

Drug Listing Inactivations An Overview

*Electronic Drug Registration and Listing Using CDER Direct
Workshop
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Background

Statutory requirements:

Section 510(b) of the FD&C Act requires that drug establishments register annually on or before December 31 each year (Oct-Dec renewal period)

Section 510(j)(2)(B) of the FD&C Act requires that registrants delist any discontinued product on file every June or December

Section 510(j)(2)(D) of the Food Drug And Cosmetic Act requires that registrants send in any material changes to any listing already on file every June or December .



Background – cont'd

Despite the requirements, here's what companies were actually doing:

- Many companies would list a product initially, then never update again:
 - One time import
 - One time or short-term repackaging contract
 - Didn't know about update requirements, or weren't as concerned with keeping all data up to date so long as imports processing, reimbursement, and insurance payments continued for current products.
 - Company may have ceased drug operations, but assigned no one to submit discontinuances/delistings
 - Underlying contract manufacturer or API manufacturer deregistered or failed to renew registration without informing owner/marketer of drug.
- Since registrants were only required to update ***when something changed***, FDA had to consider *older non-updated listings as active*
 - Electronic listings go back to 2009
 - **Some paper listings went back 20+ years!**



Background cont'd

In 2016, FDA updated its registration and listing regulations – a new 21 CFR 207 was published in August and implemented in November

21 CFR 207.57 (b)(2) *For each listed drug, certify that no changes subject to reporting under paragraph (b)(1)(iv) of this section have occurred if no such changes have occurred since the last review and update. If a drug is discontinued and FDA has received the information required under paragraph (b)(1)(ii) of this section, no further certifications are necessary for the discontinued drug. After initial electronic listing, registrants may satisfy the listing update requirement with respect to unchanged listing information by making a single “no changes” certification during the annual registration update under §207.29(b) applicable to all of the registrant's listed drugs for which no changes have been made since the previous annual registration update.*

As a result, there is now an annual requirement to update each of your listings **or at least** certify that no changes have occurred, similar to registration requirements.

If you have updated a listing during the calendar year, you do not have to certify it in the Fall!

Drug Listing Inactivations - History

- Annual requirement to update or certify drug listing data established by regulation in 2017 (from 2016 publication of the new regulation)
- FR Notice published Aug 2019 announcing the beginning of inactivations
 - Announced the beginning of inactivations in September of 2019, and reoccurring January and July rounds as well
- Inactivations commenced in September 2019
 - Incremental inactivations conducted each month through February 2020 (except December), beginning with the oldest listings first
 - In total, more than 50000 listings inactivated by February 2020



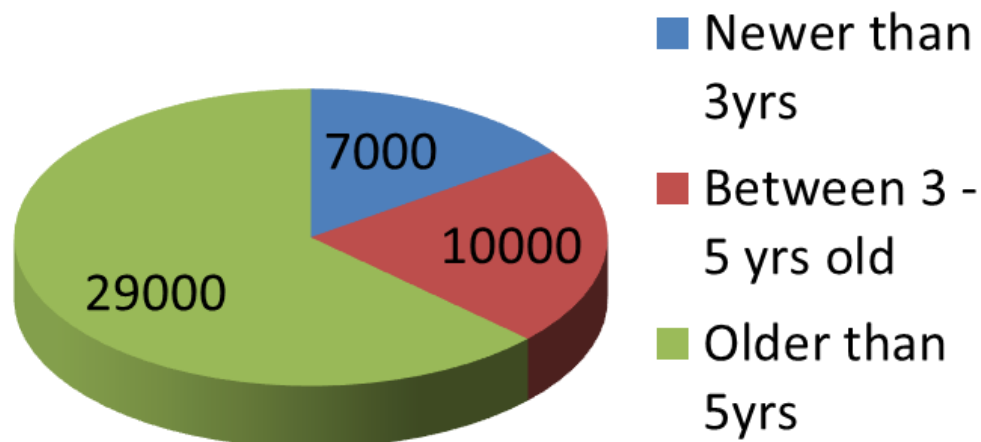
Initial Analysis of Uncertified Listings

Age of Uncertified Listings*

Listings which have not been updated in over 5 years are highly likely to be inactive and candidates for removal. Listings which are between 3-5 years old are very likely to be inactive and candidates for removal.

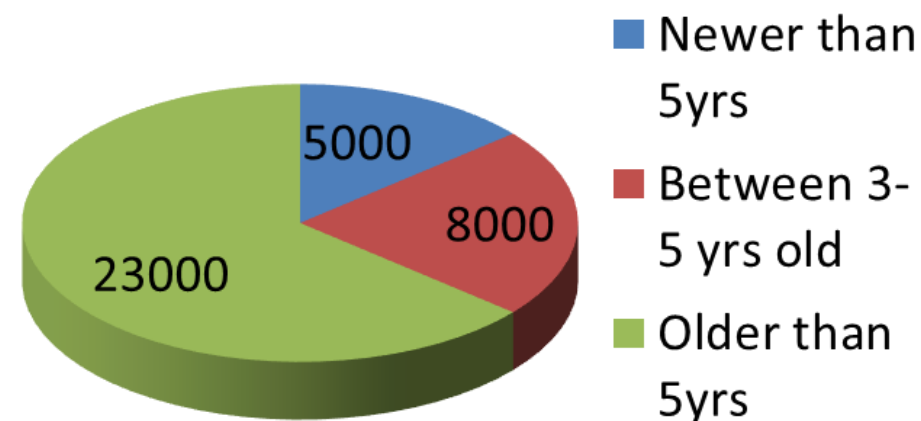
Total Uncertified Listings

(Total 46K)



Total NDC Directory Listings

(finished drugs, no API/bulks)
(Total 36K)



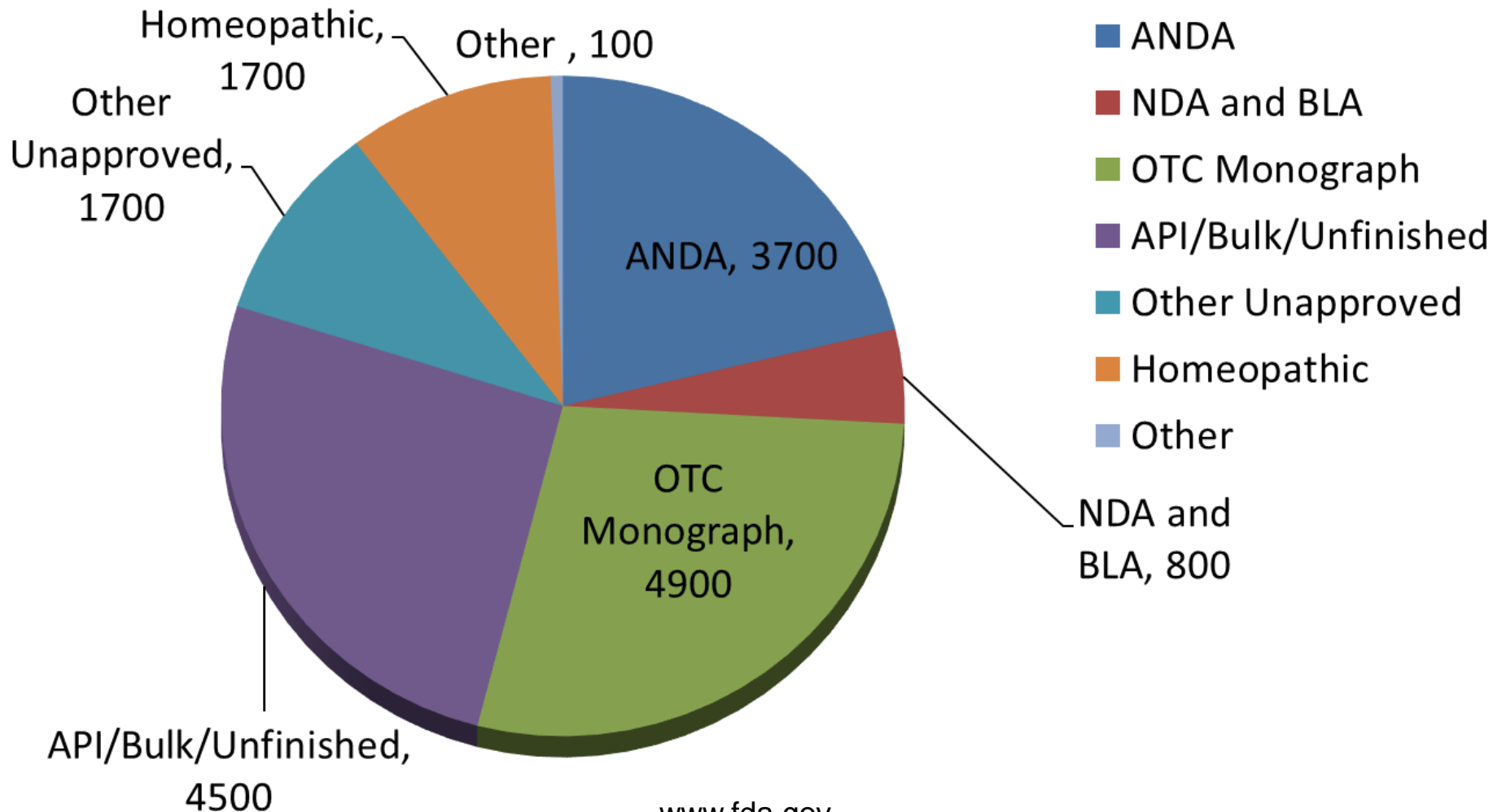
*analysis of eDRLS data, July 2019. Paper submission data not included.



Initial Analysis of Uncertified Listings

Uncertified HUMAN DRUG Listings Less Than 5 yrs old by Marketing Category

Of potential uncertified listings that may still be active, most are unapproved, unfinished, or products not usually covered by CMS or other payment plans



July Inactivations

- From the August 2019 FR notice:
 - *Thirty days after publication of this notice, and every January thereafter, FDA will begin to inactivate human drug listings that remain uncertified from the previous renewal period of October 1 to December 31. In addition, every July thereafter, FDA will begin to inactivate human drug listings that remain active and certified after the June listing update, but still contain at least one establishment that is not currently registered in accordance with FDA's requirements.*

July Inactivations

The certification process contains an *unavoidable* loophole:

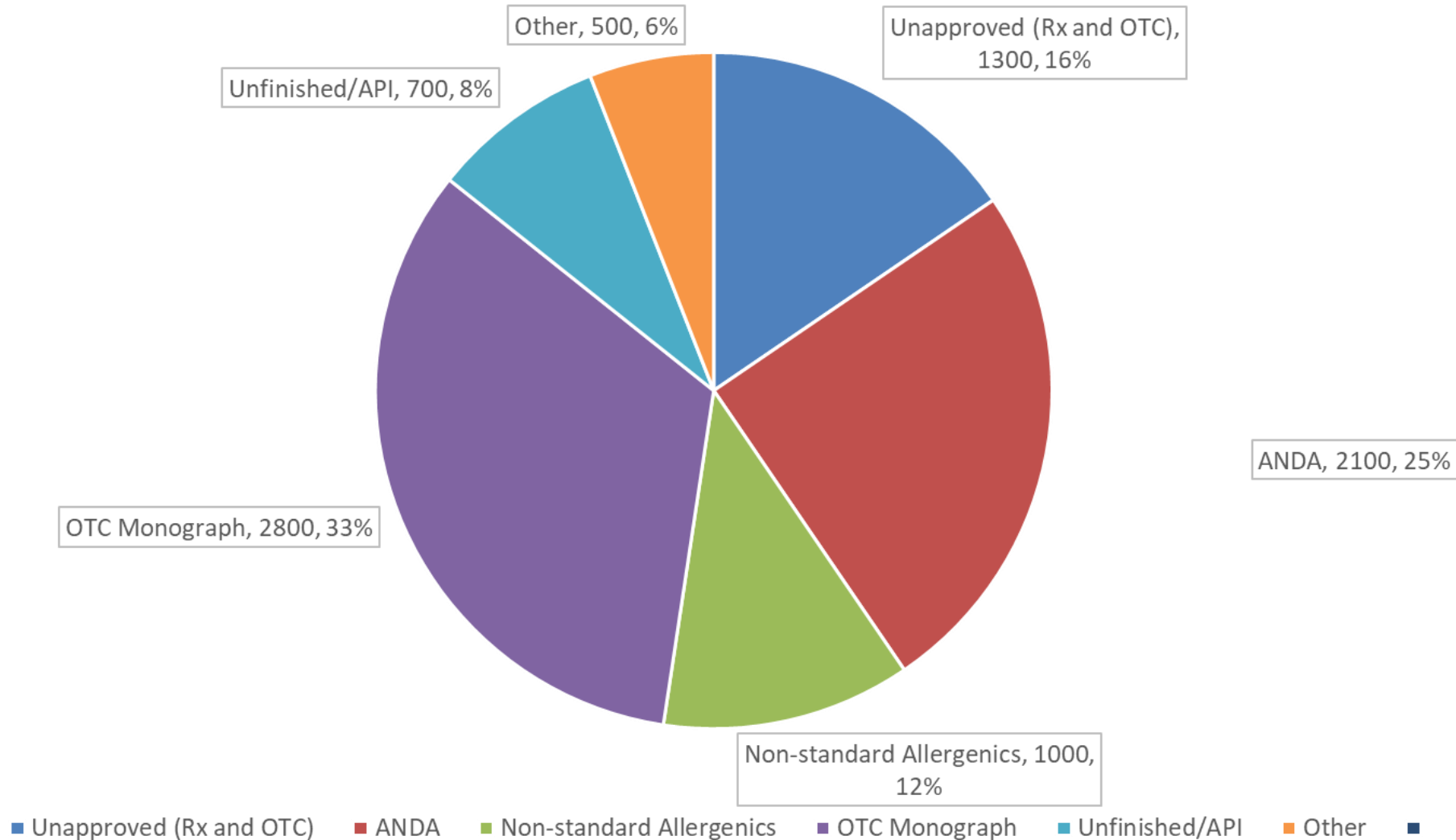
- The window to both register and certify drug listing is Oct 1 – Dec 31.
- A private label distributor (PLD) or finished drug manufacturer can certify the drug listing at anytime during that window, including *prior to* the renewal of the registration of an underlying manufacturer.
- However, any of the underlying establishments in the supply chain could fail to renew its registration by Dec 31.
 - *Consequently, on Jan 1, such a listing could immediately be deemed misbranded for being manufactured at an unregistered establishment.*
- Since the Statute requires listing updates *every June and December*, FDA allows companies with listings described above until the June update deadline to get the establishment registered or identify a new one.
 - *Therefore, in July we inactivate those active listings which are still linked to an unregistered establishment.*

Inactivation Process

- Same basic process for January and July
 - Send list of proposed inactivations to Drug Shortage Staff (DSS) for shortage consult.
 - Separately contact labeler of any product flagged by DSS.
 - Send a standard notification of inactivation email to all companies with a product in jeopardy of inactivation.
 - *Email is sent to the contact for the labeler code of the drug listing's NDC*
 - Provides 2-3 weeks notice before inactivation
 - Identifies all product NDCs under that labeler code in jeopardy of inactivation
 - Companies can request an extension if experiencing difficulty in making the update
 - Occasionally an update to listing requires a “manual override” of validations for the submission, which can take time for the FDA to process.
 - Ultimately, any product listing that is inactivated can be immediately reactivated with a full, updated, and corrected listing submission

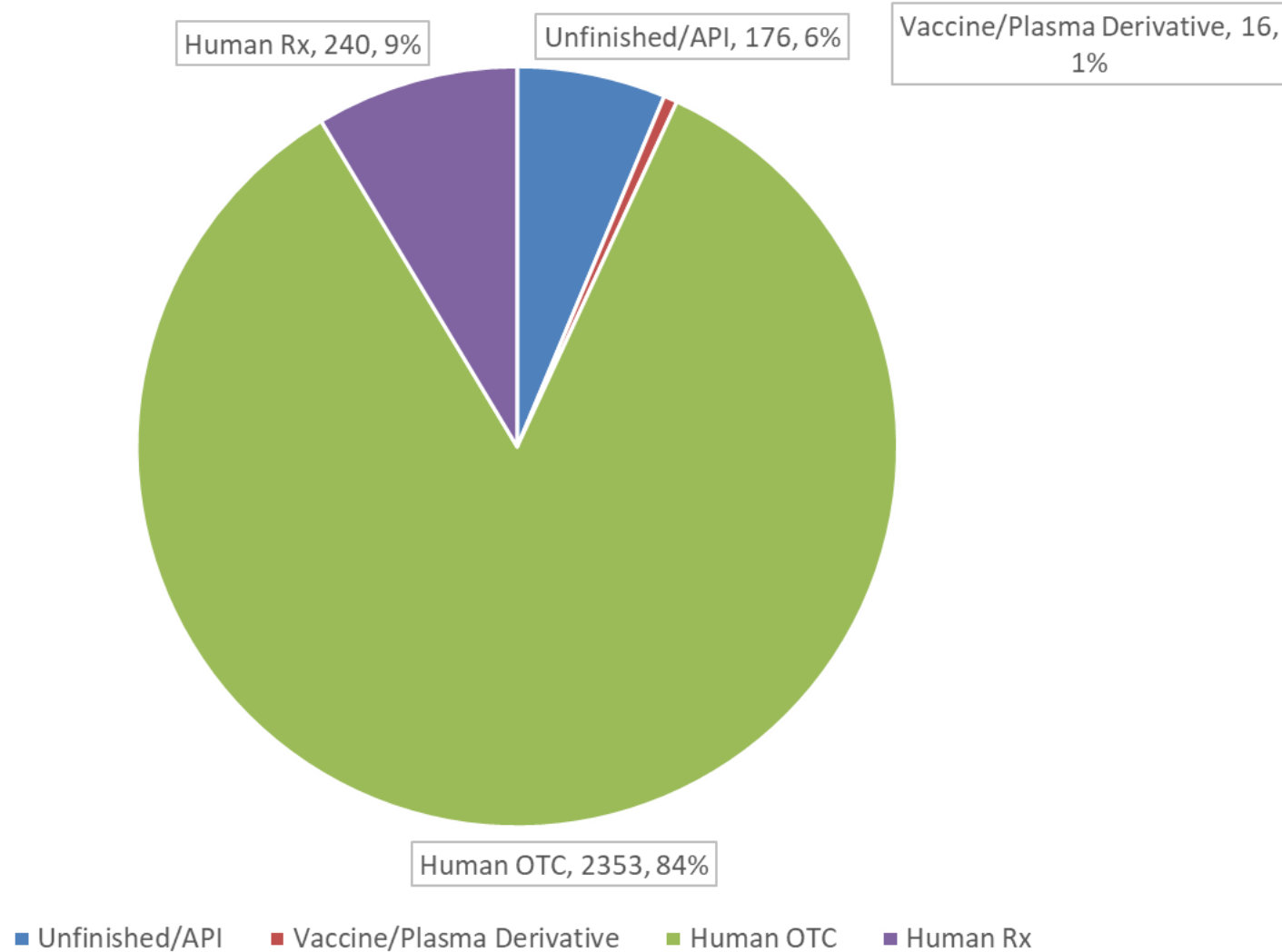
This Year – January 2021 Inactivations

Number of July inactivations Product NDCs: about 8400



This Year – July 2021 Inactivations

Number of July inactivations Product NDCs Total = 2785



Summary

- There is an **annual requirement** to review your drug listings data and make the appropriate corrections/updates or certify that the data is still accurate.
- *Each January*, FDA identifies and inactivates listings which are not updated during the previous calendar year nor certified within the Oct – Dec registration renewal period.
- *Each July*, FDA identifies and inactivates current listings which are linked to at least one unregistered establishment.
- **Prior notification is sent to the labeler code contacts** for any listing in jeopardy of being inactivated, to allow for an update.
- Any product listing that is inactivated can be immediately reactivated with a full and corrected listing submission



Finally

In short...

Please review your drug listing data frequently

FDA inactivation of the drug listing is NOT the same as delisting your product

Do not rely on Inactivation to fulfill your obligation to delist

Registrants are still required by law to delist products when they discontinue manufacturing for commercial distribution



Thank You