

Questions for the Record
HELP Committee Hearing, November 17, 2015
“Hearing on the Nomination of Dr. Robert Califf to serve as FDA Commissioner”
Dr. Robert M. Califf

Chairman Lamar Alexander

- 1. The Food and Drug Administration (FDA) has been criticized for how it restricts what drug and medical device manufacturers can tell doctors and insurers about lawful uses of their products. In particular, current regulations are unclear and heavily restrict manufacturers’ ability to provide truthful and non-misleading information to doctors and insurers, unless the information appears in the product’s FDA-approved labeling. Often, however, this information relates to medically accepted treatments that doctors can—and frequently do—prescribe for their patients, and that the federal government will even reimburse. In some instances, such “off-label” uses may even be the standard of care.**
 - a. In an era when information about medical products abounds on the Internet—some of it reputable, some of it not—do you think it is appropriate for FDA to maintain decades-old policies that block manufacturers from sharing factual, non-misleading information about lawful treatments with doctors and insurers?**

It’s important to remember the fundamental public health interests underlying the Agency’s current statutory and regulatory framework, including the requirements related to premarket review of medical products before they are distributed for new uses. This framework was developed over time in response to public health tragedies, which Congress addressed by requiring independent review of scientific evidence of the products’ safety and efficacy. The Agency is currently examining its rules and policies, with the goal of harmonizing the important public health and safety interests served by FDA’s premarket review of new uses of medical products, with the value that sharing relevant scientific information regarding unapproved uses can have in certain contexts, and with First and Fifth Amendment considerations.

I believe it is appropriate for FDA to continue examination of its rules and policies and to refine them as appropriate, in light of the important public health issues, free speech, and due process principles at stake.

- b. Several courts, including the United States Court of Appeals for the Second Circuit and the United States District Court for the Southern District of New York, have indicated that FDA’s restrictions on manufacturers’ speech may violate the First Amendment. These decisions raise the possibility that many of FDA’s regulations governing the promotion of medical products could be struck down by the courts**

unless they are substantially revised. What proactive steps will you take, if confirmed, to avoid that situation?

If I am confirmed, I will support FDA's efforts to comprehensively review its regulations and guidance documents and will make it a priority for the Agency to work on revising these documents as appropriate, in an effort to harmonize the goal of protecting the public health with First-Amendment interests.

2. Before you began your current position at FDA, you advocated publicly for changes to certain regulations. For example, you gave a presentation in 2014 in which you called regulation a "barrier to disruptive innovation," and, in 2013, you wrote in the New England Journal of Medicine about inefficiencies in the requirements for clinical trials and safety monitoring for approved drugs.

a. What are the three biggest ways in which FDA poses a barrier to innovation? If confirmed, how would you address these problems?

I think you are referring to a slide I have used in multiple lectures that characterizes regulation as a barrier to disruptive innovation.

This issue is a very important one for people proposing to develop new medical therapies. Throughout my career, I have benefitted from a close relationship with the Fuqua School of Business at Duke and the many contacts it brings in the field of health economics and health management. Among the many brilliant people I have met is Clayton Christensen ("The Innovators Dilemma"), who developed the concept of "disruptive innovation." This concept is derived from the study of the transformation of industries with the base case being the conversion of radios from the vacuum tube to the transistor. The concept is that the new product or method initially is inferior but lower priced so there is a market for it. This enables innovators to iteratively improve their product until it becomes better and supplants the old product or method. My purpose in showing this slide in multiple lectures is to explain to audiences that often include students, trainees in fellowship and scientists who are not involved in development of medical products, why the risk and investment in biotechnology is higher than most other industries, i.e., because it is a highly regulated industry, which is in fact a necessary barrier to protect public health, as discussed below. The amount of capital needed is lower and the time to return on investment is shorter in many other industries.

I have never stated, implied, or argued that the barrier should be lowered or removed. In fact I do not believe that we should be putting inferior medical products on the market, nor do the American people want inferior products to be used in medical practice. The belief that we should have evidence of benefits and risks *before* marketing in health care has been a driving force in my career and a motivation to develop more effective, efficient and unbiased ways of conducting generalizable clinical trials and implementing quality systems for learning in health care as a focus of my academic and practical work.

In summary, the purpose of the slide is to point out an issue that is motivational for people who want to develop medical products that prevent death and reduce disability:

there is a requirement to demonstrate that your product is safe and effective before you market it and that it does not put people at risk, compared to the clinical care that is currently accessible. This is a good thing and forms the basis for the benefit of a strong FDA to make these determinations, and it places a special responsibility on innovators to develop the evidence base that can ensure the FDA (on behalf of the American public) that the product is safe and effective.

With these requirements (i.e., appropriate barriers) in place, it is reasonable to ask the question, what can FDA do to enable innovators to develop new approaches and technologies, maintaining the same standards, but reducing the cost and time so that Americans can get access to new technologies that are safe and effective and so that investors continue to invest in this enterprise, which is essential to our health and vital to our economy? Among a longer list, my top three responses would be:

- Reform the clinical trials system, using the principle of Quality by Design, so that a combination of small, focused trials for precision medicine and very large trials using electronic health records for inclusion of important populations can be conducted at a dramatically lower cost per unit of knowledge. The small precision medicine trials are lower cost because of lower sample size and the very large, inclusive trials will be lower cost because they will take advantage of data already collected and the novel methods of community-based research. FDA's Sentinel project is an excellent building block with claims data on over 170 million Americans available to evaluate the safety of drugs and biologics, but the same system with modifications could be used to dramatically reduce the cost of data collection in clinical trials. Direct involvement of patients will also enable us to streamline, because a more involved public, together with more trials relevant to the needs of patients will lead to faster enrollment.
- A second key approach is to continue to improve the communication between FDA and the scientific community. In every case where FDA has offered more meetings with sponsors, the opportunity has been over-subscribed. In addition, public-private partnerships have been highly successful in promoting multi-sector dialogue and developing a common view of key issues in medical product development, including the Medical Device Innovation Consortium and the Clinical Trials Transformation Initiative.
- Finally, effective interactions between FDA and its federal partners can be an important factor in maintaining the appropriate standard while reducing the cost of medical product development. The FDA-National Institutes of Health (NIH) Leadership Council is a successful collaboration between FDA and NIH, focused on clarifying the biomarker-surrogate-clinical outcome continuum and streamlining clinical trials.

There are many other measures to achieve the goal of optimizing the efficiency of the effort to produce useful, safe, and effective medical products based on high-quality evidence.

- b. In your academic work, you have argued for expanding the size of certain clinical trials. What impact would larger clinical trials have on the cost and speed at which innovative new treatments come to market? Are there specific policies you would promote that would affect the size of future trials, and would those policies be tailored to particular types of trials?**

As discussed above, the principle of Quality by Design, an initiative that FDA is already undertaking, will lead to some trials that are “targeted,” when the therapy is expected to have a large effect in a small subpopulation, and others that will need to be much larger to ensure that the treatment is safe and effective across the spectrum of patients likely to be treated. The targeted trials are made possible by the dramatic advances in molecular biology and precision medicine methods, and the larger trials are made possible by the ubiquity of electronic health records and social media. Quality by Design is a risk-based approach to pharmaceutical development and manufacturing that has been described in numerous FDA guidance documents. In recent years, this approach has been increasingly recognized as having significant applicability to the development of clinical trial protocols and is now included in an FDA guidance document on risk-based monitoring.

Another consideration is that rare diseases will continue to need special trial considerations, especially when there is no effective treatment. As information and communication technologies advance, however, we can also develop new methods to improve enrollment in these trials.

- 3. Will you commit to requiring FDA staff to act through rulemaking, rather than through the guidance process, when (a) it intends to legally bind regulated parties or (b) it expects regulated parties to change their behavior in burdensome or costly ways?**

The Federal Food, Drug, and Cosmetic Act (FD&C Act), and FDA’s own regulations, set forth clear criteria for determining whether guidance is appropriate and provide for ample opportunity for public consideration of, and comment on, FDA guidances. I commit to working to ensure that the Agency continues to follow the requirements set forth in these authorities and issue guidance only where appropriate.¹

When issuing guidance, FDA complies with the requirements set forth in the FD&C Act as well as its own good guidance practices (GGPs). Section 701(h)(1)(A) of the FD&C Act outlines the

¹ In addition, the Administrative Procedure Act (APA) (5 U.S.C. 551-559) prescribes procedures for an agency issuing a “rule,” which is defined as “an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency” (5 USC 551(4)). For legislative and substantive rules that create a new law, rights or duties, the APA requires that agencies, among other things, provide the public with adequate notice of a proposed rule followed by a meaningful opportunity to comment on the rule’s content.

procedures that FDA must adopt when issuing guidance relating to its initial interpretations of a statute or regulation, changes in interpretation or policy, and existing practices or minor changes in policy. The FD&C Act requires that the Secretary develop guidance documents with public participation and makes clear that guidance documents “shall not create or confer any rights for or on any person.”

FDA’s GGP regulation provides greater detail regarding the circumstances when guidance is appropriate and the procedures that must be employed when the Agency issues guidance. The GGP regulation explains that guidance documents are intended to describe the Agency’s interpretation of policy on a regulatory issue, but are not intended to be binding documents or establish legally enforceable rights or responsibilities that bind the public or FDA (21 CFR 10.115). Guidance documents contain a statement of this non-binding effect.²

FDA’s guidance documents are a valued resource for many external stakeholders, including industry and patient advocacy groups, because they can serve as a means of conveying FDA’s current thinking on important issues, such as the most current scientific practices related to product development. Often the Agency’s guidance documents are issued in response to stakeholder requests. Guidance is a helpful tool that allows the Agency to inform stakeholders about its views on scientific and technical policy issues. Small businesses are often particularly interested in and reliant upon Agency guidances on such topics.

4. Food and medical products regulated by FDA increasingly are imported from other countries into the United States. Currently, FDA is not able to clear many time-critical and often temperature-sensitive shipments quickly enough for them to arrive at their destinations intact and when they are needed.

a. How do you think FDA can improve its ability to process time-sensitive shipments by commercial express carriers in a timely manner to minimize the expense and disruption that even short delays can cause?

FDA continues work on streamlining, improving, standardizing, and clarifying import processes and has initiated a number of efforts designed to process imported shipments more efficiently. FDA is a Participating Government Agency (PGA) involved in the ACE/ITDS (Automated Commercial Environment/International Trade Data System) project, which is designed to provide the import community with a single window for importing into the United States, commonly referred to as “One U.S. Government at the Border,” to streamline the entry process and provide improved messaging to the trade community.

FDA is currently running a Secure Supply Chain Pilot Program (SSCPP) for pharmaceuticals. The SSCPP is allowing FDA to assess the various entities and

² That said, in certain instances, FDA is expressly authorized by statute to promulgate guidances with binding effect. In such cases FDA clearly explains the extent to which such guidance is binding, based on the requirements in the statute, in the guidance document itself. See, e.g., *Guidance for Industry: Necessity of the Use of Food Product Categories in Food Facility Registrations and Updates to Food Product Categories* (October 2012), available at <http://www.fda.gov/RegulatoryInformation/Guidances/ucm324778.htm>.

processes involved in a repetitive-type import chain; and if found acceptable and if all information is accurately submitted at the time of entry, it would allow for more and quicker system-based releases of shipments (as opposed to having to manually verify required information). If successful, the expansion of this program will help expedite the admissibility process for pharmaceuticals originating from known sources, destined for known U.S. entities.

In addition, FDA is participating with U.S. Customs and Border Protection (CBP) in a trusted Trader Program designed to facilitate the importation process for selected firms. CBP issued a *Federal Register* Notice announcing a test program on June 16, 2014. FDA has been involved in the review of applications. The pilot will begin after the applicant awardees have been notified and CBP receives confirmation of the intent to participate.

FDA is in the process of implementing the Voluntary Qualified Importer Program (VQIP) for human and animal food to help facilitate the import entry of products from importers who demonstrate a high level of control over the safety and security of their supply chains. VQIP importers must offer FDA various assurances of compliance, including facility certifications of their foreign suppliers of VQIP products, in exchange for the expedited release of entries of those products imported into the United States. FDA continues to work on the operational design of VQIP; currently, IT requirements are being addressed and importer user fees are under development.

To improve transparency, FDA developed and deployed the Import Trade Auxiliary Communication System (ITACS), which facilitates two-way communication with the import trade community. ITACS allows users to check the status of FDA-regulated entries and lines, to submit entry documentation, and to submit the location of goods availability for those lines targeted for FDA exam. The system is currently undergoing enhancements to allow for FDA notifications to be sent directly to regulated industry via electronic means, which will allow for more timely and efficient communications.

FDA has conducted a centralized entry review pilot for courier operations. The results of this pilot are currently under review as a possible model for centralized entry review and staffing for all couriers that could expand Agency operations and better mirror the courier business model.

FDA is evaluating a dashboard intended to allow real-time monitoring of all aspects of the import process to determine if backlogs are forming and if delays are occurring, so that resources can be allocated before an issue arises.

In addition, FDA has proposed a request for new authority to assess user fees on international express courier facilities (or “couriers”) that import FDA-regulated products into the United States. These fees would support part of the cost of certain inspection-related activities at courier facilities, including processing, examining, sampling, and analysis of FDA-regulated products by FDA to improve timeliness of processing. The fees will be charged in accordance with U.S. obligations under applicable international

agreements (i.e., General Agreement on Tariffs and Trade (GATT), North American Free Trade Agreement (NAFTA), etc.).

- b. What will you do to improve FDA’s ability to use its electronic import review system—the PREDICT system—in a risk-based manner that minimizes the burdens on compliant, non-harmful shipments so that resources are allocated efficiently to the shipments carrying the highest risk?**

Since December 2011, FDA has been utilizing the Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting (PREDICT) screening tool to provide a more dynamic and risk-based assessment of imported shipments. PREDICT is designed to calculate a customized risk score based on a wider variety of factors, including, but not limited to, inherent risk of the product, data anomalies, data quality, and the compliance history of firms (e.g., manufacturer, shipper, and consignee) and the product.

FDA is continuing to improve the capabilities of PREDICT to minimize the impact on imported shipments. For example, many shipments consist of multiple commodities. Line release is a recently implemented enhancement to PREDICT that will allow FDA to evaluate a higher-risk commodity in a shipment, independent of other products that may be included in the same shipment but do not have the same level of risk.

FDA has modified the PREDICT risk evaluation process from a pool of all FDA-regulated products to a commodity-based approach in order to compare products with similar risk factors. This will improve targeting for medium- and higher-severity products and improve the “May Proceed” rate for lower-risk commodities. As of November 2015, this improvement has been implemented for medical devices and diagnostics, biologics, human foods, pharmaceuticals, radiation-emitting products, and animal foods and feeds. FDA continues to work on developing the same approach for a number of other commodities, including vitamins and supplements, cosmetics, food and color additives, infant foods, housewares, veterinary drugs, medicated feed, and tobacco products.

- 5. In recent months, FDA has sent warning letters to overseas drug manufacturing facilities, particularly in India and China, that detailed alarming violations of current good manufacturing practices. These violations include not only sanitary issues—such as bird and lizard infestations in processing facilities—but also a troubling number of instances in which data were falsified or obscured, including an instance in which an employee grabbed a memory stick and fled from FDA inspectors. While it is reassuring that FDA identified these violations, it also raises questions about the extent to which similar violations in other imports are going undetected.**
 - a. Section 706 of the Food and Drug Administration Safety and Innovation Act, signed into law on July 9, 2012, enables FDA to request records in advance or in lieu of an inspection. This authority enables FDA to detect many data integrity issues without**

having to send inspectors on site, thus improving FDA's ability to detect violations rapidly and efficiently. It is now more than three years since FDA was given this authority, but FDA still has not used it to request records from a particular manufacturer in advance or in lieu of an inspection. Why has FDA not exercised this important authority for improving its oversight of drug safety? When can we expect FDA to begin requesting records in advance or in lieu of an inspection?

FDA recognizes that the authority to request records in advance or in lieu of inspection under the Food and Drug Administration Safety and Innovation Act (FDASIA) is a potentially powerful tool for enhancing FDA's ability to assess drug manufacturers' compliance with current good manufacturing practices, and has sought to plan the use of this broad authority carefully via the several work streams described in greater detail below.

FDA is actively engaged in projects to implement this authority, for example:

- **Public Health Incident:** Recognizing that FDASIA section 706 represented a broad statutory authority that could potentially be used in many inspection contexts, FDA sought to prioritize implementation of the authority based on public health risk. To that end, in October 2014, FDA finalized procedures in the Staff Manual Guide (SMG) for requesting records in advance or in lieu of inspection in the event of a public health incident. Although FDA has not yet encountered a situation warranting use of a 706 request under this SMG, we continue to monitor appropriate opportunities for doing so.
- **Pilot to Optimize On-Site Inspection:** FDA is planning to pilot the use of the authority in advance of a small number of already-planned inspections in 2016, and the Agency will use the results of that effort to inform its strategy on a broader implementation of the authority. FDA believes that use of 706 in advance of an inspection could lead to efficiencies by allowing FDA investigators to maximize the use of their time while on site. FDA is seeking to assess the best use of this authority by gathering data through this pilot effort to evaluate, for example, the appropriate scope and volume of records to request, and the burden of producing and reviewing those records.
- **Quality Metrics:** The continued existence of product quality issues may point to increased complexities in the supply chain, a lack of innovation in manufacturing, a failure to adopt modern manufacturing technologies and robust quality management systems, or other factors. In the summer of 2015, FDA announced the availability of draft guidance for industry entitled "Request for Quality Metrics," and held a public meeting on the Agency's plans associated with a quality metrics reporting program. The draft guidance

and public meeting were intended to gain stakeholders' perspectives on various aspects of the development and planned implementation of a quality metrics program launched under the new FDASIA authority. FDA expects that quality metrics calculated from the data we intend to collect through this program will provide objective measures that, when used with additional internal data, can provide the Agency with indicators of the effectiveness of quality systems associated with pharmaceutical manufacturing. These indicators are expected to be a factor in risk-based inspection coverage, which will enable FDA to focus resources on facilities and products that present a greater risk to consumers.

In addition, FDA has implemented FDASIA section 707 and issued guidance related to this section. Section 707 deems adulterated any drug that is manufactured in an establishment that delays, limits, denies, or refuses to permit entry or inspection. In the FDA final guidance issued in October 2014, we specified that under circumstances delaying, denying, limiting, or refusing a request for records in advance or in lieu of an inspection under section 707 of FDASIA may also result in a drug being adulterated under the FD&C Act.³ In such circumstances FDA may issue an import alert that notifies FDA's field staff that the Agency has enough evidence or other information to refuse admission of future shipments of that imported product.

b. At your confirmation hearing, you stated that you have “major concerns about reimportation” of drugs from other countries, including Canada. Would you please elaborate on these concerns?

Drugs that are not FDA-approved nor manufactured in a facility inspected by FDA do not have the assurance of safety, effectiveness, and quality as do drugs subject to FDA oversight. There have been documented incidences of non-FDA-approved imported drugs found to be contaminated, counterfeit, containing varying amounts of active ingredients or none at all, or containing different ingredients than the FDA-approved product. Moreover, FDA would not be able to make safety and quality determinations for prescription drugs offered for import into the United States that have not gone through the U.S. regulatory process. In fact, FDA evaluation of non-FDA-approved imported drugs revealed that while nearly half of imported drugs claimed to be Canadian or from Canadian pharmacies, 85 percent of such drugs were actually from different countries. Typically, these products are smuggled into the United States after being transshipped to third-party countries in an effort to avoid detection and create an appearance of coming through countries that consumers may find trustworthy. Through FDASIA Title VII and the Drug Supply Chain Security Act, Congress has recognized the need to bolster this closed drug distribution system. Authorizing importation would compromise the closed drug distribution system in the United States and undermine these

³ Guidance for Industry: Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection. <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM360484.pdf>

laws, thus making it easier for unapproved drugs, which may include counterfeit or other substandard drugs, to reach American patients putting their treatment at risk. FDA is concerned that the risks of unapproved products from foreign sources outweigh any potential cost savings. We are also concerned that adverse events flowing from importation of such unapproved products could lead to diminished confidence in FDA-approved products.

- 6. The Food Safety Modernization Act was signed into law in January 2011. It took the agency over four years after the law was enacted to finalize five of the seven regulations required under the law. Congress intended this law to be flexible and risk-based, taking into account the very diverse food industry across our country. If confirmed, how will you ensure that as FDA implements this law, it focuses on and prioritizes high-risk activities in the food supply chain consistent with Congress's intent to introduce a risk-based framework that targets areas with a history of foodborne illness, is flexible, and is not overly burdensome?**

Since the passage of the FDA Food Safety Modernization Act (FSMA), the Agency has pursued a transparent process, engaging all stakeholders, to allow FDA to craft final regulations that provide sufficient flexibility across the broad spectrum of food-producing operations. Throughout the rulemaking process, the Agency has been committed to developing final regulations that are practical for businesses and that help ensure food is safe. An unparalleled outreach effort followed the original proposal of the FSMA rules. As you know, in September 2014, FDA issued supplemental proposals with a number of revisions that would add flexibility and reduce burden in key areas. FDA proposed these changes based on extensive outreach and feedback received during meetings with the public, industry groups, and consumer groups, and in the comments submitted to the Agency on the proposed rules.

In September 2015, FDA finalized preventive controls rules for human and animal food, which require modern preventive practices in food processing and storage facilities. In November 2015, the Agency published additional final rules, which establish enforceable safety standards for produce farms and make importers accountable for verifying that imported food meets the same food safety standards as domestic products. The Agency also issued a rule establishing a program for the accreditation of third-party certification bodies, also known as auditors, to conduct food safety audits and issue certifications of foreign food facilities and their foods. These rules will work together to systematically strengthen the food safety system and better protect public health.

The final rules recognize the importance of providing for flexibility within the requirements. For example, the final produce safety rule enables a state, tribe, or country to request variances if it concludes that meeting one or more of the rule's requirements would be problematic in light of local growing conditions. The state, tribe, or foreign country must demonstrate that the requested variance is reasonably likely to ensure that the produce is not adulterated and provides the same level of public health protection as the corresponding requirement(s) in the rule.

Through our sustained engagement with stakeholders, the Agency has been laying the foundation for effective, efficient, and collaborative implementation of the new standards. The Agency intends to provide guidance and technical assistance to industry so that they know what is expected and are supported in carrying out their responsibilities. For example, FDA, in cooperation with the Illinois Institute of Technology's Institute for Food Safety and Health, has established the Food Safety Preventive Controls Alliance, which is developing training courses and materials on preventing hazards for both human and animal food during production.⁴ These materials will help industry—particularly small- and medium-sized companies—comply with the new preventive controls rules. Our implementation strategy also calls for re-orienting and retraining the FDA inspection and compliance workforce, as well as our state food safety partners, so that we can provide consistent, high-quality oversight within the more preventive, systems-based and technically sophisticated FSMA framework.

Going forward, FDA is committed to continuing to ensure that its FSMA efforts are risk-based and targeted in order to achieve the greatest health benefit, without placing an unnecessary burden on the regulated industry.

- 7. In your role as Deputy Commissioner for Medical Products and Tobacco, you have overseen activities within the Center for Tobacco Products (CTP), including work to finalize a proposed rule to deem additional tobacco products subject to regulation. If that proposed rule is finalized and applies the same “grandfather date” that was written into statute for cigarettes, it will force cigars and other tobacco products, including most if not all electronic cigarettes and e-vapor products, to go through FDA’s lengthy premarket tobacco application (PMTA) process in order to stay on or enter the market. Only recently has FDA acted for the first time to authorize the marketing of new tobacco products through the PMTA pathway, which means that the agency does not have an established track record of acting quickly on PMTAs. As a result, this rule, if finalized, is expected to create significant regulatory burdens on small businesses.**
 - a. If confirmed, will you commit to ensuring that FDA reviews product submissions in a timely manner to prevent a delay of innovative and novel tobacco products from entering the market and limiting consumer choice, which could cause citizens to lose access to products they have been using as less harmful alternatives to traditional smoking? As part of this commitment, will you agree to dedicate as much funding as necessary from user fees to ensure that (a) FDA acts upon PMTAs within the statutory timeframe, and (b) adequate resources to assist applicants who previously have not been subject to FDA regulation?**

⁴ <http://www.iit.edu/ifsh/alliance/>

FDA is committed to continuing to strengthen the process for reviewing tobacco products to determine if they meet the statutory standard for marketing, including acting on applications in a timely way and working with applicants who have not previously been regulated.

As you indicated, FDA recently authorized the marketing of eight new tobacco products under the PMTA pathway. This action shows that the PMTA process is a viable pathway to market for new products, if they meet the statutory standard, which includes the requirement that permitting the product to be marketed would be “appropriate for the protection of the public health.” It took FDA eight months to issue decisions on these applications. Currently, the Agency does not have any pending PMTAs.

FDA has made significant progress in reviewing substantial equivalence (SE) applications for currently regulated products and this momentum will continue. The Agency has increased staffing, taken steps to streamline the SE review process, and established performance goals that include time frames for review of regular SE reports⁵ and review of exemption from SE requests for currently regulated products. FDA has been able to develop these performance goals because of increased capacity, efficiency, and knowledge of the scientific evidence needed to adequately review SE applications.

As of November 1, nearly 70 percent of full regular SE reports had been resolved by a final decision, either because FDA issued an Order letter, issued a Refuse-to-Accept letter, or because the submission was withdrawn.

FDA continues to improve the tobacco product review program, including hiring and training new staff and addressing the scientific policy issues that result from developing a new regulatory review program. We will continue to advance our efforts to review and act on SE reports while preparing for the PMTAs that may be submitted to FDA once the deeming rule is finalized.

FDA recognizes that manufacturers of newly deemed products will need assistance in complying with FDA regulations. The Agency is committed to providing this assistance. For example, the Agency intends to issue guidance, hold training webinars, meet with companies at their request, and increase staffing in the Center for Tobacco Product’s (CTP) Office of Small Business Assistance.

- b. If FDA finalizes this rule, it will result in an increased workload not only for tobacco-specific offices within CTP, but also for other FDA components, such as the Office of Regulatory Affairs, which oversees inspections and other enforcement activity, and the Office of Chief Counsel. Will you commit to ensuring that the increased workload attributable to deeming does not require FDA to shift resources**

⁵ SE applications submitted to the Agency are divided into two types: “provisional” and “regular.” Products that are the subject of provisional applications were received prior to March 22, 2011, and may stay on the market unless FDA issues an order finding them not substantially equivalent, or NSE. Products that are the subject of regular applications cannot be legally marketed unless FDA issues an order that they are substantially equivalent to a valid predicate product chosen by the company.

away from non-tobacco program areas? What specific steps will you take to ensure that such a shift in resources does not occur?

The workload that will result after the tobacco deeming rule is final will not shift resources from non-tobacco program areas. The TCA states that tobacco user fees are the only funds available for FDA activities related to tobacco regulation. The TCA specifically prohibits the use of funds other than tobacco user fees for tobacco regulation activities. The TCA user fees are used to hire the necessary staff in other parts of the Agency that assist CTP in the implementation and enforcement of the law.

8. FDA’s Office of External Affairs engages in a variety of patient outreach programs, often through the Office of Health and Constituent Affairs. One such program involves a partnership with the National Forum for Heart Disease and Stroke Prevention to educate patients about heart disease and stroke, and to encourage them to follow their doctors’ advice about lifestyle changes—such as improvements in diet and exercise. Although doctors’ advice regarding lifestyle changes may be beneficial to the public health, it is not clear why FDA—which regulates the safety and effectiveness of medical products, but not the practice of medicine—is the right agency to be engaging in such efforts.

a. Do you believe that FDA’s statutory mission includes encouraging patients to follow their doctors’ advice regarding lifestyle changes, such as eating better or exercising more? Or are such efforts better left to other public health agencies, such as the Centers for Disease Control?

b. What do you see as FDA’s proper role in the doctor-patient relationship?

FDA believes it is important for the Agency to keep our many stakeholders, including health care professionals and patients, informed as appropriate, when we approve important products, issue safety announcements, and take public health actions. Occasionally these communications may touch on lifestyle issues. For example, when FDA announced its approval of a medical device to treat obesity, our press release pointed out that patients who use the product must follow a medically supervised diet and exercise plan to augment their weight loss; this information is contained in the product labeling approved by FDA. We recognize that while many people learn about FDA’s products and announcements from their health care providers, others learn through FDA’s website, the news media, social media, or from family or friends, so we make sure that our communications include a recommendation that patients and consumers continue to follow their doctor’s advice or to consult their doctor if they have any questions.