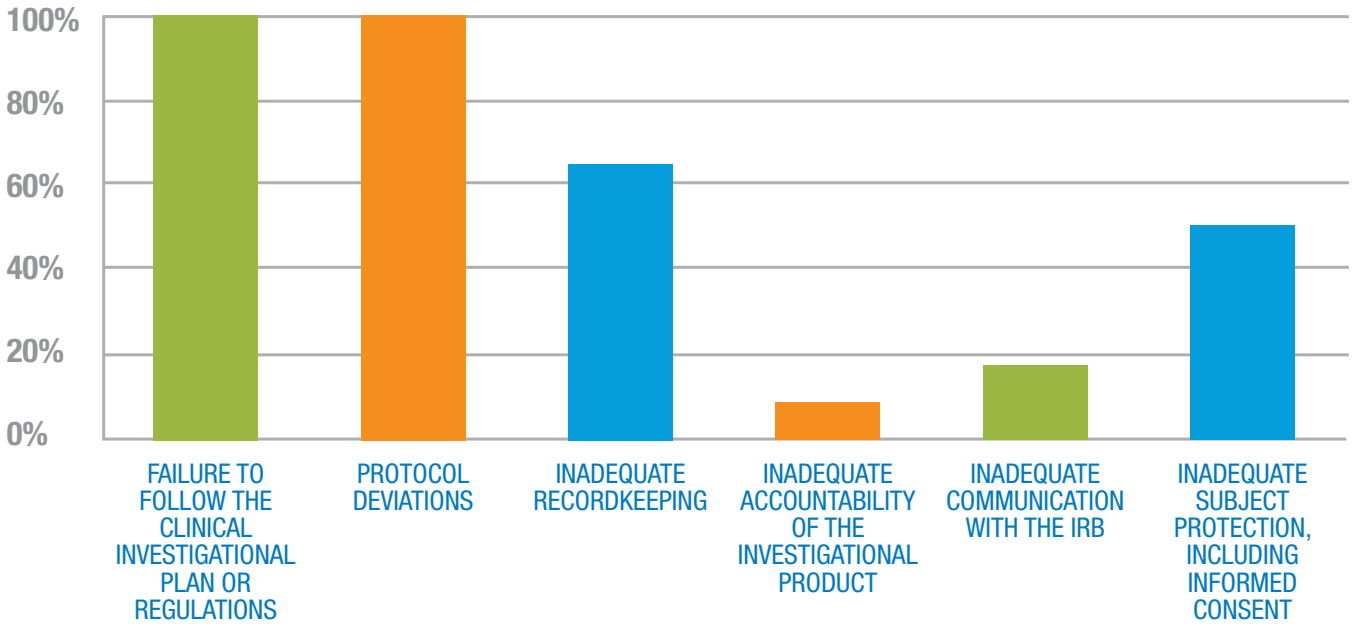
2013 FDA WARNING LETTER

Findings for Clinical Investigators, Sponsors, and IRBs

As we have done the past several years, IMARC has scoured the 2013 warning letters posted on the FDA's website to compile the top findings for investigators. This year, we took a look at the top findings for Sponsors and IRBs as well.

If, after an inspection, the FDA determines that serious violations of the federal regulations, particularly those that included human subject protection or data integrity issues, occurred at the site, they may issue a warning letter. All warning letters are available to the general public via the FDA's website[1]. 654 total warning letters were issued in 2013. This number includes not only investigational sites, IRBs, and sponsors, but also manufacturers, farms, pharmacies, and various other companies. We found twelve warning letters that were issued in 2013 for clinical investigators. Last year we provided a table of the most common deficiencies that showed up every year since 2007. Again this year, the list includes many of the same citations that have been included in prior years, as noted below:

2013 INVESTIGATOR WARNING LETTER CITATIONS



Five warning letters were reviewed for Institutional Review Boards (IRBs) from 2013. The top ten findings among the letters were:

NUMBER TEN

Failure to prepare, maintain, and follow required written procedures governing the functions and operations of the IRB

- *Examples included the IRB lacking certain SOPs, not following their SOPs for conducting initial and continuing review of research, failing to document the rationale for Significant Risk vs. Non-Significant Risk device determinations*

NUMBER NINE

Failure to prepare and maintain adequate documentation of IRB activities

- *Examples included missing protocols, safety reports, and annual progress reports from the IRB's files, no meeting minutes*

NUMBER EIGHT

Failure to fulfill membership requirements

- *Examples included allowing nonmembers to vote on clinical studies and having no physician member present during meetings*

NUMBER SEVEN

Failure to review proposed research at convened meetings at which a majority of the members of the IRB are present

NUMBER SIX

Failure to ensure that basic elements of informed consent are included in the IRB-approved consent form

- *This letter referenced failure to incorporate four risks that the IRB was informed had been left out*

NUMBER FIVE

Failure to notify investigators and the institution in writing of its decision to approve or disapprove proposed research activities or of modifications required to secure IRB approval of the research activity

NUMBER FOUR

Failure to report promptly to the FDA any suspension or termination of approval

NUMBER THREE

Failure to follow FDA regulations regarding the expedited review procedures

NUMBER TWO

Failure to prepare and maintain a list of IRB members identified by name, earned degree, representative capacity, and the relationship between each member and the institution

NUMBER ONE

Failure to determine at the time of initial review that clinical investigations involving children were in compliance with 21 CFR part 50, subpart D, Additional Safeguards for Children in Clinical Investigations

One warning letter was noted in 2013 for a Sponsor. Of note, the letter was for a Physician Sponsored IDE. The two findings noted in the letter were:

ONE

Failure to ensure proper monitoring of the investigations and to ensure that the investigations are conducted in accordance with the general investigational plan and protocols contained in the IND

- *This letter referenced inadequate monitoring, which resulted in the sponsor not identifying and correcting a clinical investigator's incorrect classification of therapeutic responses or the failure to obtain informed consent from subjects in accordance with FDA regulations*

TWO

Failure to obtain from an investigator sufficient financial information to allow the sponsor to submit complete and accurate certification or disclosure statements required under 21 CFR part 54

- *This letter referenced a failure to obtain financial information for any of the 122 subinvestigators of the study*

The purpose of reviewing the letters each year is not to poke fun at those sites or companies that were issued letters, but instead to gain insight into the current "report card" of the research industry. It helps us identify the types of issues the FDA is currently seeing as well as recognize trends of certain non-compliances. The letters are additionally a good perception into the current thinking of the FDA. Does there seem to be a particular kind of concern that was noted frequently this year that was never included in the past?

Another perk of reviewing the letters is it gives us insight into how the FDA interprets a regulation. Several regulations are purposely vague – for example, requiring "prompt reporting," but not specifying what exactly they consider prompt. Reviewing the citations and what the inspector expected of the site can provide understanding of these unclear requirements.

After reading through the citations as noted from the FDA's website in 2013, are there improvements you can make to avoid similar citations? Would training on these topics raise the bar in your daily work?

References

[1] U.S. Food and Drug Administration, Inspections, Compliance, Enforcement, and Criminal Investigations, http://www.fda.gov/ICECI/EnforcementActions/Warningletters/default.htm

Well-run, compliant studies result from well-trained staff. For more information about how you can help prepare your sites for better outcome, starting from Day One, please contact John Lehmann at 440.801.1540 or via e-mail at jlehmann@imarcresearch.com.

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WE'LL EARN YOUR APPROVAL.

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