

FDA Laws, Regulations, and Guidance Documents

SLIDE 1

This presentation will give you a very broad overview of the laws, the regulations, and the guidance documents that are important for FDA's work.

SLIDE 2

We will begin with a discussion of the legal framework under which FDA operates. Then we will give a brief introduction to, and history of, some of the laws that FDA implements. Finally, we will talk about regulations and guidance documents, two important tools that FDA uses.

SLIDE 3

We begin with the legal framework, and the structures behind the legal framework.

SLIDE 4

The U.S. Constitution is the fundamental source of authority for federal laws. (In this presentation, we will not be discussing state laws.)

The federal government is divided into three branches: Legislative, Executive, and Judicial. Let's look at what each of these branches are, and what they do.

SLIDE 5

The Legislative branch consists of both houses of Congress (the House of Representatives and the Senate). The Legislative branch enacts laws. Note that you may hear people use the terms "laws," "statutes," and "acts"; these terms are largely interchangeable. Some of the laws that Congress enacts provide regulatory agencies - like FDA - with their authority to regulate, and some may impose limits on how an agency can use this authority. Some statutes are very general, and others are very detailed.

SLIDE 6

The Executive branch consists of the President and most federal departments and agencies. The Department of Health and Human Services, which includes the Food and Drug Administration, is in the Executive branch. The Executive branch implements and enforces the laws that Congress enacts, sometimes issuing regulations to do so.

SLIDE 7

The Judicial branch consists of the Supreme Court and other federal courts. The Judicial branch makes sure that the Constitution is upheld. Among other duties, it reviews laws to make sure Congress has not gone beyond its constitutional authorities. It also reviews agencies' regulations - including those of FDA - to make sure the agency has not gone beyond its legislative and constitutional authorities.

SLIDE 8

Now, let's look at some of the statutes that Congress has passed that are particularly important for FDA in general, and FDA's Center for Biologics Evaluation and Research, or CBER, in particular. CBER works with two main statutes, the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act.

The FD&C Act is relevant to all the products that FDA regulates, including biological products. It has been amended over 100 times.

The PHS Act is very long, but there are two provisions that are very important to CBER's regulation of biological products. One is the licensing provision, under which CBER can approve biologics. Congress has amended this provision about 11 times. The other is the communicable disease provisions, which give FDA the authority to issue regulations to prevent the spread of communicable disease. These provisions have been amended about 4 times.

Next, we'll discuss the history of these laws and some of the most important amendments.

SLIDE 9

The Biologics Control Act, enacted in 1902, was the beginning of federal regulation of biological products. Indeed, it was the start of federal regulation of any medical products. Congress took this action in response to a tragedy involving an unregulated biological product.

In 1901, a diphtheria antitoxin was manufactured with materials from a horse that had tetanus. A number of people received the contaminated product and died of tetanus as a result. Because of this and a similar incident, Congress stepped in and decided that federal legislation was needed, and passed the Biologics Control Act in 1902.

This statute required, for the first time, pre-market approval and a resulting license for these biological products. It subjected any company making antitoxin or vaccines to inspections. It also included labeling requirements and provided penalties for those who violated the statute.

SLIDE 10

A federal statute for the regulation of food and drugs was put into place a few years later, in 1906. The Federal Food and Drugs Act focused primarily on enforcement - it prohibited the misbranding and adulteration of products, and provided for criminal penalties, including imprisonment and fines, for violations of the statute. In addition, it authorized product seizures. A seizure is a court action against a product, not a person, through which a court can require a product to be held in place and not be moved during legal action by the government. Once the lawsuit is resolved, a decision is made on what to do with those products that were determined to be violative, for example, the product might need to be destroyed.

The Federal Food and Drugs Act, however, did not require pre-market approval for drugs.

SLIDE 11

In 1938, Congress enacted a landmark piece of legislation, the Federal Food, Drug, and Cosmetic Act, or FD&C Act. As was the case with the Federal Food and Drugs Act in 1906, Congress enacted this statute as a result of a tragedy. In 1937, a manufacturer produced a drug, elixir sulfanilamide, which contained an unlabeled, toxic solvent. The company sent shipments of this drug all over the U.S., and within 2 months more than 100 people in 15 states had died. In response to this tragedy, Congress enacted a new law that required evidence of safety before a drug product could be marketed. The new law included many other provisions, including authorizing inspections of factories. It also added a new regulatory tool: injunctions, a court action ordering a firm to do certain things, such as shut down its production of a product. The FD&C Act also extended regulatory authority to products beyond drugs, such as cosmetics, and therapeutic devices, although the term device was not used.

The 1938 Food, Drug, and Cosmetic Act did not, however, require evidence of efficacy before a medical product could be marketed.

SLIDE 12

As mentioned earlier, the Public Health Service Act is a key statute for CBER. In 1944, Congress compiled a number of statutory provisions that existed in various laws into the Public Health Service Act. The provisions included the requirement for biologics to be licensed and authorities related to the control of communicable diseases.

Under the Public Health Service Act, FDA can issue regulations to prevent the spread of communicable diseases. That not only gives FDA authority to regulate biological medical products, but also the authority to regulate other products carrying a risk of communicable disease. For example, CBER regulates the interstate movement of turtles, because they can potentially spread salmonella. FDA has, in fact, issued regulations addressing that risk.

SLIDE 13

In 1962, Congress passed the Kefauver-Harris Drug Amendments in response to the thalidomide tragedy. Starting in 1957, thalidomide was widely sold in other countries and was prescribed to pregnant women to treat nausea. In 1960, the company applied to FDA for approval of thalidomide, but a medical reviewer who had just started working at FDA blocked its approval because of her concerns about its safety. By late 1961, it was obvious that thalidomide had caused serious birth defects in thousands of children. The following year, Congress enacted this significant legislation that put in place many important new requirements, including the requirement that manufacturers demonstrate the efficacy of a drug before it can be marketed in the U.S.

Incidentally, that medical reviewer, Dr. Frances Kelsey, received an award from President Kennedy in 1962 for her scientific judgment and her determination, in the face

of pressure from the manufacturer, to keep this product off the market. FDA later created an award, the "Dr. Frances O. Kelsey Award for Excellence and Courage in Protecting Public Health," which was first conferred on Dr. Kelsey herself in 2010.

SLIDE 14

The next significant changes to the Food, Drug, and Cosmetic Act were the Medical Device Amendments of 1976. Although therapeutic devices had been included under previous legislation, Congress specifically addressed them in this amendment. Congress revised the definition of "devices" and put into place a risk-based approach to their regulation. Congress established three regulatory classes for devices, based on the amount of control necessary to assure that the device is safe and effective. These amendments required FDA to classify each medical device, and provided for different levels of oversight depending on the device. The higher the class, the more requirements that apply and the greater the oversight that FDA has over the product.

The Medical Device Amendments also required either pre-market approval or clearance of devices. Generally, clearance - rather than approval - is used for products that can be shown to be "substantially equivalent" to another product that has already been shown to be safe and effective.

SLIDE 15

In the 1980s, Congress enacted two important statutes. Recognizing that manufacturers would often choose not to study possible treatments for diseases that affect only small numbers of people, Congress passed the Orphan Drug Act in 1983. This act provided economic incentives to companies to encourage the development of treatments for rare diseases.

Later that decade, Congress enacted the National Childhood Vaccine Injury Act. This Act amended the Public Health Service Act to require that certain information be made available to patients receiving vaccines. It also gave FDA the authority to recall not only vaccines, but also other biological products.

The National Childhood Vaccine Injury Act is a compensation statute. Vaccines, like other medical products, are not completely without risks. For any medical product, FDA must weigh its benefits and its risks; if FDA determines that the benefits of a product outweigh its risks, FDA approves the product. In the United States, children must receive a number of vaccines before they start attending school. These vaccines are considered extremely important for public health. However, there are, unfortunately, times when someone experiences an adverse event after getting a vaccine. Congress recognized that, if vaccine manufacturers were taken to court and sued for damages when this happens, they might stop making these vaccines. Because it is so important that children be vaccinated, it is also important that companies continue to make these vaccines. This statute provides an alternative to litigation - a compensation scheme for people who experience certain adverse events after receiving certain vaccines.

SLIDE 16

In 1992, Congress enacted the Prescription Drug User Fee Act, also called PDUFA. At that time, FDA reviews and approvals of drugs were taking a long time, and there was much discussion about the lack of adequate resources for FDA to review applications in a timely way. Congress, FDA, and industry developed a novel approach to this problem: FDA and industry would negotiate an agreement, and Congress would include that agreement in a statute. Under the agreement and under PDUFA, manufacturers agreed to pay fees for marketing applications they submitted to FDA, and FDA agreed to use those fees for activities related to the review process, and to meet certain target goals. For example, FDA would use PDUFA fees to hire reviewers to look at applications and safety issues, with a goal of reducing review time.

Normally, when Congress enacts a law, it remains in effect unless or until it is changed by Congress. An example would be the general licensing provisions for a biologic. Sometimes, however, Congress enacts a law that has a "sunset provision" - that is, it is written so that it expires after a particular length of time, unless reauthorized by Congress.

PDUFA had a "sunset provision," and was written so that it would expire after five years, if not reauthorized by Congress. Every five years, the provisions must be renegotiated, which may include discussions about whether the Agency needs more money, whether FDA has met its commitments, whether industry should have different expectations, or whether FDA needs to communicate its expectations differently. Although this renegotiation process is very time-consuming, the user fee approach has proven successful. The renegotiated terms have generally strengthened the process of product approval and has enhanced public health. Every five years, FDA and industry have negotiated a new agreement, and Congress has reauthorized PDUFA. In 2017, for example, PDUFA 6 was reauthorized for another five years.

As a result of the User Fee system, Congress, industry, and the public pay close attention to whether FDA is meeting its PDUFA goals.

PDUFA was the first, but not the last, user fee act for FDA.

SLIDE 17

In 1997, Congress enacted the Food and Drug Administration Modernization Act, or FDAMA. FDAMA addressed a number of issues. It reauthorized PDUFA. It provided that FDA should make efforts to harmonize the regulation of drug products and biological products. It established a clinical trials database under the Public Health Service Act, which is run by the National Institutes of Health and National Library of Medicine. It also called for a number of other broad reforms, such as accelerating the review of devices.

SLIDE 18

In 2002, Congress enacted the Public Health, Security, and Bioterrorism Preparedness and Response Act. This followed the terrorist attacks in the U.S. on September 11,

2001. This act gave FDA the authority to do more to prevent and respond to emergencies. It also required FDA to issue regulations to have greater control over imported and domestically produced commodities.

In addition, this act reauthorized PDUFA, marking the third time that user fee requirements were authorized for prescription drugs.

SLIDE 19

In 2002, Congress also enacted the Medical Device User Fee and Modernization Act, or MDUFA, which extended the user fee model to the regulation of medical devices for the first time. This legislation also provided that accredited third parties - rather than FDA - might do inspections of device manufacturers. Though not many third parties became accredited, the intent of the legislation was to increase the number of device firms that were inspected and to alleviate the burden of these inspections on the FDA.

SLIDE 20

In 2003, Congress passed the Pediatric Research Equity Act, or PREA. At this time, there was awareness that many medicines given to children had not been studied in children. Doctors sometimes had to treat children as "little adults" - making their best guesses about, for example, the appropriate dose for a child based on the child's weight. Congress recognized that regulators and medical practitioners needed to know more about the effects of drugs in a pediatric population - for example, whether a particular product worked the same way in a child as it did in an adult. This statute required sponsors to conduct pediatric testing of certain products. However, it also allowed FDA to determine whether or not such pediatric testing could be waived or deferred. For example, FDA might determine that pediatric testing could be waived if the product is used to treat a disease that does not occur in children, for example, prostate cancer. FDA could also determine that pediatric testing could be deferred if, following clinical trials in adults, an important product was ready for approval. A purpose of the statute was to ensure that pediatric studies are conducted, but Congress recognized that giving FDA flexibility about the timing or scientific necessity of such trials would be in the interest of the public health.

SLIDE 21

In 2007, Congress passed the Food and Drug Administration Amendments Act, referred to as FDAAA. This was also another very large law, which added significantly to FDA authority.

FDAAA reauthorized a number of provisions, including the Prescription Drug User Fee Act and the Medical Device User Fee Act. It also reauthorized the Pediatric Research Equity Act, including a provision to include new pediatric information in labeling. The agency also formed an internal Pediatric Review Committee, in part to provide reviews of referrals and waivers granted under PREA and to help ensure quality and consistency across the Agency.

SLIDE 22

This slide provides additional information about FDAAA.

FDAAA included a section on pediatric devices, to enhance the regulation and development of devices used in children. It also created a foundation called the Reagan-Udall Foundation, to support areas of research that would be critical to getting products to market.

FDAAA expanded the existing requirements with regard to the existing database that contains information on ongoing clinical trials. FDA works closely with the National Institutes of Health on the information to go in the database. FDAAA included a provision for the inclusion of study result information in the database. FDA participated with NIH in a public meeting on this topic.

FDAAA also contained a provision on conflicts of interest. This provision has to do with advisory committee meetings, where FDA consults with outside experts on many issues, including issues related to product approvals. Some people have raised concerns about the number of people on the advisory committees who have conflicts, and this provision contains restrictions in terms of selection of advisory committee members.

Title 9 of FDAAA contained new safety provisions. Some of these provisions gave FDA the authority to require post-marketing studies in certain instances. For instance, if, in looking at the adverse events associated with a product, there is a signal suggesting that the product may be causing the adverse event, FDA can require a post-marketing study or a post-marketing trial.

SLIDE 23

In 2010, Congress enacted the Biologics Price Competition and Innovation Act, or BPCI Act, which amended the PHS Act. This act was very important because it created, for the first time, a pathway for biological products that is somewhat like the pathway for generic drugs. Specifically, it created an abbreviated licensure pathway for biological products that are demonstrated to be "biosimilar to" or "interchangeable with" a biological product already licensed by FDA. The previously licensed product is called the "reference product."

SLIDE 24

A biosimilar product must be "highly similar" to a reference product. It cannot have any clinically important differences in its safety or effectiveness. The only differences permitted between the biosimilar product and the reference product are minor ones in clinically inactive components.

SLIDE 25

An interchangeable biological product must not only meet the requirements of biosimilarity to a reference product; it must also meet additional standards. A

pharmacist may substitute an interchangeable biologic for the reference product without consulting the prescriber.

FDA requires both licensed biosimilar and interchangeable biological products to meet the Agency's rigorous standards of safety and efficacy that are required for any biological product. That means patients and health care professionals will be able to rely upon the safety and effectiveness of the biosimilar or interchangeable product, just as they would the reference product.

SLIDE 26

In 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This act expanded FDA's authorities and strengthened our ability to safeguard and advance the public health in several ways: Through user fee reauthorization; by increasing stakeholder involvement; by promoting innovation; and by enhancing the safety of the drug supply chain.

With regard to user fees: FDASIA reauthorized the existing user fee authorities (PDUFA (5) and MDUFA (3)), and also, for the first time, authorized user fees for biosimilar biological products.

SLIDE 27

FDASIA also promoted innovation by introducing a powerful new tool, the "breakthrough therapy" designation. This new designation helps FDA assist drug developers in order to expedite the review of new drugs when there is preliminary clinical evidence that the drug may offer a substantial improvement over available therapies for patients with serious or life-threatening diseases. FDASIA also granted additional authorities with regard to the Pediatric Research Equity Act, or PREA, and made PREA permanent.

SLIDE 28

With nearly 40 percent of finished drugs being imported, and nearly 80 percent of active ingredients coming from overseas sources, protecting the global drug supply chain and making sure that patients have access to the drugs they need is a priority for FDA. New authorities under FDASIA include: Permitting FDA to switch to a risk-based system in determining the frequency of inspections; prohibitions against manufacturers' delaying, denying, limiting, or refusing inspection of their facilities; the ability to cooperate more closely with foreign regulators; and the imposition of criminal penalties for those who intentionally adulterate a product or counterfeit drugs.

SLIDE 29

In 2016, Congress enacted the 21st Century Cures Act, designed to help accelerate medical product development and bring new advances to patients faster and more efficiently.

The law built on FDA's ongoing efforts to incorporate the perspectives of patients into product development and into FDA's decision-making processes.

It also enhanced FDA's ability to modernize clinical trial designs and clinical outcome assessments, which will speed the development and review of novel medical products, including medical countermeasures.

The law established new expedited product development programs, including the Regenerative Medicine Advanced Therapy designation, which offers a new expedited option for certain biologics; and the Breakthrough Devices program, designed to speed the review of certain innovative medical devices.

In addition, the 21st Century Cures Act directed FDA to create one or more intercenter institutes to help coordinate activities in major disease areas among FDA's drug, biologics, and device centers and to improve the regulation of combination products. As a result, FDA created its Oncology Center of Excellence.

SLIDE 30

In 2017, Congress passed the FDA Reauthorization Act, or FDARA. It reauthorized PDUFA for the fifth time, MDUFA for the third time, and the Biosimilar User Fee Act, or BsUFA, for the first time. Among its other provisions, FDARA allowed FDA the flexibility to inspect medical device facilities based on risk. It authorized FDA to require a pediatric investigation into an adult cancer drug if that drug is directed at a molecular target that is relevant to a pediatric cancer. FDARA established a flexible and more efficient path to market for certain new medical device accessories. And, it streamlined the combination product review process to enhance coordination and transparency between FDA and industry.

SLIDE 31

Now that we've had a quick look at some of the history of FDA's legal authorities, let's take a closer look at the two primary statutes of importance to FDA and CBER: The Public Health Service Act and the Federal Food, Drug, and Cosmetic Act. For CBER, the PHS Act is key, because it defines biological products, and gives FDA the authority to license such products. Section 351 of that act defines what a biological product is: "A virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product...applicable to the prevention, treatment, or cure of a disease or condition of human beings." So to be a biologic, a product has to be applicable to preventing, treating, or curing diseases or conditions in people (not animals), and must be one of the listed products in the first part of the definition. Note that the definition also mentions "analogous product[s]," a term that has been the subject of discussion among applicants and FDA.

SLIDE 32

Section 351 also provides FDA with the authority to license biological products that are distributed in interstate commerce. When the PHS Act and FDA refer to "licensure" of a biological product, we mean premarket approval of, or marketing authorization for, the biologic. In other countries, people may use the term "license" to refer to something different.

In order to be licensed, a biological product must be shown to meet standards of safety, purity, and potency. The facility has to meet appropriate standards, and manufacturers have to agree to allow their facility to be inspected.

SLIDE 33

Licensure is a powerful regulatory tool. If a biological product is in violation of the statute and/or FDA's regulations, FDA has the power to suspend or revoke the license. FDA can take this action administratively, without even having to take the license-holder to court. FDA also has the power to recall products that are no longer safe, pure, or potent.

SLIDE 34

In addition to the licensing provisions, the PHS Act provides FDA with additional authority. Under section 361 of that statute, FDA can also take actions to prevent the spread of communicable diseases. This statutory provision does not prohibit shipping something in interstate commerce that might cause communicable disease. Instead, it says that the Secretary of Health & Human Services, through FDA, can issue regulations to prevent the spread of communicable disease. In other words, under section 361, FDA must issue a regulation in order to prohibit an activity.

FDA has used this authority in a number of areas. For instance, some of the blood regulations about communicable diseases have been written partly under this authority. In addition, the tissue regulations were also issued under this authority. For some tissue products, such as skin and bone, FDA does not require pre-market approval. Instead, FDA requires that there be provisions in place to prevent the spread of communicable diseases through these products. These provisions include testing the donors, screening them, and asking them questions for high-risk behavior.

SLIDE 35

Biologics have an interesting characteristic: Generally, a biological product also meets FDA's definition of a drug, and, on rare occasions, it may meet the definition of a device. Therefore, biologics are generally also subject to most of the requirements for drugs under the FD&C Act. This provides FDA with an additional source of authority when regulating biologics.

For instance, a vaccine also meets the definition of a "drug." Thus, the provisions in the FD&C Act also apply, such as the requirement that manufacturers follow good manufacturing practices, or that products must be labeled according to the requirements of the FD&C Act. Biological drugs are subject to the prohibitions and sanctions in the FD&C Act in addition to those in the PHS Act.

SLIDE 36

While the PHS Act, the FD&C Act, and their amendments are the statutes that specifically convey regulatory authority to FDA and impose requirements on it, the FDA, like other regulatory agencies, is subject to many other laws. This slide lists a few of these other laws that affect the FDA.

The Administrative Procedure Act, or APA, controls the way in which FDA can issue regulations and take other actions. FDA must follow the requirements of this act in order to produce legally-binding regulations.

The Federal Advisory Committee Act, or FACA, is a transparency statute. FDA often consults with outside experts, for example when deciding whether a product should be approved. In consulting outside experts, FDA must follow the requirements of this act, which often requires the Agency to open Advisory Committee meetings to the public to the extent possible.

The National Environmental Policy Act, or NEPA, requires FDA to take into account the effect their decisions may have on the environment - for example, a decision whether to approve a product that is made from a raw material that is endangered. In some cases, companies may need to do an assessment of what effect their product might have on the environment.

The Freedom of Information Act, or FOIA, is another transparency statute. FDA, like all federal agencies, is subject to this act. When FDA receives a request from the public for information in FDA's records, the agency must - with certain exceptions - disclose this information to the requester.

SLIDE 37

Like other regulatory agencies, FDA issues regulations under its statutory authorities. Sometimes you will hear people use the word "rule" instead; the terms mean the same thing. A regulation has the effect of law, and is binding on industry and on the Agency.

SLIDE 38

FDA's rulemaking procedures are subject to the Administrative Procedure Act and generally involve what is called "notice and comment rulemaking." This type of rulemaking generally requires an agency to publish a notice of its proposed rule in the Federal Register. The Federal Register is a daily publication, available in hard copy and on-line, used by all federal agencies to communicate with the public; it covers many topics, including rulemaking. When FDA proposes a rule, it explains its rationale. By publishing notice of the proposed rule, FDA allows interested parties all over the world the chance to comment on FDA's rationale and proposed rule. At the close of the comment period, the agency assesses all the comments received. FDA takes the comments it receives very seriously. When FDA prepares the final rule, it addresses the comments in a preamble to the rule itself. Usually, FDA makes changes to the rule that reflect information that the comments have provided. These procedures promote transparency and ensure that interested parties know what regulatory requirements FDA is considering. The procedures also ensure that FDA gets input from all possible stakeholders and can put into place well-informed rules.

SLIDE 39

The final rule published in the Federal Register is accompanied by a preamble that describes the comments received and FDA's responses. After the final rule is published, the binding language of the rule is included in the Code of Federal Regulations, or CFR.

SLIDE 40

When an agency like FDA proposes a new rule, the agency must make certain assessments, such as the impact of the rule on small businesses, on the environment, on state and local governments. FDA is also required to figure out how much paperwork the new rule would require people to do. FDA must also do an economic analysis. Rulemaking is a big undertaking and takes time.

SLIDE 41

The next few slides list some of the regulations that FDA works with regularly.

FDA's regulations are contained in Title 21 of the CFR. The first parts, 1 through 99, contain rules on general topics. For example, there are regulations about advisory committees, conflicts of interest, and the Agency's treatment of certain information.

SLIDE 42

Farther into Title 21, you have regulations that address investigational studies. Parts 50 and 56 contain the human subject protection provisions, as well as provisions related to institutional review boards.

Sections numbered in the 200s and 300s have a lot of information about drugs, which may be applicable to CBER's products, because, generally, biologics also meet FDA's definition of drugs. These drug regulations include the labeling provisions in Part 201, and the GMP provisions in Parts 210 and 211. The investigational new drug provisions in Part 312 also apply to clinical investigations of biological products.

SLIDE 43

The 600s contain the biologics-specific regulations.

Part 600 contains a number of provisions, including standards for establishments and requirements to report adverse experiences.

Part 601 contains the rules on licensing biologics.

For blood and blood components, there are specific regulations on good manufacturing practices in Part 606.

Because CBER regulates some devices, this slide refers to some device regulations, which are in the 800s.

Finally, FDA's tissue regulations are contained in Part 1271.

SLIDE 44

This series includes a separate talk on Guidances and Good Guidance Practices, so this slide will only mention them briefly.

Congress enacts statutes, and FDA issues legally-binding regulations based on those statutes. FDA also issues non-binding guidance documents. Statutes tend to be the most general, and FDA may need to interpret and implement statutes by issuing more specific Agency regulations. If the Agency needs to go into more detail about how it interprets a regulation, FDA may issue a non-binding guidance that is even more specific. Guidance documents are issued to provide a little bit more information about what people can do to comply with existing requirements. They represent FDA's current thinking on matters, but they are not binding, so industry could also do things in a different way, as long as they comply with the statutes and regulations.

FDA must follow certain procedures when it issues guidance documents. These are found in section 10.115 of the CFR.

SLIDE 45

This slide shows the Agency websites where you can find the guidance documents that relate to the different medical product Centers.

SLIDE 46

And the next three slides contain a list of helpful acronyms, including those we've used throughout this presentation.

(pause)

SLIDE 49

This concludes the presentation, "FDA Laws, Regulations, and Guidance Documents." We would like to acknowledge those who contributed to its development. Thank you.