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Association for Accessible Medicines

Biosimilars Council
A Division of the Association for Accessible Medicines

GRx+Biosims

Overview and Trends

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Engineering the Future
of Generic + Biosimilar Medicines

Overview

1. Background
2. Some basics
3. Warning letter example

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Engineering the Future of Generic + Biosimilar Medicines

Commissioner Gottlieb and Generic Drugs

- Gottlieb February 7, 2018 tweet: “Jan. ’18 had fewer generic approvals as companies work to implement new guidelines to protect patients from impurities like arsenic & lead in drugs. This is a temporary falloff in approvals. We should make up for the 1 month shortfall as the year advances.”

- “We also broke records, with the highest number of generic drugs approved in a single month multiple times in 2017, and we recorded the highest annual total of generic drug approvals (1,027) in the agency’s history. We believe that, if current trends continue, we’ll exceed this record number of generic drug approvals in 2018.”

General Enforcement Priorities

- Scott Gottlieb in 2011: “Instead of calling for targeted fixes of troubled plants, the agency has often required manufacturers to undertake costly, general upgrades to facilities. As a result, in 2010, product quality issues – and the subsequent regulatory actions taken by FDA to address these problems - were involved in 42% of the drug shortages.”

- CDER approach
  - More standards
  - More uniformity
  - Patient first focus

FDA on Data Integrity's Importance

- May conceal patient risk
- Confidence between regulator and regulated
- Enhances and sustains brand
- Provides basis for management oversight of systems and processes
- Reduced risk of enforcement action
- Level enforcement playing field and competitive advantage for firms

“ALCOA” Basics

- Attributable – e-signature
- Legible – no overwriting
- Contemporaneous – time stamp
- Original/true copy – audit trail
- Accurate – validation
- Metadata – contextual information required to understand data (e.g. data/time stamp)
- Audit trail - secure, computer-generated, time-stamped electronic record that allows for reconstruction of events relating to an electronic record
- Restricted computer system access – access only by authorized personnel

FDA List of Significant Issues (1)

- Repeated tests, trial runs, sample runs (testing into compliance)
- Changing integration parameters of chromatographic data to obtain passing results
- Deletion/manipulation of electronic records
- Altered data
- Turning off audit trail
- Sharing password
- Inadequate controls for access privileges
- Inadequate/incomplete computer validation

FDA List of Significant Issues (2)

- Inadequate investigations
- Inaccurate reporting of microbial sterility, or endotoxin data results
- Loss of data during changes to the system
- Activities not recorded contemporaneously
- Records falsely indicating that an employee completed a manufacturing step

Warning Letter Language – 1/2018

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. We strongly recommend that you retain a qualified consultant to assist in your remediation. In response to this letter, provide the following.

A. A comprehensive investigation into the extent of the inaccuracies in data records and reporting.

B. A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity, and risks posed by ongoing operations.

C. A management strategy for your firm that includes the details of your global corrective action and preventive action plan.

THANK YOU

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