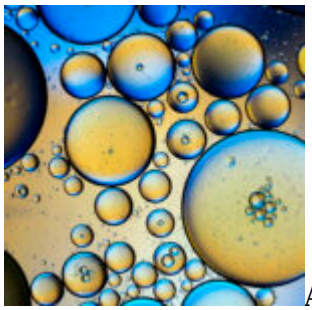
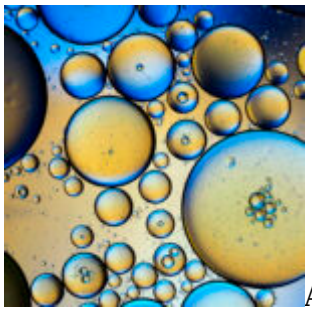
A Look Ahead in Life Sciences: What We Are Tracking in Q2 2024 and Beyond

 As the life sciences, medtech, and diagnostic industries continue to expand and grow increasingly complex, so does the legal, regulatory, and compliance landscape. To help companies and investors navigate the many evolving and emerging laws and regulations across pharmaceuticals, biologics, medical devices, diagnostics, and laboratory testing, our Life Sciences Regulatory & Compliance team has provided an overview of key developments. We update and publish a quarterly tracker detailing these developments. You can read about the Q2 2024 updates **here**.

A Look Ahead in Life Sciences: What We Are Tracking in Q1 2024 and Beyond

 As the life sciences, medtech, and diagnostic industries continue to expand and grow increasingly complex, so does the legal, regulatory, and compliance landscape. To help companies and investors navigate the many evolving and emerging laws and regulations across pharmaceuticals, biologics, medical devices, diagnostics, and laboratory testing, our Life Sciences Regulatory & Compliance team has provided an overview of key developments. We update and publish a quarterly tracker detailing these developments. You can read about the Q1 2024 updates **here**.

A Practical Look at OIG’s New Compliance

Guidance

 On November 6, 2023, for the first time in 15 years, HHS OIG issued a new reference guide for the health care compliance community – **the General Compliance Program Guidance, or GCPG**. While the GCPG does not set new legal standards and largely reinforces existing guidance, it is a tremendous tool to help health care and life sciences companies advance their compliance efforts. Indeed, within its 91 pages, the GCPG provides the most comprehensive and user-friendly trove of health care compliance insights, tips, and guidance ever provided by the federal government.

Read the full alert **here**.

Significant 340B Drug Pricing Program Litigation May Impact 340B Scope

 Two recent federal court cases signal new significant developments with respect to the 340B Drug Pricing Program. Specifically: (1) new federal district court litigation challenging a recent HRSA Notice involving 340B Program “child site” registration and eligibility; and (2) a court decision in other litigation that implicates the scope of the 340B “eligible patient” definition. Details regarding these developments are in the client alert.

Read the client alert **here**.

2023 State Drug Transparency Law Development Update

 In October 2021, we **reported** on an uptick in the passage of state drug price transparency legislation. As an update to that report, as of October 2023, approximately 22 states have now passed drug price transparency laws creating new requirements for drug manufacturers.

Each state has its own unique set of requirements, but reporting is often completed via an online portal administered by the state's implementing agency. Generally, these laws require manufacturers to report pricing and other information related to the cost, development, and sale of drugs to the state or state-affiliated entities. Some states will use this data to produce public reports about the cost of prescription drugs with the goal of creating pricing transparency for drug manufacturers as well as to educate the state legislature and public about the drug pricing process.

Read the full alert **here**.

Recent FDA Initiatives to Support Development of Individualized Cell and Gene Therapies and Rare Disease Therapies

 Last month, FDA issued a **Request for Information** (RFI) in the Federal Register seeking information and comments from interested stakeholders regarding "critical scientific challenges and opportunities to advance the development of individualized cellular and gene therapies (CGTs)." Individualized CGTs are therapies "developed for a single patient (or a very small number of patients) based on designing or engineering a product

that specifically targets the mechanism underlying a patient's (or small number of patients') illness."

FDA's request focuses on three core areas:

1. Manufacturing: Manufacturing and product quality challenges and opportunities for individualized CGTs in light of, for example, small batch sizes, tailoring of batches to individual patients, and need for rapid testing and release.

On this topic, FDA asks:

i. *Given the challenges to develop consistent manufacturing strategies for CGTs designed for a very small number of patients or an individual patient, how can manufacturers leverage their prior experience manufacturing one CGT to support subsequent development and approval of another related, but distinct CGT (potential areas for leveraging may include manufacturing process validation, control strategy, assay validation, and drug product stability studies)?*

ii. *When the batch size of a CGT is very small, what are some challenges and solutions regarding the volume of product (or number of vials) needed for batch release testing, stability testing, retention of reserve samples, and comparability studies?*

iii. *What are some challenges and solutions for individualized CGTs that need to be tested and released rapidly, either because the product has a very short shelf life or because the patient's clinical status may be rapidly declining and treatment is urgently needed?*

iv. *For many individualized CGT products, each batch is tailored to an individual patient (e.g., autologous CAR–T cells, tumor neoantigen vaccines, certain genome editing products). For such products, what are some challenges and solutions for assuring that each batch has adequate potency to achieve the intended therapeutic effect?*

v. *What are some challenges and solutions for individualized genome editing products that aim to treat monogenic diseases for which the target gene has different mutations in different patients?*

2. Nonclinical development: The use of nonclinical data to support individualized CGTs, considering the lack of relevant animal models in many instances, the uniqueness or limited applicability of individualized CGTs, and the potential of using prior knowledge from other CGTs—for example, where gene therapy vector products use the same vector backbone.

On this topic, FDA asks:

i. *What nonclinical studies could be leveraged in support of a related product using similar technologies? What nonclinical studies are important to conduct with each final clinical product?*

ii. *What nonclinical development approaches could be considered when there are no relevant animal models or animal models are unable to replicate each individual disease/condition?*

iii. *For patient-specific products where evaluating each individual product is infeasible or impractical, what is the role for nonclinical studies conducted with representative product(s)?*

iv. *What are the opportunities and challenges with using computational approaches to support*

nonclinical development?

3. Clinical Development: Clinical development of individualized CGTs, considering for example the infeasibility (for ethical or other reasons) of conducting randomized controlled studies, novel endpoints, and limitations in statistical analyses.

On this topic, FDA asks:

i. *What are challenges and strategies/opportunities with interpreting efficacy data from individual patients (including expanded access) and small groups of patients? What opportunities are there in leveraging prior and/or collective experiences?*

ii. *What strategies can be utilized to accumulate and interpret safety data in personalized/individualized CGTs?*

iii. *For genetic disorders with clear genotype-phenotype associations for disease manifestations or severity, what opportunities are there for tailoring treatments and study design to specific genotypes/phenotypes?*

FDA also requested input on several additional significant questions:

i. *What additional major scientific challenges to advance the development of individualized CGTs should be considered?*

ii. *What existing best practices or scientific approaches should be leveraged to address any of these challenges? Are there specific opportunities for collaborations to advance the development of individualized CGTs?*

iii. *Are there specific areas where flexibility in regulatory approaches would improve the feasibility of developing and commercializing individualized CGTs?*

Comments are due on November 20, 2023.

At the end of last month, FDA also **announced** a pilot program "to help further accelerate development of rare disease therapies." The program, titled Support for clinical Trials Advancing Rare disease Therapeutics ("START"), will include selected sponsors with an active IND for products meeting certain eligibility requirements. Products regulated by CBER are eligible for the program only if they are a gene or cell therapy treatment for a rare disease or condition that is "likely to lead to significant disability or death within the first decade of life." Products regulated by CDER are eligible only if they are "intended to treat rare neurodegenerative conditions, including those of rare genetic metabolic type." Participants selected for the pilot program will "be able to obtain frequent advice and regular ad-hoc communication with FDA staff to address product-specific development issues, including, but not limited to, clinical study design, choice of control group and fine-tuning the choice of patient population."

FDA will accept applications to the START program beginning January 2, 2024 and until March 1, 2024.

Federal Court Strikes Down Copay Accumulator Programs

Summary:

On September 29, 2023, the U.S. District Court for the District of Columbia **vacated** a Trump-era rule from 2021 that allowed insurers to exclude drug manufacturer co-pay support coupons and assistance from a patient's annual cost-sharing caps. This practice, commonly referred to as a copay accumulator program, is typically used by insurance companies and pharmacy benefit managers to control drug spending, especially for high-cost specialty drugs, like those required by HIV patients.

Under typical prescription drug insurance programs, patients are obligated to pay a deductible and cost-sharing (i.e. a copay) throughout the plan year, up to an out-of-pocket spend cap. Once the patient hits that spend cap, the insurance company is responsible for the patient's prescription drug costs.

Under an accumulator program, on the other hand, an insurance company does not count a manufacturer's copay support (for example, a copay card that a patient presents at a pharmacy to cover the cost of the copay) towards a patient's annual deductible or out-of-pocket maximum. By excluding manufacturer copay support and coupons from patients' cost-sharing cap, this means that, even after a manufacturer's copay support is exhausted for the year, patients remain on the hook for all cost sharing obligations up to the insurance plan's out of pocket maximums. Many states have implemented laws to ban copay accumulator programs, asserting that such programs actually increase the financial burden on patients, especially with respect to specialty or more expensive drugs. As of June 2023, 19 states have implemented copay accumulator program bans.

HIV and Hepatitis Policy Institute et al v. HHS was brought by patient advocacy groups including the HIV and Hepatitis Policy Institute and the Diabetes Patient Advocacy Coalition, among others, who challenged a May 2020 rule from HHS, the "Notice of Benefit and Payment Parameters for 2021" (85 Fed. Reg. 29164, 29230-35, 29261 (May 14, 2020)) (the "2021 NBPP") that permitted insurers to impose accumulator polices. Plaintiffs opposed the accumulator program, asserting that manufacturer copay support should count *towards* calculating patients' cost sharing obligations and should not be excluded from such calculations.

In ruling in favor of the plaintiffs on their motion for summary judgment, the U.S. District Court set aside the 2021 NBPP, largely supporting plaintiffs' challenges that the 2021 NBPP rule's language is internally contradictory, that it runs counter to the statutory definition of "cost sharing" found in the Affordable Care Act, and that it runs counter to the agencies' pre-existing regulatory definition of "cost sharing." HHS had previously defined "cost sharing" in a 2012 regulation as "any expenditure required by or on behalf of an enrollee with respect to essential health benefits," which by its terms

includes “deductibles, coinsurance, copayments, or similar charges, but excludes premiums, balance billing amounts for non-network providers, and spending for non-covered services.” *See* 45 C.F.R. 155.20. In other words, the regulation treats cost sharing is an “expenditure” by or on behalf of a plan enrollee. According to plaintiffs, and as affirmed by the court, this includes manufacturer copay assistance support.

The court disagreed with the government’s technical arguments regarding the language of the 2021 NBPP (i.e. that manufacturer copay support is actually a “reduction” in the amount the patient owes towards cost sharing or a reduction in the “actual economic impact” on the drug manufacturer and not an “expenditure”), concluding that the 2012 regulation was likely intended to define “cost sharing” as costs that are (1) required of an insurance plan enrollee and (2) paid by or on behalf of that enrollee – including manufacturer copay coupons and assistance.

It is unclear if the ruling will be appealed; however, as a result of the District Court’s ruling, the government will use an earlier 2020 version of the rule which allowed insurers to exclude from cost-sharing caps only copay support coupons for branded drugs that have available generic equivalents; if there is no generic equivalent, under the 2020 version of the rule, manufacturer copay support must be counted toward cost sharing.

Conclusions: The U.S. District Court ruling is a significant development for drug manufacturers who offer copay support as a means of providing relief to patients with respect to cost-sharing requirements under their insurance coverage as opposed to offering significant rebates, discounts, or other contracting strategies. However, manufacturers of branded drugs with a generic equivalent will still need to consider how copay accumulator programs could affect access in those states that have not yet banned the practice. Notably, in the wake of this ruling, patient advocacy organizations have indicated that they will continue to advocate for a comprehensive state and federal level ban on copay accumulator programs (*e.g.* **Immune Deficiency Foundation**).

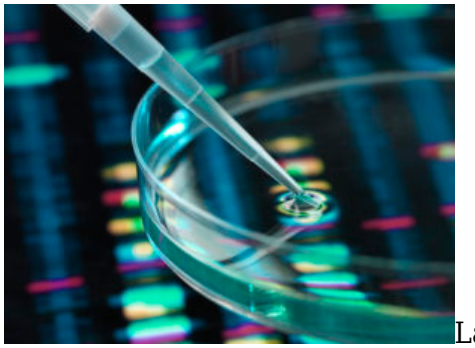
Goodwin will continue to monitor any further developments in this case and the impact of copay accumulator programs on the market.

A Look Ahead in Life Sciences: What We Are Tracking in Q4 2023 and Beyond

 As the life sciences, medtech, and diagnostic industries continue to expand and grow increasingly complex, so do the legal, regulatory, and compliance landscape. To help companies and investors navigate the many evolving and emerging laws and regulations across pharmaceuticals, biologics, medical devices, diagnostics, and laboratory testing, our Life Sciences Regulatory & Compliance team has provided an overview of key developments. We update and publish a quarterly tracker detailing these developments. You can read about the Q4 2023 updates

here.

Is it Biosimilar or Interchangeable? It Won't Be Easy to Tell Under FDA's Latest Draft Labeling Guidance



Last week, **FDA released** a draft guidance, "**Labeling for Biosimilar and Interchangeable Biosimilar Products**" that—when finalized—will revise and replace its July 2018 final guidance, "**Labeling for Biosimilar Products**." FDA noted that this 2023 Draft Guidance reflects recommendations based on the "valuable experience about labeling considerations" that FDA has gained through its approval of 42 biosimilar products, including four interchangeable biosimilar products.

Notably, the 2023 Draft Guidance provides further recommendations regarding when to use a biosimilar or interchangeable biosimilar product name, and when to use the reference product name in labeling:

- The biosimilar or interchangeable biosimilar product's proprietary name[1] (or if the product does not have a proprietary name, its proper name[2]) should be used when –
    - Information in the labeling is *specific to the biosimilar (or interchangeable biosimilar) product*, including such references to the product in the INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, DESCRIPTION, and HOW SUPPLIED/STORAGE AND HANDLING sections, and/or
    - For "directive statements and recommendations for preventing, monitoring, managing, or mitigating risk," including such references to the product in the BOXED WARNING, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and DRUG INTERACTIONS sections.

- When referring to the *drug substance* in the labeling, the biosimilar or interchangeable biosimilar product's proper name should be used.

- When information *specific to the reference product* is described in the biosimilar or interchangeable biosimilar product's labeling (for example, data from clinical trials of the reference product in the ADVERSE REACTIONS and CLINICAL STUDIES sections), the reference product's proper name should be used.

- In sections of the labeling containing *information that applies to both the biosimilar (or interchangeable biosimilar) product and the reference product*—such as BOXED WARNING,

> CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS—the labeling should use the core name of the reference product followed by the word "products."[3]

FDA acknowledges that the application of these recommendations is highly context-dependent and may not always be clear, but recommends that biosimilar and interchangeable biosimilar product sponsors evaluate all statements in product labeling carefully to determine the most appropriate product identification approach in each instance.

Another noteworthy aspect of the 2023 Draft Guidance is the Agency's recommendation regarding the biosimilarity statement and footnote in the HIGHLIGHTS section of a biosimilar or interchangeable biosimilar product's labeling.[4] Previously, FDA recommended a biosimilarity statement for a biosimilar product and an interchangeability statement for an interchangeable biosimilar product. The 2023 Draft Guidance now recommends a statement and footnote in the HIGHLIGHTS section that the product is biosimilar to the reference product, *regardless of* whether the product is a biosimilar or an interchangeable biosimilar to the reference product. In the **Federal Register notice** announcing the 2023 Draft Guidance, FDA acknowledges that this marks an "evolution in our thinking" and explains that "a labeling statement noting that certain products within a 351(k) [Biologics License Application] have been approved as interchangeable, and explaining the interchangeability standard, is not likely to be useful to prescribers, who can prescribe both biosimilar and interchangeable biosimilar products in place of the reference product with equal confidence that they are as safe and effective as their reference products." FDA further states that "information about interchangeability is more appropriately located in the Purple Book rather than labeling."

Other notable elements of the 2023 Draft Guidance include recommendations regarding how to describe pediatric use data in a range of scenarios and how to incorporate immunogenicity data. With respect to immunogenicity data, the 2023 Draft Guidance suggests that a contextual paragraph[5] generally be included in the relevant CLINICAL PHARMACOLOGY subsection before describing the available immunogenicity data for the reference product and the biosimilar or interchangeable biosimilar product. The 2023 Draft Guidance also outlines the Agency's expectations for patient labeling—such as a Medication Guide, Patient Information, or Instructions for Use—for a biosimilar or interchangeable biosimilar product, if the reference product has such patient labeling.

Information on how to submit comments on the 2023 Draft Guidance can be found at **https://www.regulations.gov/docket/FDA-2016-D-0643.**

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[1] The proprietary name of a biosimilar product is a brand name determined by the sponsor. The fictitious example provided in the 2023 Draft Guidance is "NEXSYMEO."

[2] The proper name of a biosimilar product is the nonproprietary name designated by FDA that consists of a biological product's core name plus a unique four-letter suffix. The fictitious example provided in the 2023 Draft Guidance is "replicamab-cznm."

[3] The fictitious example provided by FDA in the 2023 Draft Guidance is "replicamab products".

[4] The fictitious example provided by FDA in the 2023 Draft Guidance is "NEXSYMEO (replicamab-cznm) is biosimilar* to JUNEXANT (replicamab-hjxf)" and the accompanying footnote is "Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of *[BIOSIMILAR OR INTERCHANGEABLE BIOSIMILAR PRODUCT'S PROPRIETARY NAME]* has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration) described in its Full Prescribing Information."

[5] The Agency's suggested paragraph is, "The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of [*proper name of reference product*] or of other [*core name*] products."

Modernizing the FDA's 510(k) Program for Medical Devices: Selection of Predicate Devices and Use of Clinical Data in 510(k) Submissions

 On September 6, 2023, the US Food and Drug Administration (FDA) released a trio of draft guidances in its efforts to "strengthen and modernize" the 510(k) Program and provide for more "predictability, consistency, and transparency" for the 510(k) premarket review process. In this post, we discuss the two new draft guidances with broad applicability to the 510(k) Program:

- "**Best Practices for Selecting a Predicate Device to Support a Premarket Notification [510(k)] Submission**"
- "**Recommendations for the Use of Clinical Data in Premarket Notification [510(k)] Submissions**"

The two draft guidances address a number of fundamental issues of concern with the 510(k) process.

Read the full client alert **here**.