Evolution of FDA Companion Diagnostics: 25 Years of Growth, Consolidation, and Technological Shift

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Background

- Companion diagnostics (CDx) are tests used to identify patients who are most likely to benefit from specific therapies.[1]
- A classic example is trastuzumab in HER2-positive breast cancer, where HER2 testing has been required since 1998 to identify eligible patients.[2]
- CDx have become a key component of precision medicine, particularly in oncology and hematology.[3]
- Since the first FDA-approved CDx in 1998, the field has expanded substantially in both number and technological complexity.[2]
- CDx development has evolved from mainly single-gene, tissue-based assays toward more advanced platforms such as next-generation sequencing and liquid biopsy.[3]

Objective

- To characterize the evolution of FDA companion diagnostic (CDx) approvals from 1998 to 2024.
- To assess trends in approval type, technology, specimen type, timing relative to drug approval, and manufacturer distribution.

Methods

Study design

- Retrospective cross-sectional study of FDA-approved or -cleared companion diagnostics (CDx).[2]

Data source

- FDA's official List of *Cleared or Approved Companion Diagnostic Devices* was used to identify CDx approvals from 1998 to 2024.[2]

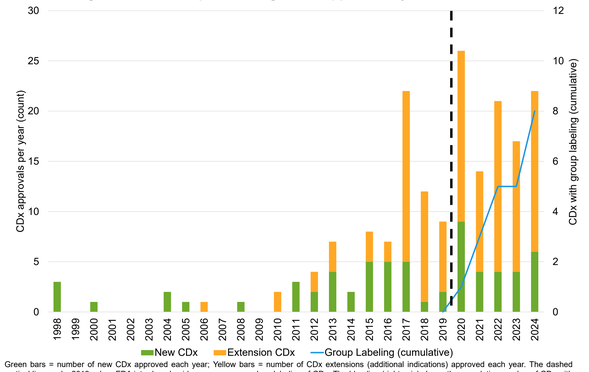
Study sample

- All devices meeting the FDA definition of a CDx were included.[1] For each approval, we extracted test name, manufacturer, approval type, approval date, indicated drug(s)/biomarker(s), and specimen type.
- Each approval was classified as either a new CDx (first FDA approval/clearance of a unique assay) or an extension (subsequent approval expanding the indication of an existing test).
- We summarized annual approval trends and evaluated, among new CDx, technology platform (NGS, PCR, FISH, IHC, other) and specimen type (tissue, plasma, other).
- We also assessed the lag between drug approval and CDx approval for drug–indication–biomarker combinations and examined manufacturer concentration based on the number of new CDx approvals.

Results

1. Approval trends over time

Figure 1: FDA Companion Diagnostic Approvals by Year, 1998–2024



Green bars = number of new CDx approved each year; Yellow bars = number of CDx extensions (additional indications) approved each year. The dashed vertical line marks 2019, when FDA introduced guidance on group or class labeling of CDx. The blue line (right axis) shows the cumulative number of CDx with group labeling indications (by year-end).

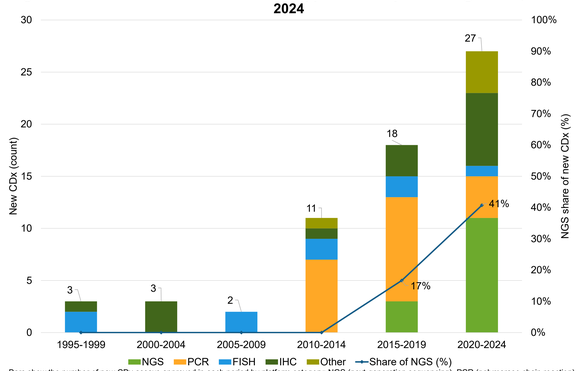
- We identified 185 FDA companion diagnostic (CDx) approval actions between 1998 and 2024, including 64 new CDx assays and 121 approval extensions for previously approved tests (Figure 1).
- Approval activity remained modest in the early years, with only 0–2 new CDx approvals per year through much of the early 2000s.
- A clear acceleration occurred in the mid-to-late 2010s, paralleling the expansion of biomarker-driven oncology therapies and the broader adoption of precision medicine.
- The highest annual approval volume was observed in 2020, with approximately 20 total approvals, including around 8 new CDx assays and 12 extensions.
- From 2017 onward, annual activity remained consistently higher than in earlier periods, with roughly 4–8 new CDx approvals per year plus multiple extension approvals.
- Extensions outnumbered new CDx by roughly 2:1, suggesting that once a CDx platform is established, it is frequently reused and expanded across additional drugs, biomarkers, and indications.

Results (continued)

- The dashed line marks 2019, when FDA introduced draft guidance on group or class labeling for oncology CDx, later finalized in 2020.[5] Approval activity remained strong after this point, suggesting that this policy did not slow innovation and may have supported additional labeling expansions (Figure 1).
- The cumulative number of CDx with group/class labeling reached 8 by 2024, indicating a gradual but meaningful shift toward more flexible labeling approaches in settings where multiple therapies target the same biomarker.

2. Shift in platform technology

Figure 2: Platform Distribution of New FDA-Approved Companion Diagnostics, 1998–2024

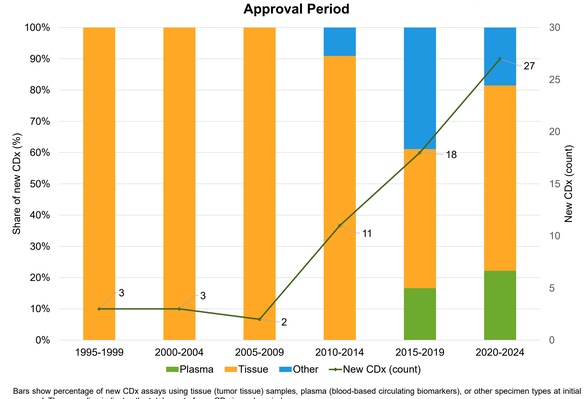


Bars show the number of new CDx assays approved in each period by platform category: NGS (next-generation sequencing), PCR (polymerase chain reaction), FISH (fluorescence in situ hybridization), IHC (immunohistochemistry), and Other. The blue line (right axis) denotes the percentage of new CDx in each period that were NGS-based.

- The technological composition of newly approved CDx changed substantially over time, moving from single-analyte assays toward broader genomic platforms (Figure 2).
- NGS-based CDx were absent from 1998–2014, highlighting how recent the transition to multigene testing has been.
- During 2015–2019, NGS began to emerge, accounting for approximately 17% of new CDx approvals in that period.
- By 2020–2024, multigene NGS panels accounted for approximately 41% of new CDx approvals (11 of 27 new tests), indicating a major shift in the technological basis of companion diagnostics.
- Across the full study period, the distribution of new CDx by platform was: PCR 21 (33%), IHC 15 (23%), NGS 14 (22%), FISH 9 (14%), and Other 5 (8%).
- Although PCR remained the single largest platform overall, the rapid growth of NGS suggests that the field is increasingly prioritizing assays that can evaluate multiple biomarkers simultaneously.
- All NGS-based CDx identified in this analysis were used in oncology, often as broad multigene panels. An important example is the first broad NGS companion diagnostic, approved in 2017.
- FISH continued to play an important role for selected biomarkers, particularly gene amplifications and rearrangements, while the Other category reflected specialized technologies used in a smaller number of niche settings.

3. Evolution in specimen type

Figure 3: Specimen Type Distribution for New FDA Companion Diagnostics, by Approval Period

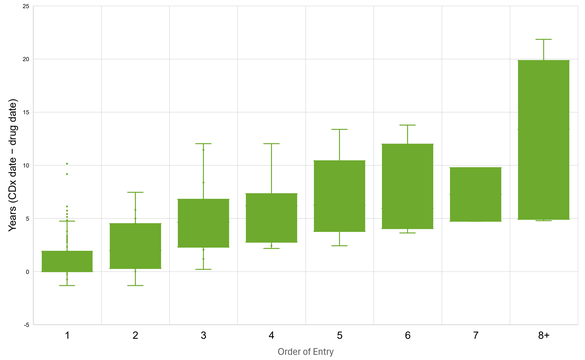


Bars show percentage of new CDx assays using tissue (tumor tissue) samples, plasma (blood-based circulating biomarkers), or other specimen types at initial approval. The green line indicates the total count of new CDx in each period.

- Most FDA-approved companion diagnostics were initially developed as tissue-based tests, reflecting the central role of tumor biopsy in early precision oncology.
- In 1998–2014, essentially all newly approved CDx were tissue-based, consistent with the use of tissue specimens for IHC, FISH, and many early PCR assays (Figure 3).
- Tissue remained the dominant specimen type overall, with about two-thirds of all new CDx through 2024 using tumor tissue at initial approval.
- A major recent development was the emergence of plasma-based (liquid biopsy) CDx, which detect circulating tumor DNA or other blood-based analytes.
- The first FDA-approved liquid biopsy CDx in this dataset appeared in 2016, specifically a plasma-based EGFR mutation test for detection of EGFR T790M mutations in lung cancer.
- Plasma-based assays represented about 15% of new CDx in 2015–2019, increasing to approximately 30% in 2020–2024.
- Overall, 9 new CDx (14%) used plasma at launch, often providing an alternative when tissue is unavailable or inadequate.
- High-profile examples include multigene blood-based companion diagnostics approved in 2020, supporting targeted treatment decisions.
- The other specimen category accounted for 13 tests (~20%) and included settings such as whole blood, saliva, or bone marrow aspirates, often for hereditary or hematologic biomarkers.
- The growth of liquid biopsy is important because it reflects a shift toward less invasive testing, broader clinical accessibility, and compatibility with newer genomic technologies. Even so, tissue remains the dominant and often preferred specimen type in many settings.

4. Timing of CDx relative to drug approval

Figure 4: Lag Between Drug Approval and CDx Approval, by Order of Test Entry



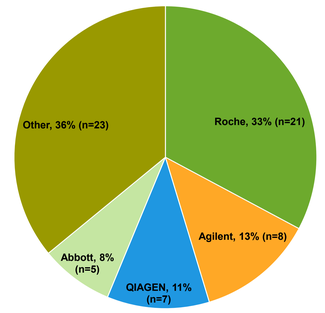
Each boxplot represents the distribution of (CDx approval date – drug indication approval date) for CDx tests that were the 1st, 2nd, 3rd, etc., approved for the same drug–biomarker combination. The y-axis (years) is truncated at 25 years for display. Negative values (if any) indicate CDx approval before the drug approval.

- To examine timing, we analyzed 114 drug–indication–biomarker combinations requiring a companion diagnostic and compared drug approval dates with the approval dates of corresponding CDx tests.
- For the first CDx entrant in a given drug–biomarker combination, the median lag was approximately 0 years, indicating that the initial CDx was usually approved at or very near the time of drug approval (Figure 4).
- Many first CDx were approved on the same day as the drug, reflecting coordinated review and the regulatory expectation that a required diagnostic should be available when the therapy launches.
- In a smaller number of cases, the first CDx was approved slightly after the drug approval, typically within about 1 year, potentially creating a short-term gap between therapeutic approval and availability of an FDA-authorized test.
- For second entrants, the median lag widened to about 2–4 years after drug approval, suggesting that additional diagnostic suppliers generally enter the market only after the initial drug–diagnostic pairing is established.
- This pattern indicates that the CDx market evolves over a therapy's life cycle: the first test is usually available at launch, while competing or alternative tests continue to emerge over time.
- Two drug–biomarker pairings stood out for the number of approved CDx options: HER2–trastuzumab, which had 11 FDA-approved companion tests, and EGFR–osimertinib, which had 9 tests.
- Later entrants often appear to compete on features such as broader genomic coverage, alternative platforms, or less invasive sampling, rather than simply duplicating the original test.
- Overall, these findings suggest that FDA policy and market dynamics support both timely initial co-approval and subsequent entry of additional test options, which may expand access and competition over time.

5. Manufacturer distribution and market concentration

- The market for FDA-approved CDx involved more than 20 manufacturers, but approvals were concentrated among a relatively small number of firms.
- Roche and its affiliates (including entities such as Ventana and Foundation Medicine) accounted for 21 of 64 new CDx approvals (33%), making Roche the dominant manufacturer in this dataset (Figure 5).
- Roche's large share likely reflects its longstanding role in the CDx space, including early HER2 testing, PCR-based diagnostic platforms, and the later addition of NGS-based portfolio assets through affiliated companies.

Figure 5. Distribution of FDA-Approved New Companion Diagnostics by Manufacturer



- Beyond Roche, there was a second tier of manufacturers with multiple CDx approvals, including companies such as Agilent/Dako, QIAGEN, Abbott Molecular, Thermo Fisher, and Myriad Genetics (Figure 5).
- In total, seven manufacturers had more than one CDx approval, and together these firms accounted for about 78% of all new CDx approvals.
- The figure also shows that the top four manufacturers accounted for 64% of the market, reinforcing the idea of moderate-to-high concentration at the top of the industry.
- Overall, the manufacturer landscape suggests a market characterized by one leading player, several established multi-CDx firms, and a broader tail of smaller entrants, consistent with an innovation-driven but still concentrated regulatory space.

Regulatory and HEOR Implications

- CDx are increasingly central to precision medicine and should be treated as essential components of targeted treatment pathways.[1,3]
- Continued coordination of drug and diagnostic development is important to ensure timely test availability at treatment launch.[4]
- Growth in extension approvals suggests that reuse of existing platforms may improve regulatory efficiency.[2,5]
- The rise of NGS and liquid biopsy CDx highlights the need for reimbursement and coverage frameworks that can accommodate more complex diagnostic technologies.[3,6]
- Group/class labeling and similar regulatory innovations may help streamline access and reduce duplication.[5]
- As multiple manufacturers and tests enter the market, policies should support both competition and consistent quality standards.[2,7]

Conclusions

- FDA-approved CDx expanded markedly from 1998 to 2024.
- The field evolved from mainly single-marker tissue-based assays to NGS- and liquid biopsy-based technologies.
- Most first CDx were approved at or near drug approval, with later entrants expanding options over time.
- Existing CDx platforms are increasingly extended to additional drugs and indications.
- These trends reflect a maturing regulatory and technological landscape for precision medicine.

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