Importing and Exporting CBER-Regulated Products

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Biological Drug and Device Compliance Branch

Center for Biologics Evaluation and Research (CBER)

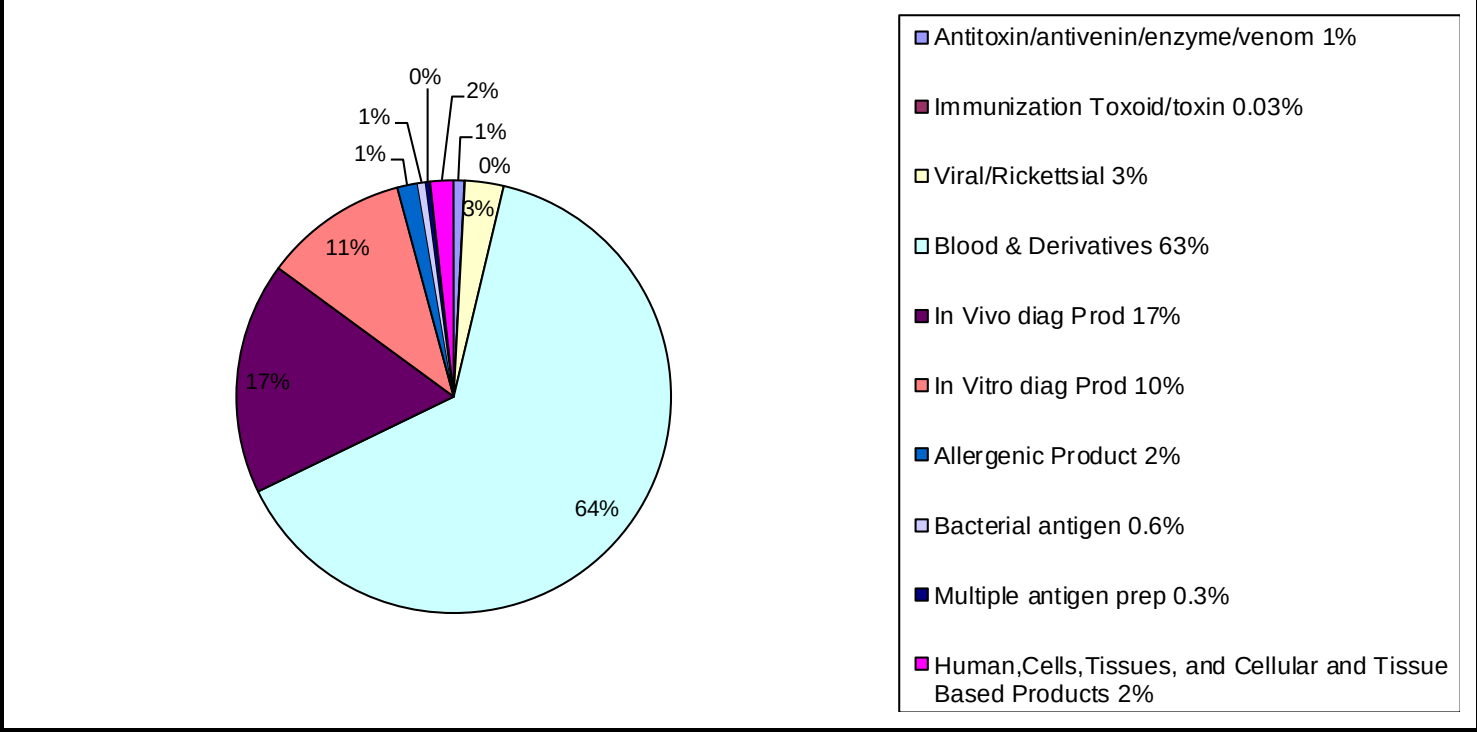
Regulates biological and related products, including blood and blood products, vaccines, allergenics, tissues, cellular and gene therapies, and some devices. For example:

- Antitoxins and Antivenins
- Vaccines
- Blood and Blood Components
- Blood-Derived Products
- Blood bags with anti-coagulant
- Certain devices involved in the collection, processing, testing, manufacture, 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.

CBER-Regulated Imports



- CBER products constitute <1% of all FDA Imports
- FY2014: 82,730 CBER-regulated lines

CBER-Regulated Imports Cont.

- 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.

Importation: Special Circumstances

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

Samples

- Drugs (including biologics):
  - Intended solely for testing in vitro or laboratory research in animals if in compliance with 21 CFR 312.160
  - 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)
  - Shipments of IVDs for other research/testing purposes if in compliance with 21 CFR 809.10(c)(2)

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 (3002905110, 3002100220, and 3002100290).

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

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

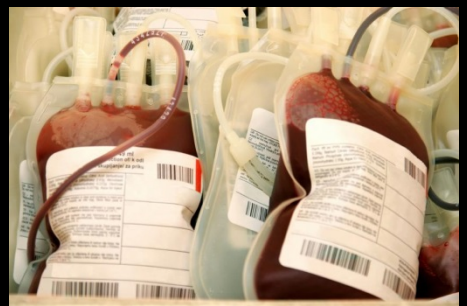
Admissibility Documentation that May be Requested

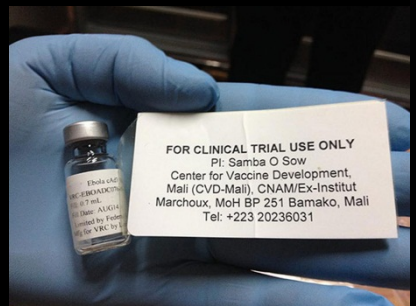
- Labeling for product
- Short supply agreement
- Import-for-Export Approval Letter under Section 801(d)(4) – where applicable
- Documents required by other agencies
- HCT/P accompanying records

Ebola Virus Disease

- Large coordinated inter-agency/global effort to import vaccines necessary for prophylaxis treatment of US healthcare workers caring for repatriated US Ebola patients and to begin clinical trials (FDA, CBP, HHS/BARDA, CDC, USDA/APHIS, DOT, FWS, DOC/BIS, NIH, PHAC).

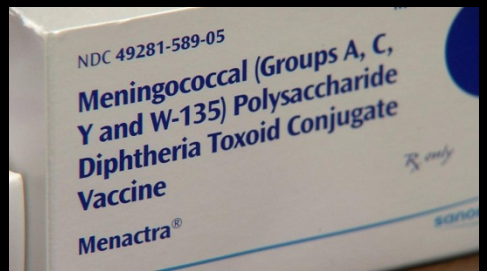
- Noted increase in Ebola R&D inquiries





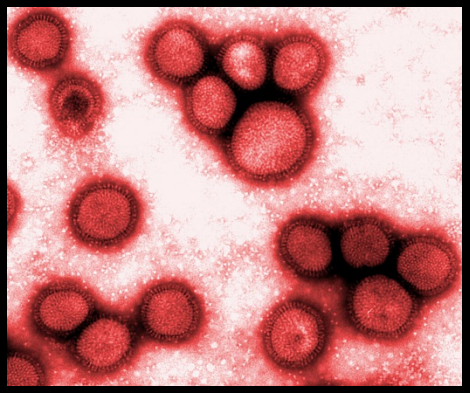
Meningitis B

- Meningitis B outbreaks were reported at Princeton University and UC Santa Barbara.
- US licensed vaccines for serogroups (A, C, Y, W-135).
- INDs were expeditiously established to import Meningitis B vaccines to treat students at Princeton University and UC Santa Barbara.
  - 8 confirmed cases at Princeton; >13,000 doses administered
  - 4 confirmed cases at UCSB; >17,000 students were vaccinated
- 2 serogroup B meningococcal vaccines have since been licensed (Trumenba, Bexsero).



Influenza Vaccines

- Annual strain change supplement approval occurs near the end of June-early July.
- CBER works closely with Districts and receives many inquires 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.



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)

Export - FD&C Act Section 801(e)

801(e)(1):

Export of any food, drug, device, or cosmetic that is adulterated or misbranded under the FD&C Act unless it meets the specifications of the foreign purchaser, is not in conflict with the laws of the country to which it is intended for export, is labeled on the outside of the shipping package that it is intended for export, and not sold or offered for sale in the US.

801(e)(2):

Export of a unapproved device that doesn't comply with section 514 or 515 of the Act, is exempt from either such section under section 520(g) of the Act, or is a banned device under section 516 of the Act. FDA must determine that the device's exportation is not contrary to public health and safety, and has the approval of the country to which it is intended for export.

Export – FD&C Act Section 802

802(b)(1)(A):

Export of any drug, biological product, or device any country if it complies with the laws of the importing country and has a valid marketing authorization in a “listed country.”

802(b)(2):

Export of unapproved/unlicensed drugs and biological products to an “unlisted country.” The product must comply with the laws of the foreign country and possess a valid marketing authorization by the responsible authority in that country. FDA must determine that the foreign entity has statutory or regulatory requirements pertaining to product safety and effectiveness, cGMPs, adverse event reporting, and labeling/promotion must be in accordance with the product’s approval.

Export – FD&C Act Section 802

802(b)(3):

Export of unapproved/unlicensed drugs and biological products to an "unlisted country" if the conditions for 802(b)(1)(A) and 802(b)(2) cannot be met. Scientific evidence must be submitted and reviewed by FDA and the foreign health authority to demonstrate that the products would be reasonably safe and effective. Exports via this mechanism are situation specific (i.e., they pertain to a specific drug intended for export to a specific country).

802(c):

Export of new drugs and biological products for investigational use in a "listed country."

Export of Investigational Drugs and Biological Products - 21 CFR 312.110

- An IND is in effect, the product complies with the laws of the country to which it is being exported, and each person who receives the drug is an investigator of the IND; or
- FD&C Act Section 802(b)(1)(A) (see previous description); or
- FD&C Act Section 802(c) (see previous description); or
- The person exporting the product sends a written certification to the Office of International Programs which should affirm the items detailed in 21 CFR 312.110(b)(4); or
- A foreign national emergency necessitates exportation of the investigational product or the product is to be stockpiled in anticipation of a national emergency.

Export of Partially Processed Biological Products – PHS Act Section 351(h)

- Export of a biological product requiring purification, inactivation, fractionation, or significant chemical modification before being used in the formulation of a final product.
- The product must “not be in a form applicable to the prevention, treatment, or cure of diseases or injuries of man,” and not be intended for sale in the US.
- Intended for further manufacture into final dosage forms outside the US.

CBER Import/Export Team

For import compliance issues and information contact:

CBER/OCBQ: Division of Case Management:

- Robert Sausville, DCM Division Director
- Maria Anderson, MS, BDDCB Chief
- LT Shannon Aldrich, MPH
- Marc Alston, MS
- Kimberly Cressotti
- Jessica Dunn, PhD

CBERImportInquiry@hhs.fda.gov
(240) 402-9155

CBER Import Website:
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ComplianceActivities/BiologicsImportingExporting/ucm143371.htm