

Importing FDA Regulated Products: Biological Products

Office of Enforcement and Import Operations
Division of Imports Operations

US Food and Drug Administration
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Agenda

- FDA Authority and Definitions
- FDA Regulatory Requirements for CBER Regulated Biological Products
- Making ACE Work for You: Importing Biological Products
- Entry Screening/Admissibility



FDA Authority to Regulate

- Public Health Service Act (PHS Act)
 - Section 351
- Title 21 Code of Federal Regulations
 - 21 CFR 601.2 – Biologic License application
 - 21 CFR 312 – Investigational New Drug (IND)

Definitions

A **Biologic Product** is defined in Section 351 of the Public Health Service Act as, “a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.”

Human cells, tissues, or cellular or tissue-based products (HCT/Ps) are defined in Section 361 of the PHS Act as “Human cells, tissues, or cellular or tissue-based products (HCT/Ps) means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.”

Definitions

Drugs are defined as articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; articles (other than food) intended to affect the structure or any function of the body of man or other animals; and articles intended for use as a component of a drug.

– Section 201(g) FD & C Act

Definitions

Devices are defined as an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

– Section 201(h) FD & C Act

FDA Biological Products

- Blood and blood products
- Vaccines
- Allergenic
- Gene therapies
- Human cells and tissue products (HCT/PTs)
- Some medical devices, test kits and certain drugs
- *Therapeutic Biological Products (CDER)

Import Requirements for Biologics

- Registration and Listing
 - Under Section 510 of the Federal Food, Drug and Cosmetic Act and 21 CFR part 207, manufacturers of biological products must:
 - Register their establishments annually each year and,
 - List all their products in commercial distribution at the time of initial registration, with bi-annual updates to their listings

Import Requirements for Biologics

- Blood Establishment
 - Manufacturers must register unless they are exempt per 21 CFR 607.65, and
 - Register and list within 5 days of beginning operation and annually between Oct. 1-Dec. 31
 - List every blood product manufactured, prepared, processed for commercial distribution
 - Blood product listings must be updated every June and Dec.

Import Requirements for Biologics

- Medical Device Establishment
 - Manufacturers must register per 21 CFR 807, and
 - Medical devices require listing, including identification of all proprietary names.



Import Requirements for CBER Regulated Drugs

- Drug Registration & Listing
- Biological License Approval & Drug Approval
 - Depending on the type of application (Biologics License Application (BLA), New Drug Application (NDA) or Abbreviated New Drug Application (ANDA), there are a variety of A of C codes that might be used.

Import Requirements for CBER Regulated Drugs

- Affirmation of Compliance for Approved products
 - DA# followed by the qualifier which is the actual NDA (prefix BN)
 - DA# followed by the qualifier which is the actual AND (prefix BA)
 - BLN followed by the qualifier which is the actual Biologics License Number
 - STN followed by the qualifier which is the Biologics Application Number (Systems Tracking Number)
- Affirmation of Compliance Investigational products
 - IND followed by the qualifier which is the actual IND Number

Import Requirements for CBER Regulated Medical Devices

- CBER regulates medical devices for screening, collection, processing, testing, manufacture and administration of blood and tissue.
- CBER regulated medical device manufacturers
 - All register and list with Center for Devices and Radiological Health (CDRH) medical devices requirements.
- CBER regulates medical devices under two provisions
 - Licensing provisions
 - Medical devices intended to screen
 - Blood donors
 - HCT/P donors
 - Medical Device provisions
 - Medical devices intended to diagnose

Import Requirements for CBER Regulated Medical Devices



- CBER regulated medical devices regulated under the **licensing provisions**
 - BLN followed by the qualifier which is the actual Biologics License Number
 - STN followed by the qualifier which is the Biologics Application Number (Systems Tracking Number)
 - IND followed by the qualifier which is the actual IND Number



Import Requirements for CBER Regulated Medical Devices

- CBER regulated medical devices regulated under the **medical device provisions**
 - Meet the entry admissibility requirements of CDRH and may need additional Affirmations of Compliance:
 - DEV - Device Foreign Manufacturer Registration number
 - DFE - Device Foreign Exporter Registration number
 - DDM - Device Domestic Manufacturer Registration number
 - LST – Device Listing number
 - And one of the following Affirmations of Compliance
 - PM# followed by the Premarket Notification 510(k) number (prefix BK)
 - PM# followed by the Premarket Approval number (prefix BP or BM)
 - IDE followed by the Investigational Device Exemption number (IDE)



Import Requirements for Clinical Research/Lab Research

- Biological specimens that are used **for testing in a clinical laboratory or for basic scientific research only** are not regulated by FDA and should be disclaimed.
- Work with your FDA local division if you have any questions regarding a specific product.
- 4 HTS Codes:
 - 3002.12.0010, 3002.12.0020, 3002.12.0090, and 3002.90.5110

<https://www.fda.gov/industry/fda-basics-industry/what-information-do-i-need-import-biological-product-research-use-only>

Import Requirements for USGR and PGAs



- US Goods Returned (USGR)
 - Expected to meet the same requirements as any biological product
 - Must be covered under a biologics license or an active IND
- Partnering Agencies' Requirements (PGAs)
 - A product may be held or detained due to another agency's requirements so be sure to check with other related agencies such as Center for Disease Control and Prevention or United States Department of Agriculture.

COVID-19 Related Products

- Top priority for FDA
- Currently, there is only one FDA approved vaccine. Other COVID-19 vaccines and COVID-19 immune globulins authorized by FDA.
 - IND or EUA
- Expedite entry of COVID-19 shipments
- CSMS #44720893 - Food and Drug Administration (FDA) New Center for Biologics Evaluation and Research (CBER) Product Code
 - 57C[][]33/COVID 19 Vaccine
 - 57U[][]46/COVID 19 Immune Globulin

Making ACE Work For You



What is ACE?

- Centralized system for all transactions related to imports and exports.
- Filers (brokers) electronically submit all information related to an inbound shipment and the government processes the transaction systematically and sends status updates.



ACE – Information Needed for Submission

- Mandatory information
 - FDA Country of Production
 - Complete FDA Product code
 - Full Intended Use Code
 - Affirmation of Compliance requirements depend on the Intended Use Code
 - Importer of record contact information

ACE – Look-up failures

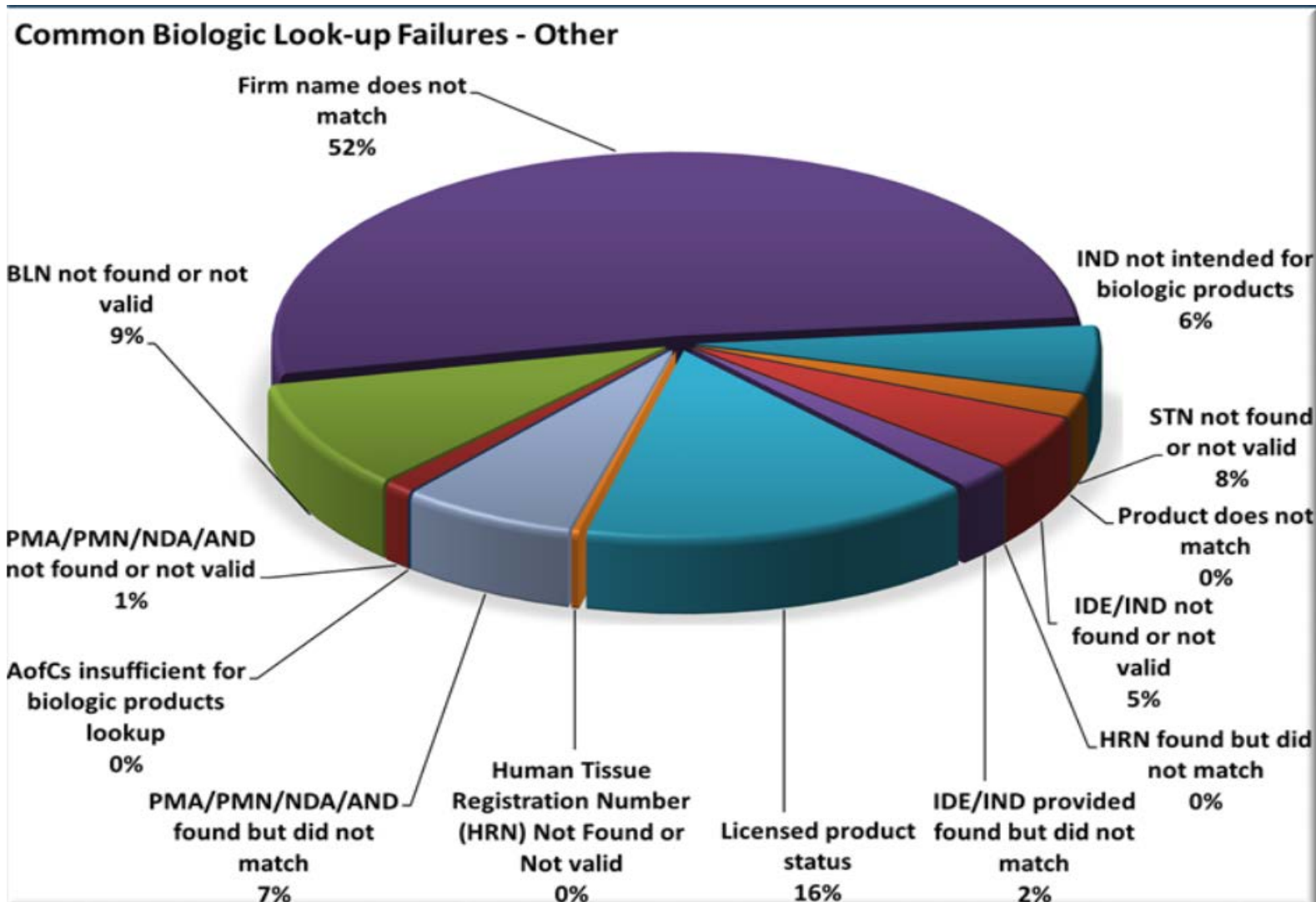
- Correct and accurate entry data
 - Use the Product Code Builder
 - [ORA Import Product Code Builder](#)
- Relevant and appropriate A of C codes
- Accurate qualifiers
- All these factors transmitted help our system “look up” and validate the info

ACE – Look-up failures - Overall

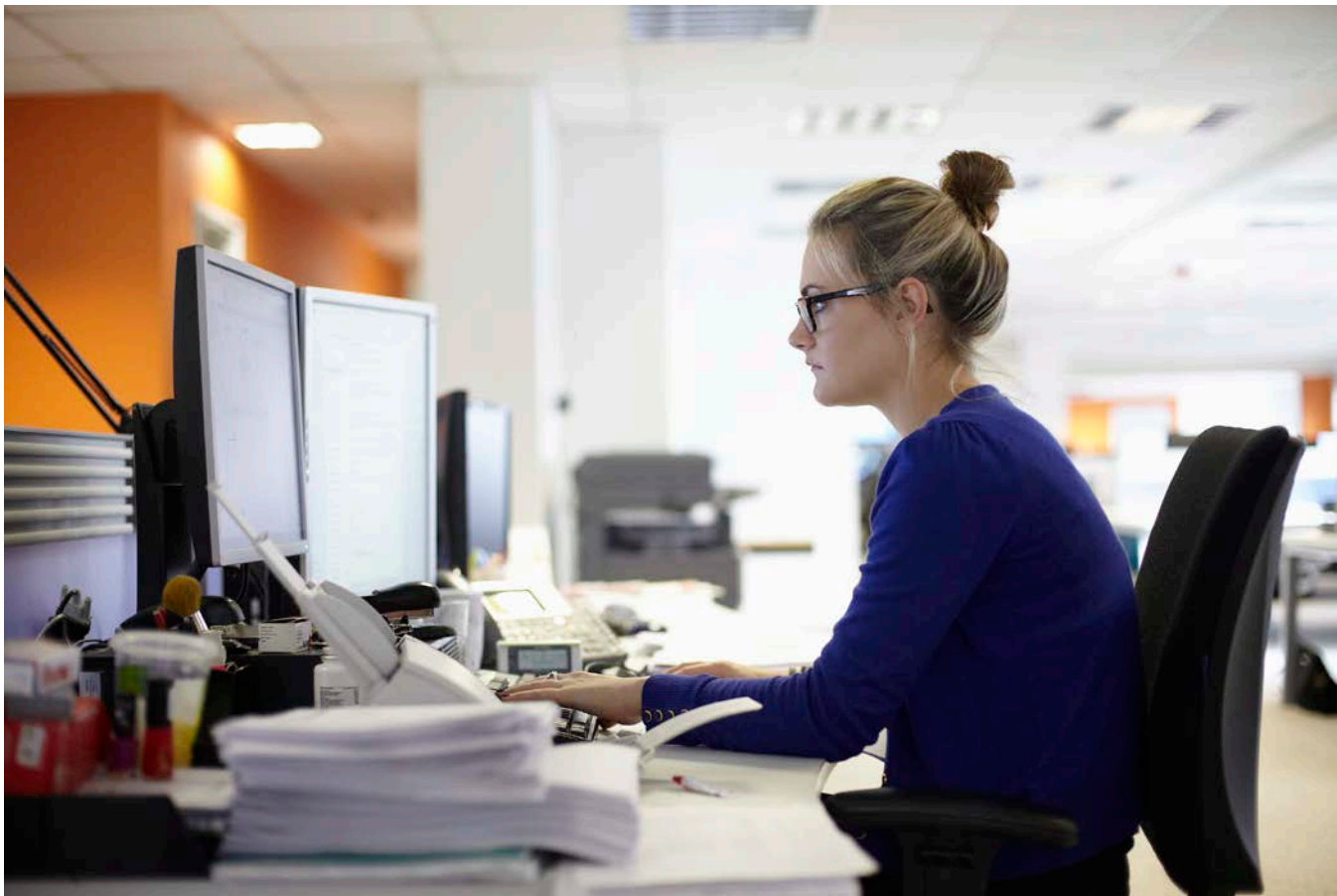
Common Biologic Look-up Failures - Overall



ACE – Common Look-up failures



Entry Screening



Import Entry Screening Process

- Risk-based approach
- Analytical tools
- FDA's screening tool: PREDICT
- Accurate data should be provided to FDA

Screening Process

- Screening:
 - Firm's previous compliance history, inherent risk of a product, and previous history of importers, manufacturers and shippers.
- FDA begins the admissibility process, conducts an onscreen review, and determines admissibility by assessing compliance with appropriate requirements.

Initial Admissibility Decision

- High risk product
- Normal surveillance
- Previously encountered manufacturer, shipper, importer of products (violative shipment history)

Initial Admissibility Decision, cont.

- Release the product
- Request additional info such as entry documentation
- Set up the product for examination or sampling/lab analysis
- Request compliance review

Verification

- FDA will verify compliance with the applicable product requirements
- Entry reviewers use the information provided in the entry transmission to compare against the FDA's internal databases
- <https://www.fda.gov/industry/regulated-products/cber-regulated-products>

Summary

- Know the product being imported and associated requirements
- Understand the data elements
- Provided complete and accurate information
- Compliance with FDA U.S. requirements

Import Resources

- Import Program Internet page
 - <https://www.fda.gov/ForIndustry/ImportProgram/default.htm>
- Regulated Products page
 - <https://www.fda.gov/industry/import-basics/regulated-products>
- CBER FAQ's for Importing CBER Regulated Products into the US
 - <https://www.fda.gov/vaccines-blood-biologics/exporting-cber-regulated-products/importing-cber-regulated-products-united-states>

Biological Product Resources

- Biologics Products & Establishments
 - <https://www.fda.gov/vaccines-blood-biologics/biologics-products-establishments>
- CBER Regulated Products
 - <https://www.fda.gov/industry/regulated-products/cber-regulated-products>
- Biologics Registration and Listing info
 - <https://www.fda.gov/vaccines-blood-biologics/biologics-establishment-registration/important-registration-and-listing-reminder-manufacturers-biological-drug-products-subject-21-cfr>

Biological Product Resources

- Devices Regulated by CBER
 - <https://www.fda.gov/vaccines-blood-biologics/510k-process-cber/devices-regulated-center-biologics-evaluation-and-research>
- FDA Product Codes for CBER Regulated Products
 - <https://www.fda.gov/vaccines-blood-biologics/exporting-cber-regulated-products/fda-product-codes-importing-cber-regulated-products>

Biological Product Resources

- Compliance Program Guidance Manual - 7342.007: Imported CBER-Related Products
– <https://www.fda.gov/media/85664/download>
- Compliance Program Guidance Manual - 7342.007 Addendum: Imported Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps)
– <https://www.fda.gov/media/73960/download>

ACE Resources

- FDA Supplemental Guide
 - <https://www.cbp.gov/document/guidance/fda-supplemental-guide>
- FDA ACE External Outreach Presentation Biological Products
 - <https://www.fda.gov/media/107178/download>
- FDA ACE Affirmation of Compliance Codes
 - <https://www.fda.gov/industry/import-systems/automated-commercial-environmentinternational-trade-data-system-aceitds>
- Industry Quick Reference Guide to the FDA ACE Supplemental Guide
 - <https://www.fda.gov/media/112800/download>

Point of Contacts

Area	Contact Information	Area of Focus
Local FDA Offices	Import Offices and Ports of Entry	First-line support for product coding and entry-specific questions
FDA Imports Inquiry	FDAImportsInquiry@fda.hhs.gov	General questions regarding FDA import operations and policy, including product classification and declaration.
ACE Support Center	ACE Support@fda.hhs.gov	Technical issues related to the FDA supplemental guide, required data elements, and general ACE submission questions, including entry rejections.
CBER Inquiries	CBERImportInquiry@fda.hhs.gov	CBER related emails should be sent to CBER Import Inquiry mailbox

Questions



