CAPITOL STREET

March 31, 2026

FDA: Where Are We?

One Year Report Card Since Commissioner Makary's Confirmation

Relevant Companies: ALL BIOPHARMA

Our Take & Next Up

The FDA latest and greatest. While we have fielded questions about who may lead the Center for Biologics, we wanted to provide an overall agency review and policy update as well as where the FDA may be going.

We believe that the agency is trending in a better direction for therapeutics. That is, in a backdrop of no-AdComs resulting in decisions that tend to fall in FDA's favor (i.e., lack of patient & stakeholder voices) while FDA reviewers are scrambling to get to meetings, often with no agenda furnished in advance. We do not foresee PDUFA dates to be missed, but less experienced staff will do things 'by the book' and will instead ask for more data or issue a CRL.

Looking ahead, we expect FDA policy on speeding first in human (FIH) trials. Given that China & Australia are speeding FIH to the point where the US is disadvantaged, per the 2025 FDA leader roadshow, we envision policy changes to toxicology studies along with centralizing IRBs to be a strong possibility in 2026.

Key Points

We provide an FDA report card as Commissioner Makary, MD, MPH, was sworn in one year ago, on April 1, 2025. We provide thoughts on likely pending policy as well as the state-of-play with therapeutic reviews (CDER & CBER), leaving CDRH out of the picture for now, given its relative competency over the last 12+ months under Michelle Tarver, MD. She was named permanent director of CDRH in October 2024 and has remained stable in her role.

TRENDING IN A BETTER DIRECTION

Capacity is diminished at the agency therefore less experienced reviewers and leaders are doing things 'by the book.' There are serious delays, no doubt, and differences in opinion between sponsors and FDA tend to be resolved in favor of the agency.

Delays are most serious in the early stage IND phases as FDA leadership understand the need to not miss PDUFA dates.

- FDA is aware of the clear need to adhere to PDUFA deadlines. Therefore, we do not expect approval delays given user fee commitments.
- Instead companies are experiencing delays in early stage investigational new drug (IND) phase as well as Phase 2→3 transition.

Why are there delays? There are fewer people overall at CDER/CBER and they are stretched thinner. All divisional resources are being spent on approvals, especially CNPV (Commissioner National Priority Voucher) applications which promise 1-2 month deadlines for approval.

Anecdotally, agency-manufacturer meetings are often haphazard. FDA officials are scrambling to make it to meetings, often the right people are not present, and agendas (which are supposed to be provided in advance) are not delivered on time.

Any differences in opinion between the FDA and sponsor tend to land in the agency's favor. Recall, the new FDA is not relying on Advisory Committee meetings. AdComs are where the patient voice is heard, as well as company and other stakeholder perspectives. We have all witnessed AdCom meetings where a few voices sway a committee, one way or another. This robust discussion of outside experts is essential in our view; and we hope that they are reinstated at FDA going forward.

2025 FDA COMMISSIONER ROADSHOW SHAPES 2026 NEW POLICY

In 2025, the FDA conducted a national listening tour to engage directly with biopharma CEOs. The forum was led by Commissioner Makary, along with Principal Deputy Commissioner Sara Brenner, MD, MPH, and CBER Director Vinay Prasad, MD, MPH. Dr. Makary has publicly referenced CEO feedback from the forums including concerns on the frustrating pace of FDA communications with sponsors.

Two major themes emerged from the 2025 FDA Commissioner roadshow.

- China and Australia first in human times are quicker than the US.
- If there are issues to discuss as the agency reviews an application, sometimes a 15-20 minute conversation clears things up.

This year, we could see FDA policy that accelerate the speed to first in human trials. Specifically we could see somewhat of an overhaul of toxicology reviews. As an example, the FDA many times will request a 400 rodent study if they see a GI issue early on; many experts find this to be unhinged from reality. Centralized Institutional Review Boards (IRBs) could also be established in some form or shape.

A first-in-human (FIH) trial is the very first time a new drug (or biologic) is tested in people after completing preclinical (lab and animal) studies. It's a critical early step in the approval pathway. FIH trials are not about proving the drug works; instead they focus on basic human safety and the drug's mechanism of action:

- **Safety & tolerability**: What side effects occur? At what dose?
- **Dose finding**: What is a safe starting dose and how high can you go?
- **Pharmacokinetics (PK)**: How does the body absorb, distribute, metabolize, and eliminate the drug?
- **Pharmacodynamics (PD)**: Are there early signals of biological activity?

CBER DIRECTOR OUTLOOK

We believe that HHS/CMS leader Chris Klomp is key to selecting the new Center for Biologics (CBER) Director. We believe a low-key competent individual is being sought to place trust back into the FDA and someone could be named that no one considered. Potential candidates include: Amy Comstock Rick J.D., Associate Director for Rare Disease Strategy at CDER; Peter K. Honig, MD, MPH, ex-FDA, first Director of the Office of Drug Safety at CDER; Katherine Szarama, PhD, Current Deputy Center Director for CBER; and Tracy Beth Høeg M.D., Ph.D., Acting Director of CDER.

We expect the FDA to reconsider some therapies rejected under Vinay Prasad's watch on a case-by-case basis. Sponsors who can provide new, incremental data as well as those with manufacturing issues may still see a path to approval.

We envision a near-term focus on rare diseases and cell & gene therapies to "make up for" the discrepancies under Dr. Prasad. The FDA Commissioner, who has stood by Vinay Prasad, to the point of bringing him back in 2025, has likely sent the message internally to immediately stop denying rare disease drugs, overall.

FDA STAFFING STILL NOT GREAT

In 1H25 when FDA reviewers and leaders were shown the door, some opted to come back. In those situations, mid-tier managers and above have come back into roles they held. However, staffing still remains a challenge as the FDA lost ~3,870 and 587 employees in FYs 2025 and 2026, respectively, according to the Office of Personnel Management.

New FDA reviewers take a long time to train. The agency is looking to hire 1500 more scientists per Makary and we note the significant training time means that new hires are not fully functional for some years.

OUTLOOK FOR COMMISSIONER VOUCHERS & PLAUSIBLE MECHANISM

Commissioner's National Priority Voucher (CNPV) approvals continue; FDA has held off on new designations for now. There are 13 outstanding vouchers left as the FDA has approved 4 CNPV products and rejected 1 (here).

- Generic antibiotic Augmentin (USAntibiotics)
- Hernexeos (Boehringer Ingelheim) for the treatment of non-small cell lung cancer
- Tec-Dara (JNJ) for the treatment of multiple myeloma
- Wegovy HD (NVO) for weight loss.
- One product has been rejected via CNPV: bitopertin (IRON) for treatment of erythropoietic protoporphyria (EPP). Disc Medicine intends to refile.

FDA may be seeking CNPV codification in the upcoming PDUFA bill to address longevity and litigation risk. CNPV currently lacks the statutory authority to have staying power past the current administration. Current PDUFA negotiations and upcoming reauthorization by Fall 2027 presents an opportunity to establish statutory authority. We could also see draft guidance in 2026 that provides the details needed for codification efforts. The FDA is hosting a public meeting on June 12 to collect public feedback.

Draft guidance on the plausible mechanism pathway offers clarity. In February 2026, the FDA launched their plausible mechanism pathway for n of 1 therapies (or n of a few) via draft guidance (here). This is one of

the few formal draft guidance released by the FDA under Trump and represents some adherence to procedures. Benefits of the pathway include approval based on a single controlled clinical investigation (not a broad clinical trial) with confirmatory evidence.

Separately, the focus on non-animal testing and AI will likely continue in 2026. In March 2026, FDA released guidance on new approach methodology (NAM) validation, which provides a regulatory framework for assessing NAM in drug development. FDA continues to push for phasing out mandatory animal testing and we may see applications approved without animal testing in the pre-IND stage. On AI, FDA has launched Elsa and a separate agentic AI tool that handles complex management tasks. FDA is likely to further expand their AI use, particularly for postmarketing monitoring, due to the current investments into their AI tools and staffing pressures at the agency.

Ipsita Smolinski
Managing Director I Capitol Street
ipsita@capitol-street.com

202.250.3741 I www.capitol-street.com

900 19th St NW 6th Fl
Washington, D.C. 20006

CAPITOL STREET
