow at a CAGR of 12%
Market Driver	Increasing Prevalence of Cancer Worldwide
Market Opportunity	Emerging economies
CAGR: Compound Annual Growth Rate	

market generated approximately US$59.1 billion in revenue in 2023 and is projected to reach US$104.0 billion by 2028, growing at a compound annual growth rate (CAGR) of 12% during the forecast period (Figure 4). The complete market metrics are summarized in Table 1 [MarketsandMarkets, 2023]. Growth in the biomarkers market is driven by the increasing adoption of companion diagnostics, rising prevalence of cancer and cardiovascular diseases, growing investment in biomarker research, continuous product innovation, and expanding applications of biomarkers in disease diagnosis and drug development [By Application, 2023].

Dynamics of the Biomarkers Market

The major factors influencing the biomarkers market are summarized in Figure 5 [MarketsandMarkets, 2023].

Drivers

The increasing global burden of cancer is one of the major drivers of market growth. Cancer is a complex disease involving multiple molecular pathways, and the identification of novel biomarkers is essential for improving diagnosis, prognosis, treatment selection, and therapeutic monitoring. The growing prevalence of cancer is therefore expected to increase the demand for biomarker-based technologies and services.

Restraints

Biomarker discovery, development, validation, and regulatory approval require substantial financial investment and lengthy development timelines. The high costs associated with clinical trials, analytical validation, and regulatory requirements can limit innovation, particularly among small and emerging companies. In addition, the gap between biomarker discovery and successful clinical validation remains a significant challenge for the industry.

Opportunities

Emerging economies such as China and India repre-

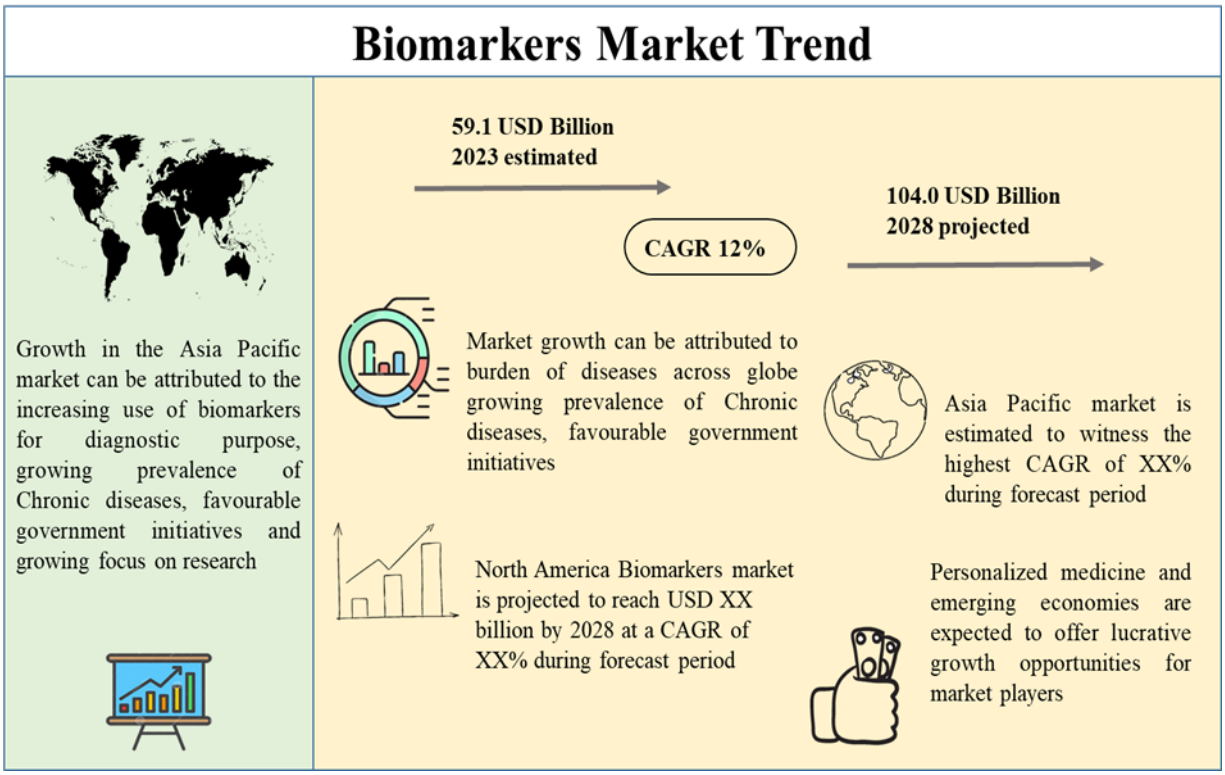

FIGURE 5. Market Trend of Biomarkers

sent important growth opportunities for the biomarkers market because of their large patient populations and increasing prevalence of chronic diseases, including cancer and cardiovascular disorders. Growing investments in research infrastructure, training programs, and collaborations between academic institutions and industry are expected to support biomarker research and development in these regions.

Challenges

Sample collection, processing, storage, and quality control remain critical technical challenges in biomarker research. The reliability of biomarker studies depends heavily on specimen integrity and standardized handling procedures. Appropriate biobanking practices, ethical considerations, patient privacy protection, informed consent, and efficient sample-tracking systems are essential for maintaining sample quality and ensuring reliable research outcomes.

Biomarkers Market Revenue and Trends

Recent market analyses indicate continued growth across multiple segments of the biomarkers industry [Precedence Research, 2023; Coherent Market Insights, 2023]. Consumables, including biomarker testing kits and related products, accounted for a significant share of the market owing to their essential role in biomarker testing workflows and the need for repeated use. Safety biomarkers continue to represent an important market segment because of their applications in drug development, clinical trials, precision medicine, and regulatory assessment.

Among disease areas, oncology remains the largest application segment because biomarkers play a critical role in cancer diagnosis, prognosis, treatment selection, and disease monitoring. Likewise, diagnostic applications account for a substantial share of the global biomarkers market owing to their importance in early disease detection, companion diagnostics, precision medicine, clinical laboratory testing, and point-of-care testing.

The growing demand for personalized medicine, increasing prevalence of chronic diseases, and expanding use of biomarker-based diagnostics are expected to continue driving market growth. The global biomarker technologies market is segmented by product, technology, indication, and geography, as illustrated in Figure 6.

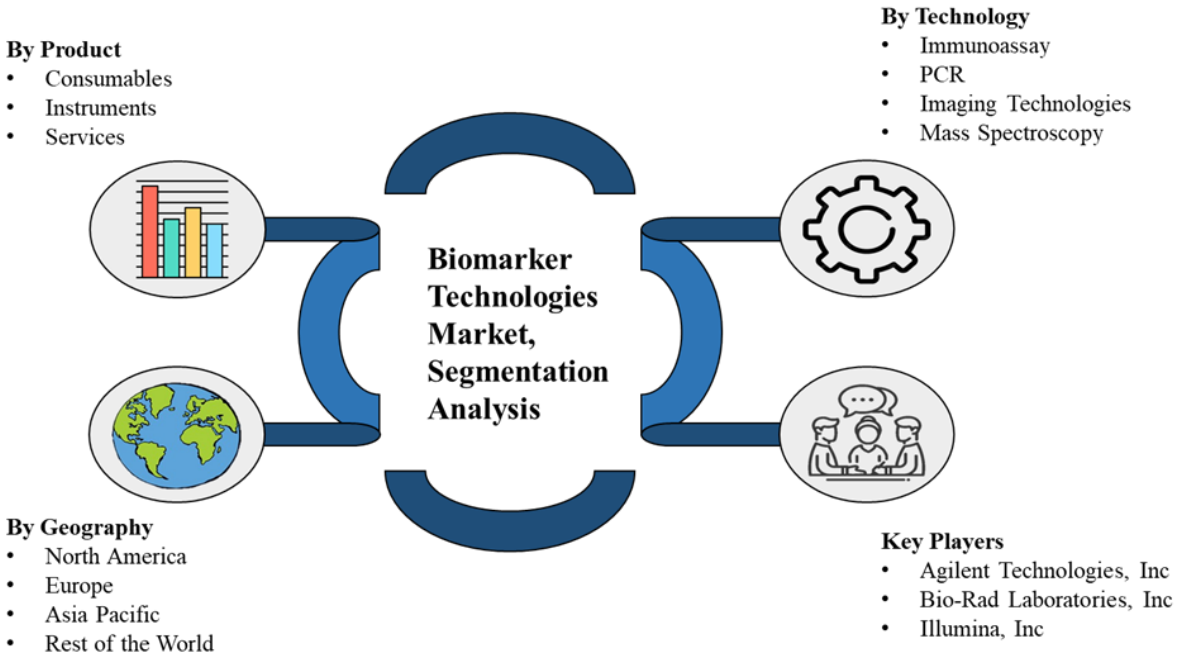

FIGURE 6. Segmentation and Analysis of Biomarkers Market

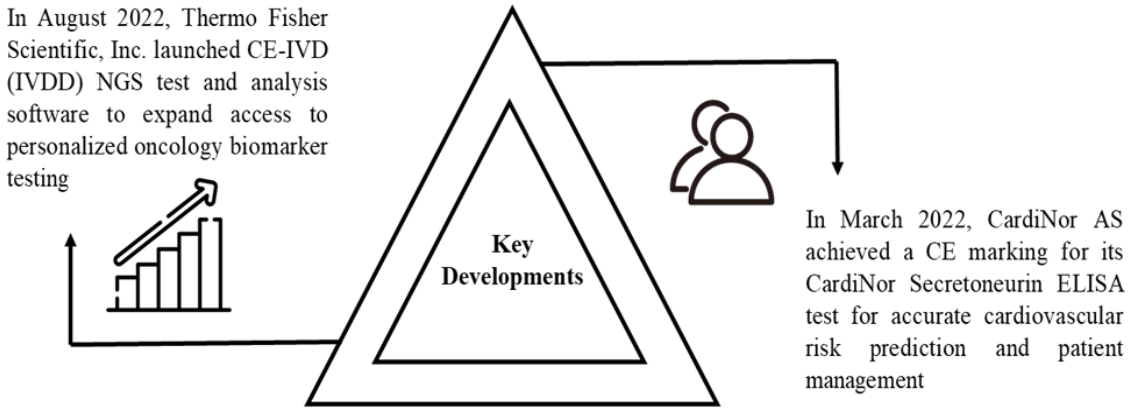

FIGURE 7. Biomarkers Key Developments

Regional Outlook and Key Players Competing in the Market

Regions with strong research and development infrastructures continue to lead biomarker discovery and application. Significant investments in biomarker research have been made in the United States, Europe (particularly Germany, the United Kingdom, Italy, Spain, Denmark, Sweden, Norway, and France), and Japan [Grand View Research, 2023]. In addition, countries in the Asia-Pacific region (China, India, South Korea, Australia, Thailand, and Japan), the Middle East and Africa (South Africa, Saudi Arabia, UAE, and Kuwait), Latin America (Brazil, Mexico, and Argentina), and Canada are emerging as important contributors to biomarker research and development.

The global biomarkers market is characterized by the presence of several companies with strong research and development capabilities. Major market participants include Bio-Rad Laboratories, Qiagen, Epigenomics AG, Abbott, Hoffmann-La Roche Ltd., Agilent Technologies, Johnson & Johnson Services, Siemens, and Thermo Fisher Scientific. Recent developments in the biomarkers market are summarized in Figure 7 [Verified Market Research, 2023].

TABLE 2: Patents granted for biomarkers used in cardiac diseases

Application/ Publication number	Title	Publication date	Country
20230128775	"Biomarker Identification for Imminent and/or Impending Heart Failure"	27.04.2023	US
4162278	"Biomarker Identification for Imminent and/or Impending Heart Failure"	12.04.2023	Europe
202347017677	"Device and Method for Measuring the Level of Biomarkers and Pathogens in Substances"	31.03.2023	India
202111043591	"DNA Aptamers"	31.03.2023	India
2022126690	"Development and Parameter Assessment for Vertically Aligned Platinum Wire Aptasensor Arrays for Impedimetric Detection of Cardiac Biomarkers"	30.08.2022	Japan
20220243249	"Antagonists of Camkii-delta 9 and uses thereof"	04.08.2022	US
2020482731	"Method and Apparatus for Determining Biomarkers of Vascular Function Utilizing Bold cmr images"	30.06.2022	Australia
3986436	"Antagonists of Camkii-delta 9 and uses thereof"	27.04.2022	EU
20220032074	"Spreading Depolarization and Repolarization as Biomarkers of Neurological Recovery after Cardiac Arrest"	03.02.2022	US
3189613	"Device and Method for Measuring the Level of Biomarkers and Pathogens in Substances"	24.02.2022	Canada
20210401356	"Biological Marker and Methods"	30.12.2021	US
2021283390	"Biomarker Identification for Imminent and/or Impending Heart Failure"	09.12.2021	Australia
3164482	"Non-invasive Diagnostics of Proximal Heart Health Biomarkers"	22.07.2021	Canada
2021207530	"Non-invasive Diagnostics of Proximal Heart Health Biomarkers"	22.07.2021	Australia
20200118679	"Transdermal Optical Detection of Cardiac Biomarkers"	16.04.2020	US
20190093169	"Biomarkers and Treatments for Heart Failure"	28.03.2019	US
20190383809	Autophagy-related Nourin gene-based RNA Network as Early Biomarkers for" "Cardiac Patients	19.12.2019	US
108458999	"Method and Kit for Jointly Detecting Various Cardiac Biomarkers"	28.08.2018	China
20180172703	"Future Cardiac Event Biomarkers ccl3, ccl5, and ccl18"	21.06.2018	US
20170121772	"Biomarkers and Treatments for Heart Failure"	04.05.2017	US
201741004864	A Novel Method for Identification of Biomarkers for Genetic Diagnosis of Car-" "diovascular Diseases	24.02.2017	India
3105350	Transcriptomic Biomarkers, Method for Determination thereof and Use of Tran-" scriptomic Biomarkers for Individual Risk Assessment of Developing Post-infarc-" "tion Heart Failure	21.12.2016	Europe
20150329907	"Biomarkers and Treatments for Heart Failure"	15.11.2016	US
720185	"Biomarker for Cardiac Disorders"	30.05.2016	New Zealand
2995957	"Future Cardiac Event Biomarkers"	16.03.2016	EU
20160054334	"Future Cardiac Event Biomarkers"	25.02.2016	US
2983581	System and Method for Imaging Biomarkers Indicative of Cardiac Thermal Ab-" "lation Lesions	17.02.2016	Europe

Patentability of Biomarker Technologies

The patentability of biomarker technologies varies among jurisdictions. Although many biomarker-related inventions are eligible for patent protection, the patentability of inventions based solely on biological correlations remains challenging in some regions, particularly in the United States. In contrast, practical applications of biomarkers, such as their use in disease diagnosis, prognosis, or treatment selection, may be patentable in several jurisdictions, including Europe [Appleton et al., 2022].

Diagnostic method claims are generally subject to specific legal requirements and may be excluded from patentability if they consist solely of clinical diagnostic steps. Therefore, patent eligibility often depends on the practical application and implementation of the biomarker technology. Patents granted for various biomarkers and disease conditions in different countries are

TABLE 3: Patents granted for biomarkers used in kidney diseases

Application/Publication number	Title	Publication date	Country
Wo/2023/096326	"Composition Comprising LGK974 for Preventing or Treating Inflammatory Renal Disease"	01.06.2023	International Application
202217020042	"Non-invasive Method to Quantify Kidney Function and Functional Decline"	02.09.2022	India
20220252617	"Biomarkers of Fast Progression of Chronic Kidney Disease"	11.08.2022	US
114509573	"Diabetes Kidney Disease Early Warning Model Established based on Synchronous Detection of Urine Markers"	17.05.2022	China
114200141	"Application of Gdf15, Upar and il1rl1 in Preparation of Auxiliary Diagnosis Reagent or Kit for Acute Kidney Injury"	18.03.2022	China
113943802	"Application of golt1b in Prognosis of Kidney Cancer"	18.01.2022	China
3929308	"Diagnostic Methods on Renal Recovery in Individuals Suffering from Acute Kidney Injury and Suitable Biomarkers Therefor"	29.12.2021	Europe
3904883	"Biomarkers of Polycystic Kidney Disease and uses thereof"	03.11.2021	Europe
Wo/2021/138611	"Reliable Metabolite Biomarkers for Multiple Urological Cancers"	08.07.2021	
3165653	"New Protein Markers of Renal Damage"	01.07.2021	Canada
112714871	"Biomarkers and Test Models for Chronic Kidney Disease"	27.04.2021	China
2020343654	"Non-invasive Method to Quantify Kidney Function and Functional Decline"	11.03.2021	Australia
112226500	"Application of Long-chain Non-Coding RNA as Biomarker to Diagnosis of Contrast-Induced Acute Kidney Injury (ci-aki)"	15.01.2021	China
3761034	"Urine Biomarkers for Prediction of Recovery after Acute Kidney Injury: Proteomics"	06.01.2021	Europe
20200292558	"Prognosis and Progression Biomarkers for Chronic Kidney Disease"	17.09.2020	US
20200150132	"Biomarkers of Renal Injury"	14.05.2020	US
3635139	"Micro vesicle Nucleic Acids and/or Proteins and uses Thereof as Markers of Renal Transplant Rejection"	15.04.2020	Europe
3554357	"Sweat Sensing Device Kidney Biomarker Measurement"	23.10.2019	Europe
268477	"Use of Serum 2-cysteine Peroxiredoxins (2-cys-prdx) as Biomarkers of Chronic Kidney Diseases"	26.09.2019	Israel
1020190094966	"Biomarkers for Diagnosing or Predicting Inflammation after Kidney Transplantation"	14.08.2019	Republic of Korea
20190085397	"Urine Biomarkers for Detecting Graft Rejection"	21.03.2019	US
3444363	"Biomarkers for Predicting and Assessing the Responsiveness of Thyroid and Kidney Cancer Subjects to Lenvatinib Compounds"	20.02.2019	Europe
3410115	"Tryptophan as a Biomarker for Kidney Function and Methods using the same"	05.12.2018	Europe
20180289306	"Method for the Early Detection of Acute Kidney Injury in Critical Patients, using Fibroblast Growth Factor 23, Klotho and Erythropoietin as Biomarkers"	11.10.2018	US
2018066733	"Markers for Renal Disease"	26.04.2018	Japan
733717	"Biomarkers Related to Kidney Function and Methods Involving Their Use"	28.07.2017	New Zealand
106526156	"Method for Detecting, Screening and Identifying Kidney-yang Deficiency Metabolism Biomarkers"	22.03.2017	China
3135774	"Complex Sets of miRNAs as Non-invasive Biomarkers for Kidney Cancer"	01.03.2017	Europe
2015301278	"Biomarkers of Polycystic Kidney Disease and uses thereof"	09.02.2017	Australia
2017003589	"Pathological Biomarkers for Kidney Diseases"	05.01.2017	Japan
201628022597	"Prognostic Biomarkers for the Progression of Primary Chronic Kidney Disease"	31.08.2016	India
2016205886	"Biomarkers Related to Kidney Function and Methods Involving Their Use"	14.07.2016	Australia
20150330975	"Urinary Biomarkers for Predicting Long-term Dialysis"	12.07.2016	US
20160116486	"Biomarkers related to Kidney Function and Methods using the same"	28.04.2016	US

TABLE 4: Patents granted for biomarkers used in Diabetes

Application/ Publication Number	Title	Publication Date	Country
Wo/2023/104788	"Reactive Aldehyde Biomarkers of Type 2 Diabetes and Diabetic Nephropathy"	15.06.2023	International Application
Wo/2023/072261	"Serum Lipid Marker Related to Fundus Hard Exudates in Diabetic Retinopathy, and Application Thereof"	04.05.2023	International Application
115598264	"Glucometabonomics Related Biomarker for Early Diagnosis and Prediction of Diabetic Retinopathy Progress and Application of Glycometabonomics Related Biomarker"	13.01.2023	China
115575534	"Application of Isovaleric Acid as Marker in Preparation of Kit for Detecting Diabetic Nephropathy and Kit for Detecting Diabetic Nephropathy"	06.01.2023	China
Wo/2022/186592	"Biomarker for Diagnosing Pre-Diabetes or Predicting Onset of Diabetic Complications and Use Thereof"	09.09.2022	International Application
114959017	"Application of Reg1a Gene and Runx3 Gene as Diabetic Nephropathy Biomarkers"	30.08.2022	China
202241020204	"New Approach on Platelet Count Indices as Predictive Biomarkers to Detect the Vascular Complications in Type 2 Diabetes Mellitus"	22.04.2022	India
114167066	"Application of Biomarker in Preparation of Gestational Diabetes Diagnostic Reagent"	11.03.2022	China
11202200045w	"Combination of Biomarkers for Diagnosing Diabetic Retinopathy and Use Thereof"	25.02.2022	Singapore
102357260	"Method for Predicting and Diagnosing Diabetic Neuropathy Using MicroRNA and Kit for the Same"	08.02.2022	Republic Of Korea
202018042051	"Biomarkers Associated with Pre-Diabetes, Diabetes and Diabetes Related Conditions"	24.09.2021	India
20210208165	"Protein Biomarkers for Nephropathy and Applications Thereof"	08.07.2021	US
20210116467	"Diabetes-Related Biomarkers and Treatment of Diabetes-Related Conditions"	22.04.2021	US
3775282	"Biomarkers For Diabetes Therapy"	17.02.2021	EU
Pi 2021007622	"Combination of Biomarkers for Diagnosing Diabetic Retinopathy and Use Thereof"	07.09.2020	Malaysia
110441366	"Biosensor and Method for Detecting Glucose Concentration in Diabetes Biomarkers"	12.11.2019	China
3343226	"Biomarkers Associated with Pre-Diabetes, Diabetes and Diabetes Related Conditions"	04.07.2018	EU
2017223682	"Biomarkers Associated with Pre-Diabetes, Diabetes, and Diabetes Related Symptoms"	21.12.2017	Japan
2251/Che/2015	"Set of Biomarkers to Identify Early Diabetic Retinopathy, Retinal Angiogenic Diseases and Resistance to Ocular Anti-Vegf Therapy"	01.12.2017	India
107133470	"Method for Forecasting Diabetic Retinopathy by using Lipid Biomarkers"	05.09.2017	China
2016151442	"Biomarker for Slow Progress Type 1 Diabetes, and its Utilization"	22.08.2016	Japan
2391654	"Urine and Serum Biomarkers Associated with Diabetic Nephropathy"	29.04.2016	Poland

summarized in Tables 2–6 [WIPO, 2023].

Selected Examples of Biomarker Patents

Proteomics International Laboratories Ltd. received an Indian patent (No. 390245) for PromarkerD, a predictive diagnostic test for diabetic kidney disease. The patent, entitled *"Biomarkers Associated with Pre-diabetes, Diabetes, and Diabetes-related Diseases,"* extends until September 2031 and forms part of the company's international intellectual property portfolio [Proteomics International, 2022].

In the United States, researchers from the Texas Tech University Health Sciences Center were granted a patent for *"MicroRNA-455-3p as a Peripheral Biomarker for*

TABLE 5: Patents granted for biomarkers used in Cancer

Application/ Publication Number	Title	Publication Date	Country
20230227914	"Biomarkers of Oral, Pharyngeal and Laryngeal Cancers"	20.07.2023	US
20230194554	"Use of Biomarker in Preparation of Lung Cancer Detection Reagent And Related Method"	22.06.2023	US
4197431	"Skin Cancer Biomarker Detection by Infrared Spectroscopy"	21.06.2023	Europe
4196771	"A Sers-Nanotag and A Diagnostic Kit for Detecting Breast Cancer Biomarkers"	21.06.2023	EU
202217038847	"Use of Biomarkers to Evaluate The Efficacy of a Composition In Reducing The Effects of Cancer Therapeutics on Skin"	18.11.2022	India
114959021	"Cervical Cancer Biomarker and Application Thereof"	30.08.2022	China
114945662	"Use of Biomarkers to Evaluate The Efficacy of a Composition In Reducing The Effects of Cancer Therapeutics on Skin"	26.08.2022	China
202041055348	"A Non-invasive Diagnostic and Prognostic Biomarkers for Breast Cancer and Method of Detection Thereof"	24.06.2022	India
202217001765	"Tumour Infiltrating Lymphocyte Therapy and Uses Thereof"	18.03.2022	India
20220057403	"Modulating Biomarkers Such as Spp to Increase Tumor Immunity and Improve the Efficacy of Cancer Immunotherapy"	24.02.2022	US
202041030017	"Blood-Based Biomarkers for Early Diagnosis and Follow-Up of Breast Cancer"	21.01.2022	India
Wo/2022/013880	"Blood-Based Biomarkers for Early Diagnosis and Follow-Up of Breast Cancer"	20.01.2022	International Application
3181609	"Biomarkers for Detection of Lung Cancer"	04.11.2021	Canada
2020405513	"Use of Biomarkers to Evaluate The Efficacy of a Composition In Reducing The Effects of Cancer Therapeutics on Skin"	24.06.2021	Australia
3825693	"Methods of Identification and Diagnosis of Lung Diseases Using Classification Systems and Kits Thereof"	26.05.2021	EU
102222002	"Stomach Cancer Biomarkers Derived from Target Glycoprotein Detected by Middle-Up-Down Analysis"	02.03.2021	Republic of Korea
20210054462	"Next-Generation Biomarkers to Detect Sun Damage and Predict Skin Cancer Risk"	25.02.2021	US
112359118	"The Invention also Discloses Application of Long-Chain Non-Coding RNA Ac073352.1 as Breast Cancer Diagnosis Marker and Treatment Target"	12.02.2021	China
20210018506	"Autoantibodies and Autoantibody-Autoantigen Complexes as Biomarkers of Small Cell Lung Cancer"	21.01.2021	US
201921028045	"Biomarker Panel for the Detection of Prostate Cancer"	15.01.2021	India
201937044042	"Plasma-Based Protein Profiling for Early Stage Lung Cancer Prognosis"	02.10.2020	India
20200300857	"Modulating Biomarker to Increase Tumor Immunity and Improve the Efficacy of Cancer Immunotherapy"	24.09.2020	US
111518914	"Mirna Marker Combination, Kit and Method for Detecting Breast Cancer"	11.08.2020	China
3654036	"Stomach Cancer Biomarker and Detection Method"	20.05.2020	Europe
Wo/2019/171110	"Salivary Protein Biomarkers for the Diagnosis and Prognosis of Head and Neck Cancer, and Precancers"	12.09.2019	International Application
109470787	"Method for Identifying Breast Cancer Biomarkers and Detection Kit for Breast Cancer"	15.03.2019	China
3058481	"Plasma-Based Protein Profiling for Early Stage Lung Cancer Prognosis"	11.10.2018	Canada
2018248293	"Plasma-Based Protein Profiling for Early Stage Lung Cancer Prognosis"	11.10.2018	Australia
20180180618	"Method of Detecting Lung Cancer"	28.06.2018	US
2018202963	"Biomarkers Useful for Detection of Types, Grades and Stages of Human Breast Cancer"	10.05.2018	Australia
20160245817	"Mucin 5b as a Pancreatic Cyst Fluid Specific Biomarker for Accurate Diagnosis of Mucinous Cysts and Other Markers Useful for Detection of Pancreatic Malignancy"	25.08.2016	US

Table 5 to be continued

Application/ Publication Number	Title	Publication Date	Country
20160208334	"Biomarkers for Detection of Colorectal Cancer"	21.07.2016	US
2015360694	Use of Markers Including Filamin A in the Diagnosis and Treatment Of" "Prostate Cancer	16.06.2016	Australia
20160067229	"Biomarker for Response to Rapamycin Analogs"	10.03.2016	US

Alzheimer's Disease." The patented technology is based on elevated levels of microRNA-455-3p in plasma or serum and may facilitate the early diagnosis of Alzheimer's disease. MicroRNA-455-3p has also been associated with several physiological processes and disease conditions, including cancer and neurodegenerative disorders [Lundin, 2023].

Commercialization Process of an In Vitro Diagnostic (IVD) Biomarker

According to the BIC consortium model, commercialization of an IVD biomarker involves a series of sequential stages, including biomarker discovery, verification and early validation, prototype assay development, laboratory performance evaluation, pre-industrial maturation, industrial assay development, and finally clinical implementation and commercial launch. Different stakeholders, including researchers, technology transfer offices (TTOs), industry partners, and commercial enterprises, contribute at various stages of the process. Figure 8 provides an overview of the phases involved in the commercialization of an IVD biomarker [Myszczyński et al., 2021]. Tables 7–9 summarize diagnostic biomarkers approved during 2021–2023 [FDA, 2023].

Biomarker Regulatory Aspects

Biomarkers are typically researched and evaluated within the context of a specific drug-development program. The simultaneous development of drugs and biomarkers can be challenging because both require substantial financial investment and resources [Sinha et al., 2018]. The regulatory landscape for biomarkers continues to evolve, encompassing both publicly available biomarkers and those developed for specific research programs. Increased accessibility to biomarker information may help drug developers and regulatory authorities reduce costs and optimize resources.

Since the early 2000s, biomarker regulations have developed rapidly, largely in parallel with the emergence of personalized medicine, which aims to tailor treatment strategies according to an individual's genetic and epigenetic characteristics. The concepts of pharmacogenomics (PGx) and pharmacogenetics (PGt) were defined in the ICH E15 Guideline and have become important components of biomarker-based drug development [ICH, 2007]. Genomic biomarkers, including RNA- and DNA-based characteristics, play a significant role in therapeutic development and regulatory decision-making [Phillips et al., 2005].

Genetic biomarkers are increasingly used in drug development to explain variability in treatment response, pharmacokinetic (PK) and pharmacodynamic (PD) parameters, patient stratification, and clinical trial enrichment. They also contribute to understanding treatment failure, adverse effects, and drug–drug interactions [Maliepaard et al., 2013]. Both the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have published extensive guidance on the use of pharmacogenomics and pharmacogenetics in drug development [CHMP/EMA, 2011; FDA, 2007; FDA, 2007; FDA, 2013; FDA, 2018].

Although biomarkers are increasingly used to support regulatory decision-making during pharmaceutical development, particularly in clinical trials, their application remains subject to ongoing scientific and regulatory debate. One important objective is to demonstrate that biomarkers can improve the efficiency of clinical trials and potentially increase their success rates, thereby reducing the costs associated with drug development [Kaitin, 2010]. The use of biomarkers as surrogate endpoints is particularly important because they may accelerate clinical development; however, their use requires careful evaluation and validation [FDA-NIH Biomarker Working Group, 2016].

Recognizing the importance of biomarkers, the FDA identified the development of biomarker validation and

TABLE 6: Patents granted for biomarkers used in various other diseases

Application/Publication Number	Title	Publication Date	Country
Wo/2023/147669	"Blood Biomarkers in Long-COVID-19"	10.08.2023	International Application
Wo/2023/052742	"Skin Biomarker"	06.04.2023	International Application
20230084402	"Biomarkers for Risk Prediction of Parkinson's Disease"	16.03.2023	US
4125999	"Therapeutic Agents, Pharmaceutical Compositions, and Associated Biomarkers based on Trk-B"	08.02.2023	EU
115641912	"Biomarker for Treating and Diagnosing Gastric Cancer Metastasis and Identification Method Thereof"	24.01.2023	China
4114950	"Genetic Biomarkers for Use in the Diagnosis and Follow-Up of Chronic Venous Insufficiency"	11.01.2023	EU
Wo/2022/269116	"Sensor Devices, Electrical Connection Systems and Methods for Detecting Genetic or Biochemical Material as Disease Biomarkers"	29.12.2022	International Application
4100548	"Biomarkers for Risk Prediction of Parkinson's Disease"	14.12.2022	EU
115029430	"Biomarkers for Evaluating Risk of Aortic Dissection and Application of Biomarkers"	09.09.2022	China
Wo/2022/129029	"Use of Alarmins as Biomarkers For Assessing Ischemia-Reperfusion Injury Severity After Solid Organ Transplantation"	23.06.2022	International Application
114176586	"Method and Device for Detecting and Acquiring Biomarkers"	15.03.2022	China
11257594	"System and Method for Biomarker-Outcome Prediction and Medical Literature Exploration"	22.02.2022	US
113936796	"Biomarker-Based Bleeding Event Risk Assessment System"	14.01.2022	China
102331854	"Novel Biomarkers for Skin Aging Diagnosis"	01.12.2021	Republic Of Korea
Wo/2021/231504	"Systems and Methods for Isolating and Testing Blood for Biomarkers and Genetic Material"	18.11.2021	International Application
2021248268	"Therapeutic Agents, Pharmaceutical Compositions, and Associated Biomarkers based on Trk-B"	07.10.2021	Australia
1/2020/050032	"Rs3883013 and Rs12734338 as Genetic Biomarkers for Systemic Lupus Erythematosus"	20.09.2021	Philippines
113130004	"Correlation Analysis Method for Identifying Alzheimer's Disease Related Biomarkers"	16.07.2021	China
20210109111	"New Biomarkers of Human Skin Aging"	15.04.2021	US
2020343336	"Systems, Methods, and Compositions for the Rapid Early-Detection of Host Rna Biomarkers of Infection and Early Identification of Covid-19 Coronavirus Infection in Humans"	11.03.2021	Australia
3784802	"Tumor Functional Mutation and Epitope Loads as Improved Predictive Biomarkers for Immunotherapy Response"	03.03.2021	EU
3775284	"Biomarkers for Inflammatory Skin Disease"	17.02.2021	EU
Wo/2021/007651	"System and Method for Camera-Based Quantification of Blood Biomarkers"	21.01.2021	International Application
Wo/2020/242976	"Methods for Diagnosis of Polygenic Diseases and Phenotypes from Genetic Variation"	03.12.2020	International Application
Wo/2019/173703	"Genetic Marker and/or Biomarkers for Traumatic Brain Injury, and Ultrasensitive Assays for Biomarkers of Traumatic Brain Injury"	12.09.2019	International Application
108660206	"Genetic Biomarkers for Predicting or Assisting in Predicting Risk of Radiation Pneumonitis After Pulmonary Radiation and Application of Genetic Biomarkers"	16.10.2018	China

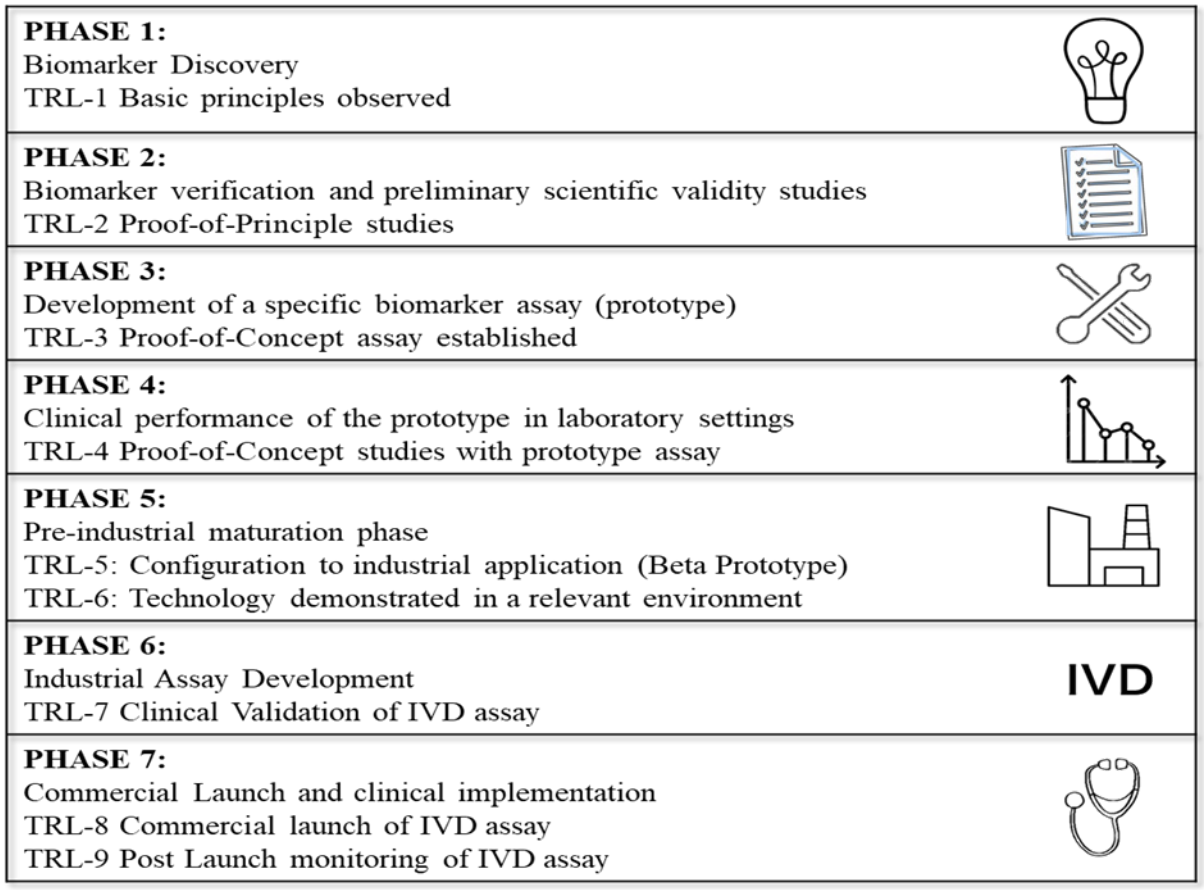

FIGURE 8. Different phases for the commercialisation process of IVD Biomarker

qualification pathways as a key opportunity in its Critical Path Opportunities List in 2006 [Weintraub et al., 2015; Fleming et al., 2012; Alonso et al., 2008; Baker et al., 2003; Psaty et al., 2008]. Subsequently, collaborative efforts involving the FDA, EMA, the Critical Path Institute, industry, and academic experts led to the development of biomarker qualification procedures. One notable example was the Predictive Safety Testing Consortium (PSTC), which assembled extensive data on seven novel kidney injury biomarkers and established a model submission and review process in consultation with the FDA and EMA [Goodsaid et al., 2006]. Based on these efforts, the FDA and EMA qualified several kidney safety biomarkers for regulatory use and established additional criteria for biomarker qualification [Sistare et al., 2010; Dieterle et al., 2010; Mattes et al., 2010; Harpur et al., 2011; Engle et al., 2009].

Biomarker Validation and Qualification

Biomarker validation and qualification are essential processes that ensure the reliability and regulatory acceptance of biomarkers. However, establishing a scientifically robust and clinically meaningful biomarker remains one of the major challenges in the field [Mattes et al., 2018].

Biomarker validation refers to the analytical assessment of performance characteristics such as accuracy, precision, robustness, sensitivity, and detection limits. In contrast, biomarker qualification involves demonstrating the relationship between a biomarker and a specific biological process, clinical endpoint, or therapeutic outcome [Hunter et al., 2010; Lee et al., 2006].

The importance of biomarker validation and qualification was highlighted in the FDA Critical Path Opportunities Report published in 2006 [FDA, 2006]. In collaboration with the EMA and the PSTC Nephrotoxicity Working Group, the FDA developed a pilot qualification program for biomarkers. As a result, seven kidney safety biomarkers were qualified for limited use in non-clinical and clinical studies in 2010. This milestone

TABLE 7: List of cleared diagnostic biomarkers in the year 2023

Manufacturer	Biomarkers	Biomarker detail	Grant date
Invivoscribe Technologies, Inc.	FLT3 (ITD/TDK)	IDT mutations and TKD mutations D835 and I836	07/20/2023
ARUP Laboratories	Anti-AAV5 Antibodies	Antibodies to the adeno-associated virus serotype 5 (AAVS) viral vector	06/29/2023
Foundation Medicine, Inc.	BRAF	BRAF V6O00E alteration	06/08/2023
Foundation Medicine, Inc.	EGFR (HER1)	Exon 20 insertion mutations	05/03/2023
Tempus Labs, Inc.	KRAS	KRAS wild-type (absence of mutations in codons 12 or 13)	04/28/2023
Tempus Labs, Inc.	KRAS and NRAS	KRAS wild-type (absence of mutations in exons 2, 3, or 4) and NRAS wild-type (absence of mutations in exons 2, 3, or 4)	04/28/2023
Guardant Health, Inc.	ESR1	ESRI missense mutations between codons 310 and 547	01/27/2023

TABLE 8: List of cleared diagnostic biomarkers in the year 2022

Manufacturer	Biomarkers	Biomarker detail	Grant date
Resolution Bioscience, Inc.	KRAS	KRAS G12C	12/12/2022
Qiagen Manchester, Ltd.	KRAS	KRAS wild-type (absence of mutations in codons 12 and 13)	12/02/2022
Abbott Molecular, Inc.	IDH1	R132 mutations (R132C, R132H, R132G, R132S, and R132L)	12/01/2022
One Lambda Inc	HLA	HLA-A*02:01	11/28/2022
Ventana Medical Systems, Inc.	FOLRI	FOLRI protein expression	11/14/2022
Ventana Medical Systems, Inc.	ERBB2 (HER2)	HER-2 protein overexpression	09/30/2022
LifeTechnologies Corporation	RET	RET mutations (SNVs, MNVs, and deletions)	09/21/2022
Guardant Health, Inc.	ERBB2	ERBB2 Activating Mutations (SNVs And Exon 20 Insertions)	08/11/2022
Ventana Medical Systems, Inc.	Proficient mismatch repair (pMMR) proteins	MLH1, PMS2, MSH2 and MSH6	06/16/2022
Foundation Medicine, Inc.	NTRKI1, NTRK2 & NTRK3	NTRK1, NTRK2 and NTRK3 fusions	06/07/2022
Ventana Medical Systems, Inc.	Deficient mismatch repair (dMMR) proteins	MLH1, PMS2, MSH2 and MSH6	03/21/2022
Foundation Medicine, Inc.	MSI-High	Microsatellite instability-High (MSI-H)	02/18/2022
Prevention Genetics, LLC	POMC, PCSK1 and LEPR	Variants (Pathogenic/Likely Pathogenic)	01/21/2022

demonstrated the commitment of regulatory agencies to collaborative biomarker development and provided the foundation for the biomarker qualification framework that continues to evolve today.

Biomarker Qualification in the EU

Supporting advances in precision medicine, biomarkers, and omics technologies are among the key priorities of the EMA Regulatory Science Strategy to 2025. Proposed actions include enhancing early engagement with biomarker developers to facilitate regulatory qualification and reviewing the EMA biomarker qualification process, including timelines and opportunities for early discussion of validation strategies, to encourage broad-

TABLE 9: List of cleared diagnostic biomarkers in the year 2021

Manufacturer	Biomarkers	Biomarker Details	Grant Date
Ventana Medical Systems, Inc.	PD-L1	PD-LI1 protein expression	10/15/2021
Agilent Technologies	Ki-67	Ki-67 protein expression	10/12/2021
Life Technologies Corporation	EGFR (HER1)	Exon 20 insertion mutations	09/15/2021
Pillar Biosciences, Inc.	KRAS	KRAS wild-type (absence of mutations in codons 12 and 13)	07/30/2021
Foundation Medicine, Inc.	MET	MET single-nucleotide variants and indels that lead to MET exon 14 skipping	07/15/2021
Foundation Medicine, Inc.	FGFR2	FGFR2 fusions/rearrangements	05/28/2021
Ventana Medical Systems, Inc.	ALK	ALK protein expression	03/03/2021
Dako North America, Inc.	PD-L1	PD-LI protein expression [Tumor Proportion Score (TPS) > 50%]	02/22/2021

er adoption and use of biomarkers. The EMA supports evidence generation throughout the product lifecycle, from preclinical development to marketing authorization [EMA, 2020; Hines et al., 2019].

Figure 9 illustrates the various EMA engagement pathways through which applicants can obtain scientific advice and feedback regarding evidence generation strategies for marketing authorization applications [EMA Innovation Task Force, 2014]. The outcome of the qualification process may be either Qualification Advice (QA) or Qualification Opinion (QO), depending on the level of evidence available and the intended context of use (CoU) of the biomarker.

Qualification Advice is a confidential procedure intended to support the early stages of biomarker development. It provides a forum for discussion between the applicant and the EMA regarding the scientific rationale, proposed context of use, available exploratory data, and plans for evidence generation. Qualification Opinion is granted only when sufficient evidence has been generated to support the proposed context of use. Before formal adoption, a draft Qualification Opinion is published on the EMA website for a two-month public consultation period to encourage scientific discussion and transparency.

Where promising preliminary data are available but additional evidence is required, the EMA may issue a Letter of Support to encourage data sharing and further research that may eventually lead to qualification [Manolis et al., 2011; Hendrikse et al., 2022].

The EMA guidance document *"Qualification of Novel Methodologies for Drug Development"* describes a voluntary procedure for qualification of biomarkers and other innovative methodologies, including animal models, clinical outcome assessments, and statistical methods [EMA, 2018]. Qualification activities involve both the Scientific Advice Working Party (SAWP) and the Committee for Medicinal Products for Human Use (CHMP), resulting in either Qualification Advice or CHMP Qualification Opinion. Figure 10 summarizes the EMA qualification pathway for novel methodologies [EMA, 2014].

The biomarkers qualified by the EMA are summarized in Table 10. Of the innovative methodologies reviewed by the EMA SAWP/CHMP, several have involved biomarker-based approaches, and additional biomarkers have received Letters of Support with the potential for future qualification [EMA, 2018].

Biomarker Qualification in the United States

The biomarker qualification process in the United States has evolved considerably since the qualification of the first biomarkers and continues to be refined. The framework has been described in both scientific publications and FDA guidance documents and has been expanded to support multiple categories of Drug Development Tools (DDTs) in addition to biomarkers [Amur et al., 2015; Parekh et al., 2015].

The FDA Center for Drug Evaluation and Research (CDER) and the Center for Devices and Radiological Health (CDRH) recognize three major categories of DDTs: biomarkers and biomarker assays, clinical out-

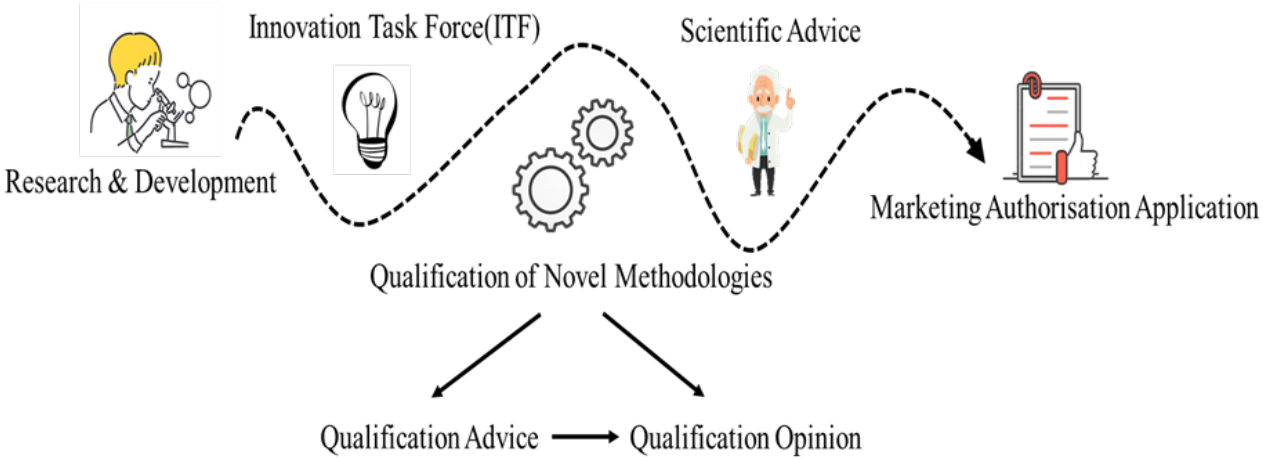

FIGURE 9. EMA techniques for evidence development of Biomarkers

come assessments (COAs), and animal or non-clinical models. The CDER qualification process generally consists of three stages: initiation, consultation and advice, and qualification review. Sponsors are required to submit a Letter of Intent (LOI), a Qualification Plan, and a Full Qualification Package during the qualification process.

Biomarkers may currently be qualified through the Biomarker Qualification Program (BQP) administered by the CDER under the FDA Drug Development Tools Program. The qualification process is voluntary and free of charge and follows a three-stage framework, as illustrated in Figure 11 [FDA, 2018; FDA, 2019].

To implement Section 3011 of the 21st Century Cures Act of 2016, which introduced Section 507 (Qualification of Drug Development Tools) into the Federal Food, Drug, and Cosmetic Act, the FDA updated its guidance on the qualification process for drug development tools. The revised guidance replaced earlier draft guidance and established a more formal framework for qualification activities [Lee et al., 2006; FDA, 2017].

As shown in Table 11, several biomarkers have received qualification through the FDA CDER Biomarker Qualification Program, including biomarkers associated with kidney injury and disease. Qualified biomarkers currently include safety, diagnostic, prognostic, and monitoring biomarkers [FDA, 2021]. In addition, numerous biomarker submissions remain under review within the FDA qualification framework.

SWOT Analysis for Biomarkers

A SWOT analysis is a strategic tool that can be used to assess the current situation, future possibilities, and risks of biomarker development and application in clinical medicine, diagnostics, and biomedical research.

Strengths

Use of biomarkers improves the accuracy of diagnosis and helps to detect disease in its early stages, thereby providing time for effective treatment and better outcomes. They are key to the personalized medicine field, aiding in patient stratification and personalized treatment based on the biological characteristics of each patient. Biomarker is also a major part of understanding the pathophysiology of disease, disease monitoring and measuring a therapeutic response. Moreover, many biomarkers can be measured in blood, urine, saliva, or imaging in a minimally invasive manner, particularly in clinical setting and research, which is useful (Henry and Hayes, 2012; Strimbu and Tavel, 2010).

Weaknesses

Even though there is potential for them, biomarker discovery, validation and qualification are still complicated, time-consuming and expensive processes. The variability in the expression of these biomarkers can be affected by genetic variation, environmental exposure, demographic and lifestyle factors, which can make them difficult to reproduce and standardise across populations. Moreover, some biomarkers do not have adequate sensi-

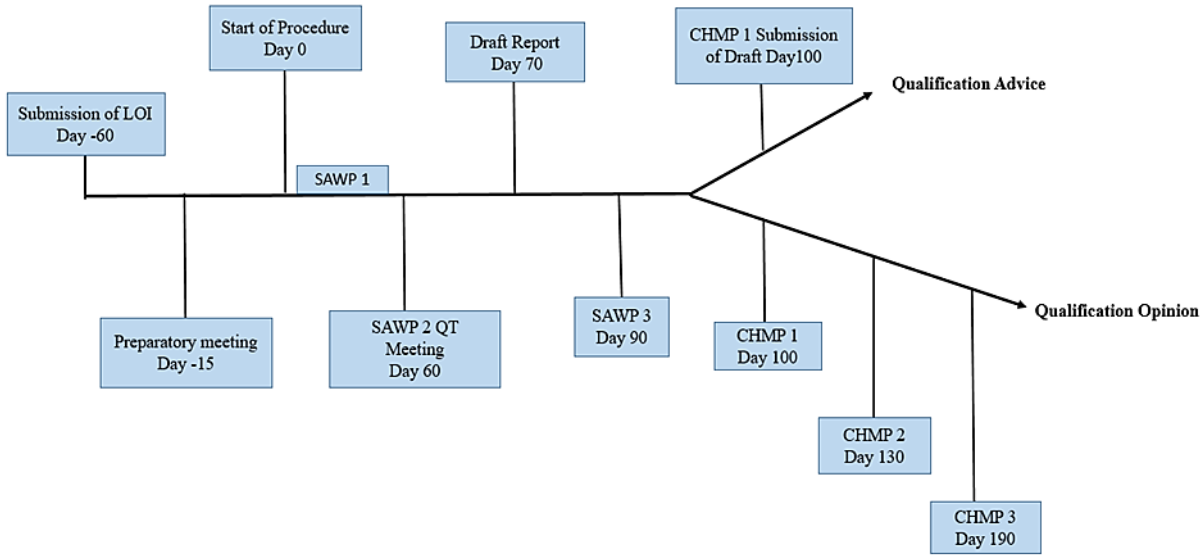

FIGURE 10. Novel methodology Qualification procedure of EMA

TABLE 10: Biomarker Qualifications by EMA

Name of the Biomarker	Description
Kim-1, albumin, total protein, β2- microglobulin, cystatin C, clusterin, and trefoil factor 3	The urinary kidney biomarkers are considered acceptable in the context of nonclinical drug development for the detection of acute drug-induced nephrotoxicity, either tubular or glomerular, with associated tubular involvement.
Clusterin, renal papillary antigen (RPA-1)	The urinary kidney biomarkers are considered acceptable in the context of nonclinical drug development for the detection of acute drug-induced nephrotoxicity in good laboratory practice (GLP) toxicology studies, which are used to support renal safety in clinical trials.
Two cerebrospinal fluid (CSF) related biomarkers: Aβ1-42 and total tau	The CSF biomarker signature based on a low Aβ1-42 and a high total tau qualifies to identify mild cognitive impairment (MCI) patients who most nearly equate to the prodromal stage of Alzheimer's disease (AD) and who are at risk of evolving into AD-dementia. Collection, handling, and measurements of all CSF samples should be performed according to GLP and to the specific international standards for these measurements.
Two CSF biomarkers (Aβ1-42 and t-tau) and PETamyloid imaging (positive/negative)	CSF biomarker signature based on a low Aβ1-42 and a high T-tau and/or amyloid-related positive/negative PET signal qualifies to identify patients with a clinical diagnosis of mild to moderate AD who are at increased risk of having an underlying AD neuropathology, for the purposes of enriching a clinical trial population
Plasma fibrinogen	Plasma Fibrinogen can be a useful enrichment biomarker in the context of a trial where all-cause mortality or hospitalised exacerbation is an outcome of interest, but several additional factors outlined by CHMP have to be considered.
Dopamine transporter (DAT) density imaging, Critical Path Global Ltd. 's	Dopamine transporter neuroimaging is qualified to be used as an enrichment biomarker in Parkinson's disease clinical trials targeting patients with early Parkinsonian symptoms
Ingestible sensor (IS) system for medication adherence	The CHMP agrees in considering the use of the Proteus technology (IS) as a qualified method for measuring adherence in clinical trials
Total kidney volume (TKV)	CHMP supports baseline total kidney volume, in combination with patient age and eGFR, as a prognostic biomarker to identify patients likely to experience a progressive decline in renal function, as characterised by a decline in eGFR or progression to end-stage renal disease

SAWP: Scientific Advice Working Party; CHMP: Committee for Medicinal Products for Human Use

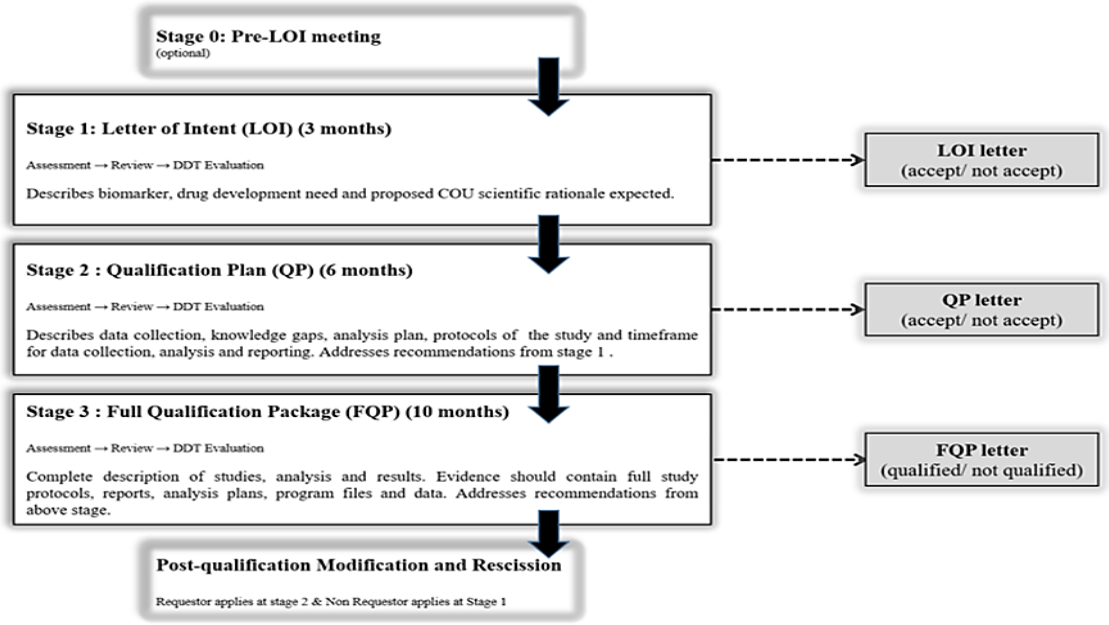

FIGURE 11. Qualification procedure of Biomarkers in the US

tivity or specificity, thus restricting their value in clinical use. There are a number of challenges to the translation of promising biomarkers from research to routine clinical practice, including methodological inconsistencies, insufficient validation studies and concerns about the reliability of surrogate endpoints (Mayeux, 2004; Pepe et al., 2001).

Opportunities

The need for precision medicine has given rise to significant opportunities in the healthcare sector that depend on the use of biomarkers. Biomarkers can be used to facilitate predictive, preventative and personalized therapeutic approaches, by identifying patients who might be at risk for the development of disease and allowing for targeted interventions. The discovery and validation of biomarkers has been accelerated by advances in high-throughput technologies, bioinformatics, molecular databases and systems biology. Moreover, biomarkers are becoming more common in drug development as patient stratification tools, as potential drug targets, for safety assessment and to evaluate treatment responses. A joint effort between academia, industry and regulatory bodies is anticipated to further broaden the clinical utility of biomarkers and ease their incorporation into the health care system (Hasin et al., 2017; Alyass et al., 2015).

Threats

There are a number of challenges that can hinder the successful use of biomarkers in clinical practice. Qualification and acceptance of biomarkers in relation to regulatory requirements continue to be a challenge and could postpone the translation of the biomarker into approved diagnostic or therapeutic tools. A false-positive or false-negative result can have a negative impact on clinical decision making and patient outcome. Complicated biomarker datasets can be difficult to interpret and may be subject to misinterpretation if the analyst or computer is inexperienced. Plus, privacy issues, intellectual property rights, reimbursement policies and the absence of consistent international regulatory policies could stall the widespread uptake. Emerging biomarker technologies are also increasingly competing with each other, which poses challenges for clinical and commercial implementation (Parkinson et al., 2016; Vasan, 2006).

Conclusion

Biomarkers have become an integral component of

TABLE 11: Biomarkers qualified by the FDA

Qualified Biomarkers	Biomarker Description	Context of Use of Biomarkers
Albumin, β2- Microglobulin, Clusterin, Cystatin C, KIM-1, Total Protein, and Trefoil factor-3	Urinary nephrotoxicity biomarkers as assessed by immunoassays	A safety biomarker to be used with traditional indicators to indicate renal injury in rats
Clusterin, Renal Papillary Antigen (RPA-1)	Urinary nephrotoxicity biomarkers as assessed by immunoassays	A safety biomarker to be used with traditional indicators to indicate renal injury in rats
Cardiac troponins T (cTnT) and I (cTnI)	Serum/plasma cardiotoxicity biomarkers as assessed by immunoassay	Safety biomarker to indicate cardiotoxicity in rats, dogs, or monkeys when testing known cardiotoxic drugs, and may be used to help estimate the non-toxic human dose
Galactomannan	Serum/broncho-alveolar lavage fluid biomarker: as assessed by immunoassay	Diagnostic biomarker used with other clinical and host factors to identify patients with Invasive Aspergillosis
Fibrinogen	Plasma biomarker as assessed by immunoassay	A prognostic biomarker used with other characteristics to enrich for COPD exacerbations.
Total Kidney Volume (TKV)	TKV as assessed by MRI, CT, and US	Prognostic biomarker with patient age and baseline glomerular filtration rate for Autosomal Dominant Polycystic Kidney Disease
Clusterin (CLU), Cystatin-C (CysC), Kidney Injury Molecule-1 (KIM-1), N-acetyl-beta-D-glucosaminidase (NAG), Neutrophil Gelatinase-Associated Lipocalin (NGAL), and osteopontin (OPN)	Urinary nephrotoxicity biomarker panel as assessed by immunoassays	Safety biomarker panel to aid in the detection of kidney tubular injury in phase 1 trials in healthy volunteers
Plasmodium 18S rRNA/rDNA	Plasmodium falciparum 18S rRNA/rDNA (copies/ml) measured in blood samples by a nucleic acid amplification test	Monitoring biomarker informs initiation of treatment with anti-malarial drug following controlled human malaria infection (CHMI) with P. falciparum sporozoites in healthy subjects in clinical studies for vaccine and/or drug development.

COU: Context of Use; BQP: Biomarker Qualification Program; CDER: Center for Drug Evaluation and Research

modern medicine and play an increasingly important role in disease diagnosis, prognosis, therapeutic monitoring, and personalized healthcare. Their successful translation from discovery to clinical application requires rigorous validation, qualification, and regulatory evaluation to ensure reliability, safety, and clinical utility.

Regulatory frameworks established by agencies such as the FDA and EMA have contributed significantly to the development and qualification of biomarkers, promoting their use in drug development and clinical decision-making. Continued harmonization of regulatory approaches may further facilitate global collaboration and accelerate the translation of biomarker research into clinical practice.

Patent protection remains an important driver of innovation and investment in biomarker research; however, a balance must be maintained between intellectual property protection and equitable access to diagnostic and therapeutic technologies. In parallel, growing demand for precision medicine and biomarker-based diagnostics continues to expand the global biomarker market.

Overall, the development and implementation of biomarkers require coordinated efforts among researchers, healthcare professionals, regulatory agencies, and industry stakeholders. Continued advances in biomarker science are expected to improve disease management, support personalized treatment strategies, and ultimately enhance patient outcomes.

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Conflict of Interest

The authors declare no conflict of interest.

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