Compliance Case Process and Manual Overrides

Leyla Rahjou-Esfandiary, Pharm. D.
Lead CSO
DRLS/ Office of Compliance
CDER/ US FDA
Electronic Registration and Listing Using CDER Direct
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Learning Objectives

- Describe FDA's registration and listing compliance program
- Identify when an NDC product code must change
- Describe the manual override request process

Registration and Listing Requirements

- Included in Section 510 of the Food, Drug and Cosmetic Act

  https://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapV-partA-sec360.htm

- Outlined in 21 CFR Part 207

  https://www.ecfr.gov/cgi-bin/text-idx?SID=fa8d7e9c3c27e094261bf903b897eb6e&mc=true&node=pt21.4.207&rgn=div5#se21.4.207_117

Registration and listing Compliance Program

- Began in 2015
- Mission: Achieve accuracy and integrity of establishment registration and drug listing data
- Phases
  - Surveillance
  - Deficiency letter
  - Data removal
  - Final action: untitled letter, warning letter, data inactivation

R&L Compliance Lifecycle - 1

Surveillance

- Compliance case created
- Deficiency letter sent

30 Days to Fix

Correction made

- SPL is reviewed
- Case is closed

Case is closed

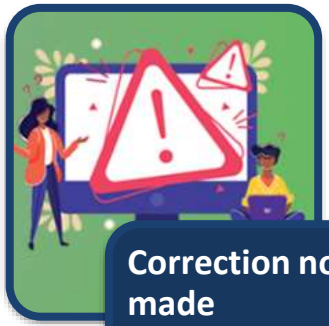
- No further action is needed

R&L Compliance Lifecycle - 2

Surveillance

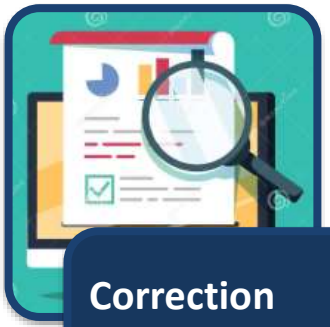
- Compliance case created
- Deficiency letter sent

30 Days



Correction not made

- Data is removed from the public sites
- **Removal notification sent**



Correction made

SPL is reviewed

Case closed

Case is closed

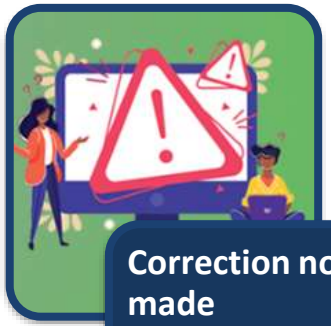
Data is released back for publication

R&L Compliance Lifecycle - 3

Surveillance

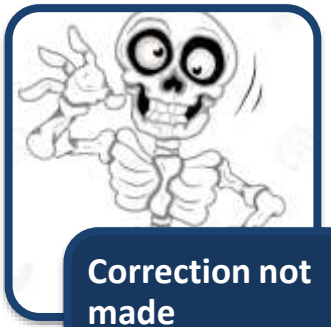
- Compliance case created
- Deficiency letter sent

30 Days



Correction not made

- Data is removed from the public sites
- Removal notification sent



Correction not made

Warning letter

Untitled letter

Data inactivation

Final Action

- Severity of the case
  - Public health concerns
- Company's efforts to address the deficiencies
- Agency's priorities
  - Public health emergency

Manual Override Process for Compliance Cases

Manual Overrides

Overrides are sometimes necessary to bypass the automated validations and allow certain corrections to be made to a record

- An override bypasses ALL business validations
- Done by the SPL office
- Initial CDER approval is required for CDER submissions
- The entire SPL file must be reviewed
- Submitted file is compared to previous version to prevent other errors from being introduced

Manual Overrides – How to Request

- *Core ID/ submission ID must be provided when requesting a manual override or requesting a review for approval of a manual override,*
- *Inclusion of a core ID/submission ID displayed as part of a screen image will not be accepted – the ID should be provided as text in the body or subject line of an e-mail message to afford the ability to copy the ID instead of retyping the ID,*
- *Be sure that core IDs/submission IDs are prominent and not buried in e-mail traffics,*
- *Barely legible images of screens, etc. included as supportive material for a manual override request may not be accepted,*
- *Be sure that the request is very clear and does not contain confusing or contradictory details,*
- *Manual override request e-mail messages with multiple core IDs/submission IDs are preferred to be formatted as one core ID/submission ID per manual override request.*

Manual Overrides – Reason for Delay

- Providing inaccurate or incomplete data at the time of request
- Discrepancies between the stated errors and the number of issues in the actual error message
- Providing a partial core ID or submission ID
- Referencing a previous message but not including that message as an attachment
- Duplicate requests
- No email subject line or subject lines not related to the message in the content

Errors

- Data errors included in a submission
  - Can generate or not generate automated errors
    - If doesn't pass validation rules:
      - Must be resolved before the submission in accepted
      - SPL Implementation Guide and Validation Procedures: https://www.fda.gov/media/84201/download
    - If passes validation rules: candidate for compliance case

Submission Errors

(Generating Automated Error Messages)

- Can be technical errors, or compliance errors
- Can be generated in an initial submission
- Can be generated in subsequent revisions:
  - Correcting a deficiency identified by FDA
    - Changes made to any key data element within the SPL
  - Updating data (registration renewal/ listing update periods)
    - Changes made to any key data element within the SPL
    - New validation rules implemented since previous submission

Some Common Errors

- Set ID issues
- DUNS issues
- Strength conversion for certain dosage forms (i.e., liquids, patches)
- Proprietary name issues
- Incorrect labeling

CDER Approval for Manual Overrides

- The change is made due to a deficiency
  - FDA deficiency letter
  - Company's internal review of its R&L data
- Other changes made:
  - Only if the start marketing date is not reached

A New NDC Product Code is Required

- Drug's established name or proprietary name
- Any active ingredient or its strength
- Drug’s Dosage Form
- A change in drug's status, between prescription and nonprescription
- A change in the drug's intended use between human and animal

Compliance Program Webpage

https://www.fda.gov/drugs/drug-registration-and-listing-system-drls-and-edrls/electronic-registration-and-listing-compliance-program

- Updated periodically
- Includes helpful resources and links
  - Strength conversion in drug listing
  - Active Moiety vs. Active Ingredient: Application of salt policy
  - Includes list of all published R&L WLs to date

Challenging Question #1

- All revisions made to correct a deficiency, will result in a submission validation error.

  A. False

  B. True

Challenging Question #2

- A pending revision, awaiting a manual override, will put a stop on all actions below, except for:

  A. NDC Directory removal

  B. Warning letter

  C. Untitled letter

  D. Deficiency letter

Biggest Take Away

- Invest in data submission infrastructure
  - Appropriate hiring
  - Trainings
- AVOID ERRORS
  - Manual overrides can take a long time

Measure twice, cut once!

Questions?

Leyla Rahjou-Esfandiary, Pharm. D.
Lead CSO
DRLS/ Office of Compliance
CDER/ US FDA
Leyla.Rahjou-Esfandiary@fda.hhs.gov
eDRLS@fda.hhs.gov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