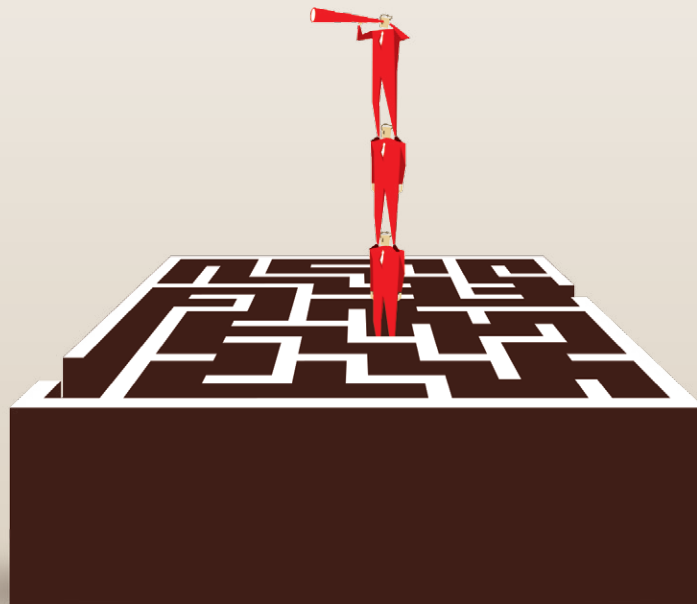


Working with Regulators A Focus on the FDA

Based on the educational program of the
Cancer Policy Institute at the Cancer Support Community
In partnership with Uniting a Community (UaC)
Policy, Advocacy, Education and Action Network



September 15, 2015

A Toolkit for Advocates

The Cancer Policy Institute *at the* 
CANCER SUPPORT COMMUNITY

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ABOUT THE CANCER SUPPORT COMMUNITY

The Cancer Support Community (CSC) is an international nonprofit dedicated to providing support, education and hope to people affected by cancer. CSC offers a menu of personalized services and education for all people affected by cancer. Its global network brings the highest quality cancer support to the millions of people touched by cancer. These support services are available through a network of professionally-led, community-based centers, hospitals and community oncology practices as well as online at www.cancersupportcommunity.org and over the phone at 1.888.793.9355, so that no one faces cancer alone.

I. Introduction

“The leaders of the FDA want to learn from patients and the advocacy community. They want to have the conversation with you.”

–Linda House, MSM, BSN, RN, President, Cancer Support Community

Working with Regulators: A Focus on the FDA is the second in a series of meetings hosted by the Cancer Policy Institute at the Cancer Support Community in partnership with the members of Uniting a Community. The goal of these seminars is to provide patient advocates with usable information about how to access, work with and have an impact on the regulatory process. The focus is on providing basic information on the U.S. Food and Drug Administration’s (FDA’s) organization, operations and interactions with Congress and the health care community.

The regulatory world is increasingly complex and interactions should be driven by evidence. There is still a powerful role for patient testimonials, but today the individual voice must be elevated to a collective voice that addresses the key factors that determine how decisions are made and policy is implemented. It is critical to have a working knowledge of the agencies making these decisions as well as the skills and resources to interact successfully with the regulators and the process.

This is particularly important when dealing with the FDA, a huge and very influential agency charged with assuring that drugs and medical devices are safe and effective before they are made available and marketed to the American public. The FDA is currently engaged in or involved with a number of programs and initiatives designed to improve that process and to accelerate the rate at which promising new therapies become accessible to patients who need them. The agency is also on the cusp of several key congressional decisions related to clinical research and the upcoming reauthorization of user fees.

THIS TOOLKIT PROVIDES BASIC INFORMATION ABOUT:

- The roles and responsibilities of the FDA.
- The FDA’s organization and how to access decision makers.
- Key initiatives that are changing how patients access new therapies.
- The FDA and Congress.
- Advocacy.
- Resources for working with the FDA.

II. The FDA 101

“The FDA wants what you want—safe, effective therapies. They are not there to say no. Slamming the FDA is not helpful. It is much more useful to work with them.”

–Joshua Sharfstein, MD, Associate Dean for Public Health Practice and Training, Johns Hopkins Bloomberg School of Public Health

THE FDA

“A place where law, science and other things—public health, politics, beliefs—intersect.”

–Susan Wood, PhD, Associate Professor and Executive Director, Jacobs Institute of Women’s Health, George Washington University

The FDA is the government agency “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 more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health. FDA also has responsibility for regulating the manufacturing, marketing and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.” The Food and Drug Administration. (2015, December 7). About the FDA. Retrieved from: <http://www.fda.gov/AboutFDA/WhatWeDo/default.htm>

The FDA is part of the executive branch of the U.S. government. It is one of the agencies of the Department of Health and Human Services, and a part of the Public Health Service.

“The FDA has a different mission than the other agencies in the health cadre of government. We are the regulators. The rest are service providers.”

–Richard Klein, Director, Patient Liaison Program, Office of Health and Constituent Affairs, FDA

WHAT THE FDA DOES:

- Reviews and approves new drugs.
- Inspects manufacturing facilities.
- Conducts field inspections.
- Monitors post-market adverse events.
- Maintains oversight of drug advertising.
- Recalls unsafe or ineffective products.
- Manages drug shortages.
- Provides information to the public.
- Conducts research to promote the science of drug and device evaluation.

THE FOOD AND DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD. 20993
888-463-6332

www.fda.gov

FDA PUBLIC HEALTH ACTIVITIES:

Review activities:

- Human drugs.
- Human biologics.
- Over-the-counter (OTC) drugs.
- Vaccines.
- Blood products.
- Cell and gene therapy.
- Tissue therapy.
- Medical devices.
- Radiation-emitting equipment.
- Veterinary drugs.
- Cosmetic regulation.
- Food safety.

Enforcement activities:

- Field inspections.
- Drug advertising.
- Recalls of defective products.
- Seizures/prosecutions.

Public health activities:

- Laboratory research.
- International coordination.
- Drug shortage management.
- Information/guidance for industry.
- Information for health care professionals.
- Information for public.

Regulated products are:

- Safe and efficacious.
- Honestly, accurately and informatively represented.
- In compliance with laws and regulations.

WHAT DOES THE FDA REGULATE?

The scope of the FDA's regulatory authority is very broad. The FDA's responsibilities are closely related to those of several other government agencies. Often frustrating and confusing for consumers is determining the appropriate regulatory agency to contact. The following is a list of traditionally recognized product categories that fall under the FDA's regulatory jurisdiction; however, this is not an exhaustive list.

In general, the FDA regulates:

Foods, including:

- Dietary supplements.
- Bottled water.
- Food additives.
- Infant formulas.
- Other food products (although the U.S. Department of Agriculture plays a lead role in regulating aspects of some meat, poultry and egg products).

Drugs, including:

- Prescription drugs (both brand-name and generic).
- Non-prescription (over-the-counter) drugs.

Biologics, including:

- Vaccines.
- Blood and blood products.
- Cellular and gene therapy products.
- Tissue and tissue products.
- Allergens.

Medical Devices, including:

- Simple items like tongue depressors and bedpans.
- Complex technologies such as heart pacemakers.
- Dental devices.
- Surgical implants and prosthetics.
- In vitro diagnostic kits.

Electronic Products that give off radiation, including:

- Microwave ovens.
- X-ray equipment.
- Laser products.
- Ultrasonic therapy equipment.
- Mercury vapor lamps.
- Sunlamps.

Cosmetics, including:

- Color additives found in makeup and other personal care products.
- Skin moisturizers and cleansers.
- Nail polish and perfume.

Veterinary Products, including:

- Livestock feeds.
- Pet foods.
- Veterinary drugs and devices.

Tobacco Products, including:

- Cigarettes.
- E-cigarettes.
- Cigarette tobacco.
- Roll-your-own tobacco.
- Smokeless tobacco.



The FDA regulates over \$1 trillion worth of products, which account for 20 cents of every dollar spent by American consumers.

WHAT THE FDA DOES NOT DO

“Don’t expect the FDA to do things it doesn’t have the legal authority to do, and remember, the FDA is required to make its decisions based on science. It does this through both internal and external evaluation.”

–Susan Wood, George Washington University

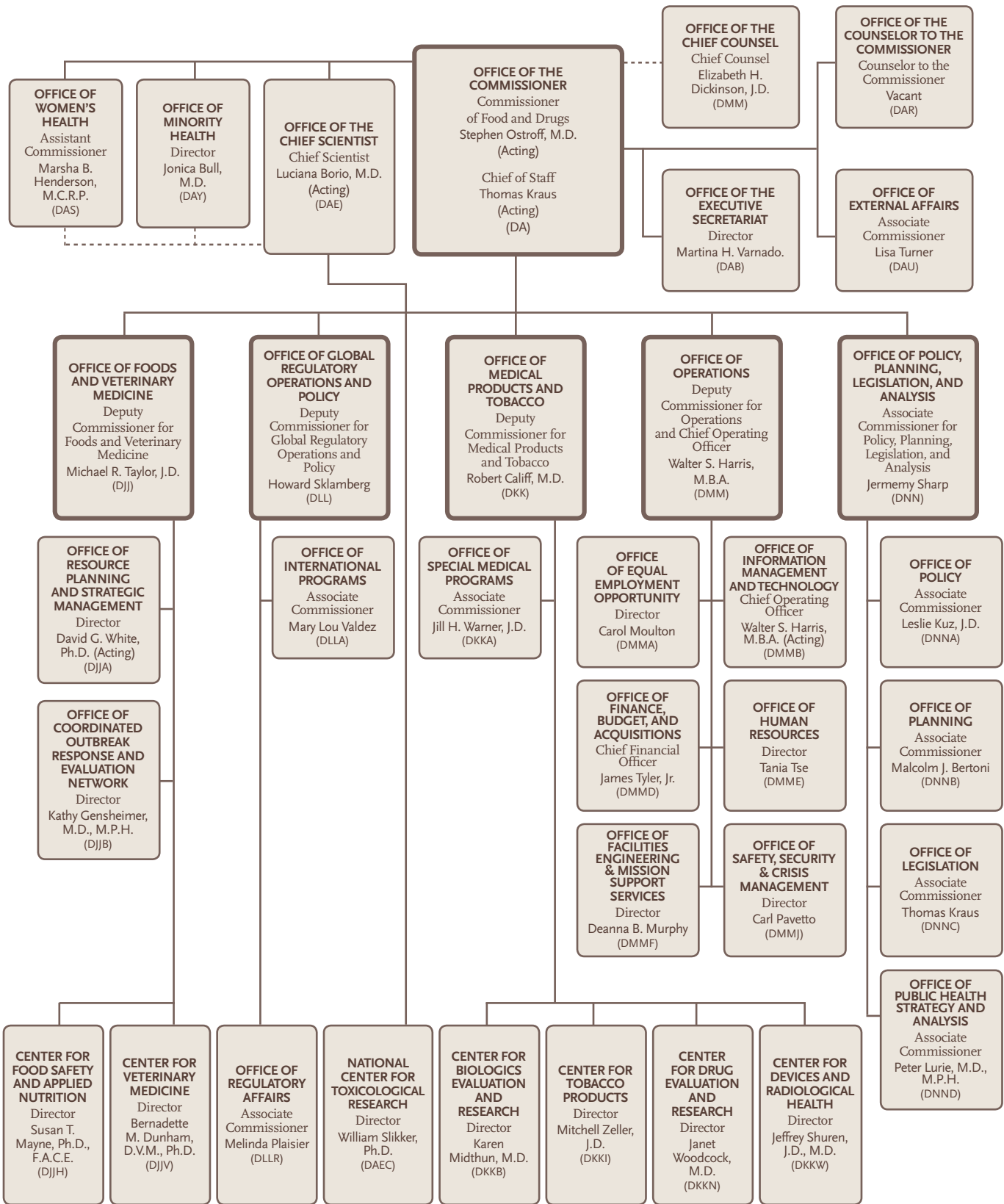
- Develop drugs and devices.
- Design or run clinical trials.
- Regulate the practice of medicine.
- Regulate the cost and price of medicines or devices.

“Changes in policy are often not just up to the FDA. It is more complex. The Department of Health and Human Services (HHS), the White House, Congress can all have a role, but the FDA can be your best advocate.”

–Joshua Sharfstein, Johns Hopkins Bloomberg School of Public Health

THE ORGANIZATION OF THE FDA

FOOD AND DRUG ADMINISTRATION



The FDA's organization consists of the Office of the Commissioner and four directorates overseeing the core functions of the agency: Medical Products and Tobacco, Foods, Global Regulatory Operations and Policy, and Operations.

HOW THE FDA IS FUNDED

"The FDA people can't say this but the agency needs more money, not necessarily in user fees but in direct dollars."

–Susan Wood, George Washington University

Congress allocates money on an annual basis. In 2015, this budget was \$4.7 billion. A significant portion of this budget, approximately \$2 billion, is generated by user fees paid by pharmaceutical, medical device and tobacco companies. The user fee program, managed by the Office of Financial Management, was created to help the FDA balance the responsibility of protecting the public health while accelerating innovation. Companies who wish to have a product approved by the FDA will pay a specified amount of money in user fees to bring their product to market (the Prescription Drug User Fee Act [PDUFA] requires an initial application fee of almost \$2.4 million).

USER FEE ACTS:

The User Fee Acts (Prescription Drug User Fee Act [PDUFA], Medical Device User Fee and Modernization Act [MDUFMA] [MDUFA], Biosimilar User Fee Act [BsUFA], etc.) all operate on the same principle. A fee is paid by the pharmaceutical industry, and the FDA uses this fee to help streamline the drug approval process, saving money in the long run and ensuring that safe medication gets to consumers faster. For example, since its first passage in 1992, PDUFA fees have gone towards increasing the number of review staff at the FDA, enabling clinical development time to drop by 10%, average drug approval time to drop nearly 60%, and ensuring that patients have gained access to nearly 1500 new drugs and biologics.

All of the User Fee Acts are reauthorized and approved in the same way. The Secretary of Health and Human Services (HHS) consults with the House Energy and Commerce Committee; the Senate Committee on Health, Education, Labor, and Pensions; and concerned professionals in the medical and pharmaceutical industry. After these meetings, a set of recommendations is put forth by the HHS Secretary and integrated into legislation that reauthorizes the bill in Congress. Per the structure of the legislation, the User Fee Acts are reauthorized every five years.



WHO DOES ALL OF THIS?

Six Centers

- Drug Evaluation & Research (CDER).
- Biologics Evaluation & Research
- Medical Devices & Radiologic Health (CDRH).
- Food Safety & Applied Nutrition (CFSAN).
- Veterinary Medicine (CVM).
- Tobacco Products (CTP).

Field Staff Activities

- Inspections, Compliance, Enforcement, and Criminal Investigations.

Over 16,000 staff

"We have to protect the FDA from politics coming in and influencing decision making. You make the decisions based on the science and the data presented to the FDA."

–Susan Wood, George Washington University

THE FDA'S JURISDICTION

- Congress passes laws, all FDA authority comes from Congress. These are usually “broad strokes,” and frequently unclear in terms of their actual impact and implementation.
- The FDA is based on the The Food, Drug, and Cosmetic Act (FD&C Act) which regulates products, components and packaging that involve interstate commerce.
- FDA writes “implementing regulations.” (Chapter 21 of the Code of Federal Regulations) These interpret the law at a more detailed level and involve an extensive administrative process that includes:
 - Notice and comment rulemaking—The proposal is published in the Code of Federal Regulations that describes regulation, rationale and interpretation of the law.
 - Paperwork Reduction Act requirements— The agency has limited budget to determine how much burden it can put on the public, including industry, to collect information.
 - Economic analysis—This measures the impact on industry and the American economy.
- The above process usually takes 60-120 days depending on complexity of proposal—but once comments are received, the FDA has to analyze and address them. It can take years for a regulation to actually get on the books.
- Once the regulations are established, they have the force of law.
- The FDA then makes a series of regulatory decisions—based on law and regulations—that establish regulatory policy:
 - These can be challenged in court—and often are, on the basis of jurisdiction or authority. Court rulings can change regulations.
 - They establish the framework for regulations to operate on a day-to-day basis.
- Guidance Documents:
 - Some regulations require more detailed interpretation to allow them to evolve as science and technology change.
 - Guidance documents are not binding but explain the reasoning and general approach that companies should take for a product.
 - The FDA is open to other approaches to achieve the desired outcome.
 - The FDA will listen—and does not have authority to require that companies follow guidance.
 - Guidance documents are typically open to comments and are initially issued as “draft” and later become “final.”

The FDA cannot make ad hoc or “one-off” decisions.

Decisions must be fair and consistent, not arbitrary and capricious.

Decisions must be made within a policy framework.

The regulatory world is complex.

THE APPROVAL PROCESS WORKS

“We have to make sure the data are enough to establish safety and efficacy. So, with these new expedited approaches, we have to assure they still hit a standard to make sure we get safe and effective products available to patients.”

–Susan Wood, George Washington University

INVESTIGATIONAL NEW DRUGS

Every experimental drug given to a human must be under the oversight of the FDA through an Investigational New Drug Application (IND). There are 1,800 new INDs filed yearly. An IND can stay active for many years. There are currently 12,000 active INDs, and the FDA

reviews/acts on 5,000 INDs per year. The IND is the basis for doing clinical trials. Each IND application includes:

- Chemical composition.
- Animal studies, which must precede human trials.
- Methods to assure safety, including range of possible doses.
- Recommendations for size and scope of clinical trials.
- What the drug will be compared to, and the study endpoints.
- Multiple points of interface between the FDA and the industry sponsor to assure that every clinical trial is addressed in detail, the development program is well designed and to establish safety profile and determine efficacy.

PHASED DRUG DEVELOPMENT

Clinical trials are done in phases, moving from preclinical animal studies to large, international trials involving hundreds or thousands of patients. These phases are described in the chart below.

Preclinical studies: Chemical and animal toxicology studies			
Phase 1	Phase 2	Phase 3	Phase 4
<ul style="list-style-type: none"> • Initial human studies to assess toxicity, Pharmacokinetics, initial efficacy. • May examine special populations (e.g., renally-impaired patients). • 20 – 80 patients per study. • \$25,000 - \$40,000/patient. 	<ul style="list-style-type: none"> • Small-scale efficacy/safety studies. • Dose/regimen selection/optimization. • 30 – 200 patients per study. 	<ul style="list-style-type: none"> • Rigorous controlled efficacy/safety studies. • 100 – 10,000 patients per study. • \$10,000/patient. 	<ul style="list-style-type: none"> • Post-approval studies of new uses or populations. • Similar in scope and rigor to Phase 3 trials.

SAFETY AND EFFECTIVENESS

There are several new paradigms that the FDA now considers as well. These are intended to move the FDA away from its traditional approach to a more patient-focused definition of risk and benefit. These include:

- Public perception of risk—how do people feel about a specific risk?
- How much risk are patients willing to tolerate in return for particular benefits? This is often heavily influenced by the severity of disease or condition, how sick the patients are, and what other therapies are available.
- Do user actions raise the level of risk?
- What tools can lead to the safest use of the product?

DRUGS ARE SAFE & EFFECTIVE

Safe

- Risks are managed.
- Quality is assured.
- Advertising is appropriate.
- Information is available.

Effective

- Studied with proper endpoints & standards.
- Demonstrated effect for intended use in the intended population.
- Quality is maintained.

“Advertising is determined by the label, and the label is based on the clinical trial data. That information is available.”

Richard Klein, FDA

NEW DRUG APPLICATIONS (NDA)

DRUG APPROVAL

After clinical trials but before a drug is marketed, it must be reviewed and approved by the FDA through a New Drug Application (NDA)

New drug applications*
200-300

Approved new products
25-30

Generic drugs
250-350

*Not all are for truly new drugs - may be for new uses of already marketed drugs, new doses, etc.

Once a drug completes clinical trials, but before it is marketed, it must be reviewed and approved by the FDA through a New Drug Application (NDA) or Biologic Licensing Application (BLA). No new drug or biologic can be marketed commercially in the United States unless it has been approved as safe and effective by the FDA.

The FDA receives 200-300 new drug applications each year. Some of these are for new uses for already marketed drugs (known as a supplemental application). Each application must contain acceptable scientific data including the results of tests to evaluate safety and substantial evidence of effectiveness for the condition for which the drug is being offered.

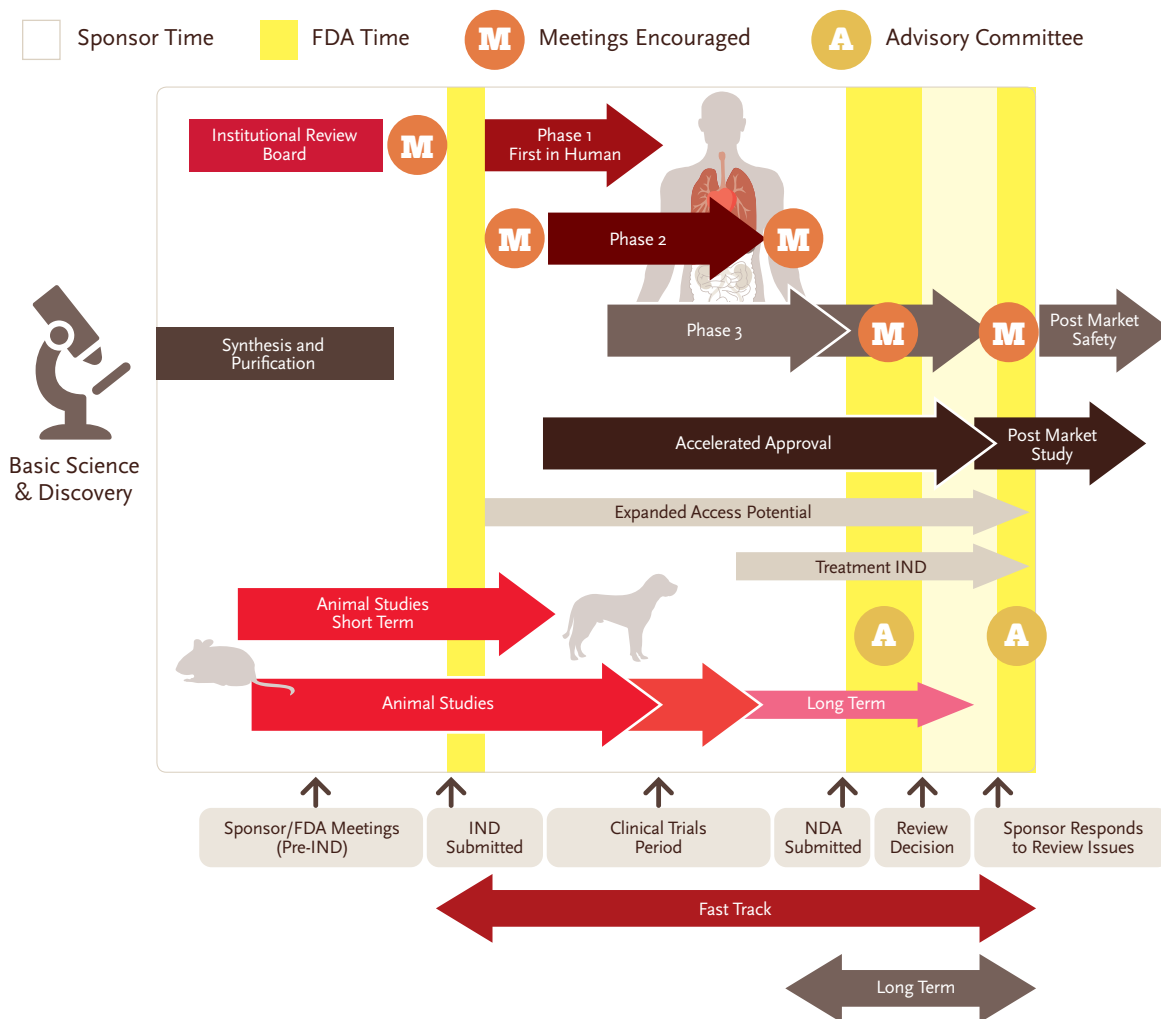
The FDA reviews primary data—a practice that is not done in Europe. This helps make the FDA the gold standard for drug review in the world.

The FDA has a responsibility to ensure that clinical trials supporting drug approval both include people representative of the population with the disease and meet special requirements for testing in children. The Pediatric Research Equity Act (PREA) requires that sponsors conduct trials in children, even for drug approval in adults, unless such studies are waived. The Best Pharmaceuticals for Children Act (BPCA) is a voluntary program administered by the FDA in which sponsors can conduct and submit pediatric studies in exchange for additional product exclusivity.

Each drug is reviewed by a multidisciplinary team that includes a project manager, biopharmacologists, chemists, clinicians, microbiologists, pharmacology/toxicologists and statisticians, safety and plant inspectors and others.

The FDA can seek public advisory committee input from medical experts, researchers, patient representatives and safety experts to help determine whether to approve a drug or device. These meetings are open to the public with opportunity for the public to present comments. They provide an excellent opportunity to be heard.

DRUG DEVELOPMENT REGULATORY OVERVIEW



After reviewing all the data, the FDA makes a final decision. Once the drug is on the market, the FDA still maintains oversight of adverse event (AE) monitoring, according to these guidelines:

- Companies are required by law to report AEs to the FDA.
- Doctors and patients can utilize the voluntary Medwatch AE.
- The Sentinel Program, established by the Center for Biologics Evaluation and Research (CBER) in 2008, is a national risk identification program that uses electronic health care data to monitor the safety of drugs, biologics and devices.
- The Office of Surveillance and Epidemiology monitors all reported AEs.
- Manufacturing is also monitored for safety.

III. History and Timeline

“The history of the FDA is intimately tied in with women’s health. It turns out that the FDA’s establishment and changes in law and policy over the decades have often been tied to tragedies in women’s health.”

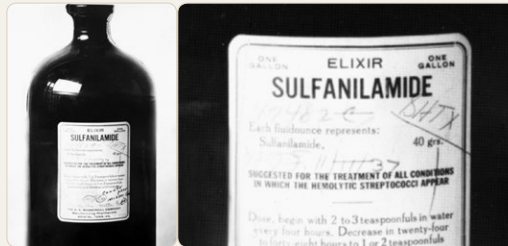
–Susan Wood, George Washington University

1906: THE PURE FOOD AND DRUG ACT—ULTIMATELY LED TO THE FDA

- Signed by Theodore Roosevelt.
- First of a series of significant consumer protection laws.
- Main purpose was to ban interstate and foreign traffic in adulterated or mislabeled food and drug products.
- Largely focused on patent medicines.
- Required drugs to meet standards of strength and purity:
 - Limited by the fact that it did not require factory inspections.
 - Put burden on the FDA to demonstrate problem—not the manufacturer to demonstrate safety and effectiveness.
 - Did not include provisions for safety testing.
 - Did not include a means of enforcement.

The FDA was initially part of the Department of Agriculture.

Regulatory changes were usually precipitated by tragedies



1906-1938 A PARADE OF DISASTERS

1937 Elixir Sulfanilamide

- Solvent: diethylene glycol.
- 107 deaths.
- Drug seizure by FDA (for misbranding).

1938 FOOD, DRUG, AND COSMETIC ACT—BEGINNING OF THE MODERN FDA

- The act resulted from the tragedy of the drug sulfanilamide which was treated with a solvent that caused 107 deaths, mostly in children.
- Was the first legislation to require pre-market safety testing.
- Shifted burden to the manufacturer to demonstrate safety and effectiveness.
- Was limited by the fact that it did not require any risk-benefit assessment.

INTERSTATE COMMERCE AND THE FOOD, DRUG, AND COSMETIC ACT (FD&C)

The FD&C federal involves interstate commerce, which is defined as:

- Commerce between any state or territory and any place outside thereof, and
- Commerce within the District of Columbia or within any other territory not organized with a legislative body.

The law applies to components and packaging as well as to finished products.

1951: DURHAM-HUMPHREY AMENDMENT—CREATED THE CONCEPT OF PRESCRIPTION DRUGS

- Defined prescription and over-the-counter drugs.

Prior to 1951, there were no prescription drugs.



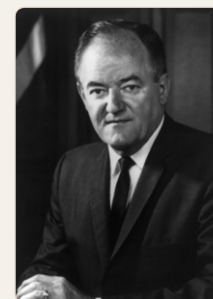
DURHAM-HUMPHREY AMENDMENT 1951

Explicitly defined two specific categories for medications:

- Prescription (Rx).
- Over-the-counter (OTC).

Required any drug that is habit-forming or potentially harmful to be dispensed under the supervision of a health practitioner as a prescription drug and must carry the statement, "Caution: Federal law prohibits dispensing without a prescription."

The amendment defined prescription drugs as those unsafe for self-medication which should therefore be used only under a doctor's supervision.



1962: KEFAUVER-HARRIS AMENDMENT—STRENGTHENED THE AUTHORITY OF THE FDA

- Was passed as the result of the thalidomide tragedy, which caused approximately 10,000 deformities in children in over 46 countries.
- Drug was never tested in pregnant women.
- Amendment required proof of efficacy.
- Required risk/benefit analysis.
- Required labeling for intended use.
- Required manufacturers to report adverse effects.
- Seen as the birth of the modern clinical trial.

1976: MEDICAL DEVICE AMENDMENTS

- The Dalkon Shield, a birth control device, was shown to be dangerous, which led to the inclusion of medical devices under the FDA aegis.

2012 FDASIA (FOOD AND DRUG ADMINISTRATION SAFETY AND INNOVATION ACT)

- Section 907 requires the FDA to publish and provide Congress with information on clinical trial participation and the inclusion of safety and effectiveness data by demographic subgroups including gender, age, race and ethnicity.

THALIDOMIDE TRAGEDY



July 15, 1962:

Thalidomide, a newly developed sleeping pill, is found to have caused birth defects in thousands of babies born in Western Europe. News reports on the role of FDA medical officer Dr. Frances O. Kelsey in keeping the drug off the American market arouse public support for stronger drug regulation.



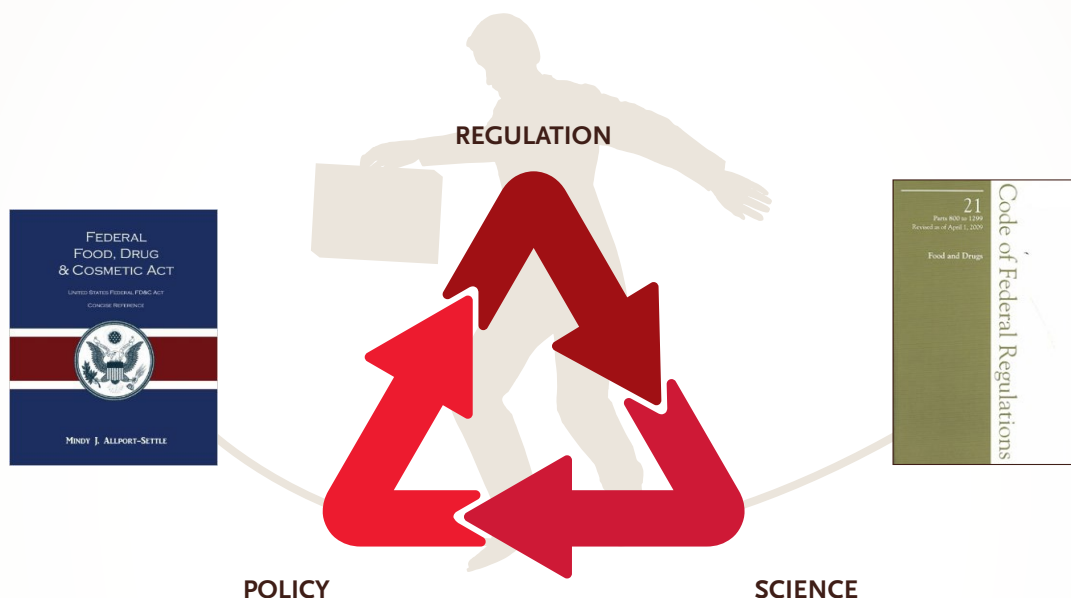
1950s -60s

- It's estimated that more than 10,000 children in 46 countries where the sleep aid had been approved were born with deformities as a consequence of their mothers using the drug while the women were pregnant.

IV. Innovative Approaches to Accelerating FDA Approval and Improving the Process

“Over the years, people have charged FDA with being much too slow... it takes too long to get drugs to market. There have been a lot of efforts to speed access to important new therapies, and I think very successfully.”

–Richard Klein, FDA



In recent years, the FDA has undertaken a number of initiatives to speed access to new therapies. These new approaches are the result of pressure from a variety of patient groups, notably the HIV/AIDS community, to make drugs available to people suffering from life-threatening diseases. They also reflect the rapid pace of progress against a number of serious illnesses, including many forms of cancer.

Priority Review, Fast Track, Breakthrough Therapy and Accelerated Approval are all intended to make therapeutically-important drugs available sooner without compromising the standards of safety and effectiveness of drugs for serious conditions.

While all of these programs are designed to meet the same goal, they each employ somewhat different procedures, use different selection criteria and target different parts of the drug development and approval process. The following information is courtesy of the Friends of Cancer Research website, www.focr.org/fda-expedited-review-programs and Richard Klein’s excellent summary.

PRIORITY REVIEW

“This is done after the IND phase when a drug comes to review by focusing resources on the review process. It also allows for rolling review of data as it becomes available and the trial is ongoing. It is applicable when you have a significant change in effectiveness, diagnosis or prevention of serious illnesses compared to standard applications.”

–Richard Klein, FDA

- Cuts a drug’s FDA review period from ten months to six.
- Priority Review can be requested alongside a Biologics License Application (BLA) or New Drug Application (NDA) submission.
- Drugs qualifying for Fast Track, Breakthrough Therapy and Accelerated Approval can also be eligible for Priority Review.

FAST TRACK

“The additional, close consultation between FDA and the sponsor can make a big difference, because the FDA will consult on the endpoints, and ask how many people do you need to have in a study of this type, how many people are affected by this disease. Are the endpoints valid and how are you going to measure them?”

–Richard Klein, FDA

- Requested as early as an Investigational New Drug (IND) application and prior to a BLA or NDA submission.
- Intended for drugs that address unmet medical need by either treating a condition for which no other treatment exists or offering some substantial benefit over existing treatment.
- Sponsors get extra opportunities to meet with FDA, discuss approval requirements and study design, and identify their most efficient path through drug development and review.
- Sponsors may also gain access to rolling review, wherein portions of their marketing application may be reviewed before the complete application has been submitted.

BREAKTHROUGH THERAPY

“This is a more recent approach. These are products for serious diseases where there is a substantial improvement over current therapy. That can be something that works better, but it can also be something that is easier to take, and make it more likely that people will continue on their therapy.”

–Richard Klein, FDA

- Requested as early as IND application and preferably prior to the end-of-Phase 2 meeting.
- Similar to Fast Track, but breakthrough drugs must show early clinical evidence of substantial improvement over existing therapies.
- Same benefits as Fast Track, with an even greater emphasis on early meetings and coordination with experienced and senior FDA personnel.
- Due to their large early clinical effect, breakthrough drugs can sometimes skip portions of the standard FDA review process without compromising safety and efficacy standards.

ACCELERATED APPROVAL

“This came about as a result of the AIDS epidemic. It shortens IND phase. It can take many years to determine if there is a survival difference, a clinical benefit, with a new therapy. Drugs for serious conditions can be approved based on surrogate endpoints—a measurement that is considered likely to predict the clinical benefit, but is not itself a measure of clinical benefit. This is used quite a bit in viral diseases and cancers. Why wait for people to die to show that something has benefit?”

–Richard Klein, FDA

- Sponsors should discuss Accelerated Approval with the FDA during development.
- Intended for drugs with long-term endpoints, such as increased survival or decreased morbidity, that are difficult to measure efficiently in trials.
- Allows approval based on surrogate endpoints—more easily measured outcomes that are reasonably likely to predict clinical benefit (e.g., tumor shrinkage can be used as a surrogate endpoint for survival benefit in some instances of cancer).
- Sponsors are required to confirm a drug’s efficacy in post-market clinical trials.
- Priority Review, Fast Track and Breakthrough drugs can also be eligible for Accelerated Approval.

This chart provides a quick comparison of these programs.

	PRIORITY REVIEW**	FAST TRACK DESIGNATION	BREAKTHROUGH DESIGNATION	ACCELERATED APPROVAL
Eligibility	1. Offer major advances in treatment over existing therapies	1. Intent to treat broad range of serious diseases 2. Potential to fill an unmet medical need	1. Treat serious or life-threatening diseases 2. Early clinical evidence of substantial improvement over existing therapies	1. Treat serious or life-threatening diseases 2. Provide meaningful therapeutic benefit over existing therapies 3. Surrogate endpoint reasonably likely to predict clinical benefit
Designation	Requested by sponsor at time of NDA/BLA submission; FDA has 45 days to respond	Can be requested by sponsor at any time; FDA has 60 days to respond	Can be requested by sponsor at any time after IND submission; FDA has 60 days to respond	No formal process
Clinical Development	Not applicable	Earlier and more frequent communication	Abbreviated or condensed development; earlier and more frequent communication; delegation of senior reviewers and cross disciplinary review team	Conditional approval granted using surrogate endpoint from phase 2 trials or interim phase 3 data; controlled trials with hard clinical endpoints required to confirm clinical benefit
Review Process	NDA/BLA data submitted in one package; review time shortened to 6 months	Option for rolling NDA/BLA submission. Official review clock begins when last module is submitted	NDA/BLA data submitted as they are accumulated; review time shortened	NDA/BLA data submitted in one package; standard 10-month review

* Not an exclusive category.

V. The Intersection of the FDA and Congress

“The timing of this conversation is really great. One of the unique things about this time is the degree to which people are focused on supporting innovation, on engaging with the FDA, and on growing and supporting the FDA in ways that are largely bipartisan, are really heartfelt. There’s a lot of energy going into that.”

–Craig Burton, Health Policy Strategist and Founder, Strategic Health Policy Solutions

CRAIG BURTON’S “TOP LINE” SUGGESTIONS FOR DEALING WITH CONGRESS (“THE HILL”)

- Why are you there? It is important to have a clear, concise message that can be articulated in a brief period of time.
- What’s the issue? This means not only knowing your side of issue—but both sides of the issue. It also requires knowing what you are asking from the Hill.
- Who are you meeting with? This applies both to the office and the people. For FDA legislation, the Senate focus is in the Health, Education, Labor and Pensions Committee (HELP); in the House, it is Health, Energy and Commerce, as well as in Appropriations Committees in both the Senate and the House. Within those committees, there is a significant range of experience and insight both among members and staff.

“You need to understand when you can and should go very deep because the staff person you are talking with has a PhD and has spent five years working on FDA legislation vs. the staff who got sent as a last minute fill-in to your meeting and may know very little.”

–Craig Burton, Health Policy Solutions

- Where is FDA on this? This often one of the first questions you will get, so either having engaged with the FDA, or planning to engage is very important. If you don’t know, say it.
- What the Hill can and can’t, or won’t do. It is important to differentiate between policy engagements and applications. The Hill will be very hesitant to engage with FDA on a pending application, but will be more likely to engage on policy issues.

SARAH WALINKSKY’S OVERVIEW OF FDA’S INTERACTION WITH CONGRESS

“We bring together the different parts of the agency to decide how we are going to engage on policy and go forward with the different initiatives.”

–Sarah Walinsky, JD, Congressional Affairs Specialist, FDA

- The FDA Office of Congressional Affairs is the conduit between the agency and Congress. This office works closely with the Office of Health and Constituent Affairs to respond to consumer and patient inquiries and provide meeting preparation and technical assistance for bills.

“As a patient group, you would not reach out and contact the Office of Congressional Affairs to address your concern, but you might want that office to know about your concern.”

–Libby Mullin, Principal, Mullin Strategies

VI. The FDA and Elevating the Patient Voice

“Before 1988, the FDA had a paternalistic view of balancing risks and benefits. They thought they knew better. Then the activists actually showed up at FDA, the HIV activists, and they said, ‘We think we have something to say. You’re speaking for us. Let us speak for ourselves.’”

–Deborah Miller, PhD, MPH, MSN, RN, Health Programs Coordinator, Cancer Patient Liaison Program, Office of Health and Constituent Affairs, FDA

Since 1988, The FDA has taken a number of major steps to address issues related to patient involvement, incorporate patient-reported outcomes into the data review process and elevate the patient voice.

After 1988 the FDA responded by:

- Seeking ways to speed review time and access to promising therapies without jeopardizing patient safety or compromising scientific rigor.
- Creating the Office of Health and Constituent Affairs (OHCA).

PATIENT-FOCUSED DRUG DEVELOPMENT

In 2012, under the Prescription Drug User Fee Act (PDUFA V), the FDA committed to a new initiative called Patient-Focused Drug Development. The goal is to systematically gather information from the patient point of view on the risks and benefits of the drugs they are using. It asks what patients are willing to accept in terms of risk to gain a particular benefit. This adds perspective to the data generated by clinical trials by providing a direct mechanism for patient feedback.

As part of this program, the FDA is holding 23 public meetings during the five-year span of PDUFA V (through 2017), each focused on a different disease area. The input provided by patients and patient representatives at each of these meetings is summarized in [The Voice of the Patient Report](#).

1991 was the first time a patient representative was included on any advisory panel. It was deemed so successful that all divisions started to include patient representatives. In 1996, patient representatives were given voting privileged on the CDER (Center for Drug Evaluation and Research) and the CBER (Center for Biologics Evaluation and Research). In 2001, the role of the patient consultants was expanded to include virtually every disease site.

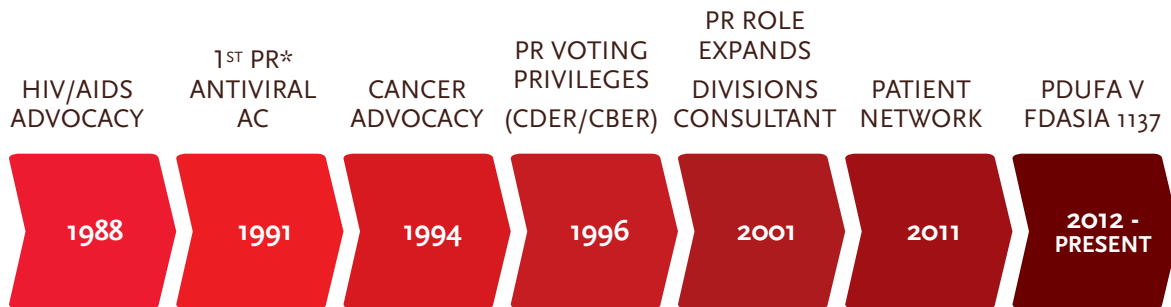
This information has become a “critical aspect of FDA decision making as it establishes the context in which the regulatory decision is made.”

www.fda.gov/ForIndustry/User-fees/PrescriptionDrugUserFee/ This website contains a full description of the Patient-Focused Drug Development Program and a full listing of the The Voice of the Patient Report.

“I think the benefit of Patient-Focused Drug Development, and programs like it, is down the line. There are already clinical trials in play. Those are not going to change, but the FDA is there, industry is there listening to all these patients, and everybody is very much aware of what is important as an outcome for patients. For industry, that’s marketing benefit. For FDA, it’s safety and effectiveness benefit.”

–Richard Klein, FDA

PATIENT PARTICIPATION MILESTONES



* PR: Patient Representative.

THE OFFICE OF HEALTH AND CONSTITUENT AFFAIRS (OHCA)

“Our office was created as a way that people could come in, talk to us, discuss their concerns. It also gave FDA a way to educate the public on FDA process and its policy and procedures, so they can understand why FDA does what it does. It’s a mutual learning curve between OHCA and patients and advocacy groups.”

–Deborah Miller, FDA

OHCA was created to work directly with patients and patient advocates to encourage and support their active participation in FDA decision making and policy formulation. It serves health care providers and includes the MedWatch program, a voluntary program for physicians and patients (mandated for industry) that allows them to report adverse events. The form to report AEs is now online and easy to use.

OCHA can be reached by calling 301-796-8460 or through its website <http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofExternalAffairs/ucm343095.htm>

“We get more complete MedWatch forms from patients than from many physicians.”

–Deborah Miller, FDA

THE PATIENT REPRESENTATIVE (PR) PROGRAM

There are currently about 200 patient representatives. The number is expanding because of increased presence from the rare disease community and the remarkable expansion in the number of specific cancer types and subtypes. It is expected that precision medicine with its identification of diseases by genetic profile will add to this trend.

The program strongly favors patients, but will consider caregivers under special circumstances or if the disease affects children. A recent panel included a group of children speaking for themselves, which may be a sign

OHCA ACTIVITIES

Responds to Emails and Telephone Calls

- From patients, family members, healthcare providers and others asking for information on clinical trials, drugs, biologics, medical devices, foods, tobacco, expanded access and other FDA-regulated issues.

Patient Network

- Maintain website.
- Host annual patient network meetings/webinars.
- Issue bi-weekly patient network newsletter.

Manage Health Professional Liaison Program

- Maintain website.
- Issue bi-weekly health professional newsletter.
- MedWatch Program – FDA’s Safety Information and Adverse Event Reporting Program <http://www.fda.gov/Safety/MedWatch/default.htm>.



- Coordinate outreach and educational activities with health professional organizations.

of things to come in the future. Patient representatives are also required to demonstrate awareness and involvement in their communities. All patient representatives receive initial training, attend an annual workshop and participate in monthly teleconferences and webinars.

Patient representatives have three primary roles as defined in the chart below.

PATIENT REPRESENTATIVES

- | | | | |
|---------------------------|-------------------------|---|---|
| • AIDS/HIV. | • Depression. | • Lupus. | • Obesity/weight control. |
| • Alzheimer's Disease. | • Diabetes. | • Macular Degeneration. | • Parkinson's Disease. |
| • Asthma/COPD. | • Fabrey Disease. | • Major Depressive Disorder. | • Polio. |
| • Cancer (various types). | • Fibromyalgia. | • Methicillin-Resistant Staphylococcus Aureus (MRSA). | • Sickle Cell Disease. |
| • Cardiovascular Disease. | • Hepatitis B. | • Neuropathy. | • Short Bowel Syndrome. |
| • Cerebral Palsy. | • Hepatitis C. | | • Temporomandibular Joint (TMJ) Disorder. |
| • Chronic pain. | • Infantile spasms. | | |
| • Crohn's Disease. | • Lung transplantation. | | |

PATIENT REPRESENTATIVE PROGRAM

Three Roles

Patient Representative

- Patient representatives serve on advisory committee panels.
- Voting member of advisory committee panels for the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER).
- Non-voting member of advisory committee panels for the Center for Devices and Radiological Health (CDRH).

Patient Consultant

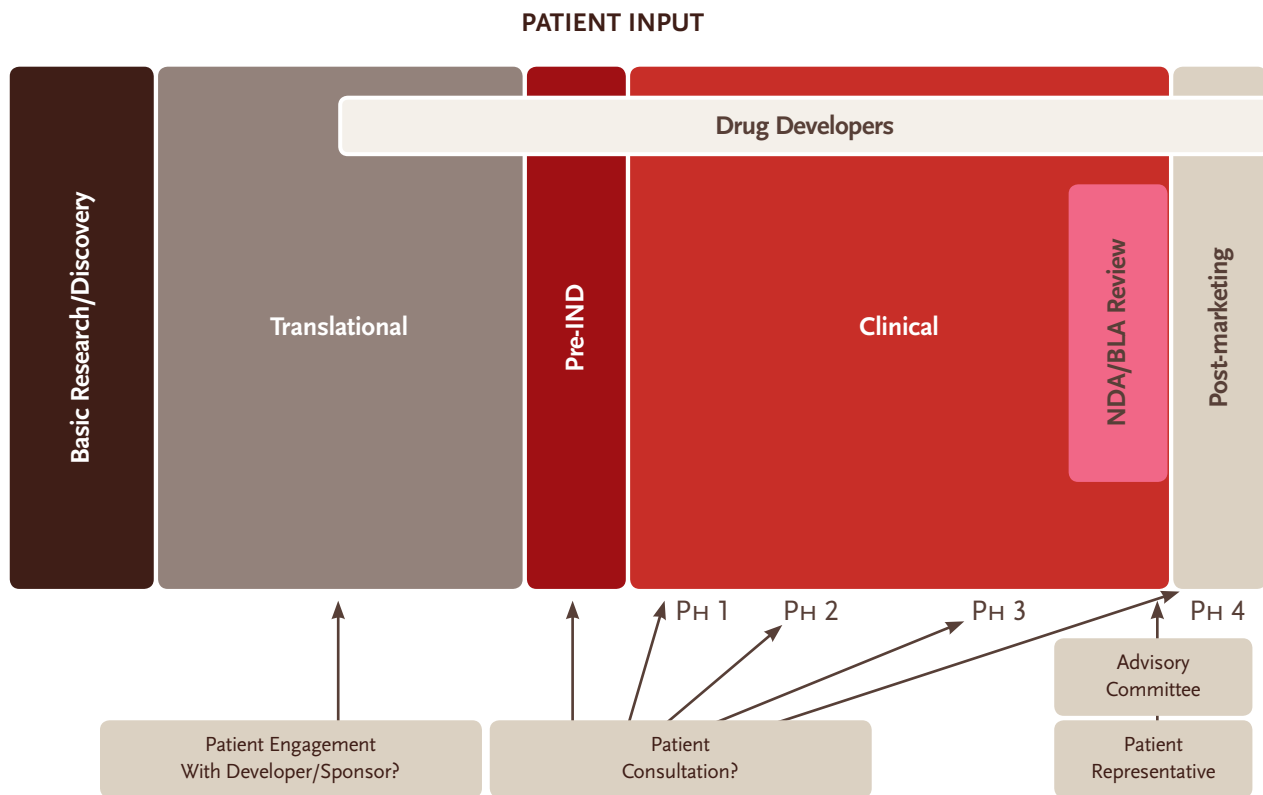
- Patient representatives participate in divisional meetings.

Informal Consultant

- Patient representatives keep FDA informed of new issues/concerns in their disease areas.

WHAT ARE THE CRITERIA FOR BEING CONSIDERED FOR THE PATIENT REPRESENTATIVE PROGRAM?

- Personal experience with the disease or condition as either a patient or primary caregiver.
- Patient community awareness: active in patient advocacy organizations, knowledgeable about treatment options and research, other advocacy activities.
- Someone who is analytical and objective, doesn't need to be a scientist but should grasp scientific principles and understand issues, experienced with decision making based upon complex information.
- Minimal or no conflict of interest.



Patient representatives provide value to the FDA in several key areas. These include:

- Perspective on specific products and their use.
- The patient point of view on risk/benefit.
- Quality of life data specifically for labeling.
- Input on better designs for clinical trials.
- Inclusion of women and minority populations in trials and patient-reported outcomes.
- Serving as community ambassadors and educators.

“Patient reps are so educated these days. They come with such great ideas, issues or topics that we may not think about.”

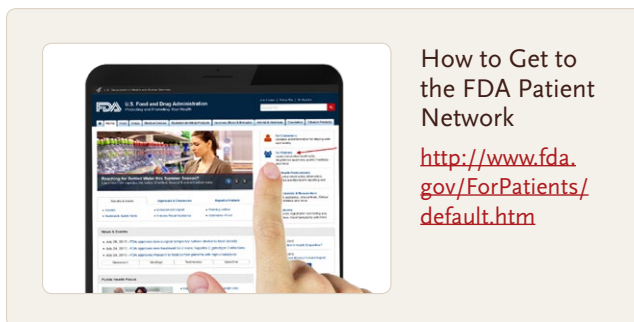
–Deborah Miller, FDA

THE PATIENT NETWORK WWW.FDA.GOV/FOR PATIENTS/DEFAULT.HTM

“The Patient Network was designed by patients and for patients.”

–Steve Morin, RN, BSN, Commander U.S. Public Health Service, Health Programs Coordinator, Cancer Patient Liaison Program, Office of Health and Constituent Affairs, FDA

The FDA Patient Network was created in 2014 to enhance OHCA's educational and advocacy activities by instituting a more proactive approach to patient engagement. It is a resource for patients and caregivers, independent patient advocates and patient advocacy organizations. The web page can be reached by clicking on the icon on the right hand side of the FDA's home page.



Patients can submit comments on a wide variety of topics. The website contains information on how to submit a comment and advice on writing a useful comment. Patients can also attend FDA-sponsored public meetings which are listed on the site as well. Another page provides information on clinical trials and a link to clinicaltrials.gov, the comprehensive resource that lists all open trials in the United States. The website provides access to webinars led by FDA experts, dating back to 2009.

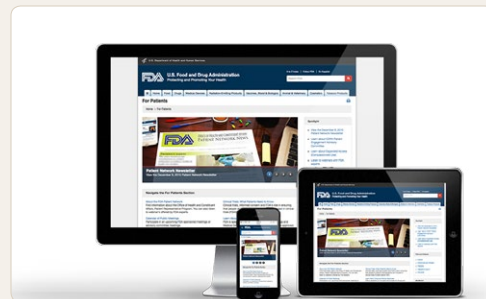
“Knowing how the (clinical trials) process works is important to meaningful advocacy and engagement.”

–Steve Morin, FDA

Additional resources include: the Patient Network Newsletter posted on the web and sent through a group email list and a series of Patient Network meetings and webinars developed in conjunction with patient advocacy organizations.

“Patients and the public can submit questions for any patient-focused meeting. It can often have just as much impact to write a question and submit it through regulations.gov as it does to stand up in the room and ask that question.”

–Steve Morin, FDA



FDA PATIENT NETWORK

- Outgrowth of the Patient Representative Program.
- Broadening opportunities for patient engagement:
 - Website.
 - Bi-weekly Email Newsletter.
 - Webinars & In-person Meetings.
- Scale up of Office of Health and Constituent Affairs educational and advocacy activities.
- Institute a more proactive approach to patient engagement by keeping interested patients informed.
- Develop an active FDA educational and advocacy resource designed for patients including:
 - Patients & Caregivers.
 - Independent Patient Advocates.
 - Patient Advocacy Organizations.



PATIENT NETWORK NEWSLETTER

A bi-weekly newsletter containing FDA-related information on a variety of topics, including:

- New product approvals.
- Significant labeling changes.
- Safety warnings.
- Proposed regulatory guidances.
- Opportunities to comment and other information. important to patients and caregivers.

INCLUSION OF WOMEN AND MINORITIES

“FDA must require adequate inclusion of women and meaningful analysis of data by sex and sex/race groups...It is really hard to do this, but we have to keep pushing on it.”

–Susan Wood, George Washington University

For many years, the research community was reluctant to include women in clinical trials because of fears of harming either them or potentially unborn children. Beginning in 1977, women were excluded from early, Phase I studies designed to establish safety and dosing. In 1993, this policy was reversed to allow for the evaluation of gender differences in clinical trials.

Minorities continue to be underrepresented in trials. While progress in this arena has been slow, the agency has taken steps to ensure that women, minorities and older people are adequately represented and served in clinical research and in the FDA review process.

Today, there are still significant issues related to including women and people of different ethnicities as well issues related to analyzing data from studies to document distinctions.

Example: Cardiovascular disease is a leading killer of women but many studies do not analyze data to differentiate between men and women.



Office of Health and
Constituent Affairs



FDA WHITE OAK CAMPUS

10903 New Hampshire Ave.,
Building 32

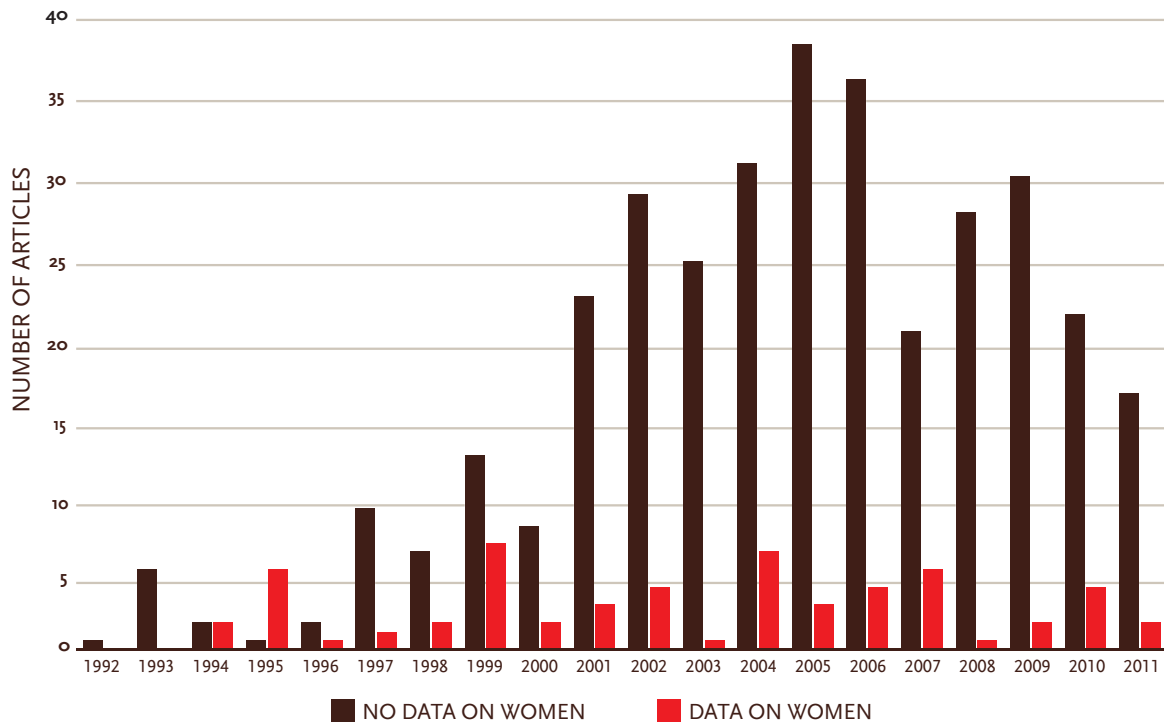
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JOURNAL ARTICLES ON TREATMENT OF CORONARY ARTERY DISEASE



Source: Dolor, R. J., Melloni, C., Chatterjee, R., LaPointe, N. M. A., Williams, J. B., Coeytaux, R. R., et al., Treatment Strategies for Women With Coronary Artery Disease, Agency for Healthcare Research and Quality, August 2012.

The passage of FDASIA in 2012 directed the FDA to provide Congress with a report on the extent to which clinical trials included safety and effectiveness data by demographic subgroups. A report was released in 2014 that established an action plan to address these issues.

Section 907 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) directed the FDA to publish and provide to Congress a report:

“addressing the extent to which clinical trial participation and the inclusion of safety and effectiveness data by demographic subgroups, including sex, age, race, and ethnicity, is included in applications submitted to the Food and Drug Administration.”

For newly approved drugs, the FDA now provides “Drug Snapshots” that detail who was in the study and any possible side effects by subgroups. There is also pending legislation called the *Research for All Act* that will enhance and expand both inclusion of subgroups and analysis of data from studies.

HR 2010 RESEARCH FOR ALL ACT

Sponsored by Rep. Jim Cooper (TN)

- Ensures the best medicine is available for both men and women.
- Directs NIH to update its guidelines to better enforce the current law on clinical research.
- Increases the study of female subjects and the analysis of sex differences in basic research.
- Speeds new drugs to market that will be safer and more effective for both men and women.
- Codifies NIH's existing sex differences research network program.
- Any new legislation (21st Century Cures) should include these provisions.

**Why do we need
The RESEARCH FOR ALL Act?**

Most medical research focuses on men.

Studying women is suggested, but not required.

Heart disease: the #1 killer of all Americans



Only 1/3 of subjects in cardiac clinical trials are women.

Only 30% of cardiac studies with women report outcomes by sex.



Diabetes drug study:

Drug may **lower** women's risk of heart failure but **increase** men's

The Fight Against Alzheimer's Disease

2/3 patients are women

Men are 50% less likely to get it

“Medical research that is gender-neutral or skewed to male physiology puts women at risk for **missed opportunities** for prevention, **incorrect diagnoses**, **misinformed treatments**, **sickness**, and even **death**.”
Researchers at Brigham and Women's Hospital

cooper.house.gov

VII. A Case History: Duchenne Muscular Dystrophy

Pat Furlong, BSN, RN, Founding President and CEO, Parent Project Muscular Dystrophy

Setting the stage: Duchenne Muscular Dystrophy (MD) is a neuromuscular degenerative disease affecting mostly boys. It is diagnosed at approximately age 4-6 and progresses until it causes death, usually in the late teens or early 20s. It is a horrible, devastating disease.

2001: The Muscular Dystrophy Care Act was passed and re-authorized in 2008: This legislation “galvanized” the field and was the most important step forward in research, next to the cloning of the gene. This stimulated the interest of industry in research and potential therapies for MD.

2009: A clinical trial using a promising new drug was terminated because the dose was wrong.

The Muscular Dystrophy Association’s Interaction with the FDA:

- Met with Center for Drug Evaluation and Research (CDER) Neurology to talk about unmet need in Duchenne.
 - *“We told them that we understand that, while you have to know about these diseases, we know more, because we have to live with them.”*
- Looked at how Duchenne fit into new policies for increasing speed of approval and access to therapies.
- Duchenne Muscular Dystrophy wrote a white paper that looked at Duchenne in the context of policy:
 - Recommend Duchenne treatments for accelerated approval.
 - Looked for guidance on surrogate outcome measures.
 - Recommended the use of conditional approval.
 - Pushed understanding of the unmet need and the difference in the benefit/risk equation for patients with limited prognoses and few available treatment options.
- Met again with CDER Neurology:
 - Reinforced the benefit/risk issue—willingness of this population to take on risks.
 - *“Coming and telling our story is reasonable and valid, but the FDA works on data.”*
 - Duchenne Muscular Dystrophy embarked on a benefit/risk survey:
 - + Hired Johns Hopkins University expert.
 - + Explored equation of benefit/risk in rigorous systematic way.
 - + Finished pilot in six months—quantified that caregiver preference was for slowing or stabilizing progression of the disease; while the lowest priority for parents was their own health. Slowing progression was rated higher than more years of life—quality meant more than quantity.
 - The group held another meeting with CDER Neurology:
 - + Data presented—what else do you need to know;
 - + CDER accepted but wanted to know if equation was the same in young adults/ adolescents and whether the equation changes over the course of the illness; and
 - + Refined data

- The European Medicines Agency (EMA) released guidance on Duchenne which the group did not like:
 - + Wrote letter to EMA describing specifically their issues.
 - + Focused on failure to include the patient voice.
- The group’s next meeting was with CDER Neurology:
 - “Who is better to write the guidance for the FDA than the community that is affected.”
 - + Offered to work with them to rewrite the guidance—partnership.
 - + MD wrote the guidance.
 - + Reached out to HIV community.
 - + Hired a science writer.
- They then held a policy forum to discuss issues in December 2013:
 - + 213 Families.
 - + 19 members of the FDA.
 - + Wanted to discuss outcome measures and trial design.
- Formed a steering committee with working groups with a range of representatives from industry, academia and the patient community.
- Created Draft Guidance within six months:
 - + All published data.
 - + Submitted to open docket for public comment.
- The FDA used this as a platform and in June 2015 issued its own guidance on MD.
- They are now in active discussion about the details including cardiac and pulmonary issues.
- Webinars have been used along the way to inform patients about what is happening and to ensure that we are speaking collectively.

“This is an example of an extraordinary partnership with the FDA, and an extraordinary way to educate them, and they us about what their struggles are and what our struggles are, and we have engaged the entire community so we could deliver a robust document.... We want to be your partner so you understand what living with this disease means.”

Summary:

“For our community, this was a journey through the disease.”

The community was incredibly pleased with the process and the results. Drafting guidance really informed our community. It was an education and a reassurance that there is an FDA that wants to learn and listen and do the best for us.

VII. Case Study II: Breakthrough Therapy Designation

Jeff Allen, PhD, Executive Director, Friends of Cancer Research

Setting the Stage: Friends of Cancer Research (FOCR) has worked for many years with the FDA. There are a number of key phases: relationships, data, bringing stakeholders together. The FDA is a scientific organization. It is important to translate anecdotal or emotional approaches into effective data-based engagement.

There has been a change in the overall understanding and approach to the FDA because the agency has been able to participate more actively in patient-based discussions.

- Initial efforts were to gain multistakeholder understanding of the challenges that oncology was facing—not to address a problem with the FDA, or in industry or in academia.
 - Held a series of workshops throughout the year to propose solutions to identified problems.
 - Did not intend to seek legislation.
 - Wanted to bring to bear the emerging issue of what happens when you see an unprecedented treatment effect very early—in phase 1 or 2—what steps should be taken to do business differently.
 - Fueled by a melanoma drug that was in clinical trials at the time—made people question whether the requirement for a large-scale trial was always necessary.
 - Needed a formalized process with a sponsor to bring acceptable trial designs to the FDA for review—purely scientific at this point.
 - Looked at other endpoints and outcome measurements that could expedite the development of the drug while minimizing the danger to patients.
- Developed a white paper to lay out strategies.
 - Leading up to 2012 PDUFA—Issue was not lowering standards but developing a new approach to demonstrating that standard.
 - Saw an opportunity to talk to the FDA and people on the Hill.
 - Brought together advocacy organizations and researchers.
 - Made an effort to formalize the approach to breakthrough drugs.
 - Used precedents of previous drugs and models of collaboration.
 - Put together an alternative to what was being proposed on the Hill.

“This has been powerful because it aligned a lot of different stakeholders and gave the FDA the opportunity to formalize a process around things that they thought were scientifically appropriate for the drugs that we are seeing now in many cases. It established something that the FDA could use to say to sponsors, ‘if you are seeing this early effect, we are here for you and we want to talk to you. We want to work with you and we are going to get it across the finish line as soon as possible.’”

Breakthrough therapy is being used more than anticipated with over 100 drugs given this designation in the three years since it has been in effect.

IX. Key Messages

- The FDA is a huge agency with a very broad and deep range of responsibilities and authority.
- The FDA is the “honest broker” when it comes to assuring that drugs and medical devices made available in the United States are safe and effective.
- Advocacy groups should view the FDA as a positive force and an important agency to engage in their efforts.
- It is critical to know what the FDA does and does not do before engaging with the agency. Fundamentally, the FDA is a scientific, regulatory agency. It does not conduct research (other than regulatory science research) or regulate the practice of medicine.
- The FDA is actively interested and involved in engaging patient and advocacy groups and has established a number of mechanisms and tools to enhance and facilitate this involvement. These include patient representatives on advisory boards, the Office of Health and Constituent Affairs (OHCA) and the Patient Network. The FDA is also willing to engage with patient groups on specific issues.
- As a scientific agency, the FDA relies on data and evidence to make its decisions. Anecdotes, individual stories and unpublished data, while they may be powerful, have little influence on the regulatory decision-making process.
- When approaching the FDA, it is important to gather key stakeholders and to have a clear, concise idea of what the goal is as well as the potential risks and benefits to the affected community.
- It is also important to understand the relationship between Congress and the FDA and to be aware of what Congress can and cannot do with regard to the regulatory process.

CONTACTING THE FDA

Call:
1-888-INFO-FDA
(1-888-463-6332)

Email:
See **Contact FDA Centers and Offices below** or **search the employee directory**.

Write to:
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

IF THERE ARE THREE BASIC TAKE-AWAY MESSAGES, THEY ARE:

1. Sitting down with the FDA is critical to identifying mutual challenges.
2. Data drive the process.
3. It takes time.

X. Glossary of Terms

Accelerated Approval: An FDA program that allows for provisional approval of a drug using a lower threshold of evidence. This type of approval is only available for drugs that treat serious diseases and fill an unmet need. Approval can be obtained using a surrogate endpoint, but accelerated approval comes with requirements for the drug sponsor to provide additional data at a later time. Failure to provide additional data can result in the cancellation of a drug's approval.

Adverse Event: Any undesirable experience associated with the use of a drug or medical device in humans. These may or may not be caused by the drug.

BLA: Biologic Licensing Application is a request for permission to introduce a new biologic product. It is the equivalent of the new drug application (NDA) for a biological product.

Breakthrough Therapy: An FDA process designed to expedite the development and review of drugs that demonstrate substantial improvement over available therapies.

BsUFA: Biosimilar User Fee Act of 2012 (BsUFA), authorizes the FDA to assess and collect fees for biosimilar biological products from October 2012 through September 2017. The FDA dedicates these fees to expediting the review process for biosimilar biological products.

CDER: Center for Drug Evaluation and Research.

Clinical Benefit: A documented, objective response that leads to improved overall survival. It is a traditional endpoint for clinical trials.

CTP: Center for Tobacco Products.

Endpoints: The measurable, targeted outcomes of a clinical trial.

Fast Track: An FDA process designed to facilitate the development and expedite the review of drugs that treat serious conditions and fill an unmet need.

FD&C Act: The Food, Drug, and Cosmetic Act, passed in 1938, is the authorizing legislation for the FDA.

FDASIA: The Food and Drug Administration Safety and Innovation Act, passed in 2012, expands and strengthens the agency's authority.

Guidance Document: These represent the FDA's current thinking on a particular subject. They do not have the force of law and are not binding.

IND: Investigational New Drug application allows a sponsor to begin clinical trials and ship an investigational agent across state lines. It is issued before the drug is approved.

Market Exclusivity: Exclusive marketing rights granted by the FDA upon approval of a drug and can run concurrently with a patent or not. Exclusivity is a statutory provision and is granted to an NDA applicant if statutory requirements are met.

Medical Device User Fee and Modernization Act (MDUFMA): Under the user fee system, medical device companies pay fees to the FDA when they register their establishments and list their devices with the agency, whenever they submit an application or a notification to

market a new medical device in the U.S. and for certain other types of submissions. These fees help the FDA increase the efficiency of regulatory processes with a goal of reducing the time it takes to bring safe and effective medical devices to the U.S. market.

MedWatch: An FDA program, mandated for industry and voluntary for patients and physicians, that provides a mechanism for reporting adverse events.

NDA: New Drug Application is the vehicle through which sponsors formally apply for FDA approval to market a new drug or pharmaceutical in the United States.

OHCA: The Office of Health and Constituent Affairs is the liaison between the FDA and patients, advocacy groups, health professionals and consumers.

Patient-Focused Drug Development: This is a program of the FDA that conducts meetings and webinars on a range of disease-specific topics for patients and health care consumers under the PDUFA V Act.

Patient Network: A user-friendly resource for patients that includes a website and newsletter.

Patient Representative: Patient Representatives provide the FDA with the unique perspective of patients and family members affected by a serious or life-threatening disease. Patient representatives may serve on FDA Advisory Committees, as a consultant for the review divisions (doctors and scientists who review data to determine whether a medical product's benefits outweigh the potential risks), or as presenters at FDA meetings and workshops on disease-specific or regulatory and health policy issues.

PDUFA V: The Prescription Drug User Fee Act of 2012 provides substantial funding to the FDA and also specifies activities and responsibilities for the agency.

Phased Drug Development: A system of conducting clinical trials, from Phase 1 to Phase 4, that begins with small trials designed to establish safety dosage and moves through increasingly larger, more specific studies of effectiveness and safety.

Priority Review: An FDA program that directs resources and attention to evaluating new drugs that could offer significant improvements in the safety or effectiveness of treatment, diagnosis or prevention of serious diseases.

Regulation: A binding ruling by the FDA on the use and marketing of a drug or medical device.

Surrogate Endpoint: An outcome of a clinical trial that measures endpoints other than overall survival.

21st Century Cures: Legislation passed by the House of Representatives in July 2015 designed to support innovative research and increase the pace of scientific discovery.

XI. Partners and Sponsors

PARTNERS



SPONSORS



The Cancer Policy Institute *at the* 
CANCER SUPPORT COMMUNITY

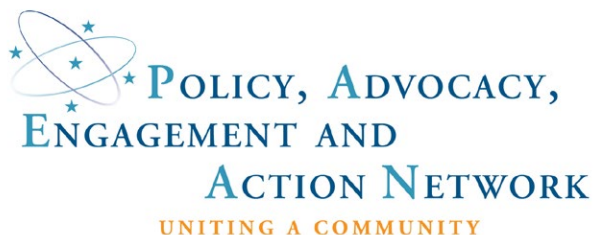
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www.CancerSupportCommunity.org

*The Cancer Support Community
Cancer Policy Institute would like
to thank the members of Uniting a
Community for their partnership.*



American Cancer Society
Community Oncology Alliance
International Myeloma Foundation
Leukemia and Lymphoma Society
Ovarian Cancer National Alliance
Prevent Cancer Foundation