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FDA Inspections

Findings for Clinical Investigators

INTRODUCTION

IMARC annually reviews the findings of FDA inspections to understand the current state of clinical research and how we can best help our clients as a trusted compliance partner. We closely reviewed the 2019 FDA warning letters issued to clinical investigators to pinpoint common threads within Bioresearch Monitoring (BIMO) program inspection findings.

There were many types of deficiencies noted during BIMO inspections for clinical investigators and sponsor-investigators, ranging from protocol deviations to inadequate records, failures to comply with the Form FDA 1572 and IRB requirements, failures to report adverse events, and more.

In 2019, there were 779 BIMO inspections of clinical investigators and 13 inspections of sponsor-investigators. Of those, three resulted in official action indicated, meaning that regulatory action was needed to address non-compliant, objectionable conditions or practices observed.

Key Issues

From the 2019 FDA warning letters for these 2 Investigators, the key issues included:

- Failure to ensure that the investigation was conducted according to the investigational plan [21 CFR 312.60]; and
- Failure to submit an IND for the conduct of clinical investigations with an investigational new drug that is subject to 21 CFR 312.2(a) [21 CFR 312.20(a) and 312.40(a)].

Failure to Follow the Investigational Plan

Three investigators failed to follow the investigational plan, or study protocol. They did not ensure that subjects met all inclusion and exclusion criteria before their enrollment in the study or before progressing on the study into the next phase.

At one site, screening potential patients to confirm eligibility before enrollment was not conducted properly; therefore, ineligible patients were enrolled in the protocol and treated with an investigational drug.

At the other, eligibility should have been confirmed before randomization into the next phase of the study and patients should have been discontinued from the study if they did not meet the criteria. In several cases, patients were randomized improperly. Some were treated at higher doses than they should have been. Additionally, several patients continued on the study when they should have been discontinued based on their lab results falling out of range.

Eligibility criteria are carefully developed. For all studies, eligibility criteria are meant to minimize risk for potential patients and optimize the ability to interpret study data. Following these 2019 inspections, the FDA had significant concerns about the adequacy of the protection of subjects enrolled and about the integrity of the data collected.

Failure to Submit an IND Application

Another investigator was cited for failing to submit an IND application to the FDA. Some studies are exempt from needing to submit this application; however, the investigator was studying an unapproved drug that did not meet the exemption conditions. Despite the regulations, patients were enrolled and treated with the study drug prior to the investigator submitting an IND application to the FDA.

Processes such as an IND application have been put into place because of the unfortunate history of clinical research. Many clinical trials were conducted in the past that did not protect the safety and well-being of research participants. By implementing ethical standards and guidelines, Institutional Review Boards, and FDA oversight of clinical research, we are striving for a world with greater knowledge and reduced risk for patients. The steps involved with FDA oversight are essential to protecting patient safety.

Because the investigator missed this step, the FDA warning letter indicated that the investigator should address the deficiencies and establish procedures to ensure any ongoing or future studies follow the FDA regulations.

Honorable Mention - CAPAs

We reviewed many of the 2019 FDA warning letters to Clinical Investigative Sites and other groups (i.e., Institutional Review Boards (IRBs), Sponsors, Monitors, Contract Research Organizations (CROs), Clinical Laboratories).

Most of the FDA inspection warning letters discussed the importance of providing sufficient corrective and preventative action plans (CAPAs) with measures and procedures to address the inspection findings. In some cases, the plan was provided to the FDA, but supporting documentation was missing. In other cases, the response provided to the FDA was not clear enough to demonstrate plans to resolve the issue, address it with relevant staff, and ensure the same problem does not continue in the future.

Our Goal

At IMARC, we strive to help our clients ensure they are following the federal regulations, signed agreements, investigational plans, and requirements of the IRB. We take pride in helping strategize ways to avoid FDA warning letters and to improve processes related to clinical research. Contact us to find out more about our approach and how we can be your compliance partner.

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WE'LL EARN YOUR APPROVAL.

As a global, ISO 9001:2015-certified, full-service medical device CRO, IMARC has over 20 years of experience helping manufacturers conduct compliant clinical research and ultimately earn approval.

Conducting clinical research is an immense responsibility. Are you ready?

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