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Decoding FDAspeak

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

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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 strictures at various stages mean.

Form 483

When any conditions 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, can 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 appropriate regulations.

Such written document is issued with the expectation of receiving a response stating clarification or documentary evidence or commitment, with specific time, to comply with all the observations.

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

Form 483, though, 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 further action.

While a response to Form 483 is not compulsory, addressing each item with a good response can typically help the company steer 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 timely. Each observation should be addressed individually.

Warning letter

When the FDA is satisfied with the firm's response, a warning letter is not 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.

Otherwise, 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 warning letter.

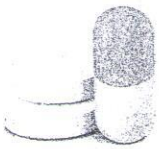
Some strong reasons for the regulator to issue warning letters are – lack of data integrity, import of substandard, mislabelled or unapproved drugs into the US; forging, counterfeiting, simulating or misrepresentation of any data, alteration of whole or any part of data, certificate of analysis, record, false statement, or false submission to FDA. A warning letter may not immediately lead to stoppage in exports.

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 detentions, 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.



Dr Reddy's

Inspected by FDA in November 2014, January 2015, and February 2015

Warning letter issued in November 2015

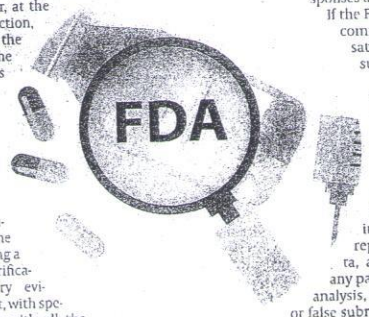
Number of NDAs and ANDAs filed in FY-16 is 14, versus 13 in FY-15

Cadila Healthcare

Inspected by FDA in August-September and December 2014

Warning letter issued in December 2015

Number of ANDAs filed in FY-16 is 30 with 10 approvals, versus 38 and 8 in FY-15



Miscellaneous