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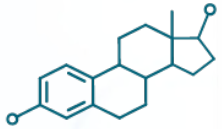

Welcome to the 3rd Annual Puerto Rico Pharmaceutical Summit 2024!

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Pharmaceutical Summit 2024

State of the Pharmaceutical Industry in Puerto Rico

PANELISTS:
Francisco E. Colón-Ramírez, Of Counsel, Porzio, Bromberg & Newman, P.C.
Humberto Mercader, Deputy Secretary for Strategic Initiatives, Department of Economic Development and Commerce
Iván Román, Advisor to the Board of Directors, Pharmaceutical Industry Association (PIA)
Eric Santiago, President, PR Manufacturers Association (PRMA)

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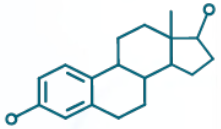


Imports and Exports: The U.S. Food and Drug Administration's Perspective

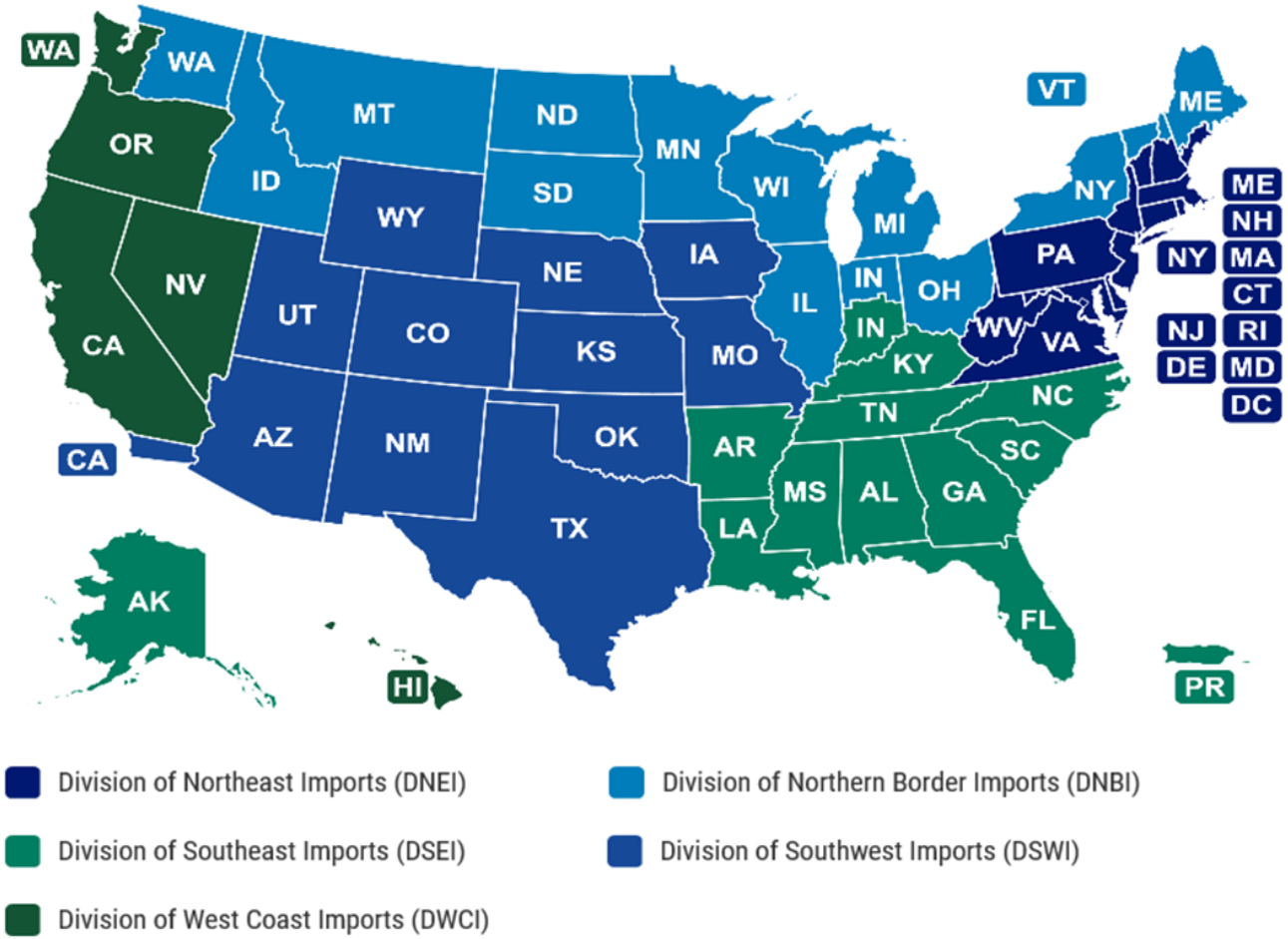
Zuleika Pineiro, Compliance Officer, Office of Import Operations, Division of Southeast Imports
Ivonne Vincente, Supervisory Consumer Safety Officer, Office of Import Operations, Division of Southeast Imports

U.S. FOOD & DRUG ADMINISTRATION

IMPORTATION OF DRUG PRODUCTS INTO US AND ITS TERRITORIES

Ivonne Vicente, Supervisory CSO
Zuleika Piñeiro, Compliance Officer
Division of Southeast Import (DSEI)
February 2024

Import Program Divisions



https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/import-offices-and-ports-entry

Regulatory Authority
Section 801

- **Section 801**: Covers FDA Imports
- **Section 801(a)**: Allows for refusal of imported FDA-regulated products for <u>appearing</u> to be adulterated, misbranded, or unapproved new drugs

"If it <u>appears</u> from the examination of such samples or otherwise that…"

1) such article has been manufactured, processed, or packed under insanitary conditions… or
2) such article is forbidden or restricted in sale in the country in which it was produced … or
3) such article is adulterated, misbranded, or in violation of section 505 (Unapproved New Drugs)

"then such article shall be refused admission…"

Regulatory Authority
CBP and FDA

- FD&C Act in 801(a)

  “The Secretary of the Treasury shall deliver to the Secretary of Health and Human Services, upon his request, samples of food, drugs, devices, and cosmetics which are being imported or offered for import into the United States, giving notice thereof to the owner or consignee, who may appear before the Secretary of Health and Human Services and have the right to introduce testimony……”

Regulatory Authority
CBP

- Customs and Border Protection (CBP) has initial authority over all imported products
  - 19 United States Code
  - Title 19 Code of Federal Regulations
  - Harmonized Tariff Schedule of the United States (HTSUS)

- All products regulated by the FDA must meet the same requirements, whether imported or produced domestically.

https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/import-basics

Import Basics

Products offered for entry into the United States must be declared to U.S. Customs and Border Protection (CBP). CBP refers all FDA-regulated products to the FDA for review.

FDA screens **all** imported shipments of FDA-regulated products.

The importers hire a licensed customs broker or entry filer to assist with importer by submitting necessary entry information and appropriate payments to CBP on behalf of the importer. CBP's website has a map with specific ports, and under each port, you will find a list of brokers.

http://uscode.house.gov/view.xhtml?path=/prelim@title21/chapter9/subchapter8&edition=prelim

Import Basics

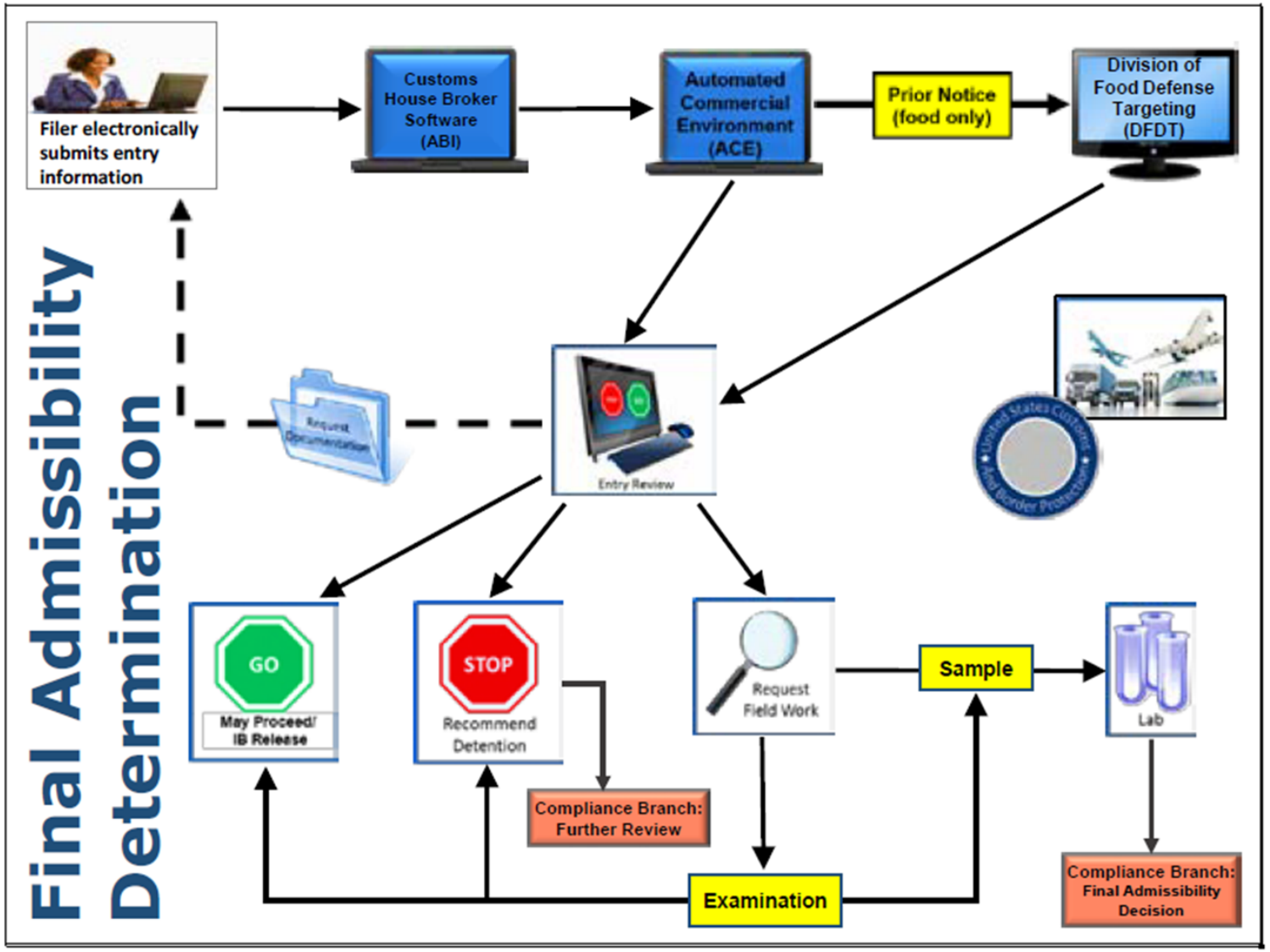
Imported shipments of FDA-regulated products are reviewed by the FDA and must comply with the same standards as domestic products. The FDA determines whether products are admissible into U.S. commerce and may refuse entry to any that violate or appear to violate any provisions of Section 801 (21 USC 381) of the Federal Food, Drug & Cosmetic Act.

During the entry review process, the imported products must be held and may not be distributed into U.S. commerce until the FDA has determined their admissibility.

FDA Regulated Products

- Human foods (exceptions: most meat and poultry)
- Animal food/feed
- Cosmetics
- Drugs (both human and animal)
- Biologics (including human cells and tissues)
- Medical devices
- Electronic products that emit radiation
- Tobacco products (including e-cigarettes)

Imports process to determine final admissibility of a product



Drug definition

The FDA defines a drug, in part, as “intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” and “articles (other than food) intended to affect the structure or any function of the body of man or other animals.” Refer to section 21 CFR 201(g) of FD&C Act.

- New Drug Definition –Section 21 CFR 201(p)
- Prescription Drug Products (RX) Definition –Section 21 CFR 503(b)(1)
- Over the Counter (OTC) Drug Product Definition –Section 21 CFR 330.1
- Investigational New Drug Definition —Section 21 CFR 312.3
- Active Pharmaceutical Ingredient (API), also known as Bulk Drug Substance Definition –Section 21 CFR 207.1

Drug definition

Imported drugs must meet FDA's standards for quality, safety and effectiveness. FDA will verify compliance with the following requirements as applicable:

- Foreign establishment Registration
- Drug Listing
- Drug application
- Drug labeling
- Drug current good manufacturing practices (cGMPs)

Drug definition

FDA entry reviewers are trained to verify compliance with applicable product requirements. The FDA entry reviewers use the information provided to FDA in the importer's entry transmission, such as:

- Declared Manufacturer
- Declared Importer/Consignee
- Product Description
- Affirmations of Compliance
- Intended use

Registration and Listing requirements

Foreign drug establishments that manufacture, repack, re-label or salvage drug products and whose drugs are imported or offered for import into the United States are required to register with the FDA before offering a drug for import and renew annually.

These regulations also require foreign drug establishments to identify a U.S. Agent and include all known importers in their drug registration.

Registrants are also required to list with FDA each drug manufactured at their establishment(s) intended for commercial distribution and submit updated drug listing information to FDA twice each year, in June and December, notifying FDA if this information has changed.

https://www.fda.gov/industry/importing-fda-regulated-products/importing-human-drugs#registration

Types of Drug Applications

Drugs may require an approved marketing application before being imported into the U.S.

Types of drug applications include:

- New Drug Application (NDA),
- Abbreviated New Drug Application (ANDA),
- Investigational New Drug Application (IND), and
- Biologic License Application (BLA).

If the product requires a NDA, ANDA, BLA or IND and does not have one, it will be subject to refusal.

Drug Labeling

- All drug products offered for importation into the United States are subject to labeling requirements.

- The FDA may review drug labeling at the time the product is offered for import to verify compliance with the regulations.

- Specific drug labeling requirements depend on the type of drug product.

Affirmations of Compliance (A of C) codes for human drugs

FDA-regulated products are expected to be in compliance at the time of entry. **To help expedite FDA's review of product compliance**, the entry filer can submit additional information at the time of entry, such as *registration, listing, and approval numbers.* This information can be submitted by using Affirmation of Compliance codes (A of C codes).

By using an A of C code, the entry filer affirms that the firm and/or product identified in an FDA line meets the requirements specific to each code. Depending on the product you are importing, submission of certain A of C codes might be mandatory, and others are voluntary A of C.

A of C are three letter codes that are provided at the time of import to facilitate FDA review.

Some of the
A of C codes used for drug products include:

Code	Affirmation of Compliance
DA	New Drug Application No. or Abbreviated new Drug Application No. or Therapeutic Biologic Application No.
DLS	Drug Listing Number
REG	Drug Registration Number
IND	Investigational New Drug Application Number

U.S. FOOD & DRUG ADMINISTRATION

Foreign Trade Zones

Foreign Trade Zones (FTZ)

- Authority for establishing these facilities is granted by the Foreign-Trade Zones Board under the Foreign-Trade Zones Act of 1934, as amended.

- Secure areas under CBP supervision that are generally considered outside CBP territory upon activation located in or adjacent to CBP ports of entry.

- FDA will make an admissibility decision when products are withdrawn from the FTZ for consumption.

- FDA still has jurisdiction for products in FTZs under the domestic provisions for the Act.

https://www.fda.gov/industry/import-basics/foreign-trade-zonesweekly-entry-filing

Foreign Trade Zones (FTZ) Program

- Encourages companies to maintain and expand their operations in the United States.
- Encourages U.S.-based operations by removing certain disincentives associated with manufacturing in the United States.
- Treats products made in the zone, for the purpose of tariff assessment, as if it were manufactured abroad.

Foreign Trade Zones (FTZ) and FDA

- FDA has jurisdiction over FDA-regulated products in an FTZ and has inspectional authority over FDA-regulated processes conducted in an FTZ.
- Products admitted to an FTZ are subject to FDA admissibility review when the articles are withdrawn from the FTZ for domestic consumption.

Foreign Trade Zones (FTZ) and FDA
Entry Admissibility

- Articles which may otherwise be inadmissible can be brought into an FTZ
- FDA does have jurisdiction:
  - FDA can take action if there are issues
  - Other sections of law have to be used
  - Using 801(a) to refuse is not an option

What is Weekly Entry Filing (WEF)?

CBP has implemented a weekly entry filing (WEF) program allowing customs brokers (entry filers) to submit a weekly estimate for repetitive, high-volume entries of low-risk products. Under this program, a customs broker (entry filer) can submit a single entry estimating the amount of product that will be withdrawn from the FTZ and offered for consumption into the U.S. during the subsequent week.

- Human Drugs-CDER has determined that human drug products are not amenable for WEF processing.
- Animal Drugs-CDER has determined that human drug products are not amenable for WEF processing.

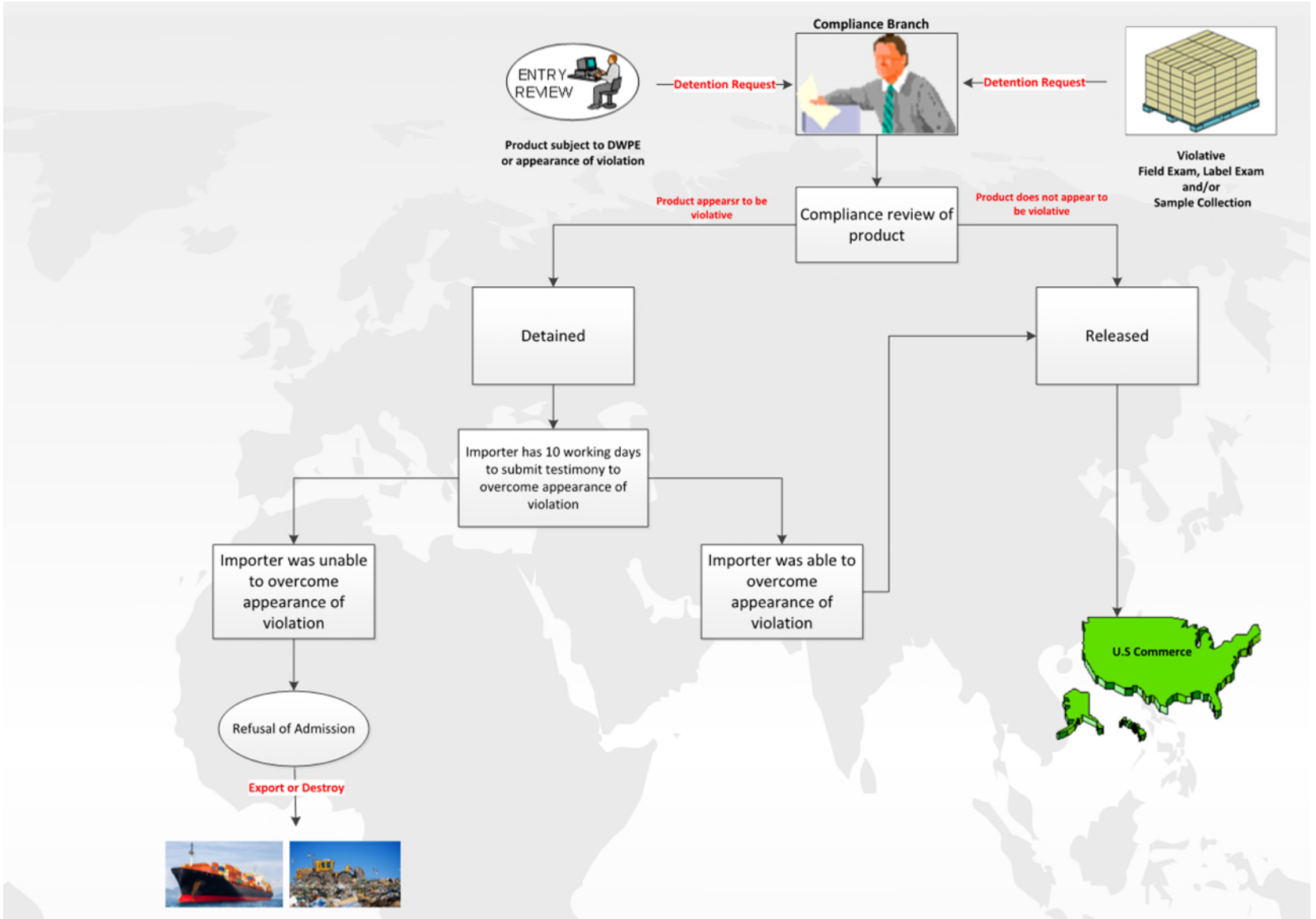
FDA Import Law
Entry Admissibility (FTZ)

- FDA does make an 801(a) admissibility determination on goods withdrawn from the FTZ for US consumption
  - Product must be compliant with laws & regulations
- If products in an FTZ are withdrawn for domestic consumption, an entry must be filed with CBP and the import process begins.
- FDA's policy regarding FTZs can be found in the Compliance Policy Guides CPG 110.200 and 110.600.

FDA Imports Overview

ACTIONS & ENFORCEMENT

Compliance Overview



FDA-regulated products are refused entry if they appear to be or have been found to be:

- **Adulterated:** product is contaminated, is not safe, unapproved, or does not meet applicable standards.

- **Misbranded:** labels contain false or misleading information, or the product is not registered and listed.

- forbidden or restricted for sale.

Products that do not comply with U.S. requirements may be refused admission. Refused products must be destroyed or exported from the United States within 90 days.

Actions & Enforcement

Import Actions

- Import Alerts (DWPE)
- Requesting Bond Actions
- Screening Criteria
- For-cause Filer Evaluation

https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/actions-enforcement

Actions & Enforcement

Judicial Actions

- Seizure
- Injunction
- Inspection Warrants/Search Warrants
- Criminal Prosecution
- Debarment

Actions & Enforcement

Administrative Actions

- Regulatory Meetings
- Recalls
- Administrative Detention
- Civil Money Penalties
- Inspectional Follow-up

Actions & Enforcement

Advisory Actions

- Untitled Letter
- Warning Letter

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities

Admissibility, Detention, and Hearing Process

- For products where the FDA does not find any apparent violations, the Notice of FDA Action will indicate the release of those products.

- If a review of the entry, a physical examination or analytical results indicate that the product **is** or **appears** to be in violation, a Notice of FDA Action will be issued with the detention information.

https://www.fda.gov/industry/actions-enforcement/detention-hearing

Admissibility, Detention, and Hearing Process

- Through the detention and hearing process the Importer/Owner/Consignee has the right to:
  - Submit evidence (also called testimony)
  - Submit a request to recondition the product to correct the violation

- After review of the evidence/reconditioning, the detention will either stand (refusal) or be overturned (release)

Options for Detention and Hearing Process

- Contest the charges
  - Submit testimony/evidence to overcome the appearance of violation
  - Submit private laboratory analysis

- Request authorization to recondition or relabel (FDA 766).
  - FDA supervision and charges may apply

- Request refusal
  - Export or destroy

https://www.fda.gov/industry/actions-enforcement/reconditioning

Import Refusals

- If the appearance of a violation is not overcome, or if the product cannot be brought into compliance, FDA will refuse admission of the product.
- CBP issues redelivery notice upon refusal.
- FDA and CBP verify refusal activities.
- The importer incurs liquidated damages (3x declared value) if products are not exported or destroyed.

The 'life' of an FDA entry ends with FDA Release or FDA Refusal

https://www.fda.gov/industry/actions-enforcement/import-refusals

Import Refusals

Section § 801 of Food, Drug, and Cosmetic Act (FFD&C Act) outlines FDA refusal authority for the following violative articles:

- § 801(a)(1) – articles manufactured, processed, or packed outside of cGMP's.

- § 801(a)(2) – articles forbidden or restricted for sale in a country where they are produced, or from which exported.

- § 801(a)(3) – articles which are adulterated, misbranded, or are unapproved new drugs.

Use of CBP Enforcement Actions

- CBP seizure
- Cargo restrictions
- Suspension or revocation of Custom Broker's license

Contact FDA

- **General Import Questions**
  - Find FDA contact information for general import questions on FDA's Import Contacts and Office Locations webpage at https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/fda-import-contacts-and-office-locations

- **Import Entry Questions**
  - Find your local FDA office or port for questions regarding specific import entries on FDA's Import Offices and Ports of Entry webpage at https://www.fda.gov/industry/import-program-food-and-drug-administration-fda/import-offices-and-ports-entry


FDA
U.S. FOOD & DRUG
ADMINISTRATION

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Coming and Going: Exporting FDA Regulated Products from Puerto Rico

PANELISTS:
Dara Katcher Levy, Director, Hyman, Phelps & McNamara, P.C.
Karla L. Palmer, Director, Hyman, Phelps & McNamara, P.C.

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Pharmaceutical Summit 2024

A View from Washington: A Regulatory and Legislative Outlook

PANELISTS:
- **Nolan Ahern,** Deputy Policy Director for House Republican Whip Tom Emmer
- **Elizabeth Fowler, J.D., Ph.D.,** Director of the Center for Medicare and Medicaid Innovation, U.S. Department of Health and Human Services
- **Nick Uehlecke,** Principal, Todd Strategy Group

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Pharmaceutical Summit 2024

Navigating Global Turbulence: Drop Your Anchor in Puerto Rico

PANELISTS:

- **Carlos Fontan,** Director, Office of Incentives for Businesses in Puerto Rico, Department of Economic Development and Commerce
- **Aurelio Fuentes,** Co-Founder & Partner, DECA Analytics
- **Isabel Hernández, CPA**, Partner, Kevane Grant Thornton, LLP
- **Robert M. Schechter,** Principal, Porzio, Bromberg & Newman, P.C.
- **Colton Wandke, CAIA,** Co-Founder & Partner, DECA Analytics

Global Growth Headwinds and Risks

World Bank, *Global Economic Prospects,* January 2024

"The forecasts in *Global Economic Prospects* imply that most economies - advanced as well as developing- are set to grow more slowly in 2024 and 2025 than they did in the decade before COVID-19. Global growth is expected to slow for a third year in a row – to 2.4 percent – before ticking up to 2.7 percent in 2025".

- INFLATION
- SUPPLY CHAIN DISRUPTIONS
- MIDDLE EAST CONFLICT
- RUSSIA-UKRAINE CONFLICT
- RESTRICTIVE CREDIT CONDITIONS
- ANEMIC GLOBAL TRADE AND INVESTMENT
- ELEVATED INTEREST RATES
- WEAKER THAN EXPECTED GROWTH IN CHINA
- CLIMATE CHANGE
- ENERGY PRICE VOLATILITY

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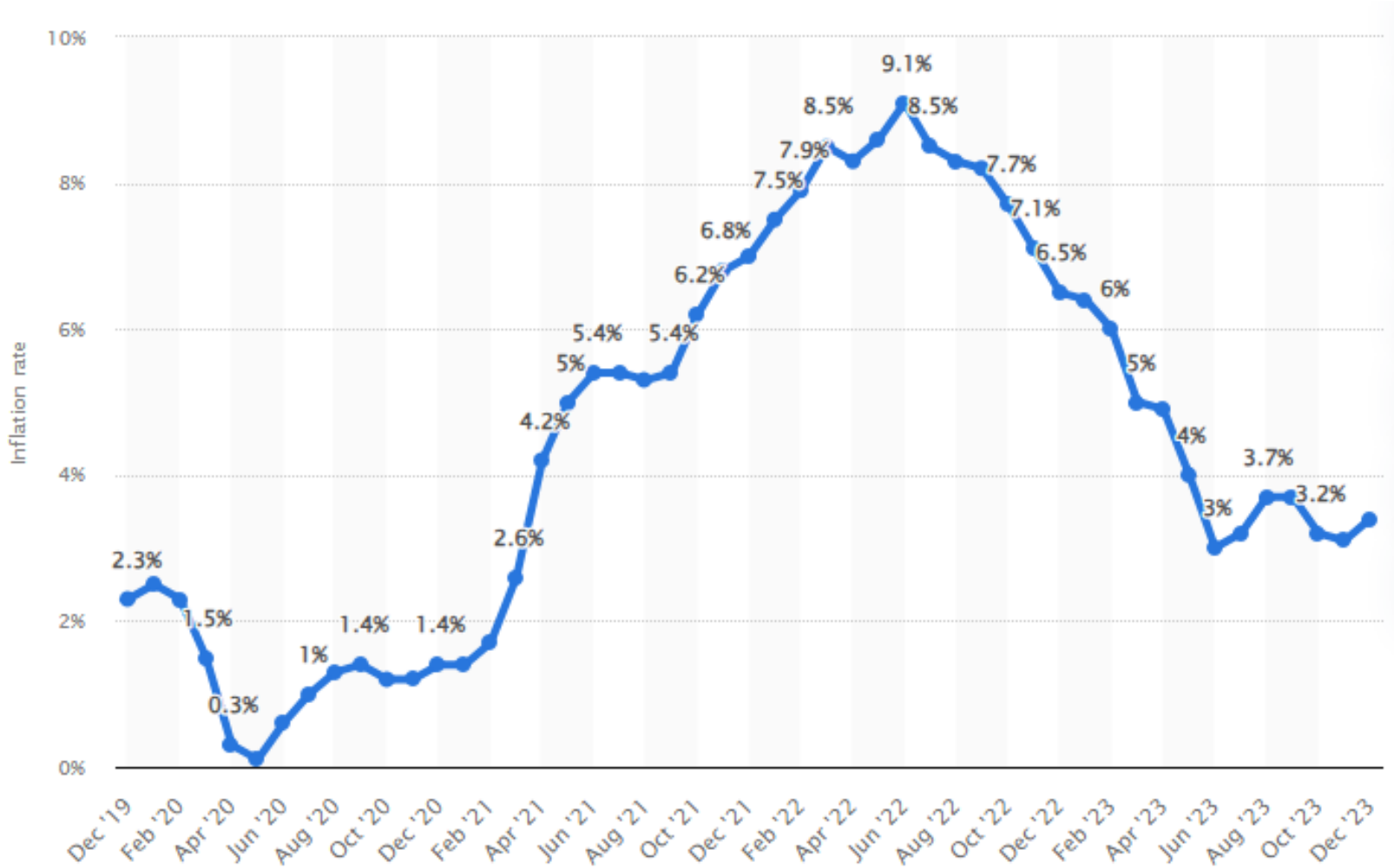
Global Challenges

Source: Monthly 12-month inflation rate from December 2019 to December 2023, Published by Statista Research Department, Jan 15, 2024



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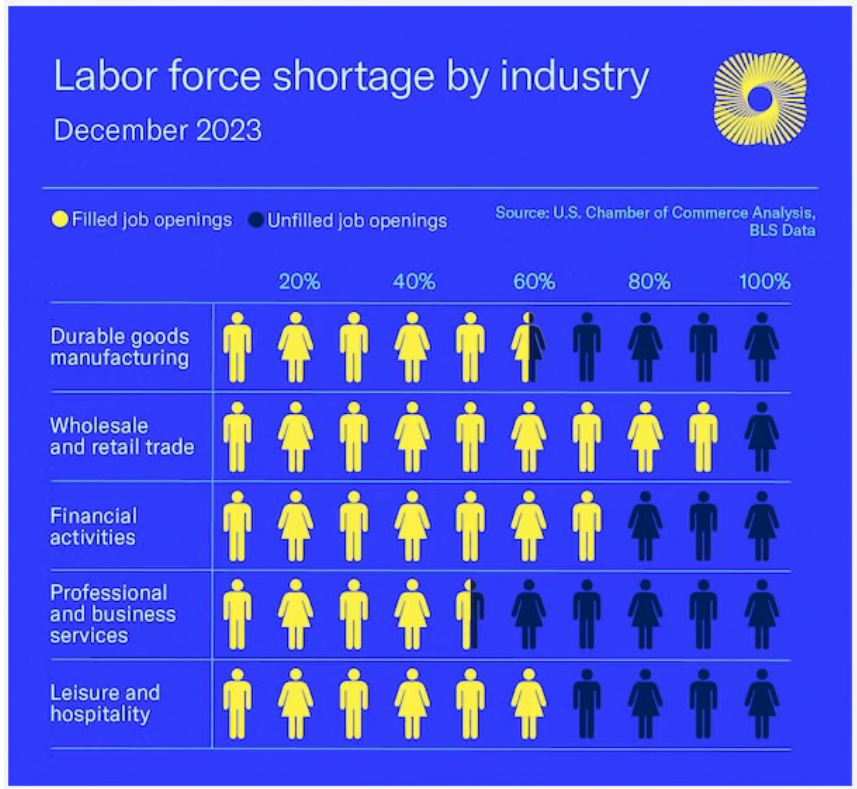
A Closer Look at Labor



"If the labor force participation rate were at the February 2020 level, we would have an additional 2.2 million people in the workforce— and this shortage is impacting all industries in nearly every state. Even if every unemployed worker were to fill an open job within their respective industry, there would still be millions of unfilled job positions, highlighting the widespread labor shortage."

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U.S. Chamber of Commerce, *Understanding America's Labor Shortage: The Most Impacted Industries,* January 9, 2024

Population
Millions of people

3.15

GDP, current prices
Billions of U.S. dollars

119.04

General government gross debt
Percent of GDP

17.1

High % of Stem Degree Graduates

International Monetary Fund, World Economic Outlook (October 2023), Puerto Rico; invest Puerto Rico, Talent in Puerto Rico

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Carlos Fontan

Director
Office of Incentives for Businesses in Puerto Rico, Department of Economic Development and Commerce

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