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TOP 3 REASONS AN FDA WARNING LETTER IS ISSUED TO A STUDY INVESTIGATOR

Throughout the 2016 fiscal year the Food and Drug Administration (FDA) completed inspections of study investigators, sponsors, institutional review boards (IRB) and other FDA regulated entities.

In 2016, there was a total of 1055 Bioresearch Monitoring Inspections (BIMO), including 775 inspections of Clinical Investigators (2016). At IMARC Research, Inc. these letters were reviewed, as they have been reviewed in previous years (2015, 2014, 2013). This is done to increase our understanding of FDA's current focus and highlight trends, so that as compliance partners, we can better assist our sponsors and investigators to ensure they are following current FDA guidelines.

Overall, the trends continue to be the same as in previous years, with the FDA citing the following common clinical investigator deficiencies:

- Failure to follow the investigation plan/agreement or regulations, or both
- Protocol deviations
- Inadequate recordkeeping
- Inadequate subject protection, including informed consent issues and failure to report adverse events
- Inadequate accountability for the investigational product; and
- Inadequate communication with the IRB

New this year was the deficiency of investigational product inaccurately represented as safe/effective by clinical investigators.

Warning letters issued to six clinical investigators were reviewed to garner more specific information. Listed from least to most frequent, these findings are described below:

NUMBER THREE

Failure to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects [21 CFR 312.62(a)].

- Example: Failure to maintain any drug disposition records.

NUMBER TWO

Failure to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation [21 CFR 312.62(b)].

- Example: Failure to maintain study records demonstrating that subjects met protocol-specified laboratory eligibility criteria.
- Example: Failure to accurately document who completed study procedures; including screening and follow up physical and neurological evaluations.

NUMBER ONE

Failure to ensure that the investigation was conducted according to the investigational plan [21 CFR 312.60].

- Example: Failure to ensure that study subjects met the protocol inclusion and exclusion criteria before enrollment.
- Example: Failure to send in required laboratory samples for 13 of the 14 enrolled subjects.
- Example: Failure to ensure that study subjects were on stable dose of concomitant medication at least six weeks prior to study screening.
- Example: Failure to delay subject randomization until screening lab values were collected.

Of the BIMO inspections of Clinical Investigators conducted in 2016, 2% of the Inspections resulted in Official Action Indicated and 32% had Voluntary Action Indicated. Reviewing these letters can provide us with more opportunities to assist study teams by ensuring that they are following study protocols and current FDA guidelines.

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Reference: BIMO Metrics