Arnold Ventures

June 10, 2026

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, Maryland 20852

Re: Drug Repurposing for Unmet Medical Needs; Request for Information FDA–2026–N–4492

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Dear Acting Commissioner Diamantas,

Thank you for the opportunity to provide input to the Food and Drug Administration (FDA) on its efforts with respect to generic drug repurposing to address unmet medical needs.

Arnold Ventures (AV) is a philanthropy dedicated to investing in evidence-based policy solutions that maximize opportunity and minimize injustice. As a philanthropy, we do not accept funding from industry or have a financial stake in policy outcomes. Our work within the health care sector is driven by the recognition that the system costs too much and fails to adequately care for the people it serves. Our work spans a range of issues including FDA accountability, prescription drug prices, commercial-sector prices, provider payment incentives, Medicare sustainability, and Medicaid.

AV has invested significantly in research and policy development to strengthen efforts to identify new uses for generic drugs. In response to FDA's request for information on a variety of topics related to generic drug repurposing, we drew from AV-funded research to focus our comments on Topic 4: *Barriers and Opportunities.*

Barriers and Opportunities

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 [generic] drugs to address unmet needs?*

The high cost of clinical trials to determine a drug's efficacy cannot be offset by future profits. Determining whether a generic drug can be used for a new purpose requires significant upfront investment to fund a clinical trial. The generic market is highly competitive, however, with low prices that limit potential returns. That means that manufacturers do not have strong financial incentives to invest in generic repurposing. As a result, repurposing efforts are limited and are typically led by government agencies, academic institutions, or nonprofit organizations with philanthropic support.[1]

It is difficult for non-manufacturers (e.g. nonprofit organizations) to petition FDA for labeling changes. FDA's label change process is not intended for organizations other than drug manufacturers. It was designed for the original New Drug Application (NDA) holder to petition FDA for changes to a drug's label, even once the drug is generic. This process is needlessly complicated when the company that originally held the NDA no longer exists and even more so when the drug is manufactured by multiple generic manufacturers.[2]

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Further, non-manufacturer organizations have great difficulty assuming product-liability risks that come with label change petitions. Organizations that are not drug manufacturers rarely have the insurance or compliance infrastructure necessary to take on the liability related to a new indication.[3] Most organizations in this space are small nonprofit organizations funded by philanthropy.[4]

There is limited, dedicated federal investment in late-stage clinical trials to determine whether a generic drug works for a new use.[5] Nonprofit organizations and philanthropies are trying to fill this gap, but the government should dedicate more resources to support late-stage trials to address a clear market failure and to fill a significant public health need.

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?*

Off-label use is an important and helpful option for patients and clinicians but presents various challenges and often does not sufficiently inform changes in formal treatment guidelines. Because non-manufacturer organizations face significant challenges in petitioning FDA to add a new indication to a generic drug's label, patients and clinicians can end up using these drugs "off-label." This can lead to uneven adoption and denial of coverage from some payers depending on the circumstances.[6]

Clinical practice guidelines are influential in the adoption of off-label treatments into the standard of care. These guidelines are treatment recommendations created and updated by panels of experts based on available evidence. Non-manufacturer organizations that generate data on new uses for generic drugs can work to change clinical guidelines to bolster adoption, especially since changing a drug's label is difficult.[7] But this pathway requires upfront investment to generate necessary evidence to be considered by these expert panels.

3. *What could FDA and other federal partners do to address these barriers?*

AV recommends that the FDA and other federal agencies consider the following:

- **FDA could develop a drug repurposing support program to advise non-manufacturer organizations interested in generic drug repurposing.** This program could help organizations develop research protocols and evidence needed for regulatory approval. FDA already provides similar support in other areas (i.e. patient-focused drug development, generic and OTC drugs) through guidance, workshops, and technical assistance. Extending that support to generic drug repurposing could help nonprofit and academic groups that often lead this work but lack experience navigating FDA approval.[8]
- **Non-manufacturer organizations should be able to submit strong clinical evidence that a generic drug can be used for a new purpose through a Citizen Petition**. If FDA finds, after rigorous review, that the data submitted are promising, it could issue a Federal Register Notice with the evidence and proposed label change to initiate a transparent process to update the generic drug's label.[9] To support these and other efforts, FDA should continue to ensure that sponsors publish the results of trials—even for those that failed—to clinicaltrials.gov in a timely manner.
- **Create a "labeling only" 505b2 pathway**. There are several benefits to this solution, including allowing non-manufacturer sponsors to demonstrate more easily—either through their own research or existing research—that there is substantial evidence to support the new use of a generic drug.[10] These organizations would be able to leverage FDA's previous determinations and ensure that postmarket surveillance obligations stay with the manufacturer of the product. This

pathway would have to include liability protections otherwise most non-manufacturers would not be willing to pursue approval through this pathway.

- **Build on existing federal programs and lessons learned.** NIH's NCATS, the National Institute on Aging Alzheimer's Repurposing Program, FDA's CURE ID App and Project Renewal, and ARPA-H's support of projects like MATRIX have shown promise. FDA and other federal agencies should examine what additional resources are needed to support these efforts and prioritize improved coordination across existing federal drug repurposing efforts.[11]
- **Request additional dedicated resources from Congress** to establish a coordinated repurposing program and more dedicated efforts to fund late-stage clinical trials targeting promising repurposed drug candidates.

Thank you again for the chance to provide input to FDA on ways to bolster generic drug repurposing efforts. Arnold Ventures welcomes being a resource to you as the agency addresses these issues. If you have any questions please contact Mark E. Miller, Ph.D., Executive Vice President of Health Care, at mmiller@arnoldventures.org or Andrea Noda, MPP, Vice President of Health Care, at anoda@arnoldventures.org.

Sincerely,

Andrea Noda
Vice President of Health Care

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[1] See "Nonprofits Are Ready to Repurpose Generic Drugs - Petrie-Flom Center" at: *https://petrieflom.law.harvard.edu/2025/10/02/nonprofits-are-ready-to-repurpose-generic-drugs/*
[2] See "Strategies to Advance Drug Repurposing for Rare Diseases" at: *https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2833522*
[3] See "Nonprofits Are Ready to Repurpose Generic Drugs - Petrie-Flom Center" at: *https://petrieflom.law.harvard.edu/2025/10/02/nonprofits-are-ready-to-repurpose-generic-drugs/*
[4] Ibid.
[5] *https://pmc.ncbi.nlm.nih.gov/articles/PMC10627937/*
[6] See "Regulatory Opportunities to Advance Generic Drug Repurposing" at *https://healthpolicy.duke.edu/publications/regulatory-opportunities-advance-generic-drug-repurposing*
[7] *https://pmc.ncbi.nlm.nih.gov/articles/PMC11496753/*
[8] See "Regulatory Opportunities to Advance Generic Drug Repurposing" at *https://healthpolicy.duke.edu/publications/regulatory-opportunities-advance-generic-drug-repurposing*
[9] *Ibid.*
[10] *https://pmc.ncbi.nlm.nih.gov/articles/PMC11496753/*
[11] See "Regulatory Opportunities to Advance Generic Drug Repurposing" at *https://healthpolicy.duke.edu/publications/regulatory-opportunities-advance-generic-drug-repurposing*