Charting a Conditional Approval Pathway for Rare Disease Drugs – A Top Priority for a Revamped FDA?

On April 18, U.S. Food and Drug Administration (FDA) Commissioner Marty Makary **announced plans** to roll-out a new approval pathway for rare disease drugs. Commissioner Makary's comments build on sentiments expressed across both the patient community and industry that rare disease drug development needs greater regulatory flexibility in order to speed access to treatments for patients with no or limited options. This is an initiative that has also been **trumpeted by Janet Woodcock**, former Principal Deputy Commissioner and Acting Commissioner of the FDA, in her work since retiring from the FDA. Prior legislative proposals (including the "Promising Pathway Act" **proposed** in 2024) have attempted to create a time-limited conditional approval pathway in the rare disease space, and Commissioner Makary's remarks may signal a renewed push for action.

In last week's interview, Commissioner Makary emphasized the following potential eligibility factors in how he is thinking about a new "conditional" approval pathway: rare conditions affecting only a small number of people, where a randomized clinical trial has not been conducted and is not feasible, but where a "plausible mechanism" physiologically exists. Commissioner Makary also noted that post-approval monitoring of adverse events and other data may be an important tool to support more flexible regulatory decision making about drug approvals.

Whether *and when* the FDA or Congress will take further steps in outlining a conditional approval pathway, and what form that outline may take (e.g., Agency guidance, expansion of the current accelerated approval authorities, or new legislation), remains unclear at this time. This is an area rare disease researchers and developers should monitor for developments, including any opportunities to provide comments to the FDA on its potential plans.

Goodwin's 2025 Rare Disease Symposium: Momentum Builds for Addressing Critical Diagnosis and Treatment Gaps

Attendees at this year's **symposium** were optimistic about the potential for progress, citing momentum from new FDA initiatives, growing legislative support, and increased global innovation in research and development. These efforts, alongside increased patient advocacy and a presidential administration focused on speeding patient access, could lead to significant advances in rare disease treatments and cures in 2025.

Read the full insight **here**.

How the Trump Administration Could Reshape Regulation in the Life Sciences Sector


Based on recent policy signals and statements from incoming administration officials, a picture of potential regulatory and policy changes that could affect biotech, pharmaceutical, and medical device companies in coming months and years is emerging.

Anticipated changes span multiple regulatory fronts: a revamped approach to antitrust review at the Federal Trade Commission (FTC), continued momentum on biosecurity measures, and a fundamental rethinking of agency regulation to streamline "red tape" and accelerate patient access to innovative treatments. The Trump administration's stated focus on "making America healthy again" suggests a broader transformation in how healthcare is delivered and regulated, with emphasis on nutrition, prevention, longevity, enhanced physician autonomy, and a more holistic approach to health to reduce the burdens of chronic disease.

While some changes may create opportunities for innovation and growth, others could pose compliance and operational challenges. Understanding these emerging dynamics will be crucial for industry stakeholders as they position themselves for success under the new administration.

The following six sections are based on discussions from a regulatory panel held on January 15 at the **Goodwin + KPMG 6th Annual Symposium**, which was held during the 2025 JPM Healthcare Conference.

Read the full insight **here**.

New Momentum for a Time-Limited Conditional Approval Pathway for Rare Disease Drugs

 On October 4, 2024, a US House version of the revised Promising Pathway Act (PPA) 2.0 was introduced, sponsored by Rep. Bruce Westerman (R-AR). The bill (**H.R.9938**) mirrors a US Senate version that was introduced in May 2024 (**S.4426**) that would authorize the US Food and Drug Administration (FDA) to grant time-limited conditional approval to drugs for rapidly progressive, terminal diseases with substantial unmet need for treatments that are eligible for the Orphan Drug Act and result in a substantially shortened lifespan, substantial reduction in quality of life, or other substantial adverse health effects.

Read the full insight **here**.

Common FDA Bioresearch Monitoring (BIMO) Violations: Updates from FY 2023 to Now

The Bioresearch Monitoring (BIMO) Program, operated by the U.S. Food and Drug Administration (FDA), conducts on-site inspections and data audits in order to effectively monitor the compliance of all FDA-regulated research.

As a follow up to our **July 2023 post**, we highlight the most common violations identified in Fiscal Year (FY) 2023, in addition to those observed thus far in FY 2024. BIMO conducted **1073** inspections in FY 2023. The majority of these inspections (approximately 79%) were of drug, biologic, or medical device study clinical investigators, institutional review boards (IRBs), sponsors, clinical research organizations (CROs), and sponsor-investigators. Some of the most common inspection outcomes are highlighted in our alert linked below. Our methodology included a search of FDA's Warning Letter database for FY 2023 and 2024, to date, for letters issued by BIMO and the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiological Health to IRBs, CROs, clinical investigators, sponsors, and sponsor-investigators.

Read the full alert **here**.

Form FDA 483 Response Best Practices Announced by the FDA

In Draft Guidance published this week by the U.S. Food and Drug Administration (FDA), **Guidance for Industry – Processes and Practices Applicable to Bioresearch Monitoring Inspections**, the Agency provides some wisdom on best practices for responding to Form FDA 483s, albeit in the context of its Bioresearch Monitoring (BIMO) program inspections, but very much translatable to *any* Form FDA 483 response. FDA notes the following best practices:

A response should demonstrate the establishment's acknowledgment and understanding of FDA's observations. It should also demonstrate the establishment's commitment to address the observations, including a commitment from senior leadership.

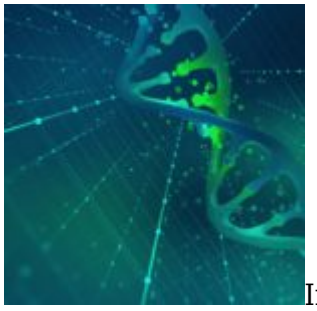
Responses should be well-organized and structured to:

- Address each observation separately
- Note whether the establishment agree(s) or disagree(s), and why
- Provide both corrective and preventive actions and timelines for completion
- Provide both completed and planned actions and related timelines
- Provide a method of verifying or monitoring the effectiveness of the actions
- Submit documentation (e.g., training, Standard Operating Procedures (SOPs), corrective action plans, records, etc.)

Importantly, FDA also states that timely Form FDA 483 responses that include "appropriate corrective and preventive actions could impact FDA's determination of the need for subsequent Agency action." FDA encourages responses within 15 business days after the end of an inspection and, helpfully, notes that any responses received within that window "will be considered before further Agency action or decision." Interested stakeholders may submit comments **here** on FDA's Draft Guidance until August 5, 2024.

*Please contact **Julie Tibbets** or any member of our **Life Sciences Regulatory & Compliance practice** with questions on FDA's Draft Guidance or on responding to Form FDA 483s.*

Designating a Platform Technology: FDA's Long-Awaited Draft Guidance



In newly released **Draft Guidance** from the U.S. Food and Drug Administration (FDA) entitled, *Platform Technology Designation Program for Drug Development*, the FDA addresses its new designation program for platform technologies, which is intended to bring efficiencies to drug development, manufacturing, and review processes for applications that incorporate designated platform technologies.

Read the full alert **here**.

Common FDA Bioresearch Monitoring Violations: Updates from FY 2022 to Now

 The Bioresearch Monitoring (BIMO) Program, operated by the U.S. Food and Drug Administration (FDA), conducts on-site inspections and data audits in order to effectively monitor the compliance of all FDA-regulated research.

As a follow up to our **June 2022 post**, we highlight the most common violations identified in Fiscal Year (FY) 2022, in addition to those observed thus far in FY 2023. BIMO conducted 766 inspections in FY 2022. The majority of these inspections (approximately 79%) were of drug, biologic, or medical device study clinical investigators, institutional review boards (IRBs), sponsors, clinical research organizations (CROs), and sponsor-investigators. Some of the most common inspection outcomes are highlighted below. Our methodology included a search of FDA's Warning Letter database for FY 2022 and 2023, to date, for letters issued by BIMO and the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiological Health to IRBs, CROs, clinical investigators, sponsors, and sponsor-investigators.

FY 2022:

BIMO conducted 504 inspections of clinical investigators (468 of which were assigned to FDA's drug, biologic, and device Centers), making up over half of BIMO's inspections conducted in FY 2022. Inspections of IRBs, sponsors, CROs, and sponsor-investigators assigned to FDA's drug, biologic, and device Centers comprised another 138 inspections in FY 2022. Of the 504 clinical investigator inspections, only 9 resulted in a classification of "Official Action Indicated" (OAI) and 87 resulted in a classification of "Voluntary Action Indicated" (VAI). The most common inspection observations included: (1) failure to comply with Form FDA 1572 requirements and protocol compliance; (2) failure to follow the investigational plan and protocol deviations; (3) inadequate and/or inaccurate case history records and inadequate study records; (4) inadequate accountability and/or control of the investigational product; (5) safety reporting and failure to report and/or record adverse events; and (6) inadequate subject protection and informed consent issues.

Of the Warning Letters that were issued in FY 2022 to clinical investigators, the most common observations were:

- **Failure to ensure that a clinical investigation was conducted according to its investigational plan.** This finding in various Warning Letters included failure to properly consent participants, failure to properly randomize participants, and/or failure to properly screen potential participants to ensure they met a protocol's inclusion and exclusion criteria prior to enrollment in an investigational plan. For example, in one **Warning Letter**, an

investigator did not ensure that subjects randomized to a specific intervention group received the assigned investigational drug for that intervention group and did not adhere to the blinding protocol.
- **Failure to submit an IND application for the conduct of a clinical investigation with an investigational new drug.** For example (and similar to trends observed in FY 2021), the FDA noted that one **clinical investigator** failed to submit an IND for the use of a product that was determined by the FDA to be a drug. The study design demonstrated that the investigational product was intended to cure, mitigate, and/or treat a disease or condition and therefore, an IND application should have been submitted to the FDA prior to commencing any research activities. Another **Warning Letter** included a finding that a protocol comprised of a combination product (a drug and device component) required an IND application.

BIMO conducted 81 inspections of sponsors and CROs in FY 2022 (all but one were assigned to FDA's drug, biologic, and device Centers). Of these, 0 resulted in a finding of OAI, though 15 were classified as VAI. The most common inspection observations included: (1) failure to ensure proper monitoring of the study and ensure the study is conducted in accordance with the protocol and/or investigational plan; (2) failure to meet the abbreviated requirements for investigational device exemptions (IDEs); (3) failure to maintain and/or retain adequate records in accordance with 21 CFR 312.57; (4) accountability for the investigational product; (5) failure to comply with Form FDA 1572 requirements; (6) financial disclosures; (7) failure to submit an Investigational New Drug (IND) application and IND safety reports; and (8) failure to submit current list of all participating investigators to FDA at the six-month interval after FDA approval of the study.

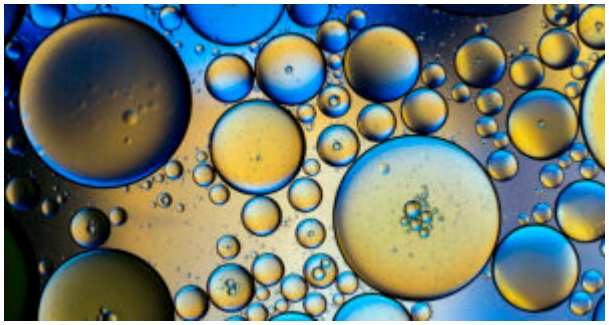
FY 2023 Trends (to date):

In 2023, we have already observed six Form FDA 483 Warning Letters issued to clinical investigators and IRBs, three involving the failure to submit an IND for the conduct of a clinical investigation with an investigational new drug, two involving failure to follow the clinical investigation according to its investigational plan, and one involving overall lack of IRB oversight and IRB compliance. For example, in a 2023 **Warning Letter** issued to an IRB, the FDA noted that the IRB: (a) failed to review proposed research at convened meetings at which a majority of IRB members were present; (b) failed to maintain adequate documentation of IRB activities, including keeping an active list of active IRB members; and (c) failed to ensure that information provided to study subjects as part of the informed consent process was done in accordance with applicable FDA regulations. Although sponsors may often make the decision to utilize a central IRB to oversee the conduct of a clinical investigation, some participating sites may be required to utilize their own local IRB, and it is important to remember that any IRB which does not adhere to FDA's requirements can introduce a compliance risk for studies it is engaged to oversee.

Sponsors, clinical investigators, CROs, and IRBs should review the FDA's **BIMO Compliance Program Guidance Manuals** regularly to ensure that they understand their responsibilities when carrying out clinical research involving human subjects. Sponsors, clinical investigators, CROs, and IRBs should ensure inspection readiness at all times while bioresearch is ongoing and following completion of bioresearch that may support marketing applications submitted to the FDA. Ensuring diligence in the research site selection process, careful monitoring during clinical trials, and corrective actions when deviations occur can help manage the risk of inspection findings of noncompliance or Warning Letters issued by the FDA. The Goodwin Life Sciences Regulatory & Compliance team provides regulatory counseling on FDA's Good Clinical Practice requirements and the resolution of BIMO inspection findings and Warning Letters when they occur.

Contact our team to learn more.

Psychedelics & Drug Development — Key Considerations for Healthcare Industry and Life Sciences Companies as Congress Seeks to Tap Into Psychedelics' Therapeutic Potential



Based on recent regulatory changes at the state and local level and the efforts by the federal government and certain foreign agencies, investors, clinical trial sponsors, life sciences companies, and investigators operating in the psychedelics industry may have reason to be optimistic about the future regulatory landscape for therapeutic psychedelic product candidate development, approval, and commercialization. The proposed Breakthrough Therapies Act is one such reason.

On March 8, 2023, US Sens. Cory Booker (D-NJ) and Rand Paul (R-KY) **introduced** an **updated version** of the Breakthrough Therapies Act. If passed, the bipartisan bill would amend the federal Controlled Substances Act (CSA) to enable the Drug Enforcement Administration (DEA) to reclassify from Schedule I to Schedule II drugs and biologics, including therapeutic psychedelics, that receive breakthrough therapy designation or are authorized for expanded access by the US Food and Drug Administration (FDA). Therapeutic psychedelics are Schedule I substances and include LSD, MDMA, and psilocybin. According to the bill's sponsors, the "legislation [would] remove regulatory hurdles that inhibit research and compassionate use access to potentially lifesaving treatments that are heavily restricted by Schedule I of the [CSA]."

The bipartisan effort behind the Breakthrough Therapies Act signals the federal government's evolving position on psychedelic substances, their therapeutic potential, and access. This evolution, discussed in greater detail in our Client Alert, presents an important opportunity for investors, clinical trial sponsors, life sciences companies, and investigators.

Accordingly, we have identified and answered 8 key questions that stakeholders should consider as they develop and innovate in the psychedelic space:

- What Is the Difference Between a Schedule I and a Schedule II Drug?
- What Diseases and Conditions Can Potentially Benefit From Therapeutic Psychedelics?
- What Are the Key Provisions of the Proposed Breakthrough Therapies Act?
- How Does a Drug or Biologic Obtain Breakthrough Therapy Designation From FDA?
- What Is Expanded Access?
- What Are Some Key Limitations in the Proposed Breakthrough Therapies Act?
- What Is the Status of Therapeutic Psychedelics at the State and Local Level?
- What Regulatory Changes Are on the Horizon for Therapeutic Psychedelics?

Read the full client alert **here**.

Seven Tips for Healthcare & Life Sciences Companies Engaging Independent Monitors and Compliance Experts

For a healthcare or life sciences company settling a government enforcement action, the prospect of being subject to an independent monitor, independent review organization (IRO), or other government-mandated compliance expert may become a reality. (We collectively refer to all of these individuals and entities as monitors throughout this update.) Hiring an independent monitor is a sensitive topic, as a company subject to a monitorship is required to open up its records and files, financial information, proprietary and confidential materials, IT assets, and employees to a third party — often at frequent and regular intervals, and often for a period of five years — not to mention the potential multimillion-dollar expense associated with the engagement.

Read the client alert **here**.