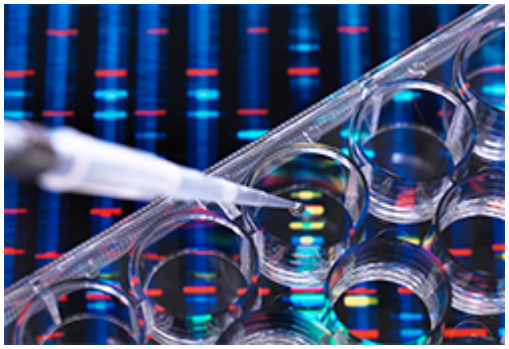
Disrupt + Innovate + Transform: Key Regulatory Issues for Digital Health Companies Webinar

Goodwin Life Sciences and Healthcare partner **Roger Cohen** and associate **Anne Brendel** along with Life Sciences and FDA associate **Steven Tjoe** kicked off Goodwin's multi-part webinar series "Disrupt + Innovate + Transform: A Healthcare Webinar Series" with "Key Regulatory Issues for Digital Health Companies" discussing the key regulatory issues affecting digital health, telemedicine and healthcare IT companies. The webinar series will be presented by a cross-disciplinary team of Goodwin lawyers exploring the topics that are most relevant for the healthcare industry today. From ever-changing regulatory guidelines to digital health, women's health and privacy, Goodwin will take attendees through these topics and more and provide guidance to help you navigate the current healthcare landscape.

View the Video:

For information on upcoming webinars in the Disrupt + Innovate + Transform: A Healthcare Webinar Series, visit our **mini site**.

Goodwin's Clinical Trials Service Offering



Given the breadth of clinical-stage companies that the Goodwin FDA and Healthcare teams advise,

our regulatory attorneys together with our commercial contracting, products liability and insurance attorneys play an integral role in counseling clinical-stage companies on matters related to the conduct of clinical trials.

Learn more about our clinical trials service offering **here**.

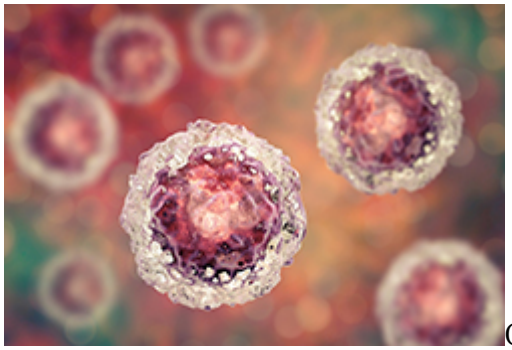
Moving from the Informed Consent to Approved Labeling: Preparing for Risks in Product Marketing & Use Webinar Recording

On February 3, 2021 Goodwin FDA Regulatory partner, **Julie Tibbets**, Products Litigation + Counseling partner, **Nilda Isidro**, and Risk Management & Insurance counsel **Brian Mukherjee** discussed what drug and biologic companies with late-stage product candidates can do to best position their products to mitigate the risks that come with transitioning from clinical trials to marketing and sales.

Our speakers – leaders in life sciences regulatory compliance, product litigation preparedness, risk management, and insurance – highlighted best practices surrounding pharmaceutical promotion, preparing for risks inherent in the marketing and sale of prescription drugs, and the ways in which insurance can help mitigate those risks. This webinar identified key takeaways for companies that are nearing FDA approval and are poised to launch their commercial products.

Click **here** to view the slides and webinar recording.

FDA Issues Guidance for Cell and Gene Therapy Manufacturers to Minimize Potential Transmission of SARS-CoV-2

 On January 19, 2021, the FDA issued **guidance** for licensed and investigational cellular and gene therapy (CGT) manufacturers during the COVID-19 pandemic. This new guidance supplements the recommendations provided in FDA's **June 2020 guidance** regarding manufacturing controls to prevent contamination in drugs, risk assessment of SARS-CoV-2 as it relates to drug safety and quality, and continuity of manufacturing operations as applied to all drug and biological product manufacturers.

The new guidance provides risk-based recommendations to minimize potential transmission of SARS-CoV-2 to patients and facility personnel with specific considerations relating to, among other things, the assessment of donors, cellular and tissue source materials, manufacturing processes, manufacturing facility control, material testing, and the number of patients that can be treated with the product. While FDA acknowledges in the guidance that is not aware of any CGT products that have been contaminated with SARS-CoV-2 or of information indicating transmission of SARS-CoV-2 via CGT products, FDA notes that "CGT manufacturers are expected to evaluate whether [the virus] poses new risks in the context of their specific products, facilities, processes, and manufacturing controls."

FDA recommends that CGT manufacturers review the current good manufacturing practice requirements and recommendations and perform a risk assessment that identifies, evaluates, and mitigates factors that may allow for transmission of SARS-CoV-2 to patients and facility personnel and include a description of the risk assessment and mitigation strategies in any investigational new drug application (IND), biologics license application (BLA), or master file. Since this is an evolving area, manufacturers should look to scientific literature to provide justification and support for their risk assessment and mitigation strategies.

CGT manufacturers should evaluate their manufacturing operations for SARS-CoV-2 risks and be sure that all risk assessments of production controls, including any follow-up and changes, are approved by their quality unit and appropriately documented within their quality management system.

Highlights for SaMD Developers: FDA's January 2021 Artificial Intelligence/Machine Learning Action Plan

 On January 12, 2021, the U.S. Food and Drug Administration (FDA) published its **Action Plan** for further development of the Agency's framework for regulatory oversight of artificial intelligence (AI) and machine learning (ML) based Software as a Medical Device (SaMD). The Action Plan identifies several opportunities for SaMD developers to engage the FDA as its regulatory framework for AI/ML-based SaMD oversight evolves:

- **Predetermined Change Control Plans:** FDA remains committed to refining a regulatory framework that would allow for some post-market SaMD modifications based largely on the establishment and utilization of SaMD Pre-Specifications (SPS) and an Algorithm Change Protocol (ACP) set forth in a "Predetermined Change Control Plan." SaMD developers can expect, and be ready to submit comments on, a draft guidance in 2021 addressing a Predetermined Change Control Plan.
- **Real-World Performance:** Real-world data collection and monitoring is another key concept in FDA's proposed regulatory framework for oversight of modifications to AI/ML-based SaMD. FDA plans to advance real-world performance monitoring pilots with stakeholders on a voluntary basis, and use the learnings from these activities to develop a framework for gathering and validating relevant real-world performance parameters and metrics.
- **Algorithm Transparency:** To identify types of information that FDA may recommend SaMD developers include in the labeling of their AI/ML-based devices, FDA intends to hold a public workshop to elicit input from the broader community on how device labeling supports transparency to users.

FDA also will continue to participate in global working groups focused on harmonizing principles of Good Machine Learning Practice (GMLP) as well as expand upon the Agency's efforts to develop methods for evaluating and addressing algorithmic bias.

The Agency recognizes that continued stakeholder engagement will be crucial for the formation of a sensible regulatory framework for oversight of AI/ML-based SaMD. SaMD developers seeking to inform the development of FDA's regulatory framework are strongly encouraged to participate in the specific opportunities outlined in the Action Plan.

FDA Announces Temporary Review Timelines for Responses to Facility Assessment-Related Complete Response Letters Due to COVID-19

 As follow-up to our October **post** on pre-approval and pre-licensure inspections impacting U.S. Food and Drug Administration (FDA) drug and biologic approvals, this blog post discusses FDA's recently announced temporary policy set forth in its **December 2020 guidance** on review timelines for company responses to a Complete Response letter (CRL) for applications requiring the conduct of manufacturing or bioresearch monitoring (BIMO) program site facility inspections prior to approval. This guidance augments FDA's **August 2020 guidance**, which described FDA's intent to issue a CRL or defer action on an application until an inspection can be completed.

FDA acknowledges in its recent guidance that it is "facing difficulties" in conducting inspections during the COVID-19 pandemic. Industry has felt the impact of this with delayed approvals of new therapies in 2020 as a result of these inspection delays. While FDA has sought to use alternative tools to mitigate the need for in-person inspections (*e.g.*, requesting records and other information directly from facilities and requesting existing inspection reports from trusted foreign regulators), FDA indicated in its December 2020 guidance that these inspection-alternatives "can be as resource intensive as inspections, if not more," thereby presenting a challenge to timely completion of required pre-approval and pre-license inspections during the application review period.

To provide greater transparency on expected timeline impacts for company complete responses where FDA issued a CRL either (a) due to its inability to perform a required inspection because of COVID-19, or (b) where the inspection involves the use of time- and resource-intensive alternative tools, the Agency provides the below timeline expectations in its December 2020 guidance for the review of applicant responses to CRLs:

- NDAs & BLAs: Resubmissions of original applications and efficacy supplements for NDAs and BLAs will be subject to a Class 2 review timeline of 6 months, which is "consistent with existing policies and practices when a facility inspection is required."
- Biosimilars & NDA & BLA manufacturing supplements: There will be no changes in the review timelines for resubmissions of original applications, supplements with clinical data, and manufacturing supplements for biosimilars, or for resubmissions of manufacturing supplements for NDAs and BLAs.
- ANDAs: Regardless of whether the CRL contains a major deficiency, amendments to original ANDAs and amendments to prior approval supplements for approved ANDAs will be treated as major amendments, subject to the timelines provided in FDA's **July 2018 guidance** on Generic Drug User Fee Amendments (GDUFA).

The December 2020 guidance enables applicants to better plan for approval timeline delay contingencies as they proceed through FDA's review process. Comments on the December 2020 guidance may be submitted to the docket for Agency consideration **here**.

Congress Enacts Amendments Affecting The Regulation Of Generic Drugs And Biosimilars

 On December 27, 2020, the President signed into law the "Consolidated Appropriations Act, 2021" (the "Act"). Included within this omnibus legislation are several provisions (in Division BB, Title III, Subtitle C) that affect the regulation of generic drugs and biosimilar medicines by the U.S. Food and Drug Administration (FDA).

Read the Alert >>

Are Pre-Approval and Pre-Licensure Inspections Limiting Approvals During COVID-19?

 In this post, we discuss FDA's conduct of inspections of manufacturing facilities for new drugs and biologics during the COVID-19 pandemic. These inspections, known as pre-approval and pre-licensure inspections (PAIs/PLIs, respectively), are performed to give FDA assurance that a manufacturing site named in a new drug or biologics license application is capable of manufacturing the product according to current good manufacturing practices (cGMPs) and producing the product at commercial scale.

In **July**, FDA resumed limited domestic on-site inspections after temporarily postponing all domestic and foreign routine surveillance facility inspections in March. Since **June**, FDA had conducted only mission-critical domestic inspections. Currently, domestic on-site inspections are pre-announced and are prioritized on a newly developed rating scale that uses real-time data on the number of COVID-19 cases in a local area to qualitatively determine when and where it is safest to conduct inspections. Foreign PAIs/PLIs continue to be temporarily postponed unless deemed mission-critical. FDA may deem an inspection mission-critical based on a variety of factors including, but not

limited to, whether the product has received breakthrough therapy or regenerative medicine advanced therapy designation.

In response to COVID-19, FDA has used, on a limited basis, various tools to conduct alternative inspections. These tools include the use of FDA's authority under Section 704(a)(4) of the FD&C Act, which enables the Agency to request records directly from facilities "in advance of or in lieu of" drug inspections. In addition, FDA has indicated that it may also look to records of recent inspections and information shared by foreign regulatory partners through mutual recognition agreements. And while the concept of virtual inspections has been floated, it remains to be seen if video-based or other virtual inspection strategies can be used to fulfill PAI/PLI requirements and how long such proposals may take to implement.

Worryingly, FDA explains in its **August 2020 guidance** that should the Agency determine that a PAI/PLI is necessary, and such an inspection cannot be completed during the review cycle due to restrictions on travel or other COVID-19-related risks, FDA generally intends to issue a Complete Response letter or may defer action. The guidance, along with a number of concerns raised quietly by sponsors regarding delayed inspections leading or potentially leading to Complete Response letters, paints a potentially ominous picture for drug and biologic approvals and the advancement of the public health over the coming months. Sponsors submitting marketing applications in the near-term would be wise to proactively prepare for discussion of alternative inspection approaches during the review of their applications.

The Continuing Saga of Lab Developed Tests, Including for COVID-19 Testing

In August, the U.S. Department of Health & Human Services (HHS) **announced** that the FDA will not require premarket review of laboratory developed tests (LDTs), whether COVID-19 related or not, absent notice-and-comment rulemaking. Labs may voluntarily seek a premarket approval, 510(k) clearance, or an emergency use authorization (EUA) for their LDTs. Importantly, labs that do not obtain such FDA approval, clearance, or authorization would not be eligible for **PREP Act** coverage.

This announcement may have come as a surprise to FDA, which historically has asserted its medical device regulatory authority over LDTs while often subjecting them to enforcement discretion. Despite this HHS announcement, FDA's May 11, 2020 **Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency** remains in effect and has not been revised since the announcement. Importantly, this guidance offers two pathways for COVID-19 related LDTs – an EUA

submission to FDA and the development of an LDT under the authorities of the State in which the laboratory resides, where the State takes responsibility for COVID-19 testing by labs in its State.

For FDA's latest statements on COVID-19 testing, see the **opinion piece** authored by CDRH Director Dr. Jeffrey Shuren and Dr. Timothy Stenzel, Director of the Office of Health Technology 7, In Vitro Diagnostics and Radiological Health, in the Hill.

The Purple Book and The Orange Book – When do Patents Expire and Regulatory Exclusivities end for FDA Approved Products?

The Food and Drug Administration (FDA) maintains two searchable online databases for approved products: the **Purple Book** (approved licensed biological products) and the **Orange Book** (approved drug products). The Orange Book provides details about an approved drug product, including the patents covering the approved drug product and the expiration dates of the patents and regulatory exclusivities, leaving investors, competitors, and the public in the dark as to when an approved biological product falls into the public domain.

For example, Sunosi® (solriamfetol hydrochloride) is a small molecule drug developed by Jazz Pharmaceuticals and was approved by the FDA on June 17, 2019 for the treatment of excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea. The NDA (new drug application) number, patents covering the product, the expiration dates of the patents, and regulatory exclusivity data are provided in the Orange Book.

Contrast this with Evenity® (romosozumab-aqqg), Amgen's monoclonal antibody approved for the treatment of osteoporosis in postmenopausal women at high risk for fracture. The Purple Book provides the approval date, proprietary name and generic name, BLA (biologics license application) number and type, date of first licensure, and a link to the product label. However, the Purple Book does not list the patents covering the product or regulatory exclusivity information. Thus, unlike patent litigation involving generic approvals for small molecule drugs, where the patents that will be involved are predictable based on the Orange Book listings, the patents that will be involved in litigation over a biosimilar approval are typically revealed for the first time during the litigation itself.