Guidelines for Regulatory Compliance.

## Regulatory Compliance for Importation into the USA

One of the primary challenges is ensuring that the correct customs classification as well as the correct permits and related documentation requirements are identified for all materials to be shipped to the USA. Detailed documentation describing material composition and use are important for the tariff determination as well as the identification of the requirement for import permits. Careful planning is critical to ensure that all items are correctly defined, to include stability data for transportation, and that appropriate documentation and literature is included when shipping materials for importation into the USA. This is necessary to reduce any delays are caused by customs or FDA inspection and/or detention.

There are three key authorities that are responsible for controlling the movement of biological agents, equipment and related materials into the USA:

- US Customs and Border Control. (Key Data – HTS Classification)
- FDA (through the Center for Biologics Evaluation and Research (CBER) (Key Data – FDA Product Code and Certificate of Affirmation)
- Center for Disease Control and Prevention (CDC) (Key Data – Import Permits)

*This Handbook will focus extensively on the interactions between these agencies - US Customs and Border Control and the FDA/CBER as well as the requirements for Permits from the CDC.*

*We have not covered the shipment planning and execution process in this handbook.*
*This can be added as needed for a variety of origin and destination pairs.*
*Models can be developed to include the inbound movement from the EU to the USA locations as well as distribution within the USA.*

Import Process into the USA – and the interaction between US Customs and Border Control, the FDA (CBER) and other agencies (for biological and potentially infectious biological substances).

A high-level overview of the import process is included below – more detail is available through the link below.

( https://www.fda.gov/vaccines-blood-biologics/exporting-cber-regulated-products/importing-cber-regulated-products-fda-interactions-other-agencies)

*PROCESS OVERVIEW*

STEP 1 Submission of entry to US Customs and Border Protection (CBP)

*The CBP has primary responsibility for regulating and facilitating international trade, collecting import duties, and enforcing United States trade laws.*

*When submitting an entry notification, the importer – or agent filing on their behalf, will determine the appropriate Harmonized Tariff Schedule (tariff) code for each 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 both products that are subject to FDA jurisdiction and 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.*
  - *Each distinct category of product in an entry will have its own "line" in the entry.*

- *For example, if a shipment of a vaccine consisted of both multi-dose vials and pre-filled, single dose syringes, the vials would be one line and the syringes another line.*

The entry information submitted to CBP and then to FDA includes:

- the identification of the product by the tariff code;
- the entry type;
- the entry number;
- the arrival date;
- the port of entry;
- the port of unlading;
- the carrier code;
- the vessel name and voyage, flight or trip number;
- the importer and ultimate consignee;
- the quantity;
- the value;
- the country of origin;
- the bill of lading or airway bill number;
- the manufacturer;
- the importer of record; and
- the ultimate consignee.

The tariff codes are flagged to indicate which products will require FDA review.

STEP 2 For materials that require FDA review the entry is electronically sent by CBP to FDA for review.

This is received through the FDA system – Operational and Administrative System for Import Support (OASIS)

The additional information that is currently transmitted to FDA includes:

- the FDA manufacturer;
- the FDA shipper;
- the FDA Country of Production (country of origin)
- the complete FDA product code;
- A description of the article in common business terms
- the quantity for each FDA line; and
- Affirmations of Compliance.

It is important to ensure that all import shipments have the correct information required for the FDA review. Key data includes:

**FDA Product Codes -** composed of a seven-character set of letters and numbers, helps FDA classify and review imports. An FDA Product Code has five parts:

- The first part is the "Industry Code." The Industry Code for all CBER-regulated products is the number "57," so the FDA Product Codes for all CBER-regulated products begin with "57".
- The second part of the FDA Product Code is the "Class Code." For CBER-regulated products, the Class Code is a letter that describes, generally, what grouping the product falls into, for example, is it a viral vaccine, blood derivative, or human musculoskeletal (tissue) product.
- The third part of the FDA Product Code is the "Subclass Code". For CBER-regulated products the Subclass Code is a letter that describes how the product will be used in the United States, for example, for further manufacturing, in final dosage form for patient use, or sample for product testing/assessment or FDA/CBER lot release.
- The fourth part of the FDA product Code is the "Process Indicator Code." CBER-regulated products do not have a Process Indicator Code so in a FDA Product Code for a CBER-regulated product, this part is filled in with a hyphen (-).
- The fifth part of the FDA Product Code is the "Specific Product Code." The Specific Product Code for CBER-regulated products is two numbers that specifically describes the particular kind of product, e.g., rabies vaccine.

  (https://www.fda.gov/vaccines-blood-biologics/exporting-cber-regulated-products/fda-product-codes-importing-cber-regulated-products)

**Description of the article in common business terms** - Description used in product catalogue and listed on the commercial invoice, packing list, insurance documentation etc. This should clearly identify the item in non-technical language.

**Affirmations of Compliance** (AOC) are voluntary data elements that a customs broker or self-filer currently may use when transmitting certain information to FDA through the CBP'electronic interface with OASIS.

- Each AOC provides a mechanism to indicate (or affirm) compliance with a specific FDA regulatory requirement.

- For example, for a licensed biological product, the AOC would be the BLN (Biologics License Number) or STN (Submission Tracking Number), while for an investigational biological drug product, it would be the IND (Investigational New Drug Application) number.

If each line of an entry is properly submitted, a lower-risk product may be allowed to enter domestic commerce without further FDA review.

There are automated systems in place to assist FDA employees in their review of import entries while targeting FDA resources on the riskiest products. These systems electronically review import entries, and highlighting risky products or entries that are incomplete or contain inaccurate data.

Systems include: (https://www.fda.gov/industry/fda-import-process/entry-screening-systems-and-tools)

PREDICT (Predictive Risk- based Evaluation for Dynamic Import Compliance Targeting) is a risk-based analytics tool FDA uses to electronically screen all regulated shipments imported or offered for import into the United States of America.

- PREDICT improves import screening and targeting to prevent entry of adulterated, misbranded, or otherwise violative goods and expedites the entry of non-violative goods.
- PREDICT uses automated data mining, pattern discovery, and automated queries of FDA databases to determine the potential risk of a shipment. It takes into consideration the inherent risk of a product and also information about the previous history of importers, manufacturers and shippers.
- PREDICT presents shipments for further review based on its analytical results. Shipments with lower risk ranks and no other potential risks may be processed through FDA review more quickly than higher risk lines.

ITACS. (https://www.fda.gov/industry/import-systems/itacs)

The FDA has deployed the Import Trade Auxiliary Communication System (ITACS) for use by the import trade community.

- ITACS was implemented in order to improve communication between the FDA and the import trade community. .
- ITACS basic functionality provides the import trade community the ability to electronically: check the status of FDA-regulated entries and lines, submit entry

documentation, submit the location of goods availability for those lines targeted for examination by the FDA, and check the estimated laboratory analysis completion dates for lines which have been sampled.

When a system flags an entry for having incomplete or inaccurate data, FDA reviewers may ask for more information or request physical exam or sampling. Additional information requested could include:

Bill of Lading (BOL), Airway Bill (AWB), invoice, and purchase order.

Where applicable, you should also provide FDA with commodity specific certifications (USDA permits, Impact Resistance test results, etc.), packing list/growers list, copies of labeling, documentation stating who the actual manufacturer is, documentation explaining why articles classified as U.S. Goods Returned are being returned, certificate of analysis, intended use statement or End Use Statement, and other related documentation as requested.

CBP forms 3461 and/or 7501 should also be provided to the FDA for manual (Non-ABI) entries.

*It is important to ensure that all potential data requirements are known and planned for to avoid this situation,*

## Roles and Responsibilities of Regulatory Agencies in Importation into the USA

Understanding the Roles, Responsibilities and Interactions between the Regulatory Agencies is important during Importation. We have therefore included more information on each of these organizations as well as some Frequently Asked Questions that should be reviewed.

### Role of US Customs and Border Control in controlling imports into the USA.

US Customs is responsible for ensuring that the correct commercial documentation and classification according to the Harmonized Tariff Schedule is applied for duties and tax purposes. US Customs are primarily focused on ensuring the safety and security of the borders, while ensuring that the trade agreements and related duties and tariffs are complied with.

## Resources available from US Customs

US Customs and Border Protection are a useful resource and have centers of excellence that can assist importers in classification for materials that have potential contingencies that could be subject to mis-interpretation..


Centers of Excellence and Expertise (Centers) are industry-focused and account-based operational organizations processing post-release trade activities on behalf of US Customs and Border Protection (CBP). Centers are aligned by 10 key industry sectors in strategic locations at Ports of Entry across the U.S. and are the strategic point of connectivity between the trade community and CBP operations. The Centers increase uniformity of practices across the Ports of Entry, facilitate the timely resolution of trade compliance issues nationwide and strengthen CBP's ability to protect the U.S. economy.

The Centers are comprised of organization units that focus on one of the following strategic areas:

### Partnership Division
Streamline trade facilitation efforts through partnership programs and increase industry-based knowledge through bi-direction education efforts.

### Validation and Compliance Division (V&C)
Validate risk factors within an industry sector and develop approaches to improve compliance.

### Enforcement Division
Develop and address risks through impactful national enforcement plans and strategies.

### Prior to importing, you may contact the CBP office at the port of entry where your merchandise will enter the United States
A complete directory of the various ports of entry can be found on this website. If you are unsure of or haven't decided the port where your shipment will arrive, or you are looking at importing through multiple ports, you may contact a service port of entry near you. Ask to speak with a CBP import specialist assigned to the commodity you are importing. Import specialists are a valuable resource for commodity specific knowledge and can provide classification advice, commodity specific requirements, advisory duty rates, and respond to questions you may have about filing an entry. At many ports, entry specialists handle questions regarding entry filing. Entry specialists work closely with import specialists and provide the technical processing expertise required to file the necessary paperwork.

When calling the port, the importer should be able to provide as much detail regarding the transaction as possible. In order for the import specialist to best assist you, it is important you be able to exactly describe the merchandise you are planning to import. In order for the import specialist to best assist you, you should provide a full and complete description of the article and answer specific questions such as: 1) the country of origin of the merchandise and manufacturer; 2) the composition of the merchandise; 3) the intended use of the item; and 4) pricing/payment information (in order to properly determine the value of the shipment). For more information on the classification of merchandise, consult the Harmonized Tariff Schedule (HTS) which contains the actual HTS number and tariff classification guidelines that explain how to properly classify merchandise.

## Applying for a Customs Ruling

In many cases it is advisable to take advantage of these resources, applying for a customs ruling to ensure that the correct HTS classification and duties and tariffs are applied at time of entry, irrespective of port of entry.

### What are Ruling Letters? (direct quotation from CBP site)

*It is in the interest of the sound administration of CBP and related laws that persons engaging in any transaction affected by those laws fully understand the consequences of that transaction prior to its consummation. For this reason, Customs and Border Protection will give full and careful consideration to written requests from importers and other interested parties for rulings or information setting forth, with respect to a specifically described transaction, a definitive interpretation of applicable law, or other appropriate information.*

*A ruling may be requested under Part 177 of the CBP Regulations (19 C.F.R. Part 177) by any person who, as an importer or exporter of merchandise, or otherwise, has a direct and demonstrable interest in the question or questions presented in the ruling request, or by the authorized agent of such person. A "person" in this context includes an individual, corporation, partnership, association, or other entity or group.*

*A request for a valuation or carrier ruling should be in the form of a letter. A request for a ruling regarding tariff classification, certain marking, origin, NAFTA and applicability of Trade Program should be submitted in the form a letter or electronically via the eRulings Template.*

**Requests for valuation rulings and carrier rulings can be e-mailed to:**
HQRulings@cbp.dhs.gov

**Requests for Valuation rulings should be addressed to:**
Chief, Valuation and Special Programs Branch
Regulations and Rulings
Office of Trade
90 K Street, NE, 10th Floor
Washington, DC 20229

**Requests for tariff classification rulings, certain marking, origin, NAFTA and applicability of Trade Program should be addressed to:**
Director, National Commodity Specialist Division
U.S. Customs and Border Protection

Attn: CIE Ruling Request
Regulations and Rulings
Office of Trade
201 Varick Street, Suite 501
New York, New York 10014

Links to Resources:
https://www.cbp.gov/trade/basic-import-export/importing-biological-materials-united-states
https://www.cbp.gov/trade/basic-import-export/importer-exporter-tips
https://www.cbp.gov/trade/centers-excellence-and-expertise-information

## Role of the FDA in Importation of Biological Products

Within the FDA the Center for Biologics Evaluation and Research is responsible for Therapeutic Products. (This includes Cell and Gene products/Car-T therapies).

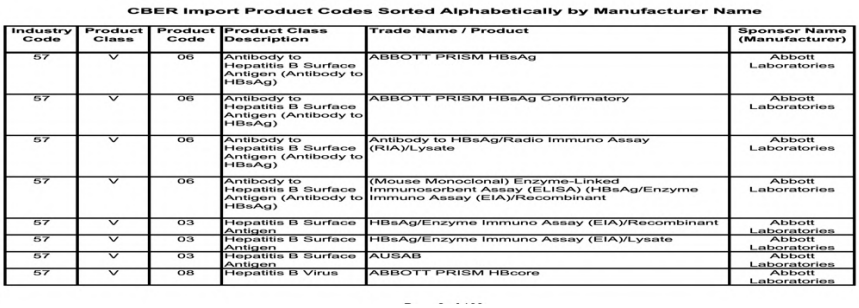
The mission of the Center for Biologics Evaluation and Research (CBER) is to protect and enhance public health through the regulation of biological and related products including blood, vaccines, allergenics, tissues, and cellular and gene therapies. CBER is making changes to its organizational structure to address the substantial growth in the development of innovative, novel products and the ever-changing public health landscape, CBER has established the new Office of Therapeutic Products (OTP). This new super office is the result of a reorganization of the Center's Office of Tissues and Advanced Therapies and includes six new offices within the super office structure.

(US Food and Drug Administration. https://www.fda.gov/ and Center for Biologics Evaluation and Research (CBER)

As this is the most important area of the FDA for the importation of cell and gene and related materials/ancillaries we have included a series of links to ensure most current information.

## Importing CBER-Regulated Products: FDA Product Codes

The FDA Product Code, a seven character set of letters and numbers, helps FDA classify and review imports.



CBER Import Product Codes Sorted Alphabetically by Manufacturer Name

| Industry Code | Product Class | Product Code | Product Class Description | Trade Name / Product | Sponsor Name (Manufacturer) |
|---|---|---|---|---|---|
| 57 | V | 06 | Antibody to Hepatitis B Surface Antigen (Antibody to HBsAg) | ABBOTT PRISM HBsAg | Abbott Laboratories |
| 57 | V | 06 | Antibody to Hepatitis B Surface Antigen (Antibody to HBsAg) | ABBOTT PRISM HBsAg Confirmatory | Abbott Laboratories |
| 57 | V | 06 | Antibody to Hepatitis B Surface Antigen (Antibody to HBsAg) | Antibody to HBsAg/Radio Immuno Assay (RIA)/Lysate | Abbott Laboratories |
| 57 | V | 06 | Antibody to Hepatitis B Surface Antigen (Antibody to HBsAg) | (Mouse Monoclonal) Enzyme-Linked Immunosorbent Assay (ELISA) (HBsAg/Enzyme Immuno Assay (EIA)/Recombinant | Abbott Laboratories |
| 57 | V | 03 | Hepatitis B Surface Antigen | HBsAg/Enzyme Immuno Assay (EIA)/Recombinant | Abbott Laboratories |
| 57 | V | 03 | Hepatitis B Surface Antigen | HBsAg/Enzyme Immuno Assay (EIA)/Lysate | Abbott Laboratories |
| 57 | V | 03 | Hepatitis B Surface Antigen | AUSAB | Abbott Laboratories |
| 57 | V | 08 | Hepatitis B Virus | ABBOTT PRISM HBcore | Abbott Laboratories |

Use the link below to learn more.

- Product Codes For Importing CBER-Regulated Products

### Importing CBER-Regulated Products: Entry Review

To learn more about FDA's Entry Review programs for imported products, click on the resource links provided below.

- PREDICT

### Importing CBER-Regulated Products: Entry Refusals

To learn more about FDA's Entry Refusal programs for imported products, click on the resource links provided below.

- Import Alerts

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

For the import of biological specimens (e.g., blood, tissue, DNA) for testing in a clinical laboratory or for basic scientific research - reference link below

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

### Importing CBER-Regulated Products: Compliance and Regulatory Resources

Additional compliance and regulatory resources related to importing CBER-regulated products:

- Compliance Program Guidance Manual - 7342.007: Imported CBER-Related Products

- Compliance Program Guidance Manual - 7342.007 Addendum: Imported Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps)
- FDA's Regulatory Procedures Manual, Chapter 9 - Import Operations and Actions
- Import and Export Guidance Documents

## Frequently Asked Questions (FAQ)

### What standards apply to imports that are regulated by the Center for Biologics Evaluation and Research (CBER)?

- CBER regulates biological and related products, including blood and blood products (which includes certain kinds of devices), vaccines, allergenics, tissues, and cellular and gene therapies.
- CBER also regulates the medical devices involved in the collection, processing, testing, manufacture and administration of licensed blood, blood components and cellular products and all HIV test kits used both to screen donor blood, blood components, and cellular products and to diagnose, treat, and monitor persons with HIV and AIDs.
- In order to import a CBER-regulated product into the United States, the product must meet FDA's regulatory requirements.
- Foreign firms which manufacture products regulated by CBER that are directly or indirectly imported into the United States must comply with applicable FDA requirements before, during, and after importing into the United States. FDA does not recognize regulatory approvals from other countries.

### Who directs and coordinates CBER's import program?

- The Division of Case Management (DCM) within CBER's Office of Compliance and Biologics Quality (OCBQ) directs and coordinates CBER's import program
- You can send questions pertaining to the importation of CBER-regulated products to CBERImportinquiry@fda.hhs.gov.

### What role does FDA play when an FDA-regulated article is offered for import?

- If the article being imported falls under FDA's jurisdiction, it is subject to FDA review.
- 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 regulations at 21 CFR 1271.420 set out the basic import standards and procedures for human tissues.
- As explained in more detail below, FDA and CBP have coordinated their efforts and work together to ensure the smooth processing of FDA-regulated imports.

## Importing CBER-Regulated Products: Roles of Other Federal Agencies

- The US Customs and Border Protection (CBP)
- Centers for Disease Control and Prevention (CDC),
- US Department of Agriculture (USDA)
- Animal and Plant Health Inspection Service (APHIS)

may have regulations that may also apply to CBER-regulated products.

## Are there any other federal agencies that may have requirements that apply to biological specimens?

**Yes.** The following organizations have regulations that may also apply to biological specimens.

- The Centers for Disease Control and Prevention (CDC);
- the US Department of Agriculture (USDA),
- Animal and Plant Health Inspection Service (APHIS);
- US Customs and Border Protection

If the material is suspected or known to contain etiologic agents or has not been tested for etiologic agents, a CDC Etiologic Agent Import Permit may be required.

(Additional reference: https://www.ecfr.gov/current/title-42/chapter-I/subchapter-F/part-73?toc=1)

CDC can be contacted at

Centers for Disease Control and Prevention
Office of Health and Safety FO5
Atlanta, Georgia 30333
Phone: (404) 639-3311 or (404) 498-2260

The following agencies regulate the import of all animal-origin materials that could represent a disease risk to United States livestock and the import and transport of infectious organisms and vectors of disease agents. This includes not only animal products and by products, but biological materials that contain or have been in contact with certain organisms and animal materials (including cell cultures).

- The U. S. Department of Agriculture (USDA)
- Animal and Plant Health Inspection Service (APHIS)
- Veterinary Services (VS),

USDA/APHIS/VS can be contacted at:

USDA, APHIS, VS
National Center for Import and Export
4700 River Rd. Unit 39
Riverdale, MD 20737
Phone: (301) 734-3277

## Role of the Center for Disease Control and Prevention in Importation of Biological Substances

An important organization for the management and control of Biological Materials is the Center for Disease Control and Prevention. Requirements for Import permits for Infectious Biological Agents (Viral Vectors) program is managed by the Center for Disease Control and Prevention– CDC.

**The CDC Import Permit Program or IPP** regulates the importation of infectious biological materials that could cause disease in humans to prevent their introduction and spread in the USA.

The CDC Import Permit program ensures that the importation of these agents is monitored and that facilities receiving permits have appropriate biosafety measures in place to work with the imported agents.

We have included some Frequently Asked Questions (FAQ) as well as some reference materials and links for access to applications and online tools.
*(Please note that these FAQ were taken directly from the CDC web site to ensure relevance)*

### FAQ - Requirements for Permits

**Is an import permit required to import material that has received approval from the U.S. Food and Drug Administration?**

**No.** Any product that is cleared, approved, licensed, or otherwise authorized under any of the following laws would not require a CDC import permit:

- The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.), or
- Section 351 of the Public Health Service Act pertaining to biological products (42 U.S.C. 262), or
- The Virus-Serum-Toxin Act (21 U.S.C. 151-159).

**What type of material requires a CDC import permit?**

- Infectious biological agent - A microorganism [including, but not limited to, bacteria (including rickettsiae), viruses, fungi, or protozoa] or prion, whether naturally

occurring, bioengineered, or artificial, or a component of such microorganism or prion that is capable of causing communicable disease in a human.

- Infectious substance - Any material that is known or reasonably expected to contain an infectious biological agent.
- Vector - Any animals (vertebrate or invertebrate) including arthropods or any noninfectious self-replicating system (e.g., plasmids or other molecular vector) or animal products (e.g., a mount, rug, or other display item composed of the hide, hair, skull, teeth, bones, or claws of an animal) that are known to transfer or are capable of transferring an infectious biological agent to a human.

### Is an import permit required to import genomic material?

- It depends. Nucleic acids that can produce infectious forms of any infectious biological agent would require a CDC import permit. For example, viral genomes which consist of positive sense RNA are infectious when the purified viral RNA is applied to permissive cells in the absence of any viral proteins. In some cases, viral genomes which are composed of double-stranded DNA are also infectious [e.g., genome of Cercopithecine Herpesvirus 1 (Herpes B virus)].
- Nucleic acids that cannot produce infectious forms of any infectious biological agent and are accompanied by an importer certification statement confirming that the material is not known to contain or suspected of containing an infectious biological agent would not require a CDC import permit.

### Is an import permit required for an infectious biological agent after dosing the infectious biological agent with an investigational new drug product under review by U.S. Food and Drug Administration?

- **Yes.** Any sample known, or suspected by the importer of containing, an infectious biological agent would require a CDC import permit. This product would not meet the exemption because the product is not approved or cleared by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).
- However, if the material is not known to contain or suspected of containing an infectious biological agent, or has been rendered noninfectious, it would not require a CDC import permit. The material must be accompanied by an importer certification statement confirming that the material is not known to contain or suspected of containing an infectious biological agent, or has been rendered noninfectious.

**Is an import permit required for a diagnostic specimen that is suspected to contain a select agent?**

**Yes.**

- Any diagnostic specimen known, or suspected by the importer of containing, any infectious biological agent would require a CDC import permit.

**Does a CDC import permit allow the importer to "hand carry" the imported material into the United States?**

No.
The issuance of an import permit is not an authorization to hand carry the imported material into the United States.

- The shipment of infectious biological agents, infectious substances, or vectors of human disease into the United States must be packaged, labeled, and shipped in accordance with all federal and international regulations. When traveling by air, the biological materials must be declared to the airline and cannot be concealed in checked luggage. Contact the airline and U.S. Customs in advance to ensure compliance with their policies and procedures.
- No person may carry a hazardous material in the cabin of a passenger-carrying aircraft or on the flight deck of any aircraft, and the hazardous material must be located in a place that is inaccessible to persons other than crew members. Hazardous materials may be carried in a main deck cargo compartment of a passenger aircraft provided that the compartment is inaccessible to passengers and that it meets all certification requirements for a Class B aircraft cargo compartment in 14 CFR 25.857(b) or for a Class C aircraft cargo compartment in 14 CFR 25.857(c).

**Does a recipient within the United States need a CDC import permit to receive an infectious biological agent, infectious substance or vector from a facility that imported the material if the condition was indicated on the issued permit for the importer?**

**Yes**. Since the requirement for approval of subsequent transfers of imported materials within the United States was noted as a condition on the issued permit to the importer, the recipient is required to obtain a CDC import permit to receive this material.

*To initiate the process for a permit, the facility would need to submit an application through eIPP.*

### Besides a CDC import permit, when would a United States Department of Agriculture (USDA) permit be needed for importing an infectious biological agent, infectious substance or vector?

The USDA's Animal and Plant Health Inspection Service (APHIS) permits are required for the import, transit and release of regulated animals, animal products, veterinary biologics, plants, plant products, pests, organisms, soil, and genetically engineered organisms.

Information on the APHIS permitting requirements is available at https://www.aphis.usda.gov/aphis/resources/permits/sa_biotechnology/brs-epermits

### Which types of materials do NOT require an import permit?

- Select agents listed in 42 CFR Part 73 and if its importation has been authorized in accordance with 42 CFR 73.16 or 9 CFR 121.16.
- With the exception of bat or nonhuman primate specimens, diagnostic specimens not known by the importer to contain, or suspected by the importer of containing, an infectious biological agent and is accompanied by an importer certification statement confirming that the material is not known to contain or suspected of containing an infectious biological agent, or has been rendered noninfectious.
- With the exception of live bats or bat or nonhuman primate products, animal or animal products being imported for educational, exhibition, or scientific purposes and is accompanied by documentation confirming that the animal or animal product is not known to contain (or suspected of containing) an infectious biological agent or has been rendered noninfectious.
- Nucleic acids that cannot produce infectious forms of any infectious biological agent and the specimen is accompanied by an importer certification statement confirming that the material is not known to contain or suspected of containing an infectious biological agent.
- Animal or animal product listed in 42 CFR Part 71 and its importation has been authorized in accordance with 42 CFR $S 71.52, 71.53, or 71.56.
- Product that is cleared, approved, licensed, or otherwise authorized under any of the following laws:

- The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.), or
- Section 351 of the Public Health Service Act pertaining to biological products (42 U.S.C. 262), or o The Virus-Serum-Toxin Act (21 U.S.C. 151-159).

**Do the issuance and expiration dates located on the import permit affect the permit conditions for importation and continued possession listed on the import permit?**

- The issuance and expiration dates located on the import permit pertain only to the dates that the importer is allowed to import into the United States the infectious biological agents, infectious substances, and vectors listed on the import permit.

- The conditions for importation and continued possession listed on the permit remain in effect until the importer is no longer in possession of the imported material.

**What if my facility receives an infectious biological agent, infectious substance, or vector that is not listed on my CDC import permit?**

You should safeguard the material and immediately report the incident to the CDC Import Permit Program either by email at importpermit@cdc.gov or by telephone at (404) 718-2077.

**If our facility does not plan to receive any more imported material from outside the United States, does our facility have to renew our permit?**

- If your facility will no longer be importing infectious biological agents, infectious substances, or vectors of human disease into the United States, your facility should not complete an application to renew your facility's import permit.
- However, the conditions specified on the permit apply until you no longer possess the material.

**What method should my facility use to render infectious biological agents non-infectious?**

- The facility should use a scientifically supportable method.
- The method used to cause permanent loss of biological activity must be reliable and based on the agent's sensitivity to the inactivating method.

- An acceptable method may consist of traditional methods that have been generally recognized in the scientific community and published in the scientific literature or a method developed in-house, but that method should be validated as applied.
- While there is no requirement to notify CDC prior to rendering an agent non-infectious, the facility should incorporate a practice of maintaining records on file in support of materials being non-infectious.

**How would an importer know if authorization for subsequent transfers of imported materials within the United States is needed?**

If the CDC Import Permit Program requires an additional permit for subsequent transfers of any infectious biological agent, infectious substance or vector within the United States, the requirement will be listed as a condition of issuance on the import permit.

*To initiate the process for an additional permit, the recipient must submit an application through eIPP.*

**How long is an import permit valid to import an infectious biological agent, infectious substance ^ or vector into the United States?**

- A permit to import, or receive through subsequent transfer, is valid only for the time period indicated on the issued permit.
- The issuance and expiration dates located on the import permit pertain only to the dates that the importer is allowed to import into the United States the infectious biological agents, infectious substances, and vectors listed on the import permit. The conditions for importation and continued possession listed on the permit remain in effect until the importer is no longer in possession of the imported material.

  *Please note that all requests for renewal of an existing import permit require the submission of a new application and current signature of the permittee.*
  *To prevent lapses in the import permit status, it is recommended that permit renewal applications be submitted at least 30 days prior to the expiration date on the current permit.*

**Is there a requirement for maintaining records of imported shipments for a specific amount of time?**

- There is no regulatory requirement in the import permit regulations for maintaining records of shipments for a specific amount of time. However, the CDC Import Permit Program recommends that the permittee maintain records of shipments for at least 3 years.

**What is the process if my permit request gets denied, suspended or revoked?**

- An applicant who wishes to make an appeal would have 30 calendar days after receiving the denial to submit the appeal in writing to the CDC Director.
- The appeal must state the factual basis for the appeal and provide any supporting documentations to justify the appeal (e.g., documents that demonstrate the facility has the appropriate biosafety measures in place for working safely with the requested imported material).
- CDC will issue a written response, which would constitute final agency action.

*The applicant can submit the appeal to the CDC Director through the CDC Import Permit Program by*
*email (importpermit@cdc.gov),*
*fax [(404) 718-2093]*
*or mail:*
*CDC Import Permit Program*
*1600 Clifton Rd, Mailstop A-46*
*Atlanta, GA 30329*

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## Information related to Packaging and Labeling

### How should we package and label shipment containing imported infectious biological agents, infectious substances, and vectors?

Imported infectious biological agents, infectious substances, and vectors classified as a Category A infectious substance must be packaged in accordance with the U.S. Department of Transportation's (DOT's) Hazardous Materials Regulations (https://www.ecfr.gov/current/title-49/subtitle-B/chapter-I/subchapter-C/part-171 and be accompanied by a shipping paper, marking, labeling, and note the appropriate emergency response information.
Please see the
https://www.cdc.gov/orr/ipp/docs/guidance_for_shippers_declaration_508.pdf
for more information.

### Labeling of Packages

The outer container of all Category A infectious substance packages must display the following:

- Sender's name and address
- Recipient's name and address
- Infectious substance label
- Proper shipping name, UN number, and net quantity of infectious substance
- Name and telephone number of person responsible for shipment
- Cargo Aircraft Only label (when shipping quantities of infectious substance over 50 ml or 50 g by aircraft). Class 9 label, including UN 1845, and net weight if packaged with dry ice and identified as Carbon Dioxide, solid, ***or*** dry ice

### What happens if a package containing an infectious biological agent, infectious substance, or vector is lost or damaged during shipment?

Requirements for All Infectious Substances

- The DOT regulations (49 CFR 171.15 and 171.16) require each person in physical possession of a hazardous material, including an infectious substance, to report specific types of transportation incidents that involve these materials.
- Immediate reporting by telephone to the National Response Center at 1-800-424-8802 is required for incidents where fire, breakage, spillage, or suspected contamination occurs that involves the shipment of infectious substances other

than a patient specimen or regulated medical waste (See 49 CFR 171.15(b)(3)).

- In addition, a written report to DOT is required within 30 days of the discovery of the incident for any unintentional release of hazardous material from a packaging during transportation, including those covered under 49 CFR 171.15 (See 49 CFR 171.16(a)).
- DOT regulations also require packages that contain infectious substances to be accompanied by several forms of hazard communication, as applicable, as well as labeled to indicate the infectious hazard (See 49 CFR 172.432 for a depiction of the required label).
- This label currently includes a statement for reporting a damaged package.


**How should vials be labeled when working with SARS-CoV-2 to ensure that they are not confused with regulated SARS-CoV?**

- Vials should be accurately labeled as SARS-CoV-2 to ensure that there is a clear distinction between the regulated virus (SARS-CoV) and the unregulated virus (SARS-CoV2).

**Is it permissible to reuse shipping and packaging material?**

- Please refer to the Department of Transportation regulations (See 49 CFR 173.22 and 24) where it refers to the integrity of the packaging.

**What are some of the specific measures required to ensure that infectious biological agents, infectious substances, and vectors are shipped safely?**

- The specific measures required to ensure that infectious biological agents, infectious substances, and vectors are shipped safely are included in the Department of Transportation Hazardous Materials Regulations (49 CFR Parts 171-180).

- A condensed version of these measures can be found in the CDC/NIH publication Biosafety in Microbiological and Biomedical Laboratories (see attachments)

## CHECKLISTS AND USEFUL LINKS

To ensure compliance with import permit regulations, the CDC Import Permit Program inspects entities using these standardized checklists to verify that facilities have implemented the appropriate biosafety measures for the infectious biological agent, infectious substance, or vector to be imported.

- Import Permit Checklist ABSL-2 [PDF – 480 KB]
- Import Permit Checklist ABSL-3 [PDF – 556 KB]
- Import Permit Checklist ACL-2 [PDF – 303 KB]
- Import Permit Checklist ACL-3 [PDF – 311 KB]
- Import Permit Checklist BSL-2 [PDF – 344 KB]
- Import Permit Checklist BSL-3 [PDF – 467 KB]

Quick links (hyperlinks to online Guidances)
Center for Disease Control and Prevention
https://www.cdc.gov/orr/ipp/eipp.htm
https://www.cdc.gov/orr/ipp/regulations.htm

### Other Organizations for Related Information for Biological Materials

**Federal Aviation Administration.** https://www.faa.gov/

All shipments must be compliant FAA regulations – based on the nature of the aircraft on which the cargo will travel (passenger or cargo aircraft).

- The shipment of infectious biological agents, infectious substances, or vectors of human disease into the United States must be packaged, labeled, and shipped in accordance with all federal and international regulations. When traveling by air, the biological materials must be declared to the airline and cannot be concealed in checked luggage. Contact the airline and U.S. Customs in advance to ensure compliance with their policies and procedures.
- No person may carry a hazardous material in the cabin of a passenger-carrying aircraft or on the flight deck of any aircraft, and the hazardous

material must be located in a place that is inaccessible to persons other than crew members.

- Hazardous materials may be carried in a main deck cargo compartment of a passenger aircraft provided that the compartment is inaccessible to passengers and that it meets all certification requirements for a Class B aircraft cargo compartment in 14 CFR 25.857(b) or for a Class C aircraft cargo compartment in 14 CFR 25.857(c).

**See Attached Packaging Instructions in Addendum.

**Pipeline and Hazardous Materials Safety Administration.**
https://www.phmsa.dot.gov/

### Transporting Infectious Substances

An infectious substance, including regulated medical waste, is regulated as a hazardous material under the U.S. Department of Transportation's (DOT's) Hazardous Materials Regulations (HMR; 49 C.F.R., Parts 171-180). PHMSA develops and enforces the HMR to ensure the safe transport of hazmat in interstate, intrastate and foreign commerce by aircraft, railcar, vessel, and motor vehicle.

The HMR apply to any material that DOT determines capable of posing an unreasonable risk to health, safety, and property when transported in commerce1, including infectious substances. An infectious substance must conform to all applicable HMR requirements when offered for transportation or transported by air, highway, rail, or water.

The HMR contain the requirements for classification, packaging, hazard communication, and, in some cases, security plans of infectious substances. Infectious substances generally fall into three classification categories:

- **Category A** – An infectious substance in a form capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animals when exposure to it occurs.

- **Category B** – An infectious substance not in a form generally capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animals when exposure to it occurs.

- **Regulated Medical Waste** – a waste or reusable material derived from the medical treatment of an animal or human.

## Transporting Infectious Substances Safely Guidance

See DOT's Transporting Infectious Substances Safely Brochure for an important overview of the general transportation requirements for infectious substances.

## Infectious Substance Oversight

Oversight responsibilities for infectious substances are shared by several Federal agencies that work together towards common goals. While the purview of the DOT is focused on the safe transportation of infectious substances, other organizations provide the expertise on classification, handling, workplace safety, waste disposal, and emergency or pandemic response.

### OSHA

The Occupational Safety and Health Administration (OSHA), part of the U.S. Department of Labor, ensures safe and healthful working conditions for working men and women by setting and enforcing standards and by providing training, outreach, education, and assistance. OSHA has standards for bloodborne pathogens and personal protective equipment to protect workers from occupational exposure to infectious substances. As such, some OSHA standards are incorporated into certain DOT packaging requirements for regulated medical waste.

### FEMA

The Federal Emergency Management Agency (FEMA), part of the U.S. Department of Homeland Security is tasked with helping people before, during, and after disasters. In the event of an infectious substance pandemic, FEMA works closely with the Department of Health and Human Services and state, local, tribal and territorial governments to execute a whole government response.

### Infectious Substance Special Permits

For important information on infectious substance special permits, including the special permit for Ebola contaminated waste, see the Infectious Substance Special Permits page.

## US Department of Agriculture – USDA. https://www.usda.gov/

The U.S. Department of Agriculture (USDA) provides leadership on food, agriculture, natural resources, rural development, nutrition, and related issues based on public policy, the best available science, and effective management. Divisions within USDA

and CDC form the Federal Select Agent Program (FSAP), which regulate the possession, use, and transfer of biological select agents and toxins that have the potential to pose a severe threat to public, animal or plant health, or to animal or plant products.

- USDA Permits – A USDA permit is also required for pandemic novel H1N1 influenza virus strains. The novel H1N1 influenza virus has genetic components of both swine and avian influenza viruses in it which result in causing infections in those species. APHIS has authority over all organisms which cause or have the potential to cause disease in animals; therefore, they issue permits for novel H1N1 influenza. For further information, contact APHIS at 301-734-3277.

The USDA's Animal and Plant Health Inspection Service (APHIS) permits are required for the import, transit and release of regulated animals, animal products, veterinary biologics, plants, plant products, pests, organisms, soil, and genetically engineered organisms. Information on the APHIS permitting requirements is available at: https://www.aphis.usda.gov/aphis/resources/permits/eauth-epermits

US Fish and Wildlife Services

USDA/APHIS and HHS/CDC import permit is required for the novel H7N9 influenza virus strains. The novel H7N9 Influenza A virus has caused infections in both humans and birds. APHIS and CDC have authority over the importation of all microorganisms which cause, or have the potential, to cause disease in animals or humans respectively, and so both agencies will issue permits for the novel H7N9 influenza A virus. For further information, please contact APHIS at 301-851-3300 (Option 1) or CDC at 404-718-2077. (Note - CDC will not issue a permit for Asian lineage H7N9 low path avian influenza until a USDA/APHIS permit has been obtained.) https://www.aphis.usda.gov/aphis/resources/permits/eauth-epermits

US Environmental Protection Agency. https://www.epa.gov/

ATTACHMENTS – pdf documents (some with hyperlinks). - second document with imbedded pdf)