

What's Ahead For FDA? New Leadership, Challenges and Initiatives

Kate Rawson

Prevision Policy LLC

Coalition for Healthcare Communication

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The Prevision Policy Team

Cole Werble
Michael McCaughan
Ramsey Baghdadi
Laura Helbling
Grace Moser



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FDA Office Of New Drugs Director Search Nearing Completion; Deputy Director Peter Stein Remains Likely Choice

FDA's Center for Drug Evaluation & Research is wrapping up its two-year search for a permanent director of the Office of New Drugs, with an official announcement expected in early December.

While no announcement has been made either internally or outside FDA, the current Office of New Drugs deputy director, Peter Stein, appears poised to become full director.

In many ways, Stein is the obvious choice. As deputy director of OND for the past two years, he is well-tuned to the current structure and leadership within the review offices and divisions – and he has worked closely with CDER Director Janet Woodcock on the design of the planned extensive reorganization and “modernization” of the Office of New Drugs.

Woodcock has been leading both the search and OND itself since the retirement of long-time director John Jenkins in January 2017. Woodcock is understood to have interviewed several candidates for the position, eventually narrowing her search down to Stein and an industry executive. In choosing Stein, Woodcock is going with a previous recruit from outside the agency (Merck) who has had time to make the key connections and adjustments to working inside government.

By many outside accounts, Stein is thoroughly enjoying his time in government service – a sentiment he himself strongly articulated during a panel discussion on the “New OND” at the fourth annual Biopharma Congress on November 14. When asked, Stein declined to comment on whether he would like the top job at OND, but expressed enthusiasm for his current position, and added that he expects to close out his career at FDA. (He also noted that he has no plans to end his career soon.)

In one sign that an announcement may be imminent, Woodcock's colleague, Oncology Center of Excellence Director Richard Pazdur, commented twice during the Biopharma Congress and the Friends of Cancer Research annual meeting the day before that that she was “down to one job.” That, of course, is not quite official yet, but an internal OND town hall, initially scheduled for November 5 but postponed for a date in December, could provide an opportunity for leadership to announce both an update on the modernization process -- and, perhaps, the agency's pick to lead the office.

Stein is still relatively new at FDA: he joined the agency just two years ago from Merck Research Laboratories, where he was VP for late-stage development, diabetes and endocrinology. The appointment was considered a big win for the agency, which has had trouble attracting and retaining candidates from industry. (See our November 8, 2016 note, [FDA Office of New Drugs Fills Deputy Position From Outside: Merck's Stein Brings Industry Experience In Endocrinology](#).)

Stein was tested early as deputy director of OND: he was still settling into his job when Jenkins, his direct supervisor, announced his move to the private sector just a few weeks after Stein joined the

PREVISIONPOLICY

1000 Potomac St. NW Suite 130 Washington, DC 20007
(202) 747-9476 • team@previsionpolicy.com • www.previsionpolicy.com

The State Of FDA



- New President, New Priorities
- Who Will Run FDA?
- State Of CDER Under Cavazzoni
- CBER's Urgent Need To Staff Up
- Lessons Learned From COVID-19
- What's In The UFAs?
- Biden's Budget Priorities for FDA

Biden's Health Care Team...So Far

**HHS Secretary
Xavier Becerra**

Senate confirmed March 18



**HHS Deputy Secretary for Operations
Andrea Palm**

Senate confirmed May 11



**COVID Response
Chief Science Officer
David Kessler**



**CMS Administrator
Chiquita Brooks-LaSure**
Senate confirmed May 25



**FDA
Commissioner
????
Janet Woodcock
is Acting
Commissioner**

COVID-19 Response Continues To Be Job One

- Three vaccines authorized; full BLAs this summer/fall
- Closing of EUA window for vaccines demonstrates progress
- Vaccine booster planning is already underway
- Inter-agency effort to combat vaccine hesitancy (with CDC, NIH)
- Greater focus on COVID-19 therapeutics coming

- 3 authorized vaccines
- 610+ drug development programs in planning stages
- 450+ trials reviewed
- 10 treatments authorized for emergency use
- 1 COVID-19 approved treatment (remdesivir)
- 400+ Emergency Use Authorizations covering nearly 800 medical products: tests, sample collection devices, personal protective equipment and ventilators.

Plus all the “regular” work within the Centers

ARPA-H Is Biden Health Care Priority

- Highlight of “skinny budget” proposal; \$6.5 million
- NIH health funding entity to support health research projects for high-priority breakthroughs
- Little impact on FDA, but big changes possible in how government is pushing into development

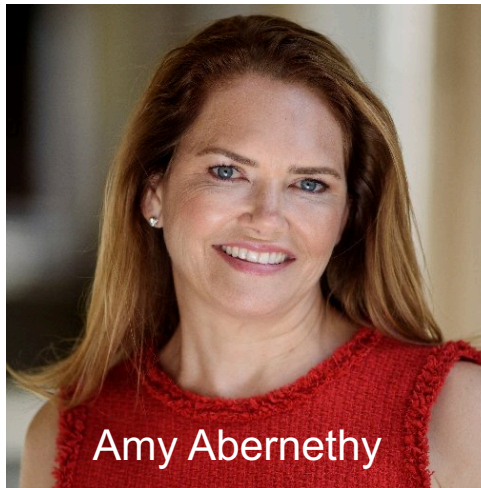
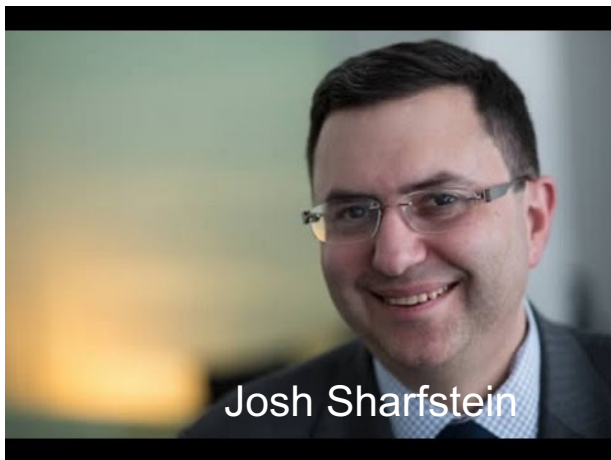
Supports IP Waiver For COVID Vaccines

- Minimal immediate impact on manufacturers
- A one-off event, or a sign of things to come?

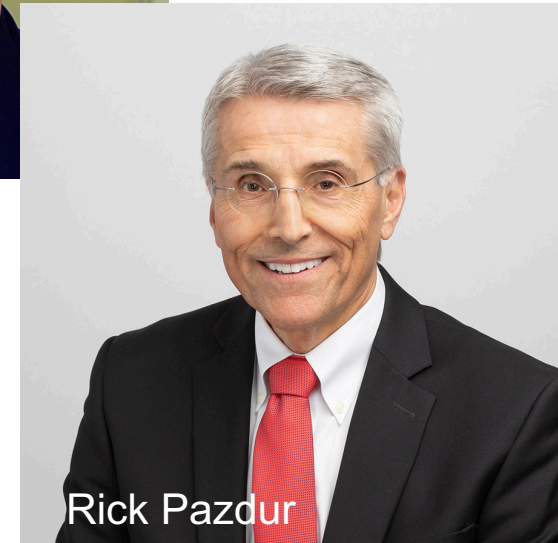
Drug Pricing: Not an immediate priority

The Next FDA Commissioner?

More Likely Picks



Dark Horses



Round Two Of Potential Candidates



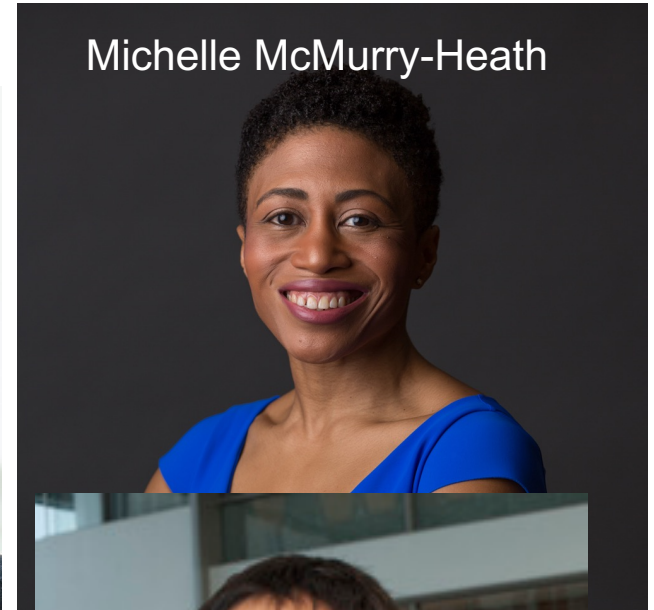
Florence
Houn



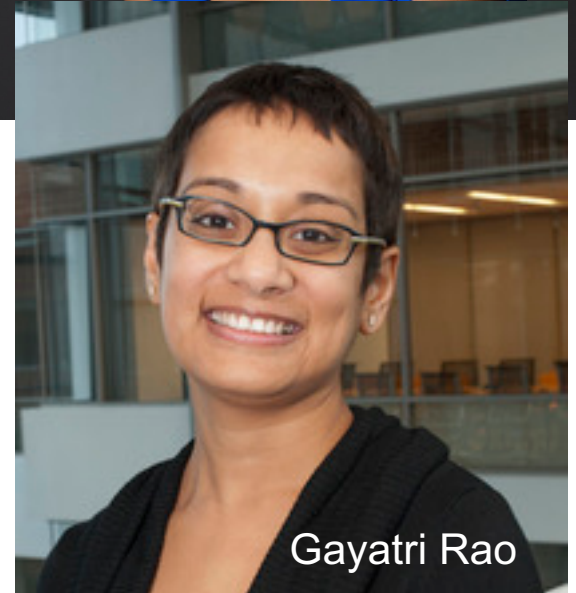
Leana Wen



Katherine Luzuriaga



Michelle McMurry-Heath



Gayatri Rao

Continuity During Crisis

- 35 years of experience at FDA
- Deep understanding of needs

Internal/External Support

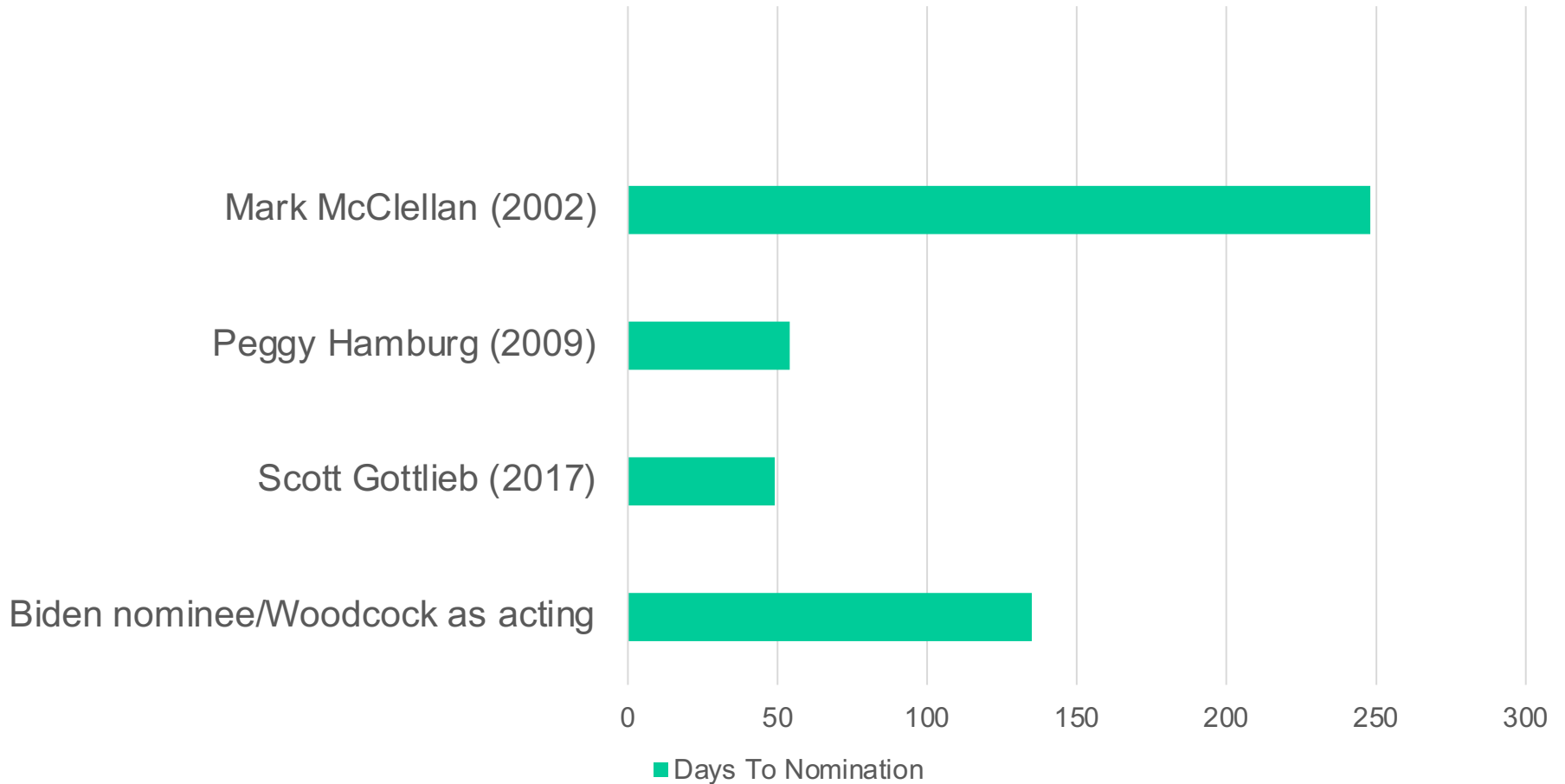
- Backing from staff, former Commissioners, some Hill
- Support from patient community

Strong FDA Advocate On Hill

- Adept at congressional testimony



Time To Nomination For FDA Commissioners By First-Term Presidents George W. Bush-Trump



The REAL Leadership Change Is At CDER

Fourth CDER director as of April 12;
acting since May 2020

Woodcock's hand-picked successor

Joined FDA from Pfizer in Feb 2018



Dr. Janet Woodcock  @DrWoodcockFDA · Apr 12

Pleased to announce the permanent appointment of Patrizia Cavazzoni, M.D., as [@FDACDERDirector](#), a position she has been serving in for the past year and providing exceptional leadership during this critical and unprecedented time.

- ✓ Steer CDER out of pandemic work
- ✓ Finish user fee negotiations, including new OTC program
- ✓ “Health Equity” – in the form of generics and biosimilars (insulin)
- ✓ Continued focus on rare and neurodegenerative diseases
- ✓ Shore up supply chain reliability
- ✓ Immediate goal: winning “hearts and minds” of the CDER staff



But CBER Is Hot New Place To Work



“We have the the most important medical product of the decade, and gene therapies which are the wave of future medicine all in one center. It’s a pretty cool thing.

“Because of that, we've been able to attract some young talent.”



Repairing A Damaged Reputation



Morale Is An Ongoing Concern...

- Staff has been going “non-stop” for 15 months
- 250 FTEs-worth of CDER work absorbed on COVID

...But Hiring Is Booming At CDER During The Pandemic

- 100+ net gains in employees in FY2020-2021
- Attrition at all-time low
- “Cures” authority now 20% of CDER staff

A “Fungible” Review Staff

- Re-assignments to busier areas helping ease strain
- FDA exploring “hybrid” work model going forward

Virtual Meetings Working (Relatively) Well

- Some sponsor meetings may be here to stay

FDA Is Continuing To Hire Through Pandemic

- Training new staff is complicated by virtual work environments

De-Centralized Trials The “New Normal”

- Patients prefer virtual visits
- More guidance from FDA coming

Investment Needed in Advanced Manufacturing

- Speedier ramp-up of vaccines for next pandemic

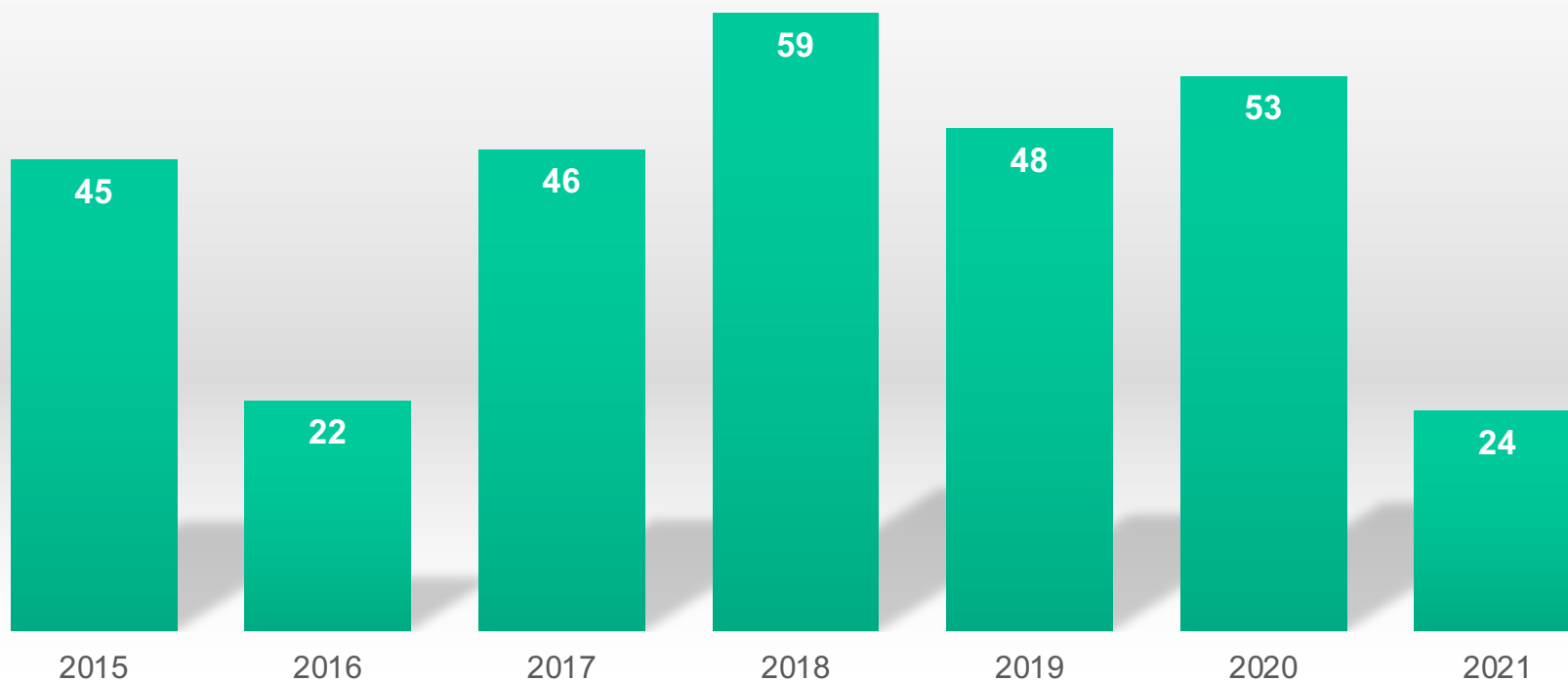
Virtual Inspections Could Replace Some Site Visits

- Flexibility after pandemic in cases where issues complicate or preclude in-person visits

Shortage Tracking Systems Are Here To Stay

- Monitoring system for COVID-related shortages to be retained and expanded

FDA Approvals of Novel Drugs/Biologics By Calendar Year

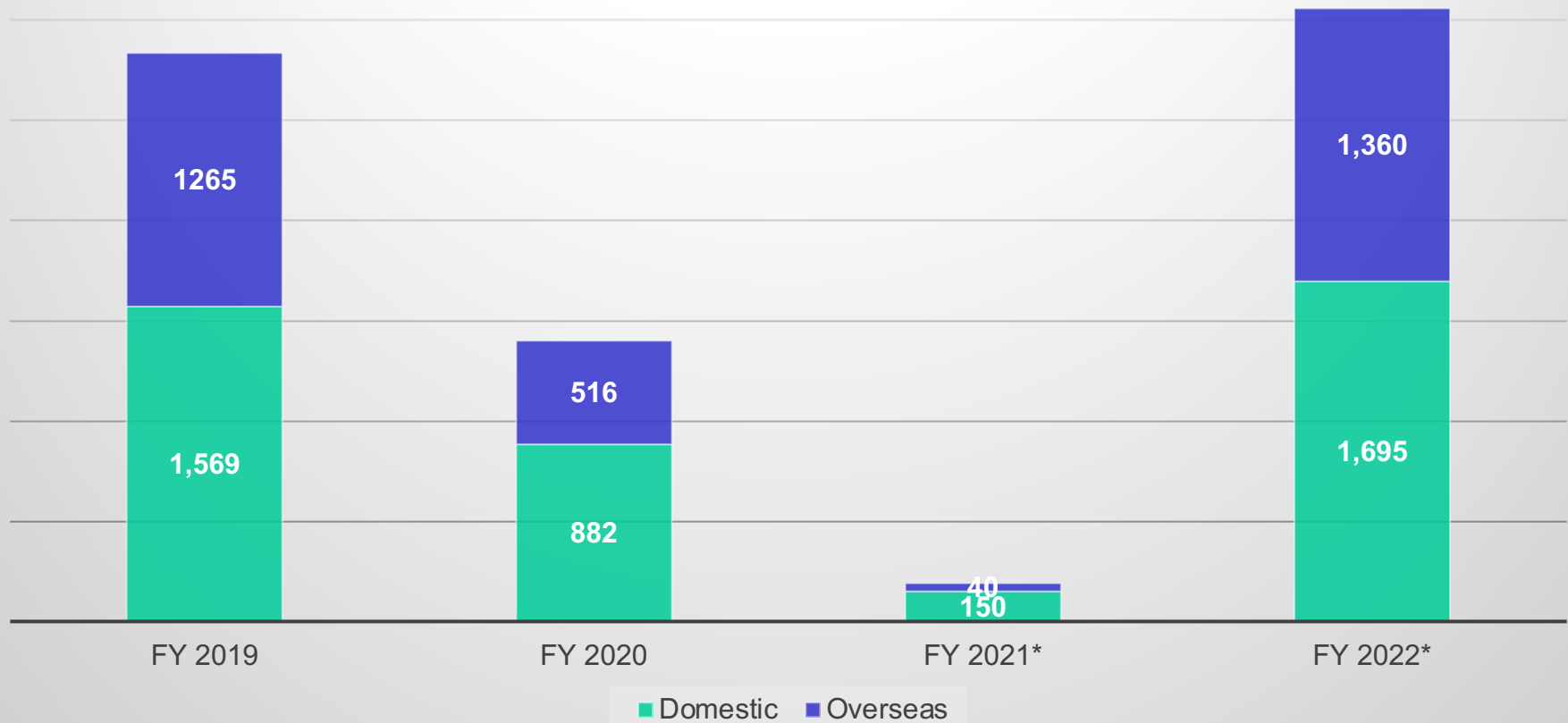


* 2021 data as of June 2

Inspections Will Be A Sticking Point



Human Drugs Establishment Inspections



SOURCE: FDA budget justification, FY 2022 *estimated

48!! NDAs delayed by travel restrictions...

- ✓ Remote Inactive Evaluations where possible, but they can take longer than in-person visits; technology does not always make them possible
- ✓ “Paper inspections” can be a black box for sponsors



...including **six** mission-critical applications

SOURCE: FDA Resiliency Roadmap

- ✓ Remarkable flexibility to ensure patient safety
- ✓ Virtual visits to measure efficacy
- ✓ But sponsors need to document any deviations

Contains Nonbinding Recommendations

Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on January 27, 2021

For questions on clinical trial conduct during the COVID-19 pandemic, please email Clinicaltrialconduct-COVID19@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Oncology Center of Excellence (OCE)
Office of Good Clinical Practice (OGCP)

Heightened understanding of FDA's public health mandate and complexity of the work it does

May (??) lead to more funding via appropriations

Potential downside: unrealistic expectations of what FDA can do – and how fast it can do it



Routine Maintenance for FDA



Congress Hauls in FDA Every 5 Years and Looks Under the Hood

Building On PDUFA VI

- ✓ Model-Informed Drug Development
- ✓ Complex Innovative Trial Designs
- ✓ Patient-Focused Drug Development
- ✓ Real-World Evidence
- ✓ REMS Changes
- ✓ Sentinel Enhancements

New User Fee Initiatives

- ✓ Cell/gene therapy \$\$, guidance, meetings
- ✓ RMAT guidance, meetings, user fees
- ✓ Emerging IT
- ✓ Digital health
- ✓ Real-Time Review

Modest Increases For FDA

- ✓ \$124 million for human drug operations (to \$2.12 billion)
- ✓ \$21 million increase for biologics (to \$458 million)
- ✓ \$18.8 million for inspections (FDA-wide)
- ✓ Much larger \$76 million increase for data modernization efforts (to \$83 million)

Drug Pricing: Punt to Congress



Thank You!

Kate Rawson

Prevision Policy LLC

1000 Potomac Street, NW

Suite 130


Washington DC 20007

202-297-6420

kate@previsionpolicy.com



@Kate_Rawson



PREVISIONPOLICY
HEALTH POLICY + BUSINESS FORECASTS

Drug Review Memorandum

11.4.2010

Ramsey
Baghdadi
202-747-9476

Michael
McCaughan
202-747-9477

Cole Werble
202-747-9478

Laura Helbling
202-747-9487

Roche/Genentech's Avastin: FDA's Decision and CMS Implications

Summary: A decision by FDA on whether to pull a major indication in breast cancer for the oncology drug *Avastin* is approaching. In this note we lay out our thinking ahead of a likely Dec. 17 action date on the issue.

We continue to believe that FDA will rescind the first-line indication for metastatic breast cancer. That conclusion is based on the overwhelming vote coupled with the tone of FDA leadership in the oncology group at the meeting.

We also note that FDA's decision may not be the critical step in determining the impact of the re-evaluation of *Avastin*'s role in breast cancer therapy. The Centers for Medicare & Medicaid Services (CMS) may also weigh in to review coverage of the indication, which would have a more dramatic impact on use of the therapy.

Finally, we include some background on precedents in the accelerated approval space that may be useful for considering potential outcomes.

Analysis: A decision by FDA on whether to pull a major indication in breast cancer for the oncology drug *Avastin* is approaching. Here is how we think FDA and CMS will respond to the changing situation.

FDA's Oncology Drugs Advisory Committee unanimously voted (13-0) on July 20 that the accelerated approval (AA) indication for first-line treatment of metastatic breast cancer should be removed from Roche/Genentech's *Avastin* (bevacizumab) label. Following the advisory committee, Roche/Genentech submitted additional data to FDA that triggered a three-month extension to the user fee deadline from September 17 to December 17.

We continue to believe that FDA will rescind the first-line indication for metastatic breast cancer. That conclusion is based on the overwhelming vote coupled with the tone of FDA leadership in the oncology group at the meeting.

The internal FDA analysis of two confirmatory studies for the breast cancer indication, AVADO and RIBBON1, found the trials did not support the improvement in progression-free survival (PFS) demonstrated in an earlier randomized study (E2100). The FDA concluded: "The magnitude of the improvement in PFS observed in these two studies failed to confirm the magnitude of PFS improvement observed in the E2100 trial, the basis for the accelerated approval."

If FDA revokes the breast cancer indication, there are several potential next steps, with CMS moving forward as the key decision-maker.

PREVISIONPOLICY
1055 Thomas Jefferson St. NW
Suite 450A
Washington, DC 20007

PHONE (202) 747-9476
E-MAIL ramsey.baghdadi@PREVISIONPOLICY.com
WEBSITE [HTTP://PREVISIONPOLICY.com](http://PREVISIONPOLICY.com)