

Improving Regulatory Cooperation Between the U.S. Food and Drug Administration and the EU

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Abstract

Rapid growth in trade and innovation in the medical product arena, as well as lengthening international supply chains for foods and drugs, have accelerated the importance of greater cooperation among governmental entities in different countries. We review the U.S. Food and Drug Administration's regulatory scope, and characterize the state of cooperation between FDA and European Union entities. We review memoranda of understanding (MOU) between FDA and selected European entities. We analyze available information about FDA's international cooperation and find that there is very little publicly available information to evaluate the accomplishments and outcomes. Finally, we make practical recommendations for better management of FDA's international activities so as to improve cooperation between FDA and EU entities in a manner consistent with current federal statutes.

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The U.S. Food and Drug Administration (FDA) is responsible for ensuring the safety of a very broad class of products, and enjoys substantial authority, including an ability to ban medical products for which it has not granted marketing approval. A large part of FDA's activities goes beyond simply sending warning letters that threaten or initiate the closure of facilities or the recall of products. Rather it involves collecting information about risks of certain products or classes of products, organizing and analyzing this information to reach conclusions about risk, and then disseminating these conclusions to manufacturers or distributors of FDA-regulated products, as well as to members of the public, health care professionals and staff at other U.S. and non-U.S. government entities. Seen in this way, FDA's activities offer ample opportunities for sharing information, i.e., cooperating with other government entities to collect, organize, analyze and evaluate information and to disseminate information about the risks associated with certain products.

Seeing FDA in part as an information management organization suggests that there may be opportunities for more meaningful cooperation between the FDA and entities around the world with similar responsibilities. Such cooperation could in principle help focus regulatory efforts on areas of greatest risk and thereby reduce both risk and regulatory burdens on lower risk activities around the globe. It could improve efficiency by allowing for more coordinated activities among major trading partners such as the U.S. and the EU and its member countries.

The EU does not have any single government entity with the same responsibilities and authorities as FDA. We endeavor to distinguish among the different EU entities, as necessary. Within the EU Commission, for example, the Directorate General for Health and Food Safety (DG SANTE) has health and food safety responsibilities.⁵ As a regulatory authority it drafts laws, and its proposals become official only once the College of Commissioners adopts them.⁶ The European Food Safety Agency is a decentralized agency with responsibilities for risk

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⁵ See, e.g., European Commission, D G Health and Food Safety, *About Us*, http://ec.europa.eu/dgs/health_food-safety/about_us/who_we_are_en.htm

⁶ See, e.g., European Commission, *About the European Commission*, http://ec.europa.eu/about/index_en.htm#directorates

assessment and communications, but not for risk management; thus it does not issue or enforce regulations.⁷ The European Medicines Agency is also a decentralized agency, and its evaluations of marketing-authorization applications submitted through the centralized procedure provide the basis for the authorization of medicines in Europe.⁸

In this report we analyze the scope and effectiveness of FDA's efforts to cooperate with entities in the EU, using publicly available information. We find that FDA provides ample information about its agreements with foreign regulators but no meaningful information about its progress in implementing such agreements. We recommend a high-level agreement and commitment for periodic disclosure of information regarding implementation of international agreements for regulatory cooperation. The development of performance plans and goals and of quantitative measures of progress to achieve those goals is routine for many of FDA's programs, despite the existence of some goals that are not easily quantifiable. The FDA's Office of International Programs should follow the practice of other FDA offices in adopting such planning and reporting procedures.

This report begins by summarizing the scope of FDA's regulatory activities. We then turn to a description and analysis of FDA's multilateral and bilateral efforts at international cooperation, including a careful consideration of various memoranda of understanding and confidentiality commitments. We then provide a critical review of the effectiveness of FDA's management of its program of international cooperation. We provide a description of opportunities for better cooperation, based on our analysis, and then conclude with some policy recommendations.

Background

A Summary of FDA's Regulatory Activities

The U.S. Food and Drug Administration has very broad regulatory authority, covering most products sold in supermarkets, and many products sold to hospitals. FDA has estimated that the products that it regulates represent between twenty and twenty-five percent of all consumer spending.⁹

Regulatory Scope

In addition to food and drugs, FDA regulates cosmetics, food additives, food contact substances, dietary supplements, animal feed, veterinary medicines, and biologics—a category of medical products that includes vaccines and 21st century biotech innovations. It also regulates tobacco

⁷ See, e.g., European Food Safety Agency, *About EFSA*, <http://www.efsa.europa.eu/en/aboutefsa>.

⁸ See, e.g., European Medicines Agency, *What We Do*, http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000091.jsp

⁹ See, e.g., U.S. Food and Drug Administration. *Global Engagement*. <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM298578.pdf>

and vaping products, products that emit radiation such as microwave ovens, as well as medical devices—a category that spans products from X-ray machines to tongue depressors, and includes sonograms and pregnancy tests. We elaborate briefly on its program to regulate two major classes of products.

Medical Products

With respect to medical products, FDA regulates all aspects of clinical testing, manufacturing, and marketing of drugs and biologic products and medical devices, from the first trial with human subjects to production, labeling and post-marketing surveillance of safety concerns. It also approves and regulates products that do not need clinical trials, that is, generic drugs approved because they are shown to be bioequivalent to innovator products¹⁰ and medical devices that are substantially equivalent to devices already legally marketed in the U.S.¹¹ Beyond regulating products, FDA oversees the research of principal investigators involved in trials of the medical products that it regulates.¹² FDA also regulates Institutional Review Boards that oversee trials of medical products regulated by FDA.¹³ FDA can put a hold on such clinical trials if it believes they cannot be conducted without unreasonable risks to subjects/patients.¹⁴

Food

FDA regulates foods for humans and animals (with the major exception of meat, poultry, and egg products which are the responsibility of the U.S. Department of Agriculture) in a manner that is only slightly less comprehensive than the way that it regulates medical products. Any food offered for sale in the U.S. must meet the content, processing, packaging, labeling and storage requirements specified by FDA in Title 21 of the United States Code of Federal Regulations. All facilities that produce, store and handle the food must be registered with the United States

¹⁰ U.S. Food and Drug Administration. “Drugs: Abbreviated New Drug Application (ANDA): Generics.” <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm>

¹¹ U.S. Food and Drug Administration. “Medical Devices: Overview of Device Regulation.” <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/> .

¹² U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, & Center for Devices and Radiological Health. *Guidance for Industry Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects*. October 2009. <http://www.fda.gov/downloads/Drugs/.../Guidances/UCM187772.pdf>

¹³ See, e.g., U.S. Food and Drug Administration. “Science & Research: Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors.” <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm> .

¹⁴ U.S. Food and Drug Administration. “Drugs: Drug Development and Review Definitions.” <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm176522.htm>

according to the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. The registrant of a facility agrees that FDA will be permitted to inspect the facility at times and in the manner authorized by the United States Food Drug and Cosmetic Act even if that facility is located outside the borders of the United States.

If FDA determines that food manufactured, processed, packed, received, or held by a registered food facility has a reasonable probability of causing serious adverse health consequences or death to humans or animals, FDA may suspend the registration of a facility that:

1. Created, caused, or was otherwise responsible for such reasonable probability; or
2. Knew of, or had reason to know of, such reasonable probability; and packed, received, or held such food.

Importers of food must notify U.S. officials of pending shipments prior to their arrival in the United States. FDA may inspect imported foods at the point of entry. Once a food has been allowed to enter the U.S., it is subject to inspection at any time by federal, state or local officials. Additionally, FDA's Reportable Food Registry is open for industry and regulators to report situations in which they believe that there is reasonable probability that an article of food will cause serious adverse health consequences. The Registry is intended to help the FDA better protect public health by tracking patterns and targeting inspections.

Outbreaks of foodborne illness or the discovery of food that is adulterated or mislabeled by U.S. standards prompts investigations. FDA uses transaction records required of industry to trace the implicated food back to the cause of the contamination at the manufacturer, repacker or warehouse, even if it is located overseas.

Administrative Procedures

The scope of these routine enforcement activities comports not only with multiple statutes, but also with FDA's regulations interpreting statutory requirements. As required by the Administrative Procedure Act, FDA must publish proposed rules in the *Federal Register* and solicit public comment on them, before publishing them in the *Federal Register* in final form.¹⁵ The Administrative Procedure Act also requires FDA to respond to public comments at the time it issues final rules. FDA typically treats all public comments equally, without regard to citizenship, place of legal residence, or whether the author is a private or government entity.

FDA issues economically significant regulations at a relatively slow pace, compared with the scope of its regulatory oversight. For the 10 years between October 1, 2004 and September 30, 2014, the U.S. Office of Management and Budget identifies only 5 economically significant

¹⁵ 5 U.S.C. §552: Public information; agency rules, opinions, orders, records, and proceedings

regulations issued by the FDA.¹⁶ It also reports that the annual benefits and costs of these regulations are between \$0.4 billion and \$14 billion for benefits and \$0.2 billion and \$0.5 billion for costs, in 2010 dollars. These regulations do not include recent rules that FDA has issued to implement the Food Safety Modernization Act (FSMA), such as the Preventive Controls for Human Food and the Preventive Controls for Animal Food. Also excluded are the Foreign Supplier Verification Rule and the Produce Rule, two economically significant rules for which OMB completed review on October 30th, 2015. OMB’s list of economically significant final rules also does not include additional rules implementing FSMA, which FDA has proposed and is expected to issue soon in final form.¹⁷

In addition, FDA issues a large number of regulations that are not economically significant. The entry for FDA in the *Unified Agenda* provides information on all final and proposed regulations expected through the end of 2016.¹⁸ For proposed rules, as of November 11, 2015, FDA lists 28 separate regulatory actions, of which 22 had no statutory deadline. In addition, FDA reports that it plans to issue 29 final rules by the end of 2016, 18 of which have no statutory deadline. The list of those final rules includes some economically significant regulations as well as some with “projected” publication dates that are prior to when the list was most recently updated in July of 2015.

Regulatory Guidance

FDA also issues many guidance documents that describe to FDA staff, applicants and sponsors of medical products, and to the public generally, its interpretation of regulations or its policy on specific regulatory issues. These guidance documents cover a very broad range of topics, from purely procedural requirements to outlining safe harbors in regulatory areas where technology is rapidly changing.

In issuing guidance, FDA follows a regulation that it issued in 2000 setting forth Good Guidance Practices—FDA’s policies and procedures for developing, issuing, and using guidance documents.¹⁹ This regulation, which we believe to be unique among federal regulatory agencies, essentially guarantees an opportunity for the public to comment on all FDA guidance documents that are “Level 1.” Level 1 guidance documents are those that present initial interpretations of

¹⁶ Office of Management and Budget. *2015 Draft Report to Congress on the Benefits and Costs of Federal Regulations*. Table 1-2.

https://www.whitehouse.gov/sites/default/files/omb/infocore/2015_cb/draft_2015_cost_benefit_report.pdf

¹⁷ For a reasonably up to date list, please see FDA’s list at

<http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm>.

¹⁸ See <http://www.fda.gov/AboutFDA/Transparency/track/ucm351742.htm> We note that some of these rules have release dates in the past. We have not ascertained whether these are rules that in fact have been issued, or are ones still to be issued in the future.

¹⁹ 21 C.F.R. 1, §10.115. <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=10.115>

statutory or regulatory requirements, set forth changes in interpretation or policy that are of more than a minor nature, include complex scientific issues, or cover highly controversial issues. As with proposed regulations, this opportunity to comment is open to all entities, regardless of residency or citizenship.

Guidance documents include, but are not limited to, documents that relate to the design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies. FDA has issued more than 260 proposed (draft) and final guidance documents since January 1, 2015.²⁰ FDA specifically identifies 15 of these guidance documents as being related to imported products, but given the large percentage of FDA regulated products that are imported, almost all of these guidance documents are likely to have indirect international impacts.

International Regulatory Cooperation

FDA has cooperated with foreign regulators for many years, but in 2011 it announced a new effort to improve international cooperation and outlined a collection of strategies for global engagement:²¹

- International offices and posts
- Strengthening regulatory capacity
- Harmonizing science-based standards
- Leveraging knowledge and resources
- Risk-based monitoring and inspection
- Global Surveillance, Preparedness and Emergency Response
- Advancing Regulatory Science

FDA's international regulatory program may be seen in light of Kingsbury, Krisch and Stewart's work describing "global administrative law."²² They recognize the growth of trans-governmental regulation in an increasingly global economy.

“[V]arious transnational systems of regulation or regulatory cooperation have been established through international treaties and more informal intergovernmental networks of cooperation, shifting many regulatory decisions

²⁰ See, e.g., U.S. Food and Drug Administration. “Regulatory Information: Search for FDA Guidance Documents.” <http://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

²¹ See, e.g., U.S. Food and Drug Administration. *Global Engagement*. 2011. p. 8. <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM298578.pdf>

²² Kingsbury, Benedict, Nico Krisch, and Richard B. Stewart, “The Emergence of Global Administrative Law,” *Law and Contemporary Problems*. Vol 68. pp. 15-61. 2005.

from the national to the global level. Further, much of the detail and implementation of such regulation is determined by transnational administrative bodies—including international organizations and informal groups of officials—that perform administrative functions but are not directly subject to control by national governments or domestic legal systems or, in the case of treaty-based regimes, the states party to the treaty.”²³

Kingsbury, et al. note that these networks and coordination arrangements need transparency.²⁴ Their observations are consistent with our recommendations for improved reporting on the activities of FDA’s international programs.

FDA’s activities to promote international cooperation can be divided into multilateral and bilateral efforts. We briefly review FDA’s multilateral cooperation before turning to bilateral cooperation between the FDA and entities of the EU.

Multilateral Efforts

FDA’s Activities to Promote International Cooperation

In 1963 the Food and Agriculture Organization of the United Nations and the World Health Organization jointly established the Codex Alimentarius Commission (CODEX) to develop harmonized international food standards to protect public health and promote fair trade practices for foods. Over 300 standards, guidelines, and codes of practice have been developed.²⁵ The issues addressed by CODEX cover a broad range of topics from seafood to vegetables, organic to biotech products, and sanitation to labeling.²⁶

Both FDA and the EU Directorate General for Health and Food Safety are major participants in the CODEX processes. FDA reports that CODEX is “the major international mechanism for encouraging fair international trade in food while promoting the health and economic interest of consumers.”²⁷ Nations are not bound to adopt CODEX standards. However, FDA considers CODEX standards when making regulatory decisions to meet World Trade Organization obligations while at the same time protecting the health of U.S. consumers.

²³ Ibid, p. 16.

²⁴ Ibid, p. 38.

²⁵ See <http://www.codexalimentarius.org/standards/en/>.

²⁶ CODEX Alimentarius International Food Standards. “Thematic Compilations.”<http://www.codexalimentarius.org/standards/thematic-publications/>.

²⁷ U.S. Food and Drug Administration. “Food: International Cooperation.”
<http://www.fda.gov/Food/InternationalInteragencyCoordination/InternationalCooperation/default.htm>

In 1990 the European Community initiated the International Conference on Harmonization (ICH) of pharmaceutical regulation.²⁸ The ICH (now the International Council on Harmonization) involves a number of developed countries in an endeavor that seeks to make recommendations towards achieving greater harmonization in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration, thereby reducing or obviating duplication of testing carried out during the research and development of new human medicines.²⁹ FDA implements these ICH recommendations in the form of guidance documents, which fall under four categories: ICH Efficacy, ICH Joint Safety and Efficacy, ICH Quality and ICH Safety.³⁰ Each of these is an area of major activity. For example, the ICH Efficacy recommendations alone have led to 30 different FDA guidance documents made public between March 1995 and July 2015. FDA has issued three of these in draft (proposed) form, and 27 as final documents.

Examples of Multilateral Cooperation

On several occasions, FDA has endeavored to cooperate with foreign entities on an *ad hoc* basis, because of the exigencies of particular circumstances. These cases illustrate active behind the scenes cooperation.

In early spring of 2007, FDA became aware of deaths of cats subjected to taste tests for different varieties of pet food. FDA, working with independent researchers eventually identified melamine as the responsible contaminant, especially when it was present along with cyanuric acid, another industrial contaminant.³¹ FDA is credited with developing and disseminating a test for melamine, which apparently had been fraudulently added in China so as to make flour from wheat and rice appear higher in protein than it actually was.³² The European Food Safety Authority (“EFSA”) acknowledged, if indirectly, prior work by FDA identifying the contaminant in animal food products originating from China.³³

²⁸ See e.g., ICH. “History.” <http://www.ich.org/about/history.html>.

²⁹ ICH. “Vision.” <http://www.ich.org/about/vision.html>.

³⁰ U.S. Food and Drug Administration. “Drugs: International Council on Harmonisation – Efficacy” <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm065004.htm>.

³¹ U.S. Food and Drug Administration. “Animal & Veterinary: Melamine Pet Food Recall - Frequently Asked Questions” <http://www.fda.gov/AnimalVeterinary/SafetyHealth/RecallsWithdrawals/ucm129932.htm>

³² See, e.g., FDA’s April 2007 public notice at <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048192.htm> and also a scientific presentation of its scientists at <http://acs.confex.com/acs/mwrm07/techprogram/P51682.HTM>

³³ See e.g., European Food Safety Authority. *Scientific Opinion on Melamine in Food and Feed: EFSA Panel on Contaminants in the Food Chain (CONTAM) and EFSA Panel on Food Contact Materials, Enzymes, Flavourings*

As a second example, in January of 2008, FDA relaxed a voluntary moratorium on the sale of food products from animal clones because it had completed a scientific risk assessment that concluded that such foods were as safe as foods from traditional animals.³⁴ The issue of safety of food from animal clones had been controversial, because such foods were not labeled and many people reacted emotionally to news reports that the meat they were bringing home from the supermarket came from animal clones. Months after the FDA decision, which was issued only after public notice and extensive comment, the EFSA released a complementary finding.³⁵ The FDA officials responsible for coordinating the January 2008 announcement were aware of the status of the EFSA work because of unofficial communications with EFSA, and anticipated correctly that EFSA would likely reach a similar conclusion. Back-channel communications of the pending EFSA work helped reassure U.S. government officials that the FDA finding was trustworthy.

The International Medical Device Regulators Forum (“IMDRF”) began in 2011 to discuss the harmonization of medical device regulations. The current members are: Australia, Brazil, Canada, China, Europe, Japan, Russia, and the U.S. IMDRF has developed a number of guidances and standards to harmonize regulatory activities such as definitions for software that acts as a medical device, processes and standards for recognizing auditing organizations, unique identifiers for devices, and standards for reports of device manufacturer audits.³⁶ An example of progress in harmonization related to the IMDRF is a pilot program on applying a common standard for medical device manufacturer audits in order to most efficiently allocate inspection resources.³⁷

The International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (“VICH”) is an international industry/government effort that was launched in April 1996. The founders were the World Organization for Animal Health, the International Federation of Animal Health, Japan, the U.S., and the EU. They wanted the VICH

and Processing Aids (CEF). April 2010.

http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/1573.pdf

³⁴ U.S. Food and Drug Administration. “FDA News Release: FDA Issues Documents on the Safety of Food from Animal Clones. Agency Concludes that Meat and Milk from Clones of Cattle, Swine, and Goats, and the Offspring of All Clones, are as Safe to Eat as Food from Conventionally Bred Animals.” January 15, 2008. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116836.htm>

³⁵ European Food Safety Authority. “Food Safety, Animal Health and Welfare and Environmental Impact of Animals derived from Cloning by Somatic Cell Nucleus Transfer (SCNT) and their Offspring and Products Obtained from those Animals.” July 2008. <http://www.efsa.europa.eu/en/efsajournal/pub/767>

³⁶ International Medical Device Regulators Forum. “IMDRF and GHTF documents.” <http://www.imdrf.org/documents/documents.asp>

³⁷ U.S. Food and Drug Administration. “Training and Continuing Education: International Medical Device Regulators Forum (IMDRF) Medical Device Single Audit Program (MDSAP) Pilot.” <http://www.fda.gov/Training/CDRHLearn/ucm372921.htm>

to develop consensus guidelines that describe the study protocols and designs for the testing required to demonstrate product safety, quality and efficacy for the purpose of licensing or registering veterinary medicines.³⁸ In addition to preapproval study requirements, VICH has also developed guidance for post-marketing monitoring and reporting of adverse drug events.

Bilateral Regulatory Cooperation

FDA's Activities Promoting Cooperation with the EU

Regulatory cooperation between the FDA and EU organizations can be seen both in terms of high-level efforts at cooperation and efforts initiated by FDA. We consider each in turn.

High-level efforts to promote regulatory cooperation between the U.S. and the EU date to at least 2007, when the White House and the European Commission created the Transatlantic Economic Council (“TEC”). The current workplan of the TEC includes only a few topics related (somewhat indirectly) to FDA. Moreover, these differ substantially in terms of the attention they have received in recent years. For example, among all the topics related at least indirectly to FDA, since 2011, e-Health received seven updates, the Innovation Action Partnership received two, Limiting Regulatory Divergence received two but both were prior to December 2011, and Nanotechnology received one in November 2011.³⁹ We could not find up to date information on the current status of these initiatives at the FDA or USTR websites.

Past cooperation topics of the Transatlantic Economic Council include six items, of which five, (all but “Finance”) are fairly directly related to FDA:

- Finance⁴⁰
- Innovation and Technology⁴¹
- Intellectual Property Rights⁴²
- Pharmaceuticals⁴³
- Safety and Regulations⁴⁴

³⁸ See <http://www.vichsec.org/what-is-vich.html>

³⁹ U.S. Department of State. “Current Workplan of the Transatlantic Economic Council.” <http://www.state.gov/p/eur/rt/eu/tec/c33533.htm>.

⁴⁰ U.S. Department of State. “Transatlantic Economic Council: Specific Cooperation Topics--Finance.” <http://www.state.gov/p/eur/rt/eu/tec/c33621.htm>

⁴¹ U.S. Department of State. “Transatlantic Economic Council: Specific Cooperation Topics--Innovation and Technology.” <http://www.state.gov/p/eur/rt/eu/tec/c33625.htm>

⁴² U.S. Department of State. “Transatlantic Economic Council: Specific Cooperation Topics--Intellectual Property Rights.” <http://www.state.gov/p/eur/rt/eu/tec/c33624.htm>

⁴³ U.S. Department of State. “Transatlantic Economic Council: Specific Cooperation Topics--Pharmaceuticals.” <http://www.state.gov/p/eur/rt/eu/tec/c47302.htm>

- Use of Standards⁴⁵

The State Department website, however, provides no information on any activity in any of these six topics in the last four years. The topic “Safety and Regulations” itself includes eight subtopics, and five of these involve FDA, but this report of the TEC provides no information on the status of these cooperation topics since March 2010, more than five years ago.⁴⁶ For two of these items, the links to additional information, in the form of a final report or an annual activities report, lead to defunct website addresses.⁴⁷ The lack of a single annual report on implementation of these agreements contributes to an impression of relative inattention to implementation.

FDA Memoranda of Understanding with Foreign Government Entities

Turning to FDA-level cooperation with foreign government entities, we find that FDA provides to the public substantial information on its website about the nature of its interactions with foreign entities.⁴⁸ Specifically, it lists and provides MOUs and confidentiality commitments with foreign entities. Before analyzing the MOUs that FDA has finalized with EU entities, however, it is worth reviewing FDA’s criteria for entering into an MOU with a foreign government entity. On its website, FDA describes the process for developing MOUs with entities in foreign governments or with international organizations. The description was last modified in 1995, but appears on a website that was updated in 2015, and thus appears to have withstood the test of time.⁴⁹ Interestingly, it represents part of the FDA’s Compliance Policy Guides, which predate its 2000 Good Guidance Practice regulation, requiring public notice and comment for guidance documents.

The criteria for a new MOU include:

⁴⁴ U.S. Department of State. “Transatlantic Economic Council: Specific Cooperation Topics--Safety and Regulations.” <http://www.state.gov/p/eur/rt/eu/tec/c33620.htm>

⁴⁵ U.S. Department of State. “Framework for Promoting Transatlantic Economic Integration, Annex I: Fostering Cooperation and Reducing Regulatory Barriers, A. Horizontal--Standards.” <http://www.state.gov/p/eur/rt/eu/tec/131810.htm>

⁴⁶ See <http://www.state.gov/p/eur/rt/eu/tec/c33620.htm>

⁴⁷ See 07/27/11 Transatlantic Administrative Simplification Action Plan - Final Report on implementation, and 06/01/11 Interactions Between the European Medicines Agency and U.S. Food and Drug Administration September 2009-September 2010 (2011 FDA/EU Annual Activities Report)

⁴⁸ U.S. Food and Drug Administration. “About FDA: FDA Memoranda of Understanding.”

<http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/default.htm>

⁴⁹ U.S. Food and Drug Administration. “Inspections, Compliance, Enforcement, and Criminal Investigations: CPG Sec. 100.900 International Memoranda of Understanding.”

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073828.htm>

- Health Benefits (Including Risk Reduction) Associated with Products or Programs: FDA should consider the benefits to public health (particularly for the United States population) when it sets priorities for its international activities.
- Products Imported into the United States: FDA should place a higher priority on international activities that are directed toward improving the quality, safety, or efficacy of products offered to consumers in the United States. For example, FDA should give a low priority to investing resources in developing a memorandum of understanding with a foreign country that covers a product where there is little likelihood of significant exports to the United States or significant risk to the public.
- History of Compliance Problems: FDA should place a higher priority on international activities directed toward remedying product defects that have been demonstrated to be previous compliance problems or where there is a demonstrated scientific basis for increased surveillance.
- Comparative Costs of Alternative Programs: FDA should pursue international programs and activities that provide the greatest benefit in relation to the resources required to administer them. For example, the costs of developing, implementing, and monitoring an agreement should be weighed against the costs of higher sampling levels to obtain the same degree of confidence in rates of compliance in the absence of an agreement.
- Regulatory Burden on Industry: FDA should consider the regulatory burden on industry that could be diminished by harmonization efforts. However, these activities need to be compatible with FDA's primary public health mission, the act, and other laws and regulations that FDA enforces.
- U.S. Foreign Policy Objectives and Priorities of Other U.S. Government Agencies: FDA should be knowledgeable of U.S. foreign policy objectives and international programs and policies of other U.S. Government agencies and appropriately balance these interests with those of FDA's primary mission.

These criteria have an understandable focus on FDA's mission to protect and promote public health in the United States. The list also includes, however, reducing the regulatory burden on industry and balancing interests of other U.S. government agencies with those of FDA's primary mission. FDA's approval of drugs for the U.S. President's Emergency Plan for AIDS Relief program to provide low-cost anti-retrovirals to fight AIDS in very low-income countries may be seen as an example of such balancing.⁵⁰

⁵⁰ U.S. Food and Drug Administration. "International Programs: Approved and Tentatively Approved Antiretrovirals in Association with the President's Emergency Plan." <http://www.fda.gov/InternationalPrograms/PEPFAR/ucm119231.htm>

FDA lists on its website one MOU, and four different confidentiality commitments with entities of the EU. Table 1 below summarizes key characteristics of these documents.

The memoranda of understanding and confidentiality commitments between FDA and the EU primarily serve to set forth the standards of the U.S. Freedom of Information Act (“FOIA”) and the U.S. Administrative Procedure Act (“APA”), as well as FDA regulations for sharing information between the parties. Specifically, FDA commits to sharing with the EU certain information, and FDA is open to receiving information from the EU. FDA also commits to respecting the protections from disclosure under FOIA to confidential commercial information, trade secret information and personal privacy information. The confidentiality commitments also extend to information that the EU shares with FDA on law enforcement and internal, pre-decisional matters — the same protections that would be afforded to parts of the U.S. federal government beyond the FDA.

**Table 1: Memoranda of Understanding and Confidential Commitments
Between the U.S. Food and Drug Administration and Entities in the European Union**

Type of Document	Memorandum of Understanding	Confidentiality Commitment			
Date	2005	2005	2007	2009	2010
Products Covered	Foods	Foods, Drugs, Biologics, Medical Devices, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, Tobacco Products	Foods	Drugs, Biologics, Animal & Veterinary Drugs	Drugs, Biologics, and Animal and Veterinary Drugs
EU Entity	European Commission’s Health and Consumer Protection Directorate General ⁵¹	European Commission’s Health and Consumer Protection Directorate General ⁴⁷	European Food Safety Authority	European Directorate for the Quality of Medicines & HealthCare ⁵²	European Medicines Agency
Selected Issues Addressed	Documents required to be made public under the APA	Non-public documents and/or information related to products that are regulated by both entities.			
	Documents relating to controls to ensure effective inspections (“verification”) enforcing the 1999 Agreement on foods of	Bilateral commitment on confidentiality of FOIA exempt information--confidential commercial information; trade secret information; personal privacy information; law enforcement information; and internal, pre-decisional information			

⁵¹ This Directorate General was reorganized in 2015 to the Health and Food Safety Directorate General.

⁵² A directorate of the Council of Europe, the European Directorate for the Quality of Medicines and Health Care facilitates the development, implementation, and application of quality standards, such as the European Pharmacopeia, for safe medicines and their safe use. The European Pharmacopeia is legally binding in the 37 states and the EU which have signed the Convention on the Elaboration of a European Pharmacopoeia.

	animal origin	
	Information relating to outbreaks of foodborne illness	FDA commits to inform the foreign party if it receives requests for information that would otherwise be protected by FOIA through mechanisms such as subpoenas or Congressional document requests.

Underlying these provisions is an FDA regulation that strengthens its ability to protect information provided to it by foreign governments and information that it provides to foreign governments.⁵³ Specifically, under limitations on exemptions, it states “communications with foreign government officials shall have the same status as communications with any member of the public, except that”:

Investigatory records compiled for law enforcement purposes by foreign government officials who perform counterpart functions shall be exempt from public disclosure to the same extent to which the records would be so exempt (pursuant to other provisions on equal access by all members of the public), as if they had been prepared by or submitted directly to FDA employees.

Disclosure of investigatory records compiled for law enforcement purposes by the FDA to foreign government officials who perform counterpart functions to the FDA in a foreign country as part of cooperative law enforcement efforts does not invoke the provision that such records shall be made available for disclosure to all members of the public.

This same FDA regulation allows designated FDA officials to “authorize the disclosure to, or receipt from, an official of a foreign government agency of nonpublic, predecisional documents concerning the FDA’s or the other government agency’s regulations or other regulatory requirements, or other nonpublic information relevant to either agency’s activities, as part of cooperative efforts to facilitate global harmonization of regulatory requirements, cooperative regulatory activities, or implementation of international agreements.”⁵⁴ This authority may be noteworthy.

The confidentiality commitments between FDA and the various EU organizations are very similar.

The MOU between the FDA and the EU does not address medicines or medical devices, although these products are the subject of MOUs between the FDA and decentralized agencies of individual European countries, both within and outside the EU. Table 2 provides some selected information about such MOUs.

⁵³ See 21 CFR 20.89.

⁵⁴ Ibid.

**Table 2: Selected Memoranda of Understanding
Between the U.S. Food and Drug Administration and Foreign Government Entities**

Type of Document	Memorandum of Understanding			
Date	1972	1986	1988	2010
Country	Sweden	United Kingdom (UK)	The Netherlands	Russian Federation
Products Covered	Inspection of Drug Manufacturing Plants	Medical Device	Good Laboratory Practices	Drugs
Foreign Government Entity	Swedish National Board of Health and Welfare	Department of Health and Social Security of the UK and Northern Ireland	Ministry of Welfare, Health and Cultural Affairs	Federal Service on Surveillance in Health Care and Social Development
Selected Issues Addressed	Provides for joint inspections and annual or periodic review.	“will exchange such information as is necessary for the mutual recognition of inspections related to medical devices manufactured in one country and intended for import into the other”	<ul style="list-style-type: none"> - Provide the other party, regularly, with the names and addresses of nonclinical laboratories operating within their country, the dates the laboratories were inspected, and their compliance designation; - Provide upon request of the other party, further information regarding whether or not a specific laboratory or study is in compliance with the good laboratory practice standards; - Honor a request by the other party to conduct a GLP inspection or data audit at a specified nonclinical laboratory 	Simplification of information exchange and emergency notification procedures to be followed in case of contamination or counterfeit, whether occasional or deliberate, of drug products and their ingredients.

Table 2 and the single MOU in Table 1 represent only an illustrative selection of the 20 MOUs that FDA reports having with other nations and international organizations. The focus on information sharing in each MOU emphasizes that information sharing is one of the primary activities and values that FDA has in its international interactions. However, the lack of uniformity in the MOUs is also notable. Without more information on the background of the MOUs it is impossible to know whether the differences in MOUs or the lack thereof is because of barriers on the FDA side of the negotiations or on the side of the other parties. It may also be the result of a lack of interest or lack of perceived need by both potential parties.

Additionally, the existence of international cooperation in the absence of specific MOUs indicates that MOUs are not required for FDA and the EU to have productive working relationships. However, without reports on international accomplishments, it is impossible to judge whether refinement of existing MOUs or the establishment of additional MOUs would improve cooperation and information sharing between FDA and the EU.

Program Management

Since 2008 the FDA has taken a variety of steps to strengthen its international program. It has created an Office of Public Health and Trade and an Office of Strategy, Partnerships and Analytics within its Office of International Programs.⁵⁵ It has opened several offices overseas, including one in Brussels, substantially increasing its international program. Regarding its Brussels office, the FDA states

The mission of FDA's Europe Office is to strengthen the safety, quality, and effectiveness of medical products and food produced in Europe for export to the United States. The objective of the Europe Office is to foster collaboration and to share knowledge and information with FDA's counterpart regulatory authorities throughout the region.⁵⁶

The FDA lists five activities of its Europe Office:⁵⁷

⁵⁵ U.S. Food and Drug Administration. "About FDA: IOP Offices." <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/ucm245229.htm>

⁵⁶ U.S. Food and Drug Administration. "About FDA: Europe Office." <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/ucm243678.htm> (downloaded November, 2015)

⁵⁷ U.S. Food and Drug Administration. "About FDA: Europe Office." <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/ucm243678.htm>

1. Transatlantic Economic Council High Level Regulatory Cooperation Forum
2. Memoranda of Understanding and Other Cooperative Arrangements
3. European Medicines Agency
4. Confidentiality Commitments
5. Transatlantic Task Force on Antimicrobial Resistance

Four of these five items, although described as activities, are in fact documents (items 2 and 4), foreign government agencies (item 3), or a new transnational bureaucratic entity (item 5). The exception, the TEC High Level Forum (“TECHLRFC”) is a process of ongoing U.S.-EU consultation involving a series of meetings among designated officials. FDA’s website provides a description of the TECHLRFC, and lists 14 separate projects with the EMA and the European Commission. (See Appendix A.) It does not, however, provide any information about the status of these projects, e.g., whether they have been initiated, are on schedule, or have ended or already been completed. A recent State Department report on the TECHLRFC is also silent on these projects and indeed on the FDA, although these projects may be encompassed by the ongoing Transatlantic Trade and Investment Partnership talks.⁵⁸ The USTR website, however, provides no additional information about FDA’s implementation of those measures.⁵⁹

FDA does not appear to provide information about the accomplishments or performance of its international programs, and specifically its Brussels office. At least, we were unable to find information about the results or accomplishments of the activities of its international program or its Brussels office.

International Activities in the FDA Budget Justification

FDA’s most recent budget justification provides additional information about its international activities, which involve two different offices: FDA’s Office of Regulatory Affairs (“ORA”), which is responsible for enforcement, and the much smaller FDA Office of International Programs. However, FDA provided little information on the expected public health achievements (outcomes) of its international programs in the budget justification.

⁵⁸ U.S. Department of State, Bureau of European and Eurasian Affairs. *Transatlantic Economic Council (TEC) Facilitators Report to Stakeholders*. March 27, 2015.

<http://www.state.gov/p/eur/rls/or/2015/240826.htm>

For TTIP, see Executive Office of the President, Office of the United States Trade Representative.

“Transatlantic Trade and Investment Partnership (T-TIP).” <https://ustr.gov/ttip>

⁵⁹ Executive Office of the President, Office of the United States Trade Representative. “T-TIP Issue-by-Issue Information Center.” <https://ustr.gov/trade-agreements/free-trade-agreements/transatlantic-trade-and-investment-partnership-t-tip/t-tip>.

The ORA's FY2016 budget request listed "Extending FDA's Global Presence" among its most significant accomplishments. In particular, it stated:

The foreign inspection program is critical to FDA's mission to protect public health. The global supply of FDA regulated products continues to grow in volume and complexity. In response to the growing trend, ORA conducted 3,000 inspections in 2014, a 300 percent increase from ten years ago. In addition to using its domestic staff, FDA is increasing the number of personnel stationed in its foreign offices.⁶⁰

In another section, entitled "Analyzing and Utilizing Global Data to Manage Risk," FDA ORA states "FDA performs routine surveillance inspections both within the U.S. and globally to assess regulated industry compliance with appropriate regulations and conducts for-cause inspections when violations are discovered or outbreaks occur."⁶¹ It does not elaborate, however, how FDA will use new technologies or new institutional arrangements with foreign government regulators to facilitate such work.

FDA's most recent budget justification includes an additional \$20.5 million for Import Safety, the Foreign Supplier Verification Program Implementation.⁶² FDA describes this program, which is primarily directed at facilitating imports of food product, as follows:⁶³

One of FDA's best opportunities for return on investment is helping foreign governments ensure the safety of food and feed before it is even shipped to the U.S. FDA continues to invest in this effort in three ways by:

- placing staff in foreign offices
- increasing the number of foreign inspections
- developing partnerships with its counterparts overseas.

Some of those efforts are focused more on technical assistance, such as helping other nations strengthen their regulatory systems and upgrading their public health laboratory methods and training.

FDA's budget justification for FY2016 includes some information about the activities of its foreign offices, but this activity is primarily in terms of outputs not outcomes that

⁶⁰ U.S. Food and Drug Administration, Office of Regulatory Affairs. *Narrative by Activity: Office of Regulatory Affairs - Field Activities*. p. 142.

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM438022.pdf> p. 142.

⁶¹ Ibid, p. 146.

⁶² Ibid, p. 151.

⁶³ Ibid, p. 152.

matter to policy makers and the public. Outputs represent FDA activities, e.g., inspections completed, but not accomplishments that matter more directly to people's welfare, such as reductions in the occurrence of pathogens on food or reductions in incidence of foodborne illness or reduced harm from medical products with poorly understood risks.

Regarding international inspections, FDA reports:

In FY 2014, FDA implemented six new Confidentiality Commitments to promote information sharing with foreign counterpart agencies and international organizations; these include agencies in Denmark, Italy, Estonia, Spain, the United Kingdom, and one Confidentiality Commitment with the World Health Organization in support of information sharing related to Ebola.⁶⁴

FDA goes on to describe collaboration and communication in India, and overseas offices in India, China, Mexico, and Chile, and inspections and short-term assignments of FDA inspectors to various countries.

These budget justifications fail to describe quantitatively the performance of FDA's foreign offices in terms of outcomes or accomplishments that ought to matter directly to the public's health and welfare. They do not provide quantitative descriptions of cooperation in responding to outbreaks of foodborne illness, tainted or mislabeled drugs, or even sharing of news about positive or negative inspection results, technical cooperation developing risk assessments to address novel threats like melamine, etc.

FDA Offices in Foreign Countries

FDA issued a report to Congress in 2012, as required by the FSMA, on the offices that FDA has established in foreign countries.⁶⁵ The report describes the progress of those foreign posts in working with foreign government counterpart regulatory authorities and others in the countries. FDA has a senior technical expert embedded in the European Medicines Agency in London.. The foreign posts enable FDA and border officials to make better-informed decisions about product entry into the United States by activities such as inspecting facilities in the EU, obtaining information about products to be exported to the U.S., reporting on adverse events in Europe that could affect products

⁶⁴ U.S. Food and Drug Administration, FDA Headquarters. *Narrative by Activity: FDA Headquarters*. <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM438025.pdf>

⁶⁵ U.S. Food and Drug Administration. "Food: Report to Congress on the FDA Foreign Offices." <http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm291803.htm>

destined for the U.S., and speeding bilateral information flows and enhancing working relationships. However, even with all of these activities, the report to Congress does not provide quantitative measures of accomplishments (outcomes) of the FDA's foreign offices.

FDA in other contexts has accepted a collection of quantitative performance goals, in terms of outputs and outcomes. FDA's user fee programs, for example, have expanded over the years to cover new drug review, generic drug review, new animal drug review, generic animal drug review, medical device review, and others. In these programs FDA receives additional resources in the form of user fees collected from all firms covered by a given regulatory program, e.g., all innovative drug manufacturers, in exchange for committing to meet certain performance goals. For example, the performance goals for the Prescription Drug User Fee Act have FDA reviewing 90 percent of all standard new drug applications (for marketing approval) within 6 months.⁶⁶

The U.S. Department of Health and Human Services, of which FDA is a part, has developed a set of quantitative performance goals, Health People 2020, which FDA uses outside of the user fee context. These goals include reductions in incidence of illness from foodborne pathogens to prescribed levels, and improvements in use of safe food handling practices.⁶⁷ FDA does post information on inspections completed by type of product and by region or foreign country.⁶⁸ But it provides no quantitative information about the effectiveness of its international program and efforts at cooperation. We are unaware of the existence of quantitative goals or performance measures focusing on the outcomes of FDA's international programs.⁶⁹

Cooperation Under Existing Statutes

Opportunities for Greater Efficiencies

If we step back from the details of international agreements and program management, it is easy to see that there are substantial opportunities for greater cooperation between FDA and the EU to yield more efficient risk management. These opportunities are most obvious regarding food because millions of Americans travel to the EU and enjoy food regulated by the EU standards without any special interventions by the FDA or any

⁶⁶ See <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>.

⁶⁷ U.S. Department of Health and Human Resources, Office of Disease Prevention and Health Promotion. "Food Safety." <https://www.healthypeople.gov/2020/topics-objectives/topic/food-safety/objectives>.

⁶⁸ U.S. Food and Drug Administration. "Data Dashboard: Global Inspections." <http://govdashboard.fda.gov/public/dashboards?id=140>.

⁶⁹ FDA's 2014 strategic priorities report includes a strategic plan but few specific quantitative performance goals. See <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM416602.pdf>.

adverse consequences. The Centers for Disease Control and Prevention offers no warnings to travelers for eating in the EU that are different from eating in the U.S. We know of no evidence that there is a higher incidence of foodborne illness among U.S. travelers to the EU than for the U.S. population in general (or EU travelers to the U.S.). If U.S. travelers are able to treat the regulatory food standards of the U.S. and the EU as essentially equivalent, then there are no clear reasons why FDA and the EU cannot recognize this fact. Doing so would allow regulators on both sides of the Atlantic to more efficiently target resources on areas of greatest risk.

Our point is not that regulations need to be made uniform but that the regulatory systems for foods can be recognized as already providing essentially equivalent levels of public health protection. In 1999 the U.S and the EU concluded an agreement on sanitary standards for live animals and foods of animal origin. Under that agreement the U.S. Department of Agriculture has acknowledged the equivalence of sanitary standards for meat and poultry produced in numerous EU countries. FDA has not acknowledged equivalent standards for any EU countries on any of the products that it regulates.

Case Study: Foreign Food Safety Controls for Shellfish

The case of shellfish illustrates how difficult it has been for FDA to recognize foreign food safety controls as equivalent. In 2010, during bilateral discussions with the European Commission, FDA considered the role of the CODEX Guidelines on the Judgment of Equivalence of Sanitary Measures Associated with Food Inspection and Certification Systems⁷⁰ in making equivalence determinations of each other's food safety controls for shellfish. FDA determined that systems recognition assessments would provide FDA with an objective basis for applying the CODEX concept of relying on FDA's knowledge, experience, and confidence in the EU system to support this equivalence determination.

In 2011, FDA began work with the EU regarding an equivalence determination on molluscan shellfish, including a systems recognition assessment. To date FDA has not reported on the progress toward either recognition of systems or equivalence even for this narrow category of products. By contrast, after only two years FDA and New Zealand were able to establish a bilateral agreement recognizing that the food safety systems of each other's countries provide a comparable level of safety for the food regulated by FDA.⁷¹ This recognition will allow FDA to use data from New Zealand to make

⁷⁰ See *Codex Guidelines on the Judgment of Equivalence of Sanitary Measures Associated with Food Inspection and Certification Systems* (CAC/GL 53/2003). <http://www.fao.org/fao-who-codexalimentarius/standards/list-of-standards/en/>

⁷¹ See *FDA - New Zealand MPI, Food Safety Systems Recognition Arrangement*. <http://www.fda.gov/InternationalPrograms/Agreements/MemorandaofUnderstanding/ucm331907.htm>

decisions about imports and as a factor in prioritizing resources dedicated to foreign facility inspections, import field exams, and import sampling.

Identifying the Low-Hanging Fruit

A 2012 GAO report indicates a significant barrier to recognition between the US and the EU.⁷² FDA's approach to comparability of international food safety systems with the U.S. domestic system requires comparability with a foreign government's *entire* domestic and export food safety systems for *all* FDA regulated food products. Given the very different approaches to cheese between the FDA and the EU, this prevents the FDA from leveraging the resources of countries with comparable systems for anything less than the entire food supply. In the GAO's assessment, "FDA can only take full advantage of comparability assessments if it modifies its approach for selecting comparable foreign countries and uses comparability assessments to identify countries that have similar food safety systems for targeted food products." In 2013 FDA indicated a willingness to entertain suggestions on how systems comparability could be pursued on a commodity-specific basis.⁷³

Given some fundamental differences within both the U.S. and the EU regarding some products (cheese from unpasteurized milk, for example), that will preclude overall systems recognition, and the long-lasting stalemate over molluscan shellfish, FDA and the EU should try a different approach. They should identify opportunities for easy success. In 2012, FDA issued its draft Qualitative Risk Assessment Risk of Activity/Food Combinations for Activities (Outside the Farm Definition) Conducted in a Facility Co-Located on a Farm.⁷⁴ FDA was concerned about food processes occurring on farms because of the proximity to animal waste and the potential for contamination of the food. However, the qualitative risk assessment identified many products that FDA considers low risk, including:

- Hard candy, fudge, taffy, toffee;
- Cocoa products from roasted cocoa beans;

⁷² U.S. Government Accountability Office. *FOOD SAFETY: FDA Can Better Oversee Food Imports by Assessing and Leveraging Other Countries' Oversight Resources*. (GAO-12-933). September 2012. <http://www.gao.gov/assets/650/649010.pdf>

⁷³ U.S. Food and Drug Administration. "Information for Foreign Governments: Frequently Asked Questions on Systems Recognition." September 5, 2013. See the answer to question 19: <http://www.fda.gov/Food/InternationalInteragencyCoordination/ucm367400.htm#QAs>

⁷⁴ U.S. Center for Food Safety and Applied Nutrition, Food and Drug Administration, & U.S. Department of Health and Human Services. *DRAFT Qualitative Risk Assessment Risk of Activity/Food Combinations for Activities (Outside the Farm Definition) Conducted in a Facility Co-Located on a Farm*. August 2012. <http://www.fda.gov/downloads/Food/FoodScienceResearch/UCM334110.pdf>

- Honey;
- Jams, jellies and preserves from acid foods;
- Maple syrup;
- Soft drinks and carbonated water;
- Sugar from sugarcane and sugar beets;
- Intact fruits and vegetables, grains and grain products, peanuts and tree nuts, coffee beans, and cocoa beans;
- Mixed intact fruits and vegetables, grain and grain products, peanuts, tree nuts, honey, maple sap and maple syrup, coffee beans, and cocoa beans;
- Coated or seasoned intact fruits, vegetables, peanuts and tree nuts;
- Shelled/hulled intact fruits and vegetables, peanuts, tree nuts, and cocoa beans;
- Chopped peanuts and tree nuts;
- Ground/milled/cracked/crushed grains (e.g., corn meal), coffee beans, cocoa beans, and peanuts and tree nuts;
- Dried/dehydrated intact fruits and vegetables (without sulfiting), grains and grain products, peanuts and tree nuts, coffee beans, and cocoa beans;
- Oils from grains; and
- Fermented cocoa beans and coffee beans.

These products represent an opportunity for FDA and the EU to come to an agreement on comparability for selected products and in the process to develop trust and cooperation upon which to build future agreements. Also, FDA and the EU may be able to develop a streamlined or simplified approach to agreeing on equivalent standards for public health protection. As suggested here, risk assessment and epidemiology should play a greater role in the identification of products for agreement and in the judgment of equivalence of effect. The standard for equivalence should be an equivalent level of public health protection as seen in epidemiological estimates of effects associated with regulated products (i.e., cases of foodborne illness) and not solely through the testing standards of the different entities.

Recommendations

FDA has a track record of engaging in dialogue with both multilateral regulatory organizations and foreign entities. Recent years have seen both high-level regulatory initiatives involving the Executive Office of the President and the European Commission and FDA-level initiatives, such as opening new offices in countries around the world. The effects of this cooperation on outcomes that matter to people's welfare, such as fewer or shorter outbreaks of foodborne illness, reduced risks associated with medical products or a greater variety of products available at lower cost, is not at all clear.

Although FDA has long provided information on its performance in reports mandated by user fee statutes or statutes such as the Government Performance and Results Act, we are unable to find any publicly available information about the effectiveness of FDA's international program at improving outcomes related to safety of products that it regulates. FDA has developed its international program without developing a plan with quantitative milestones to denote progress toward clear programmatic goals, and thus has not reported progress in achieving those milestones in a manner that allows systematic evaluation. This should change.

We recommend that FDA leadership prepare a draft plan with quantitative milestones regarding outputs and outcomes for its international program and all international cooperation activities, in the same way that FDA regularly prepares quantitative performance plans for many of its other programs. We believe that this plan should include quantitative measures for international sharing of information about risk, recognizing differences in completeness and timeliness of information.

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Appendix A

FDA Projects to Implement

The Transatlantic Economic Council High Level Regulatory Cooperation Forum⁷⁵

FDA has reported under the TEC umbrella for several areas of EU-US cooperation. It states “The most robust of these concern FDA activities with the European Medicines Agency and the European Commission. Those projects include the following:”

1. Collaboration on inspections
2. Collaboration on third country inspections
3. Dedicated facilities for high risk products
4. Biomarkers
5. Regulatory collaboration on the outputs of the Critical Path and Innovative Medicines Initiatives
6. Combating counterfeit medicines
7. Collaboration on product specific risk management activities
8. Convergence of risk management formats
9. Parallel scientific advice
10. Exchange of information on herbal medicines
11. Collaboration on biosimilar medicinal products / follow-on biologics
12. Collaboration on development of medicinal products for children
13. Advanced therapy medicinal products
14. Safety reporting from clinical trials

⁷⁵ See <http://www.fda.gov/InternationalPrograms/Partnerships/ucm389495.htm>. Downloaded November 6th, 2015.