

# **U.S. FOOD AND DRUG ADMINISTRATION**

## **U.S. Food and Drug Administration**

The **U.S. Food and Drug Administration (FDA or USFDA)** is an agency of the United States Department of Health and Human Services and is responsible for regulating and supervising the safety of foods, dietary supplements, drugs, vaccines, biological medical products, blood products, medical devices, radiation-emitting devices, veterinary products, and cosmetics. The FDA also enforces section 361 of the Public Health Service Act and the associated regulations, including sanitation requirements on interstate travel as well as specific rules for control of disease on products ranging from pet turtles to semen donations for assisted reproductive medicine techniques.

### **HISTORY**

The Food and Drug Administration is the oldest comprehensive consumer protection agency in the U. S. federal government. Its origins can be traced back to the appointment of Lewis Caleb Beck in the Patent Office around 1848 to carry out chemical analyses of agricultural products, a function that the newly created Department of Agriculture inherited in 1862. Although it was not known by its present name until 1930, FDA's modern regulatory functions began with the passage of the 1906 Pure Food and Drugs Act, a law a quarter-century in the making that prohibited interstate commerce in adulterated and misbranded food and drugs. Harvey Washington Wiley, Chief Chemist of the Bureau of Chemistry in the Department of Agriculture, had been the driving force behind this law and headed its enforcement in the early years, providing basic elements of protection that consumers had never known before that time.

The FDA and its responsibilities have undergone a metamorphosis since 1906. Similarly, the marketplace itself, the sciences undergirding the products the agency regulates, and the social, cultural, political, and economic changes that have formed the context for these developments, all have witnessed upheavals over the past century. Yet the core public health mission of the agency remains now as it did then. This web site features a variety of portals that offer insight into these changes, from overviews on how consumer protection laws evolved, to case studies that explore and interpret the agency's work and policies. In addition, the visitor will find links to key related web sites as well as citations to valuable sources to help understand the history of FDA.

FDA Inspector William Ford is at the center of activity in dealing with the 1937 flooding of the Ohio River and its impact on regulated commodities.

### **LEGAL AUTHORITY**

Most federal laws administered through the FDA are codified into the Food, Drug and Cosmetic

Act, also called Title 21, Chapter 9 of the United States Code. Other significant laws enforced by the FDA include the Public Health Service Act, parts of the Controlled Substances Act, the Federal Anti-Tampering Act, as well as many others. In many cases these responsibilities are shared with other federal agencies.

Important enabling legislation for the FDA includes:

- 1902 – Biologics Control Act
- 1906 – Pure Food and Drug Act
- 1938 – Federal Food, Drug, and Cosmetic Act
- 1944 – Public Health Service Act
- 1951 – Food, Drug, and Cosmetics Act Amendments PL 82–215
- 1962 – Food, Drug, and Cosmetics Act Amendments PL 87–781
- 1966 – Fair Packaging and Labeling Act PL 89–755
- 1976 – Medical Device Regulation Act PL 94–295
- 1987 – Prescription Drug Marketing Act
- 1988 – Anti-drug Abuse Act PL 100–690
- 1990 – Nutrition Labeling and Education Act PL 101–535
- 1992 – Prescription Drug User Fee Act PL 102–571
- 1994 – Dietary Supplement Health and Education Act
- 1997 – Food and Drug Modernization Act 105-115
- 2002 – Bioterrorism Act 107-188
- 2002 – Medical Device User Fee and Modernization Act (MDUFMA) PL 107-250
- 2003 – Animal Drug User Fee Act PL 108-130
- 2007 – Food and Drug Administration Amendments Act of 2007

## **SCOPE AND FUNDING**

The FDA regulates more than \$1 trillion worth of consumer goods, about 25 percent of consumer expenditures in the United States. This includes \$466 billion in food sales, \$275 billion in drugs, \$60 billion in cosmetics and \$18 billion in vitamin supplements. Much of the expenditures is for goods imported into the United States; the FDA is responsible for monitoring a third of all imports.

The FDA's federal budget request for fiscal year (FY) 2008 (October 2007 through September 2008) totaled \$2.1 billion, a \$105.8 million increase from what it received for fiscal year 2007.<sup>[4]</sup> In February 2008, the FDA announced that the Bush Administration's FY 2009 budget request for the agency was just under \$2.4 billion: \$1.77 billion in budget authority (federal funding) and \$628 million in user fees. The requested budget authority was an increase of \$50.7 million more than the FY 2008 funding - about a three percent increase. In June 2008, Congress gave the agency an emergency appropriation of \$150 million for FY 2008 and another \$150 million for FY 2009.

The FDA receives user fees submitted with New Drug Applications under the Prescription Drug User Fee Act (PDUFA)<sup>[citation needed]</sup>; the company submitting an application pays a fee for the review of the new product. A similar process is used for medical devices under the Medical Device User Fee and Modernization Act (MDUFMA)<sup>[citation needed]</sup> and for animal drugs under a similar act. These fees are typically waived or reduced for small businesses.

## **WHAT FDA DO?**

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

### **A) MISSION STATEMENT**

- The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.
- To participate with representatives of other countries to reduce the burden of regulation, coordinate regulatory requirements, and achieve appropriate equivalent arrangements.
- As determined to be appropriate by the Secretary of Health and Human Services, to carry out the tasks above by consulting with experts in science, medicine, and public health, and by cooperating with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.
- FDA accomplishes its task by establishing and enforcing high product standards and other regulatory requirements authorized or mandated by the Federal Food, Drug and Cosmetic Act (FD&C Act), its amendments, and other public health laws.

### **B) WHAT FDA REGULATES**

FDA is the federal agency responsible for ensuring that foods are safe, wholesome and sanitary; human and veterinary drugs, biological products, and medical devices are safe and effective; cosmetics are safe; and electronic products that emit radiation are safe. FDA also ensures that these products are honestly, accurately and informatively represented to the public. Some of the agency's specific responsibilities include:

#### **Biologics**

- product and manufacturing establishment licensing
- safety of the nation's blood supply
- research to establish product standards and develop improved testing methods

#### **Cosmetics**

- safety
- labeling

## **Drugs**

- product approvals
- OTC and prescription drug labeling
- drug manufacturing standards

## **Foods**

- labeling
- safety of all food products (except meat and poultry)
- bottled water

## **Medical Devices**

- premarket approval of new devices
- manufacturing and performance standards
- tracking reports of device malfunctioning and serious adverse reactions

## **Radiation-Emitting Electronic Products**

- radiation safety performance standards for microwave ovens, television receivers, diagnostic x-ray equipment, cabinet x-ray systems (such as baggage x-rays at airports), laser products, ultrasonic therapy equipment, mercury vapor lamps, and sunlamps
- accrediting and inspecting mammography facilities

## **Veterinary Products**

- livestock feeds
- pet foods
- veterinary drugs and devices

## **C) WHAT FDA DOES NOT REGULATE**

The following are the fields, which are not regulated by FDA, but it is regulated by some other agencies, which are closely related to FDA.

### **I) ADVERTISING**

The [Federal Trade Commission](#) is the federal agency, which regulates all advertising, excluding prescription drugs and medical devices. FTC ensures that advertisements are truthful and not misleading for consumers.

### **II) ALCOHOL**

The labeling and quality of alcoholic beverages are regulated by the Treasury Department's [Bureau of Alcohol, Tobacco, and Firearms](#).

### **III) CONSUMER PRODUCTS**

While FDA regulates a large portion of the products that consumers purchase, the agency has no jurisdiction over many household goods. The [Consumer Product Safety Commission](#) (CPSC) is responsible for ensuring the safety of consumer goods.

### **IV) DRUGS OF ABUSE**

legal drugs with no approved medical use--such as heroin and marijuana--are under the jurisdiction of the [Drug Enforcement Administration](#). FDA assists DEA in deciding how stringent DEA controls should be on drugs that are medically accepted but that have a strong potential for abuse.

### **V) HEALTH INSURANCE**

FDA does not regulate health insurance, the cost of health care products or procedures, or reimbursement for health and medical expenses. [Medicare](#) should be directed to the [Health Care Financing Administration](#).

### **VI) MEAT AND POULTRY**

The U.S. Department of Agriculture's [Food Safety and Inspection Service](#) is responsible for the safety and labeling of traditional meats and poultry. (FDA regulates game meats, such as venison, ostrich and snake.)

### **VII) PESTICIDES**

FDA, [USDA](#) (US Department of Agriculture), and the EPA ([Environmental Protection Agency](#)) share the responsibility for regulating pesticides. EPA determines the safety and effectiveness of the chemicals and establishes tolerance levels for residues on feed crops, as well as for raw and processed foods.

### **VIII) RESTAURANTS AND GROCERY STORES**

Inspections and licensing of restaurants and grocery stores are typically handled by local county health departments.

### **IX) WATER**

The regulation of water is divided between the [Environmental Protection Agency](#) and FDA. EPA has the responsibility for developing national standards for drinking water from municipal water supplies. FDA regulates the labeling and safety of bottled water.

## **ABOUT FDA**

### **1) ORGANIZATION**

The FDA is an agency within the United States Department of Health and Human Services responsible for protecting and promoting the nation's public health. The FDA is headquartered in Rockville, MD with 223 field offices supported by 13 laboratories located throughout the United States, the U.S. Virgin Islands, and Puerto Rico. In recent years the agency began undertaking a large-scale effort to consolidate its DC-metro area operations from its main headquarters in Rockville and several fragmented office buildings in the vicinity to the former site of the Naval Ordnance Laboratory in the White Oak area of Silver Spring, MD. The first building, a Life Sciences Laboratory, was dedicated and opened with 104 employees on the campus in December 2003. The project is slated to be completed by 2013.

**The agency is organized into the following major subdivisions, each focused on a major area of regulatory responsibility:**

Sr. No	Component	Full Form	Regulates
A	CBER	Center For Biologics Evaluation And Research	Biological Products
B	CDRH	Center For Devices And Radiological Health	Safety and Effectiveness of New Medical Devices Before they are Marketed
C	CDER	Center For Drug Evaluation And Research	Health of by Assuring Prescription and OTC Drugs are Safe and Effective
D	CSFAN	Center For Food Safety And Applied Nutrition	Food Supply is Safe, Sanitary, Wholesome, and Honestly Labeled, and Cosmetic Products are Safe and Properly Labeled.
E	CVM	Center For Veterinary Medicine	Assure that Animal Food Products are Safe.
F	NCTR	National Center For Toxicological Research	Human Toxicity
G	OC	Office Of The Commissioner	
H	ORA	Office Of Regulatory Affairs	Products Comply with Appropriate Public Health Laws and Regulations.

The FDA frequently works in conjunction with other Federal agencies including the Department of Agriculture, Drug Enforcement Administration, Customs and Border Protection, and Consumer Product Safety Commission. Often local and state government agencies also work in cooperation with the FDA to provide regulatory inspections and enforcement action.

## A) CBER

It is Center for Biologics Evaluation and Research which,

- Regulates biological products.
- Current authority for this responsibility resides in Section 351 of the Public Health Service Act and in specific sections of the Food Drug and Cosmetic Act.
- CBER's review of new biological products, and for new indications for already approved products, requires evaluating scientific and clinical data submitted by manufacturers to determine whether the product meets CBER's standards for approval.
- After a thorough assessment of the data, CBER makes a decision based on the risk-benefit for the intended population and the product's intended use.
- Although medical products are required to be safe, safety does not mean zero risk, since all medical products are associated with some level of risk.
- A safe biological product is one that has reasonable risks, given the patient's condition, the magnitude of the benefit expected, and the alternatives available.
- The choice to use a biological product involves balancing the benefits to be gained with the potential risks. CBER is committed to a product approval process that maximizes the benefits and minimizes the risks to patients of the biological product.

## PRODUCTS REGULATED BY CBER

- A. Blood.
- B. Devices.
- C. Vaccines.
- D. Cellular therapy.
- E. Tissue.
- F. Xenotransplantation products.
- G. Human Tissue & Cellular products.
- H. Allergenics.

### A. Blood

- The FDA is responsible for ensuring the safety of nation's blood supply. □ The Center for Biologics Evaluation and Research (CBER) regulates the collection of blood and blood components used for transfusion or for the manufacture of pharmaceuticals derived from blood and blood components, such as clotting factors, and establishes standards for the products themselves.
- CBER also regulates related products such as cell separation devices, blood collection containers and HIV screening tests that are used to prepare blood products or to ensure the safety of the blood supply.
- CBER develops and enforces quality standards, inspects blood establishments and monitors reports of errors, accidents and adverse clinical events.
- CBER works closely with other parts of the Public Health Service (PHS) to identify and respond to potential threats to blood safety, to develop safety and technical standards, to monitor blood supplies and to help industry promote an adequate supply of blood and blood products.

- In 1997, the FDA initiated the Blood Action Plan to increase the effectiveness of its scientific and regulatory actions, and to ensure greater coordination with our PHS partners.

**(a). Role of FDA in regulation**

- FDA/CBER is responsible for regulatory oversight of the U.S. blood supply.
- FDA promulgates and enforces standards for blood collection and for the manufacturing of blood products, including both transfusible components of whole blood, pharmaceuticals derived from blood cells or plasma, and related medical devices.
- FDA also inspects blood establishments and monitors reports of errors, accidents and adverse clinical events.
- The Department of Health and Human Services (HHS) accepted this plan in March 1998.
- The plan is being jointly implemented by CBER, other FDA components (i.e., Office of Regulatory Affairs, Office of Chief Counsel, and Office of Policy), the Centers for Disease Control (CDC), the National Institutes of Health (NIH), and the Health Care Financing Administration (HCFA).

**(b). Documents published as part of the Blood Action Plan includes --**

- Updating Blood Regulations
- Reinvention of Blood Regulation
- Emerging Infectious Diseases
- Insuring Compliance of Plasma Fractionation Establishments
- Notification and Lookback
- FDA Response to Emergencies and Class I Recalls Affecting Blood Safety
- Monitoring and Increasing the Blood Supply

<b>ISSUE</b>	<b>Emerging Infectious Diseases</b>
	There are constantly emerging potential threats to the blood supply which require timely action and a coordinated approach. Examples include new HIV variants; new hepatitis agents; human herpes virus type 8; Creutzfeld-Jakob Disease; human parvovirus B19; and bacterial contamination of blood products.
<b>NECESSARY STEPS</b>	a) CBER will develop and maintain a database characterizing the effort underway to manage potential threats to the blood supply; b) FDA will work closely with NIH and CDC to develop for each recognized emerging agent strategies that lead to appropriate studies, risk assessment, communication, and

	<p>any needed prevention strategies or regulatory controls to protect the blood supply;</p> <p>c) Proposed prevention strategies or regulatory controls will be brought to public meetings and Advisory Committees as appropriate to assess implementation proposals; and</p> <p>d) CBER will meet with PHS agency and other public representatives to discuss current risk assessment every 6 months</p>
<b>OUTCOME</b>	<p>a) Improved coordination of FDA efforts with other PHS efforts to address emerging infectious diseases, and</p> <p>b) Prevention of transfusion transmitted disease</p>
<b>ISSUE</b>	<b>Insuring Compliance of Plasma Fractionation Establishments</b>
<b>NECESSARY STEPS</b>	<p>a) FDA will complete draft Team Biologics Action Plan;</p> <p>b) FDA will implement Team Blood as defined in the Team Biologics plan;</p> <p>c) FDA staff will be trained in the newly defined procedures and develop compliance programs as needed to implement Team Blood; and</p> <p>d) The existing transition will require periodic oversight. The Deputy Director, CBER and the ACRA will meet with appropriate staff until all blood related regulatory activities are in conformance with ORA standards.</p>
<b>ISSUE</b>	<b>Notification and Lookback</b>
	<p>Recipients of blood and plasma products are not routinely notified in a timely manner when products are recalled. Permanently deferred donors are not routinely notified of the medical conditions resulting in their deferral. Current look-back requirements address only a narrow range of conditions.</p>
<b>NECESSARY STEPS</b>	<p>a) Regulations will be written by FDA that require adequate record keeping and an effective mechanism to identify and notify recipients when a product is implicated in a health hazard;</p>

	<p>b) Regulations will be written that require "look-back" for relevant infectious agents. The list of "relevant" infectious agents will be developed by a team of FDA, NIH, and CDC scientists and reviewed by the appropriate Advisory Committees; and</p> <p>c) CBER will develop a regulation for notification of permanently deferred donors. (Assigned to the Updating Blood Regulations Group)</p>
<b>OUTCOME</b>	<p>a) Donors are notified of their medical deferral leading to opportunities for treatment and reduced secondary transmission, and</p> <p>b) Recipients are notified of potential transfusion related risks leading to opportunities for treatment and reduced secondary transmission.</p>
<b>ISSUE</b>	<b>FDA Response to Emergencies and Class I Recalls Affecting Blood Safety</b>
<b>NECESSARY STEPS</b>	<p>a) Finalize emergency procedures and develop checklists where useful;</p> <p>b) Train FDA staff;</p> <p>c) Systematically evaluate FDA's response to blood emergencies to assure that the process functioned smoothly and appropriately; and</p> <p>d) Early decisions on Class I product recalls</p>
<b>OUTCOME</b>	<p>a) Increase speed, efficiency, and coordination of FDA response to an emergency affecting blood safety, and</p> <p>b) Enhanced public health protection in the face of threats to blood safety.</p>
<b>ISSUE</b>	<b>Monitoring and Increasing the Blood Supply</b>
<b>NECESSARY STEPS</b>	<p>a) Monitor the blood supply;</p> <p>b) Encourage more donations by eligible donors;</p> <p>c) Improve donor relations as part of recruitment and retention;</p> <p>d) Remove restrictions to safe donation; and</p>

	e) Address economic issues facing the blood industry.
<b>OUTCOME</b>	a) Improve the ability to predict and respond to blood shortages; and b) Increase the availability and elasticity of the blood supply.

**(c). Blood Establishment Registration and Product Listing (BER)**

- All owners or operators of establishments that manufacture blood products are required to register with the FDA, pursuant to section 510 of the Federal Food, Drug, and Cosmetic Act, unless they are exempt under 21 CFR 607.65.
- A list of every blood product manufactured, prepared, or processed for commercial distribution must also be submitted.
- Products must be registered and listed within 5 days of beginning operation, and annually between November 15 and December 31.
- Blood product listings must be updated every June and December.

**(d). Electronic Blood Establishment Registration (eBER) Public Query application.**

- Blood establishments located outside of the United States that import or offer for import blood products into the U.S. are required to register with FDA.
- The name of the United States agent, the name of each importer, and each person who imports or offers for import these blood products must also be provided.
- Form FDA-2830, Blood Establishment Registration and Product Listing, is used for submission of registration and product listing information to the FDA.
- The form (and accompanying instructions) may be downloaded to complete and submit by mail. Alternatively, the information may be submitted electronically. Instructions for completing the electronic form are available.

**B. Devices**

- The Center for Biologics Evaluation and Research (CBER) regulates the medical devices involved in the collection, processing, testing, manufacture and administration of licensed blood, blood components and cellular products.
- CBER also regulates all HIV test kits used to screen donor blood, blood components and cellular products, and to diagnose, treat and monitor persons with HIV and AIDS.
- CBER has developed a Device Action Plan to facilitate the device provisions of the 1997 Food and Drug Administration Modernization Act and to ensure consistency between the policies and procedures of CBER and FDA's Center for Devices and Radiological Health.

**(a). 2006 Biological Device Application Approvals**

Tradename	Description and Indication for Device	Number	Applicant	Approval Date
<u>HLA Visual Software version 1.0</u>	Accessory for the evaluation of test results from One Lambda Inc products for molecular typing and antibodies detection	BK050070	One Lambda, Inc 21001 Kittridge St. Canoga Park CA 91303	1/30/2006
<u>HLATools Software Version 1.0</u>	To aid in assigning Major and /or Minor Histocompatibility Compexes	BK050071	One Lambda, Inc 21001 Kittridge St. Canoga Park CA 91303	1/30/2006
<u>Pall Acrodose PL System</u>	Intended to be used to pool and store whole-blood-derived, leukocyte-reduced platelets in the CLX HP extended storage bag for up to 5 days	BK050074	Medsep Corporation 19 Pepperwood Lane Pepper Pike, OH 44124	1/26/2006
<u>ThromboType (HPA 1-6, 15) and ThromboType 1 (HPA 1)</u>	Alternatives to platelet serological testing and an adjunct to HLA matching in selecting compatible platelets for recipients	BK050040	GTI, INC 20925 Crossroads Circle Waukesha, WI 53186	1/20/2006
Genetic Systems HbsAg EIA 3.0 Ortho Assay Protocol Disk	Contains the pipetting parameters and analysis algorithms for Ortho Assay Software and/or processing method for the Ortho Summit Processor to run Bio-Rad's Genetic Systems HBsAg EIA 3.0, the assay specified on the disk label	BK050046	Ortho-Clinical Diagnostics, Inc 1001 U.S. Highway 202 P.O. Box 350 Raritan, NJ 08869-0606	1/13/2006

### C. Vaccines

- The Center for Biologics Evaluation and Research (CBER) regulates vaccine products. Many of these are childhood vaccines that have contributed to a significant reduction of vaccine-preventable diseases.
- According to the Centers for Disease Control and Prevention, vaccines have reduced preventable infectious diseases to an all-time low and now few people experience the devastating effects of measles, pertussis and other illnesses.
- Vaccines, as with all products regulated by FDA, undergo a rigorous review of laboratory and clinical data to ensure the safety, efficacy, purity and potency of these products.
- Vaccines approved for marketing may also be required to undergo additional studies to further evaluate the vaccine and often to address specific questions about the vaccine's safety, effectiveness, or possible side effects.
- CBER and the Centers for Disease Control & Prevention (CDC) jointly manage the Vaccine Adverse Event Reporting System (VAERS), a cooperative program for vaccine safety.

- VAERS is a post-marketing safety surveillance program, collecting information about adverse events (side effects) that occur after the administration of US licensed vaccines.
- Reports to the VAERS program are welcome from all concerned individuals:
- Patients, parents, health care providers, pharmacists, and vaccine manufacturers.

## **D. Cellular Therapy**

- Recent discoveries in cellular therapy research present new opportunities for cellular products to be used in disease areas with critical, unmet medical needs. □ The Food and Drug Administration (FDA) regulates cellular therapies to ensure that they are safe and effective, and that persons enrolled in clinical trials using cellular products are protected from undue risk.
- Cellular products come from a variety of sources, such as stem cells from bone marrow and peripheral blood, and myoblasts from skeletal muscle cells.
- FDA is committed to supporting cellular therapy research and development, and future licensure of cellular products, and wants the public to understand both the promise and the challenges presented by this exciting new therapy.

### **(a). Role of FDA**

- The Food and Drug Administration (FDA) has a long history of effectively safeguarding the public health and strong experience in regulating drugs and biological products.
- FDA's regulatory framework is based, in part, on manufacturing procedures, the use of investigational devices in some studies, the different use of cellular products, and safety concerns associated with administration of these products.
- FDA's main priority is to ensure safe human cellular therapy studies.
- FDA will hold future BRMAC meetings to discuss the regulatory issues associated with late phase clinical development of these cellular products.

## **E. Tissue**

- Human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient is regulated as a human cell, tissue, and cellular and tissue-based product or HCT/P.
- The Center for Biologics Evaluation and Research (CBER) regulates HCT/Ps under 21 CFR Parts 1270 and 1271.
- Examples of such tissues are bone, skin, corneas, ligaments, tendons, dura mater, heart valves, hematopoietic stem/progenitor cells derived from peripheral and cord blood, oocytes and semen.
- CBER does not regulate the transplantation of vascularized human organ transplants such as kidney, liver, heart, lung or pancreas.
- The Health Resources Services Administration (HRSA) oversees the transplantation of vascularized human organs.

## **F. Xenotransplantation Action Plan**

- Xenotransplantation is any procedure that involves the transplantation, implantation, or infusion into a human recipient of either live cells, tissues, or organs from a nonhuman animal source, or Human body fluids, cells, tissues or organs that have had ex vivo contact ith live nonhuman animal cells,

tissues or organs.

- The development of xenotransplantation is, in part, driven by the fact that the demand for human organs for clinical transplantation far exceeds the supply.

**(a). Purpose**

To provide a comprehensive approach for the regulation of xenotransplantation that addresses the potential public health safety issues associated with xenotransplantation and to provide guidance to sponsors, manufacturers and investigators regarding xenotransplantation product safety and clinical trial design and monitoring.

**G. Human Gene Therapy and the Role of FDA**

- One of the most exciting and highly publicized areas in biomedical research today is human gene therapy - the replacement of a person's faulty genetic material with normal genetic material to treat or cure a disease or abnormal medical condition.
- Over time and with proper oversight, human gene therapy might become an effective weapon in modern medicine's arsenal to help fight diseases such as cancer, diabetes, high blood pressure and heart disease.
- The FDA's authority includes any human gene therapy product sold in the United States.

**(a). FDA's Role With Regard To Human Gene Therapy**

- FDA's Center for Biologics Evaluation and Research (CBER) regulates human gene therapies, which fall under the legal definition of a "biologic."
- Manufacturers of gene therapy products must test their products extensively and meet FDA requirements for safety, purity and potency before they can be sold in the United States.
- A manufacturer who is considering selling a gene therapy product in the United States first must tell FDA of its intentions, and then must test the product in a laboratory and then in research animals.
- When a manufacturer is ready to study the gene therapy product in humans, it must obtain a special permission exemption from FDA before starting.
- This exemption is called an investigational new drug application or (IND).
- In the IND, the manufacturer explains how it intends to conduct the study, what possible risks may be involved and what steps it will take to protect patients, and provides data in support of the study.
- As part of the IND process, the manufacturer also must get approval from a committee of scientific and medical advisors and consumers (called an Institutional Review Board), which focuses on protecting persons who may participate in the study.
- FDA has not yet approved for sale any human gene therapy product.
- However, gene-related research and development is continuing to grow and FDA is very involved in overseeing this activity.
- Since 1989, FDA has received about 300 requests from medical researchers and manufacturers to study gene therapy and to develop gene therapy products.
- Presently, FDA is overseeing approximately 210 active IND gene therapy studies.

## **H. Allergenics**

- Patch test used to diagnose the cause of contact dermatitis.
- Prior to release standardized products are compared with US reference std. for potency.
- CBER maintains these ref. std. and distributes them.
- There are currently 19 standardized allergenic extracts available.

## **B) CDRH**

It is Center for Devices and Radiological Health which,

- To makes sure that new medical devices are safe and effective before they are marketed.
- The center also monitors devices throughout the product life cycle, including a nationwide postmarket surveillance system.
- And it assures that radiation-emitting products, such as microwave ovens, TV sets, cell phones, and laser products meet radiation safety standards.

Many of these devices are the first of a kind, such as a robotic arm that can operate a variety of surgical tools with tremendous precision. Other high-tech devices are designed to prevent, diagnose or treat cancer, heart disease, impaired vision and hearing, and other health problems.

In the near future, CDRH will be challenged to resolve complex issues connected with emerging technological and demographic developments, including:

- Diagnosis and treatment options related to the human genome project
- Radiation safety issues, including those associated with new medical imaging technologies
- Breakthrough devices using artificial intelligence, nanotechnology and robotics
- Special needs of our aging population for prosthetics, cardiac interventions, and home health care.

## **C) CDER**

- CDER does not test drugs, although the Center's Office of Testing and Research does conduct limited research in the areas of drug quality, safety, and effectiveness.
- It is the responsibility of the company seeking to market a drug to test it and submit evidence that it is safe and effective.
- Under current law, all new drugs need proof that they are effective and safe before they can be approved for marketing.

- No drug is absolutely safe; there is always some risk of an adverse reaction. CDER decides--as quickly as a thorough evaluation allows--whether the studies submitted by the drug's sponsor (usually the manufacturer) show it to be safe and effective for its intended use.
- When a proposed drug's benefits outweigh known risks, CDER considers it safe enough to approve.
- From aspirin to cancer treatments drugs, CDER regulates products like fluoride toothpaste, dandruff shampoos and sunscreens.
- However, in case of disaster( disease like AIDS, cancer) or terrorists attack, FDA has established programs to allow patients who have exhausted standard therapeutic options may be willing to accept additional risks and potentially dangerous side effects from drug products still under study, these programs allow patients access to investigational drugs.

### **Drug information provided by CDER**

The following types of drug information is provided by CDER.

- New Prescription Drug Approvals
- Prescription Drug Information
- Drug Information Pathfinder
- Major Drug Information Pages
- Consumer Drug Information
- Over-the-Counter Drug Information
- Drug Safety & Side Effects
- Drug Preparedness and Bioterrorism Response
- Clinical Trials Information
- Public Health Alerts & Warning Letters
- Reports and Publications
- Special Projects & Programs

### D) CFSAN

The Center for Food Safety and Applied Nutrition, known as CFSAN, is one of six product-oriented centers, in addition to a nationwide field force, that carry out the mission of the Food and Drug Administration (FDA).

The mission of CFSAN is in conjunction with the Agency's field staff, is responsible for promoting and protecting the public's health by ensuring that the nation's food supply is safe, sanitary, wholesome, honestly labeled, and that cosmetic product is safe and properly labeled.

Scope of responsibility of CFSAN is,

- The safety of substances added to food, e.g., food additives (including ionizing radiation) and color additives

- The safety of foods and ingredients developed through biotechnology
- Seafood hazard analysis and critical control point (**HACCP**) regulations
- Regulatory and research programs to address health risks associated with food borne chemical, and biological contaminants
- Regulations and activities dealing with the proper labeling of foods (e.g., ingredients, nutrition health claims) and cosmetics
- Regulations and policy governing the safety of dietary supplements, infant formulas, and medical foods
- Safe and properly labeled cosmetic ingredients and products
- Food industry postmarket surveillance and compliance
- Consumer education and industry outreach
- Cooperative programs with state and local governments
- International food standard and safety harmonization efforts

Some of caftan's current areas of food safety concern are:

- Biological pathogens (e.g., bacteria, viruses, parasites)
- Naturally occurring toxins (e.g., mycotoxins, ciguatera toxin, paralytic shellfish poison)
- Dietary supplements (e.g., ephedra)
- Pesticide residues
- Toxic metals (e.g., lead, mercury)
- Decomposition and filth (e.g., insect fragments)
- Food allergens (e.g., eggs, peanuts, wheat, milk)
- Nutrient concerns (e.g., vitamin d overdose, pediatric iron toxicity)
- Dietary components (e.g., fat, cholesterol)
- Radionuclides
- Tse-type diseases (e.g., chronic wasting disease in elk)
- Product tampering

## E) CVM

The FDA's Center for Veterinary Medicine (CVM) affects millions of consumers by helping to assure that animal food products are safe. Its prime aim is to Safeguarding animal health to protect consumers.

CVM also evaluates the safety and effectiveness of drugs used to treat more than 100 million companion animals. Nearly 300 drugs currently on the market have been approved by the FDA for America's dogs, cats and horses.

CVM has two top priorities:

- Prevent the establishment of bovine spongiform encephalopathy (BSE), "mad cow disease."
- Counter the risk of antibiotic resistance in humans from food animals.

The Center for Veterinary Medicine (CVM) regulates the manufacture and distribution of food additives and drugs that will be given to animals.

- These include animals, from which human foods are derived, as well as food additives and drugs for pet (or companion) animals.
- CVM is responsible for regulating drugs, devices, and food additives given to, or used on, over one hundred million companion animals, plus millions of poultry, cattle, swine, and minor animal species. (Minor animal species include animals other than cattle, swine, chickens, turkeys, horses, dogs, and cats.)

## F) NCTR

All of the research performed at the National Center for Toxicological Research is targeted to fulfill three strategic research goals in support of FDA's public health mission.

The mission of the National Center for Toxicological Research is to conduct peer-reviewed scientific research that supports and anticipates the FDA's current and future regulatory needs.

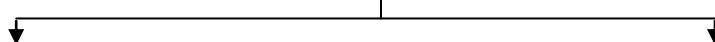
This involves fundamental and applied research specifically designed to define biological mechanisms of action underlying the toxicity of products regulated by the FDA.

This research is aimed at understanding critical biological events in the expression of toxicity and at developing methods to improve assessment of human exposure, susceptibility and risk.

The Center's goals include:

- Developing new strategies and methods to test/predict toxicity and assess/detect risk for FDA-regulated products, both new and those already on the market (**Risk Assessment for Regulated Products**).
- Developing computer-based systems (knowledge bases) that predict human risk to enhance the efficiency and effectiveness of premarket product reviews (**Knowledge Bases that Predict Human Toxicity**).
- Conducting research to understand mechanisms of toxicity, assess new product technology, and provide methods for use in FDA standards development and product risk surveillance (**Methods for Use in FDA Standard Development and Product Risk Surveillance**).

NCTR includes



CENTRE OF EXCELLENCE	NCTR RESEARCH DIVISION
<ul style="list-style-type: none"> <li>• Center for Toxicoinformatics</li> <li>• Center for Phototoxicology</li> <li>• Center for Functional Genomics</li> <li>• Center for Structural Genomics</li> <li>• Center for Hepatotoxicology</li> <li>• Center for Metabolomics</li> <li>• Center for Proteomics</li> </ul>	<ul style="list-style-type: none"> <li>• Biometry and Risk Assessment</li> <li>• Biochemical Toxicology</li> <li>• Genetic and Reproductive Toxicology</li> <li>• Microbiology</li> <li>• Molecular Epidemiology</li> <li>• Neurotoxicology</li> <li>• Systems Toxicology      Veterinary Services</li> </ul>

## G)OC

The Office of the Commissioner is made up of several components (organizational chart),

- Ethics Program
- Good Clinical Practice Program
- History Office
- Office of Combination Products
- Office of Crisis Management
- Office of Equal Employment Opportunity and Diversity Management
- Office of Financial Management
- Office of International Programs
- Office of the Ombudsman
- Office of Orphan Products Development
- Office of Pediatric Therapeutics
- Office of Planning
- Office of Policy
- Office of Public Affairs
- Office of Special Health Issues
- Office of Women's Health

## G) ORA

Office of Regulatory Affairs ensure that FDA regulated products comply with appropriate public health laws and regulations.

ORA specialists compromise of,

- Consumer safety Officers (CSO) and Inspectors conduct domestic and foreign inspections a year to ensure that regulated products destined for the US market meet the agency's standards. Plants are inspected both before the FDA approves a product to make sure that the firm has the capacity for high-quality production and periodically afterwards, to ascertain that it follows appropriate manufacturing processes. CSO also monitor clinical trials.
- Scientists in ORA's laboratories analyze product samples to determine their adherence to the FDA's standards. Products (domestic as well as foreign) that do not measure up to FDA standards are not allowed on the U.S. market.
- Public affairs specialists reach out to consumer groups, health care professionals, and state health authorities to explain FDA policies and encourage compliance with FDA standards. In addition to briefing interested groups and responding to press inquiries, these specialists work together with the rest of the field staff to rapidly respond to public health emergencies caused by natural disasters and product problems.

Compliance strategies of ORA includes,

- Providing information to industry
- Highlighting areas of significant violations and impact on public health
- Prioritizing and targeting high-risk areas
- Cooperating with state and local public health authorities and regulators

- Focusing on covering products imported into the US through border coverage and foreign inspections.

## H) COSMETICS

FDA is only able to regulate cosmetics after products are released to the marketplace. Neither cosmetic products nor cosmetic ingredients (except color additives) are reviewed or approved by FDA before they are sold to the public.

Includes,

- I) Animal Testing for Cosmetic Products
- II) Inspection of Cosmetics
- III) Shelf life
- IV) Federal Food, Drug, and Cosmetic Act (FD&C Act) and
- V) Fair Packaging and Labeling Act (FPLA)

## **2)LAWS ENFORCED BY FDA**

- Federal Food, Drug, and Cosmetic Act
- Food and Drug Administration Modernization Act (FDAMA)
- Infant Formula Act of 1980
- Orphan Drug Act
- Drug Price Competition and Patent Term Restoration Act of 1984
- Medical Device Amendments of 1992
- Prescription Drug User Fee Act (PDUFA) of 1992
- Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994
- Dietary Supplement Health and Education Act of 1994
- Food and Drug Administration Modernization Act (FDAMA) of 1997
- Best Pharmaceuticals for Children Act
- Medical Device User Fee and Modernization Act (MDUFMA) of 2002
- Animal Drug User Fee Act of 2003 PDF
- Minor Use and Minor Species Animal Health Act of 2004
- Food Allergen Labeling and Consumer Protection Act of 2004
- Federal Anti-Tampering Act
- Sanitary Food Transportation Act
- Mammography Quality Standards Act (MQSA)
- Bioterrorism Act of 2002
- Public Health Service Act
- Trademark Act of 1946
- Controlled Substances Import and Export Act
- Egg Products Inspection Act
- Lead-Based Paint Poisoning Prevention Act
- Federal Advisory Committee Act
- Government in the Sunshine Act
- Government Patent Policy Act of 1980

- Federal Anti-Tampering Act
- Sanitary Food Transportation Act
- Mammography Quality Standards Act (MQSA)
- Bioterrorism Act of 2002 Project BioShield Act of 2004

### **3)FDA ADVISORY COMMITTEES**

#### **Office of the Commissioner**

Science Board to the FDA

Risk Communication Advisory Committee

Pediatric Advisory Committee

#### **Center for Biologics Evaluation and Research**

Allergenic Products Advisory Committee

Cellular, Tissue, and Gene Therapies Advisory Committee

Blood Products Advisory Committee

Transmissible Spongiform Encephalopathies Advisory Committee

Vaccines and Related Biological Products Advisory Committee

#### **Center for Drug Evaluation and Research**

Anesthetic and Life Support Drugs Advisory Committee

Anti-Infective Drugs Advisory Committee

Antiviral Drugs Advisory Committee

Arthritis Advisory Committee

Cardiovascular and Renal Drugs Advisory Committee

Dermatologic and Ophthalmic Drugs Advisory Committee

Drug Safety and Risk Management Advisory Committee

Endocrinologist and Metabolic Drugs Advisory Committee

Gastrointestinal Drugs Advisory Committee

Nonprescription Drugs Advisory Committee

Oncologic Drugs Advisory Committee

Peripheral and Central Nervous System Drugs Advisory Committee

Pharmaceutical Science, Advisory Committee for

Psychopharmacologic Drugs Advisory Committee

Pulmonary-Allergy Drugs Advisory Committee

Reproductive Health Drugs, Advisory Committee for

#### **Center for Food Safety and Applied Nutrition**

Food Advisory Committee - Full Committee and Subcommittees

### **4)FDA STRATEGIC PLAN**

- Efficient Risk Management
- Improving Health Through Better Information
- Improving Patient and Consumer Safety
- Protecting America From Terrorism
- More Effective Regulation Through a Stronger Workforce

#### **I) EFFICIENT RISK MANAGEMENT**

- The Most Public Health Bang for Our Regulatory Buck

- Use science-based, efficient risk management in all agency regulatory activities, so that the agency's limited resources can provide the most health promotion and protection at the least cost for the public.
- Enforcement: Targeting Limited Resources for Maximum Protection
- New Drug Development: A Need for Greater Productivity
- Manufacturing: Need for Greater Efficiency in Producing Safe and Effective Medical Products
- Imports: Need for Safety Oversight to Catch Up to Quantum Growth in Volume of Entries
- Foods: Foodborne Disease Remains a Major Public Health Threat
- Objective 1 -- Provide timely, high quality, cost-effective process for review of new technologies/premarket submissions.
- Objective 2 -- Provide high quality, cost-effective oversight of industry manufacturing, processing and distribution to reduce risk.
- Objective 3 -- Assure the safety of the U.S. food and cosmetics supply to protect consumers at the least cost for the public.
- Objective 4 -- Develop methodological strategies and analyses to evaluate options, identify the most effective and efficient risk management strategies, and optimize regulatory decision-making.

## **II) EMPOWERING CONSUMERS: IMPROVING HEALTH THROUGH BETTER INFORMATION**

Empowering Consumers: Improving Health Through Better Information able consumers to make smarter decisions by getting them better information to weigh the benefits and risks of FDA-regulated products.

- Objective 1 – Develop an FDA-wide consumer communications infrastructure.
- Objective 2 – Enhance the FDA's efforts to help ensure that industry communications to consumers and health care providers are truthful and not misleading, provide information about product risks and benefits, and appropriately convey the degree of scientific uncertainty associated with such product messages.
- Objective 3 -- Improve and increase FDA-initiated health benefit-risk information

## **III) IMPROVING PATIENT AND CONSUMER SAFETY**

- Objective 1. Enhance the ability to quickly identify risks associated with FDA-regulated products.
- Objective 2. Increase capacity to accurately analyze risks associated with medical products, dietary supplements, and foods.
- Objective 3. Take appropriate actions to communicate risks and correct problems associated with medical products, dietary supplements and foods.

## **IV) PROTECTING AMERICA FROM TERRORISM**

- Objective 1. Facilitate the development and availability of medical countermeasures to limit the effects of a terrorist attack on the civilian or military populations.
- Objective 2. Enhance the agency's emergency preparedness and response capabilities to be better able to respond in the event of a terrorist attack.

- Objective 3. Ensure the safety and security of FDA personnel, physical assets, and sensitive information.
- Objective 4. The FDA must uphold its responsibility for ensuring the safety of approximately 80 percent of the nation's food supply.
- Objective 5. Protect the safety and security of human drugs, biologics (vaccines, blood and blood products, gene therapy, human tissues, and cellular therapies), medical devices (including radiation-emitting and screening devices), veterinary drugs, and other FDA-regulated products.

## **V) MORE EFFECTIVE REGULATION THROUGH A STRONGER WORKFORCE**

Ensure a world-class professional workforce, effective and efficient operations, and adequate resources to accomplish the agency's mission.

- Objective 1 -- Ensure a high quality, diverse and motivated workforce.
- Objective 2 -- Increase efficiency and effectiveness of agency management.
- Objective 3 -- Ensure effective communication and working relationships with key external stakeholders to enhance U.S. and global health outcomes.
- Objective 4 -- Transition Information technology from an enabler to a strategic tool for realizing the FDA's policy goals and objectives.
- Objective 5 -- Provide a consolidated FDA headquarters campus to improve operations for employees.

## **VI) FDA CUSTOMER SERVICE STANDARDS**

- All FDA customers are entitled to:
  - Fair, courteous and professional treatment;
  - Information that is accurate and current;
  - Timely responses to requests;
  - Reasonable access to appropriate staff;
  - Confidence that efforts are made to assure that regulated products in the marketplace are in compliance with FDA laws and regulations;
  - Two-way communication;
  - Opportunities for collaboration and partnerships, as appropriate;
  - Participation in the agency's decision-making process; and
  - Consideration of their opinions and concerns by the agency.
- In addition,
- Consumers are entitled to:
  - Accurate and timely health information about regulated products.
  - Health professionals are entitled to:
  - Timely information that will assist them in advancing and protecting the public health.
  - Other government agencies are entitled to: Regulated industry is entitled to: Timely review of product applications;
  - Professional treatment in resolving disputes;
  - Fair application of laws and regulations in enforcement activities;
  - Fair and consistent inspections and product application reviews.
  - Respect in the agency's performance of duties and responsibilities.

## **HOW TO PREPARE FOR US FDA INSPECTION**

Elaborate preparations are necessary during an FDA inspection. Before the inspections, the units should conduct internal audits and analyze quality data - deviations, OOS, rejects etc. Management has to review all the processes and systems. Training to key staff, review of SOPs, following procedures and monitoring processes and analysis of complaints etc. are a must as part of the preparation.

Before the FDA team arrives, ensure necessary regulatory follow-ups are done. Discarding of warning letters may render all products unacceptable and finding of significant deficiencies can result in discontinuation of inspection and issuance of further warning letters. Findings like all systems are not compliant and follow-up could result in further enforcement action and freezing of products in pipeline.

Ideally, create a company statement on audit behavior, be honest with the team and cooperate with them. Train personnel to answer the question directly and concisely. Be careful not to volunteer information and if you are unsure of the answer, do not guess. The procedure for responding to FDA activities includes prompt supply of photographs, electronic data, entering controlled areas and sampling. Identify the inspection team members, and define their roles and responsibilities (including back-up) like receptionist, trained facilitators and employees, note takers and subject experts.

Identify the logistics of the inspection, especially Who?, What?and Where?

Develop a strategy to manage the inspection from acceptance of the FDA-482 (Notice of Inspection) to the inspection closeout.

During the inspection, ask for a scope of the audit, timeline, or agenda so that you can have key personnel available. Encourage a daily closeout discussion and have a clear understanding of issues. Attempt to address concerns and request the corrections appear clearly in the EIR. After FDA leaves each day, note takers should create a summary report for management review. Then prepare for the "next step" of the inspection, assure documents/items are ready and available. It is necessary to effectively control your documents, so that it is readily available on demand.

Monitor observations made by the team during the inspection and compare it with the observations listed on the FDA-483. During a FDA inspection, the management has to play a key role by meeting the investigators, periodically checking with investigators, facilitate any decisions, help and resolve conflicts concerning the application of company policies, review daily inspection memoranda, facilitate and participate in the close out meeting, review and assist in responding to the 483 etc.

At the end of inspection, accept the FDA-483 and check out whether all statements during inspection closeout are included in the EIR. This is the time to clarify any issues and identify any inaccuracies. Discuss them openly with the team, and promise a written response. The management should discuss the issues, communicate it, and should correct errors. Promise corrective actions and ensure the management is present and actively participating in the meetings. Also analyse, how many observations did you miss?

After the inspection, plan, discuss, and respond in writing to the FDA-483 and determine if a regulatory attorney or consultant should review the FDA-483 and the response before delivery. Assure that promises for corrective action can be reasonably met.

## **BUDGET AND FINANCE**

- The Office of Financial Management (OFM) oversees agency-wide budget formulation and execution, accounting, payment processing, financial reporting, and financial systems. It monitors and tracks the expenditure of an annual total budget of nearly one billion dollars, including three separate appropriations and four separate kinds of user fees. OFM pays over 80,000 invoices per year, and processes vendor payments of over \$133 million, with over \$62 million made via wire transfer. OFM develops, operates and maintains FDA's central financial systems, which are being continuously updated and improved.
- In 1996, OFM implemented a new open-budget execution process to allocate agency resources efficiently, increase management awareness of cost/benefit implications, provide incentives to reduce costs, and allow for increased financial flexibility to support unfunded high priority initiatives. This budget process is designed to identify the program goals, objectives, and performance measures that best support the agency's mission, support the management of agency resources in a collaborative and coordinated fashion, introduce sound management principles to the lowest accountable levels within the agency, and promote greater accountability for resource management.
- OFM helped the agency to withstand a 17 percent reduction in its operating budget in FY 1996 without having to execute a reduction-in-force. Also, resources were redistributed to support a number of key agency initiatives such as improving the review of food additive petitions, developing strategic systems, and helping to support the tobacco initiative. OFM continues to refine the budget formulation and execution process and determine how it can serve as a better vehicle for strategic planning.

## **COMBINATION PRODUCTS**

### **A)Definition**

Combination products are defined in 21 CFR 3.2(e). The term combination product includes:

- (1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- (2) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
- (3) A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product

would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

(4) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

## **B) Other Types of Combinations of FDA Regulated Products**

A combination product as defined in 21 CFR § 3.2(e), is a product comprised of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product .

Some products are used together in a way that does not meet the regulatory definition of a combination product, but that may raise similar development or regulatory issues.

These kinds of products may include the concomitant use of drugs, devices, and/or biological products that are not “individually specified” in the product labeling (see 21 CFR 3.2(e)(3)); and combinations of drugs, devices and/or biological products with other types of FDA-regulated articles, such as dietary supplements, cosmetics, or foods.

This website will provide links to information on recently approved products of this type and other related information in an effort to keep stakeholders informed.

### **-Examples of These Types of Products**

- FDA Approves First Head & Neck Cancer Treatment in 45 Years Data Shows Treatment with Erbitux Extends Survival
- Actonel with Calcium Supplements
- Vectibix (panitumumab) and EGFR pharmDx(r) Test Kit
- DakoCytomation's c-Kit (9.7) pharmDx and Gleevec

## **C) Examples of Combination Product Approvals**

The following is a listing of example combination product approvals.

- FDA Approves Neupro Patch for Treatment of Early Parkinson's Disease
- FDA Approves Methylphenidate Patch to Treat Attention Deficit Hyperactivity Disorder in Children
- FDA Approves Emsam (Selegiline) as First Drug Patch for Depression
- FDA Approves First Ever Inhaled Insulin Combination Product for Treatment of Diabetes
- Absorbable Collagen Sponge with Genetically Engineered Human Protein
- Device - biological product gel for surgical hemostasis
- Iontophoretic transdermal system for fentanyl
- Dermal Iontophoresis System
- Surgical Mesh with Antibiotic Coating
- Antibiotic Bone Cement<sup>14</sup>

- Iontophoretic Drug Delivery Patch and Controller
- Methylaminolevulinate Cream with Halogen Light Source

## **APPROVALS OF FDA-REGULATED PRODUCTS**

Approval information by product type

### **-Drugs**

Human drugs and therapeutic biologicals (proteins and other products derived from living sources used for therapeutic purposes)

- [Drug Approval Reports by Month](#)
- [Drugs@FDA](#)
- [Postmarket Drug Safety Information for Patients and Providers](#)
- [Prescription Drug User Fee Act \(PDUFA\)](#)

### **Biological Products**

Vaccines, tissue, blood, and other products derived from living sources

- [Biologics Products & Establishments](#) -

### **Medical Devices**

Instruments or products used for treating or diagnosing disease (such as thermometers, artificial hearts, and home pregnancy test kits)

- [Device Approvals and Clearances](#)
- [Recently-Approved Devices](#)
- [Medical Device User Fee and Modernization Act \(MDUFMA\)](#)

### **Animal Drugs**

- [Animal Drugs @ FDA](#)
- [Animal Drug User Fee Act \(ADUFA\)](#)
- [Animal Generic Drug User Fee Act \(AGDUFA\)](#)

### **Food Additives**

- [Food and Color Additives: Final Rules by Year](#)

## **ABOUT FDA PRODUCT APPROVAL**

The Food and Drug Administration's regulatory approaches to marketing approval of the products it regulates are as varied as the products themselves. These differences are dictated by the laws FDA enforces and the relative risks that the products pose to consumers.

Some products — such as new drugs and complex medical devices — must be proven safe and effective before companies can put them on the market. The agency also must approve new food additives before they can be used in foods. Other products — such as x-ray machines and microwave ovens -- must measure up to performance standards. And some products — such as cosmetics and dietary supplements — can generally be marketed with no prior approval.

At the heart of all FDA's medical product evaluation decisions is a judgment about whether a new product's benefits to users will outweigh its risks. No regulated product is totally risk-free, so these judgments are important. FDA will allow a product to present more of a risk when its potential benefit is great — especially for products used to treat serious, life-threatening conditions.

FDA reviews the results of laboratory, animal and human clinical testing done by companies to determine if the product they want to put on the market is safe and effective. FDA does not develop or test products itself. The Agency does this pre-market review for new human drugs and biologics (such as vaccines, blood products, biotechnology products and gene therapy), complex medical devices, food and color additives, infant formulas, and animal drugs.

FDA has streamlined its review process for medical products in recent years to help speed important new treatments to patients. For example, the average review time for an innovative new drug is now only 6 months, and some have been approved even faster.

### **What is the approval process for a new prescription drug?**

Drug companies seeking FDA approval to sell a new prescription drug in the United States must test it in various ways. First are laboratory and animal tests. Next are tests in humans to see if the drug is safe and effective when used to treat or diagnose a disease.

After testing the drug, the company then sends FDA an application called a New Drug Application (NDA). Some drugs are made out of biologic materials. Instead of an NDA, new biologic drugs are approved using a Biologics License Application (BLA). Whether an NDA or a BLA, the application includes

- the drug's test results
- manufacturing information to demonstrate the company can properly manufacture the drug
- the company's proposed label for the drug. The label provides necessary information about the drug, including uses for which it has been shown to be effective, possible risks, and how to use it.

If a review by FDA physicians and scientists shows the drug's benefits outweigh its known risks and the drug can be manufactured in a way that ensures a quality product, the drug is approved and can be marketed in the United States.

## **FDA IMPORT PROCESS PROCEDURES**

### **1)Understanding How FDA Processes Imported Products**

All FDA regulated products that are imported into the U.S. must meet Bureau of Customs and Border Protection (Customs) requirements in addition to FDA's.

If it **appears** from the "**examination of samples or otherwise**" that the product may be adulterated, or misbranded, or unapproved, or not permitted entry into the U.S., then FDA may **detain** it upon entry. If the apparent violation is not overcome (with evidence) FDA will ordinarily **refuse admission** to the detained medical device. When FDA refuses admission to a medical device, the law requires that it be destroyed, unless it is exported within 90 days of the date of FDA's refusal of admission.

### **2)The Entry**

The FDA import process begins with the importer or customs broker submitting the necessary entry information to the local Customs port office. Most entries are filed electronically. Customs forwards the electronic data to FDA for that agency to conduct its review.

### **3)FDA Detentions**

FDA's regulations authorize FDA to detain an imported product under FDA jurisdiction if it appears to be out of compliance with the law. If a product appears to be out of compliance, the FDA district office will issue a "Notice of FDA Action" to the importer of record, the owner, consignee and the customs broker. The Notice will specify the nature of the violation and cite the relevant statutory provision. Under the Food Drug and Cosmetic Act, the owner or consignee of an imported product is entitled by law to an informal hearing during which he may provide testimony to FDA regarding the admissibility of the product.

### **4)FDA Refusals of Admission**

If an importer fails to overcome the appearance of a violation on an FDA detained entry, or fails to respond to FDA within the time frame, FDA will ordinarily refuse admission to the product and issue an **FDA Refusal of Admission**. If a product is refused by FDA, it must be exported or destroyed within 90 days of the date of the refusal.

### **5)FDA Examinations or Sampling for Analysis**

Upon entry of an FDA regulated product, FDA may examine the product to assure it complies with all applicable requirements. When this occurs, FDA will issue a notice of examination or sampling to the importer of a record, again on a form titled "Notice of FDA Action."

### **6)Reconditioning or Relabeling**

Under certain conditions, the importer of record of an FDA-detained product is given an opportunity to submit an application for authorization to bring the product into compliance with the Food Drug & Cosmetic Act by reconditioning or relabeling it.

## **IMPORT FOR EXPORT**

Import for Export can be located in the Regulatory Procedures Manual (RPM). The Regulatory Procedures Manual is a reference manual for FDA personnel. It provides FDA personnel with information on internal procedures to be used in processing domestic and import regulatory and enforcement matters. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public

- [Regulatory Procedures Manual](#)

## **CHALLENGES FACED BY FDA**

Today, more than ever, FDA needs to respond to a rapidly changing world. There are many obstacles to overcome if we are to continue our high standards of consumer protection.

The most important of these challenges are:

### **A) SCIENTIFIC BREAKTHROUGHS**

- FDA scientists will need to keep up with rapidly- advancing technologies in all product areas.
- More sophisticated products
- These technologies will translate into products with new complexities and risks.

### **B) NEW PUBLIC HEALTH THREATS**

We'll need to be prepared to respond rapidly to unexpected health risks, such as the threat of terrorism, tougher strains of antibiotic-resistant bacteria or more dangerous foodborne illnesses.

### **C) INTERNATIONAL COMMERCE**

Monitoring of imports and cooperation with foreign regulators will become more important as international commerce continues to grow.

### **D) CONSUMER INFORMATION**

Finally, today's sophisticated consumers and the wide availability of information about FDA-regulated products will challenge us to be sure consumers are getting the information they need from the right sources.

### **E) WORKING WITH PARTNER TO MEET CHALLENGES**

- As we respond to these challenges and future challenges, we will be changing our ways of doing business while maintaining our high standards for consumer protection.
- We will work more collaboratively with our partners in government, industry, health professions, and educational institutions. We are also asking these partners and the general public what they think about how FDA can do a better job.

## **REFERENCE**

[www.fda.gov](http://www.fda.gov)

[www.hhs.gov](http://www.hhs.gov)

## **STUDY QUESTIONS**

### **August 2007**

what are the centers and office of USFDA to satisfy its mission toward quality and safety of food and medicines in USA.

what USFDA does not regulate? what is strategic plan to achieve its mission? Compare this system and scope to be applicable by Indian FDA

### **September 2006**

Classify the centers which the department of health and human services are regulated in USA through FDA. Compare the system and scope with Indian FDA. Under small business assistance programme how will you file an application for marketing new drug in USA?

Major activities regulated by CDER?

Product regulated by CBER?

International pharmacopoeia activities are governed by USFDA. Write a note

### **September 2005**

What CBER regulate. How blood and blood product are regulated.