
# GREENLEAF HEALTH
## CELL & GENE THERAPY CAPABILITIES

## OUR EXPERIENCE.
## YOUR SUCCESS.

Greenleaf Health is a leading FDA regulatory consulting firm guiding companies through the changing FDA landscape.

# ABOUT GREENLEAF HEALTH

**300 YEARS**
OF FDA EXPERIENCE

## WHY GREENLEAF

Founded in 2007, Greenleaf Health is a leading FDA regulatory consulting firm that provides strategic and technical guidance to pharmaceutical, biotechnology, and medical device companies researching, developing, and manufacturing innovative solutions to pressing global public health challenges.

Greenleaf's robust blend of technical skill and FDA institutional knowledge enables the firm to provide reliable, objective guidance to companies developing medical products for the U.S. market.

## UNMATCHED EXPERTISE

Greenleaf's team brings unmatched expertise that companies need when navigating today's evolving FDA regulatory environment. The firm includes former leaders and regulatory professionals from the FDA, Capitol Hill, top global pharmaceutical and medical device companies, leading law firms, and the U.S. biotechnology trade organization.

Greenleaf experts draw on a combined total of more than 300 years of FDA experience and a network of technical specialists. This wealth of experience informs Greenleaf's understanding of the broad life sciences industry and allows us to deliver valuable insight throughout the product lifecycle.

# COMPREHENSIVE SERVICES

## PRODUCT QUALITY, MANUFACTURING & COMPLIANCE

Greenleaf experts identify and promote practices and procedures that will align a client's approach with the FDA's quality, safety, and compliance expectations.

## MEDICAL DEVICE & COMBINATION PRODUCTS

Greenleaf applies extensive regulatory expertise to guide medical device clients from early-stage development to marketing authorization and throughout the product lifecycle.

## DRUG & BIOLOGICAL PRODUCTS

Greenleaf serves as a trusted regulatory partner, advising companies on the complex process of bringing new therapeutics to market in today's evolving FDA environment.

## COMPLIANCE AUDIT, TRAINING & REMEDIATION

Greenleaf works with a network of independent technical experts who provide comprehensive on-site compliance assessments, remediation, and inspection readiness.

## DIGITAL HEALTH SERVICES

Greenleaf experts provide guidance to clients developing, commercializing, utilizing, and investing in innovative digital health technologies as they navigate the evolving landscape of FDA digital health requirements.

## CELL & GENE THERAPY

Greenleaf assists sponsors of cell and gene therapies by optimizing FDA interactions and submissions to support product development, manufacturing, quality, compliance, and regulatory review.

## ADVISORY SERVICES

Greenleaf understands the complex environment within which life sciences transactions take place and performs in-depth regulatory risk assessments tailored to investors' needs.

## LITIGATION SUPPORT SERVICES

Greenleaf and our network of experts work closely with litigators representing FDA-regulated clients in disputes related to medical devices, drug and biological products, and product quality, manufacturing, and compliance.

## REGULATORY POLICY SERVICES

Greenleaf supports the needs of small and large clients to understand, implement, and comply with the FDA's regulatory programs and policies and to enhance patient access to products.

# CELL & GENE THERAPY TEAM

Greenleaf is comprised of the foremost experts in the regulatory field, including former leaders in the FDA's offices overseeing cell and gene therapies, drugs and biologics, drug product quality, and compliance, as well as medical devices and combination products. The Cell and Gene Therapy Team draws on decades of regulatory experience in senior FDA positions, international public health organizations, academia, and industry.

## JOHN TAYLOR

**President and Principal, Compliance & Regulatory Affairs**

Former FDA senior official, acting in high-profile positions at the Agency and senior leadership roles within industry.

## CYNTHIA SCHNEDAR

**Principal, Regulatory Compliance**

30-year career as a compliance expert; formerly Director of the Office of Compliance for the FDA's Center for Drug Evaluation and Research (CDER).

## JOHN JENKINS, M.D.

**Principal, Drug & Biological Products**

Former Director of the Office of New Drugs within the FDA's Center for Drug Evaluation and Research (CDER).

## SANDRA KWEDER, M.D.

**Principal, Drug & Biological Products**

Former Deputy Director of the FDA's Office of New Drugs and Deputy Director of the FDA's Europe Office and Liaison to the EMA.

## KAREN MIDTHUN, M.D.

**Principal, Drug & Biological Products**

28-year career in public service, including as Director of the FDA's Center for Biologics Evaluation and Research (CBER) from 2009-2016.

## WILSON BRYAN, M.D.

**Executive VP, Drug & Biological Products**

FDA career of 19 years, serving as Director of CBER's Office of Tissues and Advanced Therapies (OTAT) from 2016-2023.

## BOB MEYER, M.D.

**Principal, Drug & Biological Products**

A leader in drug and biological product lifecycle management with 30 years of regulatory and academic leadership.

## MADELEINE GIAQUINTO

**Director, Regulatory Affairs**

Legal and policy expertise, with a robust portfolio of experience advising on FDA regulatory compliance for a range of product types.

# CELL & GENE THERAPY SERVICES

Greenleaf assists sponsors of cell and gene therapy products by optimizing FDA interactions, submissions, manufacturing technology, and quality systems. Working cross-functionally, Greenleaf's experts ensure that clients have the specialized strategic insight and multidisciplinary perspective needed to navigate the rapidly evolving regulatory landscape for cell and gene therapies.

## PRODUCT DEVELOPMENT & REVIEW

Greenleaf helps sponsors understand and respond to the FDA requirements and guidance applicable to cell and gene therapies, including aspects of device and combination product regulation when relevant. Our experts specialize in:

- strategic FDA interactions throughout development, including formal meetings
- clinical trial design
- submissions and expedited programs
- FDA review communications and labeling discussions
- postmarket requirements

## MANUFACTURING & QUALITY CONTROLS

Greenleaf experts provide clients with strategic and technical support for establishing manufacturing and quality controls and complying with the FDA's multiple current GXP regulations, in addition to:

- pre- and postapproval inspection readiness
- compliance assessments
- evaluating and responding to FDA regulatory correspondence
- engaging with CBER's Advanced Technologies Team

## RARE DISEASE GUIDANCE

For sponsors developing cell and gene therapies to treat rare and ultra-rare diseases, Greenleaf offers guidance on maximizing trial design using appropriate clinical endpoints and natural history study data in support of efficient product development. Our experts also assist sponsors preparing requests for orphan drug and rare pediatric disease designations.

## REGULATORY LANDSCAPE

Greenleaf monitors and analyzes the regulatory environment for emerging trends in cell and gene therapy regulation that could potentially impact current development programs, as well as changes to the competitive landscape.

Our Advisory Services Team also offers focused due diligence and regulatory risk assessment in this space.

# QUALITY & COMPLIANCE SERVICES

Greenleaf's Product Quality, Manufacturing, and Compliance Team, along with our network of independent compliance experts, offers a full portfolio of strategic and technical services to support compliance with the FDA's regulatory requirements.

## COMPLIANCE ASSESSMENTS

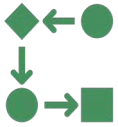
Greenleaf works with life science entities to evaluate and strengthen compliance functions with an eye toward optimizing processes, mitigating risks, and creating a culture of compliance, while continuing to meet business objectives.

## COMPLIANCE REMEDIATION

Greenleaf experts bring an unmatched level of credibility and trust when interacting with the FDA. The team has the experience and insight to successfully guide companies along the remediation pathway.

## INSPECTION READINESS

Greenleaf experts strengthen clients' readiness for FDA preapproval and surveillance inspections through consulting, training, audits, and mock inspections.



## SUPPLY CHAIN OPTIMIZATION

Greenleaf uses a systemic approach to help clients strengthen and safeguard the integrity of their supply chain management practices and comply with the regulatory requirements of the Drug Supply Chain Security Act.

## FDA COMMUNICATIONS

Greenleaf's best-in-class experts bring value to any communication with the FDA, including formal regulatory communication, in-person meetings, and responses to compliance actions and regulatory correspondence.

## CONSULTATION, TRAINING & REGULATORY GUIDANCE

Greenleaf delivers insight and guidance that help clients achieve business and regulatory objectives. The team also develops and delivers training on a variety of regulatory subjects.

## GCP SERVICES

Greenleaf specialists use a risk-based methodology to develop and improve clinical quality systems. Because there is no one-size-fits-all approach to GCP compliance, each solution is built to fit the targeted needs of the client.

## CELL & GENE THERAPY

Greenleaf helps sponsors establish manufacturing and quality controls and engage with the FDA to address potential technical and regulatory challenges related to emerging manufacturing technologies.

# DRUG & BIOLOGICAL PRODUCTS SERVICES

Greenleaf's Drug and Biological Products Team specializes in providing strategic and technical guidance on medical product development, regulatory review, and postmarket requirements, working closely with clients to navigate today's evolving FDA regulatory environment.

## UNMATCHED REGULATORY EXPERIENCE

Greenleaf serves as a trusted regulatory partner, advising clients on the complex process of bringing new therapies to market. The team's multidisciplinary expertise helps companies evaluating and prioritizing their drug development pipeline to understand and effectively manage regulatory risk.

## PREMARKET REVIEW PROCESS

Greenleaf's team of experts provides strategic and technical consultation on: scientific and regulatory practices for clinical programs and regulatory submissions, including endpoint and biomarker selection and development; identification of and eligibility for expedited programs (e.g., breakthrough therapy designation, fast track, and accelerated approval); use of real-world evidence in regulatory submissions; and preparation for FDA milestone meetings (e.g., EOP2, pre-filing, mid-cycle, and end-of-review meetings).

## REGULATORY POLICY SERVICES

Greenleaf offers strategic regulatory policy insight to support stakeholders' participation in and compliance with FDA programs and improve patient access to innovative medical products. Our team draws on deep expertise and institutional knowledge related to FDA regulatory policy, including novel programs; product designations and access to expedited programs; regulatory issues arising both pre and post market; regulatory intelligence and scientific policy; and building clients' capacity to effectively advance their regulatory policy priorities.

## CELL & GENE THERAPY

The Drug and Biological Products Team helps sponsors of cell and gene therapies understand and respond to FDA requirements and guidance for these products and optimize FDA interactions and submissions at all stages of development and review. The team also provides guidance on clinical trial design for cell and gene therapies to treat rare and ultra-rare diseases and assists sponsors preparing requests for orphan drug, RMAT, breakthrough therapy, fast track, and rare pediatric disease designations.

# MEDICAL DEVICE & COMBINATION PRODUCTS SERVICES

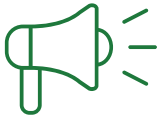
Greenleaf's Medical Device and Combination Products Team applies extensive FDA experience to determine the best regulatory approach for a product and develop a comprehensive strategy to achieve a successful result.

## UNMATCHED REGULATORY EXPERIENCE

Greenleaf guides clients through the complex regulatory process, from the earliest stages of product development, through the FDA review process, to marketing authorization and compliance with postmarket requirements and quality systems.

## PREMARKET REVIEW PROCESS

Greenleaf provides expert direction on scientific and regulatory strategies for clinical programs and regulatory submissions. Experts also provide recommendations and preparation for FDA meetings, including medical device advisory panel meetings, and FDA communications.



## MARKETING & PROMOTIONAL PRACTICES

Greenleaf offers strategic guidance to medical device firms on labeling requirements, promotional materials, direct-to-consumer advertising review processes, and use of social media. Experts also guide companies in remediation of untitled and warning letters.

## LITIGATION SUPPORT SERVICES

Greenleaf's deep bench of experts can offer litigators a high-level institutional knowledge of the FDA as well as more granular expertise regarding FDA regulation of a variety of product types across the product lifecycle. Greenleaf professionals have experience preparing expert declarations, drafting professional expert reports and depositions, and testifying at trial, and have worked with litigators representing FDA-regulated clients in a wide array of disputes involving complex FDA issues.

# COMBINATION PRODUCT SUPPORT SERVICES

Greenleaf provides strategic advice throughout the combination product lifecycle, including all potential premarket pathways (NDA, ANDA, BLA, PMA, 510(k), De Novo). Our experts have extensive experience with drug-coated devices and a wide range of drug delivery systems including subcutaneous, inhaled, injected, topical, intrathecal, and closed loop. We also have knowledge of, and experience with, designation and development of companion diagnostics.

Additionally, Greenleaf has expertise to help sponsors determine the regulatory identity (classification) of their product as a drug, device, biological product, or combination product and can prepare Requests for Designation (RFDs) and pre-RFDs to determine the regulatory identity and responsible FDA Center.

## PREMARKET STRATEGY & SUBMISSIONS

- Preparation and/or assistance with preparation of RFDs and pre-RFDs to determine primary mode of action (PMOA) and lead FDA Center assignment for combination products; strategies to help influence PMOA determination in line with company's objectives
- Strategic considerations in filing single vs. separate marketing application(s) for the drug, biological product, and/or device constituent parts of a combination product
- Strategies to help avoid the need for cross-labeling of constituent parts and advice on post-approval changes and bridging strategies for combination products
- Review of/recommendations for sufficiency of device design control documentation, including verification and validation plans, protocols, and reports for the device constituent part and combination product as a whole
- Review of/recommendations for human factors plans, protocols, and reports, including comparative use protocols for generic combination products
- Training in combination product statutory requirements, regulations, policies, and procedures
- Assessment of regulatory precedents and guidance to inform desired regulatory outcomes

## FDA INTERACTIONS

- Advice on communicating with the FDA, including help translating between "CDER speak" and "CDRH speak"
- Strategies to break logjams or obtain assistance navigating Centers
- Advice on working effectively with the Office of Combination Products (OCP)
- Review of/recommendations for responses to FDA deficiencies to investigational/marketing applications and responses to OCP questions on pre-RFD submissions

## CGMP & POSTMARKET COMPLIANCE

- Review of/advice on company procedures to comply with regulatory requirements for combination products
- Advice on cGMP requirements for single-entity, co-packaged, and cross-labeled combination products, including compliance with quality system "call-out" requirements for drugs, devices, and biological products
- Audits of company facilities for compliance with cGMP requirements for combination products
- Advice on postmarket reporting requirements for single-entity, co-packaged, or cross-labeled combination products
- Training on both cGMP and postmarket reporting requirements for combination products

# REGULATORY POLICY SERVICES

Regulatory policy is an essential component of the FDA regulatory landscape – it helps shape how regulators make decisions about the development, approval, and marketing of drugs, biological products, medical devices, and combination products. These policy decisions determine the feasibility of the development and use of new technologies and directly affect patient access to medical products.

Greenleaf's regulatory policy services are designed to support the needs of large and small clients as they navigate FDA regulations and regulatory policies. The firm's team of experts works cross-functionally to assist pharmaceutical and biotechnology companies, medical device manufacturers, patient groups, trade associations, and other stakeholders in communicating effectively about FDA regulatory policy issues and in understanding, implementing, and complying with the FDA's regulatory programs.

## EXPERT INSIGHT

Greenleaf's well-regarded professionals have each spent decades working in leadership roles at regulatory agencies and within regulated industry. The Regulatory Policy Services Team provides advice and recommendations based on extensive institutional knowledge of the FDA's overarching regulatory approach, as well as deep and granular expertise regarding FDA regulation of medical product types across the product lifecycle.

## TARGETED CAPABILITIES

Greenleaf offers unmatched insight on pre- and postmarket regulatory policy issues, product designations, expedited programs, regulatory intelligence, and scientific policy. Clients utilize our depth and breadth of knowledge to understand regulatory policy issues and build their capacity to implement, comply with, and communicate about FDA regulatory policy.

## COMPREHENSIVE SERVICES

Greenleaf's regulatory policy services address FDA regulations and regulatory policies to support clients' participation in FDA programs and regulatory compliance and to enhance patient access to innovative medical products. Comprehensive services include:

- Assistance with designing and implementing regulatory policy strategies to effectively advance priorities
- Guidance on policy issues related to development programs, combination products, submissions for marketing authorization, and the postapproval phase
- Stakeholder engagement and alliance development to achieve regulatory policy goals
- User fee negotiation support, impact assessment, and program development
- Strategic regulatory guidance for sponsors seeking access to FDA programs and designations, including orphan drug, breakthrough therapy, RMAT, and other expedited pathways
- Advice on incorporating novel tools and approaches into development programs

# ADVISORY SERVICES

Greenleaf's in-depth knowledge and understanding of the FDA equips clients with a trusted partner when considering life sciences transactions. Greenleaf's advisory services are more than a compilation of public data. Greenleaf goes a step further by using the firm's vast institutional knowledge to provide in-depth analyses tailored to our clients' specific needs.

The firm's multidisciplinary team uses its extensive expertise to perform risk assessments that take into account business objectives, transaction timelines, and the industry landscape. The end result is an unbiased analysis identifying a target company's key regulatory risks, likelihood of the risks materializing, potential impact on the business, and opportunities to manage and mitigate risks in order to achieve desired regulatory outcomes. Greenleaf's comprehensive due diligence services evaluate a company's pipeline, or a specific asset, in the following areas:

## PRODUCT DEVELOPMENT & REVIEW

Analysis of the target company's regulatory filings and product development plans, including approvals and clearances, special designations, advisory committee decisions, labeling review, and investigational products.

## QUALITY MANUFACTURING

Assessment of the target company's manufacturing practices, compliance with quality system regulations (QSRs), good manufacturing practices (GMPs), and identification of inconsistencies that may affect the regulatory risk of a product or the company.

## IDENTIFICATION OF REGULATORY RISK

Evaluation of the target company's compliance with FDA regulations and identification of issues that may require attention and resources for remediation.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