Import Admissibility Process

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Prescription Finished Dosages Entry Validation

- Drug Approval
  - New Drug Application
  - Abbreviated New Drug Application
  - (CDER-Regulated) Biologic License Application
- Approved Foreign Source
  - Foreign Drug Manufacturer must be approved in the application
- Foreign Drug Manufacturer Registration
  - Foreign Drug Manufacturer must list all *Known Importers* in their registration
- Drug Listing

APIs for Rx Manufacturing Entry Validation

- Finished Dosage Drug Approval
  - New Drug Application
  - Abbreviated New Drug Application
  - (CDER-Regulated) Biologic License Application
- Approved Foreign Source
  - Foreign API Drug Manufacturer must be approved in the finished dosage application
- Foreign Drug Manufacturer Registration
  - Foreign Drug Manufacturer must list all *Known Importers* in their registration
- Drug Listing

Over The Counter Finished Dosages Entry Validation

- Must conform to an OTC Monograph or have an approved OTC NDA/ANDA
- Foreign Drug Manufacturer Registration
  - Foreign Drug Manufacturer must list all *Known Importers* in their registration
- Drug Listing

APIs for OTC Manufacturing
Entry Validation

- Finished dosage must conform to an OTC Monograph or have an approved OTC NDA/ANDA
- Foreign Drug Manufacturer Registration
  - Foreign Drug Manufacturer must list all *Known Importers* in their registration
- Drug Listing

Investigational New Drugs
Entry Validation

- For Human Use
- IND Application Must be Active
- IND Drug Name Must be Verified in the Entry
- IND Sponsor Must Appear in Entry Documents
  - Importer of Record or Consignee Must be Sponsor or Domestic Agent
- Active INDs are Exempt from Registration and Listing

Non-Human R&D Drugs
Entry Validation

- In-Vitro or Laboratory Animal Use Only
- Exempt from Registration and Listing

Drug Label Requirements

Per FDCA, all drugs must bear:

- 502(b) – The name & place of manufacturer, packer, or distributor (also see 21 CFR 201.1)
- 502(b)(2) – Accurate statement of the quantity of contents 502(c) – Must be understandable, must be in English (also see 21 CFR 201.15)
- 502(e) – Established name and quantity of each active ingredient (also see 21 CFR 201.10)

Drug Label Requirements (Continued)

- 502(f)(1) – Adequate directions for use unless exempt (21 CFR 201.5)
- Finished dosage form Rx drugs are exempt if they meet all conditions in 21 CFR 201.100
- 502(f)(2) – Warnings against unsafe use
- 21 CFR 201.17 & 211.137 – Expiration dates
- 21 CFR 201.18 – Lot number

APIs for Commercial Use
Specific Labeling Requirements

- "Caution: For manufacturing, processing, or repacking" (21 CFR 201.122)

Human Use INDs
Specific Labeling Requirements

- "Caution: New Drug--Limited by Federal (or United States) law to investigational use.“ (21 CFR 312.6)

Non-Human R&D Drugs Specific Labeling Requirements

- "CAUTION: Contains a new drug for investigational use only in laboratory research animals, or for tests in vitro. Not for use in humans." (21 CFR 312.160)

Entry Review Decisions

Five Possible Decisions on Each Line

1)May Proceed (System or Manual)

2)Request Additional Documents from Broker/Filer

3)Refer to FDA District Compliance Branch for Possible Detention and Refusal

4)Physical Examination or Label Examination

5)Sample Collection

Foreign Drug Firm Registration & Drug Listing

21 CFR 207

- All foreign firms that manufacture, prepare, propagate, compound, or process a drug imported or offered for import into the U.S. shall, through electronic means …
- Register the name and place of business
- Designate a U.S. Agent
- Provide names of each known importer & person who imports or offers for import
- List all drug products imported or offered for import into the U.S.

Affirmations of Compliance for Drug Entries

- Broker/Filer Submits Electronically with Entry
- Provide Specific Additional Information
  - DLS Drug Listing Number
  - DA Drug Approval
    - New Drug Approval Number (NDA)
    - Abbreviated New Drug Approval Number (ANDA)
    - (CDER-Regulated) Biologics License Application Number (BLA)
  - REG Drug Facility Registration Number

CDER Pre-Launch Activities Importation Requests (PLAIRs)

- FDA's policy to exercise enforcement discretion on the importation of a limited amount of an unapproved finished dosage form product in preparation for the market launch based upon anticipated approval
- Drug product must be in final packaged form or require only minimal further processing such as final packaging and/or labeling
- CDER-regulated NDA, ANDA or BLA
- CDER-OC-PLAIR@fda.hhs.gov
- If CDER grants the PLAIR then CDER notifies DIO
- Entry Reviewers verify pending approval and quantities

Import for Export (IFE)

Allows Unapproved New Drugs to be Imported for Further Manufacturing and Re-exportation with

- A statement that article is intended to be further processed and that it will be exported under
  - sections 801(e) or 802 of the FD&C Act [21 U.S.C. 381 (e) or 382]
- Chain of Custody
  - Information to identify the manufacturer of the article and each processor, packer, distributor, or other entity in chain of possession from manufacturer to importer
- Certificates of Analysis
  - as necessary to identify the article

Common Errors in Drug Entries

- Incorrect Foreign Drug Manufacturer Site Address
- Listing, Approval and Registration Not Provided
- Dosage Not Provided for Finished Dosage Imports
- Incorrect IND Sponsor or None Provided
- Incorrect IND Drug Name or None Provided

Tips for Importing Drug Products

Expedite FDA's Processing by Providing:

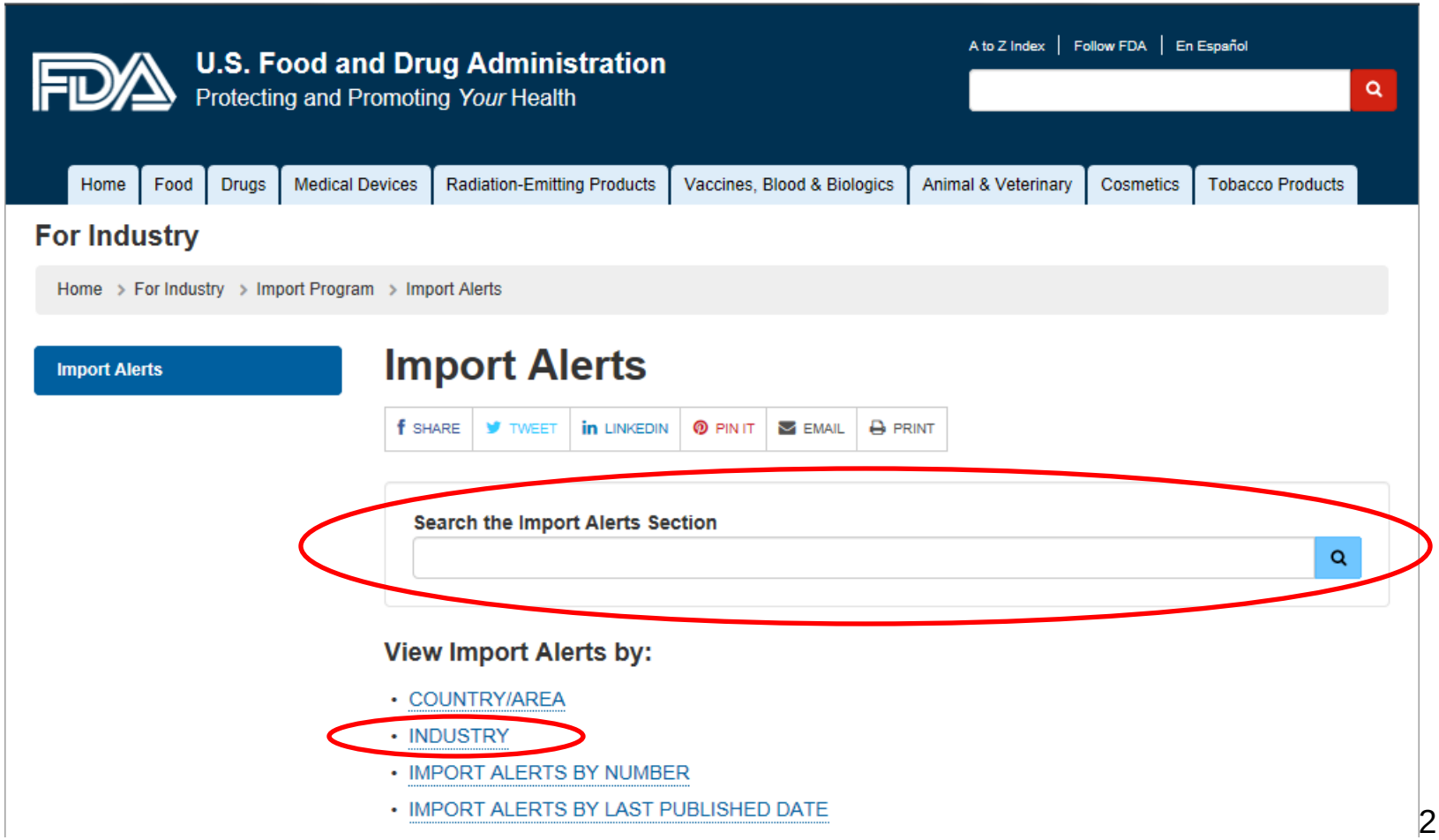
- Correct Product Code and Intended Use Code
- Active Ingredient Name and Dosage
- Brand Name
- Name, Address (and DUNS or FEI number if known) for:
  - Manufacturer, Shipper, Importer, Delivered To Party, and API Producer
- Affirmations of Compliance: (required based on Intended Use)
  - REG (Drug Registration)
  - DLS (Drug Listing)
  - DA (Drug Application Number: NDA, ANDA or BLA)
  - IND (Investigational New drug)

Import Alerts

- Information Causing Categories of Products to Appear Violative
  - All Products from a Geographic Area of Concern
  - Certain Products from Certain Geographic Areas of Concern
  - All Products from Certain Firms
  - Certain Product from Certain Firms
- DWPE
  - Detention Without Physical Examination

Accessing Import Alerts

http://www.fda.gov/ForIndustry/ImportProgram/ImportAlerts



Removal from Import Alert

- Supply Evidence to FDA that Overcomes the Appearance of a Violation
  - Resolves the Conditions
  - Prevents Future Violations
- Email Removal Petitions to ImportAlerts2@fda.hhs.gov

Executive Order -- Streamlining the Export/Import Process for America's Businesses

"…reduce supply chain barriers to commerce while continuing to protect our national security, public health…"

"…the Federal Government must increase efforts to improve the technologies, policies, and other controls governing the movement of goods across our national borders…"

"…by December 31, 2016, participating agencies shall have capabilities, agreements, and other requirements in place to utilize the ITDS and supporting systems, such as the Automated Commercial Environment…"

https://www.whitehouse.gov/the-press-office/2014/02/19

What is ACE/ITDS?

- The Automated Commercial Environment / International Trade Data System is a single access point in which industry can electronically submit information for all government agencies involved in international trade.

Core Components

Interoperability Web Services

Interoperability Web Services (IWS) is a modern interface for Partnering Government Agencies to share information , documents, and events.

PGA Message Set

The Partner Government Agency (PGA) Message Set is a single, harmonized data set collected electronically from trade partners by CBP, on behalf of the 47 PGAs. This single data set replaces the process of trade submitting the same data set to multiple agencies.

Document Image System

The Document Image System (DIS) is a functionality that will allow trade to electronically upload documentation required for cargo release processing in image format to ACE's secure data portal.

*FDA will continue to use ITACS at this time

ACE/ITDS

- The new interface will:
  - improve communication, allow FDA and other agencies to obtain data (and respond) quickly,
  - process cargo more expeditiously
  - enhance risk management and targeting procedures.
- ACE/ITDS will mutually benefit FDA and the trade community through improved processes for submitting import data that reduce:
  - costs
  - the need for paper forms,
  - and turnaround times.

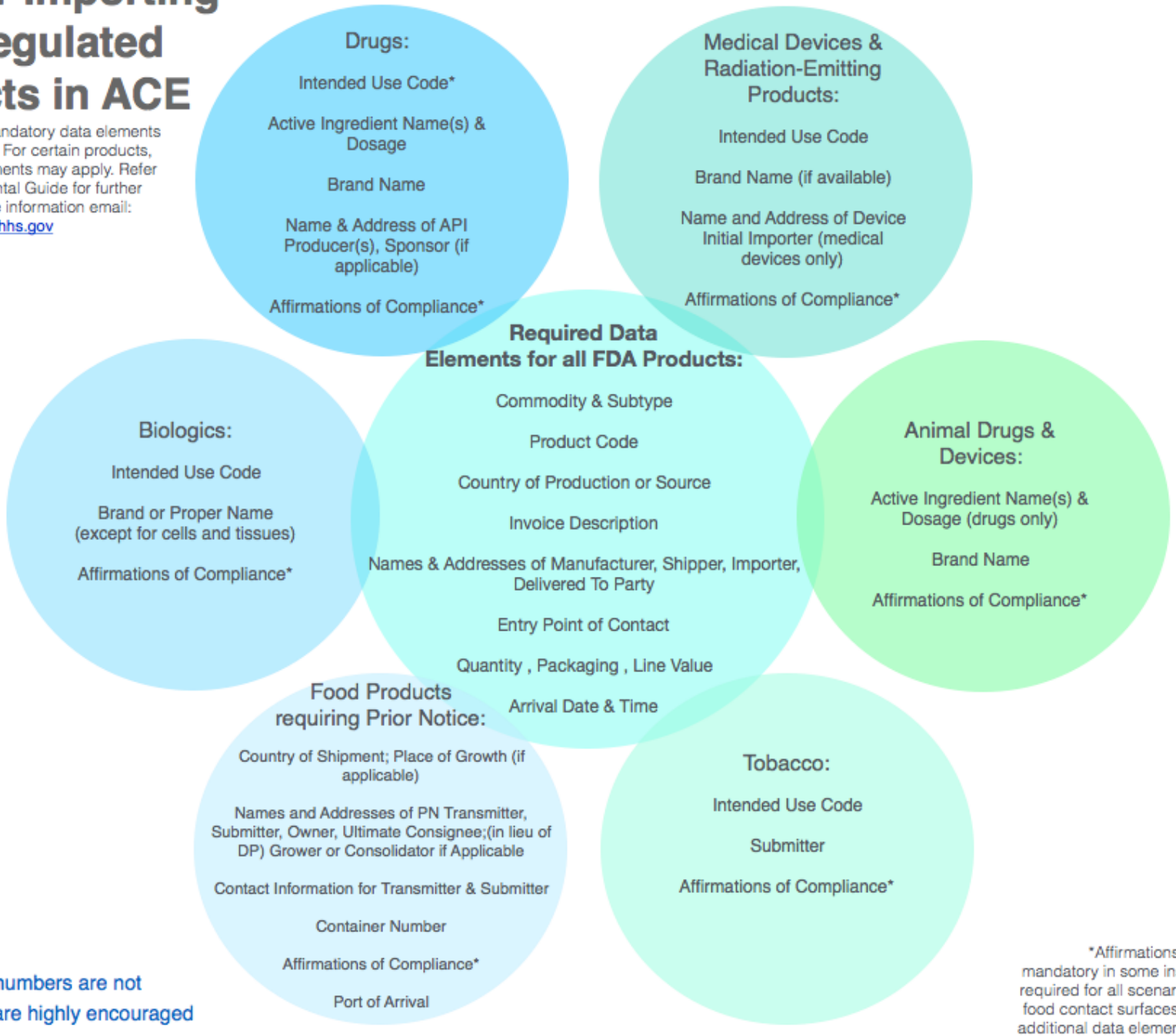
How Does ACE Change Current Business Processes?

- All entry information for all partner government agencies (PGAs) is submitted in ACE; messages from each agency are sent back to the filer
- FDA will require complete data sets at the time of transmission of the entry
- Complete and correct information will reduce the need for document requests, and improve processing times

Tips for Importing FDA-Regulated Products in ACE

FDA Division of Compliance Systems 2016

Diagram depicts mandatory data elements by commodity-type. For certain products, additional data elements may apply. Refer to FDA's Supplemental Guide for further specificity For more information email: ACE_Support@fda.hhs.gov



**DUNS or FEI numbers are not mandatory but are highly encouraged and may expedite processing.

*Affirmations of Compliance are mandatory in some instances but are not required for all scenarios. Cosmetics and food contact surfaces do not require any additional data elements other than those listed in the center of the diagram.

How CBP Licensed Brokers and Filers can Start Filing in ACE

- Get to know FDA's Requirements for importing in ACE (FDA Supplemental Guide) http://www.cbp.gov/document/guidance/fda-supplemental-guide-release-16
- Contact your software developer & work with him/her to understand changes to your software
- Keep your CBP ABI Client Representative informed
- To start filing in ACE for FDA, contact: ACE_Support@fda.hhs.gov
- Deadline for Full Implementation is December 2016

ACE References

- FDA Supplemental Guide: http://www.cbp.gov/document/guidance/fda-supplemental-guide-release-16
  (Full list of data elements required for admissibility)
- FDA DUNS Portal: www.fdadunslookup.com
  (Query or request DUNS numbers for free)