

Untitled Letters and Warning Letters

Tasneem Hussain Pharm.D.

Consumer Safety Officer (CSO) - Drug Registration
and Listing Branch

CDER | US FDA

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Learning Objectives

- Identify ULs and WLs and when they are issued
- Identify the steps to address and close ULs and WLs
- Discuss the manual override process
- Discuss the importance and impacts of the ULs and WLs
- Identify tips to avoid ULs and WLs

Registration and Listing Compliance Program



- Started in 2015
- Mission: to protect and promote public health by striving to achieve accuracy and integrity of establishment registration and drug listing data
- Four steps or actions:
 1. Random and focused registration and listing data review
 2. Issue deficiency letters
 3. Removal of uncorrected data
 4. Final action: untitled letter, warning letter, data inactivation

Untitled Letters and Warning Letters



- Official communication from FDA issued to registrants and labelers
- These can be issued if registrants or labelers do not respond to initial deficiency letters or make appropriate corrections
- Statutory and regulatory requirements



More about Warning Letters

- WLs are posted on FDA's warning letter webpage
 - [Warning Letters | FDA](#)
- Links to the issued WLs also found on
 - [Electronic Registration and Listing Compliance Program Page](#)
- DRLB has issued 21 warning letters to date
- A few include both registration and listing violations
- Most include listing violations

When Untitled Letters May be Issued



- Listing issues that can lead to ULs
 - Incorrect NDC
 - Incorrect strength of active ingredient
 - Incorrect Marketing category or Document Type

When Warning Letters May be Issued



- Registration issues that may lead to WLs
 - Failure to register or failure to list
 - Incorrect or unauthorized U.S. agent
- Listing issues that may lead to WLs
 - Incorrect or missing establishment
 - Incorrect package insert or carton label
 - Incorrect or missing active ingredient

Steps to Address and Close ULs or WLs



- Make corrections and resubmit
 - Send us the Core-ID or the Submission-ID for review
- Corrections to the errors in the UL or WL – will likely need manual overrides before acceptance



Manual Override Process

- Compliance officer will review the corrections
- Once all errors are addressed, CDER will approve a manual override
- Forward the submission and CDER's approval to the SPL Coordinator to manually load the data
- Once updated and correct file is uploaded – case is close
 - Closeout letter is issued for resolved warning letters
 - Data is released back for publication
 - Status changes to active, current, and certified

Importance and Impacts of ULs and WLs



- If UL or WL is not resolved
 - Data remains unavailable in NDC Directory
 - SPLs with WLs are indexed in DailyMed
 - Data may get inactivated at next scheduled inactivation period
 - Possible issues or delays with product importation due to open compliance case

Tips to Avoid ULs and WLs



- Follow registration and listing requirements under [21 CFR 207](#)
- Learn the latest automated validation rules
 - [SPL Implementation Guide](#)
- Make sure registration and labeler contact information is up to date and current
- Respond to the deficiency letter with corrections within 30 days

Challenge Question 1



- Which of the following may be reasons to issue an UL?
 - A. Drug not listed
 - B. Incorrect NDC
 - C. Unregistered establishment
 - D. Incorrect active ingredient



Challenge Question 2

Which of the following statements is correct?

- A. Closeout letters are issued after firm makes corrections in response to an UL
- B. ULs are posted on FDA webpages
- C. When requesting a manual override, firms need to send FDA the Core-ID or Submission-ID
- D. Failure to register an establishment may lead to an untitled letter

Summary

- ULs and WLs are issued to firms that are not compliant with R&L requirements
- Firms are legally required to submit correct and complete information to FDA
- Important to quickly review and respond with corrections – maintains data integrity

Questions?

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Consumer Safety Officer (CSO)- Drug Registration and Listing Branch

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edrls@fda.hhs.gov