FDA-2026-N-4492-0001

Research!America submits these comments in response to the Food and Drug Administration's Drug Repurposing for Unmet Medical Needs; Request for Information Docket No. FDA-2026-N-4492-0001.

July 4, 2026

Executive Summary

Research!America appreciates the Food and Drug Administration's (FDA) Request for Information (RFI) on drug repurposing for unmet medical needs. The questions posed in the RFI provide an important opportunity to examine how the pathway from scientific discovery through evidence generation, regulatory recognition, and ultimately patient benefit can be strengthened.

Drug repurposing has already improved the lives of patients across a wide range of diseases and conditions. Advances in biomedical science, artificial intelligence, and clinical research, together with growing opportunities to learn from real-world data and clinical experience, continue to expand our ability to identify promising new therapeutic uses for existing medicines.

We believe the principal challenge facing drug repurposing is the lack of sustainable resources needed to advance promising repurposing candidates from scientific discovery to patient benefit.

These comments recommend practical steps FDA and its federal partners can take to help address that challenge by strengthening evidence generation, facilitating regulatory recognition of new uses, and improving coordination across federal partners.

Introduction

Research!America appreciates the opportunity to respond to the Food and Drug Administration's Request for Information regarding drug repurposing for unmet medical needs.

Research!America is a nonprofit, nonpartisan alliance that advocates for science, discovery, and innovation to achieve better health for all. Our alliance includes patient organizations, academic research institutions, medical centers, professional societies, industry, philanthropic organizations, and other stakeholders committed to accelerating medical progress.

Research!America's comments focus on four questions posed by FDA that are central to strengthening the pathway from scientific opportunity to patient benefit:

1. In cases where there appears to be no commercial interest in adding a new use through a supplemental application, what are the barriers to repurposing drugs to address unmet needs?
2. From the perspective of patients and clinicians, what are the barriers to using FDA-approved drugs for unapproved uses when a prescriber determines a drug is medically appropriate for a patient?
3. What could FDA and other federal partners do to address these barriers?
4. How can FDA and other federal partners collect and use data about unapproved uses for FDA-approved drugs to better understand how they are being used in the community?

FDA Question 1: In Cases Where There Appears to Be No Commercial Interest in Adding a New Use Through a Supplemental Application, What Are the Barriers to Repurposing Drugs to Address Unmet Needs?

In the traditional drug development model, a commercial sponsor is responsible for generating the evidence needed to support a new indication, engaging FDA throughout the regulatory process, pursuing labeling changes, facilitating reimbursement, and promoting clinical awareness. For many repurposing opportunities, particularly those involving generic medicines, rare diseases, or other conditions that attract limited commercial interest, nonprofit organizations, academic investigators, patient organizations, or other stakeholders may be prepared to lead these efforts. However, they often lack the sustainable resources needed to move promising repurposing candidates from scientific opportunity to patient benefit.

FDA Question 2: From the Perspective of Patients and Clinicians, What Are the Barriers to Using FDA-Approved Drugs for Unapproved Uses When a Prescriber Determines a Drug Is Medically Appropriate for a Patient?

The ability of clinicians to prescribe FDA-approved drugs for unapproved uses provides important flexibility within the health care system, particularly for patients with serious, rare, or difficult-to-treat conditions. At the same time, Research!America believes the greater opportunity lies in reducing the circumstances in which patients and clinicians must rely on off-label prescribing by strengthening the pathway through which robust evidence can support new FDA-approved indications.

When evidence supporting a new use is reflected in FDA-approved labeling, patients and clinicians benefit from more consistent incorporation into treatment guidelines, clinical reference resources and compendia, reimbursement decisions, and routine clinical

practice. By contrast, off-label prescribing may be accompanied by inconsistent insurance coverage, variable institutional practices, and uneven dissemination of clinical information.

FDA Question 3: What Could FDA and Other Federal Partners Do to Address These Barriers?

The barriers described above reflect a broader coordination and incentive challenge rather than a single regulatory obstacle. The following recommendations focus on opportunities for FDA and its federal partners to strengthen evidence generation, clarify regulatory pathways for non-commercial developers, improve coordination across federal agencies, build upon existing authorities and initiatives, and better identify promising repurposing opportunities for further evaluation.

Clarifying Pathways for Non-Commercial Developers

Many promising repurposing opportunities emerge outside traditional commercial development pathways. Academic investigators, patient organizations, nonprofit organizations, philanthropic funders, and health care providers frequently play important roles in identifying and advancing new therapeutic uses for existing medicines.

FDA could further clarify how non-commercial stakeholders can engage with the agency, what types of evidence may be appropriate in different circumstances, and how existing regulatory pathways may be applied when traditional commercial incentives are absent. Greater clarity would help stakeholders understand the evidence needed to support regulatory review and enable more efficient development of promising repurposing opportunities.

Sustainable Financing

Generating the evidence needed to support new FDA-approved indications remains the principal challenge when traditional commercial incentives are absent. Achieving that objective requires substantial financial resources, sustained scientific expertise, and long-term coordination. For many promising repurposing opportunities, no organization has both the incentive and the resources to support the studies needed to advance new indications. As a result, promising therapeutic opportunities may never generate the evidence needed to support regulatory recognition, broader reimbursement, and patient access.

The federal government should consider whether additional financing mechanisms, incentives, or a combination of the two are needed to address this market failure. When successful repurposing improves health outcomes or reduces downstream health care

costs, society often realizes substantial value even though no individual stakeholder has sufficient incentive to invest in the evidence generation needed to achieve those outcomes.

Examples of potential approaches include dedicated competitive funding programs for evidence generation, shared savings models that reinvest a portion of downstream public savings into future repurposing research, bond funds, and new regulatory or other "push or pull" incentives.

Building Upon Existing Authorities and Initiatives

FDA has already established several authorities and initiatives that provide a foundation for advancing drug repurposing.

Authorities established through the MODERN Act provide a mechanism through which certain labeling updates may be considered when new scientific evidence or accepted uses in clinical practice are not reflected in approved labeling. Project Renewal demonstrates how systematic review of the published scientific literature can support labeling updates for older therapies when appropriate scientific evidence exists. CURE ID provides valuable opportunities to capture clinical experience involving difficult-to-treat diseases and novel uses of approved therapies.

Building upon these complementary efforts could enable FDA to identify promising repurposing opportunities across a broader range of unmet medical needs, strengthen the evidence supporting new uses, and facilitate broader translation of scientific advances into clinical practice.

Strengthening Coordination Across Federal Partners

No single federal agency can address every barrier affecting drug repurposing. Realizing the full health benefits of repurposed therapies will require greater coordination among FDA and other federal partners, including NIH, CMS, and AHRQ.

One particularly important opportunity is earlier coordination between FDA and CMS. Earlier engagement can help investigators generate the types of evidence needed to support both FDA review and downstream coverage decisions, reducing unnecessary delays between labeling updates and patient access. Broader coordination across federal agencies can also help align research priorities, evidence generation, regulatory review, health services research, and coverage policies in ways that more efficiently translate promising repurposing opportunities into patient benefit.

Such coordination could also help ensure that evidence generation strategies are informed early by the scientific, regulatory, reimbursement, and patient-centered evidence needs of multiple federal partners.

Convening Stakeholders to Advance Practical Solutions

FDA is uniquely positioned to convene researchers, patient organizations, nonprofit developers, manufacturers, payers, philanthropic organizations, and other federal agencies to identify practical solutions to persistent barriers to drug repurposing.

Such discussions could help align evidence generation, regulatory pathways, coverage considerations, and sustainable financing strategies while building upon existing authorities and initiatives. By fostering collaboration across the public and private sectors, FDA can help ensure that promising repurposing opportunities are more consistently translated into patient benefit.

FDA Question 4: How Can FDA and Other Federal Partners Collect and Use Data About Unapproved Uses for FDA-Approved Drugs to Better Understand How They Are Being Used in the Community?

The health care system generates substantial information regarding how FDA-approved drugs are used in clinical practice. Electronic health records, claims data, disease registries, clinical research databases, and other sources of real-world data offer valuable opportunities to better understand patterns of use, patient outcomes, and areas where additional research may be warranted. Artificial intelligence and other advanced analytical tools can help identify promising repurposing opportunities from these large and diverse data sources.

AHRQ could play a significant role in this effort. Its expertise in health services research, outcomes research, and data science could help identify, analyze, and prioritize information that warrants further investigation.

It may be fruitful to focus on patterns of insurance coverage denials based on "experimental" or "investigational" use. Such information could help identify therapeutic areas where clinically meaningful off-label use may warrant further scientific evaluation.

Large-scale research resources such as the All of Us Research Program and the VA's Million Veteran Program may offer valuable opportunities to identify promising repurposing candidates and generate hypotheses for future study.

We also perceive strong potential in partnering with the Patient-Centered Outcomes Research Institute. PCORI's research infrastructure and emphasis on real-world clinical questions could help support the evaluation of promising repurposing candidates and

accelerate the translation of evidence supporting promising repurposed therapies into clinical practice.

Conclusion

FDA has a unique opportunity to strengthen the pathway through which promising repurposing opportunities are translated into better care for patients. We applaud the agency's interest in this important effort and would welcome the opportunity to be a resource as this work moves forward.