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Client Alert

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Department of Justice Vows Vigorous Enforcement of Clinical Trial Fraud

As disruption from the COVID-19 pandemic continues, pharmaceutical and medical device companies have been working hard to keep FDA-regulated clinical trials on track. Everyone involved in clinical trials should be acutely aware that the U.S. Department of Justice ("DOJ") has promised to intensify its enforcement activity in this space. This alert provides an update on two of DOJ's recent enforcement actions and public statements related to clinical trials. It also suggests steps that compliance officers can consider to position their companies as favorably as possible to prevent enforcement actions if the government comes knocking.

DOJ'S RECENT ACTIONS AND STATEMENTS

In remarks at the November 2020 Health Care Compliance Association Virtual Healthcare Enforcement Conference, DOJ Consumer Protection Branch Director Gus Eyler specifically singled out clinical trial fraud as a "key area of drug and device related enforcement." During the pandemic, Eyler said, "good science is critical. And just as scientific breakthroughs have the potential to greatly improve public health, bad research has an equal potential to do great harm--both to patients and to trust in the system." Recognizing "the enormous potential harm of clinical trial fraud," Mr. Eyler committed the Consumer Protection Branch "to aggressively investigating and prosecuting such misconduct." He previewed that "you can expect the Consumer Protection Branch to announce many further similar actions related to clinical trial fraud in the coming months."

Mr. Eyler's comments are significant given that the Consumer Protection Branch is the principal DOJ component charged with enforcing the Federal Food, Drug & Cosmetic Act ("FDCA") against life sciences companies. The Consumer Protection Branch has tripled in size over the past several years, and has secured more than $12 billion in fines,

forfeiture, and penalties over just the past two years. His speech is not an empty warning, as two recent criminal cases illustrate.

First, just last month, a Florida resident, Lisett Raventos, pled guilty to conspiring to falsify clinical trial data. See *United States v. Raventos et al*., No. 20-20190 (S.D. Fla. 2020). Raventos was a clinical investigator who worked at a medical clinic, Unlimited Medical Research, in Miami. She contracted with the sponsor, a large pharmaceutical company, to operate a clinical trial designed to investigate the safety and efficacy of an asthma medication in children. As part of the felony plea, Raventos admitted to defrauding the company by fabricating data and falsifying medical records to make it appear as though certain children participated in the trial, when in fact those children had not.

Second, in July of this year, a grand jury in Ohio indicted a number of defendants in an alleged scheme to defraud eight pharmaceutical companies and the FDA. See *United States v. Demming et al.*, No. 20-00395 (N.D. Ohio 2020). The defendants were the President and various employees of a contract research organization ("CRO"), including a physician who acted as the principal investigator for the CRO's studies. The CRO had contracted with the pharmaceutical companies to operate various clinical trials, including studies designed to investigate the safety, efficacy, and pharmacokinetics of certain investigational drugs to treat iron deficiency, influenza, and asthma. According to the government, the defendants enrolled subjects under fake names, and fabricated and falsified medical records.

ACTIONS FDA MAY TAKE PRIOR TO DOJ INVOLVEMENT

These developments should be understood in the context of FDA's existing, longstanding focus on clinical trials. The FDA Bioresearch Monitoring Program ("BIMO") carries out domestic and foreign inspections of FDA-regulated clinical research of investigational drugs, medical devices, and biological products. FDA conducts BIMO inspections routinely as part of the process for approving marketing applications, and in response to adverse events, complaints, and whistleblower allegations. These inspections are intended to (1) protect the rights, safety, and welfare of human subjects, (2) verify the integrity – accuracy and reliability – of clinical trial data submitted to FDA in support of research or marketing applications, and (3) ensure compliance with FDA laws and regulations applicable to clinical research. In addition to its inspections of investigators, institutional review boards (ethics committees), and sponsors, FDA conducts both routine and "for cause" inspections of contract research organizations, which are entities engaged by a sponsor to conduct clinical trial functions on its behalf.

Sponsors should also be aware that although FDA has issued recommendations about changes in clinical trial conduct that are potentially acceptable for responding to COVID-19 disruption, the Agency has recently issued guidance notifying sponsors about its heightened concern for data integrity in this setting.

If FDA deems that violations of FDA's requirements have occurred that expose subjects to unreasonable and significant risk of illness or injury, compromise subjects' rights and welfare, or compromise data integrity, FDA can initiate multiple administrative actions including, but not limited to, issuance of an "Untitled Letter" or "Warning Letter" based on alleged violations of FDA's laws or regulations, initiation of disqualification proceedings for a clinical investigator (Notice of Initiation of Disqualification Proceedings and Opportunity to Explain ("NIDPOE")), rejection of clinical trial data, placement of a "clinical hold" or termination of ongoing studies, civil money penalties and debarment of individuals. DOJ also has criminal causes of action at its disposal, including potential violations of the FDCA or other more traditional criminal statutes (e.g., 18 U.S.C. §§ 2, 371, 1001, and 1341).

COMPLIANCE CONSIDERATIONS

DOJ's and FDA's focus on clinical trials raises fair questions about the types of compliance measures that pharmaceutical and medical device companies might consider. A company that uncovers, addresses, and/or reports a potential problem before the government identifies it substantially illustrates a company's own good faith and helps build defenses to charges of alleged misconduct. Indeed, according to the government, the pharmaceutical company that contracted with defendant Lisett Raventos escaped enforcement action primarily because the company first detected and reported the fraud.

To that end, companies that are sponsors[1] of clinical trials should conduct meaningful diligence regarding potential contractors–both clinical investigators[2] and contract research organizations[3]–before engaging them. Background checks, including identifying prior lawsuits, government enforcement actions, and overall financial stability, would help inform that diligence. Requiring documentation of the contract research organization's compliance program, including asking about the contractor's hard controls, policies and procedures, and training programs, also would help establish the contractor's bona fides.

Prior to initiation of a clinical trial, sponsors should also consider the following proactive steps regarding both potential clinical investigators and contract research organizations:

- Examine information that FDA publicly posts regarding the classification of BIMO inspections of sponsors, including contract research organizations, and investigators, along with identifying any Warning Letters and/or NIDPOEs;
- Conduct training of clinical investigators and staff on the conduct of the investigational plan and protocol, along with applicable FDA requirements, including the consequences of non-compliance;
- Appreciate that monitoring of a clinical trial is a core obligation of a sponsor, regardless of whether some functions are delegated to a contract research organization;
- Understand the data and processes that FDA considers critical to ensure data integrity and subjects' protection, and implement a risk-based monitoring plan[4];
- Apart from monitoring of investigators and sites, develop a plan for independent auditing of higher activity investigators (e.g., high volume enrollment), and plan audit process of the performance of the contract research organization early after trial initiation and midway through the study;

After the clinical trial begins, make sure as the sponsor to oversee the contract research organization's performance to ensure subject protection and data integrity. Include explicit audit rights in the retention contract, and then exercise those audit rights, to help document that compliance controls are maintained. Relatedly, expect the government and third parties to mine payment data associated with healthcare practitioners that may be involved in clinical trial protocols as investigators or other functions, with more scrutiny associated with higher overall payments made to any particular HCP. "It is a great point of pride in the Consumer Protection Branch that we are on the cutting edge of using data analysis tools," Mr. Eyler said last month. "These tools have been enormously important in helping us target our enforcement actions, and we apply them in the full range of our work. Do not have us be the first ones to analyze data that your companies or clients possess."

Finally, document these steps as you take them. DOJ has reiterated its promise in recent years to offer significant credit to companies that invest in compliance programs in advance of misconduct, as well as companies that take

steps to remedy problems after they occur. A contemporaneous record can be invaluable in demonstrating to the government that the company has been committed meaningfully to compliance.

These are just a few considerations for companies to evaluate as DOJ turns its sights on sponsor oversight of clinical trial investigators and contract research organizations, and the companies who use them.

We would be pleased to assist in confidential analyses of company processes for oversight of investigators and contract research organizations, conduct compliance training for investigators and staff, provide guidance as potential compliance issues emerge during clinical investigations, and provide counsel in the event of emerging or threatened federal enforcement actions. Please call or e-mail for more information on these and other compliance measures in this growing area of enforcement.

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[1] See 21 C.F.R. § 50.3(e)
[2] See 21 C.F.R. § 50.3(d)
[3] See 21 C.F.R. § 312.3(b)
[4] See FDA guidance at https://www.fda.gov/media/116754/download
Critical data and processes for sponsor monitoring, and later FDA inspections include: verification of informed consent, adherence to protocol eligibility criteria; accountability of investigational product; conduct and documentation of assessments of study endpoints, safety assessments, and reporting of serious adverse events, deaths, and subject withdrawals due to adverse events; maintenance of blinding of the study.