MORRISON FOERSTER

DOJ and FDA Regulatory and Enforcement Trends

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Food and Drug Omnibus Reform Act of 2022

Food and Drug Omnibus Reform Act of 2022

- On December 29, 2022, the President signed into law the Food and Drug Omnibus Reform Act of 2022 (FDORA) as part of the Consolidated Appropriations Act, 2023, Pub. L. No. 117-328 (2022).

- FDORA includes six subtitles:
  - Subtitle A - Reauthorizations,
  - Subtitle B - Drugs and Biologics,
  - Subtitle C - Medical Devices,
  - Subtitle D - Infant Formula,
  - Subtitle E - Cosmetics and,
  - Subtitle F - Cross-Cutting Provisions.

Sec. 3202: Improving the Treatment of Rare Diseases and Conditions

- Requires FDA to publish a report summarizing its activities related to designating and approving or licensing drugs and biologics for rare diseases.

- FDA must convene at least one public meeting to address increased and improved engagement with rare disease patients, rare disease patient groups, and experts on small population studies – all in order to improve the understanding of patient burden, treatment options, and the side effects of treatments.

- GAO report assessing FDA's policies, practices, and programs regarding treatments for rare diseases.

Sec. 3208: Rare Disease Endpoint Advancement Pilot Program

- Directs FDA to establish a pilot program to provide increased interaction with sponsors of rare disease drug development programs for the purposes of advancing the development of efficacy endpoints, including surrogate and intermediate endpoints.

- FDA must conduct up to three public workshops to discuss topics relevant to the development of endpoints for rare diseases.

- FDA must also issue guidance describing best practices and strategies for the development of such endpoints.

FDORA Sec. 3210: Modernizing Accelerated Approval

- Makes significant changes to accelerated approval.
- If no postapproval study is required, FDA must publish a rationale on its website explaining why no such study is required. If a postapproval study is required, FDA must specify conditions, which may include enrollment targets, study protocol, and milestones, including the target date of study completion.
- FDORA explicitly includes a failure to meet these conditions as being part of the determination that the sponsor failed to conduct a required postapproval study with due diligence.
- FDA is authorized to require a postapproval study or studies to be underway prior to approval, or within a specified time period after approval.

FDORA Sec. 3210: Modernizing Accelerated Approval

- Sponsors must report the progress of any required study, including progress toward any conditions specified by FDA, not later than 180 days following approval and not less frequently than every 180 days thereafter until the study is completed or terminated.
  - Previously, progress reports on these studies were only required annually.

- As additional enforcement authority, FDA may initiate enforcement actions for a failure to conduct a required post approval study with due diligence, including a failure to meet any required conditions specified by FDA or to submit timely reports.

FDORA Sec. 3210: Modernizing Accelerated Approval

- FDORA also amended the statute to describe the procedures to be used for the expedited withdrawal of approval of a product approved under accelerated approval, the details of which had previously been delegated to FDA.

- These include:
  - Notice and an explanation for the proposed withdrawal;
  - An opportunity for a meeting and written appeal;
  - An opportunity for public comment on the proposal to withdraw with the publication of the Secretary's response to such comments; and
  - Convening of an advisory committee if requested by the sponsor if no such committee had previously advised the Secretary on such issues with respect to the withdrawal of the product prior to this request.

FDORA Sec. 3210: Modernizing Accelerated Approval

- FDA must publish guidance on:
  - Identifying novel surrogate or intermediate clinical endpoints;
  - The use of novel clinical trial designs for post-approval studies; and
  - Considerations related to the use of surrogate or intermediate endpoints that may support accelerated approval.

- FDA must establish an intra-agency Accelerated Approval Council to ensure the consistent and appropriate use of accelerated approval across FDA.

Improving Diversity of Clinical Trials

- **Sec. 3601: Diversity Action Plans for Clinical Studies**
- **Sec. 3602: Guidance on Diversity Action Plans for Clinical Studies**
- **Sec. 3603: Public Workshops to Enhance Clinical Study Diversity**
- **Sec. 3604: Annual Summary Report on Progress to Increase Diversity**

Decentralized & Modernized Clinical Studies

- **Sec. 3606: Decentralized Clinical Studies**
- **Sec. 3607: Modernizing Clinical Trials**

Clinical Decision Support (CDS)

A software function will be considered CDS if it:

1. NOT intended to acquire, process, or analyze medical image or signal.
2. Intended for purpose of displaying, analyzing, or printing patient-specific medical information.
3. Intended for the purpose of supporting or providing recommendations on prevention, diagnosis, or treatment.

A software function will be considered non-device CDS if:

1. Intended for purpose of supporting or providing recommendations to HCPs.
2. Intended to enable HCP to independently review basis for recommendations so HCP does not rely primarily on the CDS recommendations in clinical diagnosis or treatment decisions.

Clinical Decision Support (CDS) Guidance

Final guidance was a shift from the previous 2019 draft guidance

Notable changes to CDS policy in the final guidance:

1. Absence of risk-based enforcement discretion policy for lower risk functions
2. Narrowed interpretation of “medical information about a patient” and “other medical information”
3. Exclusion of software that provides “specific preventive, diagnostic or treatment output or directive” that supports “time-critical decisionmaking”

In February 2023 the Clinical Decision Support Coalition filed petition requesting FDA withdraw the final guidance, claiming it oversteps the agency’s statutory authority and violates federal law.

FDORA – Predetermined Change Control Plans

FDORA amends the Food, Drug & Cosmetic Act to provide that predetermined change control plans may be approved in premarket applications

- If a PCCP is approved or cleared, then a change to a device that is consistent with such approved or cleared plan does not require submission of a supplemental PMA or new 510(k)

On April 3, 2023, FDA released its draft guidance *Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning-Enabled Device Software Functions*

- Comments to the draft guidance are due July 3, 2023

FDORA – Cyber Provisions

FDORA imposes new premarket submission requirements for "cyber devices" including a software bill of materials and plan to address cybersecurity vulnerabilities

- "Cyber devices" are those that include software (including SAMD), have the ability to connect to the internet, and contain any such technological characteristics that could be vulnerable to cybersecurity threats

FDA Rulemaking on Lab Developed Tests (LDTs)

FDA moving ahead with rulemaking on lab developed tests without waiting for Congress: BioWorld

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By Nick Paul Taylor
Contributor

Catalyst Pharms., Inc. v. Becerra

Catalyst ODE Litigation

- Catalyst sued FDA in June 2019 in the U.S. District Court for the Southern District of Florida for approving the “same drug for the same disease or condition” (i.e., RUZURGI) as FIRDAPSE during the 7-year ODE period.

- Catalyst alleged that the plain language of the Orphan Drug Act precluded FDA’s approval of RUZURGI in any LEMS patients until the expiration of the 7-year ODE period covering FIRDAPSE.

- Catalyst initially lost its case, but then appealed to the 11th Circuit.
  - *Catalyst Pharms., Inc. v. FDA*, No. 19-cv-22425, 2020 WL 5792595 (S.D. Fla. Sept. 29, 2020)
  - *Catalyst Pharms., Inc. v. Azar*, No. 19-cv-22425, 2020 WL 551487 (S.D. Fla. July 30, 2020)

Catalyst ODE Litigation

- In *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the 11th Circuit found that the scope of ODE is with respect to the designated rare disease or condition, and not with respect to the approved indication, as FDA has interpreted the statute for decades.

- Consequently, the Court held that FDA's approval of RUZURGI contravened the plain language of the Orphan Drug Act in violation of the Administrative Procedures Act and ordered FDA to rescind the RUZURGI approval – which FDA did, converting the approval to a tentative approval.

- Jacobus, an intervenor in the litigation, appealed the 11th Circuit decision to the U.S. Supreme Court, and then dropped the appeal.

Legislative Efforts to Overturn *Catalyst Pharms., Inc. v. Becerra* (11th Cir.)

- As a part of the user fee reauthorization efforts, provisions were under consideration, in both the House and Senate, that would have legislatively overturn the *Catalyst* decision.

- House
  - H.R. 7667 - the “Food and Drug Amendments of 2022”

- Senate
  - S. 4348 - the “FDA Safety and Landmark Advancements Act of 2022”
  - S. 4185 - the “Retaining Access and Restoring Exclusivity Act” (“RARE Act”)

FDA's Federal Register Notice

- FDA, Notice, Clarification of Orphan-Drug Exclusivity Following *Catalyst Pharms., Inc. v. Becerra*, 88 Fed. Reg. 4086 (Jan. 24, 2023).

- FDA says that "at this time, in matters beyond the scope of that court order, FDA intends to continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved."

- In other words, FDA will limit the scope of the Catalyst court ruling to the case and drug at hand: amifampridine for LEMS. Outside of that, the decision will not affect FDA decisions and it is "business as usual" insofar as FDA interpreting and applying the scope of orphan drug exclusivity to apply to the drug for the approved indication.

FDA's Federal Register Notice

- FDA took a similar tack in 2014 after losing another significant case in court concerning Orphan Drug Exclusivity.

- In that case, FDA's decision to continue on without regard to the Court's decision invited another litigation, which FDA also lost, and ultimately resulted in a change to the statute to address the *Depomed* Court decision.

Overview of Inflation Reduction Act

Drug Price Negotiation Program

The IRA provides Medicare with ability to negotiate "maximum fair prices" (MFP) of certain high expenditure, single source drugs through the Medicare Drug Price Negotiation Program.

For each price applicability year (which begins in 2026), CMS must:

- Identify and publish list of selected qualifying drugs.
- Enter into agreements with manufacturers of selected drugs.
- Negotiate or renegotiate MFPs for such selected drugs.
- Publish MFPs for selected drugs.

Identifying Qualifying Single Source Drugs

A negotiation-eligible drug is a "qualifying single source" Part D drug that is among the 50 of such qualifying drugs with the highest "total expenditures" under Part D.

A qualifying single source Part D drug is:

Covered Part D Small Molecule Drug that:	Covered Part D Biological that:
▪ Has been FDA approved and marketed for at least 7 years, and ▪ Is not the listed drug for an approved and marketed generic drug	▪ Has been FDA approved and marketed for at least 11 years, and ▪ Is not the reference product for an approved and marketed biosimilar

Identifying Single Source Drugs

Additional CMS guidance clarified that:

- When identifying a qualifying single source drug, the drug will include:
  - All dosage forms and strengths, with the same active moiety/ingredient and the same holder of the NDA/BLA, inclusive of products marketed pursuant to different NDAs/BLAs.
  - All products marketed per the same NDA/BLA that are repackaged and relabeled products.
- For fixed combination drugs with 2 or more active moieties/ingredients, the distinct combination will be considered one active moiety/active ingredient.

Excluded Drugs

Certain categories of drugs will be excluded when identifying qualifying single source drugs:

- Certain orphan drugs
- Plasma-derived Products
- Low-Spend Medicare Drugs
- Small Biotech Drugs (for 2026, 2027 and 2028)

Excluded Drugs – Orphan Drugs

Certain orphan drugs are excluded from qualifying single source drugs.

To be considered for orphan drug exclusion, drug or biological product must:

- Be designated as drug for only one rare disease or condition.
- Be approved only for one or more indications within such designated rare disease or condition.
  - All dosage forms, strengths and formulations of the drug must meet the criteria.
  - Multiple indications are permitted.

CMS will use the FDA Orphan Drug Product designation database and approval on FDA website to determine whether drug meets the requirements.

Excluded Drugs – Plasma Derived Products

- CMS will exclude plasma-derived products when identifying qualifying single source drugs. For purposes of this exclusion, a plasma-derived product is a licensed biological product that is derived from human whole blood or plasma, as indicated on the approved product labeling.

- CMS will refer to product information available on the FDA Approved Blood Products website and FDA Online Label Repository.

- CMS will also consult with FDA as needed.

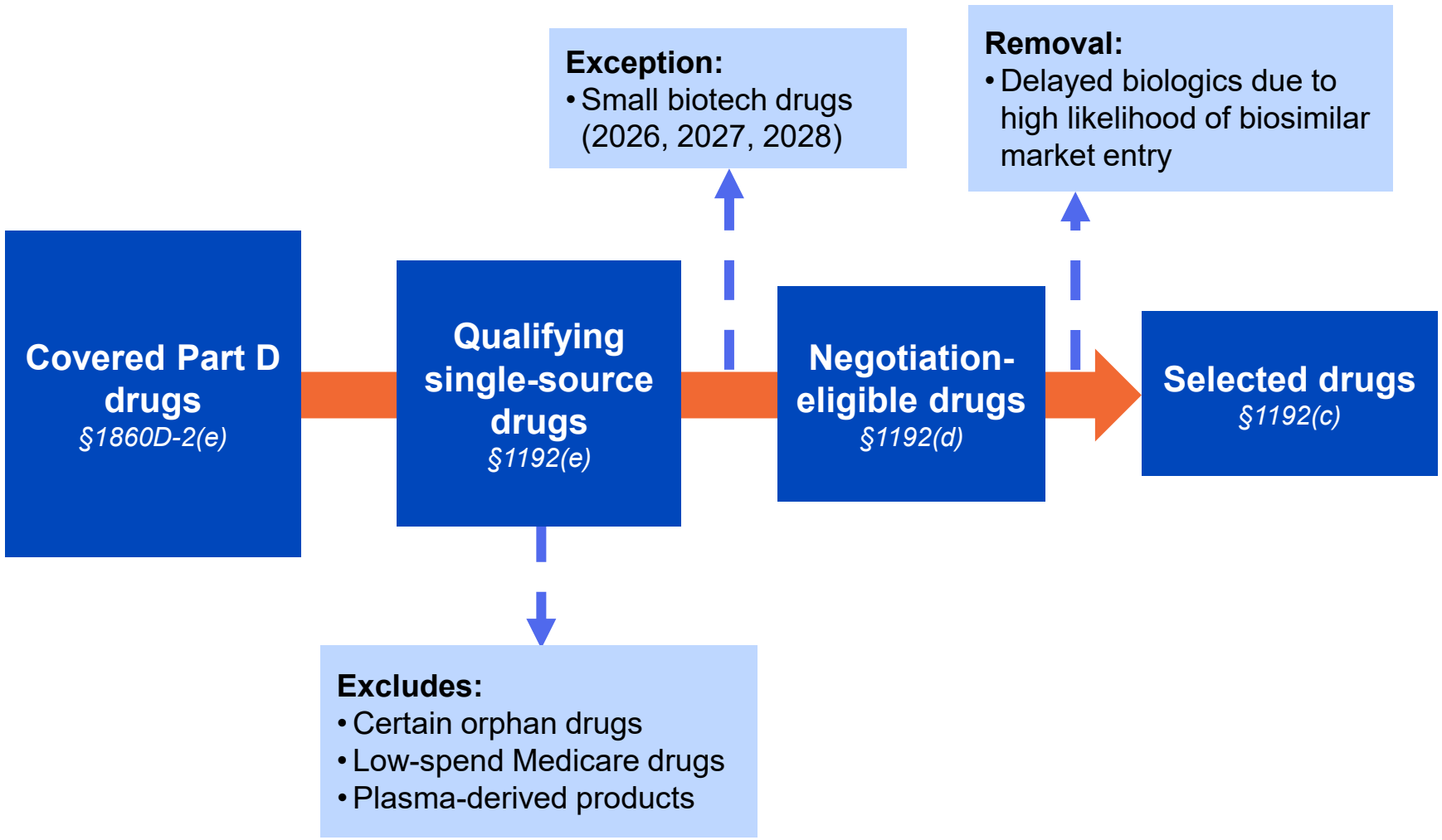
Delayed Selection for Certain Biologics

CMS will consider delaying the inclusion of a negotiation-eligible drug that includes the reference product for the biosimilar on the selected drug list for a particular year.

- Requirements include a determination that there is a “high likelihood” that the biosimilar will be licensed and marketed in 2 years.

- The biosimilar manufacturer may submit a request prior to selected drug publication date.

Summary of Process for Selecting Drugs for Negotiation



FDA Enforcement Priorities

FDA's Compliance Priorities

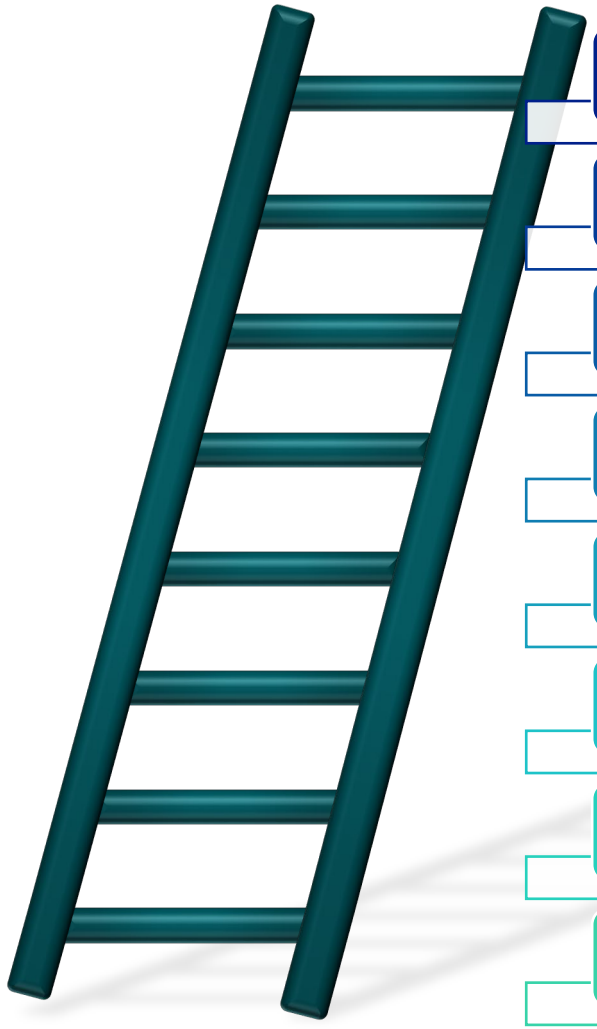
CDER Top Priorities:

- COVID-19 Fraud
- Compounding
- Opioids
- Unapproved Drugs
- Clinical Trial Oversight
- Drug Supply Chain & Security Act
- Product Recalls
- Shortages and Supply Chain Resiliency

ORA Top Priorities:

- Exceed goals for completing domestic surveillance inspections.
- Complete inspections and/or assessments in support of mission critical applications.
- Make decisions on applications reported as delayed due to a pending inspection or assessment.
- Follow up on previous inspections classified as official action indicated (OAI).

FDA Compliance & Enforcement Tools



- Civil or Criminal Referral to DOJ
- Civil Monetary Penalties
- Disqualification or Debarment
- NIDPOE/NOOH
- Warning Letter
- Rejection of Data/Complete Response Letter
- Clinical Hold
- Inspection

Overview of DOJ Enforcement Trends for Life Sciences + Healthcare Industries

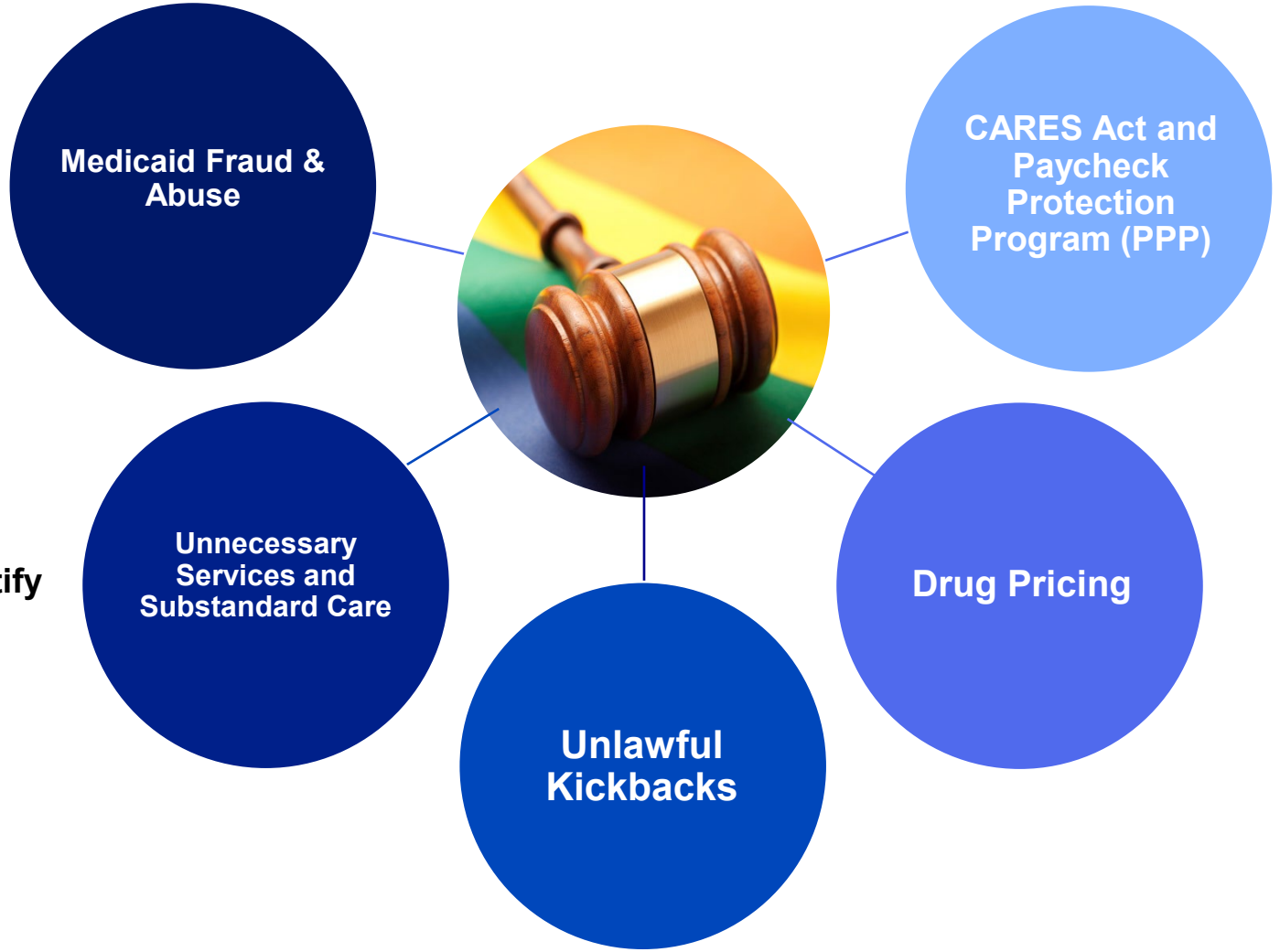
Justice Department Guidance

Renewed Focus on Corporate Malfeasance	Company's History of Misconduct Impacts DOJ Decision-making	Prevent Misconduct
▪ DOJ Revisions to Corporate Compliance Policy ▪ USAO Voluntary Corporate Disclosure Policy ▪ Surging resources to identify corporate misconduct	▪ All prior domestic or foreign criminal, civil & regulatory matters ▪ All actions against company's parent, divisions, affiliates, subsidiaries and other entities ▪ Examine Compliance Program	▪ Compensation Structure ▪ Reduce Fines for Companies that use Claw Back Provisions

DOJ's Consumer Protection Branch

DOJ's Main Areas of Focus

- DOJ's Civil Cyber Fraud Initiative designed to leverage the FCA to identify and deter cybersecurity incidents
- Settlements involving failure to protect patient data



- DOJ COVID-19 Fraud Enforcement Task Force

False Claims Act Settlements & Judgments

Last year, the DOJ obtained over $2.2 billion in FCA settlements and judgments from civil cases involving fraud and false claims against the Government

- **80% of the Recoveries ($1.76 billion) involve health care fraud.**

False Claims Act

Creates liability against any person who

- Knowingly submits a false claim to the Government;
- Knowingly makes a false record or statement to get a false claim paid by the Government; or
- Conspires with another to violate the FCA

Implied Certification Doctrine

Requesting payment from the Government without disclosing a known material breach can violate the FCA

Whistleblower Provisions & *Qui Tam* Relators

Allow private persons to sue on behalf of the Government

Known as "*qui tam*" actions, where the plaintiff is a "relator"

Relators are generally entitled to a portion of any recovery, as well as legal fees and expenses

***Qui tam* actions are filed under seal and trigger a Government investigation**

Government may either:

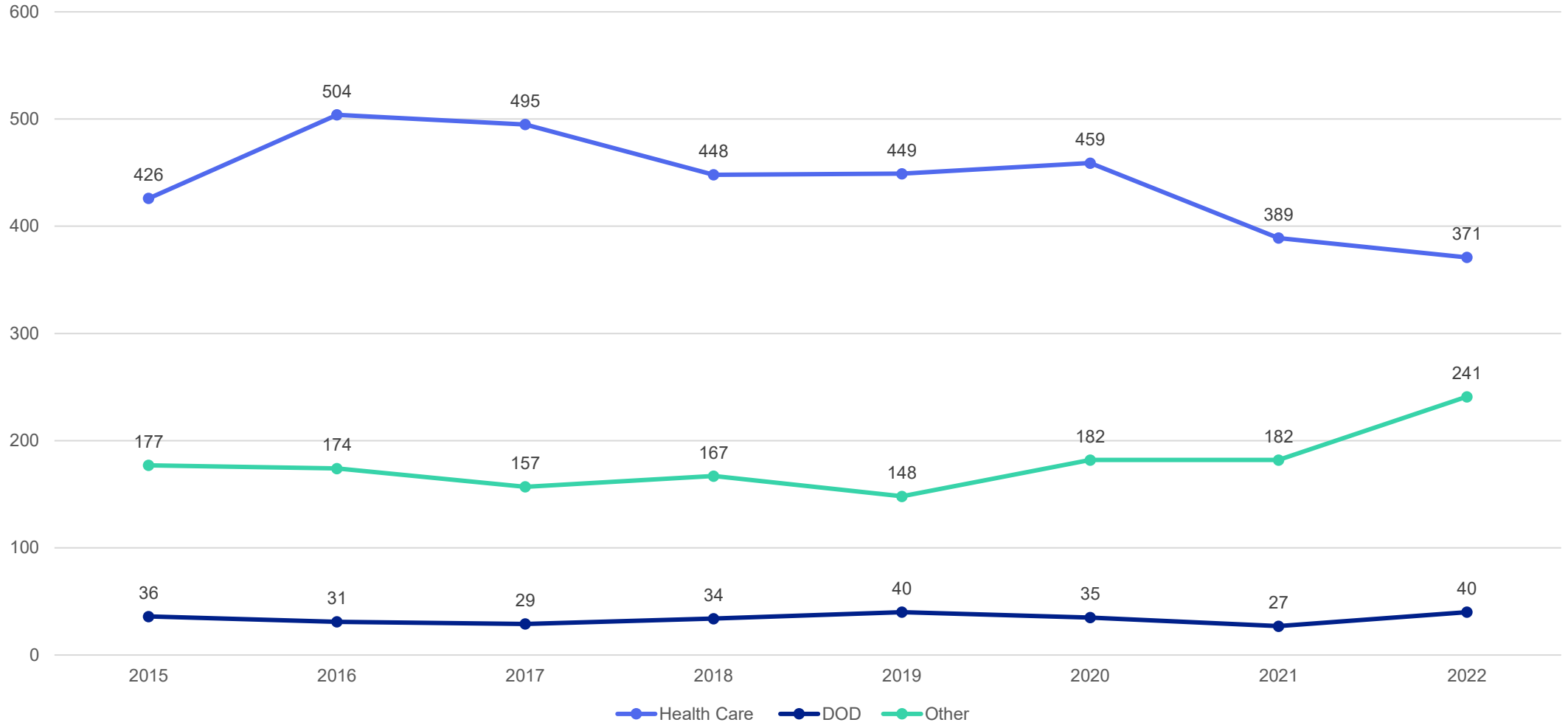
Intervene in the action
(i.e., take over the case)

OR

Decline to intervene
(relator may proceed on their own)

Government intervention can increase the likelihood of the court finding liability

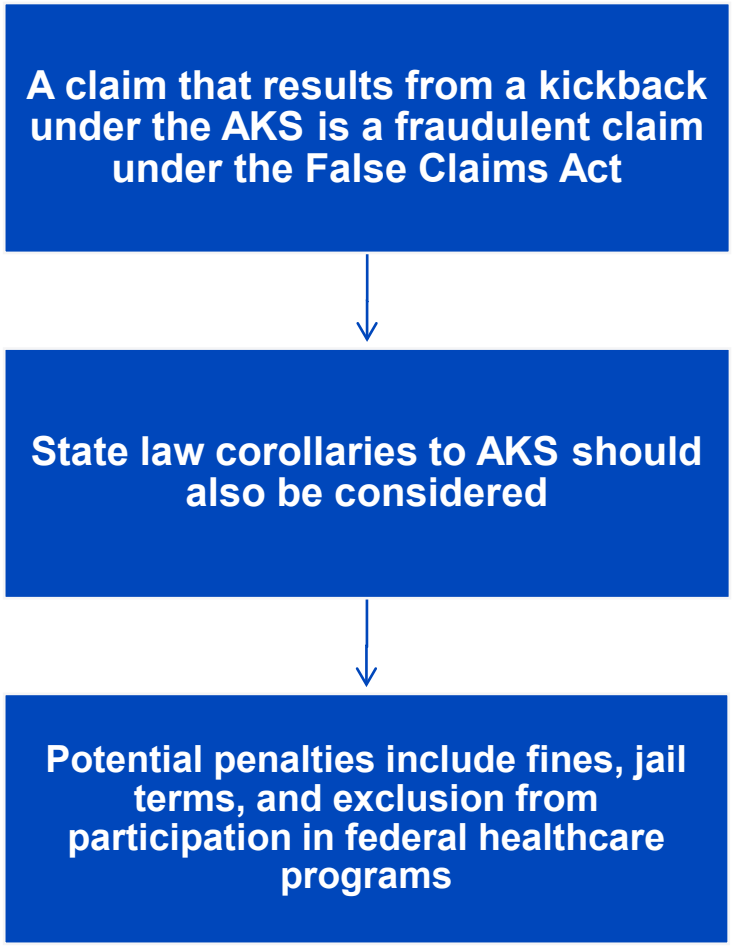
New *Qui Tam* Filings (652) – Up 9%



Anti-Kickback Statute (AKS)

AKS Overview

- AKS makes it a criminal offense to "knowingly and willfully offer, pay, solicit, or receive any remuneration to induce or reward referrals of items or services reimbursable by a federal healthcare program."
- "Remuneration" includes the transfer of anything of value, directly or indirectly, in cash or in kind.
- No actual knowledge of the AKS or specific intent required.



Expectations for Anti-Kickback Investigations

Sham agreements: little or no work required for compensation

- Speaking arrangements
- Continuing education programs
- Research

Lavish gifts: “lavish” just isn’t what it used to be

- Meals
- Alcohol
- Sporting events

Commission arrangements with third-party marketers

FCA/AKS Case Studies

Case Study: Cost Sharing Assistance Program

Pfizer sought Advisory Opinion

- **Sept. 2020 HHS Opinion that Cost Sharing program would allegedly violate AKS because it would induce Medicare patients to purchase medication**
  - Concerns of fraud and abuse – increase costs to Medicare, anti-competitive effects, could interfere with or skew clinical decision-making

The company allegedly sought to cover majority of $13,000 annual cost of a drug and eligible patients would pay $35/month.

- The company was allegedly concerned that many "middle-income" Medicare patients unable to afford medication.
- The company would not provide any financial incentives to physicians to favor medication or use the program to solicit new patients.

Second Circuit:

- Rejected the company's argument that program must be administered with "corrupt intent" to violate the AKS
- AKS prohibits "any remuneration (including any kickback, bribe, or rebate) directly or indirectly, overtly or covertly, in cash or in kind to any person to induce such person . . . to purchase . . . any good, facility, service, or item for which payment may be made in whole or in part under a Federal health care program."
- Supreme Court denied cert.
- Broader government crackdown on high-cost medications

Case Study: Speaker Programs

FCA relator filed *Qui Tam* challenging Novartis Speaker Programs as alleged illegal kickbacks to pay doctors to prescribe a drug

- U.S. declines to intervene

- Relator alleged (1) improper payments to doctors through "speaker programs" that had little educational value, were poorly attended, paid speakers for cancelled events and chose speakers on the basis of their prescription potential, and (2) found other ways to compensate these physicians including allegedly improperly outfitting medical offices, improperly producing promotional materials with the physicians' contact information, providing improper billing assistance, and "wining and dining" speakers.

Speaker Program Allegations.

- Doctors/Nurse allegedly paid to educate audience about benefits and drawbacks of a drug
- The company allegedly paid $1,500-$3,500 to its speakers at events that typically took place at high-end restaurants
- In Philadelphia, 5 speakers (4 doctors & 1 nurse) allegedly accounted for 43% of prescriptions of the drug in the region

SDNY dismisses 3rd Amended Complaint.

- Failure to plead existence of alleged kickback scheme with adequate particularity under Rule 9(b)
- The court had previously warned the relator that Rule 9(b)'s particularity rule required greater details to establish an alleged kickback scheme through "speaker programs" and gave examples: providing a list of the doctors that gave the same presentation to the same group of attendees over short periods of time – and specifically identifying the time period, the name of the presentations, the number of repeat attendees, and the alleged amounts received.

Role of the Corporate Compliance Officer

What are they thinking?

- Corporate Crime Advisory Group: all divisions with DOJ represented
- Charge: modifications to the Justice Manual and DOJ corporate criminal policies
- Monitorships: Reversing course from the Jeff Sessions/Bill Barr model. (Reasonable rationale.)

Ken Polite: CCO at heart

- CCO vignette – “That’s all I needed to see.”
- CCO as the internal champion of compliance culture.
- CCO with authority, access and experience

Certifications: logical extension

- CCO written into DOJ protocol, maximizing internal leverage and pass-through of message
- Better than a monitorship!
- With authority comes responsibility and expectations

Any Questions? Please Contact

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Stacy provides strategic regulatory and business advice to companies in the life sciences, healthcare, and technology industries. Stacy previously served as Chief Counsel of the U.S. Food and Drug Administration (FDA) and Deputy General Counsel of the Department of Health and Human Services (HHS), and held senior positions within the White House Counsel's Office and health committees in both the House and Senate. She leverages this experience to provide clients with an insider's perspective on regulatory and compliance issues, enforcement actions, and litigation challenges. As chief counsel of FDA, Stacy led an office of counselors and litigators and navigated difficult regulatory issues and litigation challenges across the agency's entire portfolio. Stacy also played a critical role in nearly every aspect of the FDA's COVID-19 pandemic response effort.

View Stacy's full bio here.

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Adam represents companies and their executives in internal and government investigations, white collar criminal defense matters, and parallel civil litigation related to allegations of bribery, government procurement fraud, COVID-19 and CARES Act fraud, anti-money laundering violations, and matters involving organized crime. Before joining MoFo, Adam spent 13 years at the U.S. Department of Justice (DOJ) where he served in senior level leadership positions in multiple administrations. As Associate Deputy Attorney General, he advised the Deputy Attorney General on litigation and policy matters and was designated to coordinate DOJ's efforts to investigate and prosecute fraud in connection with COVID-19 and CARES Act relief funds. He worked closely with all of DOJ's law enforcement agencies, other federal agencies, INTERPOL, Organized Crime Drug Enforcement Task Force (OCDETF), as well as state and local law enforcement associations.

View Adam's full bio here.

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Thank you!