August 26, 2020

FDA Releases Guidance on Civil Monetary Penalties Related to ClinicalTrials.gov Submissions

On August 12, 2020, the U.S. Food and Drug Administration ("FDA"), which has not previously undertaken enforcement action for noncompliance with ClinicalTrials.gov submission requirements, issued a final guidance document clarifying when and how FDA intends to seek civil monetary penalties for noncompliance with those standards. This marks a sea change in FDA attitudes toward noncompliance with these clinical trials transparency requirements. The document, *Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank* ("Guidance") , finalizes with little revision a September 2018 proposed guidance. It addresses how FDA intends to identify noncompliant "responsible parties" and others who violate the ClinicalTrials.gov registration and results-reporting requirements in section 402(j) of the Public Health Service Act ("PHS Act") and its implementing regulations at 42 CFR part 11; outlines how FDA will initiate enforcement actions; and describes what civil monetary penalties FDA may assess.

FDA explains that it intends to identify violations in two primary ways: first, during inspections conducted under the agency's Bioresearch Monitoring Program (BIMO), and, second, on the basis of third-party complaints. The agency will follow a "risk-based approach" to determine when noncompliance warrants enforcement. FDA announced that it intends to focus its attention on several specific forms of noncompliance, including responsible parties who fail to submit required data for applicable clinical trials of risk-high products, such as drugs intended to treat a rare or life-threatening disease or a vulnerable population, and responsible parties or other submitters who exhibit a pattern of noncompliance with clinical trial reporting and certification requirements.

When FDA determines a responsible party may have failed to submit required study records or data, FDA plans to send the responsible party a Preliminary Notice of Noncompliance (Pre-Notice) Letter, which would describe the potential violation and request that corrective action be taken within 30 calendar days of receipt. This same notice may be sent to other submitters, e.g., sponsors of FDA applications, who may have violated the certification provisions in section 402(j)(5)(B) of the PHS Act (certifying compliance with ClinicalTrials.gov reporting requirements in marketing applications). Of note with regard to inspections, FDA stated that it does not intend to include observations about possible ClinicalTrials.gov failures in FDA 483 forms, though it will include such information in Establishment Inspection Reports ("EIRs") and share it with the appropriate FDA Center for further review. FDA's reasoning is that investigators, during an inspection, may not be effectively positioned to determine whether required clinical trial information has been submitted to ClinicalTrials.gov.

If after the Pre-Notice Letter 30-day period responsible parties fail to take corrective action, FDA will publically issue a Notice of Noncompliance, as required by statute, allowing the responsible party an additional 30 days to remedy the identified noncompliance. This notice will be posted on the FDA's website and provided to the National Institutes of Health ("NIH") for posting on ClinicalTrials.gov. This may result in the NIH's withholding of grant funds, though NIH has not yet disclosed its intentions here. If the responsible party again fails to take adequate remedial action, FDA will seek civil monetary penalties.

Finally, the Guidance describes how FDA will assess the amount of civil monetary penalties according to the particulars of a given case. Civil monetary penalty proceedings are governed by regulations found at 21 CFR part 17 and are initiated by the FDA Center with primary jurisdiction over the study. Under this process, FDA presents a formal complaint with sign-off by the FDA Office of Chief Counsel, and the responsible party then has an opportunity to answer, including with agreement or objections to the FDA Center's claims, within 30 days of the date of service of the complaint. Respondents who file objections within the 30-day period are entitled to a hearing in accord with 21 CFR part

17. They may seek also to settle claims with FDA for a lower penalty. If settlement is not reached, claims will be adjudicated before an administrative law judge and, thereafter, either party may appeal to the U.S. Department of Health and Human Services' Departmental Appeals Board ("DAB"). The respondent may also appeal adverse DAB filings to the U.S. Court of Appeals for the District of Columbia or another circuit where the respondent resides or does business.

In proposing a penalty amount, the Guidance specifies that FDA will consider "the nature, circumstances, extent, and gravity" of the violation, the violator's compliance history and ability to pay, its degree of culpability, and "such other matters as justice may require." Penalties may be assessed for failing to submit required registration or results information, submitting false or misleading information, failing to submit required certifications and knowingly submitting false certifications. The Federal Food, Drug, and Cosmetic Act caps monetary penalties, permitting a maximum penalty of $10,000 for all violations adjudicated within a single proceeding, or, if a responsible party fails to remedy its noncompliance within the notice period, $10,000 per day of continuing noncompliance. These amounts may be updated to reflect inflation in accord with federal law, and the current inflation-adjusted amounts are $12,316 for 2020. Inflation-adjusted maximums are found at 45 CFR 102.3.

The Guidance is a continuing part of the federal government's effort to enforce ClinicalTrials.gov reporting requirements and respond to critics who say the government is not aggressive enough. With this Guidance, the FDA has signaled enforcement priorities and affirmed its commitment to education of responsible parties in how to fulfill their obligations voluntarily. The inclusion of the Pre-Notice Letter in the enforcement process could be viewed by some as too lenient to parties who have failed to comply with ClinicalTrials.gov registration and results-reporting requirements. Even so, the release of this new guidance signals that FDA is preparing, at least in extreme or repeated cases of noncompliance, to take enforcement action.