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Regulatory Frameworks for Companion Diagnostics in Oncology and Respiratory Disorders: A Comparative Analysis of the United States and European Union

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Abstract: Companion diagnostics (CDx) are vital in personalized medicine because they help find patients who would benefit the most from specific treatments. The rules for these tests can be different depending on where you are, which affects how easily they can be used and developed. In the U.S., the FDA has a clear process for approving CDx on the same path as the therapies they relate to. Over in Europe, they recently made their regulations stricter with the In Vitro Diagnostic Regulation (IVDR), which means more requirements for proof and oversight. Even though there are efforts to make things more uniform, the differences in approval times, data needs, and who gets reimbursed can make it tricky to roll out CDx globally. This review looks at these varying rules and how they impact developing and using CDx. CDx has become essential in treating conditions like cancer, cystic fibrosis, and asthma. In cancer, for instance, CDx helps identify genetic issues that can lead to better treatment options. For cystic fibrosis, CDx is useful in picking the right modulators for improved patient results. In asthma, new CDx methods focus on biomarkers to customize treatments. But there are hurdles, like varying approval paths in the U.S., stricter regulations in Europe needing more proof and monitoring, and challenges in getting reimbursement. There's also a need to consider genetic differences and acceptance of CDx outside of oncology. To really expand the benefits of CDx for different diseases, it's important to work on more streamlined regulations, inclusive studies, and flexible approval paths.

I. Introduction:

For a long time, medicine has had a tough time dealing with how different patients respond to treatments. Even when people have the same illness, their reactions to the same medicine can be wildly different. This can impact how well the treatment works and what side effects people experience. A survey from the early 2000s showed a lot of differences in how effective drugs were for major diseases. [1]. The majority of drugs have efficacy rates between 40% and 60%. For example, chemotherapy only works in around 25% of cancer cases. It's hard to predict how well a treatment will work for each person, which has held back how well medications can perform. But in the last few decades, there have been some big improvements in understanding how diseases work. This is especially true in blood disorders and cancer, where using predictive biomarkers has made treatments better. Now, regulatory agencies accept these biomarker tests as companion diagnostics, which help connect patients with the right treatments. [2]. Companion diagnostics (CDx) are really important in personalized medicine. They help doctors figure out which patients might benefit the most from certain drugs. These tests are done outside the body and aid in choosing the best medication for each individual. While the rules around them can differ from one place to another, CDx is usually developed alongside the drugs by working with pharmaceutical companies. By targeting specific patient groups, CDx makes clinical trials more accurate, which helps bring down the cost of drug development from about $1 billion to under $500 million and shortens the time it takes from around 10-12 years to just 5-7 years. This is especially important in cancer treatment, where drugs can have tough side effects and don't always work well. Advances in molecular biology continue to uncover new cancer markers, giving us insights into how genetic changes can fuel tumor growth. As regulatory bodies demand more reliable results for cancer treatments, CDx is becoming crucial. Tools like genetic sequencers that spot specific mutations are already affecting how doctors practice today. With all the advancements in innovation and tech, CDx is helping pave the way for more accurate and effective personal treatments in the future. **[3].**

The History of Companion Diagnostics:

Companion diagnostics (CDx) started back in 1987 when scientists found a link between HER2 amplification and bad outcomes in breast cancer. They thought that blocking this receptor might help patients. This idea turned into something real with trastuzumab (Herceptin), a drug created by Genentech in the early '90s that targets HER2. Along with the drug, a test called an immunohistochemical (IHC) assay was developed to pinpoint HER2-positive tumors, helping doctors figure out which patients could benefit from the treatment. During clinical trials, this IHC assay was crucial for finding patients who would respond well to trastuzumab. As a result, the FDA approved both trastuzumab and the HercepTest IHC assay on September 25, 1998, making history by allowing drugs and their corresponding tests to be approved together. This shift in regulations was first called "theragnostic" but later became known as "companion diagnostics," a term that gained traction thanks to an article in Nature Biotechnology.

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Acknowledging the importance of CDx in personalized medicine, the FDA laid out formal guidelines for CDx in 2014, and agencies in places like Korea, Japan, Canada, and Australia followed suit. A big step happened in May 2022 when the European Union rolled out the In Vitro Diagnostic Regulation (IVDR), which aims to improve oversight and quality for CDx, with full changes expected by May 2026. As of August 2023, the FDA had approved over 60 drugs and their associated CDx tests. CDx has really changed the game in healthcare, allowing for more precise and targeted treatments.

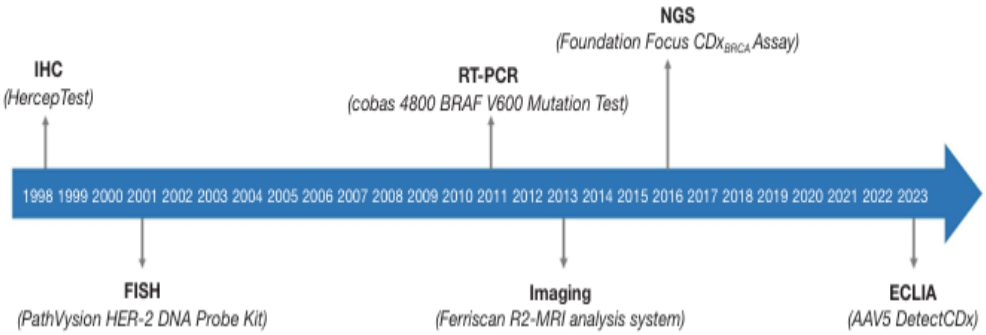

Fig : 1

Schedule for the launch of the various companion diagnostic systems [4]. RT-PCR stands for real-time polymerase chain reaction; NGS for next-generation sequencing; ECLIA for electrochemiluminescence immunoassay; IHC for immunohistochemistry; and FISH for fluorescence in situ hybridization.

https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools. Accessed August 22, 2023 .[5]

Key Considerations in Companion Diagnostics (CDx) Development

The primary goals of companion diagnostics (CDx) are to:

- Find patients who will benefit the most from a drug.
- Make sure the treatment is safe by choosing patients where the drug has shown good results.
- Anticipate serious side effects.
- Keep an eye on how patients respond to the treatment to adjust doses and ensure their safety.

But just because a companion diagnostic (CDx) is approved doesn't mean it will work perfectly in picking the right patients or that it will quickly be used in clinics. It can take up to five years for a CDx to be used in medical practice after it's approved, which can slow down access to targeted therapies. A big issue is getting the drug and CDx developed together; if they are not launched at the same time, it can lead to lost revenue, poor outcomes, and less personalized medicine. A good example of this is Gleevec from Novartis, which faced delays with its CDx from Dako Denmark, causing revenue loss and limiting patient access to the best treatment.

Challenges in CDx Development

CDx development is tied to genomic technologies and genetic testing, but several issues stand in the way:

- Low genetic diversity: More than 70% of data from Genome-Wide Association Studies come from just three countries—the U.S., U.K., and Iceland—so not all populations are represented.

- Fewer clinical trials outside Europe and the U.S. mean CDx may not work as well for non-European folks.

- Genetic differences affect how drugs are processed. For example, the CYP2C19*2 gene variant impacts how clopidogrel (a heart drug) works, making it less effective for about 70% of Asian patients compared to 25-30% of Europeans. The FDA even issued a warning about this genetic factor, showing the need for better CDx designs.

Common Problems in CDx Development

1. Not pinpointing genetic markers that are specific to populations and relevant for treatment.

2. Missing out on genetic variants that affect disease progress or treatment response.

3. Hesitation to use a wider range of biomarkers (like proteins, lipids, etc.).

4. Incorrect patient group classifications.

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5. Weak regulations that don't really support innovation and safety.

6. Issues with getting reimbursement in different countries.

To make CDx better, researchers need to boost genetic diversity in their studies, refine how sensitive biomarker tests are, and speed up regulatory approvals. These changes will help in providing more accurate and effective personalized treatment options. **[6].**

Regulations:

U.S. FDA Regulations for Companion Diagnostics (CDx)

Definition: It's a lab test that helps determine how safe and effective a treatment is going to be. Instructions on how to use the test and treatment together are included.

Classification

Most medical devices fall under Class III because they share the same risk level as the associated drug.

Some are in Class II and have a PMA (510(k)).

Procedure for Approval

According to Section 515 of the FD&C Act, Class III medical devices need Premarket Approval (PMA). As of March 2021, 40 out of 44 FDA-approved CDx had gone through this PMA process.

The Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER) looks over applications for drugs or biologics, while the Center for Devices and Radiological Health (CDRH) handles CDx applications.

Consultation Process

CDRH goes through the PMA submissions.

Applications for treatments are checked separately based on the rules for drugs or biologics.[6].

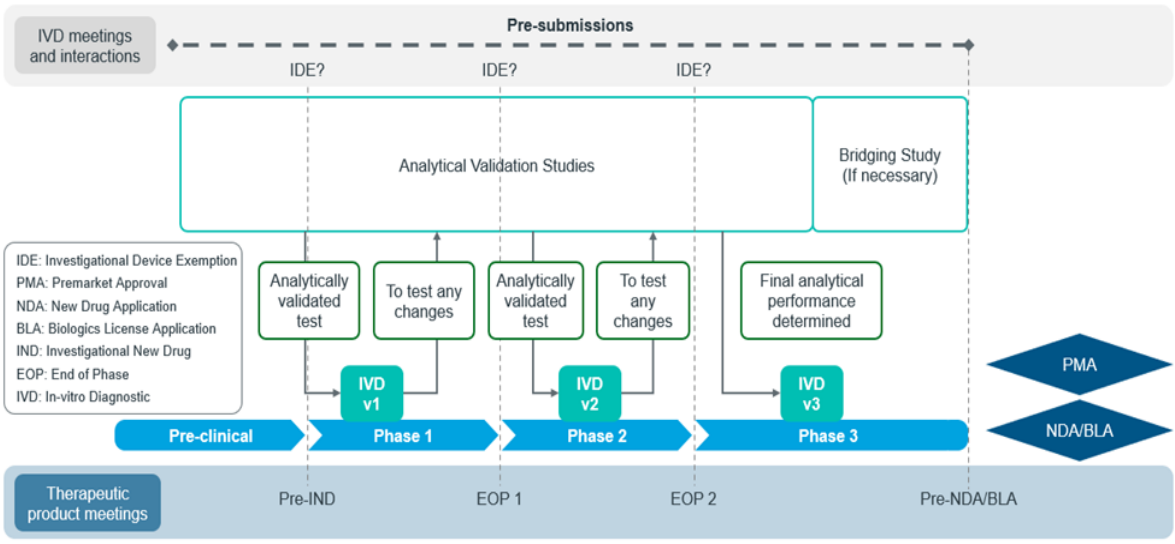

FIG 2 Adapted from US FDA CDx submission process [7]

U.S. Food and Drug Administration. (2016, July 15). Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product.

https://www.fda.gov/media/99030/download [7]

Europe—IVDR Rules for Companion Diagnostics:

Definition A companion diagnostic is a device that helps ensure a medication works safely and efficiently . It helps to:

(a) Figure out which patients are likely to benefit from the medication.

(b) Identify patients who might have serious side effects.

Classification:

According to IVDR Rule 3, these devices fall into Class C IVDs.

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Procedure for Approval:

- Under IVDR (Annex IX, Section 5.2), a conformity assessment is required, which involves a medical authority like the EMA or a national regulatory body working with a notified body.
- The notified body checks if the device is suitable for the medication.

Procedure for Consultation:

The notified body reaches out to the EMA or a medical authority for a scientific opinion on:

o A draft summary of safety and performance.

o Draft usage instructions.

o The consultation lasts 60 days, but it can be extended for another 60 days. [6]

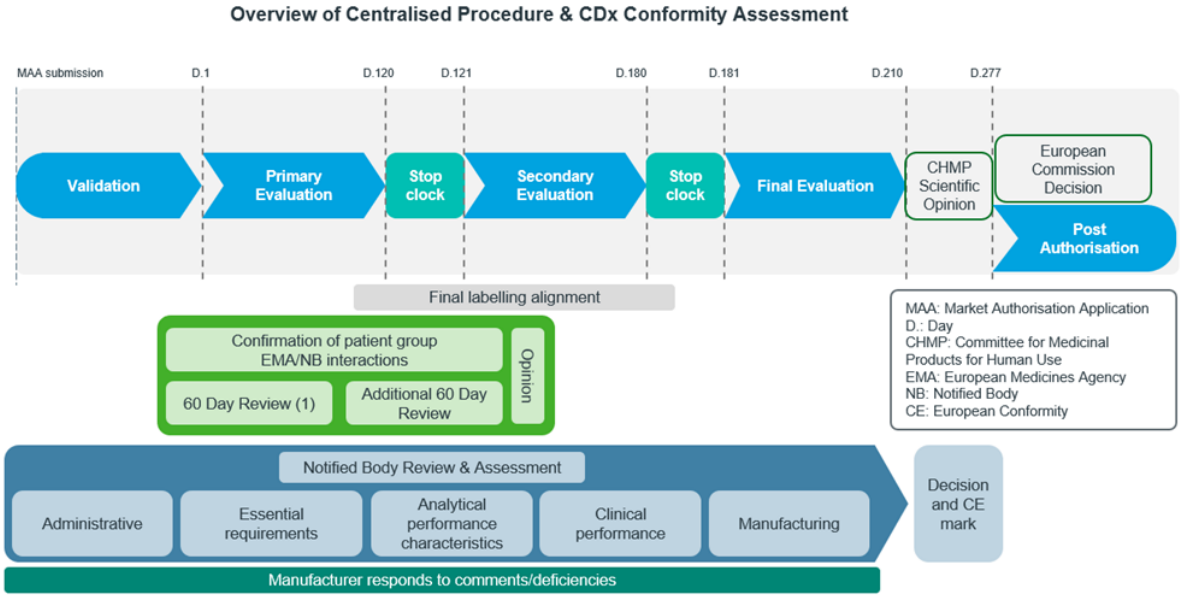

FIG 3 Adapted from EU EMA CDx submission process [8]

EFPIA & MedTech Europe. (2020). Determining the path for assessment of a Companion Diagnostic (CDx) under the In Vitro Diagnostic Medical Devices Regulation. https://efpia.eu/media/554434/2020_05_27_efpia-mte_determining-the-path-for-assessment-of-cdx-under-ivdr_final.pdf . [8]

Trends in CDx for Oncology

Precision oncology is making strides as researchers work to understand the different types of cancer better and limit side effects [9]. One big focus is finding biomarkers that can predict how well treatments will work. That's why many companion diagnostics (CDx) are made specifically for cancer treatments. The U.S. FDA has started approving these tests for groups of related drugs targeting the same mutation, which is a big help since it cuts down on the need for separate tests for each medication. For instance, one CDx for EGFR mutations in non-small cell lung cancer (NSCLC) can inform treatment choices for several therapies. This makes things smoother and helps avoid treatment delays. But there's still a problem—developing CDx tests isn't keeping up with the fast pace of new cancer drugs coming out. A study from 2020 found that nearly a quarter of advanced NSCLC patients didn't get the necessary genomic testing for important treatment targets before starting their therapy. [10]. It's a bit worrisome that around 65% of advanced NSCLC patients have mutations that can help with personalized treatment [11]. Getting genomic testing done on time is really important so patients can start the best first-line therapy for their specific cancer.

Oncology drug-companion diagnostic combinations

Drug-diagnostic The FDA's Role in Drug-CDx Co-Development :

The FDA has been a leader in bringing companion diagnostics (CDx) into the drug development process, staying ahead of other regulatory agencies. It all started back in 2005 with a concept paper that grew into a draft guideline on how drugs should work with CDx. The FDA sees these CDx tests as key to making sure specific medications are safe and effective. Since trastuzumab (Herceptin) and the HercepTest got the green light in 1998, the number of FDA-approved drug-CDx pairs in cancer treatment has steadily risen. In the last ten years, this growth has picked up pace, with 46 targeted therapies using CDx tests getting approved by June 2021.

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These treatments mainly fit into two groups:

• Small molecule inhibitors, which make up over 75% of targeted cancer drugs. This includes things like tyrosine kinase inhibitors and PARP inhibitors.

• Antibody-based therapies, which mostly consist of monoclonal antibodies, along with some newer bispecific antibodies like amivantamab (Rybrevant) and antibody-drug conjugates like ado-trastuzumab emtansine (Kadcyla).

CDx is changing the game in precision medicine, helping ensure that patients get treatments suited to their specific cancer types. [12].

Antibody Based Drugs	CDx Biomarker
Amivantamab*	*EGFR*
Trastuzumab, Pertuzumab, Ado-trastuzumab emtansine	HER2/*HER2*
Dostarlimab	MMR
Atezolizumab, Cemiplimab, Nivolumab, Pembrolizumab	PD-L1
Cetuximab, Panitumumab	*RAS (KRAS/NRAS)* /EGFR
Pembrolizumab	TMB-H
Small Molecule Inhibitors	**CDx Biomarker**
Alectinib, Brigatinib, Ceritinib, Crizotinib, Lorlatinib	ALK/*ALK*
Nilotinib	*BCR-ABL1*
Binimetinib, Cobimetinib, Dabrafenib, Encorafenib, Trametinib, Vemurafenib	*BRAF V600E or V600K*
Niraparib, Olaparib, Rucaparib, Talazoparib	*BRCA1/BRCA2*
Afatinib, Dacomitinib, Erlotinib, Gefitinib, Osimertinib,	*EGFR*
Tazemetostat*	*EZH2*
Pemigatinib, Infigratinib*	*FGFR2*
Erdafitinib*	*FGFR2 or FGFR3*
Midostaurin, Gilteritinib	*FLT3*
Olaparib	*HRR*
Ivosidenib*	*IDH1*
Enasidenib*	*IDH2*
Sotorasib*	*KRAS G12C*
Imatinib	c-KIT/*KIT, PDGFRB*
Capmatinib*	*MET*
Larotrectinib	*NTRK1/2/3*
Alpelisib	*PIK3CA*
Pralsetinib*	*RET*
Crizotinib	*ROS1*
Venetoclax	*TP53*

* Drugs not yet approved in Europe at the cut-off date of October 25, 2021.

FIG :4 List of FDA approved drugs, which have a CDx assay linked to their use

https://www.researchgate.net/publication/356425657/figure/tbl1/AS:1106038031941648@1407114248 01/List-of-FDA-approved-drugs-which-have-a-CDx-assay-linked-to-their-use-4.png [12]

Drug-diagnostics examples

Trastuzumab and the Evolution of Drug-Diagnostic Codevelopment

The creation of trastuzumab, also known as Herceptin, was a big deal in cancer treatment and marked a new step in how drugs and tests are developed together. Genentech made an immunohistochemical test to find women with HER2-positive breast cancer, making sure only those who could actually benefit were part of the trials. This approach led to the FDA approving both trastuzumab and the HercepTest in 1998, which was the first time a companion diagnostic got the go-ahead from the FDA. This method not only made drug development smoother but also lessened the number of patients needed in trials. A study later showed that if they hadn't tested for HER2, they'd have needed over 8,000 patients for a trial instead of the actual number used, which was 17 times smaller. This highlighted how crucial it is to use biomarker-guided trial designs, which are now standard in precision oncology. These days, a lot of new cancer drugs depend on multiple companion diagnostics.

Take crizotinib (Xalkori), for example—it's used for non-small cell lung cancer and targets specific proteins. It has three tests that have FDA approval:

- Oncomine Dx Target Test
- Ventana ALK (D5F3) CDx Assay
- Vysis ALK Break Apart FISH Probe Kit

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As precision medicine continues to grow, companion diagnostics will keep influencing targeted cancer treatments, helping ensure patients get the right care when they need it.

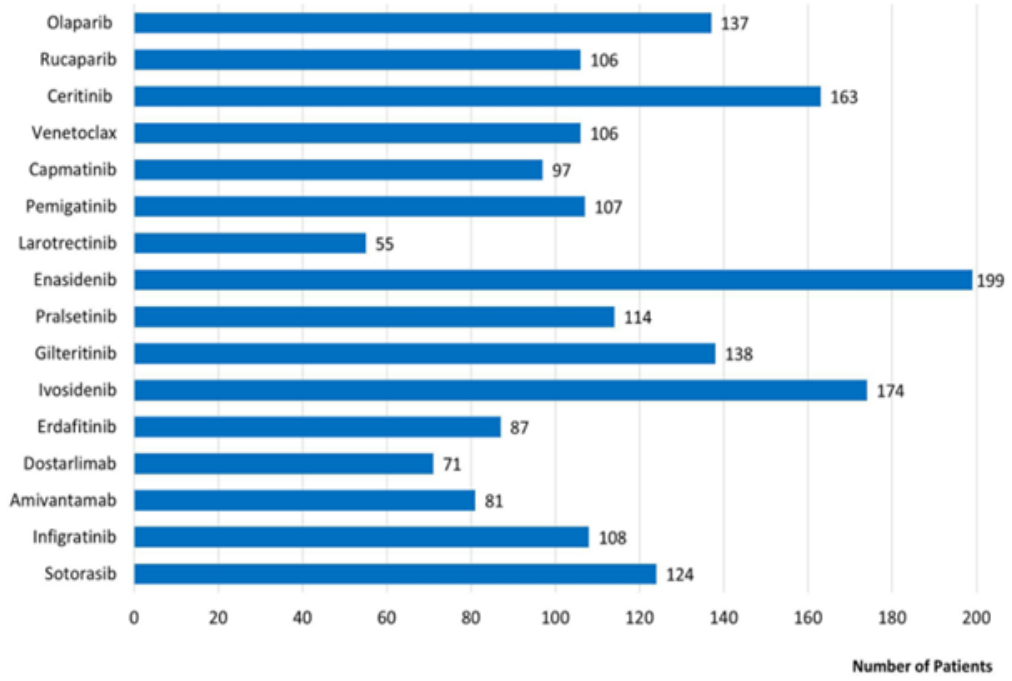

FIG: 5 Oncological and haematological drugs developed with a CDx and approved by the FDA within the past 10 years. For these drugs the efficacy populations have consisted of less than 200 patients in single arm clinical trials.

https://www.researchgate.net/profile/Jan-Jorgensen-5/publication/356425657/figure/fig2/AS:1106038031953934@1640711424786/Oncological-and-hematological-drugs-developed-with-a-CDx-and-approved-by-the-FDA-within_Q320.jpg [13] .

Recent Drug-CDx Approvals in Precision Oncology

Larotrectinib (Vitrakvi) made headlines in 2018 as the first cancer treatment that doesn't focus on a specific tumor type. Instead, it's approved based on the TRK gene fusions that can happen in different solid tumors.

Here are some other notable drug and companion diagnostic (CDx) pairings that have come out recently:

- Amivantamab (Rybrevant): This is a bispecific antibody that targets EGFR and MET, and it's used for metastatic non-small cell lung cancer (NSCLC) with specific EGFR mutations. It is used in conjunction with the Guardant360 CDx assay to detect biomarkers.
- Sotorasib (Lumakras): This was the first FDA-approved KRAS inhibitor, aimed at NSCLC with the KRAS G12C mutation, which is often linked to treatment resistance. It has a couple of diagnostics:
- Guardant360 CDx – a blood test for biomarker tracking
- Qiagen Therascreen KRAS RGQ PCR kit—a tissue test that's needed if the blood test doesn't show results, as it's less sensitive.
- Foundation One CDx assay is used to find NTRK1/2/3 gene fusions in solid tumors, which helps doctors decide on TRK inhibitor treatments like larotrectinib.

As precision medicine progresses, more biomarker-based therapies and CDx tests are changing how oncology care is approached, ensuring patients get treatments that are most effective for them. [14].

Current Status of Companion Diagnostics (CDx)

CDx has made great strides in treating tough health problems like cancer, cystic fibrosis (CF), asthma, and HIV. These illnesses often have different biological paths, so patients with the same diagnosis can react differently to treatments. CDx helps sort patients into groups based on their genetic and immune profiles, leading to better and more precise treatments. To use drugs safely and target them correctly, it's important to understand the key markers and pathways that lead to disease progression. While cancer treatments are ahead in using these markers, CDx is also making progress in infectious diseases, aging issues, and other complex health problems, moving us toward more personalized medicine across various areas.

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CDx for Cystic Fibrosis

For cystic fibrosis, this genetic disorder used to be treated mainly by managing symptoms since the causes were not well understood. CF is caused by problems with chloride ion transport, resulting in thick mucus that can clog the lungs and pancreas, causing serious infections and digestive troubles. Early treatments focused on antibiotics and bronchodilators for symptom control. Advances in genetic research showed that CF is linked to mutations in the CFTR gene, which affects how the CFTR protein works. Since different mutations lead to different problems, researchers have created targeted therapies based on these mutations. For instance, patients with the deltaF508 mutation see a lot of benefit from Orkambi (lumacaftor/ivacaftor), which helps fix CFTR function. This breakthrough helped create CDx tests that got FDA approval in 2013 to better diagnose and choose treatments for CF. These tests help ensure that patients get the best treatments for their specific mutations, moving away from just symptom management to more personalized care.

CDx for Asthma

When it comes to asthma, this disease varies greatly among patients, who need tailored treatments. Discoveries of biomarkers have been essential in guiding treatment choices. Early on, researchers linked the periostin gene, along with the CLCA1 and serpinB2 genes, to IL-13 activity in asthma patients' epithelial cells. This understanding has helped refine treatments, allowing for better-targeted therapies based on each patient's genetic makeup.

Regulatory Consideration for Compaion Diagnostics

On the regulatory side, CDx rules differ by region. The FDA in the U.S. and EMA in the EU have mostly similar guidelines but vary in their testing and labeling demands. Back in 2015, 78% of CDx-related drugs had matching labels from both agencies, even though some CDx were mandatory in the EU but only recommended by the FDA. Other countries like Japan, Canada, and Australia have their own CDx regulations, but these can differ in important ways. A review from 2014 showed that, for the same drugs, only 52% in the U.S., 63% in the EU, and 38% in Japan required biomarker testing on their labels. The U.S. and Japan often require CDx development for certain drugs, while the EU generally recommends it. Even though CDx rules are critical for safety and effectiveness, there are still inconsistencies, especially in risk classification and approval across different countries. To make things clearer and safer for patients, it would be helpful to have more global agreement through organizations like the International Council for Harmonization.

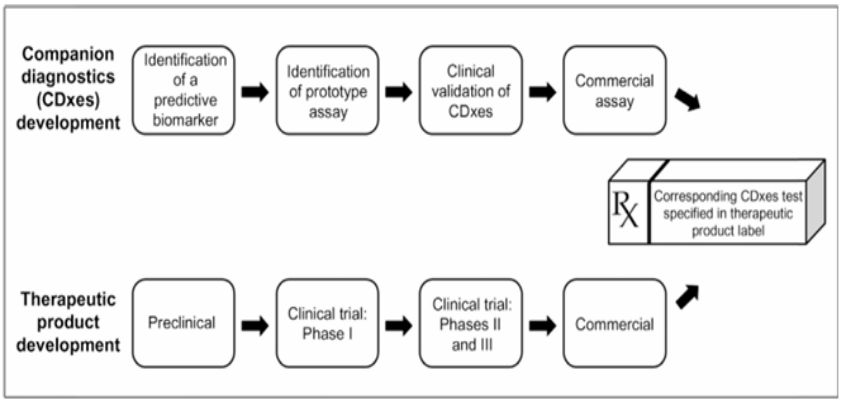

Fig: 6 Codevelopment of CDx with the therapeutic drug during clinical trial stages. CDx, Companion diagnostic.

Source: Adapted from Figure 3 in Cheng S, Koch WH, Wu L. Co-development of a companion diagnostic for targeted cancer therapy. N Biotechnol 2012;29(6):682 88 [15] .

Challenges in Using Companion Diagnostics

Companion diagnostic tests (CDx) face a tough time gaining traction in the market for several reasons. First off, they can be expensive to develop and require specialized training, which makes things tricky from a budget standpoint, even if they can save money in the long run. CDx makers also find it hard to see a good return on their investment since these tests are usually much cheaper than the treatments that go with them, making it less appealing to put money into them in the first place. These tests are often used just once for each patient, which cuts into the financial incentives—especially when dealing with rare diseases that affect only a few individuals. Another problem is the complicated reimbursement systems that treat CDx and treatments separately, which complicates their use in everyday healthcare. All these issues make it tough for CDx tests to be widely adopted and available right now. [16]

Ensuring Vigilance in Companion Diagnostics

There's a real lack of transparency in personalized medicine, especially in places like the EU and Mexico. Here, companion diagnostics (CDx) aren't really tied to specific treatments yet. Instead, the regular rules for diagnostic tests apply. In contrast, countries like the US and Japan have stricter CDx regulations that are more closely connected to drug therapies. A number of things

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can lead to problems, like wrong test results, mistakes made by doctors, or misdiagnoses that occur because of false positives or negatives. These errors can slow down treatment, cause unnecessary side effects for patients, or even prevent them from getting helpful therapies. When bad outcomes happen, it's important for drug and diagnostics companies to team up and figure out what went wrong. They need to check if the problem is due to faulty tests, drug effectiveness, or errors by healthcare providers. In the US, there's a push to improve monitoring by using electronic health records and a unique device identification system to keep track of medical devices. This UDI system includes identifiers that specify the device type and production details, which helps with traceability. To make sure investigations are thorough and reporting is accurate, clear protocols have to be laid out, and staff need proper training. Depending on what they find, companies might have to submit different reports to the FDA, which could involve talking to the CDER, CBER, or CDRH to maintain safety and accountability in using CDx.

Challenges in Commercializing Companion Diagnostics (CDx)

Getting regulatory approval doesn't mean a CDx test will actually make it to the market. Unlike drugs that get paid for based on their value, diagnostic tests usually get paid for based on the procedure costs. With personalized medicine on the rise, insurers are starting to expect biomarkers to play a role in drug development, which creates a need for covering diagnostics. But getting reimbursement for CDx is tough. These tests usually aren't paid for until their clinical usefulness is shown, which slows down the process of getting them used. The Centers for Medicare and Medicaid Services (CMS) and Palmetto GBA have rolled out Z-Codes, moving away from older payment models to ones that focus on patient outcomes. Still, it's hard to prove clinical utility, especially for people from different ethnic backgrounds. Plus, many labs would rather stick to cheaper, lab-developed tests, which creates a gap between approved tests and the ones that are commonly used.

Reimbursement policies are different around the globe:

• In the US, payment levels are going down, which worries people in the industry.

• In Japan, CDx tests are covered, but funding limits how many approved tests can actually be used.

• In Europe, it's mixed—Spain doesn't cover them, Germany has stack coding, and the UK limits the number of reimbursed tests for each disease.

• In developing countries like China, India, and Brazil, CDx isn't reimbursed, so either patients or drug companies have to pay.

• In other Asia-Pacific countries, reimbursement systems are still being developed, which delays access to personalized medicine.

Even though there's evidence showing the value of CDx tests, there's still a gap between getting regulatory approval and actually using them in clinics, pointing to a need for better reimbursement policies everywhere. [17]

Summary of current challenges to companion diagnostic implementation and recommendations for change . [18]

Challenge	Recommendation
Permission of multiple assays for a single biomarker leads to confusion.	Efficacy data from several biomarker tests will be produced in pivotal clinical trials to allow for comparison of patient benefit; robust assay concordance studies conducted by independent commercial and academic laboratories
Confusion brought on by drug labeling's use of "approved assay" terminology	• Instead, propose "analytically validated assay," providing precisedefinitions of validation. • New diagnostic tests for current biomarkers could be authorized based solely on analytical performance for simpler, single target genetic mutations .
The drug label's biomarker selection criteria are unclear.	Prior to labeling discussions, reputable academic associations involved in biomarker testing, such as the European Society of Pathology (ESP), College of American Pathologists (CAP), International Association for the Study of The Association for Molecular Pathology (AMP) and Lung Cancer (IASLC) were consulted.
For drug/diagnostic co-registration, access to an approved assay is denied.	Permit authorized companion diagnostics to be used "off the shelf" in authorized indications without requiring a pharmaceutical company and diagnostic supplier to collaborate. Eliminate the need for additional PMA. Every test must adhere to CAP/CLIA (or its equivalent outside of the US).
Because "first past the post" diagnostics define the intended use population, there is a lack of innovation in diagnostics.	Permit phase III studies to employ new diagnostics, including for the SoC arm. Clinical data should ideally inform the risk/benefit analysis, with the pivotal study incorporating efficacy data for the authorized diagnostic.

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II. Conclusion:

Companion diagnostics (CDx) are really important in personalized medicine, but the rules vary a lot from one place to another, which affects how quickly they get approved and used. In the US, the FDA requires that CDx be developed alongside therapies. Over in Europe, the IVDR has stricter rules; each has their own guidelines for clinical trials and approval. Even though there are efforts to make things more standard globally, there are still some issues, like the need for diverse trials, reimbursement problems, and the complicated rules. CDx has made a big impact in cancer treatment with therapies based on certain biomarkers, and it's also growing in areas like cystic fibrosis and asthma. To make sure CDx remains reliable and accessible, it's important to keep an eye on them after they hit the market, bring in real-world evidence, and adapt regulations as needed. Filling gaps in genetic diversity, making approval processes smoother, and getting CDx used more widely outside of cancer are all key steps to push precision medicine forward worldwide.

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