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 Following a 2015 draft guidance and replacing a 2010 guidance focused on animal studies for cardiovascular devices, this guidance document identifies general considerations for animal studies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.

NIH Again Refuses to Exercise March-In Rights to Control Drug Price

In a letter dated March 21, 2023, the National Institutes of Health ("NIH") again refused the request of petitioners to exercise march-in rights under the Bayh-Dole Act to control the price of a drug. Here, as before, the NIH found that the statutory criteria for the use of march-in rights were not satisfied by the petitioners.

March-in rights can permit the government to require a patent owner to grant additional licenses to the invention to avoid situations such as a company licensing the technology but then not commercializing it. The Bayh-Dole Act enumerates the circumstances under which march-in rights and the grant of additional licenses are warranted, for example, to achieve practical application of

the invention or to alleviate health and safety needs that are not being reasonably satisfied.

In November 2021, the Secretary of the Department of Health and Human Services ("HHS") received a petition from individuals Robert Sachs and Clare Love requesting the exercise of march-in rights under the Bayh-Dole Act to lower the price of the prostate cancer drug, Xtandi (enzalutamide). The patented drug product was invented at the University of California, Los Angeles, with funding from the NIH and U.S. Army. Xtandi, which is marketed in the United States by Astellas and Pfizer, costs more in the U.S. than it does elsewhere including other high-income countries. Petitioners argued that drug price can forbid access, specifically at prices that are allegedly unreasonable, contrary to the Bayh-Dole Act.

While the NIH's response letter expressed its concern about the high cost of drugs and the burden it places on patients, the letter explained the purpose of the Bayh-Dole Act is to promote the commercialization and public availability of government funded inventions. The overarching proposition of the Act is to permit recipients of federal government funding to retain ownership of patent rights and thereby commercialize the inventions by partnering with the private sector. Prior to the Bayh-Dole Act, most government funded inventions were not licensed or commercialized, including not one drug product.

The letter indicated that the NIH's analysis found that Xtandi is widely available to the public. The NIH stated that consistent with past march-in determinations in response to petitions for controlling drug prices, practical application of the invention is evidenced by practice of the invention and the invention's availability to the public. Astellas, the maker of Xtandi, estimated that more than 200,000 patients since 2012 were treated with the drug. Accordingly, the NIH concluded that the patent owner, the University of California, which licenses the patents to Astellas, meets the requirement for bringing Xtandi to practical application.

In addition, the NIH also stated that given the remaining patent life of the drug and the lengthy administrative procedure for the exercise of march-in rights, the NIH does not believe that the use of march-in rights would be an effective way at lowering the cost of the drug. Therefore, for these reasons, the NIH determined that march-in rights were not warranted in this situation.

The letter ends stating that the NIH and HHS would pursue a "whole of government approach," informed by public input, to ensure the use of march-in rights is consistent with the Bayh-Dole Act, promotes commercialization of federally funded research, maximizes the potential for federally funded technologies to become products, and is in the interests of the American public. To that end, on the same day as the NIH letter, HHS and the Department of Commerce ("DOC") announced a plan to review march-in authority as found in the Bayh-Dole Act with these same goals.

The NIH decision is in line with the several other petitions that have been filed for other drugs over the last few decades as well as previous petitions involving Xtandi. The exercise of march-in rights by a federal agency likely would have a negative impact on companies developing products invented using federal funding if investors believe that the price of such products could be controlled by the federal government based on public input. We will continue to monitor developments in this area, including for any recommendations from the HHS and DOC inter-agency working group on this important topic.

USPTO Director Issues Precedential Review Decision Regarding Multiple Dependent Claims

Director Katherine Vidal of the U.S. Patent and Trademark Office ("USPTO") issued a precedential review decision with respect to the interpretation of multiple dependent claims, in a case of first impression before the Patent and Trial Appeal Board ("PTAB"). In the review of the PTAB's final written Decision and Order, the Director modified it consistent with her determination of the treatment of multiple dependent claims, which are claims that refer to and incorporate by reference more than one other claim.

More specifically, at issue in the *inter partes* review captioned, Nested Bean, Inc. v. Big Beings Pty Ltd., was the interpretation of 35 U.S.C. § 112, fifth paragraph, which is the controlling statute for multiple dependent claims. The Patent Owner contended that the statute requires the PTAB to consider the patentability of each claim referenced separately. In contrast, the Petitioner argued that if any claim of a multiple dependent claim is unpatentable, then the entire claim is unpatentable. For the reasons that follow, the Director agreed with the Patent Owner.

35 U.S.C. § 112, fifth paragraph, states in relevant part, "[a] multiple dependent claim shall be construed to incorporate by reference all the limitations of the particular claim in relation to which it is being considered." The related Codified Rule, 37 C.F.R. § 1.75(c) states, in relevant part, "[a] multiple dependent claim shall be construed to incorporate by reference all the limitations of each of the particular claims in relation to which it is being considered." With other statutes and Rules considered, the Director reasoned that the plain language of 35 U.S.C. § 112, fifth paragraph, conveys that a multiple dependent claim is the equivalent of several single dependent claims.

In addition to relying upon the applicable statute and Rules, the Director also considered Federal Circuit case law, legislative history, and USPTO procedure.

More specifically, with respect to precedent, neither party identified a judicial or administrative decision addressing the issue at hand. However, the Director found that Federal Circuit cases identified were supportive of the Patent Owner's position.

The Director found that USPTO guidance and procedures further supported the Patent Owner's interpretation. For example, the Manual for Patent Examining Practice (M.P.E.P.) advises examiners that "a multiple dependent claim must be considered in the same manner as a plurality of single dependent claims." M.P.E.P. § 608.01(n)(I)(B)(4).[1] Further, as the Director found, the USPTO claim fee structure is such that applicants must pay separately for each multiple dependent combination, e.g., for a multiple dependent claim that refers to three independent claims, the USPTO charges for three dependent claims.

Thus, after reviewing the PTAB's Decision and the relevant information, Director Vidal

acknowledged that it was an issue of first impression before the Board. And based on the plain meaning of the statute, 35 U.S.C. § 112, fifth paragraph, requires that the patentability of a multiple dependent claim be considered separately with respect to each claim to which it refers. Accordingly, the Director's Review Decision modifies the PTAB's final written Decision and Order consistent with her interpretation of determining the patentability of multiple dependent claims, each separately as if multiple single dependent claims.

The Director's Review Decision clarifies the interpretation of U.S. patents containing multiple dependent claims and determining the patentability thereof. In particular, a patentee now knows that each claim of a multiple dependent claim should stand or fall by itself, independent of the invalidity of other dependent claims of the same multiple dependent claim.

[1] Eighth Ed., Rev. 7 (July 2008), which was the version in effect as of the earliest priority date of the relevant patent.

Clinical Trial Diversity Plans and Rare Diseases

Clinical trial diversity is not a new concept–the U.S. Food and Drug Administration (FDA) issued a **draft guidance** providing specific recommendations to industry on how to improve diversity in clinical trials in April 2022 which we blogged about **here**–but the passage of the Food and Drug Omnibus Reform Act, or FDORA, highlighted that the FDA will continue pushing sponsors to make progress on this front. Sponsors of rare disease trials, in particular, know that the act of *increasing* clinical trial diversity is not an easy undertaking, especially when working with already limited rare disease populations. However, the FDA's focus on ensuring diversity among trial participants may present new opportunities for designing and executing clinical trials in rare disease indications.

Under **FDORA**, sponsors of new investigational drugs will be required, unless waived by the FDA, to submit a "diversity action plan" for all Phase 3 clinical trials or, as appropriate, another pivotal study in support of a future marketing application (there is also a similar requirement for sponsors of medical devices where a trial is conducted under an investigational device exemption). Under

FDORA, this plan is required to include the sponsor's goals for enrollment in the study, the rationale for those goals, and an explanation of how the sponsor intends to meet those goals. While FDORA requires these elements to be included and that FDA issue guidance on the form and format of diversity plans, FDORA does not expressly restrict a sponsor from providing additional information with its description of goals. For rare diseases, some education and background on the disease population may be warranted in submission of sponsor diversity plan goals.

Under FDORA, sponsors must submit their plan no later than when they submit their Phase 3 or other pivotal trial protocol, and the FDA has the authority to modify the plan or to waive the requirement for a plan altogether in certain circumstances, such as if conducting a clinical trial in accordance with a diversity action plan would otherwise be impracticable.

During FDA's Rare Disease Day 2023, agency officials noted that the FDA has long encouraged diversity, including through guidances issued prior to the April 2022 draft guidance, but the passage of FDORA marks the first time that addressing diversity with a prospective plan is a *requirement* in the development process. With that in mind, speakers pointed out that developing a candidate in a rare indication is all the more reason to develop a strategy to enroll as many eligible patients as possible.

Sponsors in the rare disease space should consider the following strategies to increase diversity in their trials, where feasible:

- Engage advocacy groups and community health groups (early and often), as these groups deeply understand their populations' specific barriers to research participation and the types of accommodations that should be considered when designing trials to minimize burdens and maximize participation;
- Create more inclusivity at the study design stage, such as by widening eligibility criteria, re-enrolling early phase participants in later phase studies, where possible, or conducting cross-over extension trials, which could make a significant difference in a patient's willingness to participate;
- Simplify the complexity of trials and minimize burdens to patients to participate, where possible, such as through the use of local laboratories for testing, or consolidating assessments to be done at a smaller number of in-person visits during the trial;
- Adopt as part of the trial design access to telemedicine and technology-driven solutions, which can help promote more inclusiveness with respect to socioeconomic, travel/location, and language barriers; and
- If using a contract research organization, or CRO, partner with a CRO, or other third-party vendor, that can demonstrate experience supporting and achieving diverse population enrollment and a community-first approach.

We anticipate that the FDA's specific recommendations for sponsors will continue to evolve, as FDORA requires the FDA to issue new draft guidance or update existing draft guidance within 12 months of the enactment of FDORA. At this stage, however, sponsors have an opportunity to propose creative and innovative approaches to designing, recruiting patients for, and conducting their Phase 3 and pivotal clinical trials, even in the rare disease space.

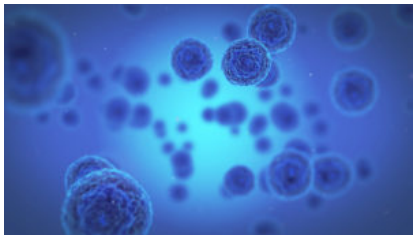
Reactions to Amgen v. Sanofi and the Future of Patent Law's Enablement Requirement

For the first time in decades, the Supreme Court will consider patent law's "enablement" requirement, in *Amgen Inc. v. Sanofi*. That requirement is often a key point in litigation when a patent claims a class of novel compounds or antibodies. In the oral argument on March 27, the Supreme Court will examine the Federal Circuit's holding that patentees must disclose enough information to "enable" people of ordinary skill in the relevant art to "reach the full scope" of the claimed invention. In this day-after webinar, litigators from Goodwin's Supreme Court and IP Litigation practices will recap the argument and explain what it could mean for the future of the enablement requirement.

Click **here** to register for the webinar.

CLE credit will be offered for California and New York.

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**.