EXPLORING THE INFORMATION ASYMMETRY GAP: EVIDENCE FROM FDA REGULATION

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Abstract: Modern models of the relationship between regulators and the firms they regulate are often built upon a principal-agent framework, most often with the assumption of an exogenously given information asymmetry gap between the principal (the regulator) and its agents (firms). Given this information asymmetry gap, considerable effort has gone into the design of optimal regulatory mechanisms. This paper contributes to the literature on the design of efficient regulatory mechanisms but does so by exploring the efficacy of regulator efforts to reduce the information asymmetry gap. We do so by assembling a data set of over 14 thousand inspections by the U.S. Food and Drug Administration (FDA) of roughly 3700 manufacturing facilities over a 14 year timeframe, and exploring the empirical determinants of inspection outcomes. Our analysis of regulatory outcomes reveals the presence of heterogeneity across individual regulators, and that this heterogeneity is seen to depend, in part, on systematic efforts by the FDA to provide specific training to inspectors designed to reduce their under-endowment of information vis-à-vis the firms they regulate. These results suggest that future models of efficient regulation may benefit by incorporating both the existence of this heterogeneity and the potential for regulators to undertake measures to overcome information asymmetries.

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1. INTRODUCTION

Government regulation consists of a set of rules by which the regulated entity must, under threat of penalty, comply. Consequently, early economic models of regulation assumed that regulatory rules were sufficiently well-specified and binding so that neither regulators nor the firms they regulate had discretion in enforcing or adhering to these regulations.[1] This early perspective of government regulation has, however, proven unrealistic. Indeed, during the past two decades economists increasingly recognized that this tight theoretical construct fails to hold in a variety of regulatory contexts. For instance, economists now recognize that rules in the regulatory "contract" commonly are sufficiently ill-specified that regulated firms have some (perhaps considerable) discretion in their response to regulations.[2] Principal-agent models of regulation, which assume information asymmetries between firms and regulators, offer the most common approach to modeling firm discretion.[3] Central to these models has been the assumption that regulators are under-endowed with information regarding the operating technology (i.e., costs or quality) of the regulated firm. This, in turn, has evoked a large and growing literature on the design of optimal regulatory mechanisms that seeks to align the interests of regulators (generally assumed to be welfare maximizing) and the firms they regulate assuming the presence of information asymmetry.[4]

While the optimal regulatory design literature has significantly advanced our understanding of economic regulation, it is less than satisfying on at least three grounds. First,

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1 See, e.g., Averch and Johnson (1962).

2 Beyond the more obvious situations in which firms discretionarily choose to fail to comply with a regulatory standard, a recent literature involves situations in which firms discretionarily engage in costly activities to *more than comply* with regulatory constraints. See, e.g., Weil (1996) and Maxwell, Lyon and Hackett (2000) and King and Lennox (2000).

3 For a recent, comprehensive survey, see Laffont and Martimort (2002).

4 See Baron (1989) and Armstrong and Sappington (forthcoming) for reviews.

although the research on optimal regulatory design mechanisms has generated considerable theoretical discussion, implementation of these schemes has been rare.[5] As a practical matter, this may spring from the significant (i.e. costly) changes to existing regulatory mechanisms that would be necessary to implement these "optimal" designs. Thus, while providing aspirant benchmarks, these design mechanism may be of more theoretical than practical importance.

Second, models of optimal regulatory design routinely begin with the assumption of an exogenously generated and immutable information asymmetry.[6] In practice, however, regulators may undertake activities to close the information asymmetry gap. Thus, the "exogenous" and "immutable" information asymmetry assumption is not congruent with the practical efforts that are made to overcome these asymmetries. It seems, then, that the design of optimal regulatory mechanisms has been the subject of considerable theoretical research while receiving little practical attention; and, conversely, considerable efforts have been made by regulators to overcome information asymmetries while research into the empirical consequences of those efforts have received little attention from researchers.

Third, in a variety of regulated industries, the common modeling assumption of a single, monolithic regulator is inapt. Regulatory agencies like the Occupational, Safety and Health Administration (OSHA), the Nuclear Regulatory Commission (NRC) and the Food and Drug Administration (FDA) are comprised of hundreds of "foot soldier" regulators. These armies of regulators are the individuals who visit firms, implement regulations, determine and report violations and individually incur effort to overcome asymmetric information and implement

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[5] Indeed, the most notable shift of regulatory design instruments, from rate-of-return regulation to price-cap regulation within traditional public utility industries, has been far from complete. See, e.g., Blank and Mayo (2006). Numerous other incentive compatible regulatory schemes have received even less attention in the actual practice of regulation. Consider, for example, the regulatory mechanisms discussed in Armstrong and Sappington (forthcoming).

[6] See Baron and Besanko (1984), Baron and Besanko (1987) and Khalil (1997) for notable exceptions.

complex regulations. If we relax the assumption of a single regulator to consider an army of regulators and allow for the potential of boundedly rational enforcement by these regulatory foot soldiers, the important possibility of significant regulator heterogeneity arises. Indeed, if regulators are not homogenous and are only boundedly-rational, then several new questions are introduced into the economics of regulation.

Indeed, once these considerations are permitted, the modern emphasis on the design of "optimal" regulatory mechanisms in the face of exogenous information asymmetries gives way to a focus on concerns about human capital development, organizational incentives, and organizational structures because these factors may become critical features of the regulatory landscape. Thus, while stylized principal-agent models of regulation have considerably enhanced our understanding of the relationship between regulators and the firms they regulate, we move here to tackle several new dimensions of the regulatory process.

To begin this effort, we address several questions: Does regulatory heterogeneity exist, and if so to what degree? What are the sources of any such regulator heterogeneity? To what extent does regulator heterogeneity and departures from perfect rationality impact the application of regulatory rules and corresponding firm behavior? If regulator heterogeneity is problematic by diminishing social welfare, how can regulators reduce or at least minimize its impact on social welfare? In short, what possibilities exist, and how effective might these possibilities be, for overcoming the much ballyhooed "information asymmetry" gap that has become such a central part of our understanding of regulation?

This paper empirically begins to tackle these questions. Specifically, we examine 14 years of inspection data for the FDA involving over 3700 manufacturing facilities, more than 700 investigators, and over 14 thousand individual inspections to analyze the extent to which

regulatory decisions are impacted by individual regulators. We explore how training, experience, and regulator-specific effects impact regulatory outcomes, controlling for a wide-variety of technology-, industry-, manufacturing-facility, and FDA-specific variables.

Our empirical analysis finds pronounced evidence of significant heterogeneity among regulators. *Ceteris paribus*, some investigators are thirty percent more likely than the median investigator to impose some type of sanction on a manufacturing facility while other investigators are twenty percent less likely to do so than the median investigator. Even after accounting for matching between type of investigator and type of manufacturing facility, we find substantial variation in investigator-specific effects. Our analysis further explores the sources of these variations. We find that regulatory outcomes differ because of variations in FDA-specific training, inspection experience, as well as investigator specific effects.

Our study provides several new insights. First, like Feinstein's (1989, 1990) prior work on NRC and OSHA regulators, we find substantial variation in regulatory outcomes by investigator. His studies in conjunction with ours provide strong evidence of a clear and consistent empirical regularity: regulator heterogeneity is a tangible empirical phenomenon that needs to be considered in the design of regulatory mechanisms. Second, beyond the extant literature, our study investigates and identifies several sources of regulator heterogeneity. Regulatory outcomes are seen to depend on the amount and type of regulatory training investigators receive and the frequency with which they participate in inspections, as well as unobserved investigator-specific factors. These findings provide strong evidence that regulatory outcomes can and do depend on investigator knowledge. Thus, at one level, we empirically confirm the oft-assumed information asymmetry gap. This information asymmetry is, however, not uniform. Indeed, we find strong evidence of heterogeneity across individual inspectors.

Importantly, this heterogeneity is seen to depend systematically on factors such as inspector training and experience. This latter finding points toward an endogenous dimension of the information asymmetry gap; thereby revealing a new tool with which economists may better design and regulators may more adroitly implement efficient regulatory policies. Third, although not an empirical outcome of our analysis, we use our findings to discuss the ways in which regulator capability, bounded rationality, and incentives might interact to affect the design of regulatory regimes. While highly prospective, our discussion offers several new considerations regarding the design of regulatory institutions and maps a new trajectory for the study of the economics of regulations and regulatory institutions.

2. BACKGROUND

2.1. Overcoming Information Asymmetries: From Theory to Practice

Early models of the regulatory process embodied the imposition of an exogenously given set of regulatory constraints imposed by total or consumer surplus maximizing regulators. [7] These models have now given way to a more sophisticated perspective that allows regulated firms to possess knowledge of its production processes (e.g., cost or quality) to which regulators are not, without expenditure of resources, privy. The incorporation of asymmetric information into economic models of regulation gave rise to the perspective of a regulatory game. In this game, firms, because of their superior knowledge, have discretion in the extent to which they comply with a particular regulatory standard or not. In the regulatory game, complying with regulations is assumed to be costly and firms, knowing they are endowed with superior information relative to regulators,[8] act to maximize profits given the imposition of a particular

[7] See, e.g., Averch and Johnson (1962)

[8] The nature of the information asymmetry may be regarding production costs, quality, safety, or, as we adopt in Section XX, whether the firm has chosen to comply with a regulatory standard.

regulatory regime. The job of regulators, who are fully aware that they are under-endowed with information, then is to design a regulatory mechanism to elicit (total or consumer) surplus maximizing behavior by regulated firms. If first-best mechanisms can be found then no regulatory monitoring is necessary and there is no unanticipated discretionary behavior on the part of firms.[9]

In the absence of a first best incentive "contract", regulatory monitoring offers an alternative mechanism to mitigate firm discretion. If monitoring is costless, detection of violations complete and regulators unbounded on the extent of fines they may impose, then any initial asymmetries enjoyed by the firm can be overcome and non-compliance with regulation ended. In reality, however, inspections are costly, detection is not perfect, and fines are bounded. In the face of these realities, regulators face the challenge of overcoming their information asymmetries by deciding whether or not to inspect a given facility and how much to invest in "detection technology." It is these issues that will be the focus of our empirical model of FDA regulation.

While most modern models that focus on firm discretion assume that the regulator is the principal a different strand of literature focuses on the regulators as agents and thereby models the potential for regulator discretion. As first demonstrated by Stigler (1971) and subsequently generalized by Peltzman (1976), regulators may use discretion to favor one or another interest group that may be affected by the regulator's decisions. Following the seminal insights of Stigler and Peltzman, considerable attention has been given to both theoretical and empirical modeling

[9] For a comprehensive survey, see Armstrong and Sappington (forthcoming)

of a general theory of capture, in which the behavior of regulators may be understood as an equilibrium consequence of competition among various interest groups.[10]

The general theory of regulator capture, while advancing considerably our understanding of regulator behavior treats the regulator as a single, monolithic, unboundedly rational agent. On its face, this simplifying assumption is in sharp contrast to empirical realities. Federal well as many state regulatory agencies are, in fact, typically comprised of hundreds if not thousands of employees who participate in regulatory oversight.

Once we relax the historical assumption of and move to this finer degree of granularity, our understanding of regulatory discretion must be reconsidered in two important ways. First, human regulators are not identical and thus we should be alert not only to the possibility of considerable variation in the behavior of individual regulators but also on the regulatory implications of this variation.[11] Indeed, Feinstein's (1989, 1990) examinations of regulators at the NRC and at OSHA found significant variations in the behavior of individual regulators responsible for the inspection of nuclear and manufacturing facilities, respectively.[12] Second, as we move away from attempts to understand the behavior of higher level bureaucrats to understanding the impact of the army of individual regulators, the historical focus on a political economy explanation of regulator behavior must confront organizational and behavioral issues

[10] See, e.g., Becker (1983), Weingast and Moran (1983), Laffont and Tirole (1993) and Beard, Kaserman and Mayo (2003). For an application to the Food and Drug Administration (FDA), see Olson (1995).

[11] For a positive theory of regulation along these lines, see Evans and Garber (1988).

[12] The observation of widely disparate behavior among individual regulators evokes the advances of Kalt and Zupan (1984, 1990) who brought the role of discretion to political actors. They note that in contrast to models of pure political capture, politicians often reveal their personal ideologies in their legislative capacities. These ideological preferences simply could not be exercised absent sufficient slack in the system to allow them this discretionary behavior.

that are present in large organizations.[13] For example, the behavior of a particular mid-level inspector is less obviously influenced by the sorts of interest group considerations than higher-level bureaucrats. Alternatively, regulatory capture of a foot soldier may be defeated under some circumstance by an agency by randomizing investigator selection for any particular inspection. Such organizational strategies are not considered in the extant literature on regulatory capture and introduce many new concerns that we will revisit in our discussion section. In this new light, considerations such as investigator capability, bounded rationality, and self-interest in the context of organizational incentives, processes, and structures become relevant factors in understanding the regulatory domain.

2.2. FDA Regulation

The mission of the Food and Drug Administration (FDA) is three-pronged: (1) to promote and protect the public health by helping safe and effective products reach the market in a timely way; (2) to monitor products for continued safety after they are in use; and (3) to help the public get the accurate, science-based information needed to improve health. At the heart of all FDA regulatory activity are judgments about whether a given product's benefits to users outweigh its risks. The FDA is made up of six centers with separate responsibilities related to food, drug product or medical device safety for both humans and animals, and one office for regulatory affairs.[14]

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[13] As noted by Olson (1995) "Given the complex hierarchy within bureaucratic agencies, many of the career bureaucrats working in the agency are less responsive to pressures from Congress." See, more generally, Moe (1985).

[14] The six centers are (1) Center for Food Safety and Applied Nutrition; (2) Center for Drug Evaluation and Research (CDER); (3) Center for Biologics Evaluation and Research (CBER); (4) Center for Veterinary Medicine (CVM); (5) Center for Devices are Radiological Health (CDRH); and (6) National Center for Toxicological Research. The Office of Regulatory Affairs (ORA) handles the general regulatory affairs of each center.

We examine the regulation of pharmaceutical drug products, which fall under the Center of Drug Evaluation Research (CDER). CDER ensures that medicinal products used for the treatment and prevention of disease are proven safe and effective before they are used by patients. Among other duties, CDER regulates not only the introduction of new drug products, but also their manufacture and distribution. Our focus in this paper is on the regulation of drug product manufacturing as opposed to the approval of new molecules.

The FDA is statutorily required to inspect all registered drug manufacturing facilities at least once every two years via the Federal Food, Drug and Cosmetic Act of 1937. Federal drug laws mandate that pharmaceutical firms manufacturing drug product for human administration operate under standards termed Current Good Manufacturing Practice (referred to as cGMP), which requires all drug products (i.e., finished dosage forms) and drug components (i.e., bulk and active pharmaceutical ingredients (APIs)) to be in conformance with guidelines related to safety and that they have "the identity, strength, quality and purity that they purport or are represented to possess" (Mathieu, 2000).

Since establishing cGMP requirements in 1962, the FDA has taken a "general regulatory approach," whereby only broad guidelines are given to pharmaceutical firms related to cGMP standards. Supplementary information typically referred to as "guidances" provide additional specificity only when necessary and usually around requirements related to manufacturing, quality control and documentation or updates for process and methods validation. The FDA centers cGMP requirements around the fundamental concept of quality assurance, such that: (1) quality, safety and effectiveness must be designed and built into drug product; (2) quality cannot be inspected or tested into finished product; and (3) each manufacturing process step must be controlled to maximize the likelihood that finished the product is safe and efficacious. (Mathieu,

2000). cGMP requirements seek to ensure the quality of drugs by setting minimum standards for all manufacturing facilities in ten separate areas (Mathieu, 2000).[15] These requirements apply both to approved drug products and experimental drug products operating under New Drug Application (NDA) status.

The FDA has an enforcement program related to manufacturing facility cGMP compliance. The Office of Regulatory Affairs (ORA) within the FDA sets the overall enforcement budget and is the organizational unit in which most investigators are housed. The 27 FDA district offices for domestic inspections located throughout the U.S. have enforcement responsibility for domestic manufacturing facilities, while ORA and CDER share enforcement responsibility for international manufacturing facilities. Typically, one or several FDA investigators take part in manufacturing facility inspections—depending upon the type of manufacturing facility and types of compounds manufactured—along the ten separate areas indicated above. FDA investigators are generally given wide latitude in cGMP-related inspections.

Any cGMP violations are communicated to manufacturing facilities after an inspection. Minor cGMP violations generally fall under the responsibility of the FDA district office that conducted the original inspection, with formal outcomes ranging from no action indicated (NAIs), voluntary action indicated (VAIs) and official action indicated (OAIs) in increasing severity—the last of which requires some response on the part of the manufacturing facility. A period of time in which to address and correct these cGMP violations is provided to these manufacturing facilities before additional FDA actions are taken. If left unaddressed, FDA can

[15] These areas are (1) organization and personnel; (2) building and facilities; (3) equipment; (4) control of components and drug product containers and closures; (5) product and process controls; (6) packaging and labeling controls; (7) holding and distribution; (8) laboratory controls; (9) records and reports; and (10) returned and salvaged drug products.

escalate the severity of these violations. Major violations generally fall under the responsibility of CDER and ORA who jointly decide upon a course of appropriate regulatory action. Major cGMP violation outcomes can result in legal sanctions, including fines, product seizures, injunctions and prosecutions. The FDA will propose such actions to the U.S. Justice Department and file cases with the appropriate U.S. District Court, if and when necessary.

3. METHDOLOGY AND EMPIRICAL ANALYSIS

3.1. Empirical Setting

Given the complexity of the various manufacturing processes and products being inspected, the standard information asymmetry gap is quite likely in the regulation of drug manufacturing processes. In the absence of perfect and costless monitoring, firms may be expected to earn rents on these asymmetries through shirking of costly implementation of sound manufacturing processes. Perhaps of greater concern than wealth transfers, unsound manufacturing processes may create higher costs to the consuming public. In light of these costs, and under federal mandate, the FDA has implemented a significant inspection effort. If effective, the outcome of this inspection process can be seen as closing the information asymmetry gap between the regulator (here the FDA) and the firms it regulates. Accordingly, in this section, we explore the empirical determinants of the outcome of the inspection process. Specifically, we explore whether characteristics of the individual regulators, including their training and experience, affect regulatory outcomes (measured by detected OAIs) after controlling for technology, product type and industry.

3.2. Data

Data for this paper were obtained directly from the FDA. Our main source of data is from the FDA Field Accomplishments and Compliance Tracking System (FACTS) database, which

provides information on completed inspections by FDA of manufacturing facilities selling pharmaceutical drug product within the United States. Facility inspections are limited to those under the responsibility of the Center for Drug Evaluation Research (CDER), which oversees both the evaluation of new drugs before they are approved to be sold and the safety and efficacy of drugs that have been approved thereafter.[16] CDER regulates both prescription and over-the-counter drugs as well as brand name and generic drugs in an effort ensure that the health benefits outweigh the known risks.

We assembled data on all inspections conducted under CDER responsibilities from 1990 to 2003. The FACTS database includes detailed information on investigations including facility identification, investigator identification, length of inspections, and the FDA district responsible for the inspection, as well as the outcomes of those inspections. We also collected a variety of facility-specific information from the FDA registration database that gave us access to the number and type of compounds (or products) produced at each facility in each year and merged these data with information from FACTS. Working with the FDA, we assembled a training database of all CDER investigators employed by FDA before and during our study window and which were engaged in pharmaceutical facility inspections over the relevant time period. This training database tracks all employer-sponsored training, and includes the total training days in which inspectors have taken part prior to a given manufacturing facility inspection and whether the inspectors have taken particular drug courses deemed critical by FDA (discussed below).

We also created a corporate ownership database for each manufacturing facility using the FDA registration database and public merger and acquisition announcements, correcting for any identifiable mismatches within the registration history records of these facilities. The registration

[16] Thus, we did not collect data for other FDA centers that evaluate biologics, veterinary products, and medical devices.

history database records the particular pharmaceutical firm or firms who own each manufacturing facility in any given year. Delineating an ownership structure is critical to our analysis, given the number of mergers and acquisitions that have resulted in the pharmaceutical industry over the time period of our study.

3.3. Variables

Using the FACTS, investigator training, and registration databases we construct several variables. These variables encompass technology, industry, manufacturing facility, and firm-level factors, as well as inspection outcomes and investigator-level factors, related to cGMP inspections. We describe below the definition and construction of each variable.

1.1.1. Inspection Outcomes

Our initial analysis examines cGMP manufacturing facility inspection outcomes, where outcomes range are no action indicated (NAIs), voluntary action indicated (VAIs), and ordered action indicated (OAIs). NAIs indicate either no objectionable conditions and practices are found during the inspection or the objectionable conditions found do not justify further regulatory action. NAIs thus require no action on the part of the manufacturing facility (as the name suggests) and signify that the manufacturing facility is in compliance with cGMP regulations. VAIs indicate objectionable conditions are found, but the FDA is not prepared to take or recommend any administrative or regulatory action as their significance is not such to demand a corrective response. The FDA may advise the manufacturing facility following the inspection of findings that should be corrected, but any corrective action is voluntarily. OAIs indicate objectionable conditions are found, and FDA will recommend regulatory and/or administrative sanctions. OAI outcomes most commonly include manufacturing facilities conducting voluntary

recalls, but actions and/or sanctions can be more severe.[17] Given the qualitative difference between an OAI outcome and either NAI or VAI, we choose as our dependent variable a binary measure that takes the value of one if the manufacturing facility inspection results in an OAI, and zero otherwise.

1.1.2. Independent Variables – Technology, Industry, Facility and Firm

Technology Variables – Our technology variables capture characteristics of production technologies of the drug products (i.e., compounds) produced in each manufacturing facility that might influence cGMP regulatory outcomes. *Prescription* is a dummy variable that equals one if the manufacturing facility produces drug products sold under prescription, and is zero otherwise. The null category indicates the manufacturing facility only produces over-the-counter (OTC) drug products. Prescription drug products are deemed higher potential for public health consequences should there be a drug defect from the perspective of the FDA (FDA, 2004) and, therefore, may generate a more rigorous inspection and a higher likelihood of an OAI.

We control for whether the drug products manufactured in each facility have any extended or delayed release profile, which represent more complex products and a potentially greater likelihood of an OAI, using two variables. The development of a desired release profile is dependent upon many different technological parameters, such as drug solubility, half life, protein binding, site of absorption, etc. *Prompt Release* is a dummy variable that equals one if any of the drug products manufactured in the facility have a prompt release profile, and is zero otherwise. *Extended/Delayed Release* equals if any of the drug products manufactured in the

[17] Recommended OAI actions include banning; certification withholding or revocation; citation; civil penalty; disqualification; emergency permit disapproved; injunction; license denial, suspension, or revocation; prosecution; provisional listing; recall (FDA initiated recalls); recommendation for denial of pending application (NDA, NADA, ANDA, PMA, etc.); recommendation for revocation of approved application (NDA, NADA, ANDA, PMA, etc.); remove from shippers list; seizure/detention; use prohibited; warning letter; demand for destruction.

facility have an extended or delayed release profile, and is zero otherwise. Our omitted category is other select technologies as classified by the FDA.

Dosage forms vary in manufacturing complexity and hence can impact the likelihood of an OAI. Accordingly, we control for the dosage form of the drug products manufactured in each facility, using nine variables. *Gel Cap* and *Soft Gel Cap* are dummy variables that equal one, respectively, if any of the drug products manufactured in the facility are in gel cap or soft gel cap form, and are zero otherwise. *Ointment*, *Liquid*, *Powder*, *Gas* and *Aerosol* are dummy variables that equal one, respectively, if any of the drug products manufactured in the facility are in ointment, liquid, powder, gas or aerosol dosage form, and are zero otherwise. *Parenteral and Large Volume Parenteral* equal one, respectively, if any of the drug products manufactured in the facility are in parenteral (e.g., intravenous or intramuscular injection) or large volume parenteral form, and are zero otherwise. *Bulk* is a dummy variable that equals one if any of the drug products manufactured in the facility are in bulk dosage form, and is zero otherwise. *Sterile* is a dummy variable that equals one if any of the drug products manufactured in the facility require sterility, and is zero otherwise. Finally, *Suppository* is a dummy variable that equals one if any of the drug products manufactured in the facility are in suppository form, and is zero otherwise. Similar to prescription drug products, *Gas* and *Sterile* are deemed by FDA as drug products with higher potential for public health consequences should there be a drug defect (FDA, 2004).

Industry Variables – Our industry-level variables control for the industry classifications for which drug products are manufactured, which might be associated with cGMP regulatory outcomes. *Vitamin* (Industry Code 54) is a dummy variable that equals one if any of the drug

products manufactured in the facility are classified as a vitamin, mineral, protein or unconventional dietary specialty product, and zero otherwise. *Necessity* (Industry Code 55) is a dummy variable that equals one if any of the drug products manufactured in the facility includes chemicals, flavors, excipients, etc., used in the manufacturing process, and zero otherwise. *Antibiotic* (Industry Code 56) is a dummy variable that equals one if any of the drug products manufactured in the facility are produced by or derived from certain fungi, bacterial, and other organisms that can destroy or inhibit the growth of other microorganisms (e.g., penicillin or streptomycin) and zero otherwise. Finally, *Biologic* (Industry Code 57) is a dummy variable that equals one if any of the drug products manufactured in the facility is synthesized from living organisms or their products and used medically as a diagnostic, preventive, or therapeutic agent, and zero otherwise. Our omitted category is Human Drug (Industry Codes 60-66).

Facility and Firm Variables – Our manufacturing facility-level variables include factors pertaining to characteristics of the manufacturing facility which likely influence cGMP regulatory outcomes. These variables help to control for the inherent complexity that exists in a particular manufacturing facility. *Therapeutic Classes* represents a count of the number of therapeutic classes manufactured in the manufacturing facility in a facility-year. *Products* represent a count of the number of products manufactured in the manufacturing facility in a facility-year. *Product Dosage Forms* represent a count of the number of product dosage forms in the manufacturing facility in a facility-year. Dosage forms are the ways drug products are identified in their physical form, and include such factors as appearance, form, product administration, dosage frequency and handling. *Product DF Routes* represent a count of the number of different routes that the drug products manufactured can take in the manufacturing facility in a facility-year. *Sponsor Applications* represent a count of the number of sponsor

applications in the manufacturing facility in a facility-year. Finally, *Operating Firms* represent a count of the number of firms that operate within the manufacturing facility in a facility-year. This variable represents the number of customers for which the manufacturing facility provides drug product.

Our firm variables capture firm characteristics that might influence cGMP regulatory outcomes. For instance, we identify ownership changes of the manufacturing facility. Ownership Δ at t=0, 1, 2, and 3 are dummy variables indicating zero, one, two, and three years since an ownership change occurred at a focal manufacturing facility.

1.1.3. Independent Variables – FDA Inspection Decision and FDA Investigator

Inspection Decision Variables – We include a variety of characteristics associated with the inspection activity and process that may affect the likelihood of a violation being detected. For example, the length of time between inspections may be indicative of FDA's expectation of an OAI, which may influence the likelihood of such an outcome. Accordingly, we include a measure of the natural logarithm the days since the manufacturing facility was last inspected [*LN(Days Between Inspection*)].

We also utilize two variables to capture the reason for cGMP inspection. *Customer Complaint* and *Compliance* are dummy variables that equal one if the reason for inspection was due to a customer complaint of an existing manufacturing facility or due to the establishment of a new manufacturing process or change in an existing manufacturing process in a facility, respectively, and are zero otherwise. The omitted category is *Surveillance*, which represents the "regular" FDA surveillance inspection of an existing manufacturing facility that is congressionally mandated every two years. We anticipate that OAI outcomes are more likely in

response to consumer complaints and compliance inspections than regular surveillance inspections.

Domestic Inspection is dichotomous variable that equals one if the inspection is conducted in a domestic manufacturing facility and zero if the inspection is conducted in a foreign manufacturing facility. Foreign inspections are typically shared with ORA and CDER personnel and thus may be systematically evaluated differently than domestic facilities. Finally, *Last Inspection Outcome* is a dichotomous variable that equals one if the last inspection in the manufacturing facility resulted in an OAI, and zero otherwise.

Investigator Variables – Our investigator variables include factors related to each individual investigator, such as training and experience, which we argue might influence the probability of detecting noncompliance. We utilize five dummy variables to capture whether the investigator has taken any of the five "main" drug courses (DC) as deemed important by the FDA prior to the cGMP inspection. *DC_1 (Basic)* equals one if the investigator has taken the "Basic Drug School" course, and is zero otherwise. *DC_2 (Advanced)* equals one if the investigator has taken the "Advanced Drug School" course, and is zero otherwise. *DC_3 (PAI)* equals one if the investigator has taken the "Pre-Approval Inspections" course, and is zero otherwise. *DC_4 (API)* equals one if the investigator has taken the "Active Pharmaceutical Ingredient Manufacturing" course, and is zero otherwise. Finally, *DC_5 (Sterilization)* equals one if the investigator has taken the "Industrial Sterilization" course, and is zero otherwise. *Total Courses* represents a count of the total number of training courses that the investigator has taken prior to the inspection at the particular manufacturing facility, other than the five main drug courses discussed above.

As FDA investigators become more experienced in conducting inspections, they may develop storehouses of knowledge that could affect manufacturing facility inspection outcomes. This investigational expertise may lead to advantages in detecting compliant versus non-compliant manufacturing facilities with respect to cGMPs. *Current Year Inspections* represents a count of the logged number of inspections conducting by the focal investigator in the 12 months prior to the focal inspection. *Prior Year Inspections* represents a count of the logged number of inspections conducting by the focal investigator in the 12 to 24 months prior to the focal inspection. We construct these variables to examine potential "forgetting," or loss of detection capabilities over time, on the part of investigators.

1.1.4. Independent Variables – Controls

We control for unmeasured variation that might exist from differences in FDA District Offices and FDA inspectors, respectively, using fixed effects. There are 27 unique FDA district offices (including headquarters) located domestically and abroad, and hundreds of FDA investigators who inspect at least one manufacturing facility over the time period of our study. We also control for unmeasured variation that might exist from differences in manufacturing facilities (e.g., the matching of investigators to facilities for inspection) using fixed effects.

3.4. Summary Statistics

Our unit of observation is the "pharmaceutical manufacturing facility inspection," defined according to whether or not a manufacturing facility was inspected, and if inspected, the outcome of that inspection (i.e., compliance (NAI, VAI) or non-compliance (OAI)). The resulting data sample represents 14,162 unique cGMP inspections by 783 investigators of 3,753 manufacturing facilities in both the U.S. and abroad from 1990 to 2003.

Table 1 summarizes the dependent and independent variables, while Table 2 provides correlation statistics for the dependent and independent variables. The technology variables represent non-exclusive categories. For example, a given drug product inspected within a manufacturing facility might be for prescription (versus over-the-counter), in a prompt release profile, and in soft gel cap dosage form. Almost 60 percent of the drug products inspected in the dataset require a prescription. The omitted category represents not classified; bacterial antigens, bacterial vaccines and modified bacterial vaccines; and blood serum and immune serum drug products. The four industry variables (*Vitamin*, *Necessity*, *Antibiotic* and *Biologic*) are exclusive and represent roughly 55 percent of the sample, with the omitted category as Human Drugs.

Manufacturing facilities in the sample, on average, produce roughly 24 different drug products in 23 different dosage forms and more than 12 DF Routes in 13 different therapeutic classes. There are more than eight sponsor applications per manufacturing facility. All of the manufacturing facility variables show significant heterogeneity. Our firm-level variables indicate moderate ownership changes among manufacturing facilities in the years that we examine (i.e., $t = 0, 1, 2,$ or 3).

The inspection decision variables indicate the FDA tends to inspect manufacturing facilities every 500 days, on average, but this variable demonstrates significant heterogeneity. In particular, some manufacturing facilities are inspected relatively infrequently, with the maximum at more than 5000 days. Domestic manufacturing facilities receive the majority of inspections, while more than half of the inspections are re-inspections due to a prior cGMP inspection resulting in an OAI. Investigators on average take just under two courses other than the five main drug courses, but this variable also shows significant heterogeneity. The five main drug courses

are non-exclusive in that some investigators have taken all of them while others have taken none. Investigators inspect roughly six manufacturing facilities per year on average.

3.5. Econometric Method and Results

Table 3 presents the results of our FDA manufacturing facility inspection analysis. Given the categorical nature of the dependent variables, a Logit or Probit model is the appropriate choice for an estimation technique. We utilize the Probit model, with its underlying assumption of a normally distributed error term, using maximum likelihood estimation. The estimation methodology is drawn from Maddala (1983). Results from a Logit model are virtually identical.

Successive models in Table 3 incrementally add the variables of interest. Model 1 of Table 3 includes the technology and industry variables; the manufacturing facility and pharmaceutical firm variables; and the FDA inspection decision variables. Model 2 adds FDA investigator fixed effects to Model 1. Due to econometric software limitations we can include only a sub-sample of FDA investigator fixed-effect variables that represent the most active in terms of the number of cGMP inspections conducted over the time period of our sample. Model 3 adds the FDA investigator training and experience variables to Model 2. As a robustness check, Model 4 adds manufacturing facility fixed-effects to Model 3 in an attempt to control for any potential matching of FDA investigator to inspected manufacturing facility. Again due to software limitations we include only a sub-sample of manufacturing facilities that represent the most active in terms of the number of cGMP inspections over the time period of our sample.[18]

We adjust standard errors for robustness and within-firm clustering (by manufacturing facility). All of the models easily reject likelihood ratio null hypothesis tests for the inclusion of

[18] Our selection criteria for FDA investigators were those who completed at least 35 unique manufacturing facility inspections. This resulted in 309 unique FDA investigators variables. Our selection criteria for manufacturing facilities were those who received at least 35 unique manufacturing facility inspections. This resulted in 337 unique manufacturing facilities. We confirm that our results are robust to different thresholds.

fixed effects and the control and independent variables, at least at the 0.001 level. As each of the models improves the fit on its predecessor, we focus our attention on Models 3 (without manufacturing facility fixed effects) and 4 (with manufacturing facility fixed effects). We include the technology, industry, facility and firm-level independent variables in the econometric analysis, but we report only those variables germane to our study—namely the FDA inspection decision and FDA investigator training and experience variables.

In terms of the FDA inspection decision, Model 3 indicates that the probability of noncompliance increases as the number of days between cGMP inspections increases ($p < 0.05$). Manufacturing facilities inspected for reasons of compliance are much more likely to be found noncompliant than those facilities under general surveillance ($p < 0.01$), a finding that suggests new or modified manufacturing processes face an uphill battle by pharmaceutical firms in terms of gaining compliance. Domestic manufacturing facilities are more likely to be found noncompliant than foreign manufacturing facilities ($p < 0.1$). Finally, manufacturing facilities whose last inspection resulted in an OAI outcome are much more likely to be found noncompliant in the most current inspection. All of the variables except *LN(Days Between Inspections)* maintain their statistical significance when manufacturing facility fixed-effects are added and as indicated in Model 4.

Model 3 also indicates that several of the FDA investigator training and experience variables have statistically significant effects on the probability of noncompliance. Investigators who have completed either *Drug Course 3 (Pre-Approval Inspections)* and *Drug Course 4 (Active Pharmaceutical Ingredient)* are found to decrease the probability of noncompliance within a manufacturing facility ($p < 0.1$ and $p < 0.01$, respectively). By contrast, investigators who have completed *Drug Course 5 (Sterilization)* increase the probability of a manufacturing

facility being found in violation of cGMPs ($p < 0.05$). We elaborate on these results in the discussion section below. In terms of investigator experience, the Model 3 results also indicate that investigators with more recent experience increase the probability of a manufacturing facility being found noncompliant ($p < 0.05$), while less recent experience has no effect. This result suggests that investigators with more active recent investigations of pharmaceutical firms are better able to detect violations.

Our results from Model 4 continue to support our key finding regarding the role of training and experience of FDA inspectors even after accounting for manufacturing facility fixed effects and any potential matching that occurs between particular FDA investigators and particular manufacturing facility. Two differences are, however, worth highlighting. First, while the coefficient on *Current Year Inspections* remains positive and statistically significant, the coefficient on *Previous Year Inspections* remains negative, but becomes statistically significant. Second, in Model 4, we find that the coefficient on Domestic Inspection, which is positive in all the models, becomes highly significant. This result indicates that detected violations are significantly more likely in domestic plants than in foreign manufacturing facilties. While the possibility of superior compliance by foreign facilities cannot logically be ruled out, this result suggests that the information asymmetry gap is accentuated for U.S.-based regulators that inspect foreign facilities.

4. DISCUSSION

Our analysis identifies three important empirical regularities. First and foremost, we find that regulatory outcomes vary by FDA investigators. Even after controlling for a wide array of technological, industry, manufacturing facility, firm, and FDA inspection decision factors that might be correlated with regulatory outcomes, we find that investigator-specific effects can

dramatically affect regulatory outcomes. For instance, 18 percent of investigators identified in our analysis have statistically significant ($p < 0.5$) impacts on the probability of an OAI outcome compared to the mean investigator. To get an economic sense of the impact that FDA regulators have, we estimate the increase in the probability of an OAI outcome by regulator and display a histogram of the distribution of probabilities in Figure 1. On average for those investigators that yield statistically significant fixed effects, we find that an inspection by this group significantly increases the probability of an OAI outcome by 17 percentage points. The investigator with the largest effect compared to the mean investigator increases the probability of an OAI outcome by fully 44 percentage points. This analysis establishes an empirical regulatory within the FDA that regulators are heterogeneous--a regularity that echoes Feinstein's (1989, 1990) earlier analyses.

Second, we find that the probability of an OAI outcome varies with FDA investigator training. Several FDA sponsored courses–which are not initially required for investigators when they began their careers—have statistically significant effects on the probability of an OAI outcome. For instance, *Drug Course 4 (Active Pharmaceutical Ingredient)* decreases the probability of an OAI outcome ($p< 0.01$) by roughly 33 percentage points, while and *Drug Course 3 (Pre-Approval Inspections)* decreases the probability of an OAI outcome ($p< 0.10$) by roughly 22 percentage points. Conversely, *Drug Course 5 (Sterilization)* increases the probability of an OAI outcome ($p< 0.05$) by roughly 26 percentage points. Given the emphasis that the FDA places in sterility in terms of its public health and safety consequences this last finding is not surprising, but nevertheless has important implications for pharmaceutical firms and manufacturing facilities operating within the industry. These findings also indicate that regulatory outcomes depend on the level of knowledge acquired by individual inspectors. Our

analysis shows that heterogeneously trained inspectors heterogeneous are heterogeneous in their regulatory outcomes.

Third, we find that the probability of an OAI outcome varies with investigator experience. Our panel data set of regulatory actions is unparalleled in its time span and breadth, which allows us to comprehensively evaluate the effect of investigational experience on regulatory outcomes. The more inspections conducted by an investigator in the 12 months prior to a focal inspection the greater the probability the investigator will issue an OAI. To place an economic interpretation on this finding we estimate the difference in the probability of an OAI outcome for the mean investigator with 5 inspections (5^{th} percentile of investigators) during the prior 12 months compared to an investigator with 10 inspections (58^{th} percentile of investigators) and 15 inspections (75^{th} percentile of investigators). An investigator with the 10 and 15 inspections in the prior year is 20 and 24 percentage points more likely, respectively, to issue an OAI than one with the lower experience. Interestingly, the impact of learning on the probability of OAI appears to be short-term. Our results indicate that while experience gained 12 months prior to a focal inspection increases the probability of an OAI, experience gained 12 to 24 months prior to a focal inspection does not in general have a statistically significant impact. Put differently, old experience offers limited experience, perhaps because investigator experience has some component of "forgetting" associated with it.

These empirical regularities generate several new questions for the study of optimal regulatory mechanisms. An immediate question is why might investigators differ in the probability of regulatory evaluations? Perhaps the first place the extant literature would turn to answer this question is the literature on regulatory capture. Heterogeneity in investigator inspectional outcomes may arise from heterogeneity in incentives. Because all investigators have

nearly the same financial and career incentives within the FDA, the primary source of heterogeneity in incentives derives from regulatory capture at the individual investigator level. For instance, many regulators eventually leave the FDA to take positions in the industry they regulated. Hoping to gain favor with particular pharmaceutical firms, regulatory capture would suggest that individual investigators may be less likely to issue OAIs. Yet, if this were true we would not expect to find that either training or experience to *increase* the probability of a manufacturing facility receiving an OAI. On first blush it would seem unlikely that regulatory capture is a viable explanation for all of the investigator heterogeneity observed in our data.

An alternative and common sense response is that FDA investigators differ in their abilities and in the knowledge that they possess at any particular point in time. Scholars from organizational economics and transaction cost economics, in particular, will recognize these cognitive characteristics as being consistent with a model of behavior based on bounded rationality. Admitting an assumption of bounded rationality would imply that training, experience, and, more generally, the way in which the investigator force is organized and managed could have important implications for the ways in which regulations are enforced. The empirically robust findings from our estimations that training and experience are significant drivers in the explanation of heterogeneous regulatory outcomes suggests that more focus on such comparative institutional considerations (either in lieu of, or as a complement, to standard principal agent asymmetric information models) may yield considerable fruit.

Understanding the sources of investigator heterogeneity is interesting for its own sake but does not address the more important question: Does investigator heterogeneity matter for the design of optimal regulations? Unfortunately, only future research can unequivocally address this question. We posit, nonetheless, that the answer is likely to be a resounding “yes”. For instance,

models that assume complete contracts, even those sophisticated enough to account for information asymmetries, are, in an environment laden with demonstrably boundedly rational regulators, problematic. Williamson (1975; 1985; 1996) chronicles these issues in his transaction cost economics approach to the theory of the firm and may equally apply in the regulatory setting with many foot-soldier regulators.

Another potential issue arose when we familiarized ourselves the FDA and the firms it regulates. To avoid regulatory capture of individual investigators, the FDA attempts to randomly match (or at least vary) investigators with the facilities that they inspect. Yet if randomly matched investigators vary in ability and knowledge then their regulatory decisions will appear to firms as inconsistent. This inconsistency may create an incentive for firms to be risk averse with respect to welfare enhancing innovation in manufacturing. The potential risk aversion may be all the greater given that compliance inspections, which are required for substantial changes to the manufacturing process, are more likely to lead to an OAI outcome, which can impose substantial cost on the manufacturing facility. That is, altering their production process even though doing so could reduce costs and improve various quality metrics may not provide sufficient gains to outweigh the risk imposed by receiving an OAI. This risk arises because of the heterogeneity of regulators. If no aspect of production is altered then a facility may be able to argue that the prior investigator found the firm in compliance and then so too should a different investigator. Indeed, this dynamic was described to us by manufacturers as well as FDA investigators alike and recent studies of the pharmaceutical industry suggest that pharmaceutical manufacturing costs could be reduced by $50 billion a year or more if manufacturers were not risk averse (Macher and Nickerson, 2006). No regulatory economics research to date develops a

model to explain the possibility of such risk aversion in a regulatory context nor does any research use investigator heterogeneity to design welfare maximizing regulatory policies.

How might the empirical regularity of investigator heterogeneity impact the future direction of the study of optimal regulatory mechanisms? We envision two complementary broad directions. The first direction is to investigate actual regulatory outcomes by developing models and perspectives that admit the possibility of bounded rationality. As we have seen, human capital development can play a vital role in overcoming information asymmetries and may significantly affect the efficacy of regulatory practice within a given regulatory system.

A second direction is to develop normative models that design of regulatory institutions adopting the assumption of bounded rationality. Specifically, while the principal-agent framework has very constructively pointed toward the challenges created by the presence of information asymmetries for the design of efficient regulatory systems, our analysis suggests that increased focus on ameliorating the human constraints wrought by bounded rationality may prove equally, if not more, effective in the ultimate design of efficient regulatory systems.

5. CONCLUSIONS

Over the past two decades increasing theoretical sophistication has been brought to the modeling of the relationship between regulators and the firms they regulate. A principal vehicle for these advances has been the principal-agent model which most often assumes the presence of an exogenous information asymmetry between the principal (the regulator) and the agents (the firms it regulates). This focus, in turn, has led to a focused effort on the design of optimal regulatory mechanism under the assumption of these given information asymmetries. Our paper seeks to shed light on a different effort, engaged in by real-world regulators, which exert

considerable effort on an ongoing basis to overcoming information asymmetries. To do so, we have investigated the role of investigator experience and training (along with a host of other controls) in affecting regulatory outcomes. Our analysis incorporates a rich panel dataset of over 14 thousand individual regulatory inspections of over 3700 manufacturing facilities around the world during a 14 year period. Our results provide considerable evidence of: (1) the presence of considerable heterogeneity across individual regulators; (2) the significant effects of training; and, (3) the significant effects of regulator experience. These results suggest that future models (both theoretical and empirical) of the regulator-regulated firm interaction are likely to benefit from incorporating regulators' efforts at overcoming information asymmetries.

REFERENCES

Armstrong, Mark and David E.M. Sappington, "Recent Developments in the Theory of Regulation," in Handbook of Industrial Organization, M. Armstrong and R. Porter, Eds., Amsterdam: Elsevier, forthcoming.

Averch, Harvey and Leland L. Johnson, "Behavior of the Firm Under Regulatory Constraint," American Economic Review, Volume 52, December 1962, pp. 1052-69.

Baron, David P., "Design of Regulatory Mechanisms and Institutions," in Handbook of Industrial Organization, Volume II, Richard Schmalensee and Robert Willig, Eds., North Holland, 1989.

Baron, David P. and David Besanko, "Regulation and Information in a Continuing Relationship," RAND Journal of Economics, Volume 53, issue 3, Autumn 1984, pp 413-436.

——— "Monitoring, Moral Hazard, Asymmetric Information, and Risk Sharing in Procurement Contracting," RAND Journal of Economic, Volume 18, issue 4, Winter 1987, pp 509-532.

Beard, T. Randolph, David Kaserman, and John Mayo, "A Graphical Exposition of the Economic Theory of Regulation." Economic Inquiry, Vol. 41, October 2003, pp 592-606.

Becker, Gary, "A Theory of Competition among Pressure Groups for Political Influence," Quarterly Journal of Economics, Volume 98, August 1983, pp. 371-400.

Blank, Larry and John W. Mayo, "Endogeneous Regulatory Constraints and the Emergence of Hybrid Regulation, Georgetown University Working Paper, 2006.

Evans, Lewis and Steven Garber, "Public-Utility Regulators are only Human: A Positive Theory of Rational Constraints." American Economic Review, Vol. 78, June 1988, pp. 444-62.

Feinstein, Jonathan S., "The Safety Regulation of U.S. Nuclear Power Plants: Violations, Inspections, and Abnormal Occurrences," The Journal of Political Economy, Volume 97, February 1989, pp 115-154.

Feinstein, Jonathan S., "Detection Controlled Estimation," Journal of Law and Economics, Vol. 33, No. 1, April 1990, pp. 233-276.

Kalt, Joseph P. and Mark A. Zupan "Capture and Ideology in the Economic Theory of Politics" American Economic Review, Vol. 74, No. 3, June 1984, pp. 279-300.

——— "The Apparent Ideological Behavior of Legislators: Testing for Principal-Agent Slack in Political Institutions," Journal of Law and Economics, Vol. 33, No. 1, April 1990, pp. 103-131.

Khalil, Fahad "Auditing without Commitment," RAND Journal of Economics, Vol. 28, Winter 1997, pp. 629-640.

King, Andrew and Michael Lennox, "Industry Self-Regulation Without Sanctions: The Chemical Industry's Responsible Care Program," Academy of Management Journal. Vol. 43, issue 4, 2000, pp 105-116.

Klimberg, Ronald, Charles Revelle and Jared Cohon "Improving the Effectiveness of FDA Drug Inspection," Operations Research, Vol. 40, September-October 1992, pp. 845-855.

FDA, "Risk-Based Method for Prioritizing CGMP Inspections of Pharmaceutical Manufacturing Sites—A Pilot Risk Ranking Model," FDA Mimeo, 2004, pp. 1-18.

Laffont, Jean-Jacques and D. Martimort, The Theory of Incentives: The Principal-Agent Model. Princeton University Press, Princeton, NJ, 2002.

Laffont, Jean-Jacques and Jean Tirole, "The Politics of Government Decision-making: A Theory of Regulatory Capture," Quarterly Journal of Economics, Vol. 106 no. 4, November 1991, pp. 1089-1127.

Maxwell, John W., Thomas P. Lyon and Steven C. Hackett, "Self-Regulation and Social Welfare: The Political Economy of Corporate Environmentalism," Journal of Law and Economics, Vol. 43, October 2000, pp. 583-618.

Macher, Jeffrey and Jackson Nickerson, "Pharmaceutical Manufacturing Research Project: Final Benchmarking Report," Georgetown University Working Paper, 2006, pp. 1-462.

Maddala, G. S., Limited-Dependent and Qualitative Variables in Econometrics. Cambridge, Cambridge University Press, 1983.

Mathieu, Mark, New Drug Development: A Regulatory Overview Parexel International Publishers, Waltham, MA, 2000.

Moe, Terry "Control and Feedback in Economic Regulation: the Case of the NLRB," American Journal of Political Science, Vol. 79, 1985.

Olson, Mary K. "Regulatory Agency Discretion among Competing Industries: Inside the FDA" Journal of Law, Economics and Organization , Vol. 11, October 1995, pp. 379-405.

_____ "Substitution in Regulatory Agencies: FDA Enforcement Alternatives," Journal of Law, Economics and Organization , Vol. 12, October 1996, pp. 376-407.

Peltzman, Sam, "Toward a More General Theory of Regulation." Journal of Law and Economics, Vol. 19 no. 2, August 1976, pp 211-248.

Stigler, George J., "The Theory of Economic Regulation," Journal of Economics and Management Science, Vol. 2, Spring 1971, pp. 3-21.

Weil, David, "If OSHA is So Bad, Why is Compliance So Good?," The RAND Journal of Economics, Vol. 27, No. 3, Autumn 1996, pp. 618-640.

Weingast, Barry R. and Mark J. Moran "Bureaucratic Discretion or Congressional Control? Regulatory Policymaking by the Federal Trade Commission," Journal of Political Economy, Vol. 91, No. 5, October 1983, pp. 765-800.

Williamson, O. E., Markets and Hierarchies, Analysis and Antitrust Implications: A Study in the Economics of Internal Organization. New York, Free Press, 1975.

Williamson, O. E., The Economic Institutions of Capitalism. New York, The Free Press, 1985.

Williamson, O. E., The Mechanisms of Governance. New York, The Free Press, 1996.

Table 1: Summary Statistics

VARIABLE	MEAN	SD	MIN	MAX	VARIABLE	MEAN	SD	MIN	MAX
TECHNOLOGY VARS					***FIRM VARS***				
Prescription	0.59	0.49	0.00	1.00	*Ownership Δ (t=0)*	0.06	0.23	0.00	1.00
Prompt Release	0.15	0.36	0.00	1.00	*Ownership Δ (t=1)*	0.05	0.22	0.00	1.00
Extended/Delayed Release	0.07	0.25	0.00	1.00	*Ownership Δ (t=2)*	0.05	0.21	0.00	1.00
Gel Cap	0.07	0.26	0.00	1.00	*Ownership Δ (t=3)*	0.04	0.20	0.00	1.00
Soft Gel Cap	0.01	0.11	0.00	1.00					
Ointment	0.11	0.31	0.00	1.00	***INSPECTION DECISION VARS***				
Liquid	0.21	0.41	0.00	1.00	*LN(Days Between Inspections)*	6.24	1.36	0.00	8.54
Powder	0.04	0.21	0.00	1.00	*Customer Complaint*	0.84	0.37	0.00	1.00
Gas	0.02	0.13	0.00	1.00	*Compliance*	0.00	0.03	0.00	1.00
Parenteral	0.11	0.31	0.00	1.00	*Domestic Inspection*	0.96	0.19	0.00	1.00
Large Volume Parenteral	0.01	0.12	0.00	1.00	*Last Inspection Outcome*	0.54	0.50	0.00	1.00
Aerosol	0.02	0.13	0.00	1.00					
Bulk	0.25	0.43	0.00	1.00	***INVESTIGATOR VARS***				
Sterile	0.04	0.20	0.00	1.00	*Total Courses*	1.88	4.37	0.00	33.00
Suppository	0.01	0.09	0.00	1.00	*DC_1 (Basic)*	0.26	0.44	0.00	1.00
					DC_2 (Advanced)	0.06	0.23	0.00	1.00
INDUSTRY VARS									
Vitamin	0.11	0.31	0.00	1.00	*DC_3 (PAI)*	0.03	0.18	0.00	1.00
Necessity	0.10	0.31	0.00	1.00	*DC_4 (API)*	0.06	0.23	0.00	1.00
Antibiotic	0.25	0.43	0.00	1.00	*DC_5 (Sterilization)*	0.11	0.32	0.00	1.00
Biologic	0.10	0.29	0.00	1.00	*Num Insp. (Current Year)*	1.54	0.95	0.00	3.69
					Num Insp. (Prior Year)	1.83	0.95	0.00	3.71
FACILITY VARS									
Therapeutic Classes	12.87	13.56	1.00	60.00					
Products	23.58	30.03	1.00	173.00					
Product Dosage Forms	22.74	30.11	1.00	149.00					
Product D Routes	12.44	26.24	1.00	267.00					
Sponsor Applications	8.40	9.82	1.00	59.00					
Operating Firms	1.11	0.44	1.00	9.00					

Table 2: Correlation Statistics

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)	(21)
(1) Prescription	1.00																				
(2) Prompt Release	0.11	1.00																			
(3) Extended/Delayed Release	0.03	-0.21	1.00																		
(4) Gel Cap	0.09	-0.23	0.20	1.00																	
(5) Soft Gel Cap	0.01	-0.07	-0.04	-0.04	1.00																
(6) Ointment	-0.06	-0.15	-0.08	-0.09	-0.03	1.00															
(7) Liquid	-0.03	-0.24	-0.13	-0.15	-0.05	-0.09	1.00														
(8) Powder	0.03	-0.10	-0.05	-0.06	-0.02	-0.04	-0.06	1.00													
(9) Gas	0.01	-0.02	-0.01	-0.01	0.00	-0.01	-0.01	0.00	1.00												
(10) Parenteral	0.12	-0.29	-0.15	-0.17	-0.05	-0.11	-0.18	-0.07	-0.01	1.00											
(11) Large Volume Parenteral	0.04	-0.08	-0.05	-0.05	-0.02	-0.03	-0.05	-0.02	0.00	0.29	1.00										
(12) Aerosol	0.01	-0.07	-0.04	-0.04	-0.01	-0.03	-0.04	-0.02	0.00	-0.05	-0.02	1.00									
(13) Bulk	0.00	-0.14	-0.08	-0.09	-0.03	-0.05	-0.09	-0.04	-0.01	-0.11	-0.03	-0.03	1.00								
(14) Sterile	0.03	-0.14	-0.07	-0.08	-0.03	0.06	0.43	0.10	-0.01	-0.10	-0.03	-0.02	-0.05	1.00							
(15) Suppository	-0.05	-0.06	-0.03	-0.04	-0.01	-0.02	-0.04	-0.01	0.00	-0.04	-0.01	-0.01	-0.02	-0.02	1.00						
(16) Vitamin	-0.02	-0.08	0.02	0.03	0.08	-0.02	0.01	-0.02	-0.01	0.12	0.10	-0.06	-0.04	-0.05	-0.03	1.00					
(17) Necessity	-0.07	-0.20	-0.11	-0.10	-0.05	0.02	0.24	-0.05	0.01	0.16	0.15	0.02	0.00	0.17	-0.03	0.35	1.00				
(18) Antibiotic	0.11	-0.01	-0.04	-0.01	-0.08	0.04	0.01	0.03	-0.03	0.11	0.00	-0.07	-0.05	0.07	-0.02	0.22	0.20	1.00			
(19) Biologic	-0.09	-0.21	-0.09	-0.10	-0.03	-0.06	-0.05	-0.02	-0.01	0.33	0.05	-0.02	0.04	0.06	-0.02	0.25	0.29	0.20	1.00		
(20) Therapeutic Classes	0.13	0.05	-0.04	0.00	-0.02	-0.09	-0.01	-0.05	-0.02	0.11	0.04	-0.01	-0.05	-0.03	-0.05	0.25	0.37	0.48	0.38	1.00	
(21) Products	0.11	0.06	-0.04	0.01	-0.03	-0.09	-0.02	-0.04	-0.02	0.09	0.08	-0.01	-0.05	-0.04	-0.05	0.22	0.38	0.45	0.32	0.94	1.00
(22) Product Dosage Forms	0.11	0.09	-0.01	0.04	-0.03	-0.08	-0.03	0.00	-0.02	-0.03	-0.01	0.01	-0.03	-0.05	-0.04	0.15	0.27	0.42	0.30	0.89	0.93
(23) Product D Routes	0.04	-0.20	-0.10	-0.09	-0.04	-0.03	-0.01	0.00	-0.01	0.38	0.07	0.01	0.02	0.04	-0.03	0.38	0.43	0.31	0.62	0.63	0.61
(24) Sponsor Applications	0.14	0.20	0.01	0.09	0.00	-0.09	-0.07	-0.03	-0.02	-0.11	-0.05	-0.02	-0.06	-0.10	-0.06	0.00	0.10	0.39	0.07	0.77	0.78
(25) Operating Firms	0.00	-0.01	0.00	-0.02	0.03	-0.01	0.03	0.01	-0.01	-0.02	-0.03	0.00	-0.02	0.00	-0.01	-0.01	0.03	0.02	-0.01	0.01	0.00
(26) Ownership Δ (t=0)	-0.04	0.00	-0.01	0.00	0.00	-0.02	-0.04	0.00	-0.01	0.02	-0.01	0.00	0.00	-0.01	-0.01	-0.02	-0.04	0.01	0.02	0.00	0.01
(27) Ownership Δ (t=1)	-0.02	-0.01	-0.01	-0.01	0.02	-0.01	-0.01	-0.01	-0.01	0.03	0.01	-0.01	-0.02	-0.01	-0.01	0.03	0.04	0.04	0.02	0.04	0.05
(28) Ownership Δ (t=2)	0.00	-0.02	-0.01	-0.01	0.03	-0.01	-0.03	-0.01	-0.01	0.05	0.00	-0.02	-0.01	-0.03	0.00	0.01	0.03	0.01	0.00	0.01	0.00
(29) Ownership Δ (t=3)	-0.02	0.03	0.00	0.06	-0.02	0.04	0.02	-0.02	-0.01	-0.07	-0.03	0.00	-0.04	0.00	0.00	0.06	0.06	-0.08	-0.08	0.06	0.07
(30) LN(Days Between Inspections)	-0.06	-0.06	0.02	-0.03	0.01	0.03	0.00	0.03	0.01	-0.03	0.02	0.03	0.06	0.00	0.01	-0.17	-0.12	-0.28	-0.14	-0.34	-0.33
(31) Compliance	0.00	-0.04	-0.04	-0.06	-0.03	0.03	0.02	-0.01	0.01	0.06	0.03	0.03	0.03	-0.01	0.01	-0.03	0.02	-0.07	0.06	-0.01	0.01
(32) Domestic Inspection	-0.06	0.07	0.05	0.00	0.03	0.06	0.04	0.03	0.01	-0.21	-0.07	0.02	-0.03	0.00	0.02	-0.19	-0.25	-0.25	-0.50	-0.51	-0.43
(33) Last Inspection Outcome	0.04	0.02	-0.04	0.03	-0.05	-0.05	-0.04	-0.01	-0.02	0.13	0.00	-0.01	-0.07	-0.03	-0.04	0.18	0.16	0.20	0.24	0.27	0.21
(34) Total Courses	-0.06	-0.04	-0.03	-0.03	-0.01	-0.02	0.02	-0.03	0.00	0.03	0.02	0.01	-0.01	0.02	0.01	-0.05	0.05	0.01	0.11	0.02	0.02
(35) DC_1 (Basic)	-0.01	0.03	-0.01	-0.03	0.01	-0.02	-0.03	0.01	-0.01	-0.02	0.01	0.00	0.02	-0.04	0.04	0.04	-0.04	0.00	0.01	0.04	0.04
(36) DC_2 (Advanced)	0.01	-0.02	0.00	-0.03	0.01	-0.02	0.00	0.00	-0.01	0.04	0.04	0.00	0.01	0.00	0.00	0.02	0.02	-0.01	0.04	0.02	0.01
(37) DC_3 (PAI)	-0.01	0.00	0.01	-0.01	0.01	0.01	0.01	0.00	0.00	-0.02	-0.01	0.00	0.01	0.02	0.00	0.01	0.00	-0.01	-0.03	-0.02	-0.02
(38) DC_4 (API)	0.03	-0.01	0.02	-0.01	0.00	-0.02	-0.01	-0.01	-0.01	0.03	0.01	-0.01	0.03	-0.01	-0.01	0.00	-0.02	-0.02	0.02	0.02	0.01
(39) DC_5 (Sterilization)	-0.01	0.00	-0.01	-0.01	0.01	0.01	-0.02	-0.01	0.00	0.02	-0.01	0.00	-0.01	0.00	0.00	-0.02	-0.06	0.03	-0.03	0.01	0.01
(40) Current Year Inspections	0.08	0.04	0.01	0.04	0.00	-0.03	-0.03	0.03	-0.03	0.01	0.01	-0.01	0.01	-0.01	0.02	0.07	-0.02	0.06	-0.01	0.05	0.03
(41) Prior Year Inspections	0.02	0.01	-0.02	-0.01	0.01	-0.04	-0.05	0.02	-0.03	0.03	0.03	0.00	0.04	0.00	0.04	-0.01	-0.04	0.01	0.03	0.02	0.02

Table 2: Correlation Statistics (cont.)

	(22)	(23)	(24)	(25)	(26)	(27)	(28)	(29)	(30)	(31)	(32)	(33)	(34)	(35)	(36)	(37)	(38)	(39)	(40)	(41)
(22) Product Dosage Forms	1.00																			
(23) Product D Routes	0.54	1.00																		
(24) Sponsor Applications	0.81	0.22	1.00																	
(25) Operating Firms	0.00	-0.01	0.01	1.00																
(26) Ownership Δ (t=0)	0.01	-0.01	0.02	-0.05	1.00															
(27) Ownership Δ (t=1)	0.05	0.02	0.04	-0.05	-0.04	1.00														
(28) Ownership Δ (t=2)	-0.01	0.03	-0.02	-0.05	-0.05	-0.04	1.00													
(29) Ownership Δ (t=3)	0.09	-0.02	0.15	0.00	-0.03	0.03	-0.02	1.00												
(30) LN(Days Between Inspections)	-0.32	-0.21	-0.29	-0.01	0.00	0.02	0.02	-0.01	1.00											
(31) Compliance	0.00	0.07	-0.04	-0.01	0.03	0.01	-0.03	0.02	0.04	1.00										
(32) Domestic Inspection	-0.43	-0.50	-0.26	0.03	0.03	0.03	-0.04	0.06	0.24	-0.02	1.00									
(33) Last Inspection Outcome	0.20	0.30	0.20	-0.04	-0.04	-0.03	0.00	0.03	-0.22	-0.09	-0.37	1.00								
(34) Total Courses	0.02	0.03	0.01	0.01	0.03	0.02	-0.03	-0.01	-0.04	0.01	-0.03	0.04	1.00							
(35) DC_1 (Basic)	0.04	-0.02	0.04	0.01	0.02	0.02	0.02	-0.02	0.06	-0.06	-0.01	-0.05	-0.12	1.00						
(36) DC_2 (Advanced)	0.00	0.00	-0.02	-0.01	0.01	0.01	0.05	-0.01	0.13	-0.05	-0.01	-0.08	-0.09	0.27	1.00					
(37) DC_3 (PAI)	-0.02	-0.03	-0.03	0.00	-0.01	0.03	0.06	0.00	0.07	0.01	0.04	-0.10	-0.07	0.11	0.01	1.00				
(38) DC_4 (API)	0.01	0.00	-0.01	0.00	0.01	-0.01	0.01	-0.01	0.12	-0.01	-0.01	-0.12	-0.08	0.14	0.35	0.14	1.00			
(39) DC_5 (Sterilization)	0.00	-0.01	0.01	-0.03	-0.01	-0.02	0.02	-0.02	0.02	0.01	0.01	-0.05	-0.12	0.14	0.07	0.01	0.10	1.00		
(40) Current Year Inspections	0.04	0.03	0.04	0.00	-0.02	-0.02	0.03	-0.03	-0.02	-0.05	-0.08	0.04	-0.07	0.11	0.11	0.04	0.16	0.11	1.00	
(41) Prior Year Inspections	0.04	0.03	0.02	0.04	0.02	0.01	0.02	-0.06	0.00	-0.02	-0.04	-0.01	0.01	0.17	0.12	0.07	0.14	0.17	0.64	1.00

Table 3: Inspection Outcome Results

	(1)	(2)	(3)	(4)
Variable	β **(SE)**	β **(SE)**	β **(SE)**	β **(SE)**
TECHNOLOGY VARS	Yes	Yes	Yes	Yes
INDUSTRY VARS	Yes	Yes	Yes	Yes
FACILITY VARS	Yes	Yes	Yes	Yes
FIRM VARS	Yes	Yes	Yes	Yes
FDA INSPECTION DECISION VARS				
LN(Days Between Inspections)	0.071** (0.032)	0.063** (0.031)	0.068** (0.031)	0.047*** (0.018)
Customer Complaint	0.193 (0.418)	0.297 (0.415)	0.305 (0.416)	0.238 (0.356)
Compliance	0.492*** (0.066)	0.445*** (0.071)	0.454*** (0.070)	0.326*** (0.038)
Domestic Inspection	0.182 (0.129)	0.200* (0.118)	0.197* (0.117)	3.790*** (0.754)
Last Inspection Outcome	0.389*** (0.076)	0.334*** (0.071)	0.315*** (0.072)	0.507*** (0.064)
FDA INVESTIGATOR VARS				
Total Courses			0.001 (0.008)	0.001 (0.007)
DC_1 (Basic)			-0.017 (0.098)	-0.023 (0.078)
DC_2 (Advanced)			0.118 (0.144)	0.055 (0.110)
DC_3 (PAI)			-0.255* (0.147)	-0.355*** (0.138)
DC_4 (API)			-0.400*** (0.147)	-0.344*** (0.095)
DC_5 (Sterilization)			0.235** (0.122)	0.225*** (0.084)
Current Year Inspections			0.079** (0.039)	0.081*** (0.028)
Prior Year Inspections			-0.063 (0.043)	-0.100*** (0.031)
Constant	-1.563*** (0.280)	-1.609** (0.752)	-1.825*** (0.791)	-3.403*** (1.219)
FDA District Office Fixed Effects	Yes	Yes	Yes	Yes
FDA Investigator Fixed Effects	No	Yes	Yes	Yes
Manufacturing Facility Fixed Effects	No	No	No	Yes
Number of observations	15350	12613	12613	10002
Wald (χ^2)	381.51***	8621.20***	10039.39***	31725.30***
Pseudo-R^2	0.093	0.161	0.165	0.263
Log likelihood	-8125.46	-6324.63	-6294.03	-4532.05

*** p<0.01 ** p<0.05 * p<0.10.
Standard errors are robust and adjusted for clustering (by manufacturing facility)

Figure 1: Distribution of Investigator Probabilities of Finding Noncompliance