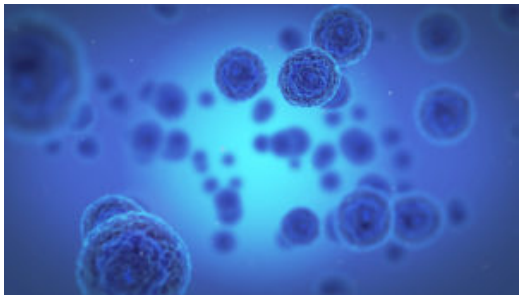
The Long (Un)Winding Road Part 2: FDA's Final Transition Guidances for COVID-19 Devices



On March 24, 2023, the FDA's Center for Devices and Radiological Health announced the issuance of two much anticipated final guidances that describe the Agency's transition plans for medical devices that fall within certain COVID-19 enforcement policies or that were issued emergency use authorizations ("EUA"s):

- **Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency** (the "Enforcement Policies Final Guidance")
- **Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) Related to Coronavirus Disease 2019 (COVID-19)** (the "EUA Transition Final Guidance")

The guidances follow the announcement in early 2023 that the Biden Administration plans to wind-down a number of pandemic-related programs and to allow the COVID-19 public health emergency ("PHE") declaration, which has been in effect since January 2020, to expire on May 11, 2023.

We summarize some of the key takeaways from FDA's finalized transition plans. Read the client alert **here**.

US Artificial Intelligence Regulations: Watch List for 2023

Companies are developing, deploying, and interacting

with artificial intelligence (AI) technologies more than ever. At Goodwin, we are keeping a close eye on any regulations that may affect companies operating in this cutting-edge space.

For companies operating in Europe, the landscape is governed by a number of in force and pending EU legislative acts, most notably the EU AI Act, which is expected to be passed later this year; it was covered in our prior client alert here: **EU Technology Regulation: Watch List for 2023 and Beyond**. The United Kingdom has recently indicated that it may take a different approach, as discussed in our client alert on the proposed framework for AI regulation in the United Kingdom here: **Overview of the UK Government's AI White Paper**.

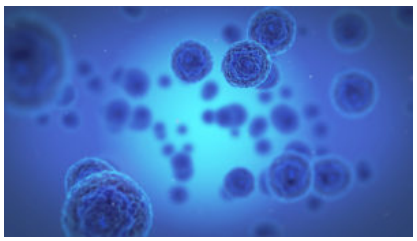
For companies operating in the United States, the landscape of AI regulation remains less clear. To date, there has been no serious consideration of a US analog to the EU AI Act or any sweeping federal legislation to govern the use of AI, nor is there any substantial state legislation in force (although there are state privacy laws that may extend to AI systems that process certain types of personal data).

Read the client alert **here**.

FDA Issues Guidance Document on Animal Studies for the Evaluation of Medical Devices

The U.S. Food and Drug Administration (FDA) recently issued **General Considerations for Animal Studies Intended to Evaluate Medical Devices – Guidance for Industry and Food and Drug Administration Staff (fda.gov)**. Following a 2015 draft guidance and replacing a 2010 guidance focused on animal studies for cardiovascular devices, this guidance document identifies general considerations for animal studies intended to provide evidence of safety, including performance and handling, in device premarket submissions "when a suitable alternative to an animal study is not available." Among other topics, the guidance provides recommendations related to personnel credentials, selecting an appropriate animal model, testing facility selection, and how to prepare an animal study report for premarket submissions to FDA. The Agency encourages sponsors with specific questions on an animal study, including the animal model selected, or compliance with FDA's Good Laboratory Practice (GLP) regulations, or who seek to use a non-animal testing method, to request feedback from FDA through the Q-Submission process.

The Long (Un)Winding Road: FDA Maps Out How the End of the Public Health Emergency Will Impact its COVID-19 Policies



Since the beginning of the COVID-19 pandemic, the United States Food and Drug Administration ("FDA") has issued more than eighty (80) guidance documents describing flexibilities that would be available to manufacturers of medical devices, drugs and biological products, and foods during the public health emergency. Several of these guidance documents have been modified, updated, or withdrawn as circumstances have changed, and on March 13, 2023, the FDA issued a **notice** in the Federal Register that outlines how it intends to unwind a large swath of COVID-19-related guidance documents that are still in effect. FDA sorted seventy-two (72) COVID-19-related guidances into several categories, based on how long and in what form they will continue to be in effect after the expiration of the public health emergency declaration, which is expected on May 11, 2023.

Read the client alert **here**.

HHS to Create New Potential Medicare Pricing Models for Cell and Gene Therapy, Drugs Subject to Accelerated FDA Approval, and "High-Value" Generics

On February 14, 2023, the U.S. Department of Health and Human Services (HHS) published a **report** identifying three models that the Center for Medicare & Medicaid Services' (CMS) Center for Medicare & Medicaid Innovation (CMMI) will test to try to improve the affordability and accessibility of prescription drugs. The report responds to the state of prescription drug costs and access in America, as well as the widespread changes introduced by the Inflation Reduction Act of 2022 and President Biden's **Executive Order 14087** (October 2022), both intended to help lower prescription drug costs for Americans. The three selected models will test the feasibility of methods to: (i) offer generic prescription drugs at $2 or less for Medicare patients; (ii)

reduce Medicaid costs for novel cell and gene therapies through outcomes-based agreements with manufacturers on a multistate level; and (iii) improve the safety and efficacy of drugs approved through the FDA's Accelerated Approval Program by aligning payment methods with stakeholders' incentives. More detail on these three models is expected, and Goodwin attorneys will continue to monitor for additional guidance and any opportunities for public comment.

Read the client alert **here**.

Leveraging Investigator-Initiated Trials in Rare Disease Drug Development

Investigators interested in rare disease treatment development have the opportunity to approach drug and biologic developers to obtain investigational drug supply for trials in which the investigators, typically at academic institutions, act as sponsor-investigators. Similarly, companies open to extending their product development pipelines can look to investigator-initiated trials as a mechanism to better understand the overall safety profile for their product candidates while exploring the potential therapeutic utility of their product candidates in diseases where unmet medical needs remain. So often, those needs exist in rare diseases where populations are small and investment returns are difficult to project. Drug developers deciding whether to supply investigational products to sponsor-investigators looking to explore therapeutic potential in areas of their research interests should evaluate what level of involvement to exercise over the investigator-initiated trial. We highlight some of these considerations below.

Ultimately, drug developers hold the decision-making power over whether to allow investigator-initiated research for their product candidates. Thereafter, the contracting process around the setup of an investigator-initiated trial and clinical supply agreement provides drug developers the

opportunity to negotiate their level of involvement in the research of their candidates. In negotiating the setup of investigator-initiated research supply, drug developers often balance their support of research into what are often unmet needs with limited company resources, limited supply that may be available and any potential risks that may flow from trial learnings in the proposed disease space. As an upside, investigator-initiated trials afford developers the opportunity to extend their research reach and product development pipelines, so any interest by investigators to conduct research with industry candidates warrants consideration.

340B Drug Pricing Program Reform Considerations

 The 340B Drug Pricing Program is a government program, administered by the Health Resources and Services Administration (HRSA), that allows qualifying hospitals and clinics that treat low-income and uninsured patients to buy certain prescription drugs at a steep discount from drug manufacturers. Drug manufacturers participate in the 340B Program as a condition of obtaining Medicaid coverage of their drugs. For the many drug manufacturers who want their products to reach the broadest patient population, participation in the 340B Program is essentially mandatory.

The program is intended to help safety-net health care providers' financial resources reach more financially vulnerable patients and deliver comprehensive services.[1] At the same time, drug manufacturers have concerns about the program:

- Manufacturers are concerned that deeply discounted prescription drugs should only go to covered entity patients and not diverted to individuals who are not covered entity patients, i.e., a practice commonly known as drug diversion.
- Manufacturers are concerned that the covered entities do not get both a deep Section 340B discount and any additional discounts and rebates under Medicaid, i.e., duplicate discounts.

Balancing the interests of covered entities and drug manufacturers has been a challenge, and one that has come under scrutiny in recent years. Drug manufacturers have no way of tracking how covered entities use the discounts paid under the Section 340B program, and there is no legal requirement for covered entities to pass the savings they received from manufacturers to patients.

There are four emerging areas of tension between the interests of covered entities and drug manufacturers related to the 340B program :

- Section 340B telemedicine standards and patient eligibility;
- Contract pharmacy utilization;
- Section 340B covered entity child sites; and
- Drug manufacturer audit limitations.

Until these four key areas are addressed, the Section 340B program will not serve its true goals; and drug manufacturers and covered entities will face increasing conflict over ambiguous and outdated regulations.

For more information regarding these controversies in the 340B Program, please see our recent Health Law360 and Life Sciences Law360 article, "**4 Key Issues Driving Drug Discount Abuse Must Be Addressed**" (Jan. 9, 2023) as well as our recent Goodwin Procter LLP client alert, **Federal Court of Appeals Rejects HHS Stance on Section 340B Contract Pharmacies** (Feb. 1, 2023).

[1] Health Resources & Servs. Admin., 340B Drug Pricing Program (Dec. 30, 2022).

Understanding Data Monitoring Committee Conflict of Interest Limitations

For sponsors utilizing a data monitoring committee in their trial designs to monitor for emerging safety signals, lack of effect, and/or futility of treatment, understanding data monitoring committee conflict of interest limitations is important to ensuring an objective view of the data from a trial. Where we see these conflict of interest considerations put to the test most often is in rare disease trials where the available pool of informed experts can be just as small as the patient populations under study. As explained in FDA's final **guidance** for industry on this topic, core considerations for avoiding potential conflicts of interest in data monitoring committee member selection include:

- **Financial interests.** Here, careful consideration must be given to whether any prospective committee member holds ownership interests in the sponsor entity or stands in a position to benefit financially from the outcome of the trial. This can include equity or stock interests, employee or temporary employee status, paid consulting or advisory board relationships with the sponsor, prior research funding from an institution involved in the study, whose product is being evaluated in the study or competes with a product being evaluated in the study, among other things. FDA generally recommends against appointing any committee members with *ongoing* financial relationships to the trial's sponsor.

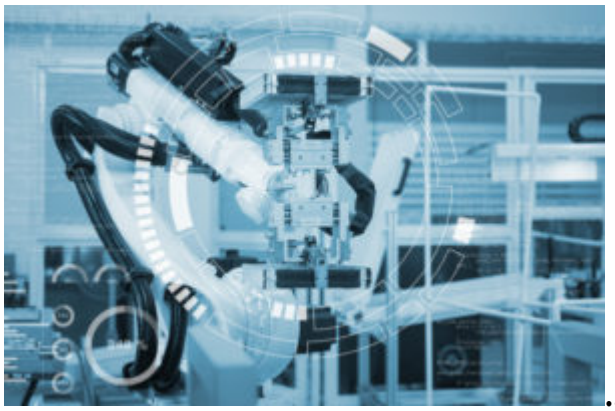
- **Other roles in the trial.** Those individuals entering subjects into and conducting a trial stand in a considerable conflict position given their knowledge of interim data emerging from subjects at their trial site which could influence the recruitment or monitoring trends of those individuals for the trial. As such, FDA generally recommends against appointing any committee member who is serving as an investigator in the trial the data monitoring committee would oversee. Additionally, FDA disfavors appointment of any members that have

had input into the design of the trial or are involved in the conduct of the trial in any other role for similar reasons.

- **Intellectual conflicts.** Perhaps most challenging to evaluate and navigate in rare disease trials is the risk to objectivity that strongly held views of prospective data monitoring committee members could play in their ability to review the data in a fully objective manner. This could include prospective committee members with strong views on the relative merits of the intervention under study vs. others under development. Additionally, FDA recommends against appointing committee members with strong relationships to or personal differences with trial investigators or to sponsor employees which are likely to cloud their objectivity.

FDA recognizes the tension that sponsors must navigate between placing a high value on independence and avoidance of conflicts of interest in the composition of its data monitoring committees, on the one hand, and understanding the importance of a well-informed data monitoring committee to the effective oversight of emerging data from a trial, on the other. While there is no one-size-fits all approach, data monitoring committee charters and sponsor conflict of interest policies can be helpful in this regard to establish and document the sponsor's limitations on engagement and interaction with the committee and vice versa. The more interconnected the sponsor-developer and investigator communities become, the more challenging it may become for sponsors, particularly those in the rare disease space, to ensure the objectivity of its data monitoring committees.

The European Commission Proposes to Extend the Transition Deadline in the EU Medical Device Regulation



... a major change to the Regulation is needed to prevent shortages of life-saving medical devices...

Background

On Friday 9 December 2022, the European Commission proposed to extend the transition deadline in the **Medical Device Regulation (EU) 2017/745** (**MDR**). According to the European Commissioner for Health and Food Safety, Stella Kyriakides, a major change to the Regulation is needed to prevent shortages of life-saving medical devices, from implants and prosthetics to ventilators and pacemakers.

Medical devices in the EU are regulated under the MDR, and the MDR replaced the previous Medical Devices Directive 93/42/EEC (**MDD**) and the Active Implantable Medical Devices Directive 90/385/EEC (**AIMDD**) on 26 May 2021. Currently, medical devices can be placed on the EU market under a CE mark certificate issued under the MDD or AIMDD until 26 May 2024 (**Transition Deadline**). After the Transition Deadline, these products will require a CE mark certificate issued under the MDR so that they remain available on the EU market – a potentially costly and time-consuming process.

A broad range of stakeholders in the medtech sector consider the Transition Deadline to be unattainable. The pandemic, shortages of raw materials caused by the conflict in Ukraine and low Notified Body capacity have collectively put a strain on the ability for medical device manufacturers to meet the Transition Deadline. Without an extension to the Transition Deadline, it is anticipated that a significant number of medical device manufacturers would need to take their products off the EU market due to an inability to comply with the new requirements under the MDR within the required timeline.

Key Proposals

The European Commission has proposed the following legislative amendments:

- Extension of the Transition Deadline in the MDR based on the risk class of each device:
  - 26 May 2027 for Class III and Class IIb medical devices; and
  - 26 May 2028 for Class IIa and Class I medical devices.
- Extension of the validity of CE mark certificates issued under the MDD and AIMDD if needed for legal and practical reasons (e.g. to access markets outside of the EU that accept products with a CE mark), provided that:
  - the device does not present an unacceptable risk to health and safety;
  - the device has not undergone significant changes in design or intended purpose; and
  - the manufacturer has already undertaken the necessary steps to launch the CE mark certification process under the MDR (e.g. lodged an MDR application with a Notified Body by 26 May 2024).
- Elimination of the "sell-off" date under the MDR and under the **In Vitro Diagnostic Medical Device Regulation (EU) 2017/746** (**IVDR**) to avoid safe medical devices and in vitro diagnostics (e.g. blood glucose meters) that are already on the EU market from having to be discarded by 27 May 2025.

Next Steps

The European Commission intends to provide these legislative amendments to the EU legislature for consideration at the beginning of 2023.

The European Commission also intends to undertake a comprehensive evaluation of the MDR by May 2027. The purpose of the evaluation is to identify structural problems with the MDR and potential medium and long-term solutions to these concerns.

As a final note, except for the elimination of the "sell-off" date, none of the proposed legislative amendments applies to in vitro diagnostics. Given that there are still few Notified Bodies under the IVDR, similar amendments might also be required for in vitro diagnostics in the near future.

Congress Expands Pathway for Drug & Device Manufacturers' Pre-Approval Communication of Health Care Economic Information to Payors, Formularies, & Similar Entities

The legislation previously introduced as the **Pre-Approval Information Exchange Act of 2022** ("PIE Act") was passed as part of Congress's December 23, 2022 omnibus spending bill. Once signed into law, this legislation will amend the Federal Food, Drug, and Cosmetic Act's (FDCA's) provisions on misbranded drugs and devices to formally allow drug and medical device manufacturers to proactively share investigational drug and device information, including health care economic information, with payors, health plans, formulary committees, and other similar entities *prior* to the clearance or approval of the drug or device or new use of the drug or device but with now-statutory strings attached.

The US Food and Drug Administration (FDA) has long had the authority to enforce against pre-approval *promotional* communications, and a pathway for pre-approval communication of health care economic information regarding the selection of drugs for coverage and reimbursement was enacted under the Food and Drug Administration Modernization Act of 1997. **Current guidance from FDA**, finalized in 2018, expressly permits drug and device companies to provide some details about investigational products or investigational uses of marketed products to payors, formulary committees, and similar entities prior to approval or clearance of the product or its new use; however, for device companies this has come in the form of non-binding guidance that lacks a formal anchor in the statutory language. The inclusion of the legislation previously known as the PIE Act in the omnibus spending bill formally establishes a statutory pathway built on FDA's 2018 final guidance for both drug and medical device companies to engage in pre-market communications about health care economic information with payors, formulary committees, and similar entities.

Read the client alert **here**.