eDRLS and the National Health Emergency

Paul Loebach
Director, Drug Registration and Listing Staff

Office of Program and Regulatory Operations, Office of Compliance
CDER | US FDA

SBIA eDRLS Using CDER Direct Conference – October 8, 2020

Learning Objectives

- Identify at least one use of registration and listing data by FDA during the National Health Emergency
- Identify potential problems encountered by FDA when registration and listing data is missing or inaccurate.
- Recognize and prevent situations of compliance issues

Background

Remember this?

- ***January 31, 2020*** – The Secretary of Health and Human Services declares a public health emergency, in response to COVID-19
- ***March 13, 2020*** – The President of the United States declares the corona virus outbreak a national emergency, effective March 1, 2020.
- ***March 13, 2020*** – DRLS Staff began 100% Telework
- ***Late March 2020*** – FDA publishes three separate guidances related to alcohol based hand sanitizers:
    - Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) Guidance for Industry
    - Guidance for Industry: Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)
    - Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency

What Happened Next…

What Happened Next

By the Numbers (New Registrations)

Month	Number of New Registrations
January	113
February	95
March	784
April	2083
May	1412
June	718
July	600
August	366
September	260*

***Slide recorded prior to end of month, number is extrapolated**

What Happened Next

By the Numbers (New Labeler Codes)

Month	Number of Labeler Codes Assigned
January	61
February	65
March	731
April	2117
May	1402
June	829
July	620
August	452
September	284*

***Slide recorded prior to end of month, number is extrapolated**

What Happened Next

By the Numbers (New Drug Listings*)

Month	Number of New Drug Listings
January	1569
February	1461
March	1922
April	4954
May	4848
June	4019
July	3536
August	2988
September	2750**

**All new listings (Rx, OTC, and bulk) identified by SPL version **Slide recorded prior to end of month, number is extrapolated*

How Did They Do That?

- *Additional staff temporarily assigned to DRLS*
- *Extended hours for helpdesk into nights and weekends*
- *Tens of thousands of emails through the eDRLS Helpdesk*
- *Hundreds of hours on the phone assisting companies and consultants*
- *Streamlined operations*

How Did They Do That?

- Standardized instructional email for the complete registration and listing process including:
  - Step by step process description
  - User guides with screenshots,
  - Links to helpful resources,
  - Contact information for various helpdesks.
- Two pre-filled drug listing templates in CDER Direct for alcohol and isopropyl alcohol hand sanitizers including:
  - Formulation information based on temporary guidance
  - Content of labeling based on temporary guidance
  - Placeholders for establishment name and DUNS
  - Users could edit/customize nearly all fields as needed to match actual product being listed

Scrutiny of the Data

Scrutiny of the Data

Labeler codes requests and assignments usually number about 1000 per year

From March to August we used up 6871 (about 7 years' worth!) of available labeler codes.

Numbers are trending back downward but are still elevated and expected to stay elevated for as long as the National Health Emergency is in effect.

Month	Number of Labeler Codes Assigned
January	61
February	65
March	731
April	2117
May	1402
June	829
July	620
August	452

Scrutiny of the Data

Most of the new registrations and listings are from non-traditional drug manufacturers trying to meet the high demand for hand sanitizer

- Domestic brewers, distillers, wineries, etc trying to supplement business by making hand sanitizers
- Chemical and other companies that produce ethanol or isopropyl alcohol for other uses
- Distributors, brokers, importers with a connection to a foreign manufacturer of hand sanitizer

Scrutiny of the Data

Non-traditional also means new to the drug industry, and its processes, regulations, terminology, and its data!

Despite our best efforts to provide detailed instruction, training, and support for registration and listing, the data still came in with some unintended errors…

Scrutiny of the Data

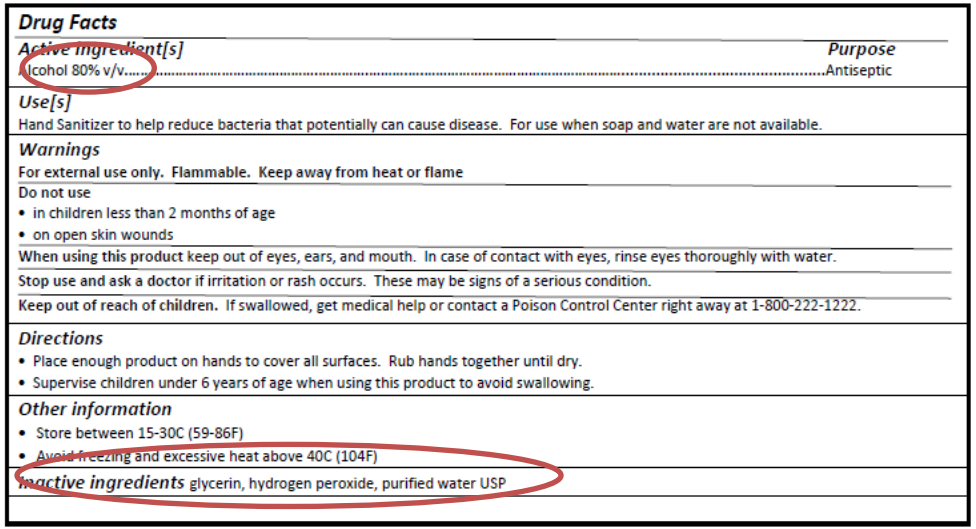
Scrutiny of the Data

For drug listings, it appears many companies did not bother to modify the default values from the two hand sanitizer templates

- *Marketing category remained OTC Monograph when product was not compliant*
- *Additional active ingredients left out of data even though named on the label*
- *Additional inactive ingredients left out of data even though named on the label*
- *Strength remained at 80% Ethyl Alcohol even though product labeled as much less*
- *Name of product remained "Hand Sanitizer" despite more specific name on labeling*
- *Dosage form remained Solution when product was a gel*

Scrutiny of the Data

Even if the data elements were updated appropriately, many companies didn't bother to update the Drug Facts label sections in the template



Drug Facts

Active ingredient[s] — **Purpose**

Alcohol 80% v/v..... Antiseptic

Use[s]

Hand Sanitizer to help reduce bacteria that potentially can cause disease. For use when soap and water are not available.

Warnings

For external use only. Flammable. Keep away from heat or flame

Do not use

- in children less than 2 months of age
- on open skin wounds

When using this product keep out of eyes, ears, and mouth. In case of contact with eyes, rinse eyes thoroughly with water.

Stop use and ask a doctor if irritation or rash occurs. These may be signs of a serious condition.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away at 1-800-222-1222.

Directions

- Place enough product on hands to cover all surfaces. Rub hands together until dry.
- Supervise children under 6 years of age when using this product to avoid swallowing.

Other information

- Store between 15-30C (59-86F)
- Avoid freezing and excessive heat above 40C (104F)

Inactive ingredients glycerin, hydrogen peroxide, purified water USP

Additional actives left out, or

Strength not modified (e.g. 70% v/v)

Additional inactives left out (fragrances, dyes, gel polymers)

Scrutiny of the Data

Regarding Contacts and US Agents…

- *Invalid email addresses*
- *Invalid phone numbers*
- *Valid DUNS, email, and/or Phone numbers for companies who have no affiliation with the foreign establishment*
- *Virtual offices such as residences, storage facilities, and other non-traditional business locations where the named US Agent does not operate.*

How the data has been used

The "Do Not Use" List

Tracking Down the Distributors and Their Products

The "Do Not Use" List

Tracking Down the Distributors and Their Products

- When methanol was discovered in several hand sanitizer products, registration and listing submissions were analyzed to determine:
  - Manufacturer(s)
  - NDC numbers and product names of all other alcohol based hand sanitizers manufactured at the same facility
  - US Agent and other contact information for firm
  - Distributors
  - Label identification

Unfortunately, our efforts were hampered by:

Manufacturer(s)	*API manufacturer not identified*
NDCs	*Incorrect assignment of NDCs led to delays for FDA staff in identifying affected products*
Product names	*Many just used the default "hand sanitizer" from the listing template as the product name*
Distributors	*Incorrect NDC assignments and non-descriptive drug names required review of individual JPGs to determine distributor identity*
US Agent	*Some foreign manufacturers simply identified customer as US Agent, or Identified the SPL consultant (or any other valid US entity) as the US Agent just to fill in the value*

Investigations

Authorized vs Unauthorized Submissions

Wall Street Journal Article about a single company linked to a house in Delaware that had registered more than 1300 firms (device firms).

DRLS data was searched and analyzed for:

- Presence of same company name, address, or email identified in WSJ
- Presence of any affiliate companies
- Patterns of any US Agent, email address, or phone number appearing in an unusual number of files

Investigations

Authorized vs Unauthorized Submissions

Various investigations and other analysis shows that some companies' information is being used or referenced as contact information or US Agent without their knowledge

How can you find out if your information is being used?

Download the DECRS file and search for your company name and info!
(We have a presentation later today about our publications)

Labeling Review

DRLS Staff conducts its own review hand sanitizer listings, in addition to consults from other offices' investigations

Listing data compared to submitted labeling and other evidence presented (e.g. photo of tested sample)

Errors encountered

- *Incorrect marketing category (not monograph compliant)*
- *Incorrect strength representation*
- *Incomplete ingredient list*
- *Incorrect dosage form*
- *Incorrect/missing package presentations*
- *Incorrect NDC assignment*
- *Inadequate Drug Facts labeling*

COVID-19 HS Project listing deficiency template

FDA Listing Deficiency Letter --#LABELER_NAME#-- Action Required #CURRENT_DATE#

#LABELER_CONTACT_NAME#
#LABELER_NAME#
#LBLR_CONTACT_ADDR#
#LBLR_CONTACT_CITY#, #LBLR_CONTACT_STATE#
#LBLR_CONTACT_ZIP#

Dear #LABELER_CONTACT_NAME#,

This letter is to notify you that we have identified an apparent problem with your firm's alcohol-based hand sanitizer listing submission to the Food and Drug Administration (FDA). The specific National Drug Code(s) (NDC) and associated error(s) or
omission(s) that we identified are itemized at the end of this letter. As explained below, if the submitted data are inaccurate or incomplete, that can have adverse results for public health and may constitute a violation of the law. Therefore, please examine the listing information for the drug(s) included in the table below, and within 14 days of receipt of this letter, ensure that you have provided complete and accurate listing information. Within that time period, please notify us at edrls@fda.hhs.gov that you have made corrections, or if you believe that your listing submission is accurate and complete without revision, please provide your reasoning and any supporting information for our consideration.

New listing information or updates to existing listing files should be submitted via Structured Product Labeling (SPL) using the FDA's electronic Drug Registration and Listing System

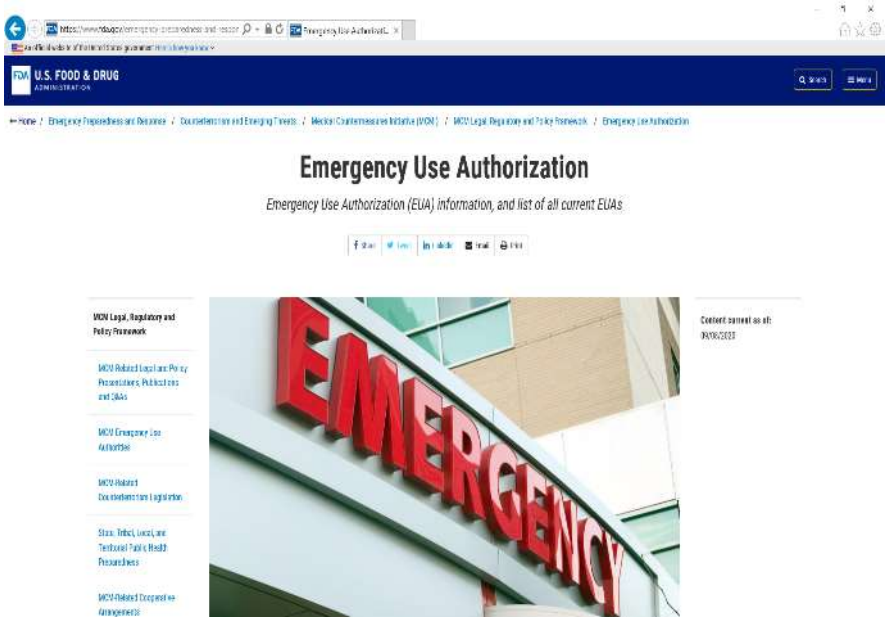
Emergency Use Authorizations

Registration and Listing Prior to Approval

Many drugs and vaccines have been granted an Emergency Use Authorization (EUA), usually as a part of a phase III trial.

Normally, phase III trials are exempt from the registration and listing requirement

However, adding registration and listing as a part of the EUA facilitates importation, and provides greater surveillance, tracking, and recall ability to FDA



Things to look forward to

Looking Forward

How has the last 8 months affected the next 8 months?

The surge in registrations, listings, and labeler code requests raises questions and necessitates certain actions which will dominate our efforts in the coming months

Looking Forward

How has the last 8 months affected the next 8 months?

More registered firms means more requests for assistance.

We have newly revised webpages available on the DRLS [website]

Looking Forward

How has the last 8 months affected the next 8 months?

The two listing templates for hand sanitizer were not only extremely popular, they save the eDRLS Helpdesk an enormous amount of time and effort providing support

New templates are being considered for other types of drugs

Looking Forward

How has the last 8 months affected the next 8 months?

Data issues encountered during the surge in new records has already led to increased number of compliance cases and deficiency emails.

An increase in the number of inactivations this January is also expected as companies choosing not to renew their registration for the new year will also let their listings go uncertified

Please don't do this and delist!

Looking Forward

How has the last 8 months affected the next 8 months?

Problems with contact information and US Agent data has already led to increased scrutiny and validations of registrations and labeler code requests

FDA collaborates with Dun and Bradstreet when it encounters problematic DUNS records

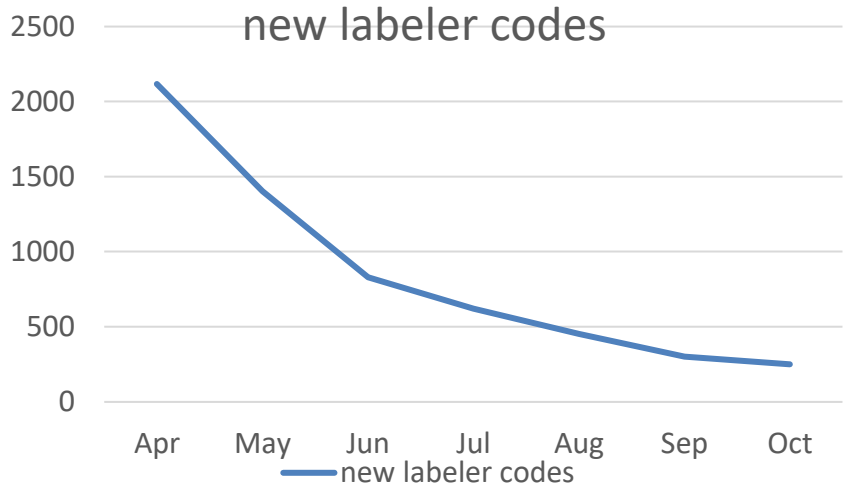
FDA is considering other avenues of action against the submission of false US Agent data

Looking Forward

How has the last 8 months affected the next 8 months?

Even though it is trending downward, FDA expects to have burned through as much as 9-10 years worth of available unused labeler codes by the end of the year.

FDA will need to find ways to address the issue of available 5 digit labeler codes



Conclusion

Conclusion

Registration and listing plays a fundamental role for FDA in our mission to protect and promote the public health.

Incomplete or inaccurate information hampers FDA response to crises ***and can endanger consumers****.*

Challenge Question #1

Which of the following uses of registration and listing data has not yet been employed:

A. Compliance investigations

B. Recalls of products containing methanol

C. Hurricane response

D. Vaccine importation

Challenge Question #2

Which of the following statements about quality and accuracy of the DRLS data is NOT true?

A. Incorrect manufacturer and lack of API manufacturer hampered efforts to track the source of methanol contamination.

B. No specific product name (e.g. proprietary name = ‘Hand Sanitizer’) made it difficult to search for records in the database.

C. Invalid contact information and US Agent data delayed/obstructed communications with firms.

D. Using different NDC Product codes for differences only in package size created confusion among consumers.

Challenge Question #3

What's the quickest way to see if a foreign manufacturer is using your data as a contact or US Agent?

A. Hire a private investigator.

B. Download the DECRS file and search for your company's information.

C. Inform FDA when in receipt of a regulatory communication for a company you don't represent.

Thank You

Thank you for listening to this presentation

Thank you for taking the time out of your day to attend the SBIA eDRLS 2020 Webinar.

Thank you for taking the time to ensure your submissions are complete and accurate.