Federal Rulemaking and the US Food and Drug Administration: International Regulatory Policy Cooperation in the 21st Century

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The globalization of food and biopharmaceutical drug industries and product supply chains increases the risks for public health and consumer protection in the United States. The weak or absent science-based food and drug regulatory policies, inspection, and surveillance systems in many countries that import goods to the US increases the need for FDA action. The FDA is rapidly working to strengthen food and drug safety regulation in the US, and "beyond the borders" through international regulatory policy cooperation. Overtime, the FDA is building global regulatory networks and coalitions of regulatory authorities to strengthen national and regional capacity for science-based systems of prevention, detection, and management of food and drug safety risks. The impacts and implications of globalization for domestic food and drug safety regulation are being addressed through the rulemaking process. To achieve its mission, the FDA must work to strengthen understanding, awareness, and support of international regulatory policy cooperation by the federal government, states, territories, tribal authorities, and the public.

I. INTRODUCTION

In the United States, international regulatory policy cooperation is an important and growing area of public policy, public management, governance and regulation (ACUS 1991).[1] One prominent example of this is the mitigation of carbon dioxide emissions which requires cooperation among countries to address global environmental effects that negatively impact the protection of clean air and water in the United States (McCarthy 2011). However, the growth in international influence and standards harmonization threatens the capacity of executive agencies to achieve their missions and goals. In the federal government, the executive branch and independent agencies historically develop national regulatory policy and rules based on domestic considerations. State governments traditionally base policy mandates and general regulatory agendas on local issues. In the early 20th century, national regulatory agencies

1 International regulatory policy cooperation is required for US federal agencies to achieve their missions in the United States.

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began to use science and technology innovations, public administration, management, and industry expertise to strengthen policy implementation, rulemaking, and goal attainment.

By the end of the century, increasing globalization of markets and the expansion of free trade and industries exceeded the national regulatory capacity and jurisdiction of federal government regulatory agencies such as the US Food and Drug Administration (FDA), US Department of Agriculture (USDA), and the Environmental Protection Agency (EPA). The FDA is one of the oldest public health, scientific, regulatory, and consumer protection agencies in the United States federal government (FDA "History"). In this role, the FDA is responsible for food products (except meat and poultry which are controlled by the USDA), human and veterinary drugs, biological agents, medical devices, and radiation emitting devices (FDA "History"). In order to understand the impacts of these new pressures, statutory requirements and obligations of the FDA require democratic oversight by citizens, states, and federal government authorities. This, however, is itself challenged by the growth in complexity and the narrow range of actors involved in providing evidence in support of science-based rulemaking.

In 2009, the FDA reported that regulated food, drug, and medical device products were produced in over 150 countries. The food and drug products were manufactured in over 300,000 plants and factories outside of the United States (FDA "Global Initiative"). The FDA currently estimates that millions of food products enter the US food system every year, with approximately 15 percent of the US food supply originating outside of the country. Consequently, the FDA requires international regulatory policy cooperation to accomplish the agency mission and to protect food, drug, and medical device safety (FDA 2011).

In the 21st century, international regulatory policy cooperation is now required for national regulation of the following strategic sectors: food safety, biopharmaceutical drug safety, climate change mitigation of carbon emissions, renewable and efficient energy, consumer protection, product safety, transportation, automotive fuel standards, consumer protection, public health, free trade, public safety, industry standards, and national security (GAO 2013). Global threats, unregulated free trade, and lack of global industry regulation increase risks to American consumers, society, and the nation. Therefore, national regulation of food safety and drug safety by the FDA requires international regulatory policy cooperation to protect citizens, consumers, public health, and the public good of the United States (FDA 2012).

This article examines the implications of globalization on federal rulemaking in the US Food and Drug Administration (FDA). In the context of globalization and FDA rulemaking for food and drug safety, the following public laws are examined:

1. Food Safety – FDA Food Modernization Act ("The FDA Act"): Public Law 111-353, 124 STAT. 3885, [H.R. 2751]. This Act amends the Federal Food, Drug, and Cosmetic Act. The FDA regulatory policy reform modernizes the human food and animal feed system. In this process, the FDA creates a science-based preventative regulatory framework for the protection of the entire national food system and

supply chain. The FDA Act regulates domestic and foreign firms and industries that supply human food and animal feed from "farm to table."

2. Drug Safety – Food and Drug Administration Safety and Innovation Act: Public Law 112-144, 112nd Congress, 126 STAT. 993, [S. 3187].[2] This regulatory reform is intended to strengthen the agency's capacity to protect the integrity of the national drug supply chain in the context of biopharmaceutical industry globalization. The regulations enforce compliance with mandatory standards for imported drugs, importing companies, and manufacturers to the US.

International regulatory policy cooperation for food safety and drug safety is examined relative to the following federal rulemaking issues:

- The impacts of food and drug industry globalization and free trade on FDA national regulatory capacity.

- The jurisdiction, product standards, compliance and enforcement, factory inspections, role of the states, and accountability.

- Opportunities to strengthen international regulatory policy cooperation and integration, such as the roles of NAFTA, TTIP, and UN global science-based standard harmonization bodies – the UN World Health Organization (WHO) and the World Organization for Animal Health.

II. BACKGROUND

The US Congress has legal authority to make laws in and for the United Sates. The growing scale and scope of shared public health, product safety, and public goods management challenges – such as infectious diseases, clean air, and water – has led to a focus on science-based regulation by federal regulatory agencies (Vogel and Kagan 2004, US-EU 2009). Globalization of regulation is used by independent regulatory agencies and national governments to protect society and the collective good of nations (Drahos and Braithwaite 2001). This follows a trend at the international level for empirical evidence-based analysis, using techniques such as cost-benefit analysis. Overtime, national rulemaking processes have become increasingly influenced by globalization (Strauss 2006). In turn, federal rulemaking and regulatory agency mission achievement is challenged by shared threats to public health, food and drug product safety, climate change, and environmental pollution. Local accountability and transparency requirements are also impacted as the scope of threats amplifies the need for multi-level regulation (Levi-Faur 2011).

The growing need for FDA cooperation with foreign counterpart agencies, international standards bodies, and multilateral institutions such as the World Health Organization, gives rise to multi-level regulation and governance. FDA international regulatory cooperation increasingly involves regional and global agency networks for food and drug safety regulation and standards harmonization (Peel 2010). International regulatory cooperation introduces

2 The Food and Drug Safety and Innovation Act (FDASIA). http://www.gpo.gov/fdsys/pkg/PLAW-112publ144/pdf/PLAW-112publ144.pdf; https://www.federalregister.gov/articles/2013/06/19/2013-14549/food-and-drug-administration-safety-and-innovation-act-title-vii-drug-supply-chain-standards-for

multi-level regulation that encompasses local, state, federal, regional, and global systems of science-based regulation of food and drug safety. International regulatory cooperation presents challenges and opportunities for innovation in federal rulemaking to achieve the missions and goals of domestic regulatory agencies.

III. GLOBALIZATION, FDA NATIONAL FOOD AND DRUG SAFETY REGULATION, AND MISSION ACHIEVEMENT

In the domestic policy process, executive and independent agencies develop regulations for the protection of citizens, consumers, society, states, and the collective good of the nation. Rulemaking procedures require that state legislatures provide broad public policy and public management framework and mandates. Based on guidelines provided by the states, the federal government, and independent regulatory bodies develop the detailed implementation strategy to achieve national policy goals and objectives.

In the United States, food and drug safety are among the most important and strategic regulatory goals. Since colonial times, America has faced food and drug safety threats from unregulated and imported agricultural and medicine products (FDA "Overviews of FDA History"). The government created customs laboratories in response to American industrialization and public health risks from imported food and drugs. The customs laboratories introduced scientific methods and regulatory practices to prevent unsafe and poor quality drugs and medicine imports from Europe and other foreign countries. By the early 20th century, US federal government agencies adopted science cooperation, technology innovation, and public management standards to achieve their statutory missions and policy goals.

FDA AGENCY MISSION, REGULATION, AND GLOBALIZATION

The FDA is an independent federal regulatory agency that sits within the US Department of Health and Human Services. Through inter-agency collaboration in the areas of public health, chemistry, agriculture, and social services, the FDA was created as a science-based regulatory body in 1906. The FDA is responsible for US food and drug industry regulation, and for security of the national food and biopharmaceutical drug supply. The FDA regulates all food, feed, and biopharmaceutical drug ingredients and their manufacture.

As an independent regulatory agency, the FDA historically relied on the Food and Drug Act of 1906 to protect food and drug safety in the United States (FDA "Federal Food and Drugs Act of 1906"). By the 1990s, globalization of US food and biopharmaceutical drug industry manufacturing, product sourcing, and trade exceeded the national regulatory capacity of the FDA. It became clear that the FDA could no longer protect food and drug safety as a domestic-focused agency that operated primarily within US borders and jurisdictions. Instead, international regulatory policy cooperation by the FDA was required to achieve its statutory mission.

In response to these external threats, the FDA reorganized food and drug safety regulatory operations. In this process, the FDA increasingly builds regulatory oversight of food and drug imports at their source of origin around the world through international regulatory

policy cooperation (FDA 2011, FDA "Global Initiative"). The FDA implemented a Beyond Our Borders initiative to globalize regulatory operations and inspection strategies to protect food and drug safety in the United States (FDA 2008). Despite this internal strengthening, the FDA continues to face growing threats and challenges. Empirical approaches have been adopted as a way to measure risks and evaluate interventions. The FDA's strategic plan for 2011-2018 explicitly states the need for stronger regulatory science, science-based regulation, and risk management (FDA 2014).

The following FDA mission requires science-based regulation, risk management, and international policy cooperation to protect public health, consumer protection, and food, drug and medical device safety:

FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of food, human and veterinary drugs, biological products and medical devices…FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use food, human and veterinary drugs, biological products and medical devices (Institute of Medicine 2006).

GLOBALIZATION IMPACTS OF FDA FOOD AND DRUG SAFETY REGULATION

The FDA once relied on food and drug factory and port inspections to protect public health, consumers, and product safety. The globalization of national food and biopharmaceutical drug supply chains has increased food and drug import risks (FDA 2011, FDA "Food and Drug Administration Safety and Innovation Act"). The source of the growing risks to US public health and consumers is due to the inability to regulate global food and drug supply chains across several countries and regions. As a result, counterfeit, substandard, contaminated, and intentionally adulterated food and drug products can enter the US market (FDA 2011). Technological innovations by food and drug firms have accelerated global industry consolidation and cross-border free trade. The outsourcing of US manufacturing, sub-contracting of food and drug production, and their re-importation increase the risks to American public health and product safety. An indicator of the need for stronger regulatory measures to achieve the agency's national mission and responsibilities is the share of products that are imported. The FDA reported that 80 percent of all active biopharmaceutical drug and medicine ingredients, 80 percent of all seafood, 40 percent of all finished dosage drugs, and approximately 50 percent of all fresh fruit are produced outside the United States (FDA 2011, FDA "Global Initiative").

As market globalization and free trade accelerate, the growing scope of national regulation is a source of conflict within state and local governments as authority and autonomy are eroded. At the same time, the growing impact of globalization on FDA food and drug safety regulation is now a source of public concern over growing threats to public health and consumer protection. Public concerns are exacerbated by the lack of transparency and local accountability in the FDA regulatory process (Wallach 2009).

GLOBALIZATION, INTERNATIONAL REGULATORY POLICY COOPERATION, AND THE FDA

In response to food and drug industry and trade globalization, the FDA is building international regulatory policy cooperation to achieve its statutory mission. The FDA has launched a globalization of regulatory agency strategy that is proactive and focuses on the prevention, detection, and rapid removal of food and drug safety threats from imported products (FDA "Global Initiative"). Earlier FDA efforts for international regulatory cooperation were limited. In response to the growing challenges of globalization on national regulation, in 1991, the Administrative Conference of the United States (ACUS) – an independent federal agency in the Executive Branch of the federal government – adopted Recommendation 91-1: Federal Agency Cooperation with Foreign Government Regulators.[3] To establish stronger cooperation between US regulatory agencies and their counterparts in foreign countries (primarily through identifying foreign bodies that have the same mission as the agency), US regulatory agencies were advised to develop harmonized regulations for common regulatory tasks such as the protection of public health, facility and plant inspections, consumer protection, food safety, drug safety, and environmental protection. This recommendation also advised the domestic agency to determine the reliability of other international agencies and to understand their technical, regulatory, and administrative standards (Aman 2001).

The goal of international regulatory policy cooperation by US government policy and federal regulatory agencies such as the FDA is as follows:

- To share human and financial resources to address common and shared regulatory problems and threats,
- To cooperate on shared regulatory compliance practices, i.e. food and drug inspections, factory visits, etc, and
- To strengthen domestic and international regulatory capacity through the improvement of regulatory practice, research and development, capacity building, and standards harmonization (ACUS 1991, Timmermans and Epstein 2010).

The ACUS also advised US agencies to engage in international regulatory cooperation to strengthen mutual recognition tests, certifications, inspection, and information gathering. The US regulatory agencies were also encouraged to work with existing bilateral/multilateral/international organizations and standards bodies to address common regulatory problems and challenges (Wessel and Wouters 2008). This has entailed the participation of US government and private industry interests (Black 2008, Wessel and Wouters 2008).

3 The Administrative Conference of the United States reports to the White House, and is responsible for providing recommendations for the improvement of administrative process through consensus driven research, non-partisan expert advice and recommendations for improvement of federal agency, public policy and regulatory policy processes.

IV. CHALLENGES FOR FDA REGULATION OF US FOOD AND DRUG SAFETY

The growing risk of naturally occurring infectious diseases, intentional adulteration, and bioterror against the US food and drug systems is now a shared threat for the FDA and other regulatory agencies such as the USDA, EPA, and Department of Defense. However, factory inspections – the dominant verification and enforcement tool of the FDA – frequently reveal non-compliance with FDA regulations for food and drug safety. In 2008, the Centers for Disease Control raised concerns and warnings about the growing incidence of allergic reactions by patients on dialysis to the blood thinner Heparin. In response, the FDA and the public expressed concerns over the growing risks from the outsourcing of biopharmaceutical drug manufacturing (Pew 2012). By 2012, the FDA announced patient injuries and deaths in the United States due to adulterated Heparin from China (Pew 2012). In 2014, factory inspections for antibiotic drugs manufactured in India for the US market revealed products that had no active ingredient (Harris 2014). In 2005, an FDA investigative operation found that 85 percent of drugs labeled as produced in Canada were in fact produced in over 25 different countries (FDA 2005). In response, the FDA seeks to protect public health and consumer safety through prescription drug import warnings (FDA "Buying Medicines Over the Internet"). Each of these examples demonstrates the need to strengthen surveillance and monitoring within those countries that export food and drugs to the United States. A preventative global approach by the FDA is emerging, which strengthens drug safety through FDA foreign plant inspections and the enforcement of US regulations.

GLOBALIZATION CHALLENGES FOR REGULATION OF FOOD SAFETY

The FDA estimates that approximately 15 percent of the US food supply originates from outside the country (FDA "Food Safety Modernization Act (FSMA)"). Approximately 60 percent of all fruits and vegetables, and 80 percent of seafood is imported (FDA "Food Safety Modernization Act (FSMA)"). Foodborne diseases are a growing threat to consumers and the public due to globalization of the food supply. The FDA estimates that every year, one in six Americans experiences food poisoning, which amounts to approximately 48 million people. In 2012, the Centers for Disease Control (CDC) reported that foodborne disease outbreaks in the United States are directly linked to imported food, specifically fish and spices. At that time, CDC research revealed that approximately 45 percent of foodborne illnesses were traced to food products from Asia (CDC 2012, CDC "New Food Safety Data for 2013").

In some cases, food exports to the United States do not meet FDA mandatory standards for food safety (CDC 2012, CDC "New Food Safety Data for 2013"). In many cases, this is due to weak regulatory systems and absent standards compliance in exporting countries and US trade partners (Wallace and Oria 2013). However, the FDA reports that it can only inspect approximately 3 percent of all food imports to the United States. The increasing supply of food sourced from outside the country challenges the accountability of the FDA as an independent regulatory agency, and threatens the achievement of its statutory mission. FDA food safety regulation requires international regulatory policy cooperation to address glo-

balization and contamination of the US food system (Demortain 2008).

GLOBALIZATION OF BIOPHARMACEUTICAL DRUG SUPPLY: REGULATION OF DRGU SAFETY THREATS

The globalization of the biopharmaceutical industry is shifting manufacturing, clinical drug trials, and drug regulation outside of the United States. By 2011, China and India were the largest sources of drugs compounding of FDA-regulated biopharmaceutical drugs in the US. China, India, and Eastern European countries will continue to grow as the main sources of US drug products (FDA 2011). However, drug regulatory capacity is weak in many emerging countries and developing regions (Weisfeld and Lustig 2013). According to the United Nations WHO, globalization of biopharmaceutical companies and industry exceeds the drug regulatory capacity of many developing countries and emerging regions (WHO 2015). The FDA is actively working to build stronger global food and drug regulatory capacity across nations and regions to strengthen the agency's ability to protect public health and product safety in the United States (FDA 2013).

The FDA has limited regulatory oversight of the pre-clinical and post-market risks of these drugs. Domestic demand for biopharmaceutical drug products is increasingly filled by human and veterinary medicines produced outside of the country. By 2002, the FDA reported that approximately 40 percent of all biopharmaceutical drugs consumed in the US were produced abroad and approximately 80 percent of the active ingredients used to manufacture the drugs used in the US were imported.

FDA human and budgetary resources, as well as jurisdictional constraints, weaken the agency's ability to inspect offshore companies, factories, or ports prior to the import of food and biopharmaceutical drug products. Between 2002 and 2007, only 1 percent of foreign companies exporting food products to the United States were inspected by the FDA (FDA 2011). During the same period, less than half of all FDA foreign drug plants – 46 percent – were inspected, while over half of all foreign drug plants – 56 percent – were not inspected by the FDA for verification of biopharmaceutical drug import safety. For example, in 2012, counterfeit and mislabeled cancer drugs entered the US market (Department of Justice 2014). In the case of Mexico, the FDA intervened to stop the illegal import of unapproved medicines through black market pharmacies that operated in California (FDA 2011).

In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law (FDA 2015). The bill addresses the growing reliance on imported drugs and increasing threats from sub-standard, counterfeit, and adulterated human and veterinary drugs. The FDASIA requires international regulatory policy cooperation to protect the safety, effectiveness, and manufacturing quality of drugs that enter the US through the global supply chain (FDA 2015). The FDA has supported this through rulemaking to enforce the new legislation.

The FDA proposed a rule to strengthen the agency's administrative authority to detain unsafe drugs for human and animal use ("Administrative Detention for Drugs Intended for Human and Animal Use" 2014). In the past, concerns over FDA regulations as the source of

US drug shortages and drug company market restrictions limited the agency's authority to place unsafe products in administrative detention.[4] The FDA issued a rule to require agency notification of the discontinuance or disruption of biopharmaceutical drug, blood product, or vaccine supplies to prevent shortages in the human and veterinary medicine supply chains.[5]

CHALLENGES FOR FDA INTERNATIONAL REGULATORY POLICY COOPERATION

The FDA has embarked on several bilateral and international initiatives to strengthen food and drug safety regulation (FDA 2014). But in spite of the investment of human and financial resources, FDA international regulatory policy cooperation initiatives have had limited impacts. Counterfeit drugs pose an increasing threat to public health in the US. Therefore, the FDA launched a counterfeit drug initiative (FDA 2009). And yet, public concerns over growing food and drug safety threats in the US requires stronger and more formal cooperation with foreign national, regional, and international regulatory organizations, and UN standards harmonization bodies.

The FDA mechanisms for international regulatory policy cooperation include: working with trusted national and regional partners; sharing regulatory resources to achieve shared food and drug inspection goals; and establishing a foreign inspection office in foreign countries to ensure compliance with FDA regulatory goals and obligations for the protection of food and drug safety in the United States. In this context, the FDA works with foreign regulatory agencies to build regulatory capacity for food and drug safety regulation, risk assessment, and science-based standards harmonization.[6]

The implementation of the FDA Food Safety Modernization Act (FSMA) and the FDSIA (drug safety) requires stronger and more formal international cooperation by the FDA, and the rules reflect the new requirements for protection of food and drug safety in the United States. The mechanisms for international regulatory policy cooperation are already in place through existing legislation, with the ACUS and the Government Accounting Office providing oversight.

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4 ibid.

5 See Frequently Asked Questions About the Drug Shortages Programhttp://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050796.htm#q2Drug Shortages: Non-Compliance With Notification Requirementhttp://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm403902.htmFederal Register-Permanent Discontinuance or Disruption in Manufacturing of Certain Drug or Biological Products, https://www.federalregister.gov/articles/2013/11/04/2013-25956/permanent-discontinuance-or-interruption-in-manufacturing-of-certain-drug-or-biological-products

6 The FDA has extensive bilateral, regional and international organization cooperation agreements in place to achieve its mission for the protection of food, drug and medical device safety in the United States.

FDA REGULATORY SHIFT FROM DOMESTIC RESPONSE TO INTERNATIONAL PROTECTION

The FDA Food Safety Modernization Act (FSMA) was signed into law in 2011. The FSMA policy shifts the focus of FDA operations from a response-driven to a preventive regulatory system that strengthens compliance through science-based and risk management-based standards for food safety. For example, rules under the Act strengthen the enforcement of agri-food firm and industry regulations to prevent human food and animal feed contamination.[7] The FSMA also makes provisions to strengthen compliance and enforcement of mandatory regulations for small businesses that produce and manufacture foods for the US.[8] This has included new rules for the sanitary transportation of human food and animal feed in accordance with the FSMA.[9] Another component of the bill includes a rule to require information and prior notice of food imports that have been rejected by other countries.

Many countries and regions still lack modern regulatory capacity, surveillance, and manufacturing inspection systems and are unable or unwilling to comply with FDA and global standards for the protection of food safety in the United States. The FDA works with other national and regional regulatory agencies to strengthen regulatory science, surveillance, and inspection capacity. The FSMA rules provide the following regulatory oversight mechanisms for the FDA:

Prevention through science/evidence based regulation to prevent contamination of the national food supply

- Mandatory compliance with food facilities controls
- Mandatory food produce controls
- Biosecurity authority to prevent deliberate contamination of the national food supply

Inspection and Compliance when problems occur

- Mandatory Inspection Frequency
- Records Access
- Food Testing by Accredited Laboratories

Response when prevention and inspection fails and problems occur

- Mandatory recall
- Extended mandatory detention
- Suspension of registration
- Enhanced product tracing
- Increased record keeping for high risk foods

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7 The FDA created a rule for the preventative control of human food and animal feed facilities. 1 CFR Chapter I [Docket No. FDA–2011–N–0251].

8 The FDA works to help small businesses comply with the mandatory registration requirements for food production and food safety in the United States.

9 See Federal Registrar – Sanitary Transportation of Human and Animal Food, https://www.federalregister.gov/articles/2014/02/05/2014-02188/sanitary-transportation-of-human-and-animal-food#h-11, The final rule is expected in March 2016.

Stronger and Wider Imports Authority to enforce US standards and consumer protection

- Importer accountability
- Third Party Certification
- Certification for High Risk Foods
- Voluntary Qualified Importer Program
- Authority to Detain Entry

Enhanced State/National/International Partnerships

- State and Local Capacity Building
- Foreign Capacity Building
- Reliance on Inspections by Other Agencies/Domestic and International

The FDA opened offices in several foreign countries and regions to strengthen partnerships with counterpart regulatory agencies. In light of the growing exports of food and drug products into the United States, the FDA has established offices in China, India, Latin America, Europe, the Asia-Pacific, Sub-Saharan Africa, and the Middle East. The main purpose of these global offices is to construct foreign food and drug plant and manufacturing inspections. The FDA works with counterpart regulatory agencies to inspect, verify and enforce compliance with US and global food and drug regulations, manufacturing quality, and product standards.

FOOD AND DRUG FACTORY AND GLOBAL SUPPLY CHAIN INSPECTIONS AND CERTIFICATION

The FSMA strengthens international food and drug factory inspections. During the factory inspections, the FDA and partner regulatory agencies share financial, human and technological resources to monitor the safety and security of food and drug supply chains in the countries that export products into the US domestic food and drug systems. As part of national biosecurity preparedness, the FDA's global strategy is used to monitor and to develop surveillance systems to detect, diagnose, and respond to infectious disease pandemics and deliberate bioterror attacks on the global food and drug supply chain. In this task, the FDA uses inter-agency collaboration with the Department of Health and Human Services, Department of Defense, Department of Agriculture, the Environmental Protection Agency, and international regulatory cooperation to protect the domestic food and drug system in the United States from bioterror and emerging infectious disease threats.[10] For example in the area of antibiotic drug resistance, the FDA hosts the National Antimicrobial Resistance Monitoring System in cooperation with state and local public health departments, the Department of Agriculture, and the Centers for Diseases Control. The inter-agency task force protects public health, consumer, and food safety through the inspection of meat products for the detection of antibiotic and antimicrobial drug resistance (FDA 2015).

The FDA also co-chairs the Inter-Agency Taskforce on Antimicrobial Resistance with the CDC and National Institutes of Health (NIH) (CDC 2014). The Department of Health and Human Services, Environmental Protection Agency, Department of Defense, and Department of Veterans Affairs are members of this

10 In the federal government, inter-agency cooperation is growing to improve policy implementation and regulatory agency goal attainment. In the context of firm, market and industry globalization, inter-agency cooperation is used to support international regulatory policy cooperation by US agencies.

task force to accelerate the innovation of safe and effective antibiotic drugs. In addition, the FDA and CDC now chair and host the Transatlantic Taskforce on Antimicrobial Resistance with counterpart agencies in the European Union. [11]

The FDA established inter-agency cooperation with the Department of Agriculture for public health and food inspection. In the event of biological or conventional warfare, the FDA and USDA cooperate to ensure the safety of the national food supply system.[12] For the protection of national and global food safety, the FDA cooperates with the Department of Defense.[13]

In the case of food contamination, toxicity, and pesticides, the FDA and the EPA have a formal agreement to cooperate on the surveillance and monitoring for food and drug products and drinking water.[14] The FDA also has a formal cooperation agreement for the inspections of fish and fisheries products with the U.S. Department of Commerce and the National Oceanic and Atmospheric Administration. The FDA uses inter-agency cooperation agreements to regulate domestic and imported food and drug safety.

V. OPPORTUNITES TO STRENGTHEN US FOOD AND DRUG REGULATION

The FDA Food Safety Modernization Act is the most extensive US food safety reform for over 70 years. The supporting rulemaking process for this includes several regulations and guidelines for the protection of the national food system.[15] The scale and scope of the policy requires a formal rulemaking process with Congressional oversight, inter-agency cooperation with federal and state governments, and international regulatory cooperation. The importance of food safety for consumers, industry, and the nation requires formal public stakeholder input prior to the proposal of rules. The FDA uses "notice and comment rulemaking" as set out in the Administrative Procedure Act of the US federal government, however, this has limited impact because of limited participation from public stakeholders, and stronger corporate and industry interest group mobilization.

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11 The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was initially launched and hosted in the EU. It is now hosted by the Centers for Disease Control in the United States.

12 The FDA and USDA cooperate in peace and wartime on food safety inspections.

13 The FDA and DOD cooperate to strengthen national and global food safety in peace time, during and after conventional and biological war attacks.

14 See the Memorandum of Understanding between the FDA and EPA for evaluation pesticide and chemical contamination of food and drug products, and drinking water. http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm115873.htm; http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm116216.htm

15 See Food Safety Law and the Rule-Making Process: Putting the FMSA to Work http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm277706.htm#primer

The FDA organizes public meetings to solicit comments and suggestions. The FDA considers public and industry comments ahead of final rulemaking and putting in place an "effective date" for company and industry compliance with the rule. The FDA prepares and issues guidance documents to assist and support compliance. As of April 2015, the following proposed FDA rules are pending final decisions:

- Proposed Supplemental Rule for Standards for Produce Safety
- Proposed Supplemental Rule for Preventive Controls for Human Food
- Proposed Supplemental Rule for Preventive Controls for Food for Animals
- Proposed Supplemental Rule for Foreign Supplier Verification Programs for Importers of Food for Humans and Animals
- Proposed Rule for Accreditation of Third Party Auditors/Certification Bodies to Conduct Food Safety Audits and Issue Certifications
- Proposed Rule for Sanitary Transportation of Human and Animal Food
- Proposed Rule for Focused Mitigation Strategies to Protect Food Against Intentional Adulteration

ROLE OF STATES: EMERGING NATIONAL INTEGRATED FOOD AND DRUG SAFETY SYSTEMS

There are approximately 3,000 state, local, and tribal governments involved in the regulation of food safety in the United States (Wallace and Oria 2010). According to the FDA, states and local territories conduct over half the mandated FSMA food facility inspections in the United States. As result, the FDA achieves its statutory goals and agency mission through frequent domestic inspections that are carried out by states (Wallace and Oria 2010). Through a more explicit statement of federal and state cooperation, the FDA Food Safety Modernization Act strengthens cooperation with food safety agencies at the federal, state, local, territorial, tribal, and international levels. Rulemaking by states is somewhat disadvantaged due to low levels of information sharing and knowledge of national and international regulatory cooperation. The FDA rulemaking process increases the scale and scope of FDA-state relations and cooperation in national food safety. In contrast to the past, the FDA rules require that federal agency staff and the state food safety regulators and inspectors have the same training.

FDA INTER-AGENCY COOPERATION, MULTI-LEVEL REGULATION, AND LOCAL ACCOUNTABILITY

The FDA is required by the FSMA to work in close partnership with several levels of government and international regulatory authorities. For this reason, FDA international regulatory policy cooperation is creating a multi-level system of food and drug safety regulation. The creation of local, state, federal, regional, and global regulatory networks for food and drug safety is used by the FDA to address the growing complexity of market globalization and economic integration. For example, the FDA actively engages in interagency cooperation with the EPA and USDA to protect meat and food safety. At the same time, FDA inter-agency cooperation for food and drug safety is also emerging at the regional and global levels. Technology and scientific methods are used to analyze and sample meat products that enter the national food system. The new FDA rules for the FSMA and FDASIA seek to strengthen

inter-agency regulatory cooperation by establishing a universal standard of science-based risk management and evaluation of interventions.

The FSMA has created a framework for building a new National Integrated Food Safety System. The FDA builds on the approved 1998 National Food Safety Initiative for the development of a new food system in the United States.[16] In the system, the FSMA will use federal budget resources to train state governments and to build infrastructure for food safety protection.[17] Building a National Integrated Food Safety System is a complex and long-term process. To be successful in aligning state programs with the FDA's new facility inspection and compliance approach, approximately 1,000 state inspectors will need training, and the states will need real-time information-sharing capacity with the FDA and other states, state laboratory accreditation, and inspector certification programs. Should the President's 2016 budget request be approved, these on-going processes will be significantly increased to help ensure that states conduct sound, consistent inspections when industry compliance with the new preventive controls rules commences in late 2016. In addition, the FDA must build state partnerships and capacity in 2016 to provide education and technical assistance to growers in anticipation of the rule starting to be implemented in 2017.

The FDA rule for food safety modernization will converge state, territorial, and tribal programs with the federal agency's mission goal, standards, regulations, and guidance. The FDA rule requires training and certification of state officials. In this regard, information sharing capacity, laboratory enhancement, and inspection capacity and standards are required for the states to implement the prevention goals of the FSMA rule.

Local accountability of the FDA for national food and drug safety regulation is impacted by the growing scale and scope of international regulatory cooperation (Coglianese, Cary, et.al. 2008). In the case of the European Union (EU) and North American Free Trade Agreement (NAFTA) countries, growing levels of regulatory policy cooperation and science-based standards harmonization for food and drug safety challenges FDA accountability. The growing role of international regulatory policy networks in the FDA is creating a multi-level system of governance for food and drug safety that are difficult for states and local actors to penetrate (Slaughter 2001). In the multi-level system states, the federal government, regions, and global organizations are involved in the implementation of FDA food and drug regulations in the United States and abroad. However, the local accountability of international regulatory policy networks to the citizens, states, and the FDA remains unclear and under-developed. Over the last decade, the FDA regulatory mission in the US has been impacted by the need for common regulatory standards that stem from closer integration with North American and transatlantic

16 See the Federal Register documentation of the 1998 National Food Safety Initiative http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/98-045N.htm

17 Building the National Integrated Food Safety System http://www.fda.gov/downloads/ForFederalStateandLocalOfficials/UCM183650.pdfhttp://www.ncsl.org/documents/environ/Reardon.pdf

economies and markets (Shapiro 2002). FDA international regulatory policy cooperation creates new opportunities for building North American and transatlantic systems for food and drug safety.

FDA FOOD SAFETY REGULATION COOPERATION IN NORTH AMERICA

In the case of the NAFTA, regulatory policy cooperation requires common regulatory policies in the United States, Canada, and Mexico (Office of Management and Budget 2013). The FDA works closely with the governments and regulatory authorities in Mexico and Canada to strengthen regulatory capacity. As major trading partners of the US, the FDA is currently building stronger regulatory policy cooperation with Canada and Mexico. The FDA is currently engaged in joint action plans and program development with Canada and Mexico to develop common approaches and standards to food safety regulation (White House 2014).

Mexico is a major exporter of fresh and processed foods to the United States. The FDA is expanding international regulatory cooperation with counterpart agencies in the Mexico to accelerate food safety modernization for the protection of the US national food system (White House 2012). However, the FDA does not engage with Mexico on drug regulation cooperation.

Regulatory policy cooperation is stronger with Canada than Mexico (White House 2014). The FDA uses international regulatory policy cooperation with Canada to strengthen the safety of drug imports. However, the FDA does not have food safety cooperation agreements with Health Canada. Instead, US livestock and meat products are regulated through the U.S. Department of Agriculture's regulatory cooperation with its Canadian Food Inspection Agency counterpart.

FDA FOOD AND DRUG SAFETY COOPERATION WITH THE EUROPEAN UNION

The FDA has an extensive relationship with its counterpart agencies in Europe. In 2007, the US and the EU launched the Transatlantic Economic Council, which now serves as the formal framework for regulatory policy cooperation and acceleration of economic and market integration between the United States and the European Union (Vogel 2012). In the Transatlantic Economic Council, the FDA and European Medicines Agency cooperate on biopharmaceutical drug safety, effectiveness, and quality regulation. The US and the EU also cooperate on manufacturing standards enforcement and inspections in other countries (FDA 2014). In spite of highly publicized regulatory conflicts and competition over food and drug safety regulation, the FDA works closely with the European Commission, European Food Safety Authority, and European Medicines Agency to converge and harmonize food and drug safety regulations.

In 2013, President Barack Obama announced the launch of formal negotiations for the Transatlantic Trade and Investment Partnership (TTIP).[18] The goal of the TTIP agreement

18 See joint US and EU press release announcement from the United States Trade Representative (USTR) February 2013 US-EU Presidents. www.ustr.gov .Also see European Commission Directorate General for Enterprise and Industry/ Transatlantic Economic Council – www.ec.europa.eu. While the global eco-

is to create an integrated transatlantic market system. The TTIP agreement will create common regulatory policies, public laws, and standards for global trade, industries, and market regulation. The FDA and European Food Safety Authority will work in cooperation to protect food safety and animal health in the US, EU, and transatlantic region.

The FDA and European Food Safety Authority have food safety regulation and standards issues that are being addressed prior to the passage of the TTIP agreement. The FDA and the European Medicines Agency have extensive drug safety, manufacturing, and other biopharmaceutical drug regulation cooperation agreements. Over the last decade, the FDA and the European Medicines Agency established the following regulatory agreements for drug safety: collaboration on transatlantic and global inspections, combatting counterfeit drugs, new biopharmaceutical drug development and accelerated innovation, and drug safety reporting for clinical drug trials and parallel scientific advice.

In addition, the US and the EU work closely in international organizations for drug regulatory standards harmonization. The FDA participates in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Within this framework, the FDA proposed and launched the International Pharmaceutical Regulators Forum to accelerate national and regional drug regulatory capacity in developing and emerging countries.[19] In the area of veterinary medicines, the FDA is a member of the International Conference on Harmonization of Technical Requirements for Registration of Veterinary Medical Products.

FDA MULTILATERAL COOPERATION FOR GLOBAL FOOD AND DRUG SAFETY

As the complexity of industry and market globalization increases, the FDA works in cooperation with international organizations and the UN scientific standard harmonization. The harmonization of national and regional regulations, standards, and laws is required to protect food and drug safety, public health, and national biosecurity. FDA rulemaking and strategic goals use international agreements and participation in international organizations to protect the American food and drug system.

In the area of food safety regulation, the FDA works on global agriculture, animal livestock, and food trade standards with the following organizations: Codex Alimentarius, UN World Health Organization, the World Organization for Animal Health, and the Food and Agriculture Organization.[20] The FDA ultimately uses

nomic crises affects all nations and regions, transatlantic economic integration is driven by accelerated science cooperation and technology innovation for market growth and knowledge based job creation.

19 See International Pharmaceutical Regulators Forum https://www.google.com/search?client=safari&rls=en&q=ICH+-+global+regulator+forum&ie=UTF-8&oe=UTF-8

20 FDA Office of Global Regulatory Operations and Policy http://www.fda.gov/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/ucm236581.htm; https://www.federalregister.gov/

international regulatory policy cooperation to build food and drug safety regulatory policy networks. The global regulatory networks and coalitions of food and drug regulators are now required to achieve the FDA's mission and regulatory responsibilities. However, the FDA is accountable to the US government, industry, citizens, and society. FDA accountability to the public is increasingly challenged by international regulatory policy networks (Slaughter 2001).

IV. CONCLUSIONS: CHALLENGES AND OPPORTUNITIES FOR NATIONAL FOOD AND DRUG SAFETY

Globalization of FDA operations and rulemaking is deeply embedded within food and drug safety regulation in the United States. The globalization of markets, industry, and free trade increase food and drug safety risks to American consumers and public health. The globalization of national food and drug systems have exceeded the FDA's ability to protect American consumers and the nation's public health. International regulatory policy cooperation is an emerging and important regulatory policy instrument for FDA rulemaking, mission achievement, and enforcement.

FDA international regulatory policy cooperation increasingly requires stronger public and citizen accountability and transparency in the area of food and drug safety regulation. The FDA is accountable to Congress and citizens, and the growing role of international regulatory agencies and standards is becoming a challenge for the democratic process and specifically the ability for non-global, non-industry actors to understand and to participate in rulemaking processes. This is currently playing out in the US and the EU over food safety regulation and standards harmonization in the TTIP agreement (EurActive 2014). While transatlantic companies and industries developed and want the TTIP agreement, there is concern by the public over differences in food safety regulation in the US and EU.

STRENGTHENING US AND GLOBAL FOOD AND DRUG SAFETY

Globalization and free trade are driving the growing use of international regulatory policy cooperation and global networks by the FDA. The use of international regulatory policy cooperation strengthens the capacity of the FDA in many ways. For example, it provides stronger regulatory tools and resources for the prevention, detection, and removal of threats to food and drug safety in the United States, and it enables the FDA to increase focus on public health and biosecurity threats to US national food and drug systems. At the same time, globalization challenges the fundamental goals and obligations of the FDA to protect food and drug safety, public health and consumers in the United States.

Since the FDA only has jurisdiction in the United States, protection of the national food and drug safety and public health require extraterritorial support. Beyond safety impacts, overtime, FDA use of international regulatory policy cooperation will strengthen the competitiveness of US food and drug exports by removing non-tariff barriers to trade.

articles/2013/08/02/2013-18631/cooperative-agreement-to-support-the-food-and-agriculture-organization

International regulatory policy cooperation offers new opportunities for the FDA to achieve its statutory goals and agency mission. Ultimately, international regulatory cooperation supports the FDA mission through the convergence and harmonization of foreign regulations to FDA science-based regulatory policy standards (Stewart 2005). In this regard, the FDA achieves its domestic mission through increasing regulatory participation, support, and inspection-sharing with comparable foreign counterparts and international standards-setting bodies. Furthermore, the FDA achieves cost-savings through information exchange, factory and facility inspection sharing, and standards verifications and compliance

CHALLENGES OF INTERNATIONAL REGULATORY POLICY COOPERATION FOR FDA RULEMAKING

In the case of the FDA international regulatory cooperation, the issues of development and/or enforcement of US public laws, regulations, and standards must be clarified in the rulemaking process. The clarification process must address the impact of globalization on the FDA, inter-agency collaboration, and international regulatory policy cooperation for food and drug safety in the United States. In the past, the FDA and other agencies have engaged in international regulatory policy cooperation to develop more a comprehensive regulatory framework and rules for the domestic policy environment.

In order to strengthen the transparency around international regulatory cooperation, during FDA consultation of the rulemaking process, foreign government bodies and US inter-agency partnerships that are used to fulfill the agency's mission should be identified. The nature and levels of international regulatory policy cooperation should be noted, for example, stating the exchange of information and coordination of national regulatory agency missions and goals in consultation prior to formal rulemaking or with reciprocal participation during rulemaking processes.

Through the use of increasing levels of mutual recognition and regulatory convergence, the FDA and other US regulatory agencies are developing a range of options for international regulatory policy cooperation. In the case of NAFTA, a tripartite framework is used to coordinate FDA regulatory policies and missions with counterpart agencies in Canada and Mexico. In contrast, the FDA mission as a science-based regulatory agency supports stronger international regulatory policy cooperation with counterpart agencies in the European Union. However, the pending TTIP agreement will require stronger alignment of US and EU regulatory missions and food and drug safety policies for the FDA to fulfill its statutory obligation to the US domestic system. To achieve this, formal and direct discussion of regulatory harmonization and agency convergence is needed by government, industry, the scientific community, and civil society.

The FDA rulemaking consultation process must address international regulatory policy cooperation in the context of the FDA's domestic mission – the regulation of the national food and drug systems. In light of the balance of authority and power that rests with the states, the challenges for the FDA will increase due to the complexity of industry globalization, free trade agreements, and international regulatory standard-setting bodies such as

the World Trade Organization, the UN World Health Organization, the World Organization for Animal Health, and the UN Food and Agriculture Organization. It is important that states, territories, and other units of government are fully involved and have the capacity to understand the impacts of internationally agreed standards for food and drug safety.

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