Decoding FDAspeak

What Form 483, warning letters, import alerts, et al, mean

Although FDA is the federal agency of the US, it exercises authority for inspections in foreign countries from which products are sourced. Here's a brief on what the observations at various stages mean.

Form 483
When any observations that may constitute significant violation(s) of the Food, Drug and Cosmetic (FD&C) Act and related Acts, including inadequate compliance with cGMP (current Good Manufacturing Practices), are observed, the investigator at the conclusion of the inspection must issue Form 483 to the firm's management. The investigator discusses these anomalies with the management at the conclusion of the inspection and outlines the agency's expectation, citing inappropriate regulations. Such written document is issued with the expectation of receiving a timely, clarifying or documentary evidence of commitment with specific time to comply with the observations.

The top items of concern that may result in the FDA to summarily issue Form 483 are absences of written procedures, weak or incorrect documentation, and inadequate corrective and preventive action.

Form 483, however, is not a final determination. It is considered along with a written report — Establishment Inspection Report (EIR) — including evidence and documentation collected on-site; and the agency then determines corrective action.

A response to Form 483 is not compulsory, addressing each item with a good response can typically help the company user clear of a warning letter. The response should reach the FDA within 15 days from the last day of inspection.

Care must be taken to ensure that such responses are comprehensive, prudent, logical, well-documented and includes such observation should be addressed individually.

Warning letter
When the FDA is satisfied with the firm's response, a warning letter is issued. If the FDA does not receive a response within 15 days, the regulator can proceed with issuing a warning letter.

A warning letter can also be issued immediately when the FDA believes that the management does not address the agency's concerns or has not addressed the agency's prior concerns or when major deficiencies are identified.

On the other hand, the company's responses are taken into account. If the FDA, after review of the company's response, is unsatisfied, it proceeds to issue a violation letter.

Some common reasons for the regulator to issue warning letters are — lack of data integrity, import of substandard, recalled or unapproved drugs into the US, forging, counterfeiting, simulating or misrepresentation of any data, alteration of whole or any part of data, certificate of analysis, false reports, false submission to FDA. A warning letter may not immediately lead to suspension in export.

Penalties, judicial actions
After issuance of warning letter, if the company continues to disregard rules and regulations, the FDA can then take enforcement action. The regulator is allowed to take one or more administrative actions, such as import alerts or product detention, revocation of product approvals, and recalls. If the FDA is not satisfied with remediation, it can call for import ban.

Further, through the Department of Justice (DOJ), the regulator can enforce legal penalties, such as seizures, injunctions and criminal prosecutions.


Miscellaneous