CAPITOL STREET

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FDA: Outlook for Drug Reviews, Policy & PDUFA

Reviews Likely Slow for Innovative Medicines, Guidance Issuances Halt, DTC Ad Reform Methods, Pandemic Preparedness

Relevant Companies: ALL HEALTHCARE

Our Take & Next Up

We believe that FDA reviews and inspections will be slowed despite the administration's exemption for reviewers and inspectors from the recent reduction in force (RIF link). The FDA is gearing up for a serious transformation with no current plans for sub-agency leadership. We expect with the departure of deputy leadership (with historical knowledge and experience) at CBER and other offices, HHS wants a more micro-managing role in shaping the agency.

Yesterday, we hosted a call with FDA experts on staff reductions, as well as impact to industry, and review timelines. Per our experts, the staffing cuts are expected to significantly impact review for innovative medicines – cell/gene, orphan, etc -- that require more work and expertise in their review process. We also hit on impact to PDUFA reauthorization, DTC advertising, and NIH cuts. Main highlights are below.

Key Points

The Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) have been hit the hardest with reduction in force (RIF). The FDA overall saw an almost 20% reduction in workforce by yesterday, according to our KOLs.

- FDA leadership that have been pushed out include **Drs. Peter Stein** (Office of New Drugs), **Hilary Marston** (Chief Medical Officer), **Julie Tierney** (CBER) and **Brian King** (Tobacco Center).
- RIFs have impacted FDA's policymaking with cuts to the Office of Drug Policy and Office of Regulatory Policy.
- Staff in clinical and medical policy, communications, program managers, and managerial and support staff at large have been cut at CBER and CDER.
- The Office of the Chief Counsel appears to have been spared as a carve out with no staffing impact so far.

Innovative medicine reviews are likely impacted/slowed, with "me toos" and supplemental applications being lower tier as well. The impact on reviews may crosscut the agency. While reviewers and inspectors are shielded from RIF, the pace of reviews will likely be impacted by the lack of program managers and support staff that keep reviews on track. Our KOLs are particularly concerned about the impact to **novel therapeutics** (cell,

gene, RNA) that require more FDA communications, and likely specific scientific and topical expertise (liver tox, pharmacokinetics, etc) to guide their reviews. Specialized support staff and experts that likely are no longer at FDA provide topical expertise to "cut through the noise" and discern safety risks.

There is no plan for agency leadership, or for who the "next Dr. Marks" will be. We have said that divisions could be combined -- like CDER & CBER. Backfilling and rehiring do not appear to be a part of the conversation after the gutting of the FDA Friday-into-Monday. Newly seated FDA Commissioner Martin Makary, MD, was reportedly in the know (link) as to Peter Marks' resignation/ouster. It is difficult to predict who will fill that role due to the emptying of deputy leadership at CBER. We believe that the leadership roles may be filled by GOP Congressional staffers, external political hires, or perhaps HHS leadership who are willing to make the transition.

Manufacturing inspections are impacted, particularly pre-approval ones. We expect that the FDA will not be able to keep up with the cadence of pre-approval inspections, particularly for novel therapeutics that may have novel manufacturing processes.

PDUFA VIII (2027) negotiations may still start this summer, but the FDA may be unable to negotiate fulfilling commitments if they don't have the authority/staff in place.

- As a reminder, every five years the FDA and industry renegotiate the *Prescription Drug User Fee Act* (PDUFA) and agree on performance goals for the next reauthorization cycle. The process of renegotiation must be done before the current user fees expire September 2027. A significant part of PDUFA negotiations is on full-time equivalent (FTE), a measure of the labor hours devoted to the PDUFA program.
- The FDA may not be ready to negotiate if they are unable to assure the industry that they can fulfill the potential FTE obligations. PDUFA 7 signed in September 2022 provided key critical staff to cell & gene products, given that CBER was grappling with a thousand cell gene therapy INDs prior to that.
- Our KOLs opined that PDUFA could include "no Ad Comms" or "no guidance document" mandates to limit the authority of the agency.
- It is possible that the FDA could have their current UFA levels extended to 2 years, as recommended by former Commissioner Scott Gottlieb (link).
- There is also the question if the user fee system would be scrapped entirely by the administration, which is unlikely.

Guidance documents – such as accelerated approval, drugs for weight reduction, advanced manufacturing -- are not expected to be finalized anytime soon.

- The chilling combination of the 10-to-1 EO (link here), new priorities, and the departure of FDA policy staff make this a new reality. We expect that key guidance documents (accelerated approvals, platform technology, artificial intelligence, etc.) are unlikely to be finalized in the near term and sit in limbo.
- We could see the FDA provide some guidance on topics (e.g., artificial intelligence) of exception where restrictions conflict with the administration's priorities.

A DTC ad ban would likely be struck down by the courts, but the FDA could find other ways to make advertising difficult.

- The first amendment is extended to commercial advertising, and commercial speech doctrine likely limits what the FDA can do. We could see the FDA increase advertising requirements beyond the final November 2023 guidance which requires clear, conspicuous and neutral advertising and/or step up enforcement of violations.
- Our experts note that the agency could also target certain companies it perceives to have onerous direct-to-consumer (DTC) violations and potentially refuse to meet with them until they fall into compliance.

Vaccines -- particularly those for pediatric populations -- face significant headwinds (liability fund, longer review, target population limits). The cost of bringing a vaccine to market will increase if the FDA begins requiring significantly more prelicensure studies vs. post-licensure real world evidence. The FDA is likely to ask developers more questions about endpoints, questions about study design, and about eligible populations. We may see scrutiny intensify particularly for pediatric and mRNA vaccines. FDA may invoke more summary reviews.

Pandemic preparedness has fallen to the wayside and remains a major public health concern despite Trump EO (here).

- The EO directs that the state and local governments, as well as individuals, should take a greater role in preparedness efforts and calls for a review of all infrastructure, continuity, and preparedness policies to modernize and simplify federal approaches. We expect that state and local governments may see an increased burden in preparedness in both responding to disasters with less financial or operational support from the federal government. The EO calls for a review of critical infrastructure policies, including the following EOs that have healthcare impacts, and recommend a risk-informed approach within 180 days (1) Supply Chain (here) and (2) America's Supply Chains (here).
- The Pandemic Preparedness bill (aka *PAHPA*) failed to pass a full reauthorization in the December 2024 CR, while some key extenders operate under short-term extensions since they expired in October 2023. *PAHPA* provisions include, among others, the authorization of the BARDA the authority of the HHS secretary to declare a public health emergency, and antitrust exemptions for the development of emergency medical countermeasures.

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