



Bipartisan Policy Center

Strengthening Regulatory Collaboration Between FDA and CMS

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HEALTH PROGRAM

Under the leadership of former Senate Majority Leaders Tom Daschle and Bill Frist, M.D., the Bipartisan Policy Center's Health Program strives to develop bipartisan policies that improve the nation's health outcomes, reduce health care costs, and make quality health care available, affordable, and accessible to all Americans. We believe the ideal health care system is one that ensures coverage for all individuals, prioritizes equity in health services, keeps people healthy, and improves care for patients.

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DISCLAIMER

The findings and recommendations expressed herein do not necessarily represent the views or opinions of BPC's founders, board of directors, funders, or advisors.

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Executive Summary

In the United States, two federal regulatory agencies are primarily responsible for the complex and important mandate of approving drugs for the marketplace and authorizing payment for them. Through the evaluation of information submitted to the agency, including clinical trial data, the Food and Drug Administration (FDA) ensures that drugs are “safe and effective” and that biologics meet the standard of “safety, purity, and potency.” The Centers for Medicare & Medicaid Services (CMS) administers the Medicare and Medicaid programs and, with respect to Medicare beneficiaries, determines if coverage for a product is “reasonable and necessary.”

The FDA’s scientific mandate allows it to intensely evaluate the technical aspects of drug development and safety. The agency does not consider payment or coverage issues. After the FDA has determined that a product can be brought to market, CMS must determine whether Medicare and Medicaid should cover and pay for it.

This policy brief lays out practical, bipartisan, and achievable steps for FDA and CMS to improve their collaboration with each other and with stakeholders. Because FDA and CMS are both agencies within the Department of Health and Human Services (HHS), the two share natural connections despite their different missions. The larger goal of enhanced agency collaboration is to provide access to safe and effective therapies to beneficiaries promptly while meeting CMS’ statutory requirements.

The following recommendations are designed to improve the information disparity between FDA and CMS by establishing a more balanced flow of information that fosters collaboration. Significantly, a majority of the policy recommendations do not rely on Congress to modify the existing statutes governing these agencies. Considering the complex, emerging challenges and the rapid pace of scientific advancement, CMS and FDA should actively coordinate messaging and decisions. The recommendations are not intended to alter statutory roles of the two agencies or adjust any of the current processes for approval or coding, coverage, and payment. Rather, the recommendations are focused on ensuring that CMS has timely information from FDA so that it can subsequently evaluate the drug products and make its independent coding, coverage, and payment decisions.

RECOMMENDATIONS

- On a quarterly basis, with consent from the respective product sponsor, FDA should provide to CMS the following materials:
 - a list of new molecular entities (NMEs) scheduled in alignment with their Prescription Drug User Fee Act (PDUFA) dates for the upcoming quarter;
 - a list of products under consideration by FDA via the accelerated approval pathway; and
 - a list of upcoming FDA Advisory Committee meetings, advanced-meeting materials, and contact information for the committee liaison. The committee liaison can serve as a resource for CMS coordination. CMS should share this information with all appropriate state Medicaid officials.
- Congress should provide additional funds, up to \$10 million per year, to the Coverage and Analysis Group (CAG) at CMS to expand its capacity.
- Congress should request that the Government Accountability Office (GAO) assess the current utilization and effectiveness of memorandums of understanding (MOUs) between CMS and FDA to identify potential areas for improvement and optimization. This review should examine whether there are any additional statutory changes required to fulfill the above recommendation related to information transfer.
- Annually, the Agency for Healthcare Research and Quality (AHRQ) should compile, organize, and analyze real-world evidence (RWE) obtained by CMS on drugs and biologics. This evidence should be shared with the FDA and the sponsors of these products.
- CMS should consider engaging with product sponsors of accelerated approval drugs before FDA market authorization in a method comparable to Transitional Coverage for Emerging Technologies (TCET). That engagement could include CMS officials observing meetings between FDA and the drug sponsor.
- With respect to surrogate endpoints, the National Institutes of Health (NIH), CMS, and FDA should convene a biomarker working group to help identify research priorities.
- To improve the understanding of the lifecycle of a drug and its development, FDA should implement informational training with state Medicaid programs to provide staff with information on the drug approval background. This would happen on an ongoing basis with a contact at the FDA to help keep Medicaid staff up to date on developments.
- CMS and FDA should create cross-agency training programs to foster a deeper understanding of each agency's functions and processes.

Introduction

“Any sufficiently advanced technology is indistinguishable from magic,” famed science fiction writer Sir Arthur Clarke tells readers.¹ A person could be forgiven for thinking this age of medical advancement is filled with magic; scientists can heal people by editing DNA, the building blocks of life. Yet, any scientist who has spent their life working on finding innovative breakthroughs will tell you, it’s not magic, it’s years of painstaking trial and error. It’s a fusion of scientific expertise and the ability to navigate a complex regulatory approval process governed by two vital entities: the Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS). This process is inherently intricate, focused not only on getting lifesaving and life-enhancing drugs to the American public but also on ensuring that only effective and appropriate drugs are being used. Ensuring the safety and efficacy of treatments that individuals rely on for their health and well-being is a responsibility that cannot be taken lightly. Is there a way to better navigate the existing legal framework to facilitate effective collaboration between FDA and CMS, ensuring that patients receive timely access to appropriate treatments without undermining the core responsibilities of each agency? Like any formidable challenge, the solution lies in breaking the issues down into manageable components, which is the aim of this project: to transform the notion of “magic” into a robust regulatory infrastructure.

In this report, the Bipartisan Policy Center lays out practical, bipartisan, and achievable steps designed to improve the exchange of information between policymakers and key regulatory bodies. These measures leverage the unique strengths of each agency to ensure that as new drugs gain approval, both FDA and CMS are well informed, enabling more-effective regulatory decisions. Our report focuses on the drug approval and payment processes by FDA and CMS. These recommendations seek to ensure that the two agencies have the benefit of each other’s knowledge and expertise, while retaining their separate processes.

Because CMS and FDA both fall under the Department of Health and Human Services (HHS), the report’s improved information-sharing mechanisms are particularly relevant, especially since the agencies respond to complex, emerging challenges and the rapid pace of scientific advancement. The recommendations are not intended to alter the current remits of the two agencies or to adjust any of the current processes for approval or coding, coverage, and payment. Rather, the recommendations focus on ensuring that CMS receives timely information from FDA so that it can effectively evaluate the drug products and make its independent coding, coverage, and payment decisions.

Improving communication and coordination between the agencies is critical to ensuring that relevant information is readily available for CMS' approval and coverage process. Better communication will improve the health care system's overall efficiency, effectiveness, and accountability, leading to better outcomes for patients and health care providers.

In the summer of 2021, FDA approved Aduhelm (aducanumab), a drug developed by Biogen for the treatment of Alzheimer's disease through the accelerated approval program.² Its approval sparked a wide range of reactions from involved parties. Some saw this development as a potential breakthrough in Alzheimer's treatment, offering hope for a solution. However, FDA's approval also raised concerns due to perceived limitations in the drug's effectiveness and to uncertainties surrounding its clinical benefits.

Before approval, FDA held an advisory committee meeting. The advisory committee expressed reservations about the drug's effects and whether the data demonstrated its effectiveness in treating Alzheimer's. Despite the committee's concerns, FDA proceeded with the approval; FDA rarely approves products after the advisory committee recommends against doing so. The FDA action led several members of the advisory committee to resign.³

Subsequently, CMS evaluated its coverage for the drug under a national coverage determination (NCD) and based upon its reasonable and necessary standard for coverage, finalized a decision to cover it under the coverage with evidence development (CED) mechanism.⁴ Stakeholders, including patient groups, criticized CMS' decision to restrict the use of an FDA-approved drug.

These outcomes prompted discussions about the need for potential changes in drug approval pathways, coverage policies, and pricing models. Furthermore, they initiated a broader conversation about striking the right balance between addressing the urgency of helping patients with unmet needs and ensuring that rigorous clinical evidence forms the basis of drug approvals.

This report does not specifically address what happened with Aduhelm, given that it is still being adjudicated, but raises many questions and anticipates additional scenarios in which FDA and CMS have different information or perspectives on a treatment's overall effectiveness and the standard of clinical benefit. The recommendations in this report aim to preserve each agency's valuable and distinct missions, while offering constructive and predictable pathways for information sharing to alleviate the burden of determining when to share information between agencies.

A Brief Primer on How CMS and FDA Interact

FDA's mandate to scientifically evaluate new treatments means staff intensely analyzes the technical aspects of drug development and safety. The agency rightly does not consider payment or coverage issues. In contrast, CMS' broader scope necessitates a diverse team capable of understanding the medical aspects and CMS regulatory structures after FDA has determined that a product is effective and is safe for the market. These differences underscore the distinct authorities of the two agencies, as well as the potential for information asymmetry where FDA might have information that would be helpful or valuable for the subsequent CMS decisions.

This report's recommendations lay out ways to address the information asymmetry, gather information in a more seamless manner, and ensure that relevant information is more readily available for subsequent CMS regulatory decisions. Improved collaboration would allow for a more balanced flow of information and collaboration while retaining the two agencies' separate missions.

The FDA assumes the crucial responsibility of ensuring that pharmaceutical therapies meet the rigorous standards of "safe and effective" (for drugs) or "safety, purity, and potency" (for biologics) before granting them legal permission to market the product within the United States. The agency reviews clinical trial data and other information submitted by drug sponsors to ensure that the medical product meets the approval standard, and that the benefits outweigh the risks for the indicated population. Marketing a drug or biologic in the United States requires FDA approval or licensure.

FDA operations contain several unique components, including:

- a dedicated team to review product submissions from a drug sponsor over several years before making the final decision regarding approval or licensure;
- public advisory committee meetings to review novel drugs or biologics or those with potential policy questions; and
- standard and predictable processes and timelines for approval or licensure established under the Prescription Drug User Fee Act (PDUFA). These processes encompass various stages, from preclinical to investigational new drug (IND), clinical trial phases, and review of submissions.

FDA's funding mechanism reinforces those statutory differences, as it receives funding from two primary sources: (1) discretionary appropriations from Congress and (2) industry user fees related to the review of medical products. For fiscal year 2022, user fees made up approximately 46% of FDA's overall budget, although it varied by each of the different centers at the agency.⁵ These user fees are part of a negotiated agreement between FDA and the pharmaceutical industry under the PDUFA, which Congress generally reauthorizes every five years. Given federal budgetary constraints, over time, the user fee percentage has increased. The FY2024 budget request related to user fees was \$3.3 billion, up from \$2.9 billion in FY2022.⁶

CMS operates under distinct criteria to determine the eligibility of therapies for reimbursement. This evaluation considers a range of factors, including the individual patient, comorbidities, and patient population. Two examples of the latter are the diverse aging population covered by Medicare and children covered through Medicaid. For Medicare coverage, CMS must rigorously assess whether a therapy is deemed "reasonable and necessary" for the specific Medicare population it serves. Within the Medicaid program, which is administered jointly with individual states, the Medicaid Drug Rebate Program (MDRP) imposes the requirement for coverage of medically accepted indications of drugs. Although states are not mandated to participate in the MDRP, all states opt to do so.

CMS' responsibilities extend beyond drug approvals to encompass a broad range of health care-related considerations, as the agency is responsible for administering the Medicare and Medicaid programs, which provide health care benefits to more than 160 million Americans.⁷ These responsibilities include payment policies for all covered services, such as hospitals, physicians, nursing homes, and dialysis; payment approaches (e.g., fee-for-service, managed care); coverage decisions at the local, state, and national levels; and overall program management (i.e., program integrity, enrollment, provider and beneficiary relationships, etc.). Not only does CMS administer Medicare and Medicaid, but it is also responsible for oversight of the Children's Health Insurance Program (CHIP) and the federal marketplace (i.e., HealthCare.gov). Given the agency's large footprint, President Biden's FY2024 budget request included \$1.5 trillion in mandatory and discretionary outlays for CMS.⁸ The majority of this funding is categorized as mandatory, leaving \$4.6 billion for discretionary funding for program management, which is less than one-half of 1%.⁹ Although CMS is responsible for all program management activities within Medicare, it shares Medicaid's and CHIP's management costs with states. As such, depending on overall state budgets and the ability to provide the required cost sharing, states could have differing levels of staff and expertise to determine coding, coverage, and payment decisions.¹⁰

CMS APPROVAL PROCESS

CMS does not consider “FDA approval or clearance alone [to] entitle that technology to Medicare coverage.”¹¹ Medicare coverage is subject to specific statutory coverage provisions, which include prohibitions on covering drugs for weight loss or weight gain as outlined in the authorizing legislation for Medicare prescription drug coverage.¹² Some coverage and payment steps may be automatic. For instance, once a drug receives a Healthcare Common Procedure Coding System code for Part B reimbursement, the statute dictates the payment methodology.

In situations where it is unclear whether it is “reasonable and necessary” for Medicare to cover a product or service, CMS can establish coverage policies at the national or local level. As of October 2023, CMS had 337 national coverage determinations (NCD), and 900 active local coverage determinations (LCD).¹³ LCDs apply at the regional level, and some of the 900 may be for the same product but in different regions.¹⁴ These policies represent a tiny fraction of the more than 1.1 billion services that Medicare paid for in 2022.¹⁵ NCDs and LCDs provide critical guidance on what Medicare beneficiaries might find covered. As part of the NCD process, CMS can utilize coverage with evidence development (CED) to collect additional data about specific populations when there is insufficient evidence to determine whether the product is reasonable and necessary, even if it has already received FDA approval. Putting a product under a CED allows for coverage and payment provided that certain parameters are met; approval is often for a limited population and is dependent on the collection of additional clinical data.

COVERAGE WITH EVIDENCE DEVELOPMENT

The Centers for Medicare & Medicaid Services uses CED as a part of coverage decisions for a variety of medical interventions and technologies, including new medical devices, pharmacogenomic tests, and other emerging technologies. By using CED, CMS generally ensures that patients have access to promising interventions while also generating evidence to inform future coverage decisions and provide clinicians with additional information about the product’s performance.¹⁶

While CMS has only used a national coverage determination with a CED for one category of on-label use of FDA-approved drugs—monoclonal antibodies for Alzheimer’s treatment—there may be instances where it would be beneficial for CMS to engage in additional discussions with drug sponsors. These discussions could be initiated in the following situations:

For drugs approved through the accelerated approval pathway, CMS might consider further dialogue if there is no consensus within the scientific community that the chosen surrogate endpoint is “reasonably likely to produce a clinical benefit.”

If FDA has held an advisory committee meeting to evaluate the data related to a drug’s approval, CMS may want to engage with drug sponsors if substantial concerns were raised about the data’s robustness and whether the drug was “reasonable and necessary” for the Medicare population.

CMS may also seek further discussions if the information provided in the FDA-approved label raises questions about whether the drug meets the “reasonable and necessary” standard for the Medicare population, particularly if the study population did not adequately represent Medicare beneficiaries or lacked diversity.

LABELING

The process of labeling pharmaceutical products is a highly structured part of FDA’s mission to ensure safety and efficacy. As part of a New Drug Application, the drug sponsor provides extensive data on the drug, including proposed labeling information regarding the indication for use. These initial indications define the medical conditions and patient populations for which the drug is intended. FDA reviews the application upon receipt, and a team of experts reviews the labeling information. The team can request additional information or changes to the labeling to make sure all usage and safety concerns are met. The agency must approve the final labeling. Because FDA monitors for safety and efficacy, if new information emerges, the agency can compel a sponsor to update the label with new indications or modifications of original ones.¹⁷

CMS is not bound by the FDA label and can utilize tools to restrict or expand coverage to Medicare beneficiaries with the most severe needs. For instance, by statute, Medicare must cover intended uses not included within the approved label of anti-cancer chemotherapeutic regimens if that use is supported in at least one of the following compendia: American Hospital Formulary Service Drug Information (AHFS DI); United States Pharmacopoeia Drug Information (USP DI); or American Medical Association Drug Evaluations.¹⁸ According to some estimates, 50%-75% of all drug (including biologics) usage in cancer care is off-label, and this percentage may be even higher for pediatric patients.¹⁹ Although there are statutory expansions, CMS’ flexibilities can lead to the narrowing of an approved, covered use of a drug. Recent research related to Part B drugs noted that “Medicare often added conditions beyond FDA approval ... and most often restricting coverage to patients with the most severe disease.”²⁰ With respect to Part D coverage, plan sponsors “covered the majority of novel therapeutics in the year following FDA approval, although access was often

restricted through prior authorization or step therapy and was dependent upon plan choice.”²¹

During interviews for this project, some provider and patient stakeholders expressed concerns regarding CMS’ current processes with respect to CED. They suggested that providing additional transparency to the CED process would be appropriate, as would finding a way to ensure provider and patient input.²² Some patient groups raised ethical concerns about a recent CED’s placebo-controlled trial. While this issue is outside the scope of this report, the Agency for Healthcare Research and Quality (AHRQ) released a report in 2022 recommending ways to improve the CED process.²³ For products without an NCD, a Medicare Administrative Contractor (a local Medicare contractor) independently evaluates coverage decisions and can opt to create an LCD using guidance from CMS.

Separately, some research and policy stakeholders expressed frustration that CMS has little flexibility in determining the overall payment for certain drugs. For instance, if CMS opts to cover a Medicare Part B drug, the statute dictates the required payment for that drug. CMS can opt to require an NCD with CED, but that only alters the pool of Medicare beneficiaries who can receive the drug product, not the amount the federal government pays. The policy challenge is particularly daunting for drugs in which the efficacy evidence may be sufficient for approval or licensure but may still have additional data or knowledge gaps making the determination of “reasonable and necessary” difficult. Despite this obvious policy conundrum and given the ongoing discussion around the Inflation Reduction Act, this report does not contain recommendations directly reforming CMS drug payment policies.

Current Coordination Efforts

EXISTING DRUG AND BIOLOGIC COORDINATION EFFORTS

Because FDA and CMS are both organizations under the HHS umbrella, they share natural connections. With respect to drugs and biologics, FDA and CMS currently coordinate on both general and specific issues, some of which are statutorily driven. Stakeholders provided insight regarding the existing coordination efforts and their utility including:

- quarterly meetings between the heads of the two agencies;
- a formal memorandum of understanding (MOU)²⁴;
- certain drug products receiving specific FDA designations that then have distinct types of payments at CMS; and
- a proposed CMS Center for Medicare and Medicaid Innovation (CMMI) model related to products receiving FDA Accelerated Approval status.²⁵

Despite that coordination, there is a significant opportunity to enhance the availability of pertinent information to support CMS in making well-informed decisions regarding complex reimbursement decisions.

Interagency Meetings

According to former staff, the CMS administrator and FDA commissioner meet quarterly to discuss items of mutual interest. While it is difficult to legislate actions of leadership, those regular meetings are an important signal that the agencies intend to work collaboratively. Midlevel center and group levels also hold coordination and ad hoc meetings. According to stakeholder feedback these are more common for devices than for drugs. However, the content or impact of these meetings is unknown, and participation is not (and likely should not be) public knowledge.

Memorandum of Understanding

In addition to regular meetings, CMS and FDA also have a process to share information. In 2010, the two agencies signed an MOU to improve information sharing by building “infrastructure and processes that meet the common needs for evaluating the safety, efficacy, utilization, coverage, payment, and clinical benefit of drugs, biologics and medical devices.”²⁶

The memorandum outlines procedures, safeguards, and decision-making processes to facilitate information sharing while adhering to applicable laws and protecting shared information. The MOU addresses information confidentiality, ameliorating concerns from stakeholders about sharing sensitive information. It also emphasizes regular oversight and re-evaluation to ensure the effectiveness and relevance of the agreement. There is little evidence that the MOU has had a substantial impact on improving the innovation pipeline, but its existence makes several of the following report recommendations easier to implement.

Differing CMS Reimbursement as a Result of FDA Designations

Beyond information sharing, Congress has established several FDA designations that enhance CMS payments. For instance, drugs that receive an orphan drug designation are eligible to receive a “transitional pass-through payment” for specific drugs or biologics administered in a hospital outpatient setting. These additional payments are temporary, lasting for at least two years but not exceeding three years. In addition, drug products receiving a qualified infectious disease product (QIDP) designation are eligible to receive CMS’ new technology add-on payment (NTAP). CMS pays 75% of drug costs in addition to the existing payment per the diagnosis-related group (DRG).²⁷

CMS Evaluation Process and Post Market Data Collection

In February 2023, CMS announced a new CMMI model known as the Accelerating Clinical Evidence Model, which tasks CMS with developing payment methods for drugs that have gone through FDA’s Accelerated Approval Process.²⁸ The goal was to test whether payment adjustments for accelerated approval drugs improve trial completion. FDA and CMS worked closely on developing and implementing the model.²⁹ The spending on these drugs is substantial. CMS spent “more than \$18 billion from 2018 to 2021 for the 18 drugs that correspond to the 35 drug applications granted accelerated approval with incomplete confirmatory trials past their original planned completion dates as of May 5, 2022.”³⁰ In March 2023, Senate Republicans sent a letter to HHS Secretary Xavier Becerra and CMS Administrator Chiquita Brooks-LaSure expressing concerns about the proposed model, which aims to encourage timely completion of confirmatory trials by reducing Medicare spending for drugs that have not yet completed the trials.^{31,32} Senate Finance Committee ranking member Mike Crapo (R-ID) and 17 of his colleagues stated that “if proposed and finalized as described, this profound policy shift would inevitably chill incentives for leveraging the FDA’s game-changing expedited regulatory avenue, which has served patients with life-threatening diseases, for decades.” CMS likely introduced this proposal to address concerns related to CMS’ coverage and payment of monoclonal antibodies designed to target amyloid in the treatment of Alzheimer’s, but the model’s basic premise overlooks the

distinctive nature of both CMS and FDA decisions regarding these drugs. Perhaps acknowledging this limitation, in October 2023, in its update on the various cost reduction models, CMS stated that it will “continue to monitor developments.”³³ Thus, at this time, there is no available information on the design or implementation of the model, and there is no guarantee that it will be implemented.³⁴

EXISTING DEVICE COORDINATION EFFORTS

Although our primary focus is on drug-related policy recommendations, CMS and FDA have also collaborated on medical devices, and certain elements of these actions could serve as a valuable template for drug models. These coordination points include investigational device exemption studies, parallel review, and Transitional Coverage for Emerging Technologies (TCET).

Investigational Device Exemption Studies

CMS covers the routine costs of care for device trials. These investigational device studies undergo centralized review, and coverage policies are established to facilitate device payment within a clinical trial context.³⁵ In 2015, FDA and CMS entered into a separate MOU on investigational devices in which FDA agrees to categorize them in a way that allows CMS to offer coverage.³⁶ The MOU outlines FDA’s responsibility in categorizing investigational devices as Category A (experimental and, as such, not covered by CMS) or Category B (nonexperimental/investigational and, as such, covered by CMS). CMS, under its regulatory authority, has issued regulations regarding the payment and coverage of Category B investigational devices, but it does not cover Category A devices.³⁷

Parallel Review

In 2010, FDA and CMS announced a pilot program called the parallel review program, which allows the two agencies to concurrently evaluate a subset of medical devices.³⁸ According to the announcement, the purpose was to “serve the public interest by reducing the time between FDA marketing approval or clearance decisions and CMS national coverage determinations.”³⁹ After a review of public comments, the agencies published their guiding principles for parallel review, which, among other things, noted that device candidates would be new technologies that “fall within the scope of Part A or Part B Medicare benefit category and are not subject to an NCD.”^{40,41} The first programmatic success was in 2014, when a colon cancer test successfully completed the parallel review process. In August of that year, the agencies made a joint announcement regarding FDA’s approval and CMS’ coverage of a cancer biomarker test.⁴² However, even though the review program has been in operation for over a decade, only two other diagnostic devices have successfully

undergone the complete parallel review process: a companion diagnostic (i.e., a medical device essential for the safe and effective use of a drug) called FoundationOne® CDx and Cologuard®, an at-home colon cancer screening test.^{43,44}

Thus, this approach has only streamlined the approval and coverage of medical devices in a limited number of devices.⁴⁵

Transitional Coverage for Emerging Technologies

In January 2021, CMS published the “Medicare Coverage of Innovative Technology” final rule. The rule included a definition of “reasonable and necessary,” guaranteeing Medicare coverage for newly approved medical devices granted breakthrough status. Later in the year, this rule was repealed by CMS citing stakeholder concerns about patient safety and benefit category designations.^{46,47} To facilitate rapid access to new technologies, CMS in June 2023 proposed a new coverage pathway, the TCET, for breakthrough devices.⁴⁸ This voluntary pathway would use current NCD and CED processes to expedite Medicare coverage of certain breakthrough devices.⁴⁹ Under the TCET program, CMS will have the opportunity to conduct an “early evidence review,” even before FDA has made a review decision.⁵⁰ As this is a newly announced program, results from its implementation are not available for evaluation. However, BPC’s recommendations below follow many of the basic constructs of this model, including ensuring that there is early communication with CMS.

Federal Policy Recommendations

The following recommendations would improve coordination between FDA and CMS by establishing a more balanced flow of information and fostering collaboration between the agencies. Importantly, most of these recommendations are not reliant on congressional action.

SHARING DRUG AND BIOLOGIC INFORMATION

Recommendation: To ensure that CMS has timely information available from FDA, FDA should provide to CMS the following materials on a quarterly basis, with consent from the respective product sponsor:

- **a list of new molecular entities (NMEs) scheduled in alignment with their Prescription Drug User Fee Act (PDUFA) dates for the upcoming quarter;**
- **a list of products under consideration by FDA via the accelerated approval pathway; and**
- **a list of the upcoming FDA Advisory Committee meetings, advanced-meeting materials, and contact information for the committee liaison. The committee liaison can serve as a resource for CMS coordination. CMS should share this information with all appropriate state Medicaid officials.**

Per the 2010 MOU, this disclosure should include appropriate safeguards to protect against disclosure of sensitive information.

Streamlining the consolidation of information will enable CMS to access potentially valuable data for its determination earlier in the process. In doing so, the FDA should rely upon established safeguards, including obtaining consent from sponsors and ensuring confidentiality, before sharing any nonpublic information.

When FDA is considering new therapies, especially those with an accelerated approval designation, this recommendation would give CMS additional preparation time for drugs lacking existing coverage and coding mechanisms. This would also reduce the time gap between FDA approval and CMS decision. Although much of this information is already publicly available, the FDA lacks a formalized mechanism to share it with CMS, and it might be difficult for CMS staff to gather this information.

With respect to the accelerated approval products, the communication does not imply that CMS would alter its decision-making process for such products.

Instead, the recommendation aims to keep CMS informed about the approval of these products, enabling it to make adequate preparations for coverage decisions following approval. Currently, such information sharing occurs informally. The recommendation is to establish a formalized process to ensure consistency across all products, recognizing that not all accelerated approval determinations are known in advance.

Finally, the communication should include any plans for holding an advisory committee meeting related to the product under review. This should include relevant meeting materials and contact information for the committee liaison. The committee liaison can serve as a resource for coordination, which may include identification of committee members who can further serve as a resource for CMS.

The FDA holds advisory committee meetings to gather insights from external experts, patient advocacy groups, and other stakeholders. These meetings provide a platform for in-depth discussions on the safety, efficacy, and approval of specific drugs.⁵¹ Sharing information about upcoming meetings with CMS would allow both agencies to align their efforts and to share their perspectives. This alignment would ensure that CMS' evaluation process considers the input and outcomes of these important meetings as part of coverage decisions.

Given that this information is not only relevant to Medicare coding, coverage, and payment decisions, but also to Medicaid decisions, CMS should share this information with the relevant Medicaid officials.

CMS and FDA can already share this information under the MOU. However, absent a required structure, FDA likely transfers the information only when there is a specific request from CMS. Therefore, BPC recommends a structured knowledge transfer process that would rely less on individual's initiative at the respective agencies. Such a process would also be more sustainable and reliable. The FDA and CMS should establish a system for ongoing evaluation and improvement of the knowledge transfer process. Regularly assessing the process's effectiveness and making necessary adjustments would ensure that it remains relevant and responsive to evolving needs. This continuous improvement approach would help CMS and FDA stay adaptable and agile in addressing challenges and fostering collaboration.

Recommendation: Congress should provide additional funds, up to \$10 million per year, to the CMS Coverage and Analysis Group (CAG) to expand its capacity.

CMS has delegated to the CAG the daunting task of reviewing all the available evidence and determining if and how a drug product should be coded, covered,

and paid within Medicare, among other key duties. Despite CAG's expansive task, Congress is not made aware of the funding for this important entity. An extensive review of the HHS budget justifications and report language indicates that the funding numbers for CAG are not readily available to the public.⁵² An additional \$10 million would provide dedicated funding for CMS to make strategic investments in expanding CAG's workforce. The CAG workforce is responsible for overseeing local and national coverage determinations and increasing technical and clinical expertise, enabling it to efficiently process a larger volume of coverage determinations.

By considering funding improvements, CMS can better manage its extensive portfolio and maintain high-quality evaluation processes; this additional funding will be necessary for CMS to implement some of the other recommendations in this report as they are functions of the CAG.

Some stakeholders, including patient advocate groups and providers, noted difficulties in accessing critical information and establishing meaningful contact with the agency. This issue raises legitimate concerns regarding the accessibility and communication effectiveness of CMS and highlights the need for dedicated attention and improvement. BPC also recommends that CMS undertake a comprehensive audit of its engagement processes with stakeholders regarding coverage decisions. The audit would also encompass a thorough examination of the processes, communication channels, and mechanisms available for stakeholders to interact with CMS within the statutory framework. And it would pinpoint areas for improvement based on the collective experiences of multiple stakeholders and the currently available communication channels at the agency's disposal.

Recommendation: Congress should request that the Government Accountability Office (GAO) assess the current utilization and effectiveness of memorandums of understanding between CMS and FDA to identify potential areas for improvement and optimization. This review should examine whether any additional statutory changes are required to fulfill the above recommendation related to information transfer.

To enhance knowledge sharing between FDA and CMS, the GAO should evaluate the existing or amended MOU for modifications and improvements. For the GAO to undertake the work of an investigation or audit, a member of the House of Representatives or Senate must directly make a request to the agency. Given competing priorities, GAO prioritizes requests that originate from senior congressional leaders and committee and subcommittee chairs and ranking members. As such, BPC suggests that at least one member of a congressional committee with jurisdiction over workforce programming make the request.

CLARITY IN POST-MARKET DATA AND ACCELERATED APPROVAL

Real-World Evidence

Recommendation: To improve the accuracy of the product label, the Agency for Healthcare Research and Quality (AHRQ) should annually compile, organize, and analyze real-world evidence (RWE) obtained by CMS on drugs and biologics. AHRQ should share this evidence with FDA and the sponsors of these drug products.

The Agency for Healthcare Research and Quality, operating within HHS, is the lead federal agency in producing and analyzing data to improve health care. AHRQ works with CMS to design and review CED studies.⁵³ The agency has the infrastructure and expertise to leverage existing health care data systems, such as CMS claims data and FDA's RWE, to provide insights regarding the safety and effectiveness of medications in the real world. AHRQ regularly undertakes systematic evidence reviews.⁵⁴ And recently, CMS proposed that under the TCET program, it will share its Evidence Preview—"a systematic literature review that would provide early feedback on the strengths and weaknesses of the publicly available evidence for a specific item or service"—with AHRQ. This positions AHRQ as the best option for a comprehensive review and distribution of RWE for CMS and FDA.

This monitoring aims to improve the accuracy of product label updates carried out by FDA, particularly in the context of coverage, by ensuring that these updates accurately mirror the real-world performance of these drugs. This is especially pertinent because the older Medicare population is rarely included in clinical trials. As the 2022 National Academies of Sciences, Engineering, and Medicine report shows, clinical trials often do not adequately represent the broader patient demographics encountered in real-world health care scenarios.⁵⁵ This shortcoming highlights the importance of how agencies could use this data.

Clinical trials for rare disease treatments have different challenges, including recruitment, trial design, and outcome measures. The criteria for participation in rare disease clinical trials can be extraordinarily complex and specific, making it challenging to gather sufficient data during the approval process. Because Medicaid is the payer for a significant portion of children with rare diseases, the collection of RWE becomes especially relevant in these cases, where it can shed light on the effectiveness and safety of drugs in populations with unique health care needs.

As the pharmaceutical landscape evolves and approved products have higher price points and less information about their durability, collecting RWE becomes even more important. For instance, it is still unknown how long gene therapies work, which is why post-market data gathering is so important.

Some products, such as one for hemophilia, have been shown to improve health outcomes for at least two years, but one model suggests that it might improve health outcomes for up to 25 years.⁵⁶ A gene therapy approved in 2017 for vision loss has an approved label, noting efficacy for at least three to four years.^{57,58} Finally, a recently approved Duchenne gene therapy has an unknown length of effect.⁵⁹ Because some gene therapies could be curative or have long-term durability, gathering long-term data is important for properly evaluating the efficacy and value of the product to the patient. Post-market surveillance via registries and other methods will likely be required for long-term data collection, filling critical knowledge gaps and ensuring that patients receive the most appropriate and beneficial treatments.

Both the FDA and CMS have mechanisms for gathering real world data and evidence on the clinical benefit of medical products. For instance, CMS uses CED to track drug usage for clinical evidence.⁶⁰ Finally, CMS has a wealth of information from claims data that may become more relevant as artificial intelligence advances.

This proposed annual compilation would supplement the work that FDA is already doing. The FDA uses a risk-based approach to prioritize its post-market monitoring activities. The agency focuses on products that pose the greatest risk to public health and uses a variety of tools to assess these risks, including epidemiological studies, randomized controlled trials, and observational studies. Additionally, FDA has several mechanisms to act when safety issues arise, including labeling changes, warnings, and restrictions on product use. To gather appropriate data, the FDA utilizes:

- the FDA Adverse Event Reporting System, a computerized database to support post-marketing safety and surveillance;
- the MedWatch program for health care professionals to voluntarily report serious reactions and problems associated with drugs and medical devices;
- the Medication Errors Reporting Program, run within the Center for Drug Evaluation and Research, which provides FDA with information to “evaluate causality, and analyze the data to provide feedback to others at FDA;”⁶¹ and
- the Sentinel Initiative, which includes epidemiology, clinical medicine, pharmacy, statistics, health informatics, data science, and network operations to support post-market safety analyses through three coordinating centers.⁶²

Further, FDA is directed by statute to develop a framework for incorporating RWE into regulatory decision-making.⁶³

The FDA’s use of Sentinel to answer CMS’ questions is unknown, which may suggest one area where the two agencies could coordinate more closely. Some stakeholders mentioned the need for continuous data gathering processes, rather than relying upon registries. This could be particularly useful in the rare

disease space, where the data is limited. AHRQ could provide some additional insight regarding Sentinel data, ideal data sources, and how to best marry FDA and CMS real-world data sets.

Accelerated Approval

Recommendation: CMS should engage with product sponsors of accelerated approval drugs before FDA market authorization in a method comparable to Transitional Coverage of Emerging Technologies (TCET). That engagement could include CMS officials observing meetings between FDA and the drug sponsor.

The accelerated approval pathway allows FDA approval based on a surrogate endpoint, which is “reasonably likely” to produce a clinical benefit. To obtain confirmation of the clinical benefit, any product approved under this pathway must be subject to confirmatory trials (i.e., post-market data). However, FDA and CMS do not necessarily coordinate with respect to the confirmatory trials (e.g., endpoints, design, and milestones for these studies), which could potentially leave sponsors with multiple and potentially conflicting requirements. As our scientific knowledge advances, the expectation is that this initial evidence will become even more robust through further research, including confirmatory trials. This becomes particularly significant because multiple ongoing studies may rely on the same surrogate endpoint for evaluation.

Having CMS observe the meetings between FDA and the drug sponsor, where they discuss trial design, interim results, and other drug development issues, could help CMS gather critical information about the drug. As such, CMS’ coverage decisions will be better informed.

Either within the same conversation or with multiple conversations, CMS and FDA could, along with the product sponsor, determine important knowledge gaps and goals for post-market studies. These expectations could be set earlier in product development and review to allow appropriate time for coordination and consultation as necessary, while still meeting PDUFA timeline goals. The PDUFA timelines specify a 10-month review period for standard applications and a six-month review for priority reviews. These timeframes are measured from the 60-day filing date (or 12 months and eight months, respectively, if counted from the date of submission of the application).⁶⁴

These activities would supplement the existing CMS process, as sponsors can always engage with CMS on these post-market studies, ensuring they understand the information required by the agency.

Recommendation: With respect to surrogate endpoints, NIH, CMS, and FDA should develop a process to help identify biomarker research priorities. This could be accomplished by CMS joining the existing Foundation for the NIH Biomarkers Consortium.

SURROGATE ENDPOINTS EXPLAINED

FDA's accelerated approval process allows the agency to approve medicines based on their impact on a **surrogate or intermediate endpoint** for drugs targeting a serious condition with an unmet need. Clinical endpoints, such as overall survival, can take years to measure. Through the accelerated approval pathway, FDA has a way to speed up this process. They can approve a new medicine based on something that is easier and quicker to measure than the ultimate outcome—an intermediate or surrogate endpoint. Surrogate endpoints may include a laboratory measurement, radiographic image, physical sign, or other measure thought to predict clinical benefit. Surrogate endpoints are not available for all diseases, but ongoing research is identifying more of them.

The FDA classifies surrogate endpoints based on the level of clinical validation, or how well they've proven to reflect actual clinical outcomes: candidate, reasonably likely (utilized for accelerated approval), and validated. In some diseases, **biomarkers** can serve as surrogate endpoints. Biomarkers are measurable characteristics of the body, including imaging studies and blood markers. However, not all biomarkers can be used as surrogate endpoints.

For instance:

- In cancer, “progression-free survival” (i.e., the tumor not expanding while the patient receives the medication) may serve as a surrogate endpoint eligible for accelerated approval.
- For women who have a history of pre term birth while pregnant with just one child and are currently pregnant with only one child, FDA has indicated that an appropriate surrogate endpoint for accelerated approval would be delivery prior to 37 weeks, provided that the drug is a progesterone analog.

For a list of all surrogate endpoints that FDA has utilized in its approval or licensure process, visit [here](#).

As discussed previously, CMS and FDA have both been actively addressing accelerated approval drugs that rely on surrogate endpoints.⁶⁵ In 2015 and 2016, FDA and the National Institutes of Health (NIH) established a working group and developed the “BEST (Biomarkers, Endpoints, and other Tools)” Resource.⁶⁶ NIH has several divisions focusing on the development of biomarkers for specific disease states. For example, the National Institute of Neurological Disorders and Stroke offers funding opportunities to research biomarkers.⁶⁷ The National Institute on Aging funds studies on biomarkers and other surrogate

endpoints, such as vision changes related to Alzheimer’s disease.⁶⁸ As part of its efforts to address chronic pain and end opioid addiction, the NIH Helping to End Addiction Long-term Initiative has funded research on pain biomarkers.⁶⁹ In all of these examples, NIH looks to the FDA’s use of surrogate endpoints, including biomarkers, in its evaluation of tests and treatments. NIH’s patient focused drug development page hosts FDA resources on developing biomarkers.

In light of the ongoing policy discussions concerning surrogate endpoints, CMS, FDA, and NIH should collaborate to identify and prioritize research on surrogate endpoints. To bridge knowledge gaps related to specific surrogate endpoints, these agencies must maintain consistent communication regarding their ongoing projects and priorities. One way in which this could occur is through utilizing existing opportunities, such as the Foundation for the NIH Biomarkers Consortium, which includes FDA and NIH, though CMS has not yet joined this initiative.⁷⁰ This absence of information sharing underscores the significance of implementing the recommendations outlined in this report. Given these agencies’ wide scopes, it can be challenging for them to remain aware of all ongoing activities. Predictable and purposeful information sharing, as proposed in these recommendations, is crucial to ensure that each agency is well-informed.

As medicine evolves, so does understanding of biomarkers and other potential surrogate endpoints. Research and medical experts should lead regulators’ use of surrogate endpoints. The FDA and CMS are tasked with evaluating the latest research when making their approval and coverage decisions; this working group would help ensure that research is at the forefront. This is particularly important when dealing with rare diseases, where neither FDA nor CMS will necessarily have a team of experts, but NIH might.

IMPROVING COORDINATION WITHIN MEDICAID

Recommendation: To improve the understanding of the lifecycle of a drug and its development, FDA should implement informational training with state Medicaid programs to provide them with information on the drug approval background. This would happen on an ongoing basis with a contact at FDA to help keep Medicaid staff up to date on developments.

The FDA, as the regulatory agency responsible for evaluating and approving drugs, possesses a wealth of information regarding the approval process, the scientific evidence supporting drug approvals, and the post-marketing surveillance that ensures ongoing safety and efficacy. To ensure that the information is most relevant to the Medicaid officials, FDA should start by surveying various staff—Medicaid directors, chief medical officers, pharmacy

directors, budget analysts, etc.—to determine which information is useful but not readily available. Once the review is completed, FDA should design a program addressing the needs identified by state Medicaid personnel.

CROSS-AGENCY TRAINING

Recommendation: CMS and FDA should create cross-agency training programs to foster a deeper understanding of each agency's functions and processes.

Cross-agency initiatives or detail positions have the potential to help staff members from both FDA and CMS gain firsthand experience of their counterparts' roles and responsibilities, enhancing communication and collaboration for more effective cross-agency cooperation. Detail positions, where an agency employee receives a temporary assignment from one government agency or organization to another for a specific time or project, already exist at the agency level and crafting rotating detail positions for agency staff to train and shadow their counterparts would be valuable. Implementing specific cross-agency rotations would allow FDA personnel to spend time at CMS, gaining insights into the intricacies of health care reimbursement, coverage determinations, and the broader health care policy landscape. Conversely, CMS staff could learn more about the FDA's regulatory processes, including drug and medical device evaluations, clinical trials oversight, and safety monitoring. This mutual exposure would empower employees to grasp the challenges and priorities of the other agency, fostering a more comprehensive perspective.

Conclusion

The gap between the regulatory bodies evaluating drugs and biologics and the pace of scientific advancement is growing exponentially. While understanding and preserving the differences between FDA and CMS, these recommendations will help undergird efforts to improve collaboration between the two agencies and support the transfer of knowledge.

At BPC, we know that smart strategic changes can have outsized effects when they are implemented thoughtfully. These recommendations were formulated after extensive stakeholder engagement, and we are confident that they will provide FDA and CMS with the essential resources to achieve heightened coordination, benefiting not only Medicare and Medicaid beneficiaries but also the wide range of health care recipients.

Glossary of Terms

AHRQ	Agency for Healthcare Research and Quality
CAG	Coverage and Analysis Group
CED	Coverage with Evidence Development
CHIP	Children's Health Insurance Program
CMMI	Center for Medicare and Medicaid Innovation
CMS	Centers for Medicare & Medicaid Services
FDA	Food and Drug Administration
GAO	Government Accountability Office
HHS	Department of Health and Human Services
LCD	Local Coverage Determination
MDRP	Medicaid Drug Rebate Program
MOU	Memorandum of Understanding
NCD	National Coverage Determination
NIH	National Institutes of Health
NME	New Molecular Entities
PDUFA	Prescription Drug User Fee Act
RWE	Real-World Evidence
TCET	Transitional Coverage for Emerging Technologies

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