2006-2022 FDA Form 483 Analysis and Top 10 Common Observations

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What is FDA Form 483?

- FDA Form 483 is an on-site inspection by US FDA inspectors of pharmaceutical companies' quality systems based on cGMP regulations, and lists a summary list of deficiencies that may violate cGMP regulations.
- The inspected enterprise needs to formally respond to the observation items in FDA Form 483, submit the formulated CAPA within the specified time, and implement it quickly.
- For pharmaceutical companies, FDA Form 483 can point out deficiencies in quality control and guide companies to improve their quality systems and meet cGMP standards.
- At the end of each year, the FDA publishes a summary of Form 483. However, it is worth noting that the data published by the FDA do not represent all observations, because some data are recorded manually.
- Analysis of FDA Form 483 observation items for drugs, it is summarized that the FDA Center for Drug Evaluation and Research (CDER) published Form 483 observation items from 2006.9 to 2022.10. A total of 651 regulatory provisions were cited in the report, with a total of 49,648 citations. Among them, 107 clauses were cited more than 100 times, with 39,373 citations, accounting for approximately 79% of the total citations.
- Most of these frequently quoted clauses come from the CGMP requirements for pharmaceutical preparations in CFR211 federal regulations, which basically reflect the common problems of pharmaceutical companies.
- The following are the top 10 most cited Form 483 observations by FDA over the past 17 years. Relevant companies can use this information to analyze their potential vulnerabilities and assess key areas where risks exist.

Top 10 observations from 2006-2022 are as follows

The observation items with the top 10 citation frequencies are concentrated in 5 aspects: organization and personnel, laboratory management, production and process control, equipment, records and reports, accounting for 25% of the total citations. Common observations are as follows:

1. Organization and Personnel

- Responsibilities and procedures applicable to quality control department, not written/fully followed (number of citations: 2479)
- Personnel are not trained in the documented procedures required by Good Manufacturing Practices (cGMP) (Number of citations: 779)
- No quality control department/quality control department, lack of permission to review records and investigate errors (number of citations: 672)

2. Laboratory Management

- The testing of closure system/intermediates/drug products does not meet the corresponding standards for identification, sampling plans, and inspection methods (number of citations: 1598)
- Testing and release of drug products not meeting final specifications/laboratory testing

appropriate to the characteristics and strength of each API (Number of Citations: 933)
- No documented testing procedures to evaluate the stability characteristics of drug products (Number of citations: 732)

3. Production and Process Control

- No documented production and process control procedures designed to ensure that a drug product has its claimed identity, strength, quality, and purity (Number of citations: 1318)
- Failure to establish control procedures to monitor the production process/validation performance that may lead to changes in the properties of intermediates and drug products (number of citations: 1022)
- Failure to follow documented procedures when controlling/recording production and processes (Number of citations: 872)

4. Equipment

- Failure to follow appropriate intervals to clean, maintain, and disinfect equipment/utensils to prevent malfunction/contamination (Number of citations: 1004)
- Failure to establish/follow documented procedures for cleaning and maintenance of equipment used to manufacture, process, package or contain drug products (Number of citations: 920)
- Failure to follow documented plans for calibrating/checking/qualifying electronic, automated, and mechanical equipment (number of citations: 820)

5. Records and Reports

- Failure to thoroughly review any unexplained deviations/batch or other deviations of raw materials and excipients not meeting quality standards (Number of citations: 1639)
- Batch production and control records: not prepared for each batch of drug products produced/does not contain complete information related to production and control of each batch (number of citations: 695)
- Written investigation records of unexplained deviations/batch or deviations of other raw materials and excipients that do not meet quality standards, not including conclusions and follow-up actions (number of citations: 510)

Source: 2006-2022 十七年 FDA483 大資料解析與 10 大常見觀察項匯總 (qq.com)