

# **FDA Importation of Biologicals**

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# Presentation Summary

- Overview of FDA Organization
- Importing FDA Regulated Biologics



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Biological Drug and Device Compliance Branch

Division of Case Management

Office of Compliance and Biologics Quality  
Center for Biologics Evaluation and Research

# FDA Organization

## **Office of Commissioner**

### **“The Field” (District Offices & Divisions)**

- Office of Regulatory Affairs (**ORA**)

### **Specialized Program “Centers” (HQ)**

- Center for Food Safety and Applied Nutrition (**CFSAN**)
- Center for Drug Evaluation and Research (**CDER**)
- Center for Biologics Evaluation and Research (**CBER**)
- Center for Devices and Radiological Health (**CDRH**)
- Center for Veterinary Medicine (**CVM**)
- Center for Tobacco Products (**CTP**)

# FDA Organization

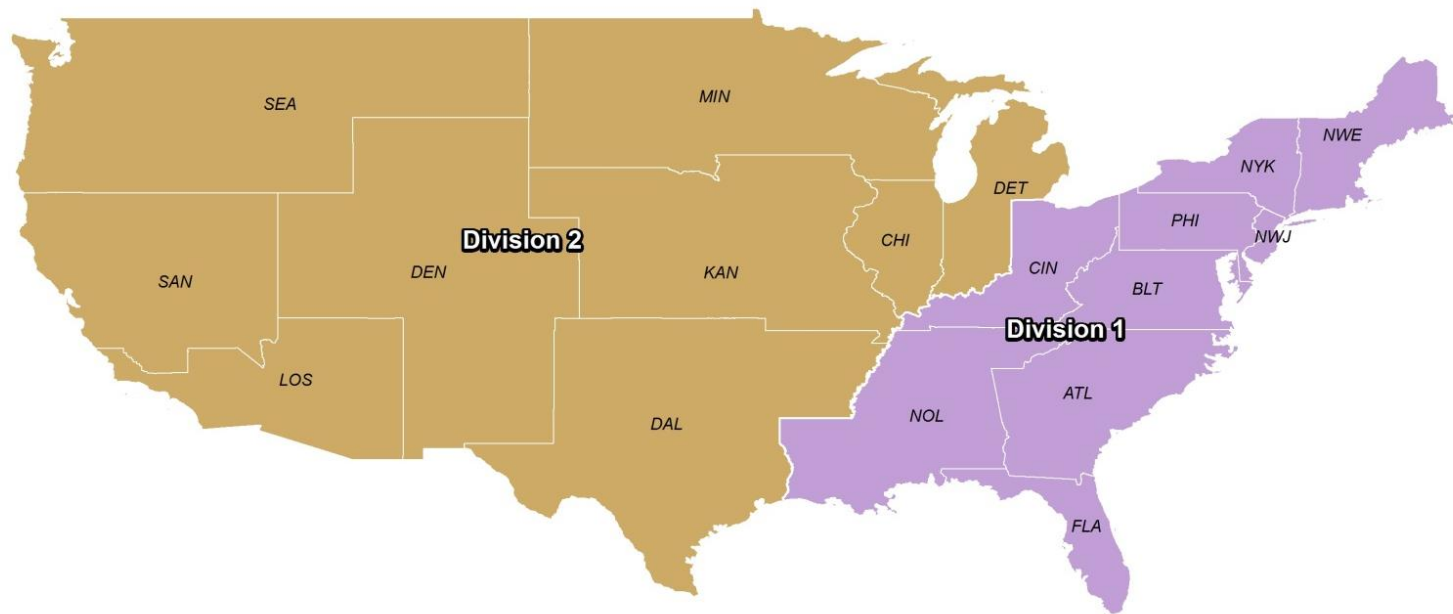
## Role of Specialized Program Centers (CBER, CDER, etc.)

- Approve/clear new drugs, medical devices, and biologics.
- Set policies, regulations and guidance documents.
- Work with ORA to construct inspectional plans
- Collaborate with Program Divisions on Regulatory Actions.
- Provide Subject Matter Experts (SME).
- Provide Policy and Guidance to ORA Field Import Staff.

## Role of ORA Program Divisions (“the field”)

- Implement Policy and Perform Work Directed by Center
- Import examinations, entry review, and sample collections
- Conduct inspections – Domestic and Foreign.
- **Office of Enforcement Import Operations (OEIO).** Agency focal point for Headquarters/Field relationships on all import programs operations.

# Office of Biological Products Operations

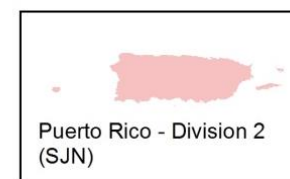
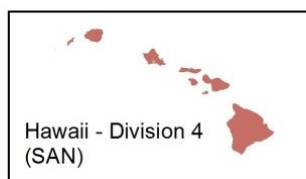
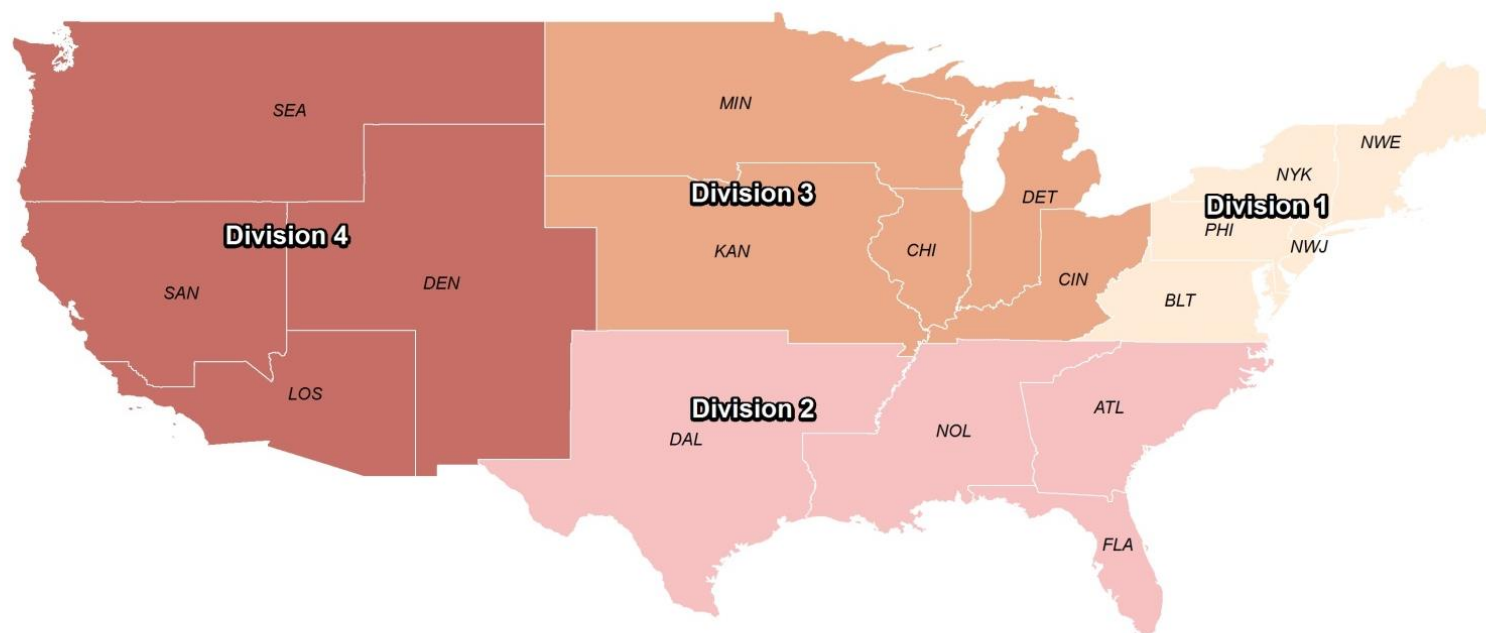


## Biologics Program Divisions

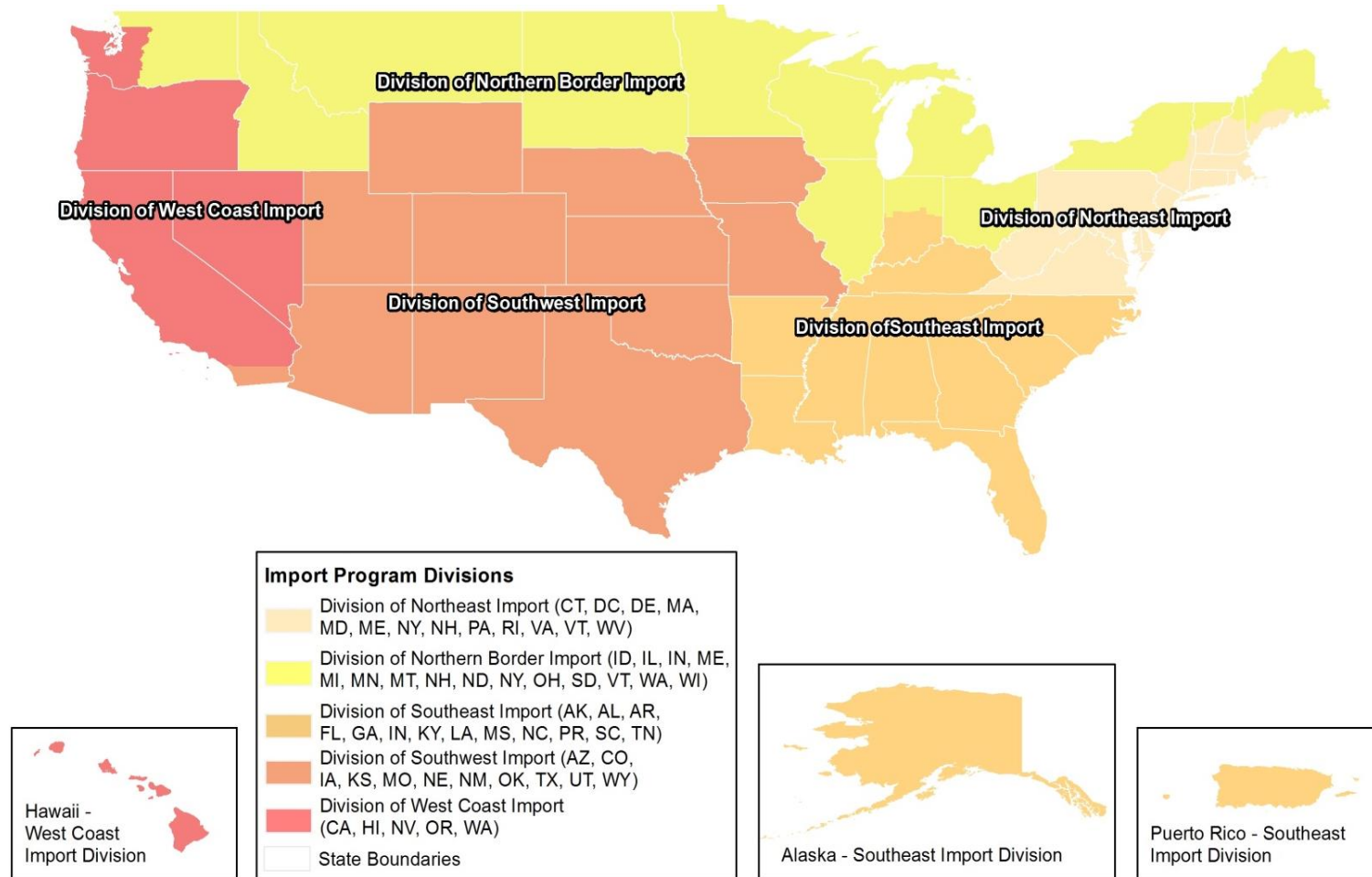
- Division 1 (ATL, BLT, CIN, FLA, NOL, NWE, NWJ, NYK, PHI, SJN)
- Division 2 (DAL, DEN, DET, KAN, CHI, LOS, MIN, SAN, SEA)
- FDA Current District Boundaries



# Office of Pharmaceutical Quality Operations

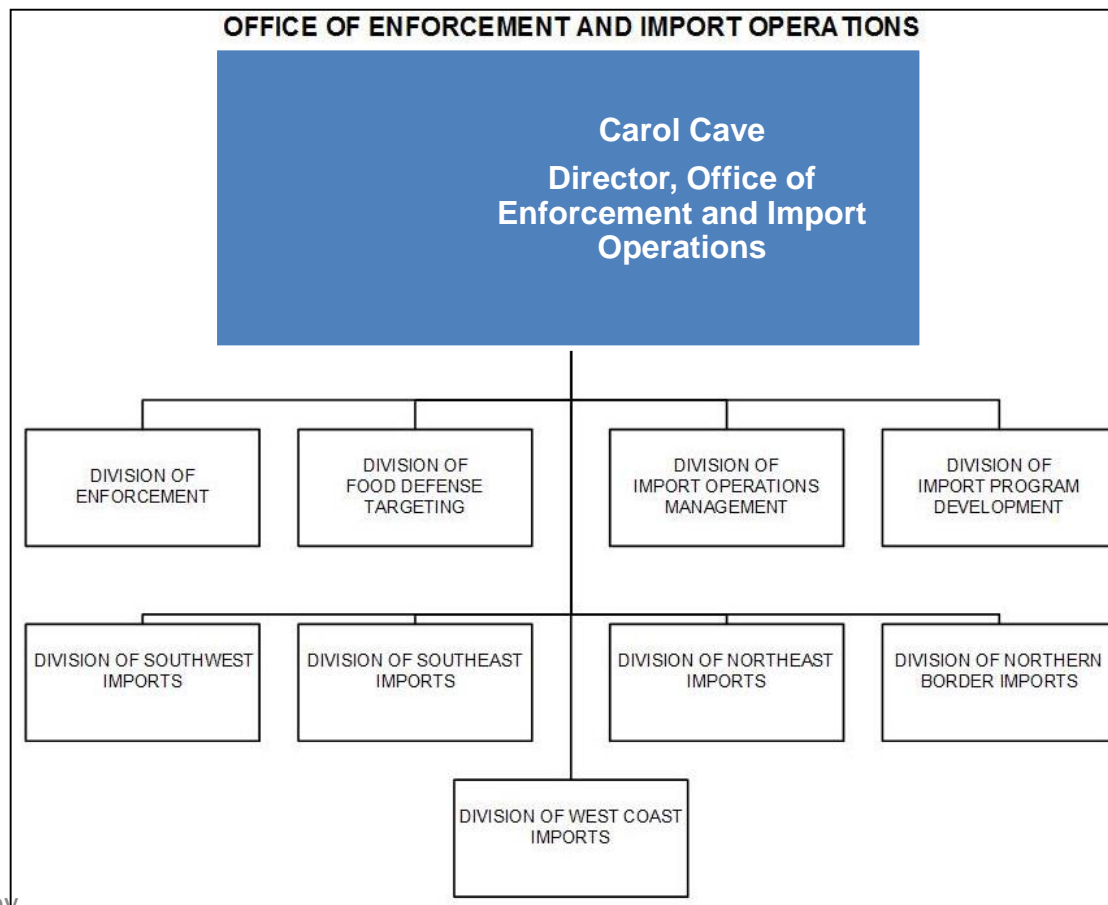


# Office of Enforcement and Import Operations





# Office of Enforcement and Import Operations



# FDA Division of Northern Border Imports Organization

## DNBI- DIVISION OF NORTHERN BORDER IMPORTS

- Keith J. Jasukaitis NB Program Division Director
- Sandra Sylvester & Eric Joneson, Investigations Branch Directors (East and West). *Detroit is in the west.* 11 Supervisory Investigative groups across NB
- Sherea Dillon – Import Compliance Branch Director (*Chicago*)
- Phenicia Petty, Supervisor - Ambassador Bridge (Detroit, MI)
- Melissa Tyrrell, Supervisor – Blue Water Bridge (Port Huron, MI)

## IMPORT STAFF

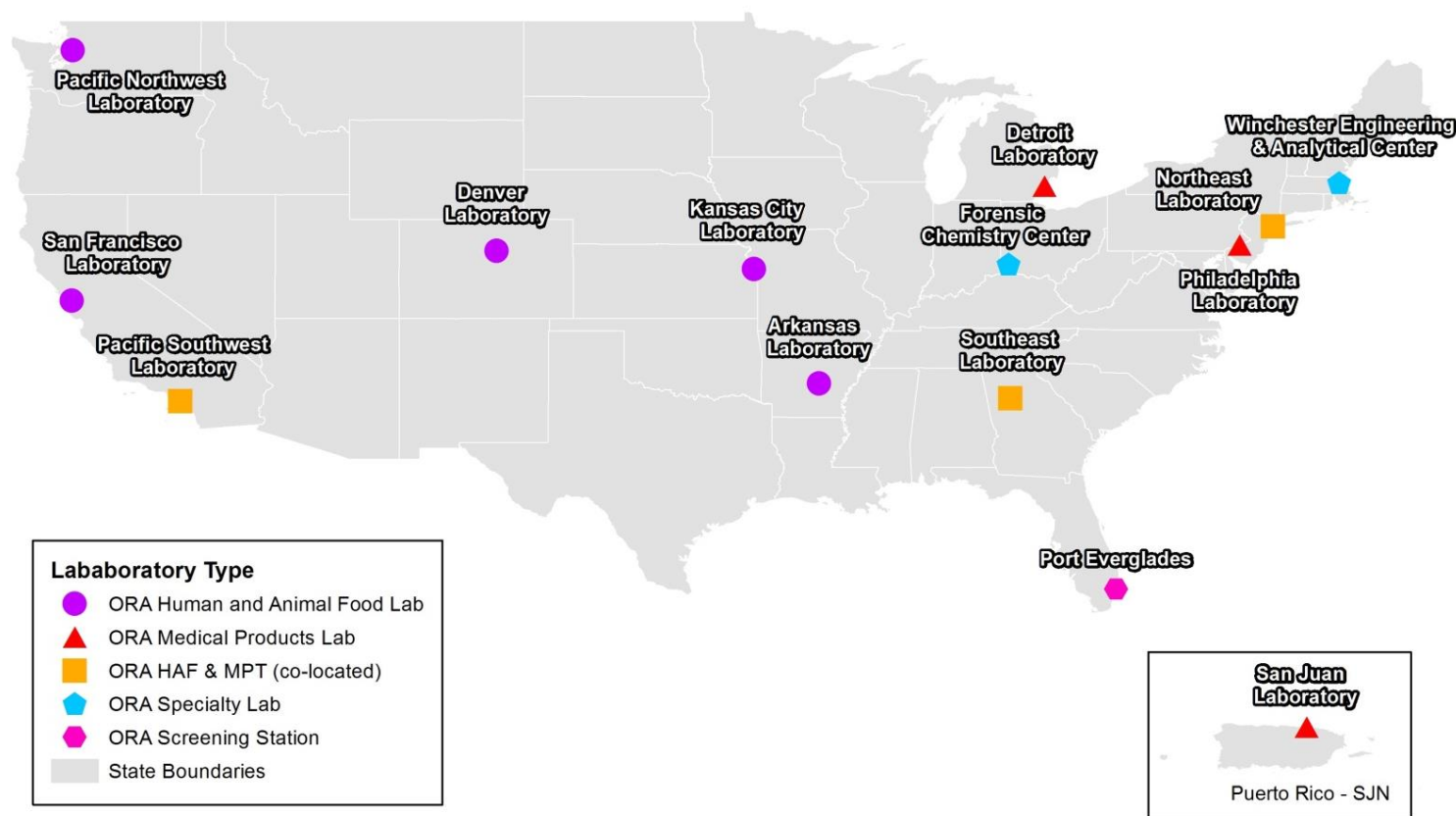
- ~100 Consumer Safety Officers, Inspectors, Technicians
- ~13 Import Compliance Officers

## OEIO- DIVISION OF IMPORT OPERATIONS

(IMPORT OPERATIONS & MAINTENANCE BRANCH)

- Jeff Hilgendorf – Division Import Area Liaison (DIAL) - Detroit Office

# Office of Regulatory Science



# Center for Biologics Evaluation and Research (CBER)

Regulates biological and related products, including blood and blood products, vaccines, allergenics, tissues, cellular and gene therapies, and some devices. For example:

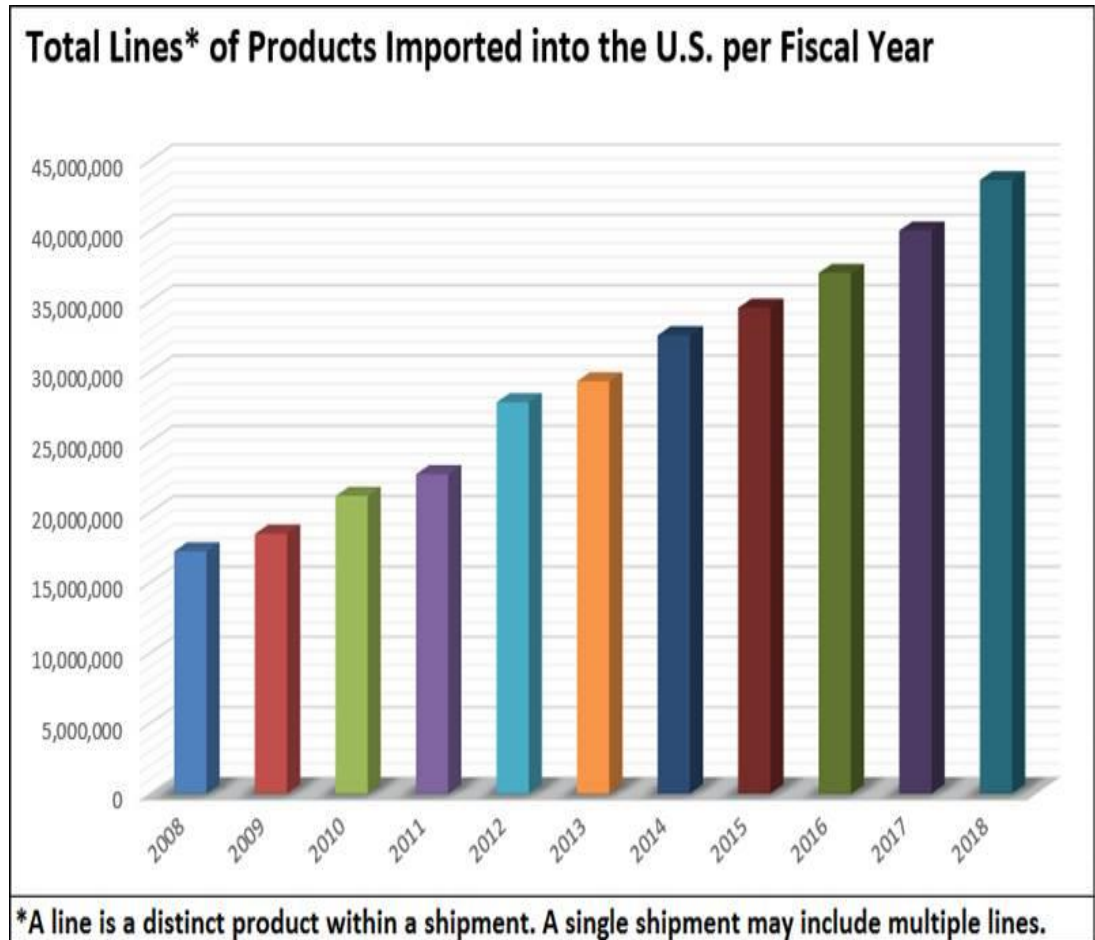
- Antitoxins and Antivenins
- Vaccines
- Blood and Blood Components
- Blood-Derived Products
- Blood bags with anti-coagulant
- Certain devices involved in the collection,, testing, manufacture processing, and administration of licensed blood components, and cellular products, etc.
- All HIV test kits
- Allergenic Products
- Cellular products licensed under section 351 of the PHS Act
- Bone, ligaments, tendons,
- Eye/Ocular tissue
- Skin
- Arteries and veins
- Pericardium, heart valve allografts
- Reproductive tissue
- Hematopoietic stem cells from cord or peripheral blood

# Imports – FD&C Act Section 801

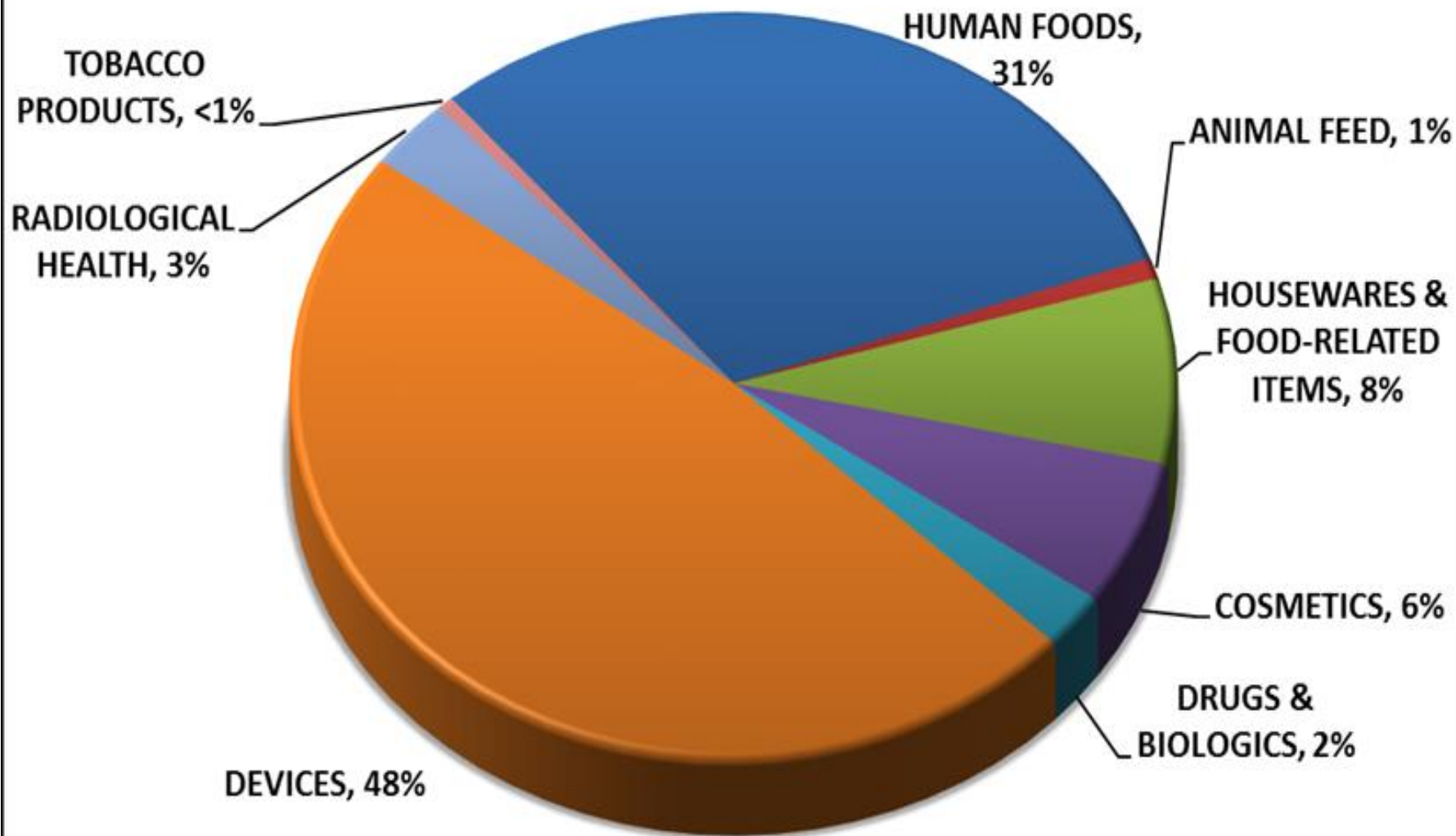
Section 801 of the Federal Food, Drug, and Cosmetic Act (21 USC 381) sets out basic standards and procedures for FDA review of imports under its jurisdiction. Section 801(a) provides for examination of imports and also authorizes FDA to refuse admission of imports that appear, from examination or otherwise, to violate FDA requirements.

# FDA-Regulated Imports

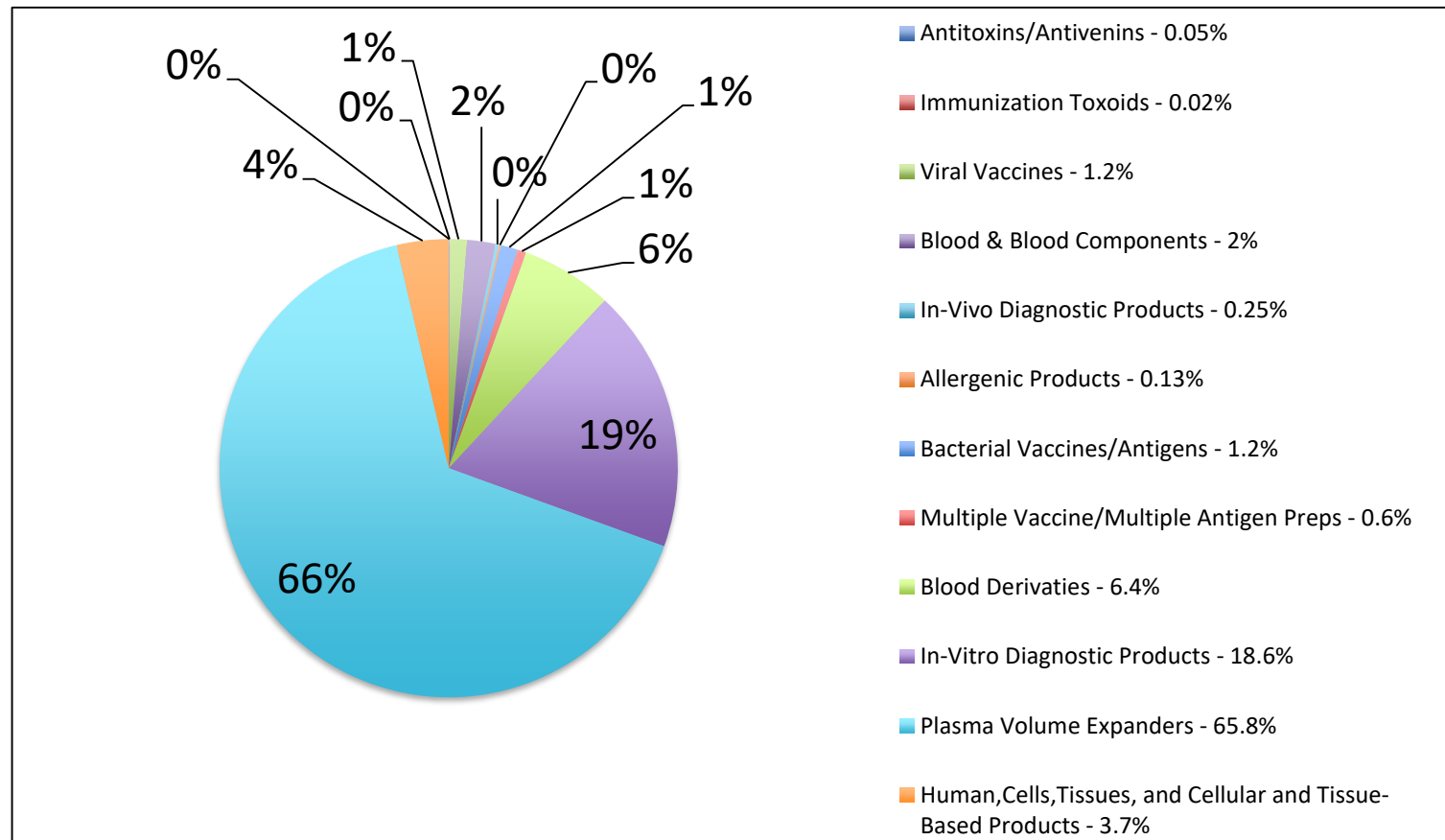
- All goods offered for entry into the US, including items for personal use, must be declared to U.S. Customs and Border Protection (CBP).
- CBP's Automated Commercial Environment/International Trade Data System (ACE/ITDS) is utilized by industry for submission of all data required by various government agencies involved in international trade.
- CBP refers all FDA-regulated products to FDA for review.



## Percentage of Imported Lines\* by Commodity for Fiscal Year 2018



# CBER-Regulated Imports



- CBER products constitute <1% of all FDA imports
- FY2018: >170,000 CBER-regulated lines

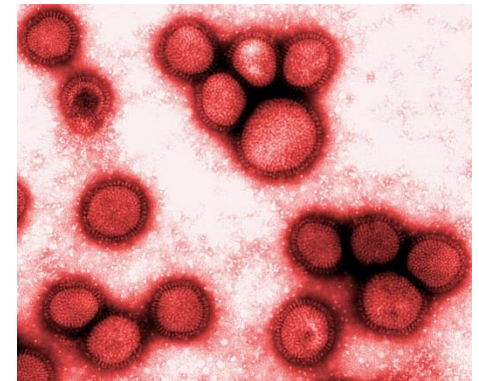


# CBER-Regulated Imports

- Compliance Program Guidance Manual 7342.007: Importation of biological products, drug, and devices regulated under **Section 351** of the PHS Act and/or FD&C Act
- 7342.007 Addendum: Importation of human cells, tissues, cellular, and tissue-based products (HCT/Ps) regulated under **Section 361** of the PHS Act and 21 CFR Part 1271.

# Example: Influenza Vaccines

- Annual strain change supplement approval occurs near the end of June-early July.
- CBER works closely with Divisions and receives many inquiries during this period due to the high influx of vaccine shipments.
- In FY2014, an intra-agency collaboration was established to aid flu vaccine importation prior to yearly strain change supplement approval. Shipments were imported and held under bond until supplements were approved.



# Importation: Special Circumstances

- Samples
- Biological specimen for research/testing
- Blood/blood components for autologous use
- Import-for-Export (IFE)

– Drugs (including biologics): **Samples**

- Intended solely for testing in vitro or laboratory research in animals if in compliance with 21 CFR 312.160; IND.
- Blood grouping reagents, reagent red blood cells, and anti-human globulin for investigational in-vitro diagnostic use if in compliance with 21 CFR 312.160

– Devices (including biologics):

- Intended for testing in vitro or in or on laboratory animals if in compliance with 21 CFR 812.5(c); IDE
- Shipments of IVDs for other research/testing purposes if in compliance with 21 CFR 809.10(c)(2); IVD



# Biological Specimens for Research/Testing

- Biological specimens NOT subject to FDA jurisdiction:



- Used only for testing in a clinical laboratory or for basic scientific research
- Not intended for the prevention, treatment, diagnosis, or cure of diseases, injuries, or conditions in humans, are not subject to FDA jurisdiction.
- Three HTS Codes were recently updated to permit filers to “disclaim” entries of clinical specimens and reagents.

## Blood/Blood Components for Autologous Use

- **Entries of unlicensed human blood or blood components for autologous use only may be imported if:**
  - the manufacturer does not ship autologous blood products in interstate commerce on a routine or regular basis
  - the product(s) are for transfusion purposes only and have not been further processed or manipulated
  - the product(s) are properly labeled (see 606.121(i)(3),(4))

# Import for Export

- Importation of certain articles that are unapproved or otherwise do not comply with the FD&C Act. The articles must be further processed or incorporated into products that will be exported from the United States by their initial owner or consignee in accordance with section 801(e) or section 802 of the Act or section 351(h) of the Public Health Service Act (PHSA).
- FDA must be provided certain information at the time of initial importation including:
  - A statement that confirms the intent to further process such article or incorporate such article into a product to be exported.
  - A statement that identifies entities in the chain of possession of the imported article.
- Types:
  - 801(d)(3): Drugs/Devices
  - 801(d)(4): Blood, Blood components, source plasma, source leukocytes

# Admissibility Documentation that May be Requested

- Labeling for product
- Short supply agreement
- Import-for-Export Approval Letter under Section 801(d)(4) – where applicable
- Documents required by other agencies
- HCT/P accompanying records



# Export

The imported product, which has been further manufactured, also must comply with applicable export requirements when the product is exported.

## Export mechanisms:

- FD&C Act Section 801(e)
- FD&C Act Section 802
- 21 CFR 312.110
- PHS Act 351(h)

# CBER-Regulated Imports Cont.

- Compliance Program Guidance Manual (CPGM) 7342.007:  
Importation of biological products, drug, and devices regulated under Section 351 of the PHS Act and/or FD&C Act.
- CPGM 7342.007 Addendum:  
Importation of human cells, tissues, cellular, and tissue-based products (HCT/Ps) regulated under Section 361 of the PHS Act and 21 CFR 1271.



# Affirmations of Compliance (AofC)

- ACE requires the intended use code for each CBER-regulated product offered for import.
- The intended use code determines which AofC is mandatory, conditional, and optional for the entry submission.
- Failure to transmit the mandatory AofC results in entry rejection by CBP.
- A list of the current intended use codes, their descriptions, and the associated AofC can be found in the FDA Supplemental Guide.

# Exceptions and Special Situations

- Reproductive HCT/Ps
- Hematopoietic stem cells
- US Goods Returned
- Nonclinical scientific or educational use
- Biological specimens for testing in a clinical laboratory or for basic scientific use
- HCT/Ps intended for further processing
- Human cell therapy and gene therapy products regulated under Section 351 of the PHS Act and the FD&C Act
- Devices composed of human tissues regulated by CDRH under the FD&C Act
- HCT/P Combination Products
- Minimally manipulated bone marrow
- Vascularized human organs
- Cells, tissues, and organs derived from animals other than humans

# Nonclinical Scientific or Educational Use Only

## [21 CFR 1271.15(a)]

- HCT/Ps imported by establishments that use them solely for nonclinical scientific or educational use are not subject to 21 CFR 1271 [21 CFR 1271.15(a)].
- Examples:
  - tissue on a slide
  - ovary in paraffin wax for research/educational use
  - Severed heads for educational use
- These HCT/Ps are not subject to FDA jurisdiction; and the filer should specify the entry is not subject to FDA regulation by "disclaiming" the entry.

# HCT/P Examples

## Section 361:

- Bone, ligaments, tendons
- Eye/ocular tissue such as corneas, sclera
- Skin
- Arteries and veins
- Pericardium, heart valve allografts
- Dura mater
- Corneas
- Reproductive tissue such as semen, oocytes
- Hematopoietic stem cells from cord or peripheral blood
- Amniotic membrane
- Umbilical cord
- Adipose tissue
- Articular and non-articular cartilage
- Lymph nodes and thymus
- Parathyroid glands
- Peripheral nerve
- Pancreatic tissue

## Section 351:

- Cultured cartilage cells
- Cultured nerve cells
- Lymphocyte immune therapy products
- Gene therapy products
- Human cloning products
- Human cells used in therapies involved in the transfer of genetic material
- Unrelated allogeneic hematopoietic stem cells
- Unrelated donor lymphocytes for infusion
- Corneal lenticules
- Preserved umbilical cord vein grafts
- De-mineralized bone combined with handling agents
- Cultured cells on synthetic membranes or combined with collagen
- Encapsulated pancreatic islet cells
- Bone-suture-tendon allografts

# Tissues Not Under FDA Jurisdiction

## [21 CFR 1271.3(d)(1-8)]

- Vascularized human organs
- Minimally manipulated bone marrow



# Cells, Tissues, and Organs Derived From Animals Other Than Humans

- CBER does not oversee the regulation of animal cells, tissues, and organs intended for use in animals.
- Contact the Center for Veterinary Medicine for additional information.





# Importing CBER-Regulated Products: Clinical Laboratories and Basic Scientific Research



- **Q1?: I want to import biological specimens (e.g., blood, tissue, DNA) for testing in a clinical laboratory or for basic scientific research. Does FDA regulate biological specimens intended only for testing in a clinical laboratory or use for basic scientific research?**
- <https://www.fda.gov/vaccines-blood-biologics/exporting-cber-regulated-products/importing-cber-regulated-products-clinical-laboratories-and-basic-scientific-research>

Answer Q1: **No. If the biological specimens you are offering for import are intended for use only for testing in a clinical laboratory or for basic scientific research** and are not articles intended for the prevention, treatment, diagnosis, or cure of diseases, injuries, or conditions in human beings, **the specimens are not considered to be biological products subject to licensure by FDA** in accordance with Section 351(a) [42 USC 262(a)] of the Public Health Service Act (PHS Act), nor would they appear to be a drug or device as defined in sections 201(g) and (h), respectively, of the Federal Food, Drug, and Cosmetic Act [21 USC 321(g) and (h)], nor an HCT/P as defined in 21 CFR 1271.3, which was promulgated under Section 361 of the PHS Act [42 USC 264].

# Importing CBER-Regulated Products: Clinical Laboratories and Basic Scientific Research



**Q2? How do I tell FDA that a biological specimen is being imported for testing in a clinical laboratory or for basic scientific research?**

Answer Q2: **When submitting an entry notification, a filer will determine the appropriate tariff code for the product being offered for importation.** CBP uses the tariff code, in part, to determine if other government agencies also need to make an admissibility determination. However, a tariff code may cover a wide range of products and may include products that are not subject to FDA jurisdiction. When this is the case, **filers are usually given the option of "disclaiming" FDA jurisdiction.** This is accomplished by disclaiming the "line" in the entry that applies to those products.

Tariff codes that cover both FDA and non-FDA regulated products have an "Other Government Agency (OGA)" flag which would allow the filer to disclaim FDA jurisdiction. If the tariff code you or your filer are using for your specimens does not have an OGA flag that will allow the filer to "disclaim" the line(s) in the entry, the filer should contact:

**FDA's Division of Import Operations & Policy at: 301-796-0356 to determine if the OGA flag for the tariff code can be modified to allow use of the disclaim process.**

# Importing CBER-Regulated Products: Clinical Laboratories and Basic Scientific Research



**Q3? What are my responsibilities as an importer of such biological specimens?**

**Answer Q3: If your biological specimens are intended for testing in a clinical laboratory or for basic scientific research, the product is not regulated by FDA.** Thus, when submitting the entry notification for the specimens, the filer should disclaim that line. Note that if the person to whom the product is shipped (the consignee) is not using the samples for testing, but instead is processing or manufacturing HCT/Ps or biological products, drugs, or devices with these biological specimens, then the products are subject to FDA jurisdiction and must meet FDA's requirements for HCT/Ps, biological products, drugs, and/or devices.

**In addition, to avoid possible delays with importation of specimens for testing or research, it is recommended that the labeling of each specimen container include the following information to make clear that the specimens do not fall under FDA regulation:**

- An accurate description of the biological specimens. For example: human blood specimen, human tissue specimen, human DNA specimen.
- A statement regarding the intended use of the specimen. For example: "Human Blood For Testing in a Clinical Laboratory," or "Human DNA Specimen for Basic Scientific Research."
- If the biological specimen has been tested for infectious agents such as the hepatitis B surface antigen (HBsAg) and/or the antibody to human immunodeficiency virus (anti-HIV), a statement relative to the test results should be included.

# Importing CBER-Regulated Products: Clinical Laboratories and Basic Scientific Research



**Q4? I want to import human tissues for educational use or for basic scientific research. Does FDA regulate human tissue intended only for educational use or for basic scientific research?**

Answer to Q4.: **No.** If the human tissues you are offering for import are intended for use only for educational use or for basic scientific research and are not intended for implantation, transplantation, infusion, or transfer into a human recipient, the tissues are not subject to FDA's human tissue regulations or FDA import review. If your broker needs to "disclaim" FDA jurisdiction, please see (link to "How do I tell FDA that a biological specimen is being imported for testing in a clinical laboratory or for basic scientific research?")

# References

**CPGM 7342.007 – Imported CBER Regulated Products:**

<https://www.fda.gov/media/85664/download>

**CPGM 7342.007 Addendum** - Imported Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps):

<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ComplianceActivities/Enforcement/CompliancePrograms/ucm095253.pdf>

**Importing CBER-Regulated Products: Clinical Laboratories and Basic Scientific Research:**

<https://www.fda.gov/vaccines-blood-biologics/exporting-cber-regulated-products/importing-cber-regulated-products-clinical-laboratories-and-basic-scientific-research>

**Importing CBER Regulated Products into the United States:**

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ComplianceActivities/BiologicsImportingExporting/ucm143371.htm>





## FDA Import Operations Michigan & DNBI Border Locations & Contacts

General Inquiry: [FDAImportsInquiry@fda.hhs.gov](mailto:FDAImportsInquiry@fda.hhs.gov);

Import Offices/Contacts: [www.fda.gov/ForIndustry/ImportProgram/ucm319216.htm](http://www.fda.gov/ForIndustry/ImportProgram/ucm319216.htm)

Biologics: [CBERImportInquiry@fda.hhs.gov](mailto:CBERImportInquiry@fda.hhs.gov) (240) 402-9155

### DETROIT AMBASSADOR BRIDGE

2810 W. Fort Street  
Detroit, MI 48207  
(313) 226-5249 (P)  
Phenicia Petty, SCSO

### PORT HURON BLUEWATER BRIDGE

2321 Pine Grove Avenue, Suite 2114  
Port Huron, MI 48060  
(810) 985-8514 (P)  
Melissa Tyrrell, SCSO

### SAULT STE MARIE

900 International Bridge Plaza  
Sault Ste Marie, MI 49783  
Periodic Coverage

### DAYS & HOURS OF OPERATION

#### DETROIT AMBASSADOR BRIDGE

Monday – Friday 6:00 am – 6:00 pm  
Saturday/Sunday 8:00 am – Noon

#### PORT HURON BLUEWATER BRIDGE

Monday – Friday 8:00 am – 4:30 pm

#### SAULT STE MARIE

Periodic Coverage

**DETROIT CROSSING OPERATIONAL ALL HOLIDAYS 8:00 AM – NOON -- EXCEPT THE FOLLOWING:**

January 1st (New Years Day)

November (Thanksgiving Day )

July 4th (Independence Day)

December 25th (Christmas Day)

### OTHER DNBI IMPORT CONTACTS

Eric Joneson, DIB-W

(313) 393-8157

Investigations Branch (from DET to Wash St)

Sherea Dillon, DCB

(312) 596-4244

Compliance Branch (All Northern Border)

Sandra Sylvester, DIB-E

(716) 846-6221

Investigations Branch (from Buffalo to ME)

Keith Jasukaitis, PDD

(313) 393-8141

Northern Border Program Division Director

# Thank You

**Questions ?**