“March-In” Rights in the Era of COVID-19: An Unlikely Scenario for Remdesivir

As the total number of COVID-19 deaths in the U.S. is expected to climb to between 180,000 to 200,000 by September 5, 2020[1][2], there currently are no FDA-approved vaccines or drugs to prevent or treat COVID-19. However, the FDA has granted emergency use authorizations to some products for use in certain patients with COVID-19, including to Gilead for its investigational antiviral drug remdesivir[3].

On August 4, 2020, a bipartisan group of 34 state attorneys general (AGs) asked the U.S. government to exercise its march-in rights under the Bayh-Dole Act and license Gilead’s remdesivir to third-party manufacturers in order to scale up production and lower the price of the drug, or allow states to do so.[4] The AGs argued that the U.S. government should exercise its march-in-rights because the price of remdesivir is too high and because Gilead “has benefited from millions of dollars of public funding, including a $30-million NIH-funded clinical trial,” and “is unable to assure a supply of remdesivir sufficient to alleviate the health and safety needs of the country.”[5]

The AGs’ request that the U.S. government exercise its march-in rights under the Bayh-Dole Act, however, does not appear to be tethered to the law.

Under the Bayh-Dole Act, in specific circumstances, the U.S. government has the right to “march-in” and either grant licenses, or require the patent holder/licensee to grant licenses, to third parties under federally funded patents.[6] The U.S. government may exercise its march-in rights if it determines that action is necessary because the patent holder or licensee:

- has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention;
- is not reasonably satisfying health or safety needs;
- is not reasonably satisfying regulatory requirements for public use; or
- has violated the U.S. industry preference provisions of 35 U.S.C § 204.[7]

If the U.S. government decides to exercise its march-in rights, the decision may be appealed to the U.S. Court of Federal Claims, and with respect to items (1) and (3) above, march-in rights may not be exercised until all appeals or petitions are exhausted.[8]

Despite having the authority, the U.S. government has never exercised its march-in rights. In its response to a 1997 petition requesting that the NIH exercise it march-in rights, the NIH noted its unwillingness “to influence the marketplace for the benefit of a single company, particularly when such actions may have far-reaching repercussions on many companies’ and investors’ future willingness to invest in federally funded medical technologies,”[9] and, with respect to drug pricing,

in response to a 2004 petition, the NIH noted that "because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by NIH, the NIH agrees with the public testimony that suggested that the extraordinary remedy of march-in is not an appropriate means of controlling prices."[10]

Given the fact that: (a) march-in rights are limited to federally funded patented inventions (and it is not clear to what extent federal funds contributed to the development or remdesivir[11]), (b) the Bayh-Dole Act is not triggered by high drug prices, (c) the NIH's unwillingness to exercise its march-in rights, particularly because it does not want to disincentivize innovation and does not believe that the Bayh-Dole Act should be used to control drug prices, and (d) the patent holder/licensee has the ability to appeal the U.S. government's decision to exercise its march-in rights, and some instances march-in rights may not be exercised until all appeals or petitions are exhausted, it seems unlikely that the Bayh-Dole Act will be invoked in response to the AGs' request that the U.S. government exercise its march-in rights.

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[1] According to the Centers for Disease Control and Prevention (CDC) COVID Data Tracker, as of August 21, COVID-19 has claimed 173,490 lives. **https://www.cdc.gov/covid-data-tracker/#cases**

[2] **https://www.cdc.gov/coronavirus/2019-ncov/covid-data/forecasting-us.html#anchor_1587397564229**

[3] **https://www.gilead.com/purpose/advancing-global-health/covid-19**

[4] **https://www.oag.ca.gov/system/files/attachments/press-docs/Remdesivir%20Letter%2020200804.pdf**

[5] **https://www.oag.ca.gov/system/files/attachments/press-docs/Remdesivir%20Letter%2020200804.pdf**

[6] 35 U.S.C. §203(a).

[7] 35 U.S.C. §203(a).

[8] 35 U.S.C. §203(b).

[9] Harold Varmus, Director, NIH, Determination in the Case of Petition of CellPro,Inc., August 1, 1997,

http://web.archive.org/web/20070102183356/http:/www.nih.gov/icd/od/foia/cellpro/pdfs/foia_cellpro39.pdf.

[10] Elias A. Zerhouni, Director, NIH, In the Case of Norvir Manufactured by Abbott Laboratories, Inc., July 29, 2004,

http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf.

[11]
https://www.statnews.com/pharmalot/2020/05/08/gilead-remdesivir-covid19-coronavirus-patents/

Real-World Evidence: Challenges and Opportunities During COVID-19

The urgent needs of the COVID-19 pandemic have more squarely brought into focus the role real-world evidence (RWE) can play in analyzing and informing product development and clinical and public health decisions. Specifically, the U.S. Food and Drug Administration (FDA) is participating in the COVID-19 **Evidence Accelerator**, in partnership with Friends of Cancer Research and the Reagan-Udall Foundation, to bring leading experts together to share insights and use RWE to help answer the most pressing research questions raised by the pandemic.

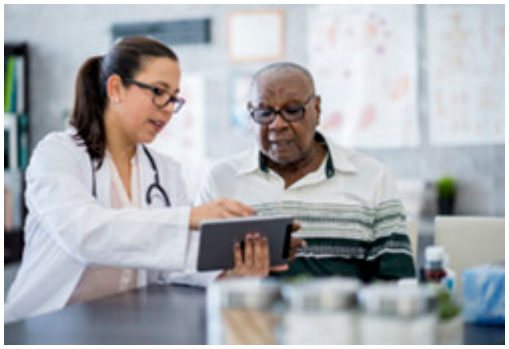
The FDA believes that RWE can play an informative role in analyzing potential therapies, vaccines, and diagnostics for COVID-19. At the recent "Establishing a High-Quality Real-World Data Ecosystem" **workshop** hosted by the Duke Margolis Center for Health Policy, Amy Abernethy, the Principal Deputy Commissioner of Food and Drugs and Acting Chief Information Officer at the FDA, highlighted the work of the Evidence Accelerator initiative, noting that RWE allows the FDA to constantly update its understanding of COVID-19 and recurrently analyze data to address changing needs. Amongst the other presenters, the general discussion focused on the many hurdles industry needs to address to establish a robust and more accurate RWE data ecosystem, including efficient capture of reliable data at the source. While internet access, smartphones, and wearable technology enable consumers and patients to keep meticulous records of their biometric data, the vast amount of collected data does not necessarily lead to efficient or fruitful analysis currently. FDA noted during the workshop that, to be more insightful, RWE stakeholders must narrowly tailor their collection to what is actually useful and relevant to clinical endpoints, fit for purpose, rather than merely what is easily accessible. Eric Perakslis, a Rubenstein Fellow at Duke University, noted that stakeholders must balance the usefulness of RWE collection against the risk of over-surveillance for each data point collected. While not discussed during the workshop, collecting massive data sets must also be weighed against the ever-present risk of data breach. Finally, speakers also discussed patient-generated health data (PGHD) and the need for aligned stakeholders who are motivated to collect this data and understand the process for doing so, including a plan for handling outlier data which is unavoidable with PGHD.

In the context of the COVID-19 pandemic, RWE presents an opportunity for real-time learnings

toward quicker identification and development of treatments and vaccines. As a result, the pandemic has only strengthened the importance of RWE in product development and, if deployed well, could help support more efficient and expedited product development plans.

*Emily Tribulski, a 2020 summer associate in Goodwin's Washington, D.C. office, contributed to this post.

What are Clinical Outcome Assessments (COAs) and Can They be Used to Support Approval and/or Labeling Claims?



The patient voice is recognized as one of the most critical sources of data in drug development, and patients play an increasingly important role in these efforts by teaching us about their experience with their condition and its impact. A common way sponsors can leverage the patient experience is by utilizing a clinical outcome assessment (COA). A COA is an assessment that describes or reflects how a patient feels, functions, or survives. Such an assessment can be a patient-reported outcome (PRO) measure, observer-reported outcome (ObsRO) measure, clinician-reported outcome (ClinRO) measure, or a performance outcome (PerfO) measure. **Alexander Varond** chaired a session on this topic in June 2020 at the Drug Information Association's Annual Meeting. Slides from his presentation can be found **here**.

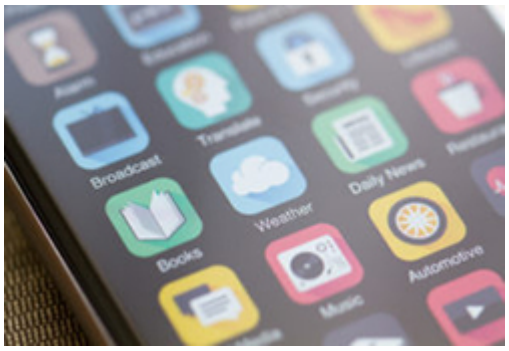
FDA plans to issue a guidance that will provide patient-focused approaches and methods to consider in the selection and/or development of COAs. This future guidance, known as Patient-Focused Drug Development (PFDD) Guidance 3, is one piece of FDA's plan to develop a series of four PFDD-specific guidances for stakeholders on how to collect and utilize patient experience data in drug development. We initially discussed this plan and background on patient experience data **here**. In the meantime, FDA has described a "roadmap to COA selection/development for clinical trials" **here**. This roadmap sets forth how to obtain an understanding of the disease or condition, conceptualize clinical benefit (i.e., how a patient feels, functions and survives), and how to select, develop and modify a COA. In Guidance 4, FDA will discuss how to incorporate COAs into endpoints for regulatory decision-making. FDA issued a discussion document related to the forthcoming Guidance 4 **here**.

As background, a COA may support approval of a product if it is a "well-defined and reliable" assessment (21 CFR § 314.126). FDA interprets this to mean that the COA must have content validity, construct validity, reliability, and the ability to detect change. But COAs can do much more.

For example, COAs can be included in labeling claims, as with CRYSVITA (burosumab-twza) for X-linked hypophosphatemia linked **here**, which incorporates both PRO and ClinRO measures. COAs can even lead to a regulatory change in thinking about a particular disease or condition. For example, just over two months after hearing directly from patients with epidermolysis bullosa (EB), a rare disorder that results in serious cutaneous manifestations, at an externally-led PFDD meeting, FDA published a draft guidance for sponsors developing therapies for EB that outlined specific examples of efficacy endpoints that would show the drug provides a clinically meaningful improvement. The finalized guidance can be found **here**.

If you are considering developing or utilizing in your clinical development program a COA, or if have questions about other PFDD initiatives such as PFDD meetings, we encourage you to contact your Goodwin life sciences lawyer for assistance on how to incorporate the patient voice–the real experts on their disease or condition—in drug development.

FDA's COVID-19 Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders



Developers of certain digital health devices for treating psychiatric disorders may be able to take advantage of an FDA **enforcement policy**, which remains in effect for the duration of the COVID-19 public health emergency. The policy applies to certain prescription computerized behavioral therapy (CBT) devices for psychiatric disorders, digital health therapeutic devices for psychiatric disorders that operate using a different fundamental technology than CBT, other variations of CBT devices, such as non-prescription devices, and low-risk general wellness and digital health products for mental health or psychiatric conditions.

Relevant psychiatric conditions include Obsessive Compulsive Disorder, Generalized Anxiety Disorder, Insomnia Disorder, Major Depressive Disorder, Substance Use Disorder, Post-traumatic Stress Disorder, Autism Spectrum Disorder, and Attention Deficit Hyperactivity Disorder. The enforcement policy's goal is "to help expand the availability" of these devices to aid those with these conditions "while reducing user and healthcare provider contact and potential exposure to COVID-19."

Under this policy, these devices may be distributed and used without complying with the following regulatory requirements, where such devices do not create an undue risk in light of the public health emergency: 510(k) submission, correction and removal reports, registration and listing

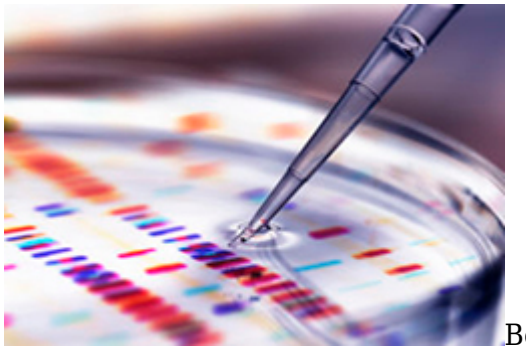
requirements, and Unique Device Identification requirements. For those software products with low-risk general wellness indications or functionality, FDA does not intend to enforce regulatory requirements consistent with the agency's existing policies, which were in effect prior to the pandemic. Finally, FDA's enforcement policy sets forth certain recommendations regarding the performance and labeling elements for these devices, such as user instructions that direct the patient to contact a physician before using the device. This enforcement policy highlights FDA's regulatory flexibility for software and app developers in this therapeutic area during the COVID-19 pandemic.

Conduct of Clinical Trials During the COVID-19 Pandemic: Recommendations from FDA

 As the COVID-19 pandemic unfolds, our drug, biologic, and medical device clients conducting or planning to conduct clinical trials may be faced with challenges related to quarantines, travel limitations, site closures or access restrictions, infection transmission concerns of site research personnel and study subjects, and supply chain interruptions. Nonetheless, it remains critical during the COVID-19 pandemic to continue to assure the safety of trial participants, comply with good clinical practice (GCP) requirements, and minimize risks to trial integrity. In this client alert which follows our earlier article on product development considerations for COVID-19 and article on FDA scrutiny of COVID-19 medical product marketing, we briefly discuss the impact the COVID-19 pandemic may have on our life sciences clients, and we provide an overview of FDA's "Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic" issued on March 18, 2020.

Read the Alert >>

Clinical Holds: Tips for Handling FDA's Call and What to Do Next

 Because life sciences companies hope to never end up on clinical hold, preparing for such a call from the U.S. Food and Drug Administration (FDA) is often not on the to-do list. But there can be significant advantages to advance preparation. Our Goodwin Insight shares some tips for life sciences companies on navigating that first call with FDA and the actions that follow.

Read the Insight >>

Q&A on FDA's Requirements Related to Financial Disclosure by Clinical Investigators

What financial arrangements between clinical trial sponsors and clinical investigators must be disclosed in a drug, biologic or device marketing application?

In a marketing application, FDA requires that four types of financial arrangements be disclosed: (1) any financial arrangement between the sponsor and the investigator whereby the value of the compensation to the investigator for conducting the study could be influenced by the outcome of the study; (2) any significant payments of other sorts from the sponsor, such as a grant to fund ongoing research, compensation in the form of equipment, a retainer for ongoing consultation, or honoraria, which are greater than $25,000 in cumulative value and given to the investigator or the investigator's institution to support the investigator's activities, exclusive of the costs of conducting the study, for the duration of the study and for one year following the study's completion; (3) any proprietary interest in the tested product held by the investigator; and (4) any significant equity interest in the sponsor held by the investigator, which is any amount for a non-publicly traded company or an equity interest in a public company valued over $50,000 for the duration of the study and for one year following the study's completion.

How is a clinical investigator defined in the context of FDA financial disclosure regulations?

In FDA’s financial disclosure regulations, the agency defines a clinical investigator as a listed or identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

What does FDA look for with regard to financial interest?

FDA looks at several factors with regard to financial interest, including the size and nature of the disclosed financial interest, the steps taken to minimize the potential for bias, and the study design. For example, FDA will evaluate whether the study has been designed with multiple investigators (most without a disclosable interest), blinding, objective endpoints, or measurement of endpoints by someone other than the investigator. FDA may initiate audits of the data from the investigator at issue, request that the applicant submit further analyses of the data or conduct additional independent studies to confirm the results. The agency could also refuse to treat the study as providing data that can be the basis for an agency action. We recommend you contact your Goodwin life sciences or FDA lawyer for further explanation of the agency’s financial disclosure regulations.